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October 17-21, 2020

These abstracts of research studies, published as submitted by the authors, are presented in the ASRM 2020 Congress sessions and are published in the order of their presentation. Abstracts of plenary lectures, symposia and interactive sessions are not included.

O-1 9:55 AM Saturday, October 17, 2020

LIBERTY: LONG-TERM EXTENSION STUDY DEMONSTRATING ONE-YEAR EFFICACY AND SAFETY OF RELUGOLIX COMBINATION THERAPY IN WOMEN WITH SYMPTOMATIC UTERINE FIBROIDS.

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OBJECTIVE: In the LIBERTY 1 and 2 trials, once-daily relugolix combination therapy (Rel-CT) reduced menstrual blood loss (MBL) volume and pain in women with uterine fibroids (UF) and was well tolerated, with preservation of bone mineral density (BMD) through 24 weeks (Al Hendy, ASRM 2019). Here we report on the long-term efficacy and safety of Rel-CT for up to 52 weeks of treatment.

DESIGN: Multinational, Phase 3, open-label, long-term extension trial.

MATERIALS AND METHODS: Women with UF-associated heavy menstrual bleeding (HMB) who completed the 24-week, double-blind, placebo-controlled LIBERTY 1 and 2 trials were eligible to enroll in a 28-week extension study. All received once-daily Rel-CT (40 mg relugolix, an oral gonadotropin-releasing hormone receptor antagonist, estradiol 1 mg, norethindrone acetate 0.5 mg). The primary efficacy endpoint was the proportion of women who achieved or maintained an MBL volume < 80 mL and a $\geq 50\%$ reduction from parent study baseline to the last 35 days of treatment, as measured by the alkaline hematin method. Secondary endpoints included mean % MBL reduction, amenorrhea rate, and improvements in anemia. Adverse events (AEs) and BMD changes by dual-energy X-ray absorptiometry were assessed. Outcomes were analyzed by treatment assignment: Rel-CT, delayed Rel-CT (relugolix 40 mg alone for 12 weeks, then Rel-CT for 12 weeks), and placebo, and were reported using descriptive statistics without statistical comparisons between groups. The Rel-CT group has the longest treatment duration (52 weeks): the other groups, where patients transitioned to Rel-CT, are supportive.

RESULTS: Of the 770 randomized LIBERTY patients, 610 completed the primary study; 477 (78%) enrolled in the long-term extension and 363 (76%) completed it. The Rel-CT group demonstrated sustained improvement in HMB through 52 weeks with 87.7% of patients meeting the definition of responder. The mean MBL volume reduction from baseline was 89.9% with most patients (70.6%) achieving amenorrhea. The reductions in MBL led to substantial improvements (> 2 g/dL) in hemoglobin concentrations at Week 52 for most (59.0%) patients with anemia (< 10.5 g/dL) at baseline. Reductions in uterine and UF volume at Week 24 were sustained through Week 52. Consistent with the change observed at Week 24, the Bleeding Pain and Discomfort scale score was reduced by 51.3 points from baseline to Week 52, indicating that reduction in measures of symptom-associated distress were substantial and sustained. There was no disproportionate increase in the incidence of either serious or nonserious AEs in the Rel-CT group through the 52 weeks. The most frequently reported AEs were headache and hot flush. BMD was preserved with a mean % reduction of –0.80% (95% confidence interval: –1.36, –0.25) for lumbar spine BMD at Week 52. Efficacy and safety outcomes for delayed Rel-CT and placebo were consistent.

CONCLUSIONS: Rel-CT showed durability of effect for both HMB and pain through 52 weeks of treatment in women with UF. No new safety concerns were identified, and bone mass was maintained.

SUPPORT: Myovant Sciences Inc.

O-2 10:10 AM Saturday, October 17, 2020

AMH HIGHLY CORRELATES WITH ASSISTED REPRODUCTION CUMULATIVE LIVE BIRTH RATE IN WOMEN WITH DIMINISHED OVARIAN RESERVE INDEPENDENT OF AGE: AN ANALYSIS OF 34,540 CYCLES FROM THE SART DATABASE FOR 2014-2016.

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OBJECTIVE: Serum antimullerian hormone (AMH) is used to predict a woman's response to ovarian stimulation. However, its ability to predict clinical outcomes per embryo transfer such as clinical pregnancy and live birth rate has been considered to be poor. We hypothesized that its association with cumulative live birth rate (CLBR) as reported by Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SARTCORS) from 2014 onward among women with diminished ovarian reserve (DOR) could be more informative as CLBR accounts for all embryos (fresh and frozen) linked to a single identified index retrieval.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: The SARTCORS database was analyzed for CLBR by assessing outcomes of all linked fresh and/or frozen embryo transfer cycles (2014 to 2016) from an index retrieval cycle (between 2014-2015). A total of 34,540 (25.9%) of 133,442 autologous index cycles with DOR (i.e. AMH<1 ng/ml) were included and analyzed. Cycles with preimplantation genetic testing, egg/embryo banking and those with embryo transfer/s from more than one ART index cycle were excluded. Multiple logistic regression (MLR) was performed for the probability of CLBR per index cycle. Data was stratified according to AMH and age and linear regression analysis of AMH and CLBR were calculated for each age strata.

RESULTS: Multiple logistic regression demonstrated that AMH is an independent predictor of CLBR (Odds ratio 1.46, 95% CI 1.28-1.66, P<0.0001) when controlling for age, body mass index, race, total FSH dose and number of embryos transferred. Serum AMH was associated with number of oocytes retrieved, number of embryos cryopreserved and percentage of index cycles that had an embryo transfer, but was not associated with number of embryos transferred. Linear regression analysis demonstrated that AMH highly correlated with CLBR in each age strata of women with DOR (Table 1), and most strongly in women <35 (R=0.95, p<0.001).

	Age				
AMH (ng/ml)	<35 N=8,290	35-37 N=7,507	38-40 N=8,999	41 – 42 N=5,548	43+ N=4,196
0.00 – 0.1	22.1%	18.7%	9.2%	6.1%	1.2%
0.11 – 0.2	29.1%	19.8%	12.5%	6.4%	1.7%
0.21 – 0.3	30.3%	26.1%	16.3%	7.9%	1.9%
0.31 – 0.4	32.0%	26.1%	17.8%	7.4%	2.4%
0.41 – 0.5	35.9%	27.6%	17.7%	7.3%	3.2%
0.51 – 0.6	34.0%	26.7%	19.1%	9.2%	3.9%
0.61 – 0.7	36.7%	30.8%	18.9%	10.1%	2.6%
0.71 – 0.8	38.2%	31.2%	21.8%	11.1%	3.0%
0.81 – 0.9	42.7%	30.2%	19.0%	10.7%	4.1%
0.91 – 1.00	41.2%	34.0%	20.6%	9.5%	4.1%
Mean CLBR	36.1%	25.5%	19.3%	5.7%	1.4%
Linear regression (R)	0.95	0.88	0.87	0.89	0.88
p-value	<0.0001	<0.0001	0.001	0.001	<0.001

CONCLUSIONS: Serum AMH is highly correlated with CLBR in women with DOR independent of age. The addition of AMH to current age-based prognostication counseling would provide more informative and personalized CLBR prediction.

O-3 10:25 AM Saturday, October 17, 2020

NEW INSIGHTS FROM ONE THOUSAND MOSAIC EMBRYO TRANSFERS: FEATURES OF MOSAICISM DICTATING RATES OF IMPLANTATION, SPONTANEOUS ABORTION, AND NEONATE HEALTH.

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OBJECTIVE: To understand how the features of chromosomal mosaicism detected in PGT-A affect implantation rates, pregnancy, and newborn health.

DESIGN: Compiled analysis from multicenter data on transfers of mosaic embryos (n=1,000) and their clinical outcome, with comparison to a euploid control group (n=5,561). Birth characteristics of neonates (n>200) from mosaic embryo transfers are compared to a euploid control group (n>200).

MATERIALS AND METHODS: PGT-A was performed on blastocyst-stage embryos with 24-Chromosome whole genome amplification (WGA)-based Next Generation Sequencing (NGS). In accordance with established guidelines, embryos were categorized as mosaic when PGT-A results indicated 20-80% aneuploid content.

RESULTS: Compared to the euploid group, mosaic embryos had lower rates of implantation (57.2% vs. 46.5%, P<0.05) and lower rates of ongoing pregnancy or birth at the time of analysis (OP/B) (52.3% vs. 37.0%, P<0.05). When only considering embryos with mosaicism involving at least one entire chromosome (no segmental mosaics), implantation and OP/B rates were 41.8% and 31.3%, respectively. Rates of spontaneous abortion for euploids, all mosaics, and non-segmental mosaics were 8.6%, 20.4%, and 25%, respectively. Mosaic embryos with percent aneuploidy ≤50% had more favorable clinical outcomes than those containing >50% aneuploidy (implantation 47.4% vs. 35.8% and OP/B 39.5% vs. 24.1%, P<0.05 for both comparisons, n=848 and n=137, respectively). Mosaics of the segmental type (n=483) had more favorable outcomes than whole chromosome mosaics involving one or two chromosomes (n=392) (implantation 51.6% vs. 43.1%, OP/B 43.1% and 34.7%, P<0.05), while complex mosaics involving three or more chromosomes (n=125) had the least favorable outcomes, experiencing implantation rates of 30.4% and OP/B rates of 20.8%. Evaluation of clinical outcomes when combining mosaic level (low ≤50% aneuploidy or high >50% aneuploidy) and mosaic type (segmental, whole chromosome, or complex) produces the following ranking system from most to least favorable: Low segmental>low whole chromosome>high segmental>low complex->high whole chromosome>high complex. Prenatal testing of >200 pregnancies from mosaic embryo transfers showed no incidence of mosaicism that matched the PGT-A findings, indicating the involvement of self-corrective mechanisms. By and large, the metrics of pregnancy and birth (e.g. length of gestation and birth weight) were similar between babies born from transfers of mosaic embryos and euploid embryos.

CONCLUSIONS: This large dataset of transferred mosaic embryo outcomes confirms that mosaic embryos have lower rates of implantation and higher likelihood of spontaneous abortion compared to euploid embryos. The data reveals that traits of mosaicism (level and type) significantly affect likelihood of positive outcome, and identifies a ranking system for mosaic embryos in the clinic. Pregnancy and obstetric data indicates that mosaic embryos prevailing through gestation and birth have similar chromosomal and physiological health compared to euploid embryos.

References: None

SUPPORT: None

O-4 10:40 AM Saturday, October 17, 2020

WHAT IS THE OPTIMAL TIMING OF INTRACYTOPLASMIC SPERM INJECTION (ICSI) AFTER EGG RETRIEVAL? A RANDOMIZED CONTROLLED TRIAL. Meghan Brooke Smith, MD, Jacqueline Ho, MD MS, Victoria Cortessis, PhD, Irene J. Chen, MS, Kristin A. Bendikson, MD, Richard J. Paulson, MD, Lynda K. McGinnis, PhD, Ali Ahmady, PhD. University of Southern California Los Angeles, CA.

OBJECTIVE: To determine if oocyte denudation/ICSI at 2.5 hours vs 5 hours post retrieval (36.5 vs 39 hours post HCG and/or Lupron trigger) influences fertilization/blastulation rates in good prognosis couples.

DESIGN: Randomized controlled trial (RCT).

MATERIALS AND METHODS: This is a RCT of oocytes obtained at time of IVF. We included couples with: female age ≤ 38 yo; AMH > 1 ng/mL; day 3 FSH < 13.5 mIU/mL; ≥ 10 oocytes retrieved; male partner < 50 years old; no male factor infertility. Oocytes retrieved from each participant were randomized in blocks of 4 to 2 groups for denudation/ICSI: 2.5 hours (Group 1) vs 5 hours (Group 2) post oocyte retrieval after 34 hr trigger. Fertilization a/blastulation was recorded for each oocyte. Regression analyses conditioned on the patient from whom each oocyte had been retrieved was used to estimate relative rates of these events, treating 2.5 hours as the reference value. A total of 200 oocytes was determined by an a priori power calculation to provide 95% power to detect rate ratio of 78% or lower in either outcome at 5% level of nominal significance.

RESULTS: 206 MII oocytes were randomly assigned, 105 to group 1, 101 to group 2. Median parameters for female patients were: age 33 (IQR 31.0-36.5); D3 FSH 5.9 (IQR 4.4-7.5); AMH 4.76 (IQR 3.7-6.5); BMI 20.96 (IQR 18.9 – 24.8); total MII oocytes retrieved 17 (IQR 11.0 – 19.8). All patients underwent controlled ovarian stimulation with antagonist protocols. No difference was observed in fertilization rate, total blastulation rate, or day of blastulation based on timing of denudation and ICSI (all p > 0.05). Fertilization was less frequent among group 2 oocytes (5 hours), estimate of relative fertilization rate 0.81 (95% confidence interval [CI]: 0.40-1.63, p=0.55). However, among women for whom any blastulation event occurred, blastulation was more frequent in group 2 oocytes (5 hours); estimates of relative blastulation rate were 1.42 (95% CI: 0.81-2.49, p=0.22) overall, and 1.76 (95% CI: 0.84-3.71, p=0.14) among women 35 or more years of age at the time of retrieval. No relative rate estimate achieved statistical significance.

CONCLUSIONS: In good prognosis couples, we observed no difference in fertilization/blastulation rates based on timing of ICSI within the currently accepted 2-6 hr window post-retrieval with 34 hr trigger. The oocyte appears to have a physiological tolerance for fertilization during this window of time. Variability in the timing of ICSI during this window is unlikely to have an impact on cycle outcome.

	Group 1	Group 2
Fertilization Rate (#2PN/#MII)	84.8%	81.2%
Total Blastulation Rate, (#Blasts/#2PN)	66.3%	74.4%
Day 5 Blastulation (#D5 Blasts/#2PN)	38.7%	43.9%
Day 6 Blastulation (#D6 Blasts/#2PN)	37.9%	38.7%
Day 7 Blastulation (#D7 Blasts/#2PN)	6.9%	6.5%

References: None

SUPPORT: None

O-5 10:55 AM Saturday, October 17, 2020

NONINVASIVE PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY EXHIBITS HIGH RATES OF DNA AMPLIFICATION FAILURE AND LACKS CONSISTENCY WITH PGT-A USING TROPHOECTODERM BIOPSY. Brent M. Hanson, MD,[1] Xin Tao, Ph.D,[2] Julia G. Kim, MD, MPH,[1] Nola S. Herlihy, MD,[3] Amber M. Klimczak, MD,[3] Ashley W. Tiegs, MD,[1] Emily K. Osman, MD,[1] Kathleen Hong, MD,[3] Emre Seli, M.D.,[1] Richard Thomas Scott, Jr., MD.[1] [1]IVI RMA New Jersey Basking Ridge, NJ; [2]Foundation for Embryonic Competence, Basking Ridge, NJ; [3]IVI-RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: Preimplantation genetic testing for aneuploidy (PGT-A) is currently performed via analyses of trophectoderm (TE) biopsies. Concerns regarding the safety of TE biopsy and the technical skill required to perform the procedure have led to increased interest in noninvasive preimplantation genetic testing for aneuploidy (niPGT-A). The noninvasive testing modality assesses an embryo's genetic composition indirectly by analyzing spent culture media. This study begins the validation process of a commercially available assay by investigating: 1) the prevalence of DNA amplification failure with niPGT-A compared to TE biopsy; 2) factors affecting amplification failure with niPGT-A, and 3) the frequency of discrepant results between niPGT-A and traditional PGT-A.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: This study was performed at a university-affiliated fertility practice. Patients were enrolled prospectively during in vitro fertilization (IVF) cycles between July and October 2019. Culture media samples were collected at the blastocyst stage immediately prior to TE biopsy. Media samples underwent whole genome amplification using the commercially available NICSInst™ sample preparation kit (Yikon Genomics) followed by NGS with the Illumina HiSeq system. Coordination with Yikon Genomics was undertaken to ensure optimization of the niPGT-A protocol. Standard PGT-A of TE biopsies was performed using targeted NGS, consistent with institutional practices.

RESULTS: A total of 170 individually cultured blastocysts were included in the study. 1) When performing niPGT-A, 62 of the 170 samples (36.47%) failed to amplify. The failure rate following TE biopsy was dramatically

lower at 0 out of 170 (0%) ($p<1*10^{-6}$). 2) Investigation into the factors that may lead to amplification failure revealed that when an aneuploid result was noted on TE biopsy, the DNA amplification failure rate with niPGT-A was 23.46% (n=19). However, when TE biopsy resulted in a euploid embryo, rates of DNA amplification failure with niPGT-A were significantly higher (48.31%, n=43, p<0.01). 3) Finally, among the 108 embryos with results from both niPGT-A and TE biopsy analyses, a discrepancy in diagnosis was noted in 37 cases (34.3%). Twenty of the 37 cases showed aneuploidy on niPGT-A where none was evident in the TE biopsy.

CONCLUSIONS: DNA amplification failures were unacceptably high when using niPGT-A. This dramatically impairs the clinical applicability of niPGT-A based on poor amplification alone. Moreover, when interpretable results were obtained with niPGT-A, results failed to correlate with TE biopsy in over one-third of cases. This study suggests that niPGT-A, in its current state, lacks the precision and accuracy to be a useful diagnostic tool and should be used with caution until prospective non-selection data allow calculation of the "no result" rate and the predictive values of normal and abnormal results.

SUPPORT: None

O-6 11:10 AM Saturday, October 17, 2020

ASSOCIATIONS BETWEEN POLYCYSTIC OVARY SYNDROME AND ADVERSE OBSTETRICAL, AND NEONATAL OUTCOMES: A POPULATION STUDY OF 9.1 MILLION BIRTHS. Ginevra Mills, MD, FRCSC, Ahmad Badeghiesh, MD, Eva Suarthana, MD, Haitham Baghlaf, MD, MPH, Michael H. Dahan, M.D. McGill University, Montreal, QC, Canada.

OBJECTIVE: The objective of this study is to determine if polycystic ovary syndrome (PCOS) confers an independent risk for adverse delivery and neonatal outcomes.

DESIGN: This retrospective population-based cohort study utilized data from the HCUP-NIS from 2004 to 2014. The HCUP-NIS is an inpatient sample database from the United States, comprised of hospital inpatient stays throughout the entire country. It provides information relating to 7 million inpatient stays per year, includes approximately 20% of admissions, and represents over 96% of the American population.

MATERIALS AND METHODS: A cohort of all deliveries between 2004 and 2014 inclusively was created. Within this group, all deliveries in women with PCOS were identified as part of the study group (n=14,882), and the remaining deliveries were categorized as non-PCOS births and comprised the reference group (n=9,081,906). Initial analysis was performed to identify the prevalence of pregnant women with PCOS over the entire duration of the study. Baseline clinical and demographic characteristics were compared between women with PCOS and those without PCOS. Logistic regression analyses were conducted to explore associations between PCOS, delivery, and neonatal outcomes through the estimation of odds ratio (OR) and 95% confidence intervals (CI). The regression models were adjusted for the potential confounding effects of maternal demographic, preexisting clinical characteristics, and concurrently occurring conditions including hypertension and diabetes. Pregnancy induced hypertension (PIH) and gestational diabetes (GDM) data is presented separately.

RESULTS: Women with PCOS were more likely to experience preterm pre-labour rupture of membranes (aOR1.48, 95%CI 1.20-1.83), preterm delivery (aOR1.37 95%CI1.24-1.53 p<0.001), placental abruption (aOR1.63, 95%CI 1.30-2.05), and cesarean delivery (C/S) (aOR1.50, 95%CI 1.40-1.61 p<0.001). Women with PCOS developed more chorioamnionitis (aOR1.58, 95%CI 1.34-1.86 p<0.001), and maternal infections (aOR1.58, 95%CI 1.36-1.84 p<0.001). With the exception of multiple gestations (aOR1.27, 95% CI1.01-1.62 p=0.04), there was no difference in the number of women who gave birth to small for gestational age infants (aOR 0.97, 95% CI 0.82-1.15 p=0.72). Intrauterine fetal deaths were comparable between the two groups (aOR1.03, 95%CI 0.68-1.59, p=0.88). However, congenital anomalies were more likely to occur in women with PCOS (aOR1.89, 95%CI 1.51-2.38, p<0.001).

CONCLUSIONS: After controlling for all potential confounding effects including PIH and GDM, women with PCOS are at an increased risk of experiencing delivery related complications, C/S, infections, and having a child with congenital anomalies. Increased risk of placental abruptions, infections and congenital anomalies are a novel finding in women with PCOS.

ACCESS TO CARE

O-7 9:55 AM Saturday, October 17, 2020

FRONTERAS Y FERTILIDAD: INSIGHTS ON LATINX INFERTILITY AND ACCESS TO CARE FROM THE ENVIRONMENT, LEIOMYOMAS, LATINAS, AND ADIPOSITY STUDY (ELLAS). Nicholas S. Raja, MD,[1] Anne Waldo, MS,[1] Torie C. Plowden, MD, MPH,[2] Lia Bernardi, MD,[3] Sonia Acosta, PhD,[4] Charo C. Ledon, NA,[5] Anita Malone, MD,[1] Erica E. Marsh, MD, MSCI, FACOG.[1] [1]University of Michigan Ann Arbor, MI; [2]Womack Army Medical Center, Fort Bragg, NC; [3]Northwestern University, Chicago, IL; [4]Centro Multicultural la Familia, Pontiac, MI; [5]Buenos Vecinos, Ann Arbor, MI.

OBJECTIVE: To investigate infertility rates and access to infertility care among Latinx females using data from the Environment, Leiomyomas, Latinas, and Adiposity Study (ELLAS).

DESIGN: Prospective longitudinal cohort study.

MATERIALS AND METHODS: Latinx females between the ages of 21 and 50 were eligible to enroll in this study. All participants were administered questionnaires collecting demographic information as well as reproductive health and fertility histories. Demographic data included age, country of birth, education history, annual household income, acculturation level, health literacy, insurance status, and body mass index (BMI). Outcomes of interest were pregnancy history, including gravidity, live births, and pregnancy loss, as well as rates of infertility and rates of accessing fertility care. The prevalence of infertility was evaluated in the general population, followed by subgroup analyses to compare outcomes of interest among infertile patients based on income, educational level, insurance status, health literacy, and acculturation level using Kruskal-Wallis and Chi-squared tests for comparison.

RESULTS: 633 participants have enrolled in the study and 569 have completed the first study visit. The average age of enrolled females was 37.6 ± 6.97 years. 90% of study participants were born outside the United States (U.S.) and 79.3% of this subgroup entered the U.S. after age 18. 59.8% of participants reported an annual household income of $30,000 or less, 48.2% had not completed high school, and 56.9% did not have health insurance. 25.1% of the participants reported having experienced infertility at some point their lives, but of these ultimately 85.3% reported a live birth. We found that participants that reported a history of infertility had a higher mean BMI (31.3 vs. 29.5, p=0.01), and that rates of infertility did not differ based on income, education level, or insurance status. Infertility was associated with lower gravidity, fewer live births, and a history of polycystic ovarian syndrome but not with a history of pregnancy loss or ectopic pregnancy. In this cohort, females with infertility did not experience differences in their ability to obtain treatment based on annual income, insurance status, educational history, health literacy, or acculturation.

CONCLUSIONS: Strikingly, 25.1% of ELLAS participants reported a history of infertility – a rate nearly four times higher than that reported by the National Survey of Family Growth (6.7%) [1]. Despite robust scientific literature documenting racial disparities in rates of infertility and access to care, studies specifically focused on Latinx females remain rare. Insights from the ELLAS study will contribute to collective knowledge of this understudied population of largely first generation Latinx females as well as inform future research into racial and ethnic disparities in the field of reproductive health and infertility.

References: 1. Chandra A, Copen CE, and Stephen EH.Â Infertility and impaired fecundity in the United States, 1982–2010: Data from the National Survey of Family GrowthÂ Natl Health Stat RepÂ (2013);67:1-18.

SUPPORT: This work was supported by NIMHD grant R01MD011570.

O-8 10:10 AM Saturday, October 17, 2020

JOURNEY LEVEL ANALYSIS OF PROGRESSION TO TREATMENT VERSUS DROP OUT IN A LARGE COHORT OF PATIENTS WITH ACCESS TO A DEFINED FERTILITY BENEFIT. Yishin Yang, BA,[1] Melody Qiu, MSc,[1] Aly Emiola, BA,[1] Dmitry Gounko, MA,[2] Joseph A. Lee, BA,[2] Alan B. Copperman, MD.[3] [1]Progyny Inc., New York, NY; [2]Reproductive Medicine Associates of New York, New York, NY; [3]Icahn School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: To evaluate variables associated with progression to ART treatment versus with patient drop-out.

DESIGN: Retrospective Multi-Center Study.

MATERIALS AND METHODS: Between January 2018 and July 2019, a total of 8,441 patient journeys were analyzed based on intention to initiate IVF treatment. Data points included factors relating to patient drop-out versus accessing Assisted Reproductive Technologies. Relevant factors in this study include the number of provider locations the patient had access to within their CBSA (Core Based Statistical Area), age at time of appointment, number of calls/emails made before an initial consultation. Further classifications were assumed based on the patient's geographic location, region, and etiology of infertility. Missing CBSA clinic options where substituted with average clinic option counts. Hypothesis tests were performed using Chi Square tests for independence of categorical variables as well a t-tests for continues variables. A multivariable logistic regression was performed in order to model the likelihood of a patient initiating treatment.

RESULTS: Hypothesis testing determined a significant difference between CBSA provider counts (P<.0001), Patient inquiries (P<.0001), male diagnosis (P<.0020), age quartiles (P<.0001) with treatment progression. No univariate significant association was determined when comparing coastal status of patients and treatment status. A multivariable analysis was also examined to adjust for confounding factors. The odds of progressing to treatment was significantly associated with an increase in CBSA clinic options (OR 1, [95% CI 1.001-1.008], p= 0.0047) as well as the number of patient inquiries (OR 1.032, [95% CI 1.020.-1.046], p< .001). Using a third quartile range age group as reference, the odds of treatment progression was significantly different amongst the first age quartiles and the third age quartile ranges (OR .605, [95% CI .526 - .696], p< .0001). For patients with a male infertility diagnosis the odds of treatment progression was determined to be 39.96% lower than other diagnosis (OR .604, [95% CI .425 - .858], p< .0049). Patients living in Coastal states where determined to have an approximately 14% lower likelihood of progressing to treatment (OR .8 63, [95% CI .763 - .976], p< .0186).

CONCLUSIONS: In the largest multi-center study to date analyzing patient drop out, we identified that patients with multiple contacts with patient care advocates were more likely to access treatment, and that patients with male factor were less likely to progress. We plan to use this data to improve support systems of the patient and the partner and increase contact points with couples presenting for fertility treatment.

References: None

SUPPORT: None

O-9 10:25 AM Saturday, October 17, 2020

ASSOCIATION BETWEEN DEMAND FOR FERTILITY SERVICES AND CHANGES IN UNEMPLOYMENT RATE IN THE UNITED STATES.

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OBJECTIVE: The effect of the economic crises on the demand for fertility services remains to be understood. This is particularly relevant nowadays as fertility centers prepare for the economic impact of the current COVID-19 pandemic. Using the 2008 financial crisis and resulting economic downturn as a proxy, this study describes and quantifies the impact of recessions on the demand for fertility services in the US.

DESIGN: Retrospective study.

MATERIALS AND METHODS: We used the SART dataset (2007-2011) to evaluate demand for fertility services in the period surrounding the 2008 economic crisis. Number of cycles per thousand women (cycles/1k) was standardized using the US Census data on the number of females of reproductive age (20-44 years). States with at least 500 cycles/year were included in the study. The historical unemployment rate was obtained from the US Bureau of Labor and its projection for 2020 from the Congressional Budget Office. Statistical associations were assessed using generalized least squares and significance set at P<.05.

RESULTS: There were 1,119,806 cycles performed in these states during the study period. While the number of cycles increased throughout the period an average of 2.3% per year, the growth significantly decreased during the economic downturn from 4.8% in 2007 to 0.2% in 2009 (Table). The number of cycles in 2009 decreased in more than half of the states, with a median change of -0.4% (Table). The change in the number of cycles/1k was significantly associated with the change in state unemployment rate. On average, an 1% increase in unemployment was associated with a decrease of 0.94% in the number of cycles, accounting for expected growth. A conservative estimate indicates that about 10,000 cycles were forgone in 2008-2010. Under the same assumptions and a projection of 5% additional unemployment in 2020, around 15,000 ART cycles are estimated to be forgone this year.

CONCLUSIONS: We used the recession of 2008 as a framework to estimate the potential impact of the current economic crisis in the demand for fertility services. Our results suggest that while fertility care is not as affected as other industries, changes in unemployment rate are associated with decreases in demand for fertility treatments. Further research is needed to evaluate the additional impact of the unique situation programs and patients are facing in the current COVID-19 pandemic, including temporary halt of fertility services, reduced mobility, and variation in state policies.

	2007	2008	2009	2010	2011
Cycles; N	215,245	222,751	223,490	225,470	232,850
Cycles/1k; N	4.35	4.50	4.51	4.54	4.66
Change from previous year; %	4.8	3.4	0.2	0.7	2.6
Change from previous year per State; median % (IQR)	3.2 (-0.7, 7.1)	2.4 (-0.7, 6.6)	-0.4 (-2.4, 2.8)	0.7 (-1.0, 2.8)	1.8 (-1.1, 5.0)

O-10 10:40 AM Saturday, October 17, 2020

ANALYSIS OF STATE MANDATED INSURANCE COVERAGE FOR INFERTILITY TREATMENT AND FERTILITY PRESERVATION IN THE UNITED STATES.

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OBJECTIVE: To characterize the landscape of state mandated insurance coverage for infertility treatment and fertility preservation in the United States (US). Furthermore, we aimed to identify the political party in power at the time these mandates were passed.

DESIGN: Retrospective analysis of US legislation mandating insurance coverage pertaining to the diagnosis and treatment of infertility and fertility preservation.

MATERIALS AND METHODS: Review of state infertility and fertility preservation insurance mandates was conducted via ASRM's ReproductiveFacts.org, the National Council of State Legislatures (NCSL), and Google search. Initial search was confirmed by primary review of current state legislation (performed April 2020). Mandate eligibility criteria, covered procedures, step-through requirements, lifetime limits, exemptions, and coverage of fertility preservation were analyzed. State political party at time of passage was derived from the NCSL.

RESULTS: Nineteen states (38%) have passed legislation mandating insurers to cover or offer coverage for the diagnosis and treatment of infertility or conditions resulting in infertility. Nine (47%) states require individuals to demonstrate a period of infertility longer than the ASRM definition of infertility to be eligible for assisted reproductive technologies (ART). Four (21%) states have an age limit, after which services are no longer covered. Utah is the only state that mandates coverage for IVF contingent on the presence of a genetic trait associated with a qualifying condition. States vary in the specific services covered, such as IVF (12 [63%]), IUI (9 [47%]), and fertility preservation for patients with cancer or other iatrogenic infertility (10 [53%]). Seven of the 12 states mandating IVF (58%) require patients to attempt less costly methods of ART prior to IVF being covered. Four (21%) states require fertilization to be performed with the spouse's sperm. Seven (37%) states require that the facility providing fertility services conform to the standards developed by ASRM, ACOG, or another governing body. Eleven (58%) states place a lifetime limit on the amount of fertility treatment

provided. Coverage exemptions exist for religious, small employer, and non-health maintenance organizations (8 (42%), 6 (32%), and 3 (16%) states, respectively). Eight (42%), 2 (11%), and 9 (47%) infertility mandates were passed by Democratic, Republican, and split state governments, respectively. Among fertility preservation bills, 6 (60%), 0 (0%) and 4 (40%) bills were passed by Democratic, Republican, and split state governments.

CONCLUSIONS: Across state infertility and fertility preservation insurance mandates, significant heterogeneity exists. Only Colorado, Connecticut, Delaware, Illinois, Maryland, New Hampshire, New Jersey, New York, and Rhode Island mandate coverage for both IVF and fertility preservation. Most states do not have an infertility mandate. Infertility mandates have passed with bipartisan state legislature support; however, no fertility preservation mandates have been passed by Republican-controlled state governments.

O-11 10:55 AM Saturday, October 17, 2020

DOES SOCIOECONOMIC STATUS PLAY A ROLE IN LONG-TERM REPRODUCTIVE OUTCOMES IN INFERTILE COUPLES? FOLLOW-UP RESULTS FROM THE FAST TRACK AND STANDARD TREATMENT TRIAL (FASTT). Carleigh B. Nesbit, DO,[1] Marlene B. Goldman, ScD,[2] June L. Fung, PhD,[2] Katherine G. Koniares, MD,[3] Denis A. Vaughan, MD,[4] Thomas L. Toth, MD,[5] Richard H. Reindollar, MD.[2] [1]Dartmouth Hitchcock Medical Center Lebanon, NH; [2]Geisel School of Medicine at Dartmouth, Hanover, NH; [3]Tufts Medical Center, Boston, MA; [4]Beth Israel Deaconess Medical Center, Boston, MA; [5]Boston IVF, Waltham, MA.

OBJECTIVE: To investigate long term reproductive outcomes in couples of different socioeconomic groups enrolled in FASTT from 2001-2006.

DESIGN: Long term follow-up of randomized controlled trial (RCT) participants.

MATERIALS AND METHODS: A telephone survey was administered to couples who had been enrolled in FASTT, an RCT which investigated time to conception and cost effectiveness of conventional treatment for unexplained infertility vs a fast track approach in women ages 21-39 years. Statistical analyses were performed using SAS v 9.2. Categorical variables were compared between groups using chi-square and Fisher's exact tests and continuous variables with analysis of variance with $P < 0.05$ as significant.

RESULTS: Of the 503 couples enrolled in FASTT, 311 (61.8%) were able to be contacted of whom 286 (56.9%) consented to participate. The distribution of reported annual household income at the time of FASTT among consenting couples was 32.5% ≥$140,000, 28.3% $100,000-139,999, 31.5% $60,000-99,999, and 5.6% <$60,000. The distribution of highest level of education of female participants at the time of FASTT was 1.8% high school diploma, 7.8% associate's degree, 7.8% some college education but no degree, 44.8% bachelor's degree, 28.3% master's degree, and 9.5% medical degree/doctorate. There were no statistically significant differences in income between those who were able to be contacted and those who were not nor in income or education level between those who consented to participate and those who did not. Women who were able to be contacted were more likely to have a bachelor's or master's degree than those who were not ($P = 0.01$). In terms of outcomes during FASTT, there were no differences in any income group in terms of achievement of live birth but couples with lower income were less likely to achieve a clinical pregnancy ($P = 0.02$.) There were no differences by level of education in achievement of live birth or clinical pregnancy during FASTT. Following FASTT, there were no statistically significant differences by income or level of education in number of couples who attempted conception, achieved a clinical pregnancy or live birth, or who reported ultimate family building satisfaction. For those who were able to conceive, time to conception was not significantly different based on couple's reported income or level of education. There were no statistically significant differences in number of couples who attempted spontaneous conception after FASTT, controlled ovarian hyperstimulation +/- intrauterine insemination, in vitro fertilization with autologous or donor oocytes, or who adopted children between groups of different income or education levels.

CONCLUSIONS: In a long term follow up of infertile couples, annual household income and level of education of female partners did not have an impact on long term reproductive outcomes. These findings reflect the success of insurance coverage for infertility treatments.

O-12 11:10 AM Saturday, October 17, 2020

PATIENT BARRIERS TO DISCONTINUING LONG ACTING REVERSIBLE CONTRACEPTION. Kacie R. Fox, MD, Alyssa M. Kameoka, BA, Bliss Kaneshiro, MD, MPH, Shandhini Raidoo, MD, MPH, Reni Soon, MD, MPH, Tiana Fontanilla, MPH. University of Hawaii Honolulu, HI.

OBJECTIVE: The objective of this study was to determine whether patients face barriers to discontinuing long acting reversible contraception (LARC), and if so, to evaluate if certain patient demographic groups are disproportionately affected. We classified the patient as having a barrier if the patient was unable to remove the device at the time they requested or desired removal.

DESIGN: Prospective online survey.

MATERIALS AND METHODS: We conducted an online survey of individuals ages 18-50 who used and discontinued (or attempted to discontinue) a contraceptive implant or intrauterine device. Estimating that about 20% would have experienced a barrier, we aimed to recruit 500 participants. Participants provided demographic information and answered questions related to their experiences discontinuing LARC, including any challenges they faced, such as, "my provider wouldn't remove it until I started another form of contraception," or "my provider stated there wasn't enough time in that visit." Flyers advertising our online survey were posted at various University of Hawaii faculty practice sites, in the University of Hawaii dormitories, and online via Instagram and Facebook. In addition, an international sample of participants was obtained using Amazon Mturk. Statistical analysis was performed using SPSS.

RESULTS: Of the 133 individuals who completed our Hawaii-based survey, 59% had experience discontinuing LARC, and of those, 21.5% encountered a barrier to discontinuation. Half of those who identified with Hispanic ethnicity experienced a barrier to discontinuation, compared to 17.6% of non-Hispanics ($p=0.03$). Those with no insurance, or government funded insurance were also more likely to face a barrier compared to those with private insurance (100% and 36.8% respectively, versus 13.6%, $p=0.05$). A greater proportion of participants who were high school or college graduates experienced a barrier when compared to those with more than a college degree, though this was not statistically different. Age, other racial groups, or prior pregnancy was not associated with experiencing a barrier in discontinuation.

In our international survey using Mturk (n=448), 29.2% of participants reported a barrier to discontinuation. Characteristics associated with facing barriers included having government-funded insurance ($p=0.005$), lower levels of education ($p=0.005$), younger age ($p<0.001$,) and having previously been pregnant ($p<0.001$). In addition, Hispanics and those of African, Middle Eastern, Asian, American Indian or Alaksa Native decent were statistically more likely to experience a barrier ($p< 0.03$.)

CONCLUSIONS: Results of our study show that patients often face barriers to discontinuing LARC. Demographic characteristics associated with meeting a barrier to discontinuation were different in the Hawaii-based survey and the Mturk international survey, but our findings suggest that insurance-status, race, education, age, and parity could play a role. Providers should remain mindful of these barriers and work towards an unbiased practice where patients have easy access to using and discontinuing LARC.

SUPPORT: Financial support for this project was generously provided by the Lakshmi Devi and Devraj Sharma Endowment Fund.

ART LAB: BASIC

O-13 9:55 AM Saturday, October 17, 2020

A NOVEL NON-INVASIVE METABOLOMICS APPROACH TO SCREEN EMBRYOS FOR ANEUPLOIDY. Sara Cabello-Pinedo, Biotechnologist,[1] Hussain A. N. Abdulla, Ph.D.,[2] Michelle Louise Seth-Smith, Master,[1] Maria Escriba, MSc,[3] Juana Crespo, Medical Director,[3] Santiago Munne, PhD,[4] Jose A. Horcajadas, PhD.[4] [1]Overture Life Alcobendas - Madrid, Spain; [2]Texas A&M University Corpus Christi, Corpus Christi, TX; [3]Equipo Juana Crespo, Valencia, Spain; [4]Overture Life, Madrid, Spain.

OBJECTIVE: The aim of this study was to develop a novel non-invasive technique for embryo selection. This was performed by identification of

metabolomics biomarkers of euploidy and aneuploidy in spent culture media after embryo culture.

DESIGN: Samples (n=80) consist of spent culture media collected in IVF clinics after embryo culture from day 3 to day 5. After collection, samples were frozen and shipped to analysis lab. Samples were analyzed using a high-resolution accurate mass (HRAM) mass spectrometer. After appropriate data processing and analysis, several critical biomarkers were identified, leading to the development of a new non-invasive technique for embryo selection based on these specific molecules.

MATERIALS AND METHODS: After embryo culture between days 3 and 5, spent culture media was collected from 80 samples with known PGT results. These samples were processed using an ultrafiltration technique to separate high-molecular weight molecules from the metabolites fraction, the relevant one for this study.

After this step, samples were analyzed using HRAM mass spectrometer. Resulting chromatograms were aligned and processed to identify and quantify different metabolites in the culture media.

Several statistical and machine learning techniques were applied to identify the most important metabolites to use as biomarkers. To test the performance of the model built, half of the samples (50%) were used to build the prediction model and the other half were used in the validation phase.

RESULTS: A total of 7,523 metabolites were detected in spent media samples. Several dimension reduction techniques were applied and, eventually, selection was performed using PLS-DA (Partial Least Squares – Discriminant Analysis), which gave the best results. Sixty (60) metabolomics biomarkers were identified as the most significant ones and a model was built using PLS-DA algorithm.

The model was tested using the other half of the dataset (27 aneuploid and 13 euploid), for validation purposes. The results gave a concordance with PGT results of 97.5% accurate prediction, with only one misclassified instance: one euploid embryo was classified as aneuploid.

CONCLUSIONS: Differences in metabolites concentration in spent culture media between euploid and aneuploid embryos were highlighted, confirming that we are able to infer metabolic status of the embryo by analyzing the compounds in culture media. In addition, a set number of metabolites were identified as potential biomarkers, facilitating its use in clinical practice instead of the total data, which is highly dimensional and difficult to handle.

This research demonstrates the power of metabolomics in IVF as a non-invasive tool for accurate selection of euploid embryos.

SUPPORT: Overture Life SL

O-14 10:10 AM Saturday, October 17, 2020

MATHEMATICALLY ADJUSTING FOR EMBRYO SIZE IMPROVES THE ACCURACY OF A SPECIFIC GRAVITY DEVICE IN PREDICTING EMBRYO SEX. Samuel D. Prien, PhD,[1] Lindsay L. Penrose, PhD.[2] [1]Texas Tech University Health Sciences Center AND Texas Tech University Lubbock, TX; [2]Texas Tech University Health Sciences Center, Lubbock, TX.

OBJECTIVE: Previous research from this laboratory has demonstrated a Specific Gravity Device (SGD) can be used to noninvasively assess embryo quality across the early stages of embryo development (zygote to blastocyst). Preliminary data also appears to suggest the system might also be useful in predicting embryo sex as embryos enter the blastocyst stage. However, as the SGD calculations assumed embryos of a consistent size, its usefulness was limited in expanding blastocyst. The objective of the current study was to determine if a corrective mathematical algorithm, based on embryo size, could enhance the ability of the SGD to predict embryo sex.

DESIGN: Lab-based trial of the SGD in predicting embryo sex.

MATERIALS AND METHODS: In this preliminary study, a proprietary algorithm was developed to account for embryos of varying sizes based upon the physics of shape and buoyancy. Data from a previous experiment of 463 bovine blastocyst stage embryos that had SGD results correlated to sex determination by Polymerase Chain Reaction (PCR) were used. Data were first corrected for size using the new mathematical algorithm and the embryo's predicted growth (expansion) from the time of blastocyst formation and exposure to the SGD, and then re-analyzed using the SGD prediction for sex. Finally, these new outcomes were compared to the PCR results to determine if correcting for embryo size improved the predictive power of the SGD.

RESULTS: Initial studies without the size correction demonstrate the SGD 65.3-78.4% accuracy selecting for female embryos with no predictive power for male embryos. With the size adjustment, the predictive power for both sexes increased; female embryos were predicted with over 80% accuracy and male embryos with 60% accuracy. While further refinement of the mathematical algorithm may be necessary, these data suggest the SGD could be an effective noninvasive means of predicting the sex of preimplantation embryos.

CONCLUSIONS: Theoretically, the differences in the buoyancy of mammalian blastocyst embryos of similar sizes must be a reflection of differences in the chromosomal weight of X and Y chromosomes or due to developmental differences of male and female embryos. However, while the size of embryos before blastocyst formation is highly conserved, embryos at the blastocyst stage show dynamic shifts in size. Data suggest the SGD can remain an accurate predictor of sex if embryo size is incorporated into the calculations.

SUPPORT: None

O-15 10:25 AM Saturday, October 17, 2020

EMBRYO DEVELOPMENT ON DAY 7 BY CULTURE MEDIA EXPOSURE: A PROSPECTIVE TRIAL. Iris Insogna, MD, MBE, Andrea Lanes, PhD, Elizabeth S. Ginsburg, MD, Catherine Racowsky, PhD. Brigham and Women's Hospital Boston, MA.

OBJECTIVE: 1) To test the hypothesis that slowly developing embryos on day 6 (D6) will be more likely to develop into good, biopsy-quality embryos when randomized to fresh culture medium on D6, compared to embryos that remain in the same medium until day 7 (D7) and that this is age-dependent; 2) To determine the overall percentage of otherwise discarded D6 embryos that would meet biopsy criteria on D7 in PGT-A cycles.

DESIGN: Prospective randomized trial within an academic IVF clinic.

MATERIALS AND METHODS: Embryos of patients ages 18-44, undergoing fresh autologous or donor cycles, with or without preimplantation genetic testing (PGT) that did not meet criteria for biopsy and/or freeze on D6, were randomized to remain in the culture medium (Global® total; GLBT) used for D3-D5 of culture (C-GLBT) or be moved to fresh medium (F-GLBT) with re-evaluation on D7. Embryos from the same cycle were randomized to the medium groups following a pre-determined algorithm. Cycles with at least 2 randomized embryos were included.

Log binomial regression was used to calculate the relative risk and 95% confidence intervals of embryos achieving good quality on D7 when exposed to fresh versus continuous media. The models accounted for patients contributing embryos from more than one cycle.

RESULTS: 1254 embryos were randomized between 3/2019 – 2/2020, with complete grading available for 603 embryos cultured in F-GLBT and 620 cultured in C-GLBT. The groups were similar for patient age, gravidity, parity, AMH, BMI, infertility diagnosis, stimulation protocol and mature eggs retrieved.

The proportion of good quality D7 blastocysts did not differ between media groups (10.1% (61/603) vs. 9.7% (60/620), F-GLBT vs. C-GLBT, respectively; RR 1.05 [95% CI 0.74 – 1.47]). No significant differences were found between groups when stratified by age (Table).

In PGT cycles, 12.3% (26/211) of embryos in F-GLBT achieved good quality on D7 compared to 10.3% (22/214) in C-GLBT, RR 1.20 (95% CI 0.72 – 2.00). 9.9% of embryos otherwise discarded on D6 met criteria for biopsy and/or freeze on D7.

Relative risk of conversion to good quality blastocysts on D7 after randomization to fresh or continuous media on D6, stratified by age

CONCLUSIONS: Refreshment of medium on D6 did not increase the incidence of D7 good, biopsy quality embryos and this was not influenced by patient age. However, our findings support culturing slow developing

	F-GLBT N (%)	RR (95% CI)	C-GLBT N (%)	RR (95% CI)	Total (F-GLBT + C-GLBT) N (%)	RR (95% CI)
<38 N = 897	50/446 (11.2%)	Ref	41/451 (9.1%)	Ref	91/897 (10.1%)	Ref
≥38 N = 326	11/157 (7.0%)	0.63(0.32–1.23)	19/169 (11.2%)	1.24 (0.69–2.22)	30/326 (9.2%)	0.91 (0.57–1.44)

embryos to D7, rather than discarding them on D6, as a significant number of good quality blastocysts become available for clinical use.

SUPPORT: Internal grant awarded from the Obstetrics and Gynecology Department of Brigham and Women's Hospital.

O-16 10:40 AM Saturday, October 17, 2020

INTRACYTOPLASMIC SPERM INJECTION (ICSI) DOES NOT PROVIDE ANY BENEFIT OVER IN VITRO FERTILIZATION (IVF) ON PLOIDY RATES IN NON-MALE FACTOR INFERTILITY CYCLES UNDERGOING PRE-IMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A). Jessica N. Tozour, MD, PhD, Alyson Brady, MS, Meredith Akerman, MS, Alicia J. Arnott, BS, Linda Sung, MD, Rani Fritz, DO, PhD. NYU Winthrop Hospital Mineola, NY.

OBJECTIVE: Early PGT-A platforms required use of ICSI to eliminate paternal DNA contamination. Advances in genetic testing platforms, such as Next Generation Sequencing (NGS), allow for the use of IVF or ICSI. Despite clinical indication, ICSI is currently the recommended fertilization method for PGT-A cycles [1]. Our objective is to evaluate whether significant differences exist in ploidy rates from PGT-A tested embryos fertilized by IVF compared to ICSI.

DESIGN: Retrospective cohort study at a single academic institution.

MATERIALS AND METHODS: All embryos from ICSI and IVF cycles performed from 1/2016 to 2/2020 that underwent NGS PGT-A from trophectoderm biopsy were evaluated. Exclusion criteria included male factor infertility, embryos tested for PGT for monogenic disorders, structural rearrangements, or HLA-typing, cryopreserved oocytes, blastomere or polar body biopsy, in vitro maturation, rescue ICSI, or split IVF/ICSI cycles. Patient demographics, infertility diagnoses, cycle characteristics, and embryo PGT-A results for euploid, aneuploid, low and high mosaicism, and no call rates were collected. Primary outcome was euploid embryo rates. Secondary outcomes were aneuploid and mosaic rates. Chi-square or Fisher's exact test and Mann-Whiney test were used for categorical and continuous variables, respectively. Outcomes of IVF vs. ICSI groups were compared using generalized linear mixed models, in which euploid and aneuploid rates were adjusted for confounding variables attained during the univariate screen. Continuous variables are reported as median with interquartile range. Outcomes variables are reported as mean (95% CI). Results were considered statistically significant with a p-value <0.05. Analyses were performed using SAS version 9.4

RESULTS: A total of 1517 embryos from 387 cycles met criteria, 789 embryos from IVF (52.0%) and 728 embryos from ICSI (47.9%) cycles. Median age in IVF vs. ICSI group were 38 (35 ,40) and 38.5 (36 ,41) years, respectively. Median AMH in IVF vs. ICSI group was 1.8 ng/ml (1 ,3.7), and 2.1 (1.18 ,2.9) ng/ml, respectively. Average embryos biopsied in IVF vs. ICSI group were 4 (2 ,6) vs. 3 (1 ,5), respectively. Euploid, aneuploid, mosaic, and no call rates demonstrated no significant differences in IVF vs. ICSI inseminated groups (Table 1).

CONCLUSIONS: The use of ICSI in non-male factor infertility cycles undergoing PGT-A does not provide an advantage over IVF for euploid or mosaic rates.

TABLE 1.

	IVF	ICSI	p-value
Euploid	0.43 (0.34, 0.51)	0.42 (0.34, 0.49)	0.76
Aneuploid	0.40 (0.31, 0.49)	0.43 (0.37, 0.52)	0.37
No call	0.02 (0.005, 0.03)	0.03 (0.01, 0.04)	0.35
Mosaic	0.15 (0.11, 0.19)	0.13 (0.09, 0.17)	0.39
Low Mosaic	0.07 (0.04, 0.09)	0.06 (0.04, 0.09)	0.79
High Mosaic	0.08 (0.053, 0.11)	0.07 (0.04, 0.09)	0.41

References: 1.Â Practice Committees of the American Society for Reproductive Medicine and Society for Assisted Reproductive Technology. Intracytoplasmic sperm injection (ICSI) for non-male factor infertility: a committee opinion.Â *Fertil Steril*. 2012;98(6):1395-1399.

O-17 10:55 AM Saturday, October 17, 2020

REDUCING THE STRESS OF CULTURE? LOW LACTATE EMBRYO CULTURE MEDIUM INCREASES USABLE BLASTOCYST RATE FOR WOMEN OF ADVANCED MATERNAL AGE. Elizabeth R. Hammond, PhD, Dean E. Morbeck, Ph.D., M.B.A. Fertility Associates, Auckland, New Zealand.

OBJECTIVE: to determine the impact of low-lactate concentration in continuous embryo culture media on useable blastocyst rates and clinical pregnancy rates.

DESIGN: prospective validation of embryology and clinical outcomes for standard-lactate (Continuous Single Culture Complete; CSCM-C) compared to low-lactate continuous culture media (Continuous Single Culture-NX; CSCM-NX, Irvine Scientific).

MATERIALS AND METHODS: from 2019 to 2020, 1673 IVF or ICSI cycles had embryos cultured in either CSCM-C or CSCM-NX at a multicentre clinic (5 clinics) during a prospective culture media validation. CSCM-NX contains a lower concentration of lactate compared to traditional culture media (6-fold lower compared to CSCM-C) enabling direct assessment of whether a reduced concentration of the energy substrate lactate is biologically relevant in human embryos. Day 5 useable blastocyst rate (D5BUR), total useable blastocyst rate (TBUR) and clinical pregnancy rate (CPR) after first fresh or frozen transfer (primary outcome) were compared using two-tailed t-Tests or Pearson Chi-squared test. A p-value of <0.05 was statistically significant.

RESULTS: low-lactate continuous media, CSCM-NX, resulted in a 7% increase in TBUR (52.8%) compared to CSCM-C (46.1%) for exclusively older patients ($\geq$ 38 years; $p=0.0186$). Young patient ($\leq$ 37 years) had a comparable TBUR for the two media (53.2% for CSCM-C and 53.6% for CSCM-NX). There was no difference in the D5BUR between CSCM-C and CSCM-NX according to female age group (40.9% and 41.9 % for $\leq$ 37 years; 32.4% and 37.3% for $\geq$ 38 years, respectively). Similarly, there was no difference in the primary outcome clinical pregnancy rate (44.4% and 47.6% for $\leq$ 37 years; 25.8% and 26.6% for $\geq$ 38 years, respectively).

CONCLUSIONS: results from this large prospective media validation provide evidence that comparatively lower levels of lactate in continuous embryo culture media provide a beneficial metabolic environment for blastocyst development in older patients. The fact that the effect was confined to older patients may reflect higher levels of metabolic stress occurring within their embryos and therefore indicate lower lactate concentrations throughout culture improve metabolic conditions.

SUPPORT: None

O-18 11:10 AM Saturday, October 17, 2020

IS MTDNA CONTENT ASSESSMENT AN INDICATOR OF THE AMOUNT OF MITOCHONDRIA (TOTAL AND ACTIVE ONES) IN THE HUMAN BLASTOCYST?: A CONFOCAL MICROSCOPY APPROACH. Marta Pérez, phD student,[1] Amparo Mercader, PhD,[2] Amparo Mifsud, PhD,[2] Diana Beltrán, Master,[2] Carmen Vidal, M.D., Ph.D.,[2] Elena Labarta, MD PhD,[3] Antonio Pellicer, MD,[4] Ma José de los Santos, PhD.[2] [1]IVI foundation Valencia, Spain; [2]IVIRMA Valencia, Valencia, Spain; [3]IVI-RMA, Valencia, Spain; [4]IVI Foundation Innovation, Valencia, Spain.

OBJECTIVE: to assess if mitochondrial DNA (mtDNA) content per trophectoderm (TE) cell (Mitoscore®) could serve as a predictor of total mitochondrial mass and activity in the human blastocyst.

DESIGN: A prospective cohort study was performed in 51 vitrified aneuploid blastocysts with known Mitoscore® data. Blastocysts were warmed, maintained 6 hours under in vitro culture conditions and stained with mitochondrial dyes. Nonyl acridine orange was used for staining the total mitochondrial content, Mitotracker Deep Red was used for staining the active mitochondrial content and Dapi was used for staining the nucleus.

MATERIALS AND METHODS: Confocal microscopy was used to take three photos of the focal plane of each blastocyst. The analysis was performed with two different methods: Adjusting a fluorescence value for each mitochondrial dye and evaluating the differences in gains values required (N=17) between embryos and setting the same gain values for each dye and calculating the differences in fluorescence emitted between embryos using the image analysis software Image J (N=34). Data was statistically analysed by linear regression and analysis of variance ratios.

RESULTS: We observed that there was no correlation ($p>0.05$) between the mtDNA content either with the number of mitochondria per cell or with the number of active mitochondria per cell using both methods of analysis (fixed fluorescence, N=17 and fixed gains values, N=34).

Most importantly, when we analyzed the variance ratios (variance of a subsample divided by variance of the global population) of the total embryos fluorescence for each dye (mitochondrial mass variance ratio=0,99 and active mitochondria variance ratio=1,89) within a group of embryos with the same Mitoscore® (Mitoscore® variance ratio=0,0096) we observed differences in terms of Mitoscore®' emitted fluorescence and vice versa (mitochondrial mass variance ratio =0,11 and Mitoscore® variance ratio = 0,79; active mitochondria variance ratio=0,007 and Mitoscore® variance ratio= 0,97).

CONCLUSIONS: Confocal approach showed that no correlation could be established between Mitoscore® and total and active mitochondrial content in human blastocysts.

The lack of correlation observed can be due to random distribution of mtDNA content in TE during embryo culture, indicating that mtDNA copy number in the TE is not a good surrogate marker of the mitochondrial mass and the metabolic state of the trophoblast and suggesting a lack of utility of mtDNA measurement as a marker of embryo implantation. Another possibility is that the confocal approach is not accurate enough for doing such correlation.

SUPPORT: This project was supported by funds from the IVF laboratory of IVIRMA Global Valencia, a grant from the IVI foundation (Instituto de investigación sanitaria La Fe, Valencia) and a grant for the recruitment of support staff in a technology transfer project (APOTI, Generalitat Valenciana).

REPRODUCTIVE ENDOCRINOLOGY

O-19 9:55 AM Saturday, October 17, 2020

MENSTRUAL CYCLE CHARACTERISTICS THROUGHOUT THE LIFE COURSE IN RELATION TO CANCER RISK.

Siwen Wang, BS,[1] Janet Rich-Edwards, PhD,[2] Edward Giovannucci, MD, Sc.D.,[3] Jorge E. Chavarro, MD, Sc.D.[1] [1]Harvard School of Public Health, Boston, MA; [2]Brigham and Women's Hospital, Boston, MA; [3]Harvard T.H. Chan School of Public Health, Boston, MA.

OBJECTIVE: Long and irregular cycles have been associated with lower risk of breast cancer and higher risk of endometrial cancer, but associations with other malignancies are less clear. Therefore, we comprehensively assessed the relation of menstrual cycle length or regularity throughout the reproductive lifespan with risk of cancer.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Between 1993 and 2015, we followed 78,947 premenopausal women in the Nurses' Health Study II without a history of cancer and who reported the usual length and regularity of their menstrual cycles at ages of 14-17, 18-22, and 28-48 years. Self-reports of newly diagnosed cancer were subsequently confirmed through review of medical records and pathology reports. Cancer was categorized into obesity-related cancer (colorectal, gallbladder, kidney, multiple myeloma, thyroid, pancreatic, esophageal, gastric, liver, endometrial, ovarian, and post-menopausal breast cancer) and non-obesity-related cancer, based on the classification from the International Agency for Research on Cancer. We fitted Cox proportional hazard models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) of the association between menstrual cycle characteristics and cancer incidence, adjusting for updated body mass index (BMI) and other known cancer risk factors.

RESULTS: We documented 6,661 incident cancer cases during 1,646,310 person-years of follow up. After adjusting for potential confounders, women who reported irregular cycles at age 28-48y had a 9% higher risk (95% CI, 0%-18%) of cancer than women reporting very regular cycles in the same age range. This association was limited to obesity-related cancers, with a 22% (95% CI, 9%-36%) higher risk, while no relation was found with non-obesity-related cancers (HR, 0.94; 95% CI, 0.83-1.07). Similarly, cycles longer than 40 days were associated with increased risk of total cancer and obesity-related cancer compared to a usual cycle length of 26-31 days [HRs=1.19 (95% CI, 1.07-1.32) and 1.30 (95% CI, 1.12-1.51), respectively]. These associations were not modified by BMI, clinical signs of excess androgens, smoking status, or family history of cancer.

CONCLUSIONS: Women with irregular or long menstrual cycles in adolescence and adulthood have a significantly higher risk of developing cancer, especially obesity-related cancers, independent of obesity. Our findings suggest that obesity-related cancers may need to be added to the spectrum of long-term health consequences of long/irregular cycles, possibly warranting targeted screening among women who experience long or irregular cycles in mid-adulthood.

O-20 10:10 AM Saturday, October 17, 2020

LOWER SERUM FSH LEVELS IN RESPONSE TO IV RECOMBINANT FSH IN OBESE WOMEN IS NOT EXPLAINED BY GNRH ANTAGONIST (CETRORELIX) PHARMACODYNAMICS.

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OBJECTIVE: ART employs GnRH suppression and FSH stimulation to induce follicular development. Obese women are known to require higher FSH doses during ART as compared to normal weight (NW) women. It remains unclear whether this higher exogenous FSH requirement for ART is related to abnormal hypothalamic-pituitary dynamics, abnormal ovarian environment or GnRH antagonist or FSH pharmacodynamics/ pharmacokinetics.

DESIGN: We have developed a model to examine IV recombinant (r)FSH levels after GnRH antagonist (cetrorelix) suppression due to the fact there is a need for higher FSH levels in obese women undergoing ART remains unexplained.

MATERIALS AND METHODS: 23 NW and 17 obese women, with regular menstrual cycles, underwent early follicular phase frequent blood sampling (q10min) for 10hrs. At 10hrs cetrorelix acetate (3 mg) was given followed by a secondary dose (0.25mg) 6hrs later. At this time, hourly IV rFSH (30IU) was initiated and frequent blood sampling continued for 10hrs. LH and FSH were measured by immunoassay (Centaur XP, Siemens). Baseline adjusted serum FSH values were used in non-compartmental analysis (WinNonlin) to assess clearance (CLss), steady state volume of distribution (Vss) and total FSH exposure. Pharmacokinetics were compared by two-tailed, unpaired t test. Cetrorelix was measured by tandem gas chromatography and mass spectrometry.

RESULTS: Baseline FSH levels were significantly lower in obese compared to NW subjects. Cetrorelix suppressed FSH by 30% in both groups. Serum cetrorelix concentrations trended lower in obese subjects but were not significantly different (see Table). Despite equivalent IV dosing and correction for baseline levels, the rate of FSH accumulation in serum and total overall FSH exposure concentration was significantly lower in obese women ($p=0.01$, for both). No differences in clearance or volume of distribution were observed.

CONCLUSIONS: FSH pharmacokinetics and Cetrorelix concentrations and efficacy were similar, implying that another factor or pharmacodynamic effect underlies the disparate endogenous post-suppression FSH profiles. This model of pulsatile, IV rFSH reveals a novel and clinically relevant, difference in pharmacodynamics between NW and obese women, which has not been previously observed. Repeated IV boluses of rFSH, after GnRH blockade, mimics endogenous FSH secretion but yields significantly lower serum FSH levels in women with obesity.

Cetrorelix Levels	Minimum (ng/mL)	Maximum (ng/mL)	Area Under the Curve (ng*min/mL)
Normal Weight	3.2	8.0	2655.9
Obese	1.75	4.75	924.4
p Value	0.3	0.27	0.26

O-21 10:25 AM Saturday, October 17, 2020

THE PHARMACOKINETICS OF FOLLICLE STIMULATING HORMONE IN WOMEN WITH POLYCYSTIC OVARY SYNDROME AND MATCHED CONTROLS ACROSS A WIDE BMI SPECTRUM. Malinda S. Lee, MD, MBA,[1] Andrea Lanes, PhD,[1] Andrey V. Dolinko, MD,[2] Alexandra Bailin, MD,[3] Elizabeth S. Ginsburg, MD.[1] [1]Brigham and Women's Hospital Boston, MA; [2]Women and Infants Hospital and Warren Alpert Medical School of Brown University, Providence, RI; [3]Children's Hospital Los Angeles, Los Angeles, CA.

OBJECTIVE: Women with polycystic ovary syndrome (PCO) have an increased ovarian responsiveness to exogenous recombinant follicle stimulating hormone (rFSH); it is unknown how obesity may affect FSH absorption and response in the context of PCO. The objective of this study was to compare pharmacokinetic and pharmacodynamic responses to rFSH between lean and overweight/obese PCO subjects and age and BMI-matched normo-ovulatory controls.

DESIGN: Prospective pilot study conducted in the clinical research center of an academic hospital.

MATERIALS AND METHODS: Fourteen women with PCO by Rotterdam criteria aged 18-42y with BMI of 18.5-24.9 kg/m^2 (normal) or 25.0-40.0 kg/m^2 (overweight/obese) and eleven normo-ovulatory controls matched by age (+/- 3y) and BMI (+/- 2.5 kg/m^2) were included. After an initial hormone washout period of at least one month, participants were initiated on combined oral contraceptive pills (COCPs) for 2-3 weeks. Following a withdrawal from COCPs, participants were administered a single subcutaneous injection of 225IU rFSH and underwent serial blood draws over the next 72 hours. The main outcome measures were the changes in serum FSH and estradiol following rFSH injection.

RESULTS: Lean women exhibited significantly higher peak serum concentration of change in FSH from baseline (Cmax) when compared to overweight/obese women (p=0.01). Lean PCO subjects exhibited a significantly higher area under the curve (AUC) of change in FSH when compared to overweight/obese PCO subjects (183.3 vs 139.8 IU*h/L, p=0.0002), and lean, normo-ovulatory women had a significantly higher AUC of change in FSH when compared to overweight/obese, normo-ovulatory women (193.3 vs 93.8 IU*h/L, p<0.0001). Lean PCO subjects similarly had the highest AUC of change in estradiol (6,095 pg*h/mL), compared to lean normo-ovulatory subjects (1,931 pg*h/mL, p<0.0001) and overweight/obese PCO subjects (2,337 pg*h/mL, p<0.0001).

CONCLUSIONS: As previous studies similarly have shown, FSH absorption and maximum circulating concentrations are mediated by BMI, with overweight/obese women having significantly lower Cmax FSH than women with a normal BMI. In our study, which was able to compare the pharmacokinetics and pharmacokdynamics of FSH between ovulatory and PCO subjects across a wide BMI spectrum, overweight/obese PCO subjects exhibited significantly higher FSH and estradiol levels following rFSH injection when compared to matched normo-ovulatory controls, but significantly lower responses when compared to lean PCO subjects. These findings suggest that PCO itself, in addition to BMI, also appears to mediate FSH absorption and metabolism.

SUPPORT: This work was conducted with support from the Department of Obstetrics and Gynecology, Brigham and Women's Hospital, Expanding the Boundaries Grant; EMD Serono; Harvard Catalyst, The Harvard Clinical and Translational Science Center.

O-22 10:40 AM Saturday, October 17, 2020

LETROZOLE "STAIR-STEP" PROTOCOL VERSUS TRADITIONAL PROTOCOL IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME. Anna Claire Reynolds, M.D.,[1] Heather R. Burks, MD,[1] Sarah Z. Gavrizi, MD,[2] Katherine Boecking, B.S.[1] [1]University of Oklahoma Health Sciences Center, Department of Obstetrics and Gynecology, Oklahoma City, OK; [2]University of Oklahoma Health Sciences Center, Oklahoma City, OK.

OBJECTIVE: Polycystic ovarian syndrome (PCOS) is the most common cause of anovulatory infertility. Prior studies have shown that increasing clomiphene citrate dosing in a "stair-step" fashion shortens time to ovulation. Although it is an off-label use, patients with PCOS have improved fertility outcomes with letrozole as compared with clomiphene citrate for ovulation induction[1]. Stair-step dosing increase using letrozole is common in clinical practice but not well studied[2].

Primary: To evaluate time to ovulation using a letrozole stair-step protocol versus traditional protocol in patients with anovulation secondary to PCOS. *Secondary*: To evaluate time to pregnancy using a letrozole stair-step protocol versus traditional protocol in patients with anovulation secondary to PCOS.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Patients with anovulation and previously diagnosed PCOS by Rotterdam criteria who underwent ovulation induction with letrozole were included from both the Reproductive Medicine Network (RMN) database of patients in the PPCOSII study and our academic REI clinic. Patients were separated into two groups: traditional (progestin-induced withdrawal bleed between cycles if no ovulation with initial letrozole dose) and stair-step (no withdrawal bleed). Interval between the first day of letrozole administration and the date of ovulation was measured and compared in both groups. For patients who conceived, the time from initiating letrozole treatment to positive pregnancy test was also measured and compared.

Patient demographic data and the time to ovulation were evaluated using Student's t-test. Chi-squared test was used to compare the rate of ovulation and pregnancy between groups.

RESULTS: 143 patients were included in this study: 35 patients in the traditional protocol group and 108 in the stair-step protocol group. There were no significant differences in patient demographics or pregnancy rates. A significant difference in time to ovulation was noted, see table below.

	Traditional Protocol n = 35	Stair-step Protocol n=108	p-value
Ovulation (Y/N)	85.7% yes (n=30) 14.3% no (n=5)	83.3% yes (n=90) 16.7% no (n=18)	0.74
Time to ovulation (days)	**75.2**	**37.2**	**< 0.01**
Clinical pregnancy (Y/N)	34.3% yes (n=13) 65.7% no (n=22)	30.6% yes (n=33) 69.4% no (n=75)	0.47
Time to pregnancy (days)	111.4	87.3	0.15

CONCLUSIONS: To expedite ovulation in PCOS patients, with the goal of expediting pregnancy, letrozole is often prescribed in a stair-step fashion. Our findings suggest there is decreased time to ovulation with a letrozole stair-step protocol, of 38 days on average, with similar pregnancy rates. In conclusion, the dose of letrozole may be increased as soon as nonresponse is noted, and menses is not required between cycles in PCOS patients.

References: 1. Legro, R. S., R. G. Brzyski, et al. (2014). "Letrozole versus clomiphene for infertility in the polycystic ovary syndrome." N Engl J Med 371(2): 119-129.

2. Hurst, B. S., J. M. Hickman, et al. (2009). "Novel clomiphene "stair-step" protocol reduces time to ovulation in women with polycystic ovarian syndrome." Am J Obstet Gynecol 200(5): 510 e511-514.

SUPPORT: None

O-23 10:55 AM Saturday, October 17, 2020

HIGH LIVE BIRTH RATES WITH LOW MULTIPLE BIRTH RATES: OVER TWO DECADES' EXPERIENCE OF PULSATILE GNRH PUMP USE FOR OVULATION INDUCTION IN PATIENTS WITH FUNCTIONAL HYPOTHALAMIC AMENORRHEA (FHA). Philipp Quaas, MD,[1] Alexander M. Quaas, MD, PhD,[2] Manuel Fischer, PhD,[1] Christian De Geyter, MD.[1] [1]University Hospital Basel Basel, Switzerland; [2]University of California San Diego, San Diego, CA.

OBJECTIVE: To analyze the experience of treating patients with FHA (functional hypothalamic amenorrhea) over the last 25 years using a subcutaneous pulsatile gonadotropin releasing hormone (GnRH) pump at a Swiss university-based tertiary referral center.

DESIGN: Retrospective cohort study of all patients with FHA undergoing ovulation induction using the GnRH pump between 1996 and 2020.

MATERIALS AND METHODS: Inclusion criteria for the study were a diagnosis of FHA and treatment using a subcutaneous pump delivering pulsatile gonadorelin acetate during the study period. Baseline characteristics including age, BMI, smoking status, AMH, AFC, endocrine profiles, and

lifestyle parameters including exercise were recorded. The primary outcome was live birth rate (LBR) per treatment. Secondary outcomes included the number of dominant follicles per cycle and ovulation rate per cycle attempt (data available for 2014-2020), biochemical pregnancy rate (BPR), clinical pregnancy rate (CPR), miscarriage rates and multiple pregnancy rates.

RESULTS: During the study period, 66 patients with FHA underwent a total of 82 separate treatment episodes involving 208 ovulation induction attempts using the pulsatile GnRH pump. Baseline characteristics of the study population included a mean age of 31.6 years, mean BMI of 20.2 kg/m^2, and a mean serum AMH concentration of 35.2 pmol/l, equivalent to 4.93 ng/ml. The ovulation rate per cycle attempt was 96% and monofollicular ovulation (one follicle of $\geq$14 mm size at time of ovulation) was observed in 67% of cycle attempts. In patients who conceived, the median number of cycles necessary to achieve a clinical pregnancy was 2. The cumulative CPR per treatment episode was 62/82 (76%) and the overall LBR per treatment was 50/82 (61%)*. The miscarriage rate was 7/62 (11%). There was one dizygotic twin pregnancy (multiple pregnancy rate 1/62 = 1.6%). The mean infant birth weight in the cohort was 3249 g. No significant adverse effects were reported by any of the patients in the study.

CONCLUSIONS: In patients with FHA, monofollicular ovulation can be achieved in the majority of patients using the subcutaneous pulsatile GnRH pump. The high observed cumulative live birth rates, with multiple pregnancy rates comparable to those in the general population suggest that the pulsatile GnRH pump represents a safer, more physiologic alternative to ovulation induction using injectable gonadotropins.

TABLE. Treatment outcomes in the study population

Clinical parameter	Outcome (n / %)
Monofollicular ovulation	31/46 (67%)
BPR per cycle	67/208 (32%)
CPR per cycle	62/208 (30%)
LBR per cycle	50/208 (24%)*
LBR per treatment episode	50/82 (61%)*
miscarriage rate	7/62 (11%)
Multiple pregnancy rate	1/62 (1.6 %)

*5 pregnancies ongoing at time of submission.

References: [1] Gordon, C. M. (2010). Functional hypothalamic amenorrhea. New England Journal of Medicine, 363(4), 365-371.

[2] Quaas, A. M., & Legro, R. S. (2018). Pharmacology of medications used for ovarian stimulation. Best Practice & Research Clinical Endocrinology & Metabolism.

SUPPORT: None.

O-24 11:10 AM Saturday, October 17, 2020

POSITIVE EFFECTS OF THYROID REPLACEMENT THERAPY ON ART OUTCOMES IN WOMEN WITH SUBCLINICAL HYPOTHYROIDISM WITH TPO^{+VE} ANTIBODIES.

Maria Bustillo, M.D,[1] Ineabelle Collazo, BS,[2] Katherine L. Palmerola, BS, MD,[2] Sabrina A. Gerkowicz, MD,[2] Juergen Eisermann, M.D,[1] Nicholas Hendon, BS,[2] Himanshu Arora, PhD.[3] [1]IVFMD South Florida Institute for Reproductive Medicine, MIAMI, FL; [2]IVFMD, South Florida Institute for Reproductive Medicine, Miami, FL; [3]University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: Thyroid function is critical to optimal reproductive function in women; and thyroid disease may exert negative effects on ovulation, menstrual function, and pregnancy success. Thyroid-stimulating hormone (TSH) is the primary marker for thyroid function, stimulates the release of thyroxine (T4) and tri-iodothyronine (T3) from the thyroid gland, exerting the metabolic effects of the thyroid gland throughout the body. Serum TSH levels and antithyroid antibodies are routinely screened in women with infertility. In a previous study, we have shown that thyroid replacement therapy (TRT) has significant effect on pregnancy outcomes in women with subclinical hypothyroidism (TSH levels > 2.5 uIU/mL and </= 4.2 uIU/mL; SCH). Whether antithyroid antibodies on thyroid replacement therapy in women with SCH remains largely unexplored. In the current study we evaluated whether TRT can overcome the adverse effects of antithyroid antibodies on pregnancy outcome in women with SCH.

DESIGN: Retrospective study of 707 patients undergoing IVF.

MATERIALS AND METHODS: Patients were categorized into 3 groups. Group 1, euthyroid, consisted of women who had pre-IVF TSH levels <2.5 uIU/mL. Patients with SCH were divided into two groups (Group 2 and 3) based on whether or not they were given low dose thyroid supplementation (treatment): group 2 included women with SCH who were not treated, and group 3 included women with SCH who were treated. Additionally, all three groups were classified into two subgroups based on thyroid peroxidase (TPO) antibody levels: TPO negative (<11ng/ml) or TPO positive (>11ng/ml). All women underwent standard IVF protocols following usual individualized practice in our practice. IVF outcomes were compared between the three groups using three-way ANOVA. GraphPad Prism (GraphPad Software) was used for statistical analysis, with $p<0.05$ considered statistically significant.

RESULTS: A total of 707 patients were included in the analysis. Group 1 (euthyroid) included 526 women: 454 patients were TPO negative (359 pregnant (P), 95 not pregnant (NP)) and 72 patients were TPO positive (54 P, 18 NP). Group 2 included 50 women: 42 patients were TPO negative (28 P, 14 NP) and 8 patients were TPO positive (3 P, 5 NP). Group 3 included 131 women: 87 patients were TPO negative (64 P, 23 NP) and 44 patients were TPO positive (37 P, 7 NP). Three-way ANOVA analyses demonstrated that women with SCH and TPO positive had significantly fewer pregnancies compared to women with SCH who were TPO negative ($p<0.001$). However, thyroid replacement therapy significantly improved the pregnancy outcomes in patients with SCH that are TPO positive ($p<0.0001$). Importantly, the difference between pregnancy outcomes between patients in Group 1 versus Group 3 is non-significant ($p>0.05$).

CONCLUSIONS: Our findings suggest that thyroid replacement therapy has significant positive effects on ART outcomes in SCH women with positive TPO antibodies. Further in-depth studies are ongoing considering parameters such as the AMH, patient's BMI etc and additional specific treatment strategies which may have an additional effect on successful IVF outcomes.

References: 1. Impact of BMI on pregnancy outcomes with respect to differential TSH levels Bustillo, Maria et al. Fertility and Sterility, Volume 112, Issue 3, e213 - e214

SUPPORT: This work was supported in part by the *IVFMD, South Florida Institute for Reproductive Medicine*

CONTRACEPTION AND COMPLEX FAMILY PLANNING

O-25 9:55 AM Saturday, October 17, 2020

POLIDOCANOL/DOXYCYCLINE FOAM FOR NONSURGICAL PERMANENT FEMALE CONTRACEPTION BABOON CONTRACEPTION STUDY: 18 MONTH DATA.

Jeffrey T. Jensen, MD, MPH,[1] Carol B. Hanna, Ph.D.,[2] Shan Yao, M.D.,[3] Philberta Y. Leung, Ph.D.,[3] Nicholas M. Kiulia, MS,[4] Ov D. Slayden, PhD.[5] [1]Oregon Health & Science University Portland, OR; [2]Oregon National Primate Research Center, Beaverton, OR; [3]Oregon National Primate Research Center, BEAVERTON, OR; [4]Department of Reproductive Health and Biology, Institute of Primate Research, Nairobi, Kenya; [5]Professor, Beaverton, OR.

OBJECTIVE: The addition of doxycycline to polidocanol foam increases the rate of tubal occlusion. We sought to determine if a single transcervical administration of polidocanol/doxycycline foam (PDF) would prevent pregnancy in female baboons and assess safety of treatment.

DESIGN: Controlled nonhuman primate cohort study.

MATERIALS AND METHODS: Healthy regularly cycling female baboons underwent laparoscopy with chromopertubation for evaluation of tubal patency and pelvic adhesions followed by transcervical infusion of either 20 mL of 5% PDF (each 5 mL of foam contains 25 mg doxycycline; n=12, 8 nulliparous, 4 parous), 20 mL of 1% control methylcellulose foam (MC; n = 6, 5 nulliparous, 1 parous), or no additional treatment (Control; n=6, all nulliparous). All of the females received an intramuscular injection of depomedroxyprogesterone acetate (DMPA, 2 mg/kg) after the treatment. After recovery, females were socially-housed with males of proven fertility, and observed for resumption of menstrual cyclicity and evidence of mating. The primary outcomes was pregnancy through 18 months of follow-up. Secondary outcomes included histologic evaluation of the fallopian tube, and peritoneal adhesions assessed at necropsy (PDF group only).

RESULTS: All females resumed normal menstrual cycles and mating activity within 3 months of treatment. After 15 months of regular cycles, 11/12

(92%) of control females became pregnant (6/6 MC control, 5/6 untreated control). Significantly fewer (2/12, 16%) pregnancies occurred in PDF-treated females ($p < .001$, Fisher's exact test). All of the pregnancies were intrauterine. Both pregnancies in PDF-treated females occurred in nulliparous females considered high-risk for failure; one progressed normally to term and one underwent spontaneous abortion. Histologic evidence of bilateral tubal occlusion (de-epithelialization, collagen obliteration of lumen) developed in all of the PDF-treated females except for the two that became pregnant (each with unilateral occlusion). New pelvic adhesions developed in 11/12 of the PDF-treated females; of these 4/11 (36%) were dense. In contrast, we found no new adhesions in a subset of control females (n=3) evaluated at necropsy.

CONCLUSIONS: A single transcervical treatment with PDF prevented pregnancy in most baboons, and resulted in histologic tubal occlusion that appears permanent at 18 months. The new onset of pelvic adhesions appears related to the addition of doxycycline, as these occurred uncommonly in a prior baboon contraception study with polidocanol foam alone [Contraception. 2016;94(5):527-33].

SUPPORT: Bill and Melinda Gates Foundation OPP1191953

O-26 10:10 AM Saturday, October 17, 2020

BLEEDING PATTERNS FROM MONTHS 60 TO 72 WITH USE OF A LEVONORGESTREL 52 MG INTRAUTERINE SYSTEM. Jeffrey T. Jensen, MD, MPH,[1] Bruce R. Carr, MD,[2] Thomas D. Kimble, MD,[3] Michael A. Thomas, MD,[4] Andrea I. Olariu, MD, PhD,[5] Mitchell D. Creinin, MD.[6] [1]Oregon Health & Science University Portland, OR; [2]UT Southwestern Medical Center, Dallas, TX; [3]Eastern Virginia Medical School, Norfolk, VA; [4]University of Cincinnati, Cincinnati, OH; [5]Medicines360, San Francisco, CA; [6]University of California, Davis, Sacramento, CA.

OBJECTIVE: Evaluate bleeding patterns during levonorgestrel (LNG) 52 mg intrauterine system (IUS) use beyond 5 years.

DESIGN: Prospective clinical trial.

MATERIALS AND METHODS: Nulliparous and parous women 16-45 years old received the Liletta® LNG 52 mg IUS in an IRB-approved multicenter trial to evaluate efficacy and safety for up to 10 years. Bleeding assessments after 24 months of IUS use occurred every 3 months, including subjective flow evaluation and how the bleeding compared to pre-insertion frequency or flow. For this analysis, we evaluated reported bleeding patterns (none, "just spotting," irregular or regular), comparison of frequency or flow to baseline, and discontinuation for bleeding complaints over 3-month intervals beginning at 60 months (5 years) and then for the following year (months 63 to 72). We performed chi-square test for trend to evaluate changes in patterns over time.

RESULTS: The dataset included 707, 645, 563, 477 and 349 women with bleeding pattern reports for months 58-60, 61-63, 64-66, 67-69, and 70-72 at the time of the data cut. The heaviest flow in the prior 3 months is reported in the Table. Amenorrhea rates remained around 40%, ranging from 39.1-43.2% (p=0.75). Most women reported their heaviest flow as none (amenorrhea) or spotting during each interval (69.8-72.6%, p=0.30). Approximately 90% of women (87.2-90.4%, p=0.58) reported their heaviest bleeding as none (amenorrhea), spotting, or light bleeding per interval. Among women with any bleeding, most reported spotting as the main pattern, ranging from 29.8-35.3% (p=0.41); the remainder reported the main pattern as irregular (6.4-7.7%, p=0.84) or regular (16.6-19.5%, p=0.52) during each interval. Approximately 1-1.5% of users reported frequency or flow worse than pre-insertion patterns and only 1 woman during months 58-60 and 1 during months 70-72 discontinued for a bleeding complaint considered an adverse event. Additionally, beginning after month 60, 1-2 persons per 3-month period discontinued because of reduced menstrual suppression.

CONCLUSIONS: Bleeding patterns remain consistent in LNG 52 mg IUS users from months 60 through 72 of use, with most women experiencing amenorrhea, spotting or light bleeding. Discontinuation for a bleeding complaint occurred in only 2/707 (0.3%) women during this period, and another 6 (0.9%) discontinued for reduced menstrual suppression. Providers and patients can be informed by this data that bleeding patterns remain favorable with use beyond 5 years.

	Heaviest flow in prior 3 months				
	Month 60 n=707	Month 63 n=645	Month 66 n=563	Month 69 n=477	Month 72 n=349
None	40.2%	40.8%	39.1%	43.2%	40.4%
Spotting	30.8%	31.8%	32.0%	26.6%	31.2%
Light	18.0%	17.8%	18.1%	17.4%	17.8%
Normal	9.2%	8.8%	9.2%	11.1%	9.5%
Heavy	1.8%	0.8%	1.6%	1.7%	1.1%

SUPPORT: Mediines360

O-27 10:25 AM Saturday, October 17, 2020

COMPARING THE CARDIOVASCULAR RISK OF NORETHINDRONE ACETATE- AND LEVONORGESTREL-CONTAINING ORAL CONTRACEPTIVES: IS THERE A DIFFERENCE? Clare Barnett, MBBS (Hons), MPH, Sophia von Stockum, PhD, Anja Bauerfeind, PhD, Klaas Heinemann, MD, PhD, MBA. ZEG Berlin GmbH Berlin, Germany.

OBJECTIVE: Norethisterone acetate (NETA) and levonorgestrel (LNG) were two of the first progestins to be introduced for medical use. From a research perspective, LNG is the first-choice progestin and it is accepted by regulators as the gold-standard since it has been shown to not increase the thromboembolic risks derived from the estrogen component. Combined oral contraceptives containing norethindrone acetate (NETA) are widely used in the US, and globally, and are recommended as first-line therapy alongside LNG-containing pills. No robust data is currently available directly comparing the cardiovascular risk profiles of LNG and NET/NETA.

DESIGN: A pooled analysis to directly compare the safety of NETA and LNG in pills containing ethinyl estradiol (EE) $\leq$30 mcg.

MATERIALS AND METHODS: We pooled cohorts of NETA (EE $\leq$30 mcg) and LNG (EE $\leq$30 mcg) users from four large prospective, controlled, non-interventional, cohort studies in 14 European countries, US and Canada. Baseline characteristics, including reproductive, contraceptive and medical history, were summarized using descriptive statistics. Propensity score sub-classification was applied to balance baseline characteristics between cohorts. Time-to-event analysis of venous and arterial thromboembolic events was carried out based on the extended Cox model to calculate crude and adjusted hazard ratios with 95% confidence intervals.

RESULTS: Overall, 235,437 study participants who were followed up for a total of 571,163 WY of exposure were included in the pooled dataset. Among these, 40,142 women were users of NET/NETA (EE$\leq$30μg) and 39,098 women were users of LNG (EE$\leq$30μg), contributing 61,976 and 84,816 WY of observation, respectively. The prevalence of prognostic factors at baseline showed typical characteristics of US and European COC user populations regarding age structure, socioeconomic and life-style factors and cardiovascular risk factor. In total, 43 validated VTE events in 61,976 WY occurred in the NET/NETA (EE$\leq$30μg) user cohort, and 75 VTE events during an observation time of 84,816 WY in the LNG (EE$\leq$30μg) user cohort. Study participants taking NET/NETA (EE$\leq$30μg) had a similar risk of encountering a VTE (IR: 6.9; 95% CI, 5.0-9.3 per 10,000 WY) to study participants taking LNG (EE$\leq$30μg) (IR: 8.8; 95% CI, 7.0-11.1 per 10,000 WY). A time-to-event analysis of the VTE data was carried out based on the extended Cox model. Validity of the model was demonstrated by the standardized differences summarized over strata as weighted average yielded upon PS sub-classification, which were consistently <0.25 and mostly <0.1. A comparison between NETA vs LNG showed no significant difference in the risk of venous thromboembolism: adjusted hazard ratio 0.73 (95% CI 0.48-1.11). A similar result was observed considering the risk of arterial thromboembolism (adjusted hazard ratio 0.89 [95% CI 0.42-1.89]).

CONCLUSIONS: Low-dose oral contraceptives containing NETA and LNG are associated with similar low risks of venous and arterial disease. This analysis provides reassurance for both women and clinicians regarding the safety of contemporary oral contraceptives.

SUPPORT: Analysis of pooled dataset was supported by a grant from Myovant Sciences. Dataset is owned by ZEG Berlin GmbH.

O-28 10:40 AM Saturday, October 17, 2020

DURATION OF CONTRACEPTIVE USE IS NOT ASSOCIATED WITH AMH LEVELS. Sharon Briggs, PhD, Talia Shirazi, MA, Avner Hershlag, MD. Modern Fertility San Francisco, CA.

OBJECTIVE: To estimate the effect of length of contraceptive use on anti-Mullerian hormone (AMH) levels in reproductive-age women.

DESIGN: Prospective analysis of serum AMH levels and survey data.

MATERIALS AND METHODS: The study included a subset of customers who used an at-home fertility hormone test between June 2018 and April 2020 ($n = 2,358$). Participants were between 21 and 46, consented to research, had not reported a previous diagnosis of polycystic ovary syndrome or primary ovarian insufficiency, and were currently using either the levonorgestrel IUD (LNG-IUD), implant, combined oral contraceptive (COC), or vaginal ring. The duration of contraceptive use was self-reported and ranged from 1-3 months up to more than 20 years.

We performed three linear regressions per contraceptive method to evaluate the relationship between the length of contraceptive use and log-transformed AMH levels. Since three regressions were run per contraceptive group, the threshold for statistical significance ($\alpha = 0.05$) was set to 0.017 to adjust for multiple comparisons. We subsequently grouped short-term use and long-term use participants into binary categories or bins and compared mean AMH levels for each contraceptive use group.

RESULTS: Our cohort included 807 women using the LNG-IUD, 112 using the implant, 1,109 using a COC, and 165 using the vaginal ring. There were no statistically significant associations between length of contraceptive use and adjusted AMH levels for any contraceptive method. This was true in regressions of the entire sample and when we limited the sample to just short-term users or just long-term users.

When the length of contraceptive use was treated as a binary variable (short-term <1 year or long-term 1+ years) or was grouped into categories spanning approximately 5 years, no statistically significant effects were observed for any contraceptive method.

CONCLUSIONS: It is known that AMH levels are lower in women using hormonal contraceptives when compared to women who aren't. However, this study shows that the duration of contraceptive use is not associated with any additional variation in AMH levels. We observe no impact of either long or short term usage on AMH levels for any of the contraceptive methods included in this study. These results are reassuring since it is still widely believed among physicians and patients alike that long term contraceptive use suppresses ovarian reserve more than short term use, particularly in users of COC.

Women are increasingly seeking testing of their ovarian reserve while remaining on contraceptives to prevent pregnancy. Reasons for getting tested for AMH while on contraceptives are varied and include seeking proactive hormone assessments, getting information about time to menopause, egg freezing, or donating eggs. Having to stop contraception to test ovarian reserve may be unwanted or inconvenient. By better understanding the effects of contraceptives on AMH, women will have more options when pursuing this testing, and physicians will be better equipped to interpret the results.

O-29 10:55 AM Saturday, October 17, 2020

MENORRHAGIA AND RISK OF INTRAUTERINE DEVICE (IUD) EXPULSION AND UTERINE PERFORATION: RESULTS FROM THE APEX IUD STUDY. Susan D. Reed, MD, MPH, MS,[1] Catherine W. Saltus, MPH, MA,[2] Darios Getahun, MD, MPH, PhD,[3] Juliane Schoendorf, MD,[4] Mary Anne Armstrong, MA,[5] Jeffrey F. Peipert, MD, PhD,[6] Tina R. Raine-Bennett, MD, MPH,[5] Mary E. Ritchey, PhD,[7] Laura E. Ichikawa, MS,[8] Xiaolei Zhou, PhD,[9] Michael J. Fassett, MD,[10] Amy Alabaster, MPH, MS,[5] Fagen Xie, PhD,[3] Maqdooda Merchant, MSc, MA,[5] Vicki Y. Chiu, MS,[3] Jiaxiao M. Shi, PhD,[3] Ann-Kathrin Frenz, MSc,[11] Theresa M. Im, MPH,[3] Harpreet S. Takhar, MPH,[3] Richard Lynen, MD,[12] Alex Asiimwe, PhD,[13] Mary S. Anthony, PhD.[9] [1]University of Washington Seattle Seattle, WA; [2]RTI Health Solutions, Waltham, MA; [3]Kaiser Permanente Southern California, Pasadena, CA; [4]Bayer OY, Espoo, Finland; [5]Kaiser Permanente Northern California, Oakland, CA; [6]Indiana University, Indianapolis, IN; [7]Med Tech Epi, LLC, Philadelphia, PA; [8]Kaiser Permanente Washington, Seattle, WA; [9]RTI Health Solutions, Research Triangle Park, NC; [10]Kaiser Permanente Southern California, Los Angeles, CA; [11]Bayer AG, Wuppertal, Germany; [12]None, Richboro, PA; [13]Bayer AG, Berlin, Germany.

OBJECTIVE: IUDs are an effective form of contraception, and the most common levonorgestrel (LNG) IUD has an FDA indication for heavy menstrual bleeding. We assessed the risk of IUD expulsion and uterine perforation in women with and without a recent diagnosis of menorrhagia.

DESIGN: APEX IUD was a retrospective cohort study that used electronic health records from three Kaiser Permanente sites (Northern California, Southern California, Washington) and Regenstrief Institute (Indiana).

MATERIALS AND METHODS: This study included 228,834 women aged ≤50 years with an IUD inserted from 2001–2018 without a delivery in the prior 52 weeks (including nulliparous women). Diagnosis of menorrhagia was identified via ICD code within 12 months before IUD insertion. Expulsion included complete and partial (IUD in cervical canal). Perforation was defined as complete (in pelvis or abdomen) or partial (embedded in myometrium). Crude incidence rates, hazard ratios adjusted for confounding with propensity scores via Cox regression, and 95% confidence intervals (CI) were estimated.

RESULTS: Expulsions occurred more often among women with a menorrhagia diagnosis. Among 31,600 women with menorrhagia, 2% of IUD insertions were copper; and among 197,234 women without menorrhagia, 20% were copper. The expulsion rate among those without menorrhagia was lower for those with LNG versus copper IUDs. For those with menorrhagia, expulsion was lower in the few with copper IUDs. Perforation rates were higher among women with menorrhagia but low in all groups. After adjusting for confounding, women with menorrhagia had a 2.84-fold increased risk of expulsion and a 1.53-fold increased risk of perforation over women without.

	Person-Years	# Events	Incidence, Per 1,000 Person-Years (95% CI)	Adjusted Hazard Ratio (95% CI)
IUD Expulsion				
Menorrhagia	**62,405**	**2,497**	**40.0 (38.5, 41.6)**	**2.84 (2.66, 3.03)**
LNG	60,053	2,450	40.8 (39.2, 42.5)	–
Copper	1,505	32	21.3 (14.5, 30.0)	–
No menorrhagia	**390,598**	**4,265**	**10.9 (10.6, 11.3)**	**Ref**
LNG	306,268	3,031	9.9 (9.6, 10.3)	–
Copper	79,930	1,197	15.0 (14.1, 15.9)	–
Uterine Perforation				
Menorrhagia	**62,405**	**61**	**0.98 (0.75, 1.26)**	**1.53 (1.10, 2.13)**
LNG	60,053	58	0.97 (0.73, 1.25)	–
Copper	1,505	2	1.33 (0.16, 4.80)	–
No menorrhagia	**390,598**	**248**	**0.63 (0.56, 0.72)**	**Ref**
LNG	306,268	185	0.60 (0.52, 0.70)	–
Copper	79,930	59	0.74 (0.56, 0.95)	–

CONCLUSIONS: Increased rates of expulsion and perforation with menorrhagia may be due to physiological differences related to menorrhagia including adenomyosis and uterine fibroids. Providers should be aware of these risks for patient counseling and exercise caution at the time of insertion. We recommend informing women regarding the higher risk of IUD expulsion and the importance of recognizing expulsion in prevention of unwanted pregnancy.

SUPPORT: This work was funded by Bayer AG which produces one of the IUD types under study, and some of the authors are employees of that company.

O-30 11:10 AM Saturday, October 17, 2020

SEXUAL SATISFACTION WITH A VAGINAL PH REGULATOR (EVO100): RESULTS FROM THE AMPREVENCE CLINICAL TRIAL. Michael A. Thomas, MD,[1] Kelly R. Culwell, MD, MPH,[2] Scott G. Mollan, MS, MBA,[3] Brandon Howard, PhD.[2] [1]University of Cincinnati Cincinnati, OH; [2]Evofem Biosciences, Inc., San Diego, CA; [3]ICON Clinical Research LLC, Durham, NC.

OBJECTIVE: EVO100 is an investigational antimicrobial vaginal pH regulator that is a non-hormonal, woman-controlled, water-based vaginal gel for prevention of sexually transmitted infection. To better understand the effects of use on sexual satisfaction and function, questionnaires were administered to women receiving EVO100 in the phase 2B/3 AMPREVENCE trial (NCT03107377) at each study visit.

DESIGN: AMPREVENCE was a randomized, multicenter, US-based, double-blinded, placebo-controlled trial conducted over 16 weeks in women aged 18–45 years who had been treated for chlamydia or gonorrhea $\leq$16 weeks before enrollment. Women were randomized to receive EVO100 or placebo vaginal gel. Primary and secondary efficacy endpoints were prevention of urogenital chlamydia and gonorrhea, respectively. Women's sexual satisfaction and function with EVO100 was an exploratory endpoint.

MATERIALS AND METHODS: To assess sexual satisfaction/function, questionnaires were administered at enrollment and at Visit 5. Women reported how EVO100 use impacted their sex life since their last study visit and provided responses on the Sexual Function Questionnaire (SFQ) and for item 10 on the Female Sexual Function Index (FSFI). All results were summarized using frequency and percentage.

RESULTS: AMPREVENCE enrolled 860 women randomized 1:1 to EVO100 (n=426) or placebo (n=434). At Visit 5, most of the women receiving EVO100 (51%, 140/273) reported a positive impact on their sex life or "no difference" (45%, 124/273) since their last study visit. With EVO100, more women reported no difficulty maintaining lubrication until completion of intercourse (74%, 203/274) at Visit 5 compared with baseline (68%, 239/350). Most women receiving EVO100 surveyed at Visit 5 reported improvements in various sexual function measures compared with baseline and reported no vaginal dryness during sexual activity (67% [181/272] vs 53% [184/349]); no pain during intercourse (71% [192/272] vs 58% [204/350]); no vaginal tightness (49% [133/272] vs 37% [131/350]); and ability to orgasm in the past month (67% [181/272] vs 57% [200/350]). Overall, 91 of 426 women randomized to EVO100 discontinued the study early; of these, 25 provided responses to the sexual impact question and to FSFI, and 24 provided responses to the SFQ. Of women who terminated the study early and reported an impact of EVO100 on their sex life, 44% (11/25) and 48% (12/25) reported a positive impact or no difference in their sex life, respectively, since their last study visit. Women who terminated the study early also described improvements in sexual function measures and reported no vaginal dryness during sexual activity (79%, 19/24); no pain during intercourse (67%, 16/24); ability to orgasm (63%, 15/24); and no vaginal tightness (42%, 10/24) in the past month.

CONCLUSIONS: In AMPREVENCE, healthy women receiving EVO100 reported positive impact on their sexual satisfaction, maintained lubrication, and reported improvement in many sexual function measures.

SUPPORT: Evofem Biosciences, Inc.

2020 SCIENTIFIC CONGRESS PRIZE PAPER SESSION 2

O-31 2:00 PM Saturday, October 17, 2020

FRESH EMBRYO TRANSFER FOLLOWING IN VITRO INSEMINATION OF FRESH VERSUS CRYOPRESERVED ANONYMOUS DONOR OOCYTES- WHICH HAS A BETTER LIVE BIRTH RATE? A SART CORS ANALYSIS.

Rachel M. Whynott, M.D.,[1] Karen M. Summers, MPH CHES,[2] G. David Ball, PhD,[3] Bradley J. Van Voorhis, MD,[2] Amy E. Sparks, PhD.[4] [1]University of Iowa Hospitals and Clinics Iowa City, IA; [2]University of Iowa, Iowa City, IA; [3]Seattle Reproductive Medicine Center, Seattle, WA; [4]University of Iowa Center for Advanced Reproductive Care, Iowa City, IA.

OBJECTIVE: To determine if transfer of fresh embryos derived from fresh anonymous donor oocytes yields a higher live birth rate compared with cryopreserved (cryo) oocytes.

DESIGN: Historical cohort study.

MATERIALS AND METHODS: All anonymous donor oocyte recipient cycles undergoing fresh embryo transfer on day 5 in the United States from 2014-2016 using the SART CORS database were included. Demographics were analyzed using t-test or Chi-square as appropriate. Generalized estimating equations were used for modeling to determine predictors of live birth, using Bayesian Information Criterion (BIC) to select the best model.

RESULTS: 24,663 transfers met inclusion criteria. 16,073 were transfers from fresh embryos created from fresh oocytes, and 8,590 were fresh embryos from cryo oocytes. Age, body mass index (BMI), gravidity, and parity were clinically similar between recipients using fresh oocytes compared with cryo oocytes. Most patients using donor oocytes identified as white non-Hispanic (66.9%), followed by Asian (13.7%), then black non-Hispanic (9.3%), and Hispanic (7.2%). When compared to other races, a larger proportion of black non-Hispanic women used cryo oocytes (37.2%), whereas a smaller proportion of women of Asian descent used cryo oocytes (19.9%) (p< .001). Intended parents using gestational carriers were more likely to use fresh oocytes than those not using gestational carriers (75.5% vs 64.6%, p<0.001). Cryo oocyte cycles were more likely to have only one embryo for transfer (9.5% vs 3.1%), while fresh oocyte cycle were more likely to utilize elective single embryo transfer (42.5% vs 37.8%) and cryo oocyte cycles were more likely to involve transfer of more than 2 embryos (2.2% vs 1.2%)(p<0.001). Fresh oocyte cycles resulted in more surplus embryos available for cryopreservation after completion of fresh embryo transfer (4.55 vs 1.16, p<0.001).

The live birth rate using fresh oocytes was 58.3% versus 49.9% using cryo oocytes (p<0.001). Negative predictors of live birth included utilization of cryo oocytes (OR 0.744, 95% CI 0.674-0.821, p<0.001), black non-Hispanic race (OR 0.597, 95% CI 0.509-0.700, p<0.001), Asian race (OR 0.752, 95% CI 0.653-0.867, p<0.001), and increasing oocyte recipient BMI (OR 0.913, 95% CI 0.876-0.952, p<0.001). Other factors in the model included age, Hispanic ethnicity, multiracial status, number of embryos transferred on day 5, and unexplained infertility diagnosis. For cycles utilizing fresh oocytes, number of live born was 1.28 ± 0.46, versus 1.21 ± 0.42 for cryo oocytes (mean difference 0.07 (CI 0.05-0.09), p<0.001).

CONCLUSIONS: Live birth rate is higher with use of fresh oocytes versus cryo oocytes in fresh embryo transfer cycles in anonymous donor oocyte recipients. Negative predictors of live birth include black non-Hispanic or Asian race, and increasing BMI.

References: N/a

SUPPORT: None

O-32 2:15 PM Saturday, October 17, 2020

STATE-MANDATED INSURANCE AND PREIMPLANTATION GENETIC TESTING (PGT) INDICATION IN THE UNITED STATES.

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OBJECTIVE: To assess associations between insurance mandates for fertility care and indications for PGT over time.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Fresh autologous IVF cycles from the 2007-2016 SART registry were analyzed in two time periods due to changes in SART cycle definitions in 2013. Given the introduction of "other" indication for PGT in 2009, we limited our analysis to 2009-2016. Frozen, cancelled, and banking cycles were excluded. Fertility clinics were categorized by level of insurance coverage mandated in their state: comprehensive, partial, and no coverage. Indications for PGT were categorized hierarchically as follows: genetic, balanced translocation, HLA typing, elective sex selection, aneuploidy, and other. Log binominal regression was used to analyze change in indication for PGT over time relative to mandate type.

RESULTS: 99,726 cycles were included. The median age of women utilizing PGT remained fairly constant over time (37 years), and median ages by mandate were comparable. The most common indication for PGT across all years was aneuploidy. For most indications, state mandate impacted the rate of change in indication. No coverage states had a greater decline in proportion of genetic cycles, and there were no statistically significant differences between comprehensive and no coverage states for HLA typing. For both periods, elective sex selection was more commonly used in states with no coverage (p<0.0001). Additionally, the yearly proportion of cycles for elective sex selection decreased significantly over both periods (β = -0.24, SE = 0.01, p<0.0001 and β = -0.18, SE = 0.02, p<0.0001), although the number of elective sex selection cycles increased.

CONCLUSIONS: This is the first study to examine differences in PGT indication by insurance mandate and the first to examine trends over a period longer than two years. Our findings suggest indications for PGT have changed over time and vary by level of insurance coverage for fertility. As

Period	1					2		
Year	2009	2010	2011	2012	2013	2014	2015	2016
Aneuploidy	1331 (36.8)	1480 (38.4)	1537 (35.5)	1522 (34.5)	1657 (33.7)	8297 (51.7)	15183 (59.0)	20029 (54.4)
Elective Sex	833 (23.0)	875 (22.7)	930 (21.5)	625 (14.2)	518 (10.5)	1312 (8.2)	1837 (7.1)	2170 (5.9)
Genetic	861 (23.8)	893 (23.2)	980 (22.6)	1061 (24.1)	938 (19.1)	1576 (9.8)	1804 (7.0)	1844 (5.0)
Translocation	331 (9.2)	325 (8.4)	516 (11.9)	816 (18.5)	1116 (22.7)	2694 (16.8)	2585 (10.0)	3703 (10.1)
HLA Typing	50 (1.4)	54 (1.4)	61 (1.4)	33 (0.7)	18 (0.4)	57 (0.4)	91 (0.4)	110 (0.3)
Other	208 (5.8)	228 (5.9)	307 (7.1)	350 (7.9)	674 (13.7)	2122 (13.2)	4243 (16.5)	8941 (24.3)

Legend: Values are n (% of PGT cycles that year).

PGT utilization increases, it is vital we understand how and why PGT is applied in order to better understand outcomes.

SUPPORT: The Center for Administrative Data Research is supported in part by the Washington University Institute of Clinical and Translational Sciences grant UL1 TR002345 from the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health (NIH) and Grant Number R24 HS19455 through the Agency for Healthcare Research and Quality (AHRQ).

O-33 2:30 PM Saturday, October 17, 2020

PULSATILE GONADOTROPIN RELEASING HORMONE (GNRH) VIA SUBCUTANEOUS PUMP FOR THE TREATMENT OF PRIMARY AMENORRHEA ASSOCIATED WITH HYPOGONADOTROPIC HYPOGONADISM.

James H. Liu, M.D.,[1] Masakazu Ando, PhD,[2] Patrick W. Heiser, PhD.[2] [1]UH MacDonald Women's Hospital Cleveland, OH; [2]Ferring Pharmaceuticals, Inc, Parsippany, NJ.

OBJECTIVE: To compare the ovulation rate in women with primary amenorrhea, hypogonadotropic hypogonadism (HH) randomized to three GnRH doses (10, 15, 20 μg per pulse) delivered subcutaneous every 90 minutes with the LutrePulse OmniPod Pump versus a placebo control.

DESIGN: Multicenter, double-blind, randomized, placebo-controlled trial.

MATERIALS AND METHODS: Reproductive-aged women with primary amenorrhea, hypogonadotropic hypogonadism and a negative progestin challenge test were randomized to receive one of three GnRH doses or placebo. Baseline serum FSH and LH were $<$5 IU/L. Follicular and endometrial development were monitored by transvaginal ultrasound until a dominant follicle of $\geq$18 mm mean diameter and normal endometrium (thickness and pattern) were confirmed. If a dominant follicle was not observed after 21 days or if menses occurred, treatment was discontinued. Urine luteinizing hormone tests were used to time sexual intercourse. The primary endpoint was ovulation rate, defined as either a serum progesterone $\geq$6 ng/mL, positive β-hCG, or presence of a gestational sac. An adaptive design included interim analyses that allowed for trial continuation, early success, or stop for futility by utilizing pooled 15 and 20 μg efficacy versus placebo as the primary analysis.

RESULTS: Across 24 trial sites, 39 subjects were randomized (N: 10, placebo; 10, 10 μg; 9, 15 μg; 10, 20 μg per pulse) and is one of the largest trials in this rare patient population. Demographics were similar across treatment arms with mean age 30.2 years and BMI 25.9 kg/m^2. Mean treatment duration days were 21.1, 23.8, 34.4, and 32.0 for the placebo, 10, 15, and 20 μg doses, respectively. The pooled ovulation rate with LutrePulse 15 μg and 20 μg was 50.0% compared to 0% with placebo with p-value for the comparison of 0.0120, i.e. below a pre-defined success threshold of 0.0130 allowing for early trial termination for efficacy success at the first interim analysis with 37 subjects (N: 10, placebo; 9, 10 μg; 9, 15 μg; 9, 20 μg). One subject who did not complete 14-day pituitary priming in the 10 μg group was excluded from the efficacy analysis. A significant difference in the number of follicles with mean diameter $\geq$14 mm was seen on treatment day 18 for 15 μg versus placebo (p = 0.0143), and 20 μg versus placebo (p = 0.0060). Biochemical pregnancy was achieved in 8 subjects (3 in the 15 μg group and 5 in the 20 μg group), of these, 7 subjects (2 in the 15 μg group [22.2%] and all 5 in the 20 μg group [50.0%]) achieved a live birth in the final efficacy dataset (N=38). The most frequently reported adverse events were breast tenderness (2 events reported by 2 subjects in the 15 μg group and 2 events reported by 2 subjects in the 20 μg group) and hot flush reported by 3 subjects (2 events reported by 1 subject in the 15 μg group and 2 events reported by 2 subjects in the 20 μg group).

CONCLUSIONS: LutrePulse administered as subcutaneous pulsatile injections with the OmniPod pump in doses of 10 μg, 15 μg, and 20 μg was well-tolerated, the pooled 15 and 20 μg doses were superior to placebo for the primary endpoint, ovulation rate, and the highest live birth rate was observed in subjects treated with the 20 μg dose.

SUPPORT: Ferring Pharmaceuticals, Inc. Parsippany, NJ

O-34 2:45 PM Saturday, October 17, 2020

SELF-CORRECTION OF MOSAICISM IN HUMAN SELF-ORGANIZING GASTRULOIDS AS POTENTIAL EXPLANATION FOR NORMAL BIRTHS AFTER TRANSFER OF CHROMOSOMAL-ABNORMAL EMBRYOS.

Min Yang, PHD,[1] Tiago Rito, PhD,[1] Jeffrey Naftaly, BA,[1] Jianjun Hu, MD,[2] David F. Albertini, PhD, MS,[2] David H. Barad, MD, MS,[2] Ali H. Brivanlou, PhD,[1] Norbert Gleicher, MD.[3] [1]Rockefeller University New York, NY; [2]Center for Human Reproduction, New York, NY; [3]Center for Human Reproduction, Foundation for Reproductive Medicine, Rockefeller University, Medical University Vienna, New York, NY.

OBJECTIVE: To recapitulate in *in vitro*in self-organizing human "*gastruloids*"the consequences of aneuploidy in cell fate determination during early human development and investigate a putative aneuploidy-correcting mechanism, suggested by birth of normal offspring following transfer of chromosomal-abnormal embryos.

DESIGN: Experimental study.

MATERIALS AND METHODS: We induced aneuploidy in the human embryonic stem cell line (RUES2) by reversion (0.5μM) treatment for 48 h. Both, induced aneuploid RUES2 and control euploid RUES, were used to generate gastruloids. To induce gastruloid differentiation, the cells grown on a micropattern in culture dishes were cultured with 2 ml induction medium (MEF-CM supplemented with 20 ng/ml bFGF, 100 μg/ml normocin, and 50 ng/ml BMP4) for 48 h. To generate mosaic human gastruloids, we treated fluorescence-tagged RUES2 line (VENUS-H2B) with reversine to generate aneuploidy line and mixed the cells at different ratios with the parental non-tagged RUES2. We used three mixing ratios: 1:3 (25% of aneuploid cells), 1:1(50%), and 3:1(75%) of reversine-treated RUES2 (VENUS-H2B). After immunofluorescent staining, quantification of VENUS-H2B line for different cell fates was performed in ImageJ.

RESULTS: In response to BMP4, euploid RUES2 cells differentiated and generate embryonic and extraembryonic fates that patterned in radially symmetrical domains with ectoderm (SOX2+) at the center, extraembryonic (GATA3+) and mesoderm (BRA+) in between. However, when aneuploid RUES2 cells were used to generate gastruloids, almost all cells were GATA3+, suggesting global conversion to extraembryonic tissue. SOX2 and BRA domains were largely absent.Strikingly, mixture with euploid cell were able to rescue the self-organization of aneuploid gastruloids. When aneuploid cells comprised 25% of the cell population, the gastruloids exhibited self-organization of completely normal spatial patterning. The mosaic micropatterned colonies containing 50% and 75% of aneuploid cells were also able to form gastruloids with normal self-organization of all lineages. However, the higher the aneuploidy ratio, the smaller the SOX2 territory became. Compared with euploid cells, a significantly lower percentage of aneuploid SOX2+ cells (18.32 %, 15.79%, 27.16% lower for 1:3, 1:1, 3:1 ratio, respectively) and significantly higher percentage of aneuploid GATA3+ cells (16.90 %, 17.22%, 30.02% higher for 1:3, 1:1, 3:1 ratio, respectively) were found in the mosaic gastruloids.

CONCLUSIONS: Results of this first analysis of aneuploid cell fate in humans demonstrate that aneuploidy exhibits a lineage preference during early specification. A small fraction of euploid cells in the mosaic gastruloid is sufficient to generate a normal self-organizing circular patterns, with aneuploid cells preferentially allocated to the trophectodermal layer. These findings offer a putative explanation for delivery of chromosomal-normal pregnancies after transfer of chromosomal-abnormal embryos, diagnosed by trophectoderm biopsy.

SUPPORT: Intramural funds from The Center for Human Reproduction and Rockefeller University.

O-35 3:00 PM Saturday, October 17, 2020

RISK OF CARDIOVASCULAR DISEASE AFTER MENOPAUSE AMONG WOMEN WITH POLYCYSTIC OVARY SYNDROME (PCOS).

Jacob Christ, MD,[1] Genevieve S. Neal-Perry, M.D., Ph.D.[2] [1]University of Washington, Seattle, WA; [2]University of North Carolina, Chapel Hill, NC.

OBJECTIVE: Women with PCOS have increased rates of premenopausal cardiometabolic dysregulation, however it is not clear if this baseline dysfunction results in increased risk of cardiovascular disease (CVD) after menopause. This study sought to prospectively assess risk of cardiovascular disease after menopause among women with and without PCOS using a validated prospective multicenter cohort.

DESIGN: A secondary analysis of data from the prospective cohort study, Study of Women's Health Across the Nation (SWAN).

MATERIALS AND METHODS: Enrollment criteria included age 42-52, presence of a uterus, at least one ovary and a spontaneous menstrual period within the past three months. Inclusion criteria for secondary analysis included complete data on baseline menstrual status and total testosterone, and at least one follow-up visit after menopause. Menopause was defined as date of final menstrual period. Among those without a recorded final menstrual period, 51 years of age (or 1 year after enrollment if 51 years or older at time of inclusion) was used to impute date of menopause. Postmenopausal outcomes included self-reported postmenopausal cardiovascular disease events as well as calculated Framingham 10-year risk score, Atherosclerotic cardiovascular disease (ASCVD) risk score and General cardiovascular risk score. PCOS cases were defined as presence of both biochemical hyperandrogenism and a history of irregular menses and non-PCOS cases were defined as a lack of both features. Between groups comparisons were completed using Student's t-test and Chi-squared test. Associations between PCOS diagnosis and CVD events as well as calculated CVD risk scores were assessed using a multivariable Cox proportional hazards model and linear regression models respectively.

RESULTS: 174 women with PCOS and 1166 women without PCOS met criteria for inclusion. At baseline women with PCOS more frequently smoked cigarettes (22.0% vs 12.7%), had higher body mass index (BMI) (31.3±8.6 vs 26.7±6.5 kg/m^2), systolic blood pressure (120.7±19.7 vs 115.8±16.3 mmHg), total cholesterol (202±38 vs 192±33 mg/dl), and fasting blood glucose (103.7±44.6 vs 89.2±21.8 mg/dl) $p < 0.01$ for all comparisons. Independent of age at enrollment, baseline BMI, smoking status and race, women with PCOS had a significantly greater odds of a CVD event after menopause (odds ratio (95% CI), 1.6 (1.1-2.4)). Independent of age at enrollment, baseline BMI, smoking status, race and age at follow up, PCOS diagnosis significantly associated with General cardiovascular risk score (β (95% CI)) (1.1 (0.3-2.0)) and ASCVD risk score (0.01 (0.0-0.2)), but not Framingham 10-year risk score (0.19 (-0.2-0.6)).

CONCLUSIONS: PCOS diagnosis prior to menopause appears to confer an increased risk of cardiovascular disease after menopause. Women with PCOS should have increased monitoring to help reduce risk of long-term disease even after the menopausal transition.

O-36 3:15 PM Saturday, October 17, 2020

PRIMARY OVARIAN INSUFFICIENCY HAS STRONG HERITABILITY, EVEN AMONG DISTANT RELATIVES; RESULTS OF A MULTIGENERATIONAL GENEALOGICAL OBSERVATIONAL STUDY.

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OBJECTIVE: To determine the heritability of primary ovarian insufficiency (POI) on a population level through examination of multigenerational genealogical information linked to electronic medical records.

DESIGN: Case Control Study.

MATERIALS AND METHODS: POI cases were identified from 1995 to 2019 using electronic medical records from the two major healthcare systems in Utah (University of Utah Health and Intermountain Healthcare), which provide approximately 80% of all healthcare to Utahns. POI cases were identified using ICD9 256.31, 256.39 and ICD10 E28.31, E28.39, and elevated FSH > 20 IU/L or AMH <0.08 ng/mL before the age of 40 years. We excluded women who had a hysterectomy, oophorectomy, endometriosis with pelvic surgery, pelvic radiation or chemotherapy before the diagnosis of POI and those with systemic lupus erythematosus or other disorders treated with cyclophosphamide using ICD codes, lab results, medication lists, cancer treatment and surgical data (using CPT codes). All medical records at the University of Utah were then examined to ensure that each subject fulfills the POI diagnosis. These cases were then linked to genealogy information extending back to the 1700s using the Utah Population Database (UPDB). All POI cases were required to have genealogy information available for 12 of 14 immediate ancestors (parents, 4 grandparents, and 6/8 great grandparents). Expected number of affected relatives were calculated based on matched (by age, sex, and birthplace) population rates of POI. Consanguinity rates in the Utah population have been determined to be the same as, or lower than, United States rates.

RESULTS: A total of 857 POI cases were identified. The table below reports number of relatives of a specific type, observed and expected number of affected relatives, p-value, relative risk (RR) and 95% confidence interval (CI). We observed a significantly increased risk of POI among first, second, and third-degree relatives.

CONCLUSIONS: We observed a strong heritability for POI, even in distant relatives, suggesting a genetic component to the ovarian lifecycle and ovarian insufficiency. While a few causative genes for POI have been identified mostly in consanguineous families, there is an opportunity to study POI genetics in non-consanguineous families.

Familial POI Cases Observed in Utah Population Database

Relationship	# Relatives	Observed	Expected	p-value	RR	95% CI
1st Degree	4632	14	4.67	<0.0004	3.00	1.64-5.03
2nd Degree	10612	12	5.53	<0.011	2.17	1.12-3.79
3rd Degree	23270	27	16.65	<0.015	1.62	1.07-2.36

SUPPORT: This study is funded by a NICHD grant: 1R01HD099487-01

ENVIRONMENT AND REPRODUCTION

O-37 2:00 PM Saturday, October 17, 2020

URINARY PHTHALATE METABOLITE CONCENTRATIONS ARE INVERSELY ASSOCIATED WITH FOLLICULAR FLUID ANTI-MÜLLERIAN HORMONE CONCENTRATIONS IN WOMEN UNDERGOING FERTILITY TREATMENT.

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OBJECTIVE: We previously showed that anti-müllerian hormone (AMH) concentrations in pre-ovulatory follicular fluid (FF) positively correlated with serum AMH, a commonly used marker of ovarian reserve, and associated with improved pregnancy outcomes among women undergoing fertility treatment. Thus, identifying modifiable lifestyles, such as environmental exposures, which are associated with FF AMH has become a public health matter and is understudied. In particular, exposure to phthalates, endocrine-disrupting chemicals commonly used as plasticizers, has been associated with infertility and premature ovarian failure. Our objective was to investigate whether urinary phthalate metabolite concentrations are associated

with pre-ovulatory FF AMH concentrations in women undergoing fertility treatment.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: FF was collected from 2-3 pre-ovulatory follicles in 162 women contributing 217 in vitro fertilization (IVF) cycles (range=1-3) enrolled in the Environment and Reproductive Health (EARTH) Study at Massachusetts General Hospital Fertility Center (2010-2016). AMH concentrations were quantified using a sandwich enzyme-linked immunosorbent assay (ELISA) in FF samples and corrected for volume. We also quantified 8 phthalate metabolite concentrations using tandem mass spectrometry in 1-2 urine samples/cycle, calculated the cycle-specific geometric mean for each metabolite, and the molar sum of di-2-ethylhexyl phthalate ($\sum$DEHP) metabolites. Linear regression models adjusted for age, body mass index (BMI), race, fertility treatment protocol, and urinary dilution were used to estimate the association between urinary phthalate metabolite concentrations, in quartiles, and FF AMH concentrations.

RESULTS: The 162 women studied had mean age of 34.0 years (+/- SD), 83% were white, and mean BMI of 22.7 kg/m^2 (+/- SD). The following stimulation protocols were used: luteal phase agonist (69%), antagonist (16%), or flare (15%). We found lower FF AMH concentrations across quartiles of urinary $\sum$DEHP (p-trend=0.07). Specifically, women in the highest quartile of urinary $\sum$DEHP (range 0.23-0.33) had, on average, 0.2 (95% CI=0.1, 0.6) ng/mL FF AMH, compared to women in the lowest $\sum$DEHP quartile (range 0.01-0.06), who had 0.7 (95% CI=0.1-0.7) ng/mL FF AMH (p=0.04). This negative association was non-linear, as mean FF AMH was similar in the second, third and fourth quartiles, and was mainly driven by individual negative associations between urinary concentrations of two DEHP metabolites, mono(2-ethyl-5-oxohexyl) phthalate and mono(2-ethyl-5-carboxypentyl) phthalate, with FF AMH. No other urinary phthalate metabolites were associated with FF AMH.

CONCLUSIONS: We observed that urinary concentrations of certain phthalate metabolites are negatively associated with FF AMH concentrations, which may have implications for fertility treatment.

SUPPORT: NIH grants R01ES022955, R01ES009718, R00ES026648 and P30ES000002.

O-38 2:15 PM Saturday, October 17, 2020

POLY AROMATIC HYDROCARBONS (PAHS) IN SEMEN OF INFERTILE MEN REVEAL DISTINCT SIGNATURES OF OXIDATIVE STRESS AND PROTEIN TRAFFICKING AS MODULATORS OF SPERM FUNCTION: A PROTEOMIC INSIGHT THROUGH SEMINAL EXTRACELLULAR VESICLES.

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OBJECTIVE: To evaluate the cut off levels of seminal poly aromatic hydrocarbons (PAHs) and its correlation with sperm function in infertile men by comparative proteomic analysis of seminal extracellular vesicles (EVs).

DESIGN: Perspective case-control study involving 42 fertile donors and 113 infertile patients. Infertile patients having PAH level above cut off (n=57) were included in the experimental group and compared with fertile donors.

MATERIALS AND METHODS: PAH levels in semen were determined by HPLC and receiver operator curve (ROC) analysis was carried out to find the cut off limits of different PAHs. Seminal EVs were isolated in both groups by ultracentrifugation and characterized by western blot, transmission electron microscopy, and nanoparticle tracking analysis followed by label free liquid chromatography mass spectroscopy (LC-MS/MS) and bioinformatics analysis.

RESULTS: A total of 13 PAHs were detected (Table 1) where Benzo (a) pyrene was exclusively detected in infertile group. A total of the 1120 proteins were detected (Control:724 and PAH:1041). Of the 272 differentially expressed proteins 210 were underexpressed and 62 overexpressed in PAH ($\log_2$ fold change ≥ 2, $p \leq 0.001$) while 79 and 396 proteins were exclusive to control and PAH, respectively. STRING-PPI and Cytoscape analysis revealed oxidoreductase activity (p value=7.5292E-5), carbonyl reductase activity (p value=1.2657E-3) and transfer of alkyl and aryl activity (p value=5.740E-3) were overexpressed in PAH while antioxidant activity (p value=4.9436E-3) was underexpressed. Ingenuity pathway analysis (IPA) showed signaling by Rho family GTPases, NRF2-mediated oxidative stress response, protein trafficking, cellular function and maintenance, molecular transport were deregulated in PAH group.

TABLE 1. Receiver Operating Characteristic (ROC) optimal cut points and operating characteristics for semen PAH metabolites.

PAH	Area Under Curve	Cut-off Value (ppm)	p Value
Benzo (A) Pyrene	0.817460	6	<0.0001
Anthracene	0.815789	62	<0.0001
Benzo (B) Fluoranthene	0.811821	40	<0.0001
Fluoranthene	0.758981	17	<0.0001
Pyrene	0.738304	32	<0.0001
Indo (123 CD) Pyrene	0.737260	8	<0.0001
Benzo(A) Anthracene	0.728488	333	<0.0001
Napthalene	0.707602	868	<0.0001
Dibenzo (AH) Anthracene	0.694653	7	<0.0001
Fluorene	0.692565	831	<0.0001
Chrysene	0.687552	6	<0.0001
2Bromonapthalene	0.682957	188	<0.0001
Benzo (GH1) Perylene	0.671053	107	<0.0001

CONCLUSIONS: Seminal EVs are reported to protect and maintain sperm function by trafficking RNA and proteins to spermatozoa. Our data indicate that PAH exposure above cut off is associated with male infertility due to impaired protein trafficking by seminal EVs resulting in oxidative damage and declined antioxidant defense.

O-39 2:30 PM Saturday, October 17, 2020

REDUCED OOCYTE QUALITY JUSTIFIES POOR ICSI OUTCOMES AMONG SMOKERS AND SUGAR CONSUMERS.

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OBJECTIVE: Considering that the human fertility rate has declined over time, it could be argued that maternal lifestyle factors, including eating, smoking and physical exercise habits, may affect fertility potential. Growing evidences link maternal lifestyle and prenatal factors with serious health consequences later in life. To date, studies have shown that both female and male germline development follow distinct paths of epigenetic events and both gametes possess their own unique epigenomes. Lifestyle factors can be adapted to enhance well-being and are ultimately under one's own control; therefore, adjusting for their influence may yield valuable information for counselling couples undergoing ICSI. Therefore, the goal for the present study was to evaluate the influence of maternal lifestyle factors on oocyte morphology.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: The study included 561 female patients undergoing ICSI cycles, in a private university-affiliated in vitro fertilization center, from January/2015 to December/2018. Prior to start of the treatment, participants were asked to complete a detailed non-validated questionnaire regarding cigarette smoking habit, consumption of items such as refined sugar, soft drinks, alcoholic beverages, milk and dairy, and white and red meat, and exercise frequency over the past 3 months. Oocyte morphology was evaluated before sperm injection and intra and extra-cytoplasmic dimorphisms were recorded. The influences of maternal lifestyle factors on oocyte morphology were evaluated by multiple multivariate regression analyses, adjusted for maternal age and body mass index, FSH dose and number of retrieved oocytes.

RESULTS: Cigarette smoking positively influenced the incidence of zona pellucida dimorphisms (B: 14.9, CI: 3.9 – 25.9, p=0.009), fragmented first polar body (PB) (B: 32.4, CI: 7.9 – 57.0, p=0.011), and oocyte shape dimorphisms (B: 14.2, CI: 4.6 – 23.8, p=0.004). The consumption of refined sugar positively influenced the incidence of centrally located granular cytoplasm (B: 19.5, CI: 0.5 – 38.4, p=0.044) and perivitelline space granulation (B: 21.6, CI: 2.6 – 40.6, p=0.027). The consumption of milk and dairy was inversely correlated with the incidence of fragmented PB (B: -26.4, CI: -51.2 - -1.5, p=0.038), and the consumption of fish was inversely correlated

with the incidence of membrane resistance (B: -8.7, CI: -16.4 - -1.0, p=0.027). There were no significant influences of other investigated maternal lifestyle factors on oocyte dimorphisms.

CONCLUSIONS: Cigarette smoking and the consumption of refined sugar appear to reduce oocyte quality. Therefore, it would be wise to advise female partners undergoing assisted reproduction treatments to abstain from smoking and consuming sugar to avoid decreased in vitro reproduction outcomes.

SUPPORT: None.

O-40 2:45 PM Saturday, October 17, 2020

INFERTILITY AND ENVIRONMENTAL, CHEMICAL, AND HAZARDOUS EXPOSURES AMONG UNITED STATES VETERANS. Abigail C. Mancuso, MD,[1] Andrea Holcombe, MS, PhD,[2] Michelle A. Mengeling, MS, PhD,[2] Ginny L. Ryan, MD, MA.[3] [1]University of Iowa Hospitals and Clinics Iowa City, IA; [2]Iowa City VA Health Care System, Iowa City, IA; [3]University of Iowa Carver College of Medicine, Iowa City, IA.

OBJECTIVE: To assess the association between infertility and environmental, chemical, or hazardous material exposures among United States Veterans.

DESIGN: Cross-sectional survey study.

MATERIALS AND METHODS: A national sample of female and male US Veterans aged 20-45 completed a computer-assisted telephone interview lasting an average of 1 hour 27 minutes assessing demographics, general and reproductive health, and lifetime and military exposures.

Infertility was defined as unprotected intercourse with a member of the opposite sex, with or without trying to conceive, for >12 months without pregnancy over a lifetime. Participants reporting never having had unprotected intercourse were excluded from analysis.

Logistic regression analysis was used to compare exposures among infertile and non-infertile groups. Odds ratios (OR) with 95% confidence intervals are reported.

RESULTS: 3,018 Veterans participated in this study. After excluding participants never reporting unprotected intercourse (216 women and 201 men), 1,194 women and 1,407 men were included in this analysis with 592 (50%) women and 727 (52%) men meeting the definition of infertility.

Exposures reported to be higher among both women and men meeting the definition of infertility than among those not meeting this definition included polychlorinated biphenyl (PCBs) (4.7% vs. 2.3% exposed in the infertile and non-infertile groups respectively; OR 2.09 (1.09-4.00) for women; 9.5% vs 6.2%; OR 1.59 (1.07-2.37) for men) and sulfur fires (2.2% vs. 0.5%; OR 4.48 (1.27-15.81) for women; 4.0% vs 2.1%; OR 1.98 (1.04-3.77) for men).

Exposures reported to be higher only among women meeting the definition of infertility than among women not meeting this definition were extreme heat (66.3% vs 59.0%; OR 1.37 (1.08-1.74)), chemical weapons (e.g., Sarin gas) (10.7% vs 6.8%; OR 1.63 (1.08-2.46)) and anthrax vaccine (54.2% vs. 45.9%; OR 1.40 (1.11-1.75)).

Exposures reported to be higher only among men meeting the definition of infertility than among men not meeting this definition included exposure to oil well fires (16.8% vs. 11.5%; OR 1.56 (1.15-2.11)), petrochemicals (71.4% vs 64.9%; OR 1.35 (1.08-1.69)), other chemicals (such as solvents, degreasers) (55.3% vs. 49.4%; OR 1.27 (1.03-1.56)), and asbestos (35.4% vs. 28.2%; OR 1.39 (1.11-1.74)).

There were no queried exposures self-reported at higher rates in the non-infertile group.

CONCLUSIONS: During their military service, Veterans commonly experience exposure to chemical, physical, and environmental hazards that may have negative effects on their future reproductive health. Our study found that Veterans reporting at least one episode of 12 months or more of unprotected intercourse without conception over their lifetime were more likely to report exposure to such hazards, especially PCBs and sulfur fires. These data provide evidence of an association between exposures encountered during military service and infertility, and thereby support recent efforts to improve coverage of fertility preservation and fertility treatment for Veterans.

SUPPORT: The research reported here was supported by the Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development (HSR&D) Service grant IIR 13-294. The content is solely the responsibility of the authors and does not necessarily represent the views of the Department of Veterans Affairs.

O-41 3:00 PM Saturday, October 17, 2020

UNIVERSAL SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 (SARS-COV-2) TESTING IN A NEW YORK CITY REPRODUCTIVE MEDICINE PRACTICE. Pietro Bortoletto, MD, Phillip A. Romanski, MD, Joshua Stewart, M.D., Glenn Schattman, MD, Zev Rosenwaks, M.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To describe our single-center experience and results of universal SARS-CoV-2 testing in asymptomatic patients undergoing controlled ovarian hyperstimulation (COH).

DESIGN: Retrospective cohort study conducted at a university-affiliated center.

MATERIALS AND METHODS: On March 21, 2020, New York-Presbyterian Hospital, where our retrieval suite is located, instituted a policy of universal SARS-CoV-2 testing prior to surgical procedures requiring anesthesia. As a result, we began testing all patients undergoing COH for SARS-CoV-2 using reverse transcription-polymerase chain reaction via nasopharyngeal swabs (Roche Cobas 6800). Tests were performed on the morning of cycle start and repeated 24 hours before oocyte retrieval. A positive test at either time point excluded patients from continuing with treatment. During the testing period, all patients and staff were required to wear surgical masks at all times when at our center and consented to symptom and temperature screening at every monitoring visit.

RESULTS: Between March 21 and May 20, 2020, 169 asymptomatic patients underwent nasopharyngeal swabs at cycle start, four of which returned positive for SARS-CoV-2 for a center prevalence of 2.4%. All four patients were asymptomatic at the time of cycle start and were not permitted to begin their COH cycle. One of these patients had previously had a positive PCR swab over 60 days prior and had been symptom-free during this interval. One patient with a negative PCR swab on cycle start subsequently converted to positive 15 days later on her PCR swab prior to retrieval, despite the absence of COVID-19 symptoms. Per our hospital policy, she was not allowed to proceed with oocyte retrieval and was started on a course of daily GnRH antagonist and asked to abstain from intercourse for 14 days. None of the 5 patients went on to develop COVID-19 symptoms following their positive test result. All patients were referred to follow-up with their primary care provider. Prior to returning for further COH treatment, all patients will be required to undergo repeat PCR testing with a negative result.

CONCLUSIONS: While rare, asymptomatic carriers of the SARS-CoV-2 virus were identified for a center prevalence of 2.4% in patients undergoing COH. Despite initial negative PCR testing, patients may convert to positive over the course of a COH cycle and not demonstrate symptoms. Strict personal protective equipment and social distancing use is essential to protect patients and staff alike.

O-42 3:15 PM Saturday, October 17, 2020

EFFECT OF THE EXPOSURE TO FINE INHALABLE PARTICULATE MATTER ($PM_{2.5}$) ON SPERM FUNCTIONAL QUALITY OF MICE. Paula Intasqui, PhD,[1] Letícia Kaory Tamashiro, BSc.,[1] Victor Yuji Yariwake, BSc.,[2] Rosana Xavier Souza, BSc.,[1] Camila Matie Kanashiro, BSc.,[1] Mariana Matera Veras, PhD.[2] [1]Sao Paulo Federal University São Paulo, Brazil; [2]Laboratory of Experimental Air Pollution (LIM05), São Paulo, Brazil.

OBJECTIVE: To evaluate the effect of exposure to pollution (fine inhalable particulate matter - $PM_{2.5}$) from the city of São Paulo on sperm functional quality.

DESIGN: Male isogenic BALB/c mice were used, distributed in two groups, control (n=6) and polluted air (n=8). For the polluted air group, after weaning (21 days), animals were daily exposed to 600 $\mu g/m^3$ of $PM_{2.5}$ for 96 days in an Ambient Particle Concentrator (APC). Control group was simultaneously exposed to filtered air in the APC. On postnatal day 118, animals were sacrificed (isoflurane overdose), body was weighted and the epididymis were collected.

MATERIALS AND METHODS: Sperm obtained from the cauda epididymis were used for the evaluation of motility, mitochondrial activity (DAB staining), acrosome integrity (PNA staining), DNA fragmentation (alkaline comet assay), oxidative stress (DHE staining) and cell viability (PI staining). Groups were compared using an unpaired Student's t test ($p<0.05$).

RESULTS: Groups did not differ regarding body weight, and sperm motility. Furthermore, air pollution did not alter sperm functional quality (Table 1).

CONCLUSIONS: Exposure to high concentrations of $PM_{2.5}$ does not affect sperm motility and functional parameters.

TABLE 1. Body weight and sperm functional quality of mice from the control and polluted air groups. Data are presented as Mean ± Standard Deviation. Groups were compared using an unpaired Student's t test.

	Control (n=6)	Polluted air (n=8)	p
Body weight	29.46 ± 4.82	28.01 ± 0.82	0.50
Motility (%)	51.67 ± 13.66	55.62 ± 18.41	0.67
Intact acrosome (%)	85.33 ± 7.65	81.94 ± 9.08	0.48
Mitochondrial activity			
DAB I (%)	7.08 ± 4.53	9.81 ± 10.19	0.56
DAB II (%)	71.75 ± 11.16	68.44 ± 61.75	0.53
DAB III (%)	20.83 ± 9.31	21.06 ± 11.55	0.97
DAB IV (%)	0.33 ± 0.61	0.75 ± 0.96	0.37
DNA fragmentation			
Comet I (%)	29.83 ± 23.17	35.07 ± 23.16	0.69
Comet II (%)	45.83 ± 10.81	36.36 ± 12.90	0.18
Comet III (%)	17.92 ± 10.88	16.36 ± 9.70	0.79
Comet IV (%)	6.58 ± 9.11	12.14 ± 11.70	0.37
Tail DNA (%)	14.11 ± 12.67	19.82 ± 15.38	0.49
Olive Tail Moment (a.u.)	5.41 ± 5.91	7.27 ± 6.60	0.61
Comet Distribute Moment (a.u.)	50.32 ± 43.00	35.80 ± 4.59	0.48
Oxidative stress			
DHE positive (%)	21.98 ± 19.71	12.63 ± 11.22	0.28
Cell viability			
PI positive (%)	51.47 ± 14.33	47.70 ± 13.74	0.63

DAB (3,3'-diaminobenzidine); DAB I: 100% of mitochondrias stained; DAB II: >50% mitochondrias stained, DAB III: <50% mitochondias unstained, DAB IV: no mitochondrias stained. Comet I: no DNA fragmentation; Comet II: low DNA fragmentation; Comet III: increased DNA fragmentation; Comet IV: high DNA fragmentation. a.u: arbitrary units. DHE (Dihydroethidium) positive: presence of superoxide anion stained with DHE. PI (Propidium Iodide) positive: permeable sperm membranes.

SUPPORT: São Paulo Research Foundation (FAPESP grant number 2019/05879-7).

GENETIC COUNSELING

O-43 2:00 PM Saturday, October 17, 2020

EXPERIENCE WITH CARRIER SCREENING FOR X-LINKED CONDITIONS. Dana Neitzel, MS, CGC, Jocelyn Leahey, MS, CGC, Sienna Aguilar, MS, CGC, Nicole Faulkner, PhD, FACMG, Swaroop Aradhya, PhD, FACMG. Invitae San Francisco, CA.

OBJECTIVE: Current ACOG carrier screening guidelines do not support routine inclusion of X-linked (XL) conditions. There are over 100 known XL conditions. Clinical presentation depends on many variables and males are typically affected while females may show varying symptoms. Despite high *de novo* mutation rates, the identification of carriers for XL conditions is important as females have a 50% chance of transmitting a disease-causing variant. The aim of this study was to determine the carrier frequency of XL conditions identified through routine carrier screening for the purpose of reproductive planning.

DESIGN: Retrospective cohort study of patients undergoing routine carrier screening to determine carrier rates of a subset of XL conditions.

MATERIALS AND METHODS: Carrier screening was performed by next-generation sequencing with full coding sequence and deletion and duplication analysis for up to 301 genes as ordered on 68,100 patients. Twenty-two of the 301 genes were XL. Pathogenic and likely pathogenic variants were reported. Ordering patterns and positive rates for XL conditions were assessed.

RESULTS: Of 68,100 patients, 68% were female and 32% were male. Most orders (87.9%; 59,865) included at least one XL condition, though female orders included XL conditions more often than male orders (91.9% vs 79.4%).

Of the 59,865 orders that include XL conditions, the overall positive rate was 60.9% and of these positives, 1.98% were for XL conditions, giving an overall positive rate for XL conditions of 1.2%. In this dataset, at least one carrier was identified for each of the 22 XL conditions tested.

When stratified by patient sex, 1.3% of females (557/42,572) tested positive for an XL condition, most frequently *G6PD*, *FMR1*, *DMD*, *COL4A5*, and *ABCD1*; 0.95% of males (165/17,293) were positive for an XL condition, most frequently *G6PD*, *FMR1*, *COL4A5*, *DMD*, and *GLA*.

CONCLUSIONS: In this cohort, 88% of all orders included at least one XL condition, indicating that clinicians are regularly ordering XL conditions as part of their routine carrier screening for both male and female patients. One point two percent of individuals were positive for at least one XL condition, and XL conditions together accounted for 2% of all positive results.

The inclusion of XL conditions on a carrier screen is controversial: ACOG does not support it; the line between carrier screening and diagnostic testing may be crossed for male patients who screen positive for variants in XL conditions; and the high *de novo* rate in many of XL conditions may lead to false reassurance after a negative carrier screening result.

However, inclusion of XL conditions in routine carrier screening is common practice. Screening for XL conditions allows patients the opportunity to make informed reproductive decisions about these often severe conditions with high reproductive risks. Additional studies are needed to determine the phenotypes and potential impact associated with males identified with XL conditions in this study.

References: NA

SUPPORT: All authors are employees and stockholders of Invitae.Â

O-44 2:15 PM Saturday, October 17, 2020

FAVORABLE OUTCOMES IN A SUBSEQUENT PGT-A CYCLE FOLLOWING ALL ANEUPLOID BLASTOCYST COHORT. Alyssa Schickedanz, M.S, C.G.C, Diane Klepacka, MS, Annette Matts, MS, Amy Bartoli, MS, Emily Anderson, BS, Mary E. Haywood, PhD, William B. Schoolcraft, MD, Mandy G. Katz-Jaffe, PhD. Colorado Center for Reproductive Medicine Lone Tree, CO.

OBJECTIVE: Preimplantation genetic testing for aneuploidy (PGT-A) has been shown to improve the likelihood of live birth per embryo transfer. However, oocyte aneuploidy is significantly associated with reproductive aging, and the probability of an IVF cycle resulting in a lack of euploid embryos becomes more significant for women of advanced maternal age (>38 years). The aim of this study was to review patient's treatment decisions following an all aneuploid PGT-A cycle to assist in future clinical management and counseling practices.

DESIGN: Retrospective cohort analysis.

MATERIALS AND METHODS: Consecutive, autologous PGT-A cycles that resulted in all aneuploid blastocysts between January 2016 and December 2019 (n=550) were included in this analysis. Individual variable analysis was performed using Wilcoxon rank sum test. Step-wise logistic regression models evaluated whether 12 clinical parameters were predictive of patient treatment decisions including parental ages, prior live birth, BMI, ovarian reserve variables and IVF cycle characteristics. Significance determined at $p<0.05$.

RESULTS: Nearly half of the couples (47.6%) decided to terminate treatment following an all aneuploid IVF cycle. Only a small number of couples pursued donor oocytes for future treatment (7.6%) and a handful naturally conceived (1.5%). The remaining couples (43.3%) pursued a second autologous PGT-A cycle, with 50.4% obtaining ≥ 1 euploid blastocyst. Interestingly, women who chose to stop treatment had significantly more oocytes retrieved ($p<0.05$) but trended towards being less likely to have had prior live births ($p = 0.07$) than women who continued infertility treatment. Other variables, including maternal age, AMH and resting antral follicle count (AFC), were not significantly different. Women with euploid blastocysts following their second IVF cycle were significantly younger ($p<0.001$, OR = 0.84) and had higher AMH ($p<0.05$, OR = 1.25) than women with a consecutive second all aneuploid cycle. Stratification of subsequent euploid frozen blastocyst transfers demonstrated the trend of lower maternal age ($p = 0.06$, OR=0.89), higher AFC ($p<0.05$, OR = 1.06) and more mature autologous oocytes ($p<0.05$, OR = 1.12) in association with a positive pregnancy outcome.

CONCLUSIONS: Following a PGT-A cycle resulting in all aneuploid blastocysts, nearly half of all couples chose to cease pursing infertility treatment. Maternal age, ovarian reserve and other clinical parameters were not significantly associated with this decision. This indicates that external variables such as, stresses of the procedure and financial burden, may be more significant in patient treatment decisions. For those couples that did pursue further treatment over half went on to have a euploid embryo transfer. This encouraging information will be useful during patient counseling for future clinical decisions following an all-aneuploid PGT-A cycle.

SUPPORT: None

O-45 2:30 PM Saturday, October 17, 2020

EMBRYO TRANSFER BASED ON PREIMPLANTATION GENETIC TESTING: A CRITICAL ASSESSMENT OF CURRENT PRACTICE AND POLICY GUIDELINES. Christina Ren, BS,[1] Andria G. Besser, MS, CGC,[2] Jon Weil, PhD,[1] Rachel Hull, BS,[3] Janey Youngblom, PhD, MS.[1] [1]California State University Stanislaus, Turlock, CA; [2]New York University Langone Fertility Center, New York, NY; [3]University of California, Davis, Davis, CA.

OBJECTIVE: To investigate the status of policies and practice of IVF clinics regarding transfer of embryos with positive or abnormal results following preimplantation genetic testing for aneuploidy and for monogenic disorders (PGT-A and PGT-M).

DESIGN: Mixed methods study, using a survey and semi-structured interviews.

MATERIALS AND METHODS: An online survey was emailed to 394 IVF clinics across the United States. In-depth interviews were conducted with a subset of 11 survey respondents. Descriptive statistics and chi-square were used to analyze survey data. Interviews were transcribed verbatim and independently analyzed by two coders using thematic analysis. Abnormal PGT-A results only included non-mosaic aneuploidies. Unaffected carriers of autosomal recessive disorders were not included in the definition of positive PGT-M results.

RESULTS: A total of 97 clinics completed a survey (25% valid response rate). 37% of clinics had written policies on transferring embryos with positive or abnormal results which they discuss with patients before testing and 54% handled patient requests on a case-by-case basis. 9% did not have a policy because they did not transfer abnormal embryos or were in the process of creating a policy. Clinics with policies were less likely to consider transfer of embryos with non-viable aneuploidy (11%) and partial aneuploidies (22%) than clinics without policies (31% and 43%, respectively; $p<0.05$). A minority of clinics reported having previously transferred one or more embryos with a non-viable aneuploidy (12%), partial aneuploidy (12%), or viable aneuploidy (7%). No clinics have transferred embryos positive for a monogenic childhood-onset life-limiting disorder. However, most clinics (69%) would consider transferring embryos positive for reduced penetrance, variable-onset monogenic disorders, and 16% of all clinics have transferred such embryos. 78% would require genetic counseling before transfer of embryos with abnormal PGT-A or positive PGT-M results.

The qualitative interviews suggested that the decision to create clinic policies was shaped by previous/anticipated patient requests and desire for either standardized or discretionary practice. Factors contributing to provider considerations for transfer of positive or abnormal embryos include individual patient circumstances and limited reproductive options, clinical uncertainty/variability of outcomes, interpretation and reliability of PGT results, liability and financial concerns, and balance of ethical perspectives.

CONCLUSIONS: Patient requests to transfer embryos with abnormal or positive PGT-A/PGT-M results do occur and there is variability in practice policies for such situations among U.S. IVF clinics. The majority of clinics do not have a policy in place regarding transfer of abnormal or positive embryos, preferring to handle these requests on a case-by-case basis. Ongoing discussion of establishing practice guidelines is critical as PGT-A results become increasingly complex, the scope of indications for PGT-M use expands, and providers increasingly encounter these requests more frequently.

SUPPORT: Grants from California State University, Stanislaus.

O-46 2:45 PM Saturday, October 17, 2020

GENETIC SCREENING IN REPRODUCTIVE AGE WOMEN IDENTIFIES A HIGH POSITIVE RATE OF ACTIONABLE RESULTS. Sienna Aguilar, MS, CGC,[1] Eden Haverfield, DPhil, FACMG,[1] Edward Esplin, MD, PhD, FACMG,[1] Robert L. Nussbaum, MD,[2] Swaroop Aradhya, PhD, FACMG.[1] [1]Invitae San Francisco, CA; [2]1400 16th Street, San Francisco, CA.

OBJECTIVE: Personal risk for actionable Mendelian genetic disease has been identified in 2-16% of the general population.[1-5] Early identification of individuals at risk allows for proactive screening and prevention to reduce morbidity. Current genetic testing guidelines designed to identify those most likely to have a genetic risk appear to miss a significant portion of at-risk individuals.[6-8] The aim of this study was to determine the frequency of pathogenic variants found in a medically actionable genetic screening panel in a cohort of reproductive age women.

DESIGN: Retrospective cohort study of reproductive age women undergoing proactive genetic screening to determine rates of medically actionable findings.

MATERIALS AND METHODS: Under an IRB-approved protocol, we analyzed de-identified data from 1,305 women of reproductive age (18-45 years) who underwent genetic screening with a panel of up to 147 genes for actionable disorders.

RESULTS: Pathogenic/likely pathogenic variants were observed in 15.6% (204 of 1,305) of individuals. Among these, 55.4% had at least one finding in a cancer-related gene, 36.8% in a cardiovascular-related gene, and 12.3% in genes causing other medically actionable disorders. At least 8.3% of positive individuals had two or more findings. Even when individuals with moderate risk (variants in F2 and F5, APC I1307K, biallelic HFE variants, and heterozygous variants in MUTYH) are excluded, one in 13 women still had a positive actionable test result.

CONCLUSIONS: Our data show that 15.6% of women of reproductive age may have risks for hereditary disease. Incorporating genetic screening for personal risk of actionable disorders in the course of preconception evaluations may be an opportunity to identify individuals at high genetic risk prior to disease onset. Outcomes-focused longitudinal data are needed to fully understand the benefits of genetic risk information identified in this population.

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SUPPORT: Authors are employees/stockholders of Invitae

O-47 3:00 PM Saturday, October 17, 2020

PATIENT EXPERIENCE WITH EXPANDED-CARRIER SCREENING: ADEQUACY OF PROVIDER COUNSELING, ECONOMIC BURDEN AND DECISION-MAKING REGARDING PARTNER TESTING. Alice J. Shapiro, M.D., Molly M. Quinn, MD. David Geffen School of Medicine University of California, Los Angeles, Los Angeles, CA.

OBJECTIVE: Expanded carrier screening (ECS) is a method for identifying individuals who are carriers for recessively-inherited genetic disorders. When couples are screened sequentially, many positively-screened individuals choose not to test their reproductive partners despite provider recommendations.[1] The patent experience with ECS and factors contributing to decision-making regarding partner testing have not been explored. The goal of this study was to evaluate the patient experience with ECS by

assessing the efficacy of provider counseling, the economic burden imposed by ECS, and the reasons some positively-screened individuals do not have their partners tested.

DESIGN: Cross-sectional patient survey.

MATERIALS AND METHODS: All individuals presenting to a university-affiliated reproductive endocrinology and infertility clinic who underwent ECS with a single test provider between 9/1/13 and 2/1/20 were contacted via e-mail to complete a confidential and anonymized online survey. All survey questions were in multiple-choice format with an optional free text response.

RESULTS: The survey response rate was 11.9% (189/1586). The cost of ECS was not covered by insurance for 54.5% (103/189) of patients and most paid over $300 out-of-pocket for testing (47.6%). ECS was covered by insurance for 34.4% (65/189) of patients. Among those who had insurance coverage, 38.5% had no co-pay. Nearly half (49.2%, 93/189) of patients were found to be carriers of at least one disorder. Among carriers, 16.1% (15/93) did not have their reproductive partners screened. The most common reason positively-screened individuals cited for not testing their partners was that the results would not alter their course when seeking conception (33.3%). Nevertheless, 73.9% (139/188) of patients knew that the largest benefit of ECS comes from knowing a partner's results as well as their own. If presented with the option again, 82.6% would choose to undergo ECS screening.

CONCLUSIONS: A significant number of patients who are found to be carriers of a recessively-inherited disorder did not have their partners screened because the results would not change what they would do when seeking conception. For many patients, ECS testing is not covered by insurance and this test may impose a significant economic burden. Providers should evaluate whether a patient's ECS result would change their treatment course prior to testing.

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O-48 3:15 PM Saturday, October 17, 2020

EGG DONORS ARE NOT GOLDEN: ABNORMAL RESULTS AFTER PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY, PRODUCTS OF CONCEPTION ANALYSIS OR NONINVASIVE PRENATAL TESTING WITH USE OF SNP-BASED METHODOLOGIES.

Katherine L. Howard, MS,[1] Wendy DiNonno, MS,[1] Melissa K. Maisenbacher, M.S.,[2] Katrina Merrion, MS.[1] [1]Natera Inc., San Carlos, CA; [2]Natera, San Carlos, CA.

OBJECTIVE: Preimplantation genetic testing for aneuploidy (PGT-A), products of conception (POC) and noninvasive prenatal testing (NIPT) are not routinely indicated for pregnancies conceived with in vitro fertilization (IVF) and donor oocytes, as lower aneuploidy rates are anticipated due to lower maternal age.[1] This study compared rates of chromosome abnormalities for IVF cycles with and without the use of donor oocytes via PGT-A, POC and NIPT.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: Trophectoderm biopsy samples for PGT-A, fresh POC samples and NIPT samples were sent to a single reference laboratory. Inconclusive results and POC results showing maternal cell contamination (MCC) were excluded. For PGT-A and POC analysis, genotyping was performed using Illumina Cyto12 SNP-based microarrays with informatics. For NIPT, cell-free DNA was isolated and amplified by massively-multiplexed PCR targeting >13,000 SNPs covering chromosomes 13, 18, 21, X and Y. Oocyte donor age is defined as ≤30 years.

RESULTS: Abnormal PGT-A and POC results had monosomy, tri/polysomy, haploidy, triploidy, deletions/duplications, and/or uniparental disomy reported. High-risk NIPT results indicated trisomy 13, 18 or 21, sex chromosome abnormality, triploidy versus suspected multiple gestation, microdeletions, or high risk Fetal-Fraction-Based Risk (FFBR) calls. The FFBR model is validated to assess SNP-based NIPT no-call low fetal fraction pregnancies given specific clinical information to determine pregnancies at an increased risk for trisomies 13, 18, and triploidy.[2]

CONCLUSIONS: In cycles that used donor oocytes, high-risk results were observed in ~30% of PGT-A cases and ~20% of POC tests. For NIPT cases, high-risk results were observed in 1.0% of cases with donor and 2.2% for those without donor oocytes. Screening and diagnostic options to detect chromosome abnormalities should still be considered for donor oocyte recipients. These results may be beneficial for counseling intended parents about the rates of chromosome abnormalities following IVF with donor oocytes.

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INFERTILITY AND CANCER

O-49 2:00 PM Saturday, October 17, 2020

DEVELOPMENT OF A FERTILITY RISK CALCULATOR TO PREDICT INDIVIDUALIZED CHANCES OF OVARIAN FAILURE AFTER CHEMOTHERAPY.

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OBJECTIVE: Individualized prediction of a patient's risk of premature ovarian insufficiency (POI) after chemotherapy is challenging. Currently, chemotherapy regimens are stratified as "minimally increased" risk of POI (<20% risk), "intermediate" (30-70%) or "high" risk (>80%). Given the wide range of possible effects, it is challenging to counsel a patient with "intermediate" risk. Our study sought to use individual patient and treatment factors to develop a model that predicts personalized risk of POI after chemotherapy for reproductive-aged women. The eventual goal is to create a user-friendly, web-based fertility risk calculator to be made publicly accessible for oncofertility counseling.

DESIGN: Retrospective analysis of existing studies

MATERIALS AND METHODS: Candidate studies that followed patients for resumption of menses or POI after gonadotoxic therapy were identified and narrowed to randomized controlled trials and cohort studies that assessed the use of GnRH agonists in various cancer patients (breast, lymphoma, leukemia, etc.). By May 2020, 5 authors shared their data for a total N of 532 patients (111 records excluded for missing outcomes). A composite outcome for POI was determined for each patient and validated by 3 separate authors. Random Forest (RF) regression classifiers for POI were trained on 75% of the

	PGT-A	POC	NIPT
Overall Sample Total (n)	138,391	63,261	1,061,540
Donor Oocytes			
Total Samples, n (%)	15,889 (11.5)	1625 (2.6)	7314 (0.7)
Excluded (Inconclusive/MCC) , n (%)	435 (2.7)	206 (12.7)	724 (9.9)
Abnormal/High Risk Result, n (%)	5109 (33.1)	300 (21.1)	76 (1.0)
Non- Donor Oocytes			
Total Samples, n (%)	122,502 (88.5)	61,636 (97.4)	1,054,226 (99.3)
Average Maternal Age (years)	37.1	33.9	31.3
Excluded (Inconclusive/MCC/Test Not Performed) , n (%)	3455 (2.8)	8603 (14.0)	48,273 (4.6)
Abnormal/High-Risk Result, n (%)	60,170 (50.5)	23,915 (45.1)	23,684 (2.2)

data, while the remaining 25% was used as a validation set. For every RF classifier, we optimized the number of variables randomly sampled at every tree split and the number of trees until maximum possible POI prediction accuracy in the test dataset was achieved. Prediction scores for each patient sample are computed as the mean predicted class probabilities of the trees in the forest. To reduce overfitting, each classifier was validated using 10-fold cross-validation procedure.

RESULTS: A prediction score of >0.5 indicated a higher probability of POI. Our classifier predicted individualized risk of POI with an accuracy of 80% (area under the ROC 0.78, 95% CI: 0.67-0.88; p <0.001). The mean prediction scores for patients who developed POI and those who did not were 0.50 and 0.27 (t-test p < 0.001), respectively. Variables weighted most highly in our model included age, chemotherapy dose, prior chemotherapy, smoking status, and presence of baseline diminished ovarian reserve.

CONCLUSIONS: Using machine learning, we developed a predictive model to estimate patient-specific risks of POI after chemotherapy. We were able to assign an individualized risk score to each patient, refining the currently-used wide ranges of risk. Ongoing work involves validating the model with institutional data and other shared data from collaborators, as well as comparing our model's outcomes with the current risk stratification system. In the move towards personalized medicine, our web-based calculator will be a useful decision aid for providers and patients, thereby improving the quality and individualization of risk prediction in oncofertility consultations.

SUPPORT: None

O-50 2:15 PM Saturday, October 17, 2020

TOWARD TARGETING COUNSELING: ASSOCIATION BETWEEN CANCER TYPE AND ADVERSE PREGNANCY OUTCOMES.

Beth Zhou, MD,[1] Milli Desai, MHS,[1] Vinit Nalawade, MS,[1] James D. Murphy, MD,[1] Brian W. Whitcomb, PhD,[2] H. Irene Su, M.D., M.S.C.E.[1] [1]University of California San Diego, La Jolla, CA; [2]University of Massachusetts, Amherst, Amherst, MA.

OBJECTIVE: At higher risk of infertility, female adolescent and young adult (AYA) cancer survivors seek care of fertility specialists, who need information on cancer-specific pregnancy risks to inform treatment decisions. Limited studies on pregnancy and perinatal outcomes in AYA cancer survivors lack data on low-incidence cancers. Hypothesizing that adverse pregnancy outcomes differ by cancer type, the objective was to estimate the association between cancer type and live birth, preterm birth, and severe maternal morbidity.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: We used OptumLabs® Data Warehouse, a longitudinal, real-world data asset with de-identified administrative claims data to identify females with pregnancies from 1/1/2001 to 6/30/2019. Primary exposures were AYA cancer type, i.e. bone, brain, breast, cervical, gastrointestinal, leukemia, lung, lymphomas, melanoma, ovarian, renal, sarcoma, thyroid, and uterine. Primary outcomes: live birth, preterm birth, maternal morbidity in pregnancy measured by the Bateman Obstetrics Comorbidity Index, and CDC-defined severe maternal morbidity. Exposures, outcomes, and covariates were defined using ICD, CPT, DRG codes, and validated algorithms. Log-binomial generalized estimating equation models estimated associations of outcomes by cancer type. Counts <11 were suppressed.

RESULTS: There were 2,220,026 pregnancy episodes, 1,549,494 singleton live births in 1,286,922 women without cancer and 5,956 pregnancy episodes, 3,708 singleton live births in 3,150 women with history of cancer diagnosed between ages 15 and 39 prior to pregnancy. In all pregnancies, 70% were live birth, 12% preterm. Compared to women without cancer, several cancer types had lower likelihood of live births: brain (relative risk [RR] 0.8, 95% CI 0.7-0.9), breast (RR 0.9, 95% CI 0.9, 0.95), renal (RR 0.8, 95% CI 0.6, 0.99), sarcoma (RR 0.8, 95% CI 0.7, 0.99), and uterine (RR 0.6, 95% CI 0.5, 0.8). Preterm birth was also increased in survivors of gastrointestinal cancers, leukemia, and thyroid cancers with relative risks of 1.8 (95% CI 1.2, 2.7), 1.6 (95% CI 1.2, 2.0) and 1.3 (95% CI 1.1, 1.5) respectively.

Severe maternal morbidity occurred at a higher rate in several cancers. Compared to a 1.8% risk in women without cancer, leukemia (RR 2.9, 95% CI 1.8, 4.7), Non-Hodgkins lymphoma (RR 3.5, 95% CI 2.0, 6.1), and sarcoma (RR 3.9, 95% CI 1.5, 9.9) survivors experienced significantly higher rates of morbidities such as eclampsia, acute heart failure, and embolisms.

CONCLUSIONS: Leveraging a large administrative claims dataset to build a sizeable AYA cancer survivor cohort, this study presents novel data on cancer types at highest risks of adverse outcomes. While impact on preterm births and live births were modest, severe maternal morbidity had increased magnitude of risk that warrants further investigation. These findings by cancer type can aid in counseling of AYA cancer survivors as they present for fertility care and prompt further investigation of the pathophysiology and prevention of these outcomes.

O-51 2:30 PM Saturday, October 17, 2020

SYSTEMATIC REVIEW OF REPRODUCTIVE OUTCOMES FOR WOMEN UNDERGOING FERTILITY-SPARING THERAPY WITH PROGESTIN AND METFORMIN FOR ATYPICAL ENDOMETRIAL HYPERPLASIA AND EARLY ENDOMETRIAL CANCER.

Jennifer Chae-Kim, MD,[1] Gunjal Garg, MD,[1] Larisa Gavrilova-Jordan, MD,[2] Lindsay E. Blake, MLIS, AHIP,[3] Tongil T. I. Kim, PhD,[4] Clifford Cal Hayslip, Jr., MD.[1] [1]East Carolina University Greenville, NC; [2]Medical College of Georgia at Augusta University, Augusta, GA; [3]University of Arkansas for Medical Sciences, Little Rock, AR; [4]Emory University, Goizueta Business School, Atlanta, GA.

OBJECTIVE: High potency progestin is a common fertility-sparing management of atypical endometrial hyperplasia (AEH) or early stage endometrial cancer (EC) in reproductive-aged women (1). Addition of metformin has been shown to have a synergistic effect in the suppression of endometrial proliferation (1, 2). Reproductive outcomes for therapies using progestin or metformin have been reported. The outcomes of progestin and metformin combined therapy (Prog+M) in comparison to progestin (Prog) alone have not yet been evaluated systematically. The aim of this study was to conduct a systematic review of the reproductive outcomes for fertility-sparing management of AEH/EC with Prog+M versus Prog therapy.

DESIGN: Systematic review and meta-analysis.

MATERIALS AND METHODS: An extensive literature search was conducted to identify studies reporting outcomes in reproductive-aged women who underwent Prog+M versus Prog therapy. Primary outcomes were clinical pregnancy and live birth rates, hyperplasia or cancer remission, as well as relapse. Databases (MEDLINE, Web of Science, Cochrane Library, CINAHL, LILACS, clinicaltrials.gov) were searched from inception through April 2020 using key terms and subject headings where available. Inclusion criteria were as follows: reproductive-aged women with a histologically confirmed diagnosis of AEH or EC, who met criteria for fertility-sparing management, and received Prog+M or Prog; and studies reporting on at least one of the primary outcomes. Data were presented as proportions and odds ratio (OR) (95% confidence interval [CI]) with fixed- or random-effects meta-analysis.

RESULTS: In total, 251 reports were identified, and 10 studies (250 Prog+M and 226 Prog comparators) met the inclusion criteria. Mean age and body mass index for Prog+M were 35.8 years and 31 kg/m^2, compared to 36.4 years and 27 kg/m^2 in the Prog group. Both Prog+M and Prog had a high percentage of nulliparous women, at 74% and 77% respectively. Results showed a pooled remission rate of 78% (95% CI 64%-91%) for Prog+M and 70% (95% CI 51%-89%) for Prog, and the odds ratio for both treatments was not statistically significant (pooled OR 1.35, 95% CI 0.86-2.12, P = 0.26). Relapse rates for AEH/EC were statistically lower for Prog+M (pooled OR 0.49, 95% CI 0.25-0.95, P = 0.035). Interestingly, while clinical pregnancy rates were not different, live birth rates were significantly lower for Prog+M (pooled OR 0.39, 95% CI 0.17-0.89, P = 0.025).

CONCLUSIONS: Reproductive-aged women with AEH/EC have similar clinical pregnancy rates and lower cancer relapse after Prog+M compared to Prog therapy alone. Prog+M therapy was associated with a lower live birth rate. Further evaluation of the optimal window between discontinuation of Prog+M and onset of pregnancy is necessary to investigate possible improvements in the live birth rates in these women.

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SUPPORT: None.

O-52 2:45 PM Saturday, October 17, 2020

OVARIAN RESERVE AND RESPONSE TO STIMULATION AMONG PATIENTS UNDERGOING FERTILITY PRESERVATION FOR CANCER (ONCOFERTILITY) COMPARED TO THOSE PATIENTS WITHOUT A CANCER DIAGNOSIS. Devora Aharon, MD,[1] Sydney Chang, MD,[1] Dmitry Gounko, MA,[2] Joseph A. Lee, BA,[2] Alan B. Copperman, MD,[1] Erkan Buyuk, MD.[1] [1]Icahn School of Medicine at Mount Sinai New York, NY; [2]Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Whether malignancy has a harmful effect on ovarian function is currently unknown, with studies demonstrating conflicting results regarding ovarian reserve and response to stimulation among cancer patients.[1-2] The objective of this study is to determine whether oncofertility patients undergoing fertility preservation have reduced ovarian reserve and cycle outcomes compared to oocyte cryopreservation patients without cancer.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients who underwent fertility preservation prior to undergoing chemotherapy and/or radiation for cancer treatment from February 2006 through May 2020 were included. Controls were other fertility preservation patients matched by age (within 2 years) and cycle year in a 2:1 ratio. Patients with a prior oophorectomy or prior chemotherapy or radiation were excluded. Age, BMI, AMH, basal antral follicle count (bAFC), basal estradiol (bE2) and follicle stimulating hormone (bFSH) values, number of oocytes and mature oocytes (MII) retrieved, and ratio of MII to oocytes retrieved were compared between the groups using comparative statistics. Linear regression was used to compare cycle outcomes and control for confounders.

RESULTS: A total of 187 cancer patients who underwent fertility preservation were identified and included in the analysis, matched to 374 controls. 146 patients had breast cancer (75.4%), 19 had hematologic cancers (10.2%), 14 had endometrial or cervical cancers (7.5%), and 13 had other cancers (6.9%). Oncofertility patients were similar to patients without cancer in terms of age, BMI, AMH, bAFC, and bFSH. Oncofertility patients had significantly higher bE2 (62.4 ±56.1 vs. 46.0 ±33.0, p=0.001). Number of oocytes retrieved was similar between oncofertility patients and egg freezers without cancer (15.5 ±11.7 vs. 13.6 ±8.8, respectively, p=0.41). Oncofertility patients had a significantly lower number of MIIs retrieved (9.44 ±9.37 vs. 9.71 ±7.06, p=0.03) and MII/oocyte ratio (0.59 ±0.29 vs. 0.70 ±0.22, p=<0.0001). After adjusting for age, BMI, AMH, bAFC, bE2, and bFSH, egg freezing in patients without cancer was not associated with number of MIIs retrieved (β=-0.733, p=0.30) but was significantly associated with a higher MII/oocyte ratio (β=0.075, p=0.007).

CONCLUSIONS: Oncofertility patients had similar ovarian reserve testing and oocytes retrieved, however the ratio of mature oocytes to total number of oocytes retrieved was lower when compared to egg freezing patients without cancer. This may be due to the effect of the underlying disease process on oocyte maturation, a shorter time frame to start and complete a cycle, or a physician bias in either the stimulation protocol or retrieval process to maximize oocyte yield in cancer patients who face potentially sterilizing treatment. Clinicians should counsel patients that while outcomes may not be identical in patients with cancer, fertility preservation with oocyte freezing can result in a satisfactory yield of mature oocytes for future use.

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SUPPORT: None

O-53 3:00 PM Saturday, October 17, 2020

IS FERTILITY PRESERVATION A PART OF COMPREHENSIVE CANCER CARE IN THE UNITED STATES? Adriana Nicholson Vest, PhD, Nelson T. Kuete, B.Sc., Akanksha Mehta, M.D., M.S. Emory University School of Medicine, GA.

OBJECTIVE: Although fertility preservation is important to young cancer survivors of reproductive age, the delivery of oncofertility care remains challenging, and utilization of fertility preservation remains low. Cancer patients increasingly utilize online health information to fill knowledge gaps in their fertility care. The purpose of this study was to evaluate the website content of NCI designated cancer centers to assess the quantity and quality of patient-oriented information pertaining to pre-treatment fertility preservation.

DESIGN: A cross-sectional review of National Cancer Center (NCI) designated Cancer Center websites.

MATERIALS AND METHODS: Cancer Centers (CC) and Comprehensive Cancer Centers (CCC) were identified based on the NCI list of designated institutions. Laboratories were excluded and centers that shared a website were counted once. Each center's website was evaluated for the presence of terms related to the etiology and treatment of cancer related infertility. The frequency with which websites included information pertaining to fertility preservation was calculated and the differences between CC and CCC were compared with Fischer's exact test using Matlab R2020a. Statistical significance was set as $p<0.05$.

RESULTS: Of the 72 identified CC and CCCs, 64 patient-facing websites were eligible for analysis. Overall, 72% of websites mentioned any effect of cancer or cancer therapy on fertility potential. Only 56% of websites had a page devoted solely to the effect of cancer on fertility; information for female patients was more common than for male patients (59% vs 50%). Sperm banking (66% of websites), embryo banking (67%), and oocyte banking (69%) were the most commonly mentioned options for fertility preservation. The least mentioned options for fertility preservation were radiation shielding of gonads (19%) and radical trachelectomy (27%). Referral information that directed a patient to a fertility provider was provided on 63% of websites.

When comparing CC vs. CCC websites, the latter were more likely to include information about the effects of cancer and cancer treatments on fertility and the option for fertility preservation ($p< .001$). CCCs were more likely to include details for fertility preservation methods, including sperm banking, surgical sperm extraction, embryo banking, oocyte banking, ovarian tissue banking, ovarian transposition and ovarian suppression ($p < .05$). CCCs were also more likely to have referral information on their website to a fertility specialist ($p < .05$).

CONCLUSIONS: Patient-directed information pertaining to oncofertility and fertility preservation is absent on greater than 25% of NCI-designated cancer center websites, and represents a gap in comprehensive cancer care and survivorship planning. Patients who rely primarily on internet-based information regarding oncofertility may not be well-informed about fertility preservation options in the critical period between cancer diagnosis and treatment.

SUPPORT: None

O-54 3:15 PM Saturday, October 17, 2020

ADVERSE PERINATAL OUTCOMES IN ADOLESCENT AND YOUNG ADULT CANCER SURVIVORS AND IMPACT OF ART. Milli Desai, MHS,[1] Beth Zhou, MD,[1] Vinit Nalawade, MS,[1] James Murphy, MD, MS,[1] Brian W. Whitcomb, PhD,[2] H. Irene Su, M.D., M.S.C.E.[1] [1]University of California San Diego, La Jolla, CA; [2]University of Massachusetts, Amherst, Amherst, MA.

OBJECTIVE: Little is known about use of assisted reproductive technology (ART) and adverse perinatal outcomes following ART in female survivors of adolescent and young adult (AYA) cancers. The magnitude of risks for preterm birth and maternal morbidity and whether these risks are moderated by ART use are unknown. We hypothesized that prior AYA cancer is associated with these outcomes, and the effect of AYA cancer differs by ART use.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: We used OptumLabs® Data Warehouse, a longitudinal, real-world data asset with de-identified administrative claims data. Eligibility criteria: female and live birth from 1/1/2001 to 6/30/2019. Primary exposures: AYA cancer preceding pregnancy, and ART. Primary outcomes: preterm birth and CDC-defined severe maternal morbidity. Exposures, outcomes and covariates were defined using ICD, CPT, DRG codes and validated algorithms. Generalized estimating equation log-binomial models estimated associations to account for repeated pregnancy episodes, and control for maternal age. We tested for effect modification of ART on the association between AYA cancer and outcomes, and stratified by birth plurality.

RESULTS: We identified 3,708 singleton and 137 multiple live births after cancer in 3,265 females with prior cancer. The most common cancer types were thyroid (22%), melanoma (21%), and breast (15%). For cancer survivors, mean age at pregnancy was 33.5 (SD 4.7). Cancer survivors used ART more than women without cancer (6% vs. 3% of singleton births, 34% vs. 21% of multiple births). The incidence of preterm birth and severe maternal morbidity in cancer survivors were 15% and 2.5%, respectively, in singleton births and 61% and 18% in multiple births.

In singleton births, compared to women without cancer, cancer survivors had a 1.2-fold higher risk of preterm birth (95% CI 1.1, 1.3) and 1.3-fold higher risk of severe maternal morbidity (1.1, 1.6) after adjusting for age. In multiple births, cancer survivors did not have significantly higher risks of these outcomes.

Cancer survivors had a higher Bateman maternal comorbidity index score than women without cancer. Adjusting for age and comorbidity index, the effect of cancer on outcomes was attenuated, suggesting mediation.

In singleton births, controlling for cancer and age, ART was associated with 1.4-fold higher risk of preterm birth and 1.6-fold higher risk of severe maternal morbidity; in multiple births, the relative risks of each outcome with ART were 1.3 and 1.5, respectively. The interaction between AYA cancer and ART was not significant for any outcomes.

CONCLUSIONS: For AYA cancer survivors, preterm birth and severe maternal morbidity risks are increased and appear to be mediated through more maternal comorbidities. ART independently increased perinatal risks, but the magnitude of increase was no higher than in women without cancer. As adverse perinatal outcomes were increased in multiples, the goal of singleton pregnancies remains paramount. AYA cancer survivors desire healthy pregnancies; ART use presents an important clinical opportunity to modify risks through singleton pregnancies.

MALE REPRODUCTION AND UROLOGY: TRAVELING SCHOLARS

O-55 2:00 PM Saturday, October 17, 2020

THE PROVIDER LANDSCAPE OF MALE INFERTILITY CARE IN THE UNITED STATES. Richard Jacob Fantus, MD,[1] Cecilia Chang, MS,[2] James Wren, MD,[3] Nelson E. Bennett, Jr., MD,[3] Robert E. Brannigan, MD,[3] Joshua A. Halpern, MD, MS.[3] [1]University of Chicago Chicago, IL; [2]NorthShore University HealthSystem, Evanston, IL; [3]Northwestern University Feinberg School of Medicine, Chicago, IL.

OBJECTIVE: Recent studies have demonstrated that reproductive endocrinologists perform sperm extraction procedures for male infertility, yet the overall proportion of male infertility care provided by non-urologists is unknown. Using a nationally representative cohort, we sought to assess male infertility visits to examine provider specialization and patient characteristics across the United States.

DESIGN: Retrospective cohort review.

MATERIALS AND METHODS: We examined all male patient visits in the National Ambulatory Medical Care Survey (NAMCS) between 2006-2016, a Center for Disease Control and Prevention (CDC) sponsored dataset designed to characterize ambulatory medical care in the US. The diagnosis of infertility was made using the International Classification of Disease (ICD) 9 codes 606.x for the years 2006-2015 and ICD 10 codes N46.x for the year 2016. Chi-squared tests were used to compare demographic and clinical information of men with and without infertility.

RESULTS: A total of 3,410,129 weighted visits were analyzed of which 1513 (0.04%) were for infertility. Men seen with a diagnosis of infertility compared to those without were on average younger (35 years vs. 58 years, $p<0.05$) and more likely to have private insurance (89.2% vs 50.4%, $p<0.05$). Urologists were responsible for the majority (N=957, 64.6%) of visits for infertility, followed by gynecologists (N=205, 13.6%). When examining the primary diagnosis for each encounter, gynecologists represented 69.4% of infertility diagnoses among non-urologists. Compared to men seen for infertility by urologists, those seen by non-urologists were more likely to be younger (31 years vs. 36 years, $p<0.05$) and Black (18.2% vs. 10.0%, $p=0.04$).

CONCLUSIONS: Over a third (35.4%) of office visits for male infertility were performed by non-urologists, primarily gynecologists. Given the high prevalence of medical comorbidity and treatable etiologies of male infertility among male partners of infertile couples, it is critical that these men undergo evaluation by a reproductive urologist. As models for delivery of care in reproductive medicine continue evolve, further studies are needed to examine referral patterns and integration of care between reproductive endocrinologists and urologists. This will aid in the optimization of access to reproductive urologic evaluation.

O-56 2:15 PM Saturday, October 17, 2020

PERCEPTIONS OF INFERTILITY AND SEMEN ANALYSIS TESTING AMONG MEN WITHOUT CHILDREN. Matthew Hudnall, MD, MPH, Mary Kate Keeter, MPH, James Wren, MD, Nelson E. Bennett, Jr., MD, Robert E. Brannigan, MD, Joshua A. Halpern, MD, MS. Northwestern University Feinberg School of Medicine, Chicago, IL.

OBJECTIVE: Adult men, particularly those in the millennial generation (age 25-40) and younger, are increasingly targeted by direct-to-consumer (DTC) companies offering diagnosis and treatment of men's health conditions, including home semen testing. However, perceptions of infertility among adult men not actively attempting to conceive and their willingness to undergo semen analysis are not well understood. We hypothesized that men proactive about their health are more likely to be concerned about infertility and undergo semen analysis without a healthcare provider recommendation.

DESIGN: Online survey study conducted via ResearchMatch.com.

MATERIALS AND METHODS: We surveyed men age 18 and older without children (n=634). Sociodemographic data (age, education, income, insurance, relationship status) were collected. Survey questions included 5-point Likert items assessing level of concern and likelihood of performing a particular action, such as discussing infertility with a physician or conducting a semen analysis test without a physician recommendation. Responses were dichotomized and logistic regression estimated the association between participant characteristics and outcomes of interest.

RESULTS: The majority of men (54.7%) were aged 18-39 and in a romantic relationship (55.2%). Only 186 (29.3%) men expressed concern about infertility, whereas 391 (62%) expressed concern about low testosterone. Among men concerned about infertility, 23.4% were unlikely to discuss infertility concerns with a health care provider. On multivariable analysis, factors associated with infertility concern included younger age (age 18-39: OR 4.48, 95% CI 2.23-9.03, $p<0.001$), being single (OR 0.65, 95% CI 0.43-0.97, $p=0.037$), and concern about low testosterone (OR 5.28, 95% CI 3.32-8.40, $p<0.001$).

Of all respondents, 10.4% would obtain a semen analysis without a health care provider recommendation. This increased to 14.2% if the test could be performed at home ($p=0.04$). Factors associated with likelihood to pursue semen analysis included post-graduate degree (OR 0.28, 95% CI 0.11-0.72, $p=0.009$), frequency of doctor visits (1-2 in last year: OR 4.05, 95% CI 1.11-14.83, $p=0.034$), concern about low testosterone (OR 2.30, 95% CI 1.12-4.74, $p=0.023$), and concern about infertility (OR 3.91, 95% CI 2.14-7.15, $p<0.001$). Regular exercise, fitness tracker use, and use of DTC services such as Hims®, Roman®, or 23andMe® were not associated with increased likelihood.

CONCLUSIONS: Millennial and younger men were more concerned about infertility than older men, but many were unlikely to discuss infertility concerns with a healthcare provider. These men were not more inclined to pursue a semen analysis without a health care provider recommendation, even after accounting for use of other DTC health care services. Concerns about low testosterone were pervasive and are strongly associated with both infertility concern and likelihood of self-initiating a semen analysis.

O-57 2:30 PM Saturday, October 17, 2020

WALNUTS IMPROVE SEMEN QUALITY IN INFERTILE MEN: A RANDOMIZED CONTROL DIETARY INTERVENTION TRIAL. John Michael Masterson, MD,[1] Howard H. Kim, MD,[1] Wendie A. Robbins, PhD.[2] [1]Cedars Sinai Medical Center Los Angeles, CA; [2]University of California Los Angeles, Los Angeles, CA.

OBJECTIVE: Walnut-enriched diets have been shown to improve semen parameters in healthy men. The objective of the present study was to measure the impact of walnut consumption on semen parameters in a clinic population diagnosed with male factor infertility.

DESIGN: A randomized, parallel two-group dietary intervention trial with single-blind masking of outcome assessors was conducted with infertility

patients at a major university. The primary outcome was improvement in conventional semen parameters from baseline to 12 weeks.

MATERIALS AND METHODS: Eligible participants were males diagnosed with male factor infertility. Men were ineligible if they had a known food allergy, were smokers, were taking medications for chronic illness, or consumed multivitamins, supplements or walnuts within the prior six months. Participants were randomly assigned to one of two parallel groups: group one received usual care but added ≥45 grams/day of whole-shelled walnuts to their diet, while group two received usual care but added a daily fertility vitamin and avoided consumption of tree nuts. Blood fatty acid/nutrient profiles, 24 hour ASA dietary recalls, and semen parameters were measured at baseline and 12 weeks. Fertility outcomes were tracked for one year.

RESULTS: A total of 75 infertile men, age 27 to 61 completed the study. The group consuming walnuts experienced improvement in sperm motility ($p = 0.02$) and progressive motility ($p = 0.08$) from baseline to 12 weeks (table 1). Both groups saw improvement in percent normal morphology from baseline to 12 weeks with the control group reaching statistical significance ($p = 0.02$), group x time interaction $p = 0.02$ (table 1). The walnut intervention group also experienced a non-significant improvement in sperm concentration (table 1).

CONCLUSIONS: Dietary modification is a safe and cost-effective method of improving semen parameters. Adding dietary walnuts can improve sperm motility for some patients. Whether increased walnut consumption alone will improve fertility outcomes remains to be proven. This is the first walnut dietary intervention randomized control trial (RCT) conducted with male factor infertility patients, however, findings are consistent with two previous RCTs showing improved motility for healthy men of unknown fertility (1,2).

	Baseline mean (SE)	Post-intervention mean (SE)	p
Concentration million/ml			
Control	41.9 (6.81)	45.9 (9.76)	NS
Walnuts	41.9 (8.08)	52.4 (8.32)	NS
Motility %*			
Control	38.3 (6.82)	32.8 (5.76)	NS
Walnuts	35.5 (5.4)	44.6 (6.64)	0.02
Progressive Motility %			
Control	23.2 (4.08)	22 (4.03)	NS
Walnuts	20.4 (3.6)	25.2 (4.49)	0.08
Morphology % Normal			
Control	4.3 (0.86)	5.7 (1.11)	0.02
Walnuts	3.4 (0.76)	4.1 (1.03)	0.09

*ANOVA time x group interaction, $p = 0.02$.

References: 1. Salas-Huetos A, et al. 2018.
2. Robbins WA, et al. 2012.

O-58 2:45 PM Saturday, October 17, 2020

AN ANALYTICAL MODEL TO DEFINE THE PROBABILITY OF AZOOSPERMIA FROM SERUM FOLLICLE STIMULATING HORMONE.

Michael B. Tradewell, MD, MS, Andrew Hany Rezk, BA, Elie Nwefo, MS, Emad Ibrahim, MD, HCLD(ABB), Ranjith Ramasamy, M.D. University of Miami Miller School of Medicine Miami, FL.

OBJECTIVE: To develop and internally validate a model to predict the probability of azoospermia from serum follicle stimulating hormone (FSH) in men with infertility.

DESIGN: We reviewed a prospectively maintained database from a male infertility clinic between 01/2016 and 03/2020. Age at semen collection, sperm concentration, FSH, LH, total testosterone, bilateral testis volume (estimated by Prader orchidometer) were extracted from the database. Only pared sperm concentration and clinical data collected within +/-90 days of semen analysis were included. Data from men using medications clomiphene, anastrozole, or human chorionic gonadotropin and from men with diagnoses of Klinefelter Syndrome or Y Chromosome Microdeletion (YCM) AZFc were included. Men with history of vasectomy, solitary testis, recent testosterone or steroid use, and YCM AZFa or AZFb microdeletion were excluded.

MATERIALS AND METHODS: Probability of azoospermia was determined from the quotient of binned FSH data (Number of Azoospermic Samples / Total Number of Samples). A quadratic model predicting probability of azoospermia from FSH was fit to these data. Logistic regression from continuous gonadotropin, testosterone, and testis volume data was used as a comparator. Accuracy and internal validity of each model were assessed via correlation, discrimination (after exclusion of men with obstructive azoospermia) and calibration. All modeling and statistical analysis was computed in *R*.

RESULTS: A total of 946 pared sperm concentration and hormone data sets from 749 men were analyzed. The quadratic FSH model (Probability of Azoospermia = $0.133[FSH]^2 - 0.965[FSH] + 10.1$) fit with a high R^2 (0.95). The model showed an undetectable FSH (<0.2 IU/mL) confers a 10% chance of azoospermia, the probability of azoospermia is least when FSH is 3.6 IU/L. Most interesting was that all men with FSH >30 IU/L were uniformly azoospermic.

On internal validation, the Pearson Correlation Coefficient between the quadratic FSH model and the logistic regression model is 0.93, suggesting excellent agreement. The logistic regression and quadratic FSH models both demonstrated good discrimination with AUCs of 0.86 and 0.84, respectively. Finally, each model is well calibrated with near ideal probabilities throughout the entire range of predictions however the quadratic FSH model's calibration is closer to ideal at higher, more clinically relevant, predicted probabilities of azoospermia.

CONCLUSIONS: Based on a single serum FSH level, our model provides an infertility specialist the ability to predict with a high degree of confidence the probability of azoospermia, especially at high levels suggesting production defect. The utility of this study presents itself during the initial infertility encounter with a male who is apprehensive about performing a semen analysis. Future work will be necessary to externally validate the model.

SUPPORT: None.

O-59 3:00 PM Saturday, October 17, 2020

CHANGES IN SEMEN ANALYSIS IN UNTREATED NON-AZOOSPERMIC PATIENTS OVER TIME: A TEMPORAL TREND ASSESSMENT OF 23 YEARS.

Nahid Punjani, MD MPH,[1] Omar Al Hussein Alawamlh, MD,[1] Soo Jeong Kim, MD,[2] Carolyn A. Salter, MD,[3] Gal Wald, BA,[1] Miriam Feliciano, BSc,[1] Vanessa L. Dudley, MSHS,[1] Philip S. Li, M.D.,[4] Marc Goldstein, M.D.[5] [1]Weill Cornell Medicine, New York, NY; [2]New York Presbyterian - Weill Cornell Medical Center, New York, NY; [3]Memorial Sloan-Kettering Cancer Center, New York, NY; [4]Weill Cornell Medical College, New York, NY; [5]Center for Male Reproductive Medicine and Microsurgery, Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY.

OBJECTIVE: To examine trends of population-level semen quality over a 23-year period at a single high-volume institution with a heterogenous patient population.

DESIGN: Retrospective study of prospectively collected data.

MATERIALS AND METHODS: We assessed a total of 12,883 consecutively collected semen samples over 23 years (1997-2019) at Weill Cornell in New York City. We included samples that had an available corresponding date of collection. To remove confounding due to patients with post-vasectomy semen samples, we excluded all patients with sperm concentrations of zero. We examined yearly trends in concentration (million/ml), total sperm count (million), pH, volume (mL), motility (%) and progressive motility (grade 1-4), and morphology (%). To determine trends in semen parameters over time in men presenting for fertility assessment restricted cubic spines were used to model the data due to its non-linearity. Furthermore, differences in estimated average outcomes at the beginning and end of the study period were assessed.

RESULTS: After exclusions, a total of 10,505 semen samples were assessed over our study period. A total of 23-time intervals were included. Semen volume decreased over time and estimate average at the beginning and end were statistically different ($p<0.001$). Similarly sperm morphology decreased overtime, with a statistically significant difference between estimated averages from start to finish ($p<0.001$). Semen pH appeared to be increasing over time, with significant differences between estimated average outcomes at the beginning and end ($p<0.001$). Sperm concentration and count displayed an increase around 2003-2005 but otherwise remained fairly constant over time ($p=0.215$ and $p=0.409$, respectively). Sperm motility appeared to remain relatively similar over time ($p=0.654$).

CONCLUSIONS: In a large subset of patients presenting to a single institution for fertility assessment at a single lab, semen volume and sperm morphology significantly worsened over more than two decades. The etiologies and driving forces changing semen parameters over time remains to be determined.

O-60 3:15 PM Saturday, October 17, 2020

VIDEO VISITS ALLOW FOR MANAGEMENT OF MALE INFERTILITY ACROSS A BROAD SPECTRUM OF DIAGNOSES. Juan J. Andino, MD, MBA, Alex Zhu, DO, Stephanie Daignault-Newton, MS, Chad Ellimoottil, MD, MS, James M. Dupree, IV, MD, MPH. Michigan Medicine Ann Arbor, MI.

OBJECTIVE: While the COVID-19 pandemic has resulted in a rapid expansion of telehealth services, it remains unknown how video visits, a form of telehealth, can be used to treat male infertility. We sought to evaluate what infertility diagnoses were see and how they were managed through telehealth. Herein we summarize a single institution's experience with video visits for male infertility prior to COVID-19.

DESIGN: Retrospective case series of patients with male infertility managed via video visits.

MATERIALS AND METHODS: We identified video visits completed at our institution between August 21, 2017 and March 17, 2020 for male infertility. All men had a previous in-person examination. We collected patient demographic and referral information, grouped primary diagnoses, categorize what management steps were taken, and determined whether in-person examinations were needed within 90 days.

RESULTS: 70 video visits were completed by 56 men. The median age was 36 years (interquartile range 32 - 40), 78.5% were white, and most patients were referred by their primary care provider or their partner's reproductive endocrinologist (47% and 33%, respectively). Most men were diagnosed with endocrinologic (29%) or anatomic (21%) contributors to infertility. See Table1A for full diagnostic categories.

73% of video visits involved reviewing results such as semen analysis and hormonal testing. 30% of visits involved counseling for assistive reproductive technologies (ART) and, in 25% of visits, hormonally active medications were prescribed. See Table1B for all management categories. There were only two in-person visits within 90 days after a video visit, both of which were planned post-operative visits.

TABLE 1. Diagnostic categories of and management through video visits

A. Diagnostic categories	Proportion
Endocrinologic (hypothalamic-pituitary-gonadal axis)	29%
Anatomic (e.g., varicocele, vasectomy, CBAV)	21%
Idiopathic	16%
Treatment-related concerns (e.g. cancer therapy or medication impact)	9%
Concurrent partner evaluation	9%
Genetic abnormalities	7%
Ejaculatory failure	6%
DNA integrity	4%
Total	100%
B. Male infertility management	Proportion*
Review of results	73%
ART counseling	30%
Medication management	25%
Sperm extraction counseling	14%
Varicocelectomy counseling	13%
Cryopreservation counseling	4%
Referral to other specialists (REI, genetics)	3%

*Visits included multiple management categories; totals do not equal 100%.

CONCLUSIONS: Video visits can be used with established patients to manage a broad spectrum of diagnoses that contribute to male infertility. In the short-term, these visits are serve as substitutes for clinic visits without resulting in additional in-person encounters.

SUPPORT: Dr. James M. Dupree receives Grant Funding from Blue Cross Blue Shield of Michigan for quality improvement work with the Michigan Value Collaborative

PATIENT EDUCATION AND SUPPORT

O-61 9:40 AM Sunday, October 18, 2020

MILITARY SERVICE AND MEDICAL ASSOCIATIONS WITH INFERTILITY IN U.S. VETERANS. Ginny L. Ryan, MD, MA,[1] Marie E. Thoma, PhD, MHS,[2] Andrea Holcombe, MS, PhD,[3] Anne Sadler, PhD, MS,[3] Bradley J. Van Voorhis, MD,[4] Alicia Y. Christy, MD,[5] Michelle A. Mengeling, MS, PhD.[3] [1]Center for Access and Delivery Research and Evaluation Iowa City, IA; [2]University of Maryland, College Park, MD; [3]Iowa City VA Health Care System, Iowa City, IA; [4]University of Iowa, Iowa City, IA; [5]Veterans Administration, Kensington, MD.

OBJECTIVE: Studies suggest U.S. military Veterans have higher rates of poor reproductive outcomes due to unique exposures and complex health challenges. Our objective was to identify associations between lifetime infertility measures and key military service/medical characteristics in Veterans.

DESIGN: Cross-sectional survey study of 1407 female and 1601 male U.S. Veterans aged 20-45.

MATERIALS AND METHODS: Data were collected using computer-assisted telephone interviews. Infertility prevalence and key military service/medical characteristics were analyzed by sex. Lifetime infertility was defined as: 1) twelve or more consecutive months of unprotected intercourse without pregnancy (UI), 2) twelve or more months of trying before any pregnancy (TTP), and 3) ever diagnosis of infertility in participant and/or partner (DX). For depression, eating disorder, and PTSD, Veterans were screened for current disease and self-reported ever diagnosis.

RESULTS: 84.9% reported ever unprotected intercourse and of those 49.6% reported having twelve or more consecutive months without pregnancy. Among those ever pregnant (65.3%; n=919), 45.3% (n=416) reported twelve or months of TTP. Overall, 11.7% (n=165) reported ever being diagnosed with infertility. There were no statistically significant associations between age of enlistment, ever deployed or duration of deployment and any of the 3 infertility measures for female or male Veterans.

Ever deployed male Veterans with infertility were more likely to have been under enemy fire or at risk of IED injury than ever deployed male Veterans without infertility (UI measure, p=0.04). Ever PTSD diagnosis was associated with the DX infertility measure for women (p=0.01) and with UI (p=0.003) and DX (p=0.04) infertility measures for men. Female Veterans with infertility (UI measure) were also more likely to screen positive for current PTSD (p=0.02).

Female Veterans with lifetime infertility (UI measure) were more likely to have ever smoked than female Veterans without infertility (p=0.046). Higher BMI was associated with infertility in female Veterans by all 3 infertility measures (p=0.02-0.0003). Neither of these associations was seen in male Veterans.

Ever diagnosis of depression was more likely in female Veterans with lifetime infertility (by TTC p=0.03 and DX p=0.0002) but not in their infertile male counterparts. Current depression, ever diagnosis of anxiety disorder, and ever diagnosis of or current eating disorder were not significantly associated with any infertility measure in female or male Veterans.

CONCLUSIONS: Consistent with general population studies, several general health-related factors were found to be associated with infertility in women Veterans but not in men. More research is needed regarding the role of traumatic deployment experiences in male Veteran infertility. The role of PTSD as a mediator or moderator, or alternatively an outcome, of infertility for both male and female Veterans also requires additional research to examine the timing of this association. Our results provide evidence to help inform Veteran- and sex-specific infertility care.

SUPPORT: The research reported here was supported by the Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development (HSR&D) Service grant HSR&D IIR 13-294. The content is solely the responsibility of the authors and does not necessarily represent the views of the Department of Veterans Affairs.

O-62 9:55 AM Sunday, October 18, 2020

THE IMPACT OF AN INTERACTIVE E-LEARNING PLATFORM ON PATIENT COMPREHENSION REGARDING INFERTILITY TREATMENT: A RANDOMIZED CLINICAL TRIAL. Ashley K. Barbour, MPhys,[1] Abigail L. Bernard, MD,[2] Jody L. Madeira, Ph.D., J.D.,[3] Steven R. Lindheim, M.D.,[4] Linnea R. Goodman, MD.[2] [1]Brody School of Medicine at East Carolina University Greenville, NC; [2]University of North

Carolina, Raleigh, NC; [3]Professor of Law, Bloomington, IN; [4]Wright State University, Dayton, OH.

OBJECTIVE: To determine the impact of a multi-media e-learning platform regarding patient comprehension of fertility pathophysiology and treatment.

DESIGN: Prospective randomized controlled trial.

MATERIALS AND METHODS: Consecutive female patients aged 18-43 years undergoing their first intrauterine insemination (IUI) or in-vitro fertilization (IVF) cycle were randomized to receive either standard fertility counseling with their physician and nursing team (Conventional group) or to standard counseling plus an interactive online learning platform (EngagedMD) before and during their first treatment cycle (EMD group). A 15-question online assessment was administered to both groups after completion of their MD consultation/nursing teaching at the start of their treatment cycle (T1) and again at the conclusion of that same treatment cycle (T2) to quantitatively evaluate initial fertility treatment comprehension and whether knowledge was learned and retained over the course of the cycle. Physicians and nurses involved in patient care during the study were also surveyed to determine if a difference in fertility comprehension between groups was noted. A power analysis was performed to determine a sample size adequate to detect a difference of four more questions answered correctly in comprehension between groups and Chi-square and Student's t-test were used as appropriate.

RESULTS: To date, a total of 77 patients have been recruited, 35 undergoing IUI and 42 undergoing IVF, with 52 completing both assessments. The average age of the cohort was 35.2 +/- 4.4 (mean +/- SD) years and the most common reason for fertility treatment was unexplained (50.7%) followed by male factor (29.9%). For both IUI and IVF patients, demographics including age, duration of infertility and education level were similar between groups. Overall, the average scores in the EMD group (n=23) were significantly higher than the conventional group (n=29) at T1 (13.7 +/- 1.6 vs. 11.76 +/- 2.05; $p<0.01$), but were similar at T2 (13.1 +/- 2.1 vs. 12.3 +/- 1.6; $p = 0.11$). When comparing IUI and IVF patients, this difference remained with the EMD group scoring higher at start of treatment in both IUI (13.2 +/- 1.8 vs. 11.0 +/- 3.4; $p = 0.01$) and IVF (14.3 +/- 1.4 vs. 12.4 +/- 1.9; $p = 0.01$) groups and at the conclusion of the IVF cycle (14.1 +/- 1.9 vs. 12.7 +/- 1.3; $p = 0.04$). The IUI group did not score higher at the conclusion of the cycle (12.2 +/- 2.0 vs. 11.8 +/- 1.7; $p = 0.52$). All physicians surveyed ($n = 6$) could not determine a difference in fertility comprehension between groups. However, all nurses (n=4) reported an improvement in comprehension, shorter teaching visits and fewer questions in the EMD group.

CONCLUSIONS: The addition of an online learning platform significantly improved patients' knowledge base at the initiation of first IUI or IVF cycles and at the conclusion of IVF cycles. These results suggest that having access to such resources improve patient understanding of their diagnosis and treatment prior to undergoing fertility therapy.

O-63 10:10 AM Sunday, October 18, 2020

READING LEVEL OF PATIENT EDUCATION MATERIAL ON INFERTILITY CLINIC WEBSITES IS ABOVE NATIONAL RECOMMENDATIONS. Holly Mehr, MD MSEd,[1] Victoria Lee, BS,[1] Tia Jackson-Bey, MD MPH,[2] Christopher Herndon, MD,[3] Molly M. Quinn, MD.[1] [1]University of California Los Angeles, Los Angeles, CA; [2]University of Illinois at Chicago, College of Medicine, Chicago, IL; [3]University of Washington, Seattle, WA.

OBJECTIVE: Patients are increasingly using the internet to answer medically related questions. Most fertility clinics offer patient educational materials (PEMs) via a practice website. The National Institutes of Health (NIH) and the American Medical Association (AMA) recommend that PEMs are written between a 6th and 8th grade reading level. In this study, we assess the reading level of PEMs on fertility clinic websites.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: Between 4/2020 and 5/2020, SART affiliated fertility clinic websites were reviewed for PEMs, defined as content intended to inform patients about the etiology, diagnosis or treatment of a specific disease beyond the purpose of advertising a service performed by the clinic. Clinic characteristics including size, type of practice, and location were collected from SART. To improve reliability of results, only sites with content on hysterosalpingogram (HSG) or intrauterine insemination (IUI) of at least 100 words in length were analyzed. Using 5 validated readability metrics: Flesch-Kincaid Grade Level, Gunning Fog Index, SMOG formula, Coleman-Liau Index and Automated Readability Index, an average reading level was calculated for each PEM. To ensure HSG and IUI were interchangeable and representative of website reading level, the reading levels of HSG were compared to IUI in 15 websites containing both topics using paired t-test. Readability levels were compared across clinic characteristics using one-way ANOVA and chi squared analyses where appropriate.

RESULTS: Of the 382 SART affiliated clinics, 355 had an active, unique website. While most (n=309, 92%) websites had some form of patient education, fewer (n=266/355, 75%) had at least 100 words of PEM on either HSG or IUI and were included in the readability analysis. Analysis of websites with both HSG and IUI material found reading levels between the two to be similar ($p=0.348$). It was more common to find PEMs for analysis in private practices than academic practices (79% vs 60%, $p=0.001$) and in practices with >1000 cycles a year than <200 cycles a year (95% vs 53%, $p<0.001$). Websites with PEM also differed by geographic region, with 62% of midwestern versus 84% southern websites containing PEMs ($p=0.014$).

The average reading level of all PEMs was 12.3 +/- 1.78 grade level (range 6.5-17.3). Only 2.2% (n=6) of PEMs were written at the AMA/NIH recommended grade level. Website reading level was similar between private and academic practices ($p=0.34$), and was not associated with practice size ($p=0.33$). The 15 most readable PEMs included 8 practices in the Western US and all (n=2) SART affiliated clinics in Puerto Rico.

CONCLUSIONS: Most fertility clinics in the United States offer patient education on their websites. However, content is written well above the NIH and AMA recommended 6th to 8th grade reading level. Patients with lower educational attainment have greater need for PEM, but patients of all levels of educational attainment prefer medical information presented in plain, easy to understand language. All infertility patients may be better served with more readable patient education material.

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O-64 10:25 AM Sunday, October 18, 2020

WHAT DO WOMEN NEED TO KNOW TO MAKE INFORMED DECISIONS ABOUT FERTILITY PRESERVATION? A DELPHI ANALYSIS OF PROVIDER-RECOMMENDED KEY FACTS. Sukhkamal Campbell, MD,[1] Aubri S. Hoffman, PhD,[2] Robert Volk, PhD,[2] Terri L. Woodard, M.D.[2] [1]Fellow, Baylor College of Medicine, Houston, TX; [2]The University of Texas MD Anderson Cancer Center, Houston, TX.

OBJECTIVE: To support national guidelines that all reproductive-age women should be offered fertility counseling prior to starting cancer treatment, this study sought to identify the key facts newly-diagnosed female cancer patients should know to make an informed decision about fertility-preservation.

DESIGN: Pilot Study.

MATERIALS AND METHODS: *Challenging Choices*: *Understanding the Specific Fertility Needs of Providers and Newly Diagnosed Female Cancer Patients in High and Low Resource Settings* was a clinical pilot study completed at MD Anderson Cancer Center and the Harris County Health System to understand and address gaps in fertility preservation counseling. A portion of the study involved engaging oncologists (medical, pediatric, young adult, and gynecologic) and reproductive endocrinologists in a Delphi survey. Providers completed three rounds of online questionnaires, with anonymized results that were reviewed and revised between rounds. Round 1: provider perception of fertility preservation counseling in a low resource setting. Round 2: A) a fertility facts quiz and B) ranking of facts in order of importance. Facts with more than 5 providers choosing "strongly agree" were retained for round 3. Round 3: provider ranking of most important final "key facts" (6 total).

RESULTS: The majority of the 33 providers were female (73%) with mean age of 51 years old. Overall, 34 reproductive endocrinologists and 25 oncologists were polled. The majority (80%) of providers agreed that

newly diagnosed female cancer patients of reproductive age should be counseled on fertility preservation options regardless of parity, partnership or financial status, or literacy level. The top ranked key-facts were: 1) Many cancer treatments can lead to infertility (the inability to get pregnant), 2) Fertility preservation should be done before starting cancer treatment, 3) Freezing eggs takes about 2 weeks, 4) If your insurance does not fully cover fertility preservation, there may be funds available through your employer (eg Johnson and Johnson, Starbucks) or other organizations (i.e. LIVESTRONG Fertility or Walgreens/Ferring Heart Beat Program) 5) Fertility preservation does not increase the risk of cancer recurrence in the future, and 6) If you choose not to do fertility preservation before cancer treatment, you can consider other family building strategies (i.e. adoption, fostering, third-party options) later.

CONCLUSIONS: Providers confirmed the importance of fertility preservation counseling for all reproductive-age women with cancer prior to initiation of treatment. Before deciding about fertility preservation, women should understand these key facts – infertility is a risk, preserve before cancer treatment (takes 2 weeks) if possible, confirm insurance coverage (or apply for funding), no increase in future cancer risk, and there are alternatives for family building. These facts may be used to guide shared decision making discussions, develop measures (knowledge tests, decision quality indices), design tools (patient decision aids), and inform reimbursement policies for high quality comprehensive cancer care.

SUPPORT: NA

O-65 10:40 AM Sunday, October 18, 2020

DESIRE FOR TWIN OR TRIPLET PREGNANCY IN INFERTILITY PATIENTS AND PATIENTS PRESENTING FOR PLANNED FERTILITY PRESERVATION (FP). Anne P. Hutchinson, M.D.,[1] Rafael Confino, BS,[2] Angela K. Lawson, Ph.D.,[1] Seth Barishansky, M.D.,[1] Mary Ellen Pavone, MD, MSCI.[1] [1]Northwestern University Feinberg School of Medicine Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Chicago, IL; [2]Northwestern Feinberg School of Medicine, Chicago, IL.

OBJECTIVE: To assess the desire for future twin or triplet pregnancy in patients presenting for planned FP and infertility.

DESIGN: Survey study.

MATERIALS AND METHODS: We designed a 40-question digital survey based on a validated survey developed at University of Iowa and approved by our IRB. Between February 2019 and May 2020, patients presenting to the clinic were asked to participate in a survey study. Those who agreed were routed to our survey which collected de-identified patient demographic information as well as treatment outcomes ranked in order of preference, specifically "no child", "singleton pregnancy, "twin pregnancy", "triplet pregnancy", obstetrical history, openness to multifetal reduction, and understanding of maternal and neonatal risks associated with twin and triplet pregnancies.

Chi-squared analysis was used to compare characteristics of planned FP who prefer twin or triplet pregnancy to those who prefer singleton pregnancy and infertility patients who prefer twin or triplet pregnancy to those who prefer singleton pregnancy.

RESULTS: 337 patients completed our survey, 14% undergoing planned FP and 86% presenting for infertility. 30% of the patients undergoing planned FP and 31% of the patients presenting with infertility identified twin or triplet pregnancy as their ideal pregnancy outcome. In the infertility population, patients who desired twin or triplet pregnancies were less likely to be open to multifetal reduction (p=0.012), had a lower annual household income (p=0.003), and had a larger ideal family size (p=0.004). Importantly, they were also less likely to understand the maternal and neonatal risks that came with twin and triplet pregnancy. While there was no significant effect of parity noted, those who received fertility treatments to conceive a previous child were less likely to desire twin or triplet pregnancy (p=0.036). There was no difference in age between the two groups.

In patients undergoing planned FP, those who desired twin or triplet pregnancy were more likely to be open to multifetal reduction (p=0.027). These patients showed similar understanding of maternal and neonatal risk of twin and triplet pregnancy as their counterparts desiring singleton pregnancy. No other parameters were noted to be significantly different between the groups.

CONCLUSIONS: Nearly one third of our patients desire twin or triplet pregnancy as their ideal outcome. This finding is consistent between our planned FP patients and our patients undergoing treatment for infertility. Our goal as providers is to help our patients achieve the healthiest possible pregnancy and baby, which is most effectively done through singleton pregnancy. While it can be helpful to recognize motivators for these desires, these findings highlight the importance of providing patient education to better align provider and patient goals.

O-66 10:55 AM Sunday, October 18, 2020

OPTIMIZING PROVIDER AND PATIENT EXPERIENCE: AN ANALYSIS OF AN ONLINE TOOL FOR PRE-IMPLANTATION GENETIC TESTING (PGT) PRE-TEST EDUCATION. Stephanie Sehnert, B.A.,[1] Sarah Yarnall, MSc,[1] Syed U. Abdul Aziz, B.S.,[1] Paul C. Lin, M.D.,[2] Maria Saketos, M.D.,[3] Dina Nusblat, MS, CGC.[4] [1]EngagedMD Washington DC, DC; [2]Seattle Reproductive Medicine, Seattle, WA; [3]NYU Langone Reproductive Specialists of New York, Mineola, NY; [4]CooperGenomics, Livingston, NJ.

OBJECTIVE: Evaluate the patient experience and utility of a digital tool for pre-test PGT education.

DESIGN: There is increased demand for PGT during in vitro fertilization (IVF) treatment, but clinician time to educate patients about testing is limited and pre-test genetic counseling is rare. This study assesses the ability of digital tools to facilitate patient education, support informed consent, and impact overall patient care.

MATERIALS AND METHODS: Patients considering PGT were provided a 15 minute video module consisting of 5 sections. Following each section, patients were required to answer comprehension questions. After completion, an optional survey was provided to assess their experience.

RESULTS: Between July 2018 and November 2019, 1562 patients completed the module and answered all comprehension questions. 246 patients completed the survey. Before the module, 50% (115/230) agreed or strongly agreed they knew what to expect before, during, and after their treatment. Afterwards, 88% (203/230) agreed or strongly agreed. 97% (224/230) felt the module was a helpful addition to the care provided by their medical team and 167/226 were more satisfied with their care after the module. Of 192 respondents, 83% felt the module made them more prepared to sign consent forms. For 92% (211/230), the module answered at least one question the respondent would have asked their medical team.

CONCLUSIONS: As fertility providers struggle to manage increased patient load and the complexities of genetic testing, digital tools can play an important role in the patient education and informed consent process. The results of this survey demonstrate the ability of digital tools to enhance patient education and improve the patient experience, with more than 70% of respondents (73.8%) reporting increased satisfaction with their overall care after completion of the modules. The average comprehension score for patients was 92%, which is evidence of patients' ability to absorb and retain the information. Digital platforms like the one studied here may be an effective way to improve the patient experience while reducing provider burden and time constraints. Further investigation of their utility for topics beyond PGT is warranted.

MALE FACTOR

O-67 9:40 AM Sunday, October 18, 2020

INCREASED RISK FOR CONGENITAL MALFORMATIONS IN RELATIVES OF MEN WITH POOR SEMEN QUALITY: EVIDENCE FROM THE UTAH POPULATION DATABASE (UPDB). Darshan P. Patel, MD,[1] Joshua J. Horns, PhD,[1] Stevie Kinnear, BS,[2] Heidi A. Hanson, PHD, MS,[1] Kelli X. Gross, MD,[1] Alexander W. Pastuszak, MD, PhD,[1] Ken R. Smith, PhD,[3] James Hotaling, MD.[4] [1]University of Utah Health Salt Lake City, UT; [2]Huntsman Cancer Institute, Salt Lake City, UT; [3]University of Utah, Salt Lake City, UT; [4]University of Utah School of Medicine Andrology and IVF Laboratories, Salt Lake City, UT.

OBJECTIVE: Male reproductive health is a marker of individual somatic health and more recently has been associated with familial health. Familial studies offer a unique opportunity to quantity the effect of genetic and shared environmental exposures on male subfertility and birth outcomes. We have previously shown an increased risk of death from congenital malformations (CM) in relatives of men with lower semen parameters. We examine the association between markers of poor semen quality in men presenting for

infertility workup and any CM in their relatives, within the Utah Population Database (UPDB).

DESIGN: This is a retrospective, population-based, cohort analysis of subfertile men who underwent semen analysis (SA) at our centers for infertility workup (cases). Their clinical records have been linked to the UPDB as part of the Subfertility, Health, and Assisted Reproduction (SHARE) study and with age-matched, fertile male controls drawn from the UPDB (5:1 ratio).

MATERIALS AND METHODS: Relatives of cases and controls were identified using the familial relationship data in the UPDB. CMs were identified using diagnosis data from the Utah Birth Defects Network, birth certificate data, statewide inpatient and ambulatory surgery records, and electronic medical records. Presence of a CM in first-degree relatives (FDR), second-degree relatives (SDR), and first-cousins (FC) were identified through logistic regression analyses among men presenting for SA as part of infertility work-up compared to age-matched, fertile controls. Total motile count (TMC) was categorized by quartiles and sperm concentration and sperm count were each categorized by World Health Organization reference criteria. Separate logistic regression models were estimated for each semen parameter and relative type (FDR, SDR, and FC) to test the association between case-control status and CMs in relatives.

RESULTS: We identified 13,628 men with SA who presented for infertility evaluation, who were matched to 68,140 age-matched, fertile controls. Male relatives had excess risk of a CM compared to female relatives among cases and controls. FDR of men with low TMC (1st quartile), oligospermic for sperm count, or oligospermic for sperm concentration, had an elevated risk of a CM (OR: 1.28 (95%CI: 1.11-1.47); OR: 1.31 (95%CI: 1.10-1.56); OR: 1.25 (1.04-1.49), respectively when compared to fertile controls. There was no significant risk difference for a CM between relatives of azoospermic, normospermic, or hyperzoospermic men or of men in the 2nd, 3rd, or 4th quartiles for TMC and relatives of fertile population controls.

CONCLUSIONS: We found that FDR of men with poor semen quality had a higher risk of CM. This suggests that genetic and epigenetic factors leading to subfertility, in addition to shared environmental exposures, may increase the risk for adverse birth outcomes.

O-68 9:55 AM Sunday, October 18, 2020

MALE INFERTILITY TESTING AND DIAGNOSES REMAIN INFREQUENT FOR INFERTILE COUPLES. Jesse Benjamin Persily, BA,[1] Sameer Thakker, BA,[1] Paxton E. Voigt, BA,[1] Bobby B. Najari, MD MSc.[2] [1]NYU Langone School of Medicine New York, NY; [2]New York University School of Medicine, New York, NY.

OBJECTIVE: To characterize the population of men specifically undergoing infertility testing using a nationally representative survey of the US male population, with a focus on the burden of male infertility diagnoses.

DESIGN: Secondary analysis of the 2011-2017 male responses of the National Survey for Family Growth (NSFG).

MATERIALS AND METHODS: We used the provided sample weights and the complex sample analysis required by the NSFG survey design. All men who sought any medical advice to conceive were included. We looked at the proportion of men who specifically underwent infertility testing. We then looked at the demographic and healthcare utilization characteristics of the men who had received a specific infertility diagnosis, which included low sperm count, varicocele, genetic disorders that alter sperm production, low testosterone, and other infertility diagnosis. We compared men who received a fertility diagnosis to the general population of men who had fathered at least one child using univariate and multivariate logistic regression. Significance was set at $p < 0.05$.

RESULTS: Of the 13,861 men surveyed, 643 sought medical help with their partner to have a baby. In 305 cases, the male underwent infertility testing. Applying the NSFG sample weights, 3,486,602.9 couples (95% Confidence Interval: 3,026,890.3-3,946,315.6), or 6.6% (95%CI: 5.9-7.4) of the population sought medical advice to have a baby, but of these couples, only 53.1% (95%CI: 47.6-58.4) of the men received infertility testing. Of the men who received testing, 30.5% (95%CI: 23.5-38.5) were given at least one specific infertility diagnosis. 25.8% (95%CI: 19.1-32.4) were diagnosed with low sperm count, 3.7% (95%CI: 1.0-13.3) were diagnosed with varicocele, 0.6% (95%CI: 0.0-3.8) were diagnosed with a genetic disorder affecting sperm production, and 3.5% (95%CI: 0.8-9.9) were diagnosed with low testosterone. Comparing men who received an infertility diagnosis to men who had completed a pregnancy, income, marital status, race, education level, whether or not they had a usual place for healthcare, and insurance status were significantly different between the groups. However, on multivariate analysis, only income ($p<0.001$) and marital status ($p=0.001$) remained significantly difference. The men who had received infertility diagnoses had a higher income and were 6.67 times more likely to have been married than not married.

CONCLUSIONS: Despite the fact that male-factor infertility has been implicated in up to 50% of infertile couples, only half the men seeking help to have a child undergo infertility testing. Very few men are being diagnosed with conditions that are quite common in the infertile male, such as varicocele. The men who ultimately receive infertility diagnoses are wealthier and more likely to be married, and thus, analyses that look at men who have presented to an infertility specialist may not be representative of the national infertile population.

O-69 10:10 AM Sunday, October 18, 2020

ICSI OUTCOMES USING SPERMATOZOA WITH OPTIMAL GENOMIC INTEGRITY. Alessandra Parrella, M.Sc., Danielle Rebecca Tavares, B.A., June Wang, B.A., Mounia Haddad, M.D., Philip Xie, B.S., Derek Keating, B.A., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To test whether selecting spermatozoa with an intact genome enhances implantation and pregnancy rates in couples undergoing ICSI.

DESIGN: During the past 3 years, semen specimens from consenting men with prior ICSI failure were screened for sperm chromatin fragmentation (SCF) and double-stranded DNA breaks (DSBs). These tests were performed on raw specimens that were processed by density gradient centrifugation (DGC) and microfluidic sperm selection (MFSS). Couples underwent subsequent ICSI cycles with MFSS processing in order to select spermatozoa with the highest genomic integrity. Embryological and pregnancy outcomes were recorded in the study groups and compared to the historical cycles.

MATERIALS AND METHODS: Consenting men underwent standard semen analysis according to WHO 2010 criteria. DGC and MFSS were used to select spermatozoa with the highest portion of progressively motile spermatozoa. SCF was assessed by terminal deoxynucleotidyl transferase dUTP nick-end labeling (TUNEL) on at least 500 spermatozoa utilizing a threshold of $\leq$15%. DSBs were measured by a neutral Comet assay using a modified in-house protocol which assessed at least 200 spermatozoa per patient considering a normal threshold of $\leq$3%. ICSI was performed in the standard fashion.

RESULTS: A total of 63 men with an average age of 41$\pm$10 years had the following average semen parameters: concentration of 26$\pm$31 x 10^6/mL, 33$\pm$14 motility, and 2$\pm$1% morphology. After DGC and MFSS, the sperm concentration was 18$\pm$23 and 8$\pm$13 x10^6/mL, with 55$\pm$33% and 97$\pm$9% motility ($P<0.0001$), respectively. The morphology remained 2$\pm$1% after DGC, and improved to 3.2$\pm$1% after MFSS ($P<0.001$). The SCF decreased from 24$\pm$8% in the raw samples to 19$\pm$10% following DGC, and fell to 1.7$\pm$1% after MFSS processing ($P<0.0001$). DSB rates were 4.1$\pm$1% in the raw samples, 3.3$\pm$2% after DGC, and only 0.3$\pm$0.1% after MFSS ($P<0.0001$). Men (n=39; 42$\pm$7 years) who underwent ICSI with their female partners (38$\pm$3 years) had an average SCF and DSB rate in their raw sample of 23$\pm$9% and 3.9$\pm$1.5%, respectively, which fell to 19$\pm$2% and 3.2$\pm$3% after DCG selection, and dropped to only 1.4$\pm$1% and 0.2$\pm$0.1% after MFSS ($P < 0.0001$). These couples underwent 25 reference ICSI cycles with DGC sperm selection and achieved a fertilization rate of 60.5% (98/162). The implantation rate was only 2.1% (1/47) with a clinical pregnancy rate of 5.0% (1/20), resulting in a pregnancy loss. These couples subsequently underwent 48 ICSI cycles with MFSS and achieved a fertilization rate of 73.1% (333/455; $P<0.01$). The implantation rate rose to 27.3% (26/95; $P<0.001$) and the clinical pregnancy rate increased to 53.3% (24/45; $P<0.001$), resulting in 46.6% (21/45) ($P<0.0001$) of deliveries/ongoing pregnancies.The pregnancy loss rate was 12.5% (3/24).

CONCLUSIONS: According to our study, SCF is strongly correlated with sperm motility. MFSS is the only device capable of yielding the highest portion of progressively motile spermatozoa that therefore have the least amount of DNA damage. Spermatozoa with an intact genome are associated with improved embryonic development and implantation rates in couples undergoing ICSI.

SUPPORT: None

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MALE FACTOR INFERTILITY AND PLACENTAL PATHOLOGY IN LIVE BIRTHS CONCEIVED WITH IN VITRO FERTILIZATION. Roisin Ryan, MB BCH BAO,[1] Caitlin R. Sacha, MD,[2] Kaitlyn E. James, PhD,[3] Drucilla J. Roberts, MD,[1] Charles L. Bormann, PhD,[3] Irene Souter, MD.[2] [1]Massachusetts General Hospital Boston, MA; [2]MGH Fertility Center, Harvard Medical School, Boston, MA; [3]Massachusetts General Hospital, Harvard Medical School, Boston, MA.

OBJECTIVE: Recent research has highlighted the role of paternal genetics in the makeup of the trophoblast. However, there is little data available on whether male factor infertility affects placental pathology. This study aimed to analyze the effect of male infertility status on placental pathology from live births arising from in vitro fertilization.

DESIGN: This was a retrospective cohort study of 1035 live births with placental pathology arising from autologous in vitro fertilization cycles performed at MGH Fertility Centre between 2004 and 2017.

MATERIALS AND METHODS: Placental pathology was reported as anatomic, infectious, inflammatory, or vascular/thrombotic. Primary outcomes were differences in placental pathology between live births arising from cycles of couples with and without male factor infertility. Male factor infertility was defined as having a total motile count of less than 15 million, with severe cases less than 5 million, in a pre-IVF semen analysis. Demographic, cycle and placental outcomes were compared with chi square tests, Student's t-tests or non-parametric tests, as appropriate. Multivariate logistic regression models were used to compare placental pathology between groups, adjusting for maternal age, race, BMI, gestational age at delivery, number of fetuses born, number of embryos transferred, transfer type, fertilization method

RESULTS: 1035 cycles were included in this analysis, 145 of which were from couples with a diagnosis of mild male factor infertility and 192 from couples with a diagnosis of severe male factor infertility. There were no differences in maternal age (p=0.083), maternal race (p=0.35) or ethnicity (p=0.37), nulliparity status (p=0.31), hormone measurements (D3 FSH (p=0.67), AMH (p=0.32) or peak estradiol (p=0.81) levels) across groups. There were no significant differences in IVF stimulation protocols (p=0.07) or numbers of embryos transferred per cycle (p=0.73) between groups. Mild and severe male factor infertility groups were significantly more likely to have ICSI as part of their fertilization method (p<0.001). Gestational age at delivery (p=0.07) and median birthweight (p=0.94) did not differ significantly between groups. Measured obstetric outcomes including mode of delivery (p=0.16), postpartum hemorrhage (p=0.38) and hypertensive disorders (p=0.63) were not significantly different between groups. There was no difference in placental pathology outcomes between couples with or without a male factor infertility diagnosis.

CONCLUSIONS: Male factor infertility status was not significantly associated with placental outcomes amongst this cohort. In the setting of an increasing prevalence of male-factor infertility, further prospective research is needed to reproduce and validate this finding.

SUPPORT: None

O-71 10:40 AM Sunday, October 18, 2020

RELATIONSHIP BETWEEN SEMEN PARAMETERS AND PATERNAL ORIGIN OF ANEUPLOIDY. Marissa L. Luck, MD,[1] Dana B. McQueen, MD, MAS,[1] Rachel Ruderman, MD, MPH,[1] Lydia Hughes, MD,[1] Melissa K. Maisenbacher, M.S.,[2] Christina E. Boots, MD, MSCI,[1] Eve C. Feinberg, M.D.[1] [1]Northwestern University, Chicago, IL; [2]Natera, San Carlos, CA.

OBJECTIVE: To evaluate the relationship between semen analysis parameters and embryonic aneuploidy of paternal origin.

DESIGN: Retrospective Cohort Study.

MATERIALS AND METHODS: Institutional Review Board approval was obtained. All in vitro fertilization (IVF) cycles utilizing preimplantation genetic testing for aneuploidy between 1/2015 and 1/2020 were reviewed. The World Health Organization 2010 criteria were used to evaluate semen parameters. The paternal aneuploidy rate was the number of embryos with paternal aneuploidy or mixed aneuploidy (maternal and paternal aneuploidy) divided by the total number of embryos tested. Continuous variables were compared with a student's t-test and categorical variables with a Chi-square.

RESULTS: A total of 1,245 IVF cycles were included; 617 cycles in men with normal semen parameters and 628 cycles in men with abnormal semen parameters. The parental origin of aneuploidy was available for 453 cycles and 1,720 embryos. The mean paternal age (38 years, SD 4.9), maternal age (36.6 years, SD 3.8), maternal body mass index (24.8 kg/m^2, SD 5.0), number of oocytes retrieved (15.8, SD 9.1), and number of blastocysts biopsied (3.8, SD 2.9) were not different between the two groups. Neither embryonic aneuploidy rates (50.3% vs 50.1%, P=0.48) nor paternal origin of aneuploidy (8.8% vs. 8.0%, P=0.54) were different between groups. Furthermore, there was no difference in the paternal aneuploidy rate between men with normal and abnormal sperm concentration, total count, motility or morphology (Table). There was also no difference in mean sperm concentration, total count, or morphology among cycles resulting in ≥50% (N=31) or cycles with 100% paternal aneuploidy (N=10), compared to cycles with 0% paternal aneuploidy (N=332). Male partners with cycles resulting in 50% or 100% paternal aneuploidy had a higher mean motility (60.5% and 66.8%), compared to cycles with 0% paternal aneuploidy (53.2%).

CONCLUSIONS: There was no association between semen analysis parameters and paternal aneuploidy rates. Couples with male factor infertility can be reassured that abnormal semen parameters are not associated with increased aneuploidy rates due to the male contribution.

Semen analysis parameters	Paternal aneuploidy rates per embryo tested		
	Normal	Abnormal	p-value
Semen analysis (any parameter)	8.8% (75/854)	8.0% (69/866)	0.54
Concentration (15 mil/ml)	8.7% (121/1390)	7.0% (23/330)	0.20
Total count (39 million)	8.5% (105/1238)	8.1% (39/482)	0.85
Motility (40%)	8.8% (127/1438)	6.0% (17/282)	0.13
Progressive motility (32%)	8.7% (122/1401)	6.9% (22/319)	0.32
Morphology (4%)	9.0% (88/979)	7.8% (40/515)	0.44
Severe oligo/ azoospermia (5 mil/mL)	8.6% (134/1567)	6.5% (10/153)	0.45

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THE RELATIONSHIP BETWEEN PATERNAL BODY MASS INDEX (BMI) AND PATERNAL ANEUPLOIDY RATES. Lydia Hughes, MD,[1] Dana B. McQueen, M.D., M.A.S.,[1] Rachel Ruderman, MD, MPH,[1] Marissa Luck, M.D.,[1] Melissa K. Maisenbacher, M.S.,[2] Eve C. Feinberg, M.D.,[1] Christina E. Boots, MD, MSCI.[1] [1]Northwestern University Chicago, IL; [2]Natera, San Carlos, CA.

OBJECTIVE: To examine the association between paternal BMI and embryonic aneuploidy of paternal origin.

DESIGN: Retrospective Cohort.

MATERIALS AND METHODS: Institutional Review Board approval was obtained. All in vitro fertilization (IVF) cycles utilizing preimplantation genetic testing between 1/2015 and 1/2020 were reviewed. Obesity was defined as a BMI ≥30 kg/m^2. Embryonic aneuploidy and paternal aneuploidy rates were compared between non-obese and obese male partners. Continuous variables were compared with a student's t-test and categorical variables with a Chi-square. Multivariable regression analysis was used to control for potential cofounders.

RESULTS: A total of 1089 IVF cycles were included; 855 cycles in men with a BMI < 30 and 234 cycles in men with a BMI ≥30. There was no significant difference in female age, anti-mullerian hormone (AMH), or number of blastocysts biopsied between groups. The non-obese group did have a significantly lower paternal age, lower maternal BMI, and a greater number of oocytes retrieved (Table). The embryonic aneuploidy rate was not different between non-obese and obese men, 50.1% versus 51.9%, P=0.37. The parental origin of aneuploidy was available for 399 cycles. The paternal aneuploidy rate was not different between non-obese and obese men, 7.9% versus 9.1%, P=0.5. In addition, there was no difference in paternal BMI among cycles with ≥50% (N=27) or 100% (N=9) paternal aneuploidy, compared to 0% (N=288) paternal aneuploidy,

All values in: Result (SD)	Paternal BMI < 30 (N=855 IVF cycles, 3292 embryos tested)	Paternal BMI > 30 (N= 234 IVF cycles, 835 embryos tested)	P-value
Paternal Age, yr	38.4 (5.1)	39.4 (5.4)	0.009*
Paternal BMI, kg/m^2	25.7 (2.5)	33.4 (3.5)	< 0.0001*
Maternal Age, yr	36.5 (3.9)	36.9 (3.4)	0.15
Maternal BMI, kg/m^2	24.1 (4.6)	27.0 (6.3)	< 0.0001*
AMH, ng/mL	3.0 (2.6)	2.8 (2.5)	0.29
Day 3 FSH, mIU/ml	8.0 (7.6)	8.1 (2.6)	0.84
Days of Stimulation	10.6 (1.6)	10.5 (1.5)	0.39
Peak E2, pg/ml	2466.9 (1463.4)	2177.6 (1215.3)	0.006*
Oocytes Retrieved	16.2 (9.5)	14.7 (7.6)	0.03*
Mature Oocytes	10.9 (7.5)	10.3 (6.4)	0.26
Fertilized Oocytes	9.1 (6.3)	8.8 (5.4)	0.51
Blastocysts Biopsied	3.9 (2.9)	3.6 (2.7)	0.16
Aneuploidy Rate per Embryo	50.1% (1649/3292)	51.9% (433/835)	0.37
Paternal Aneuploidy Rate per Embryo	7.9% (96/1209)	9.1% (30/328)	0.50

BMI 28.6 kg/m^2 ± 5.3 and 27.5 kg/m^2 ± 4.5 versus 27.5 kg/m^2 ± 4.1, respectively. After a multivariable linear regression to control for paternal age, maternal BMI and oocyte number; paternal BMI was not associated with paternal aneuploidy.

CONCLUSIONS: There was no significant difference in overall aneuploidy or paternal aneuploidy between non-obese and obese men. Thus, our findings are reassuring that paternal obesity is not associated with paternal aneuploidy rates.

PREIMPLANTATION GENETIC TESTING

O-73 9:40 AM Sunday, October 18, 2020

A MULTI-CENTER, PROSPECTIVE, BLINDED, NON-SELECTION STUDY EVALUATING THE PREDICTIVE VALUE (PV) OF AN ANEUPLOID DIAGNOSIS WITH PGT-A AND THE IMPACT OF BIOPSY. Ashley W. Tiegs, MD,[1] Xin Tao, Ph.D,[2] Yiping Zhan, Ph.D,[3] Christine V. Whitehead, BSN, RN,[4] Emre Seli, MD,[1] George Patounakis, MD, PhD,[5] Jacqueline Gutmann, MD,[6] Arthur J. Castelbaum, MD,[7] Thomas Kim, MD,[8] Chaim Jalas, N/A,[2] Richard Thomas Scott, Jr., MD.[1] [1]IVI RMA New Jersey Basking Ridge, NJ; [2]Foundation for Embryonic Competence, Basking Ridge, NJ; [3]The Foundation for Embryonic Competence, Basking Ridge, NJ; [4]IVI-RMA New Jersey, Basking Ridge, NJ; [5]IVI-RMA, Florida, Lake Mary, FL; [6]IVI-RMA, Philadelphia, Philadelphia, PA; [7]IVI-RMA Philadelphia, Philadelphia, PA; [8]IVI-RMA Southern California, Los Angeles, CA.

OBJECTIVE: Two concerns regarding PGT-A are: 1) embryos labeled aneuploid may be reproductively competent and thus may be wrongfully discarded, and 2) trophectoderm (TE) biopsy may have an adverse effect on embryo reproductive potential. This study addresses these concerns by 1) directly measuring the predictive value (PV) of an aneuploid PGT-A diagnosis, and 2) comparing sustained implantation rates (SIR) of the study group to a control group, in which biopsy/ PGT-A were not utilized.

DESIGN: Prospective, blinded, multi-center non-selection study.

MATERIALS AND METHODS: 1) We first conducted a prospective, blinded, multi-center non-selection study in which all participants (n=402) underwent ICSI and blastocyst culture. Blastocysts underwent TE biopsy followed by vitrification. In the next cycle, patients underwent single embryo transfer (SET) of the best embryo selected solely on morphology. PGT-A analysis (targeted amplification, NGS-based) was performed only after the clinical outcome was known. Clinical outcomes were compared to PGT-A results to calculate the PV of an "aneuploidy" diagnosis. 2) To determine the impact of the biopsy, the SIR of the patients in the non-selection study (n=484 transfers) was compared to that of a control group (n=1208) undergoing cryo-SET not using PGT-A. As neither had access to PGT-A results, the groups differed only in that embryos in the study group had undergone TE biopsy.

RESULTS: 1) In the non-selection study, PGT-A analysis of the TE samples diagnosed 102 (out of 484 transferred) as "aneuploidy." The SIR of embryos diagnosed as aneuploidy was 0% (0/102) (binomial proportion 95% CI 0-2.4%); therefore, the PV of an aneuploidy result for failure to deliver was 100%. The PV for a euploid result to predict SIR was 64.7% (p<0.001). 2) When compared to the control group (n=1208) who underwent cryo-SET without biopsy or PGT-A, the mean SIR of all patients in the non-selection study group (including all euploid and aneuploid transfers) was not different (47.9% versus 45.8% (OR 1.17 (95% CI 0.93-1.46)); p=0.17), demonstrating no detectable detrimental effect of the TE biopsy.

CONCLUSIONS: The PGT-A assay evaluated does not result in the discard of embryos with significant reproductive potential. Additionally, the TE biopsy has no detectable adverse impact on sustained implantation. Overall, these data support the safety and benefit of utilization of this PGT-A assay.

PGT-A Diagnosis	Ongoing Pregnancy/ Delivered	Failed or No Pregnancy	Total	Sustained Implantation (%)
Aneuploid	0	102	102	0.0%
Euploid	202	110	312	64.7%

SUPPORT: IVI-America, Foundation for Embryonic Competence

O-74 9:55 AM Sunday, October 18, 2020

IDENTITY MARKER ANALYSIS DEMONSTRATES THAT MOST INITIAL AND RE-BIOPSY PAIRS ARE CONCORDANT. Lauren Walters-Sen, PhD, FACMG, Dana Neitzel, MS, CGC, Sara L. Bristow, PhD, Asia D. Mitchell, PhD, Charlene A. Alouf, PhD HCLD, Swaroop Aradhya, PhD, FACMG. Invitae San Francisco, CA.

OBJECTIVE: To determine the identity marker concordance rate between initial embryo biopsies and re-biopsies in the context of preimplantation genetic testing for aneuploidy (PGT-A).

DESIGN: Failure to obtain an actionable result is one limitation of PGT-A independent of the testing platform. "No-results" can be categorized into two groups, 1) those with failed amplification (FA) or 2) indeterminate (IND) samples for which data from the amplified DNA is uninterpretable. An alternative to discarding or transferring no-result embryos is to re-biopsy for repeat screening. Since the process from biopsy to PGT result is not fully automated, the potential for labeling error exists due to the multiple steps involved. To determine the rate of error, we retrospectively compared single nucleotide polymorphisms (SNPs) between initial biopsy and re-biopsy material to determine identity concordance rates.

MATERIALS AND METHODS: In total, 2350 trophectoderm biopsies from previous no-result embryos from 106 IVF centers were submitted for re-analysis. Samples were analyzed using FAST-SeqS, an NGS-based assay enhanced with genome-wide SNPs (>10,000). For 2079 biopsy pairs, SNP genotypes were compared between the rebiopsy sample and all samples submitted in the initial case to determine concordance rates; data were then stratified into three categories: full match, sibling, or unrelated.

RESULTS: Actionable results were obtained in >95% of all re-biopsies (2246 of 2350). There was no apparent difference in the ability to obtain results when broken down by result type (FA or IND) or biopsy day. With an average egg age of 35 years, more than half (58%; 1317/2246) of re-biopsies with results were euploid.

Identity marker concordance analysis was performed for 2079 biopsy pairs (FA=1118; IND=961). The majority of initial IND samples had ample SNP data to determine full matches; 98.44% of biopsy pairs were full matches (946/961). For initial FA samples with limited SNP data, full matches between biopsy pairs could not be determined; 98.57% were consistent with a sibling match (1102/1118).

Of the 31 discordant re-biopsy pairs, 16 were unrelated, while 15 were identical matches to a different embryo number from the original biopsy set (sibling).

CONCLUSIONS: Ninety-five percent of re-biopsies yielded actionable results and despite the additional work and expense for the clinic, it is important that these embryos be identified as no-results, rather than be potentially resulted as abnormal, to avoid discarding embryos that may lead to a normal live birth.

As expected, our analysis confirmed that the majority of re-biopsies are in fact taken from the same embryo as the original biopsy. However, it is important to note that ~2% indicate a sample swap, thus identifying room for labeling and workflow improvement on both the IVF lab and PGT-A lab to reduce the likelihood of incorrect embryo assignment. The incorporation of SNPs into a PGT-A assay has many utilities including the ability to identify polyploidy, uniparental isodisomy, as well as to confirm sample identity matches.

References: NA

SUPPORT: All authors are employees and stockholders of Invitae.

O-75 10:10 AM Sunday, October 18, 2020

DO WE STILL NEED TO DEPRIORITIZE THE TRANSFER OF 'LOW GRADE MOSAIC EMBRYOS'?

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OBJECTIVE: The efficiency of PGT-A is currently the subject of great debate for possible embryo wastage associated with the technique. Thus, the establishment of evidence-based guidelines for transferring mosaic embryos has become a priority. In this study, we compared the clinical outcomes of over a hundred embryos diagnosed as low grade (<50%) mosaic with embryos diagnosed as euploid by Next Generation Sequencing (NGS). At the time of transfer, no prioritization of euploid embryos versus low grade mosaic embryos were applied.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Up to April 2019, our policy was to classify embryos as euploid when the percentage of normal cells in the TE biopsies was determined to be $\geq$ 50%. The genetic profiles of 896 embryos transferred in single frozen embryo transfers cycles (Jan 2018-Dec 2018) were retrospectively analyzed in order to identify those that would have been classified as mosaic if the Preimplantation Genetic Diagnosis International Society guidelines were applied. Logistic and linear regression analysis were conducted to correct the results for use of day 5 blastocyst, egg donors and gestational carriers.

RESULTS: Out of the 896 embryo transferred, 784 were euploid and 112 were mosaic (range 20-50%). Live birth rates (LBRs) were similar between euploid (58.0%) and mosaic (56.3%) blastocysts. After correction for confounders, the Odds Ratio (OR) for LBR in the mosaic group was 0.88 (95%CI 0.59-1.33, p=0.56). In the mosaic group, after stratifying by the number of chromosomes involved, the adjusted OR for LBR was 1.04 (95%CI 0.65-1.67, p=0.87) when only one chromosome was involved (n=82), and 0.65 (95%CI: 0.30-1.40) when more chromosomes (n=30) were involved, however, the difference was not significant (p=0.27). LBR was higher when a day 5 blastocyst was transferred (OR 1.61, 95%CI 1.15-2.24, p=0.005) and a gestational carrier was involved (OR 1.66, 95% CI 1.21-2.28, p=0.002). The abortion rate (ABR) in the mosaic group was not higher than the ABR in the euploid group, either when one (OR 1.11, 95%CI 0.50-2.48, p=0.79) or more chromosomes were involved (OR 1.07, 95%CI 0.23-4.9, p=0.93). The biochemical pregnancies were higher, but not statistically different, when more than one chromosome was involved (OR 2.74, 95%CI 0.87-8.69, p=0.08). Finally, the birth weights (BW) were similar between euploid (7.1 $\pm$ 1.2 lb) and mosaic (7.0 $\pm$ 1.4 lb) embryos; the adjusted BW differences in the stratified population were -0.10 lb (95%CI -0.48 to 0.29, p=0.62) when one chromosome was involved and -0.23 (95%CI -0.95 to 0.48, p=0.65) when more chromosomes were involved. One therapeutic abortion was reported for each group.

CONCLUSIONS: Our results show that low grade mosaic embryos give the same results in term of LBR, AR and BW as euploid embryos. Excluding "low grade mosaic embryos" may result in a depletion of the pool of embryos to transfer, reducing the chance for the patient to take home a baby. Due to increasing evidence, the current guidelines that advise to initiate a further PGT-A cycle before considering transferring a mosaic embryo should be loosen at least for the "low grade mosaic embryos".

References: PGDIS Newsletter, May 27, 2019 PGDIS POSITION STATEMENT ON THE TRANSFER OF MOSAIC EMBRYOS IN PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A)Â Cram DS, Leigh D, Handyside A, Rechitsky L, Xu K, Harton G, Grifo J, Rubio C, Fragouli E, Kahraman S, Forman E, Katz-Jaffe M, Tempest H, Thornhill A, Strom C, Escudero T, Jie Q, Munne S, Simpson JL, Kuliev A BASED ON MATERIALS OF 18TH INTERNATIONAL CONFERENCE ON PREIMPLANTATION GENETICS, Geneva, Switzerland, April 15-18, 2019.

SUPPORT: none

O-76 10:25 AM Sunday, October 18, 2020

IVF PGT-M VERSUS NATURAL CONCEPTION WITH PRENATAL DIAGNOSIS FOR HUNTINGTON'S DISEASE: A COST-EFFECTIVENESS ANALYSIS.

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OBJECTIVE: In 2018 The American Society of Reproductive Medicine (ASRM) published an ethics committee opinion regarding the use of Preimplantation Genetic Testing for Monogenic Disease (PGT-M) for adult-onset conditions, such as Huntington's Disease (HD). We aimed to investigate if IVF PGT-M is cost-effective for heterozygous individuals with HD versus natural conception with prenatal diagnosis (PND).

DESIGN: Cost-effectiveness analysis from a societal perspective of couples, where one individual is heterozygous for HD, undergoing IVF PGT-M compared to natural conception with PND.

MATERIALS AND METHODS: A decision-analytic model using TreeAge Pro software was developed with a theoretical cohort composed of 3,851 couples which contain one individual who is heterozygous for HD and one unaffected individual. Outcomes included procedure-related loss, spontaneous abortion (SAB), termination of pregnancy (TOP), early/normal/late onset HD in addition to cost and quality-adjusted life years (QALYs) for both parents. A willingness-to-pay threshold was set at $100,000/QALY.

RESULTS: IVF PGT-M is both lower in cost and higher in effectiveness compared to natural conception with PND among couples with one heterozygous HD individual, making it the dominant strategy. All measured outcomes were lower in the IVF PGT-M strategy including 39 fewer procedure-related losses, 116 fewer SABs, 462 fewer TOPs. Most notably, in our theoretical cohort of couples, IVF PGT-M resulted in 1,079 fewer HD-affected offspring. IVF PGT-M was also associated with 45 more QALYs and a cost saving of $65,334.757. Our results were robust over a wide range of assumptions.

CONCLUSIONS: We found IVF PGT-M to be a cost-effective strategy compared to natural conception with PND when one of the individuals is heterozygous for HD. Not only can morbidity and mortality incurred by HD be mitigated for the offspring by using IVF PGT-M, this study is the first to demonstrate the cost effectiveness of utilizing IVF PGT-M for those with HD.

TABLE 1.

	IVF PGT-M	Natural Conception	Difference
Procedure-related loss*	0	39	-39
Spontaneous abortion*	77	193	-116
Termination*	0	462	-462
HD, late onset*	0	77	-77
HD, normal onset*	0	963	-963
HD, early onset*	0	39	-39
Cost (in $millions)	$97,815,708.08	$163,150,464.74	-$65,334,756.66
Effectiveness (QALYs)	156,162	156,207	+45
Strategy**	Dominant	Dominated	

* Units are outcome occurrences within this theoretical cohort.
** Dominant strategies are those that result in lower cost and higher effectiveness.

	Not Pregnant % (n)	Biochemical Loss % (n)	Clinical Miscarriage % (n)	Ectopic % (n)	Sustained Implantation/ Live Birth % (n)
MOS (n=16)	6.3% (1)	12.5% (2)	12.5% (2)	0%	68.8% (11)
SEG (n=39)	51.3% (20)	12.8% (5)	5.1% (2)	0%	30.8% (12)
Euploid (n=312)	*17.9% (56)*	*9% (28)*	*7.4%(23)*	*1% (3)*	*64.7% (202)*
Aneuploid (n=102)	*59.8% (61)*	*16.7% (17)*	*23.5% (24)*	*0%*	*0%*

SUPPORT: IVI-America, Foundation for Embryonic Competence

O-77 10:40 AM Sunday, October 18, 2020

TRANSFER OUTCOMES OF EMBRYOS WITH PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) DIAGNOSES OF UNDETERMINED REPRODUCTIVE POTENTIAL: RESULTS FROM A PROSPECTIVE, BLINDED, MULTI-CENTER NON-SELECTION STUDY.

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OBJECTIVE: In reports describing outcomes associated with transfer of whole chromosome mosaicism (MOS) and segmental abnormality (SEG) PGT-A embryos, such embryos are typically the only available for transfer. Therefore, patients in these series likely have reduced prognosis. To truly assess the reproductive potential of PGT-A MOS and SEG embryos, transfer must be performed in a non-selected manner. The present study aimed to report clinical outcomes associated with PGT-A MOS and SEG embryos after transfer in a prospective, blinded non-selection study.

DESIGN: Subset evaluation within a larger prospective, blinded, multicenter, non-selection study.

MATERIALS AND METHODS: This was a prospective, blinded, multicenter, non-selection study including couples undergoing their first in vitro fertilization (IVF) cycle. Couples with endometrial insufficiency or antral follicle count < 8 were excluded. Routine procedures included ICSI and blastocyst culture. All usable blastocysts underwent trophectoderm (TE) biopsy but transferred prior to biopsy analysis. Targeted NGS-based PGT-A was performed only once the clinical outcome of the transfer was determined. Clinical outcomes were then compared to PGT-A results. Specifically, outcomes associated with the transfer of PGT-A MOS and SEG results were evaluated.

RESULTS: In total, 402 patients underwent 484 single, frozen, blastocyst transfers (Jan 2014 - Dec 2019). Of all embryos transferred, 3.3% (n=16) were diagnosed as MOS and 8.1% (n=39) as SEG once PGT-A results were un-blinded. Clinical outcomes are described in Table 1. Outcomes associated with PGT-A euploid and aneuploid diagnoses are provided for comparison only.

CONCLUSIONS: Transfer of embryos with PGT-A diagnosis of MOS appear to result in outcomes similar to that of euploid embryos, while those with a diagnosis of SEG appear to have lower sustained implantation and live birth rates. However, due to the low incidence of MOS and SEG PGT-A results with this NGS-based assay and the resultant limited sample size, there is insufficient power to calculate predictive values associated with such diagnoses. Further research is needed.

O-78 10:55 AM Sunday, October 18, 2020

SEGMENTAL ANEUPLOIDY RATES OBSERVED IN ~192,000 BLASTOCYSTS BY FAST-SEQS SUPPORT INCLUSION IN PGT-A ASSAYS.

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OBJECTIVE: Assessing clinical impact of transferring embryos with segmental aneuploidies (SAs) identified through preimplantation genetic testing for aneuploidy (PGT-A) is difficult as not all SAs lead to miscarriage and/or birth defects. In order to support the inclusion of SAs in PGT-A assays, we analyzed the incidence and types of SAs across all chromosomes in our cohort.

DESIGN: Retrospective cohort study of PGT-A biopsy results.

MATERIALS AND METHODS: Trophectoderm biopsies were analyzed using our modified FAST-SeqS method and bioinformatics pipeline, which detects whole chromosome and segmental aneuploidies (≥10Mb), most types of polyploidy, and many instances of single chromosome uniparental isodisomy. [1-3] Similar to other PGT-A platforms, the p arms of the acrocentric chromosomes were not analyzed. SAs derived from known rearrangement carriers and complex abnormalities (gains and losses within a chromosome) were excluded. SA rates were stratified by type (deletion [del], duplication [dup]) and location, and egg age.

RESULTS: The dataset consisted of 191,855 embryos from 40,439 cycles. Mean egg age was 35 years (range 18-55 years). Of all resulted samples, 51.3% were euploid. SAs were detected in 11.2% of biopsies, of which 4.0% were observed along with at least one whole chromosome abnormality. SAs were observed across all ages including donor eggs and had no correlation with clinical indication. Dels/dups were detected on all analyzed chromosome arms and frequency was roughly correlated with size. Among individual SAs (n=26,707), whole-arm abnormalities were more common than partial-arm abnormalities, comprising 23-25% of all SAs. Of the 10 most common SAs (n=2,363), 87% were whole-arm changes primarily involving chr9, chr1, and chr7. The most common partial-arm SAs involved 7q21-q36, 11q14-q25, and Xq21-q28.

CONCLUSIONS: To our knowledge, this is the largest study reporting SA rates in blastocysts. Our data supports the observed rates of SAs reported in the literature (8-15%[4]) and demonstrates consistency across all age groups, unlike whole chromosome aneuploidy. As expected, most dels/dups involved whole chromosome arms, with larger chromosomes having more segmental events. While it is known that whole-arm dels/dups have dire clinical consequences, the field remains divided on the utility of assessing embryos for partial-arm SAs. Of the most frequent partial-arm SAs seen in our cohort, many are associated with known syndromes that cause birth defects and intellectual disability. Additionally, the most frequently observed SAs in our dataset were not only similar to those reported in blastocysts but also miscarriage tissue.[5-7] Despite the fear of discarding embryos that may result in a healthy child, the potential to cause miscarriage and/or an affected child warrants the inclusion of SA analysis in PGT-A assays.

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SUPPORT: All authors are employees and stockholders of Invitae.

REPRODUCTIVE BIOLOGY: HUMAN STUDIES

O-79 9:40 AM Sunday, October 18, 2020

INSULIN-LIKE GROWTH FACTOR 2 PROMOTES DEVELOPMENT AND FUNCTION OF MACAQUE PREANTRAL FOLLICLES DURING THREE-DIMENSIONAL CULTURE. Shally N. Wolf, B.S., Maralee Lawson, B.S., Olena Y. Tkachenko, Ph.D., Jing Xu, Ph.D. Oregon Health & Science University, Beaverton, OR.

OBJECTIVE: This study was to investigate the direct action of insulin-like growth factor 2 (IGF2) on growth and function of primate preantral follicles in vitro.

DESIGN: Rhesus macaque (Macaca mulatta) follicles were studied individually during matrix-free three-dimensional culture.

MATERIALS AND METHODS: Ovaries were obtained from adult rhesus macaques (6-9 years old; n = 3) through an institutional tissue distribution program. Preantral follicles (diameter = 140-180 um) were mechanically isolated and cultured individually in the ultra-low-attachment plate containing alpha minimum essential medium supplemented with follicle-stimulating hormone and insulin at 20% O2 for 2 weeks. Follicles were randomly assigned to two groups (12 follicles/animal/group), including (a) control media only and (b) 50 ng/mL recombinant human IGF2 supplementation. Follicle survival was assessed and follicle diameters were measured weekly by microscopy. Media samples collected at culture week 2 were assayed for anti-Mullerian hormone and inhibin B concentrations by ELISA. Data were analyzed using mixed models.

RESULTS: IGF2 addition increased preantral follicle survival rates compared with controls at week 2 (85 $\pm$ 6 versus 68 $\pm$ 3%; $P < 0.05$). Although follicle diameters were comparable between culture groups at week 1 (control versus IGF2: 181 $\pm$ 4 versus 174 $\pm$ 3 um), follicles exposed to IGF2 had greater diameters than those of controls at week 2 (248 $\pm$ 10 vs. 210 $\pm$ 7 um; $P < 0.05$). While media concentrations of anti-Mullerian hormone were not altered by IGF2 supplementation (control versus IGF2: 7 $\pm$ 1 versus 6 $\pm$ 1 ng/ml), IGF2-treated follicles produced higher levels of inhibin B relative to control follicles at week 2 (1.4 $\pm$ 0.2 versus 0.9 $\pm$ 0.2 ng/ml; $P < 0.05$).

CONCLUSIONS: These data demonstrate that IGF2 promotes survival and growth of primate preantral follicles with increased inhibin B production. IGF2 is the predominant circulating form of insulin-like growth factors in primate species, which plays a key role during antral follicle maturation by stimulating granulosa cell proliferation and theca cell differentiation. IGF2 is also produced locally by antral follicles, which can induce paracrine signaling in the primate ovary. There is evidence that preantral follicles express the type I insulin-like growth factor receptor, which mediates most of the somatomedin-like actions of IGF2. However, data on IGF2-regulated preantral follicle development are limited. Given the fact that rodents only have trace amounts of circulating IGF2, and IGF2 expression is slight and diffuse in the rodent ovary, IGF2 action on preantral follicles appears to be species-specific. The rhesus macaque model is an adequate surrogate for understanding IGF2-regulated follicular development and function in women. The study was supported by NIH/NICHD R01HD082208, P50HD071836, and NIH/OD P51OD011092.

SUPPORT: NIH/NICHD R01HD082208, P50HD071836, and NIH/OD P51OD011092.

O-80 9:55 AM Sunday, October 18, 2020

LOSS OF EXPRESSION OF THE NONCODING RNA *H19* PROMOTES SUSCEPTIBILITY TO GONADOTOXIN-INDUCED OVARIAN DNA DAMAGE. Wang Jing, MD, PhD,[1] Lu Pingping, PhD,[2] Johnson Joshua, PhD,[3] Amanda Nicole Kallen, MD.[4] [1]Beijing Friendship Hospital Capital Medical University, Beijing, China; [2]Women's Hospital, School of Medicine, Zhejiang University, Hangzhou, Hangzhou, China; [3]University of Colorado Denver, Aurora, CO; [4]Yale School of Medicine, New Haven, CT.

OBJECTIVE: Ovarian DNA damage occurs naturally with age and is exposure to gonadotoxic agents such as chemotherapylet-7 is a negative regulator of target genes and is recognized for its importance in the regulation of DNA damage genes. We have shown that let-7 is itself regulated by the long noncoding RNA *H19*; that is, *H19* binds and antagonizes let-7, releasing its targets from suppression. We therefore hypothesized that loss of ovarian *H19* can increase ovarian susceptibility to DNA damage in mice, potentially via a let-7 intermediary.

DESIGN: Basic science research.

MATERIALS AND METHODS: We first induced DNA damage with the chemotherapeutic agent doxorubicin (DXR). 8wk *H19* knockout (*H19*KO) and wild type (WT) mice (n=5) were injected with DXR or saline and ovaries isolated 48h later. Key genes involved in detection and repair of DNA damage were evaluated pre- and post-DXR. Apoptosis was evaluated with TUNEL. Timed matings were done (n=5 mice) 2m post-DXR to determine whether recovery of fertility was impaired in *H19KO* mice. We used bioinformatic analysis to predict let-7 binding sites in DNA damage genes, and transfected a human granulosa cell (GC) line with let-7 to determine whether gene expression was decreased in the presence of let-7. Results were analyzed via t-test.

RESULTS: Expression of *ATM* and *RAD51* was decreased in H1KO at baseline as compared to WT ($p<0.05$, Student's t-test). 48 hours after DXR, gH2AX protein level was increased in both KO and WT ovaries; however, the increase was significantly larger in *H19*KO mouse ovaries ($p>0.05$). Apoptosis was detected in ovarian sections with the ApopTag Fluorescein Apoptosis Detection Kit, ovaries were counterstained with DAPI. After DXR, *H19*KO ovaries exhibited increased apoptosis (as measured by TUNEL) as compared to WT. At 8 weeks, additional H19KO and WT mice were mated and litter sizes evaluated. After DXR, *H19*KO mice were infertile, with no litters born after 8 weeks (Fig.2). By comparison, WT mice exhibited reduced litter numbers and sizes but were still fertile (n=0 pups for *H19*KO vs 5 pups for WT, $p<0.05$). After bioinformatic prediction of let-7 target sites in DNA damage genes and transfection of GCs with let-7, we observed decreased *ATM, RAD51,* and *RPA2* mRNA and protein compared to control ($p<0.05$).

CONCLUSIONS: We have discovered an important role for *H19* and let-7 in ovarian aging via regulation of DNA repair. Our findings of increased ovarian DNA damage and apoptosis and complete fertility loss in *H19* null mice after DXR, along with our observation that transfection of GCs with the *H19*-regulated miRNA let-7 decreased expression of key DNA damage mediators, suggests that loss of *H19* renders the ovary more susceptible to DXR. The *H19*/let-7 pair appears to represent a novel regulatory pathway by which ncRNAs can govern the follicular response to DNA damage. Further mechanistic studies will determine whether differential ncRNA expression in the follicle microenvironment can serve as an important regulator of ovarian sensitivity to gonadotoxins.

SUPPORT: This work was supported by the Reproductive Scientist Development Program (NIH- NICHD Project #2K12HD000849-26), the American Society for Reproductive Medicine, the Albert McKern Foundation Grant, and the NIH Loan Repayment Program.

O-81 10:10 AM Sunday, October 18, 2020

NON-INVASIVE METABOLIC IMAGING OF CUMULUS CELLS TO DETECT OOCYTE MATURITY AND FERTILIZATION. Marta Venturas, M.Sc.,[1] Kishlay Kumar, PhD,[2] Xingbo Yang, PhD,[3] Dagan Wells, Ph.D.,[4] Catherine Racowsky, PhD,[5] Dan Needleman, Ph.D.[3] [1]Universitat Autònoma de Barcelona, Cerdanyola, Spain; [2]University of Oxford, Oxford, United Kingdom; [3]Harvard University, Cambridge, MA; [4]Juno Genetics, Oxford, United Kingdom; [5]Brigham and Women's Hospital, Boston, MA.

OBJECTIVE: To investigate the association between Fluorescence Lifetime Imaging Microscopy (FLIM) of metabolic function in cumulus cells and 1) oocyte maturity; and 2) fertilization potential. The over-arching objective of this work is to determine whether metabolic function of cumulus cells can non-invasively detect maturity and fertilization of the corresponding oocytes. And to determine whether these metabolic parameters are correlated with maternal age and BMI.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: Cumulus cell clusters (n=422 from 212 patients; mean age 35.9 y, mean BMI 26.9 kg/m^2) were dissected from the

cumulus oocyte complexes prior to assisted reproduction treatments. Maturity and fertilization status of the corresponding enclosed oocytes were tracked. 60 samples were associated with immature oocytes and 362 with mature oocytes. 282 oocytes resulted in 2 pronuclei zygotes and 36 oocytes did not fertilize. Cumulus cell metabolic function was assessed non-invasively using FLIM to measure the autofluorescence of NADH and FAD+, endogenous coenzymes essential for cellular respiration and glycolysis. Quantitative information was obtained on 1) metabolite concentrations from fluorescence intensity; and 2) metabolite enzyme engagement from fluorescence lifetimes. Each FLIM measurement provides a total of 9 quantitative metabolic parameters (4 for NADH, 4 for FAD+ and Redox Ratio: NADH intensity /FAD+ intensity). These cumulus cell metabolic parameters were compared with oocyte maturity, oocyte fertilization status and patient age and BMI using multi-level generalized linear models providing information of cumulus variance within and between patients.

RESULTS: We found statistically significant correlations regarding both cumulus cell NADH metabolic parameters ($p<0.05$) and the Redox Ratio ($p=0.001$) and oocyte maturity. FAD+ intensity and fraction bound to enzyme displayed significant variation between cumulus cells associated with fertilized compared to unfertilized oocytes ($p<0.05$). All metabolic parameters of cumulus cells were significantly correlated with maternal age ($p<0.05$), but not with BMI.

CONCLUSIONS: Metabolic imaging can non-invasively detect significant metabolic variations in cumulus cells between mature and immature oocytes, suggesting the potential utility of this technique in a clinical setting. These metabolic parameters were also associated with oocyte fertilization potential and clinically relevant factors, such as maternal age, but not BMI. Moreover, we are in the process of developing machine learning based algorithms combining patient characteristics and cumulus cell FLIM data to predict the maturity of the corresponding oocyte.

SUPPORT: NIH RO1 (5R01HD092550-02).Â Becker and Hickl GmbH, and Boston Electronics sponsored research with the loaning of equipment for FLIM.

O-82 10:25 AM Sunday, October 18, 2020

ENDOMETRIAL MITOCHONDRIAL DNA SECRETED IN EXTRACELLULAR VESICLES: A NOVEL MATERNAL MECHANISM MODULATING EMBRYO BIOENERGETICS.

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OBJECTIVE: To investigate endometrial extracellular vesicles (EV) mitochondrial DNA (mtDNA) cargo internalization by the embryo as a potential mechanism by which the maternal endometrium modulates embryo bioenergetics.

DESIGN: Secreted EVs [apoptotic bodies (ABs), microvesicles (MVs) and exosomes (EXOs)] were isolated and characterized from endometrial fluid (EF) from fertile donors (n = 10) in their receptive phase. EVs populations originating from the same EF sample were evaluated in a paired design. The potential for EVs to transfer DNA from the mother to the embryo and to modify embryo energetics through ATP modulation was also investigated.

MATERIALS AND METHODS: MtDNA copy number was quantified in receptive endometrium by qPCR ratio of *β-ACTIN* (nuclear) to *ATP8* (mitochondrial) genes, and changes in metabolic gene set were studied using targeted RNAseq (Ion AmpliSeq Transcriptome Human Gene Expression Core Panel). Maternal endometrial EV DNA cargo tagged with 5-ethynyl-2'-deoxyuridine was followed by confocal imaging after co-incubation of EVs with murine embryos (n = 600). In the presence or absence of maternal EVs, embryo ATP levels was assessed by FLASC luciferase reporter system (n = 250 embryos).

RESULTS: Receptive-phase endometrium had lower mtDNA content (92 +/- 31 mtDNA relative to nuclear DNA content, versus 219.37 +/- 56 in pre-receptive phase) together with an upregulation of genes that promote mitophagy in vesicular compartments. The sequencing of EVs isolated from human EF revealed that MVs were 11.12 ± 0.53-fold enriched in the 13 mtDNA-encoded genes for electron transport chain complexes, and 7.1–26.7-fold enriched in transcription factor binding sites (TFBSs). Most TFBSs mapped to the mitochondrial genome associated with transcription factors (*SRF, GABP, E2F4, TR4, FOXA2, FOXA1, CTCF, GATA2, PAX5*) with roles in early embryo development, mitochondrial function and biogenesis. DNA transfer was demonstrated from EVs to embryos by internalization in the cytoplasm and nuclei of trophectoderm cells. Murine embryos incubated with EVs from human EF reduced their ATP content, being more dramatically with EXOs ($p < 0.001$). Since cellular ATP can't be stored, our results suggest a novel maternal mechanism stimulating ATP consumption by the embryo.

CONCLUSIONS: During the preconception period, endometrial mtDNA content is reduced through mitophagy. Processed mtDNA, both coding and regulatory are secreted through EVs to the EF and taken up by the embryo, where it modulates embryo energetics inducing ATP consumption by the embryo. Our results support a novel maternal mechanism modulating embryo bioenergetics in preparation for implantation.

CS & FV contributed equally.

O-83 10:40 AM Sunday, October 18, 2020

ALTERED BLASTOCYST METHYLOME AND IMPRINTING DYSREGULATION ASSOCIATED WITH THE PROLONGED DISEASE STATE OF INFERTILITY.

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OBJECTIVE: The increased incidence of rare imprinting disorders in children born following infertility treatments has led to questions regarding the origin of this observed epigenetic dysregulation. Epidemiological studies suggest that the underlying disease state and severity of infertility plays a significant role. Imprinting disorders frequently arise from DNA methylation errors at imprinting control regions (ICRs), leading to our investigation of the euploid blastocyst methylome in association with duration of infertility (time to pregnancy; TTP).

DESIGN: Research study.

MATERIALS AND METHODS: Surplus cryopreserved euploid blastocysts of transferrable quality (grade $\geq$3BB; n=104) were donated with IRB approval and patient consent. Blastocysts were grouped based on TTP; months of reported primary infertility prior to oocyte retrieval that resulted in a live birth (Fertile Control: 0 months, donor oocyte/donor sperm; Infertile Short: 12-24 months; Infertile Intermediate: 36-48 months; Infertile Long: $\geq$60 months). Patient demographics and total gonadotropin doses were comparable between groups. Individual blastocyst DNA underwent whole genome bisulfite sequencing (Methyl-MaxiSeq; Zymo Research) with significant methylated CpGs determined by Student's t-test adjusted using Benjamini-Hochberg FDR; $q<0.05$. Methylation validation of ICRs was performed by pyrosequencing (PyroMark Q24 Advanced; Qiagen) with significance determined by Student's t-test and one-way ANOVA where appropriate; $p<0.05$. Quantitative RT-PCR was utilized on individual blastocysts for gene expression analysis with REST 2009 Software (Qiagen) and significance determined by a pairwise fixed reallocation randomization test; $p<0.05$.

RESULTS: Prolonged TTP (Infertile Long $\geq$60 months) resulted in 6,609 significantly altered CpGs compared with blastocysts from Fertile Controls (0 months; $q<0.05$). Significant CpGs were situated at five ICRs, including *KvDMR* and *MEST*, and 36 imprinted genes, with NFAT signaling identified as the top canonical pathway (62/221 genes, q=1.28E-08). Overall, extended TTP $\geq$36 months (mean=65 months) exhibited significant hypomethylation compared to shorter TTP $\leq$24 months (mean=10 months) for *KvDMR* (39% Extended vs. 48% Shorter; $p<0.05$), *MEST* (40% Extended vs. 49% Shorter; $p<0.05$), and *H19* (29% Extended vs. 41% Shorter; $p<0.05$) while *SNRPN* trended downward without significance. Significant decreases in expression were observed for maternally imprinted genes (*KCNQ1OT1, MEST, COPG2, DNMT1*; $p<0.05$), and significant increases in expression for paternally imprinted genes (*H19*, *CDKN1C*; $p<0.05$).

CONCLUSIONS: This novel study is the first to report evidence that an extended duration of infertility correlates with altered methylation in euploid blastocysts, with a particular emphasis on genomic imprinting. Our results provide evidence to support an association between imprinting dysregulation and infertility as a prolonged disease.

O-84 10:55 AM Sunday, October 18, 2020

GENE CONVERSION IN HUMAN EMBRYOS INDUCED BY GENE EDITING. Nuria Marti-Gutierrez, PhD,[1] Dan Liang, PhD,[1] Tailai Chen, PhD,[2] Yeonmi Lee, PhD,[3] Hong Ma, PhD,[1] Amy Koski, BA,[1] Aleksei Mikhalchenko, PhD,[1] Stephen B. Heitner, PhD,[4] Eunju Kang, PhD,[5] Paula Amato, MD,[1] Shoukhrat Mitalipov, PhD.[1] [1]Oregon Health & Science University Portland, OR; [2]Shandong University, Jinan, China; [3]ASAN Institute for Life Sciences, ASAN Medical Center, Seoul, Korea, Republic of (South); [4]Oregon Health &Science University, Portland, OR; [5]ASAN Medical Center, Seoul, Korea, Republic of (South).

OBJECTIVE: Double strand breaks (DSBs) at specific loci can be efficiently induced by genome editing tools. It is believed that most DSBs are repaired by either non-homologous end joining (NHEJ) or homology directed repair (HDR) using synthetic DNA templates. Our study aims to evaluate if DNA DSBs in human preimplantation embryos also repaired by an alternative mechanism known as gene conversion (GC).

DESIGN: Pre-tested sgRNAs and Cas9 protein were co-injected into human MII oocytes or zygotes to target heterozygous *MYH7* (g.15819 C>T; NG_007884.1) and homozygous wild-type (WT) *MYBPC3* (g.9836, NC_000011.10) loci. Injected embryos were cultured for 3 days and then individual blastomeres of cleaving embryos were isolated and analyzed by sequencing at a single-cell level.

MATERIALS AND METHODS: DNA from each individual blastomere was amplified and the target region was sequenced by Sanger. Since gene conversion results in loss of heterozygosity (LOH) around target region, we evaluated the presence or loss of single-nucleotide polymorphisms (SNPs) adjacent to the target region.

RESULTS: As expected, most DSBs at the heterozygous *MYH7* locus were repaired by NHEJ (58.3%; 70/120) resulting in additional indel mutations on the mutant allele. However, remaining 41.7% (50/120) of blastomeres lost the mutant allele and were presented by the WT allele. We excluded possibility of deletions in these samples abut showed LOH at adjacent loci. When targeting both alleles at homozygous *MYBPC3* locus, we found that 40.2% (129/321) blastomeres appeared with identical indel mutations on both parental alleles, indicating that GC and NHEJ compete and interplay with each other within the same cell. In contrast, frequency of HDR via exogenous synthetic DNA templates is limited.

CONCLUSIONS: We report here that in addition to NHEJ and HDR, human embryos frequently employ an alternative repair mechanism known as gene conversion where intact endogenous homologous sequences are used as templates. While gene conversion could be applicable for gene correction, extensive LOH presents a safety concern.

REPRODUCTIVE SURGERY AND PROCEDURES

O-85 9:40 AM Sunday, October 18, 2020

ULTRASONOGRAPHIC PARAMETERS PREDICT THE IMPROVEMENT OF POSTMENSTRUAL SPOTTING IN PATIENTS UNDERGOING HYSTEROSCOPIC TREATMENT OF ISTHMOCELE. Simone Ferrero, MD PhD,[1] Franco Alessandri, MD,[2] Michele Altieri, MD,[1] Giulio Evangelisti, MD,[1] Maria Grazia Centurioni, MD,[2] Fabio Barra, MD.[1] [1]IRCCS Ospedale Policlinico San Martino Genova, Italy; [2]IRCCS Ospedale Policlinico San Martino, Genoa, Italy.

OBJECTIVE: Current literature supports a role for hysteroscopic isthmoplasty in treating isthmocele-related abnormal uterine bleeding. However, limited data is available on preoperative factors predicting successful hysteroscopic treatment. The objective of this study is to investigate the performance of bidimensional ultrasonography (TVS) and three-dimensional saline contrast sonohysterography (3D-SCSH) in predicting the improvement of symptoms in patients undergoing hysteroscopic treatment of cesarean scar isthmocele.

DESIGN: Prospective study.

MATERIALS AND METHODS: This prospective study included patients with cesarean scar isthmocele requesting hysteroscopic treatment because of postmenstrual spotting. Exclusion criteria for the study were: residual myometrium over the isthmocele (< 2.5 mm), other potential causes of abnormal uterine bleeding, previous surgical treatment of the cesarean scar defect. 3D-SCSH was performed by introducing a 5-Fr balloon catheter into the cervical canal and gently injecting saline solution into the cervical canal, niche and uterine cavity. The following parameters were assessed by TVS and 3D-SCSH: length, depth, width, residual myometrial thickness, adjacent myometrial thickness, distance between the niche and the vesicovaginal fold, distance between the niche and the external os, volume of the niche (calculated by length × depth × width × 0.52 at TVS and assessed by virtual organ computer-aided analysis at 3D-SCSH), shape of the uterine niche (assessed only by 3D-SCSH). A score number from 1 to 4 was assigned to each variable, and, for each patient, a total score was calculated for TVS and 3D-SCSH. The hysteroscopic correction of the isthmocele was performed under general anesthesia by resection of the superior and inferior edges of the defect using a resectoscopic loop and pure cutting current until reaching the muscular layer; ablation of the isthmocele base was performed. At 3-month from surgery, patient satisfaction was assessed using a 5-point Likert scale.

RESULTS: 102 patients were included in the study. The mean (± SD) age of the study population was 39.1 (± 4.3) years. The median number of previous cesarean section was 2 (range, 1-4). At 3-month follow-up, 59 patients (82.4%) were very satisfied or satisfied with the surgery. The 3D-SCSH score was superior to the TVS score in predicting patient satisfaction after surgery ($p < 0.001$). Linear regression analysis showed that patient satisfaction was significantly correlated with width ($p=0.004$), shape of the uterine niche assesed by 3D-SCSH ($p<0.001$), and the volume of the niche assesed by 3D-SCSH ($p=0.007$).

CONCLUSIONS: 3D-SCSH is superior to TVS in predicting the improvement of postmenstrual spotting following hysteroscopic treatment of isthmocele. The width, shape, and volume of the niche are associated with amelioration of the symptoms.

O-86 9:55 AM Sunday, October 18, 2020

PERSPECTIVES OF 281 PATIENTS WITH MAYER-ROKITANSKY-KÜSTER-HAUSER SYNDROME ON UTERINE TRANSPLANTATION. Nicole Mercado Fischer, MPH,[1] Helen Xun, BS,[2] Bhuchitra Singh, MD, MPH, MS,[3] James Segars, MD.[1] [1]Johns Hopkins University School of Medicine Division of Reproductive Endocrinology and Infertility, Baltimore, MD; [2]Johns Hopkins School of Medicine, Baltimore, MD; [3]Johns Hopkins University School of Medicine, Baltimore, MD.

OBJECTIVE: The aim of this study was to investigate the personal, ethical, and financial perspectives of individuals with Mayer-Rokitansky-Küster-Hauser syndrome (MRKH), a congenital uterine factor infertility condition, towards uterine transplantation (UTx).

DESIGN: Cross-sectional quantitative survey analysis.

MATERIALS AND METHODS: A 60-item anonymous electronic questionnaire was advertised to international members of the Beautiful You MRKH Foundation via social media sites (Facebook, Instagram, and Twitter). The survey contained UTx educational materials followed by questions assessing participants' baseline knowledge, global perceptions, financial concerns, and ethical considerations regarding UTx.

RESULTS: We received 281 responses (88% completion rate), with a mean participant age of 28.2 ± 9.8 years. After reviewing the UTx education material, the majority of participants considered receiving a uterine transplant (73%), felt it should be an option for all women with uterine factor infertility (86%), and believed it should be covered by health insurance (78%). Respondents perceived the benefits of the procedure to outweigh the risks (67%) and considered it to be an ethical procedure (82%). Although the majority of participants have or would consider adoption (85%) and gestational surrogacy (81%) to have children, a large percentage indicated they would prefer to give birth to their own child (79%). Almost half of participants (49%) reported a willingness to spend over $10,000 out of pocket to receive a UTx procedure. When asked to rank the risk of UTx to self, donor, and fetus in order of personal importance, (21%) ranked their own safety last.

CONCLUSIONS: The results of this analysis have important implications for the future of UTx. There is a profound desire in the MRKH community for UTx to become more widely available and affordable. MRKH patients may represent a vulnerable population requiring special considerations for informed consent and rigorous evaluation for UTx. Providers caring for MRKH patients should be prepared to educate about UTx and thoughtfully engage with news and media outlets to communicate evidence-supported information.

References: None

SUPPORT: None

O-87 10:10 AM Sunday, October 18, 2020

QUANTIFYING HETEROGENEITY OF TESTICULAR HISTOPATHOLOGY IN NON-OBSTRUCTIVE AZOOSPERMIC MEN. Nahid Punjani, MD MPH,[1] Ryan Flannigan, MD,[2] Kathleen Hart, BSN RN MA,[1] Peter N. Schlegel, M.D.[3] [1]Weill Cornell Medicine, New York, NY; [2]University of British Columbia, Vancouver, BC, Canada; [3]Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY.

OBJECTIVE: To quantify the histopathologic heterogeneity of testicular biopsies from non-obstructive azoospermic (NOA) men undergoing microsurgical testicular sperm extraction (mTESE).

DESIGN: Retrospective study of prospectively collected data.

MATERIALS AND METHODS: All patients undergoing mTESE by a high-volume surgeon at Weill Cornell in New York City between 2010 and 2019 were evaluated. Testicular histopathology from all men were reviewed. Men were included if testicular biopsy histopathology reported by the pathologist described the percentage breakdown of respective histopathologies. Men who had pathology reports without a percentage breakdown were excluded. Descriptive reports of pathology totals were reported.

RESULTS: A total of 971 men were included. The median age was 34 (IQR 30-39). Mean pathological components (Table 1) were 57.9 ± 42.9% Sertoli-Cell Only (SCO), 16.3 ± 32.6% maturation arrest (MA), 14.6 ± 25.28% tubular atrophy (TA), 8.0 ± 24.2% full spermatogenesis (SG), and 1.54 ± 8.6% germ cells (GC). A total of 411 (42.5%) had only one pathology on biopsy, 384 (39.8%) two different pathologies on biopsy, 171 (17.7%) had three or more different pathologies. Sperm retrieval rates for first time retrieval was 135/395 (34.2%) for one pathology in comparison to 246/486 (50.6%) with mixed patterns, with increasing rates of success with increasing pathologic variety. Of those with two pathologies, the most common pairs included SCO and TA (n=270, 74.7%) of which mean SCO component was 71.08 ± 29.10% and 28.26 ± 28.60% was TA, followed by MA and TA (n=26, 6.8%). Of those with three different pathologies, the most common combinations include SCO, MA and TA (n=37, 36.3%), of which mean SCO was 35.19 ± 28.38%, mean MA was 32.30 ± 31.20% and TA was 30.78 ± 24.51%, followed by MA, SG, and TA (n=23, 22.5%). Among men with KS (n=107), pathological components were 56.8 ± 48.3% Sertoli-Cell Only, 0.4 ± 2.3% maturation arrest, 0.6 ± 3.2% spermatogenesis, 33.6 ± 35.8% tubular atrophy, 0.52 ± 2.9% germ cells. For those with AZF mutations (n=17) pathological components were 53.2 ± 49.5% Sertoli-Cell Only, 38.8 ± 48.1% maturation arrest, 0.0 ± 0.0% spermatogenesis, 1.5 ± 3.4% tubular atrophy, and 6.5 ± 24.2% germ cells.

CONCLUSIONS: To the best of our knowledge, this is the first report describing the pathological breakdown of testicular histopathology in a large subset of NOA men. The most common overall pathology is SCO in our cohort, which was also the most common in KS and AZF deleted men.

O-88 10:25 AM Sunday, October 18, 2020

EVALUATING THE QUALITY OF REPORTING IN OUTCOMES OF MICROSURGICAL-TESE IN MEN WITH NON-OBSTRUCTIVE AZOOSPERMIA (NOA): A METHODOLOGICAL ANALYSIS. Brittany D. Berk, MD, John Joseph Ernandez, Jr., BA, Tracy X. Han, MD, MBA, Martin Kathrins, MD. Brigham and Women's Hospital and Harvard University Boston, MA.

OBJECTIVE: Microsurgical testicular sperm extraction (micro-TESE), since its introduction in 1999, has been demonstrated to be the optimal approach to surgical sperm retrieval for men with NOA. However, there is heterogeneity in the methodological quality of published micro-TESE approaches and outcomes.

DESIGN: We conducted a systematic methodological analysis of all published literature on the use of micro-TESE in men with NOA from 1999 to the present.

MATERIALS AND METHODS: A PubMed search was performed using the search terms "microdissection TESE" or "microsurgical TESE". Only studies on NOA patients were considered. Studies on obstructive azoospermia, case studies, and review articles were excluded. We included only the most recent publication from a given academic medical center's cohort. Adapted from previously published quality reporting criteria for prospective trials (CONSORT), we evaluated publications on their reporting of preoperative factors, intraoperative techniques, surgical and clinical outcomes, and adverse events. Two reviewers evaluated each publication for inclusion.

RESULTS: 182 articles were identified in our initial search, of which 55 met inclusion criteria. Specific reporting criteria are listed in Table 1. Surgical technique and sperm retrieval rates were the most commonly reported criteria. Reporting on the presence of an embryologist intraoperatively was observed in approximately 25% of articles, while other procedural details including method of sperm quantification, quantity retrieved, and number of cryopreserved vials were observed in fewer than 10% of articles. Clinical outcomes, including surgical complications, pregnancy rates, and live birth rates were reported in fewer than half of the articles. Fetal outcomes were rarely reported.

CONCLUSIONS: There are many inconsistencies in reporting quality of micro-TESE outcomes, specifically a lack of information on the quantity of sperm retrieved, the role of embryology intraoperatively, and clinical and fetal outcomes. Development of a reporting guideline may help standardize reported results to better assess clinical outcomes across institutions.

References: Schulz KF, Altman DG, Moher D; CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. Ann Intern Med. 2010;152(11):726-732. doi:10.7326/0003-4819-152-11-201006010-00232

SUPPORT: None

TABLE 1. Mean Percentage Breakdown of Testicular Histopathologies in NOA Men

	SCO	MA	SG	TA	GC
Overall (n=966)	57.9 ± 42.9	16.3 ± 32.6	8.0 ± 24.2	14.6 ± 25.3	1.54 ± 8.6
KS (n=107)	56.8 ± 48.3	0.4 ± 2.3	0.6 ± 3.2	33.6 ± 35.8	0.52 ± 2.9
AZF (n=17)	53.2 ± 49.5	38.8 ± 48.1	0.0 ± 0.0	1.5 ± 3.4	6.5 ±24.2

TABLE 1. Reporting Criteria

PREOPERATIVE FACTORS	INTRAOPERATIVE TECHNIQUES	SURGICAL OUTCOMES	FERTILIZATION TECHNIQUES	CLINICAL OUTCOMES
Genetic Testing	Surgical Technique	Sperm Retrieval Rate	Fresh/Frozen Sperm	Clinical Pregnancy
Diagnosis of Azoospermia	Operative Time	# of Sperm Retrieved	Method of Cryopreservation	Live Birth Rate
Hormonal Therapy	Anesthesia	Method of Quantification	# of Cryopreserved Vials	Fetal/Neonatal Anomaly
	Laterality	Adverse Events	Fertilization Rate	Growth Defects
	Embryologist in OR		Use of intracytoplasmic sperm injection	Preterm Delivery
				NICU Admission

O-89 10:40 AM Sunday, October 18, 2020

EFFECTS OF PREOPERATIVE MEDICAL TREATMENT ON SPERM RETRIEVAL RATES IN PRIMARY AND IN RECURRENT MICRO TESE CASES. Murad M. Basar, PROF. MD,[1] Hakan Kadir Yelke, MsC,[2] Gönül Özer, MD,[3] Melike Kaya-Bahcecitapar, PhD,[4] Yesim Kumtepe-Colakoglu, Msc,[2] Semra Kahraman, Prof. MD.[2] [1]MEMORIAL SISLI HOSPITAL ISTANBUL, Turkey; [2]Istanbul Memorial Hospital, Istanbul, Turkey; [3]Istanbul Memorial Hospital, İstanbul, Turkey; [4]HACETTEPE UNIVERSITY FACULTY OF SCIENCE, Ankara, Turkey.

OBJECTIVE: The aim of the present study was to evaluate the efficacy of different medical treatments in azoospermic males through comparison of the effects on sperm retrieval rate in primary and recurrent micro TESE (m-TESE).

DESIGN: This is a prospective study. A total of 1048 non-obstructive azoospermic (NOA) males were included.

MATERIALS AND METHODS: The patients were divided into two groups: Group I: Patients undergoing their first micro TESE operation (n=466) and Group II: Patients undergoing repeated m-TESE operations (n=582). A total of 623 cases were given hormone treatment, HT(+) and a total of 425 did not receive hormone treatment HT(-).
In the HT(+) group, all patients received gonadotrophine replacement, hCG, 5.000U-10,000U per week for 3 months. After 3 months, if the FSH level was suppressed, hMG, 150-225 units per week was added; if not, treatment continued with hCG. In addition, if TT/E2 ratio was less than 0.10, aromatase inhibitor of 1 mg per day was added. If, however, the patient's TT/E2 ratio was higher than 0.10, clomiphene citrate 50 mg was given daily. In all treatment groups, medication was administered for 6 to 9 months until the patients reached eugonadotropic state. Mann-Whitney U test, two sample t-test, paired-t test and Pearson's $\chi 2$ tests were used to determine the effect of medical treatment on m-TESE results. The phi correlation coefficient ($r\varphi$) is used as a measure of association for two categorical variables.

RESULTS: There was a statistically significant relationship between treatment and m-TESE variables ($\chi^2=13.19$, $p<0.001$). Spermatozoa was retrieved in 234 (55.1%) patients who had not received any treatment and in 277 (44.5%) patients who had received treatment. However, while there was no statistically significant difference in sperm retrieval between primary micro-TESE cases who had received or not received hormone treatment ($\chi^2=0.033$, $p>0.001$), there was a significantly higher sperm retrieval rate in HT(-) cases with recurrent micro-TESE. ($\chi^2=22.36$, $p<0.001$). There was no statistically significant difference between hormonal treatment types in terms of the outcome of m-TESE variable ($\chi^2=5.87$, $p> 0.05$).

CONCLUSIONS: Our results show that hormone treatment had no positive effect on sperm retrieval in NOA cases with primary and recurrent micro-TESE. Underlying etiopathologic factors and previous micro-TESE outcomes in recurrent cases are the main determinant factors.

SUPPORT: None

O-90 10:55 AM Sunday, October 18, 2020

FLUOROSCOPIC-GUIDED HYSTEROSCOPIC TUBAL CANNULATION RESULTS IN HIGH TECHNICAL SUCCESS, HIGH SPONTANEOUS PREGNANCY RATES, AND SIMILAR TIME TO PREGNANCY WHEN COMPARED TO LAPAROSCOPIC GUIDANCE. May-Tal Sauerbrun-Cutler, MD,[1] Emma Charlotte Brown, BA,[2] Gary N. Frishman, MD,[3] Phinnara Has, MS,[4] Martin D. Keltz, MD.[5] [1]Warren Alpert Medical School of Brown University; Women & Infants Hospital Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Providence, RI; [2]Brown University, Providence, RI; [3]Brown University; Women & Infants Hospital, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Providence, RI; [4]Warren Alpert Medical School of Brown University; Women & Infants Hospital, Department of Obstetrics and Gynecology, Division of Research, Providence, RI; [5]WESTMED Reproductive Services, Associate Professor at Icahn School of Medicine at Mt. Sinai, Purchase, NY.

OBJECTIVE: Tubal cannulation for proximal tubal obstruction (PTO) has historically used fluoroscopy for visualization and guidance or hysteroscopic visualization with laparoscopic guidance. This study compared women with PTO undergoing hysteroscopic tubal cannulation with fluoroscopic guidance versus laparoscopic guidance.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Infertile women with unilateral or bilateral PTO on hysterosalpingography who failed selective salpingography in the Radiology suite and had a planned hysteroscopy in the operating room for defects seen on sonohysterography were studied. All women had a Novy Catheter system® positioned hysteroscopically to cannulate the occluded fallopian tube(s). Women undergoing Fluoroscopically Guided Hysteroscopic Tubal Cannulation (FHTC) which utilized contrast and C-arm pelvic imaging at an ambulatory center were compared to those undergoing hospital based Hysteroscopic Tubal Cannulation (LHTC) with laparoscopic chromotubation. Procedural success, perforation rates, pregnancy rates and time to intra-uterine pregnancy were analyzed. T-test, Wilcoxon rank sum analysis were used to compare continuous variables and a Fisher's exact test was used for categorical variables. Kaplan Meier analysis was used to compare times to pregnancy.

RESULTS: 79 infertile women undergoing either FHTC (37 women) or LHTC (42 women) between 2017 and 2019 were included. Demographic variables were similar, though the FHTC group was older (age 37.6 vs 35.4, P =0.03). 34/37 (92%) of FHTC and 36/42 (86%) of LHTC patients had at least one tube successfully cannulated (P=0.49) and 29/37 (78%) of FHTC patients and 33/42 (79%) of LHTC patients had all occluded tubes successfully cannulated (P=0.52). Tubal perforation occurred in 2/37 (5%) FHTC cases vs. 3/42(7%) LHTC cases (p=1.0). A similar percentage of non-IVF intrauterine pregnancies were achieved in the FHTC and LHTC groups (12/37 32% and 12/42 29%, p=0.42). Two ectopics occurred in the LHTC group. Among patients who conceived without IVF, days from procedure to pregnancy was reduced in the fluoroscopically guided group compared to the laparoscopically guided group (102.9 +/-118.6 vs. 228.2 +/-216 p= .01). However, there was no significant difference in time to pregnancy when all subjects regardless of pregnancy were analyzed (hazard ratio 1.08 (95% CI 0.45, 2.57).

CONCLUSIONS: FHTC is a safe, effective, incision free procedure that results in a comparable rate of tubal patency and intrauterine pregnancies as LHTC, and may shorten the time to conception likely due to a quicker recovery. This technique should be considered in women undergoing treatment of PTO when operative laparoscopy is not otherwise indicated.

CRYOPRESERVATION AND FROZEN EMBRYO TRANSFER

O-91 1:50 PM Sunday, October 18, 2020

SUCCESSFUL PRODUCTION OF NORMAL EUPLOID HUMAN BLASTOCYSTS DERIVED FROM SPERM AFTER PARTIAL FREEZE DRYING, REHYDRATION AND ICSI: TOWARDS DEVELOPING A NOVEL METHOD FOR SAFE STORAGE OF BIOLOGICAL SAMPLES. Stoyana Alexandrova, PhD,[1] Amir Arav, PhD,[2] Kristy Hood, M.Sc,[1] Yehudit Natan, M.Sc,[2] John J. Zhang, MD, PhD,[1] Patrizio Pasquale, MD, MBE, HCLD.[3] [1]Darwin Life INC New York City, NY; [2]FertileSafe, Ltd, Ness Tziona, Israel; [3]Yale Fertility Center, Orange, CT.

OBJECTIVE: Current cryopreservation and storage methodologies have many unresolved issues including impact of cryoprotectants (CP) on cell survival, Liquid Nitrogen (LN) tank failures which may jeopardize samples integrity during storage, cumbersome and costly sample shipping. Here we aimed at replacing LN storage with ordinary freezers (-80℃) after partial sperm freeze/drying (pFD) with a CP-free solution. Rehydrated sperm were evaluated for motility and embryo competence following ICSI.

DESIGN: Prospective, experimental basic research.

MATERIALS AND METHODS: Donor sperm cryovials (n=12) were thawed and motile sperm recovered using the ESep device (FertileSafe Ltd, Israel). The separated motile sperm fractions were washed with a solution (Lyo4) containing 0.25M Trehalose and 0.25M Sorbitol in 10mL sperm wash (SW) and diluted 2:1 with SW. Volumes of 100 μL were pipetted into cooled glass vials (-25° C). Five samples were placed in the -80℃ freezer for 1 hour (frozen samples) and the other 7 samples underwent partial freeze drying (pFD). pFD was done with a lyophilizer device (Darya, FertileSafe Ltd, Israel) having preset shelf temperature at -25℃ and operated at a vacuum of <500 mTorr for 10-20 minutes. Samples were then stored at -80℃ for various time lengths (1 to 8 days). Then pFD samples were rehydrated, assessed for motility and used for ICSI with donor MII oocytes.

Thawing of frozen samples was obtained by plunging the vials in a 37℃ water bath (1 min) and sperm suspension diluted with same volume of SW.

Rehydration after pFD, was done by adding pre-warmed Sperm Wash solution (volume 1:1) at 37C to the sperm pellet.

Sperm motility was evaluated (i) at the baseline thawing after ESep preparation of the donor sperm cryovials; (ii) after Lyo4 addition and freezing/thawing and (iii) after pFD after different storage-times.

Both immotile and motile sperm after freezing/thawing and pFD were selected for ICSI of donor MII oocytes. Embryo aneuploidy screening was conducted via Non-Invasive Chromosome Screening (NICS) with DNA obtained from embryo culture media utilizing previously validated NICS platform.

RESULTS: ESep processed sperm cryopreserved at -80ºC in CP-free Lyo4 maintained had high post thaw motility (94%) at 1 hour, supporting the choice of Lyo4 as the optimal SW protocol for sperm pFD. Preliminary work (data not shown) had demonstrated that pFD-sperm without Lyo4 had no survival. Upon thawing and rehydration pFD-sperm had the following motility: 69% at 24 hrs; 43% at 7 days and 6% at 8 days.

After ICSI with immotile sperm (n=6), there were 0 fertilized oocytes and 0 blastocysts; after ICSI with motile PFD-sperm (n=13) there were 8 correctly fertilized oocytes, 6 blastocysts, 3 euploid (46XX).

CONCLUSIONS: This experiment demonstrated that sperm selected by ESep after partial freeze drying with CP-free solution maintains motility during storage at -80ºC for various lengths of time. To our knowledge this is the first report that using rehydrated motile sperm for ICSI produces human euploid blastocysts.

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EMBRYO VITRIFICATION IN SUPER COOLED SLUSH NITROGEN RESULTS IN SUPERIOR POST-THAW SURVIVAL COMPARED TO CONVENTIONAL LIQUID NITROGEN: A BLINDED, RANDOMIZED CONTROLLED TRIAL. Emily K. Osman, MD,[1] Marga Esbert, PhD,[2] Brent M. Hanson, MD,[1] Ayesha D. Winslow, MS,[3] Emre Seli, MD,[1] Richard Thomas Scott, Jr., MD.[1] [1]IVI RMA New Jersey Basking Ridge, NJ; [2]IVI RMA Barcelona, Barcelona, Spain; [3]IVI-RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: Slush nitrogen (N_2) is a mixture of solid and liquid N_2 and has a lower temperature compared to conventional liquid N_2, leading to an accelerated cooling rate. The study aim was to assess if slush N_2 for embryo vitrification is a less damaging alternative to liquid N_2 as determined by post-warming survival.

DESIGN: Blinded, randomized controlled trial.

MATERIALS AND METHODS: This study was conducted at a large infertility center from October 2019-March 2020. High quality blastocysts donated to research with a single autosomal aneuploidy, expansion grade of 4 or 5, and modified Gardner grade of BB or better were eligible. Fifty embryos were randomized to the control group and 50 to the study group. Embryos underwent repetitive vitrification-warming cycles in liquid N_2 at -196°C or slush N_2 at -210°C until deemed to have demised. One embryologist performed all cycles while a separate embryologist who was blinded to vitrification method graded embryo survival. Primary outcome was embryo survival, or the proportion of embryos surviving in good condition after each cycle. Student's *t*-test analyzed differences in oocyte age of blastocysts in each group. Chi-squared testing compared day of cryopreservation between groups. Differences in probability of survival after each freeze-thaw cycle were determined with Cox regression. Wilcoxon-rank sum testing compared the median number of survived cycles.

RESULTS: Of the 50 embryos in the liquid N_2 group, 238 vitrification-thaw cycles were performed compared to 513 cycles on 50 embryos in the slush N_2 group. Oocyte age (35.8 yrs. liquid N_2 vs 36.4 yrs. slush N_2, p =0.38) and day of cryopreservation were equivalent between groups (p =0.84). After each cycle, embryos vitrified in slush N_2 were significantly more likely to survive versus those in liquid N_2 (p <0.0001). The median number of survived cycles in the control group was 3.0 (Quartile(Q)1 1.0, Q3 3.0), compared to 7.5 in the study group (Q1 5.0, Q3 10.0), p <0.0001.

CONCLUSIONS: Blastocyst cryopreservation in slush N_2 results in superior post-thaw survival due to reduced vitrification-associated toxicity compared to liquid N_2. Use of slush N_2 for embryo cryopreservation is a promising intervention for optimization of IVF outcomes.

TABLE 1. Survival data for vitrification-warming cycles 1-10.

	Liquid N_2		Slush N_2	
Vitrification Cycle	# Survived Embryos	Survival % (95% CI)	# Survived Embryos	Survival % (95% CI)
1	41	82 (68.2-90.2)	50	100
2	31	62 (47.1-73.8)	50	100
3	24	48 (33.7-60.9)	50	100
4	12	24 (13.3-36.4)	46	92 (80.1-97.0)
5	10	20 (10.3-32.0)	40	80 (66.0-88.7)
6	8	16 (7.5-27.4)	34	68 (53.2-79.0)
7	6	12 (4.8-22.6)	27	54 (39.3-66.6)
8	3	6 (1.6-14.9)	25	50 (35.6-62.8)
9	2	4 (0.7-12.1)	23	46 (31.9-59.0)
10	1	2 (0.2-9.2)	17	34 (21.4-47.0)

p <0.0001.
N_2 = Nitrogen.
CI = Confidence Interval.

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UPRIGHT, UPSIDE DOWN, SIDEWAYS - EFFECTS OF ORIENTATION OF VAPOR SHIPPERS AND DATA LOGGERS ON HOLD TIME. William Brent Hazelrigg, M.S., Amy Suzanne Erickson Hagen, M.S. ReproTech, Ltd., Columbia, MO.

OBJECTIVE: Cryoshippers are essential for the movement of embryos. Manufacturers may sell their cryoshipper with a protective mushroom to ensure upright shipping. Labs are at the mercy of commercial transport carriers to ensure the package is kept upright. Our study presents what happens when the cryoshippers are not kept upright.

DESIGN: Prospective Experimental Design.

MATERIALS AND METHODS: In preparation for this experiment each cryoshipper (MVE Vapor Series SC4/2V; SC4/3V) was tested per MVE's annual maintenance to determine the normal evaporation rate (NER; Liters) and calculated hold time (days). Shippers from 2013 to 2015 and 2017 to 2019 were selected, fifteen SC4/2V cryoshippers and fifteen SC4/3V cryoshippers were then placed upright, horizontally or inverted. The cryoshippers were weighed daily in the respective position; temperature at the top position of the cane was continually measured using a temperature probe and wireless transmitter (Vaisala, HMT143) until the temperature reached -135 °C or 7 days*. The NER and hold time were calculated based on the weight loss of the nitrogen.

RESULTS:

	NER (Liters/Day)	Hold Time (Days)	Days to -135 °C
SC4/3V Manufacturer Stated NER (vertical)	0.20	21.00	
SC4/3V Vertical with no data logger	0.14	27.35	N\A
SC4/3V Vertical	0.29	13.79	>7*
SC4/3V Horizontal	0.47	8.45	8.13
SC4/3V Inverted	0.57	7.47	7.00
SC4/2V Manufacturer Stated NER (vertical)	0.26	13.00	
SC4/2V Vertical with no data logger	0.20	15.96	N\A
SC4/2V Vertical	0.37	8.63	>7*
SC4/2V Horizontal	0.46	6.80	6.27
SC4/2V Inverted	0.58	6.03	5.40

CONCLUSIONS: Orientation of dry shippers in transit, while important, allows for a tank to be tipped over or even set upside down for periods of time without jeopardizing the viability of the embryos. Hold times are reduced while in the horizontal or inverted positions.

We show that shipments completed within one calendar week should maintain temperatures below glass transition phase even when in the inverted position for the entire duration. The mushroom case should prevent any extended exposure of the tank to an inverted position and decrease the time the shipper may spend on its side.

The NER increased when comparing our Annual Preventative Maintenance (vertical with no logger) calculated NER to the NER calculated during this study for the tank (vertical with a data logger). While we knew that data loggers decrease the hold time of tanks in shipment, we were surprised at the severity of the decrease caused by the "heat wick" effect of the wiring between the probe within the tank and the transmitter outside of the tank. We witnessed a statistically significant ($p<0.05$) doubling of the NER in the SC4/3V model and a near doubling in the SC4/2V model when the data logger was added. This cut the hold times of the tanks essentially in half.

SUPPORT: None

O-94 2:35 PM Sunday, October 18, 2020

A NOVEL ORGAN CULTURE SYSTEM SUPPORTED GERM CELL SURVIVAL IN PRIMATES AND SPERMATOGENESIS IN MICE. Kien Tran, BS,[1] Wenbo Li, MS,[2] Sung Kwon Cho, PhD,[2] Kyle E. Orwig, PhD.[1] [1]University of Pittsburgh School of Medicine Pittsburgh, PA; [2]University of Pittsburgh, Pittsburgh, PA.

OBJECTIVE: The goal of this study is to develop a simplified, efficient culture system to induce *in vitro* spermatogenesis from fresh and cryopreserved immature testicular tissues, and translate this technology from mouse to monkeys to humans to test safety and feasibility for future clinical applications.

DESIGN: Spermatogonial stem cells (SSCs) have a tremendous capacity to regenerate spermatogenesis under proper conditions. Testicular tissue organ culture, utilizing the potency of SSCs to differentiate them into sperm outside of the body, may become a potential therapy to restore fertility in the future for pre-pubertal male patients, who encounter a permanent infertility risk as a side effect of gonadotoxic treatments. Takehiko Ogawa lab produced mouse sperm and offspring from cultures of neonatal testes in the pump-driven microfluidic (MF) device. To overcome its bulkiness and electrical-dependency, they later invented the pumpless microfluidic (PL) device. However, mouse sperm and offspring have not been produced and spermatogenesis was not reported from cryopreserved tissues or from any other species using the PL devices. This study aims to fill the gaps in knowledge on generating mouse sperm and offspring using the PL devices and translate this technology to non-human primate and/or human testicular tissues. In addition, we developed and tested a novel PDMS-roof transwell (PRT) culture system, comprised of a polycarbonate-membrane-transwell and a polydimethylsiloxane roof, to improve ease of device production and simplify the sample seeding and maintenance of cultures compared to the PL devices.

MATERIALS AND METHODS: Cultures of testicular tissues were maintained in MEM-alpha medium and 10% knock-out serum replacement at 34C with or without additional growth factors or hormones essential for in vitro germ cell development of mouse, Rhesus monkey, and human pre-pubertal tissues, respectively.

RESULTS: The efficiency of *in vitro* spermatogenesis using the PRT device was similar to PL device in cultures of fresh neonatal mouse testes (>70% tubules showed active spermatogenesis at 1 month). In the PRT system, our immunofluorescence results confirmed VASA+ germ cells in 81.6±6.63% of tubules, SALL4+ undifferentiated spermatogonia in 70.1±10.21%, STRA8+ differentiating spermatogonia in 50.0±14.01%, SYCP3+ spermatocytes in 75.9±9.2%, and SOX9+ Sertoli cells in 99.08±0.9% of tubules. A similar experiment using cryopreserved neonatal mouse testes in both culture systems also showed differentiated germ cells but with more delayed spermatogenesis. When culturing a fresh Rhesus testis tissue in the PRT for 3 months, 90.3% of tubules showed presence of VASA+ germ cells. In addition, a 2-month culture of a fresh Rhesus testis tissue under the same condition showed 74.3% of tubules with VASA+ cells, 65.52% tubules with Ki67+ proliferating cells, and 63.04% of tubules with SYCP3+ cells.

CONCLUSIONS: The PRT system could become an alternative testicular tissue culture system with simple design and equivalent efficiency compared with the PL devices to enhance in vitro tissue viability and development.

SUPPORT: This work was supported by anonymous donor funds; the *Eunice Kennedy Shriver* National Institute for Child Health and Human Development grant HD092084 and the National Institute of Biomedical Imaging and Bioengineering of the National Institutes of Health grant 5T32EB001026-15.

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OOCYTE VITRIFICATION HAS A DISADVANTAGEOUS EFFECT ON EMBRYO QUALITY: A PROPENSITY SCORE MATCHING-BASED STUDY. Jingwei Yang, M.D,[■] Xiaodong Zhang, M.D,[2] Guoning Huang, M.D.[2] [1]ChongQing Health Center for Women and Children; [2]■■■.

OBJECTIVE: To find the evidence of the effect of oocyte vitrification and warming procedures on embryos by comparing embryos developed from vitrified–warmed oocytes with those developed from fresh oocyte cycles.

DESIGN: This was a retrospective analysis of 1360 cycles of intracytoplasmic sperm injection (ICSI) involving 1293 fresh oocytes and 67 vitrified–warmed oocytes in a reproductive institude during January 2016–2019.

MATERIALS AND METHODS: Propensity score matching (PSM) was used for sampling to compare implantation rates, embryo morphological quality on days 2 and 3, and clinical outcomes between the two groups. A confocal microscope was used for imaging of the donated oocytes after ICSI.The primary outcome measure was implantation rate after embryo transfer. The secondary outcome measures included morphological quality of embryos on days 2 and 3. Confocal images were obtained to observe the alternations in vitrified–warmed oocytes.

RESULTS: A 1:1 PSM revealed significantly lower cleavage and implantation rates among the vitrified–warmed oocytes than among the fresh oocytes (97.3% vs 99.5% and 35.0% vs 48.3%, respectively; $P < 0.01$ for both) but similar clinical pregnancy rates. The rates of four-cell embryos on day 2 and eight-cell embryos on day 3 were lower among the vitrified–warmed oocytes than among the fresh oocytes (55.9% vs 63.1% and 34.1% vs 41.7%, respectively; $P < 0.05$). Lower cleavage and implantation rates were observed in the vitrified–warmed oocyte group ($P < 0.05$). In patients who accepted re-vitrification embryo/frozen-thawed embryo transfer after the failure of the first attempt, implantation and pregnancy rates were lower among the vitrified–warmed oocytes than among the fresh oocytes (16.00% vs 50.00% and 23.08% vs 72.73%, respectively; $P < 0.05$). Through confocal analysis, the first mitosis with chromosome separation failure was recorded.

CONCLUSIONS: Clinical data and image observations suggest that oocyte vitrification has a disadvantageous effect on chromosome segregation. We assume that abnormal embryo development might be related to the damage to the spindle, actin, or tubulin owing to vitrification and warming; more evidence should be accumulated on this topic.

SUPPORT: no

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DOES TROPHECTODERM BIOPSY AFFECT BLASTOCYST'S EXPANSION RATE POST THAWING? Samar Gamal El qassby, Bachelor and Samar Gamal el qassby, Manar Hozyen, Abdul ghafaar, Hana elkhader, Hosam zaki, FRCOG. Ganin fertility center Giza, Egypt.

OBJECTIVE: The expansion of blastocyst post thawing is one of an important indicator of embryo viability and affects it's implantation potential . Previous research found that there is correlation between rate of expansion and number of trophectoderm cells.Embryo biopsy involves reducing the number of trophectoderm cells . So this study looks into the trophectoderm biopsy would affect post thawing embryo expansion as a proxy of viability.

DESIGN: retrospective comparative study.

MATERIALS AND METHODS: A total of 406 vitrified/thawed blastocysts were observed from May 2019 to April 2020. Blastocysts were divided into two groups: biopsied blastocysts (n=195) and non biopsied blastocysts

(n=204).Biopsy was done using flicking technique of pre-herniated blastocysts. All vitrified blastocysts were of good quality at least 4BB according to Gardner's criteria 1999, and vitrification was done using cryotop kitazato method. We assessed the expansion rates (%) immediately post thawing (t0), after one hour (t1), and at time of transfer (t2). Data was recorded and analyzed using SPSS version -23 statistical software.

RESULTS: There is no significant difference in the female age between the non biopsed blastocyst group (29.5 years) and the biopsed blastocyst group (30.3 years). We found no significant differences between the expansion rates of the biopsied and non biopsied blastocysts at the t(0), .t(1), and t(2).

	Non biopsied blastocyst n=209	Biopsied blastocyst n=197	P-values
Expansion t(0) (%)	8.6±14	6.9±11.2	0.37
Expansion t(1) (%)	27±24.7	26.4±22.3	0.81
Expansion t(3)(%)	64±37.7	63.9±39	0.84

Data presented as mean ± standard deviation, Data are considered significant if p value $\leq$ 0.05.

CONCLUSIONS: This study suggests that embryo biopsy does not seem to affect the rate of expansion of blastocyst post thawing.

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WORKING HARD OR HARDLY WORKING: DOES PCOS IMPACT THE MITOCHONDRIAL DNA CONTENT OF THE EMBRYO. Lauren Grimm, M.A.,[1] Zoran J. Pavlovic, M.D.,[2] Jessi Anderson, MPH,[1] Christy Oso, B.A.,[1] Emma Radley, M.A.,[1] Nepheli Raptis, B.A., M.A.,[1] Hanna Mandell, M.A.,[1] Shawn Zimmerman, PhD, HCLD,[3] Angeline Beltsos, MD,[1] Amber R. Cooper, MD,[4] Roohi Jeelani, MD.[1] [1]Vios Fertility Institute Chicago, IL; [2]Rush University Medical Center, Chicago, IL; [3]Vios Fertility Institute, Swansea, SC; [4]Vios Fertility Institute St Louis, St. Louis, MO.

OBJECTIVE: This study sought to compare the mitochondrial DNA (mtDNA) content of age-matched controlled, euploid embryos in patients with Polycystic Ovary Syndrome (PCOS) compared to other infertility diagnoses.

DESIGN: Retrospective chart review at a private, multi-site fertility clinic.

MATERIALS AND METHODS: All euploid embryos from patients 35yo and younger who underwent in-vitro fertilization (IVF) with PGT-A from January to February 2020 utilizing a PGT lab that reports mtDNA (MitoScore; Igenomix) were included. Patients were divided into two groups: those whose embryos were derived from patients with a diagnosis of PCOS and those that did not. A PCOS diagnosis was defined according to the Rotterdam Criteria. Baseline patient characteristics were measured and IVF cycle statistics recorded. Two sample t-tests and chi square analysis were used to analyze the data using SPSS (SPSS Inc., Chicago, IL, USA).

RESULTS: A total of 412 embryos were analyzed. Baseline characteristics, including age and BMI, were similar between the PCOS and non-PCOS patient populations ($p>0.05$). There were a total of 202 embryos included in the PCOS group and 212 embryos in the age-matched control group. There was no statistical significance in the number of oocytes retrieved, maturation rate, fertilization rate, and blastocyst rate between the two groups ($p>0.05$). Interestingly, the average mtDNA score was also statistically similar, where the PCOS group had an average score of 22.9 (SD:6.25), compared to the non-PCOS group with an average score of 23.2 (SD:5.7) ($p>0.05$).

CONCLUSIONS: As one of the most common endocrine disorders, PCOS occurs in 5-10% of reproductive age women, and is a leading cause of infertility. It is well established that reactive oxygen species (ROS) are significantly increased in patients with PCOS compared to the average population, where elevated intracellular levels of nitric oxide (NO) and advanced glycation end products (AGE) have been found. This increase in ROS is thought to result in the inducement of PCOS pathogenesis, where accumulating evidence suggests that increased AGEs may play a role in the abnormal steroidogenesis seen in PCOS patients by affecting enzyme function and inflammatory responses during steroid biosynthesis. Similarly, this ROS excess is also thought to result in poor oocyte health. For women undergoing IVF, there are a limited number of ways to appropriately assess oocyte/embryo quality for optimal success. Yet, the quantification of mtDNA may offer a promising new parameter in assisted reproductive technologies (ART). Increased mtDNA have been linked to decreased pregnancy rates and is thought to be indicative of poor embryo quality due to oxidative stress; while lower mtDNA scores have been associated with improved outcomes. Our results show that while women diagnosed with PCOS may have increased rates of oxidative stress, this does not seem to significantly impact blastocyst quality or metabolic health. Further investigation into the underlying biological causes associated with elevated levels of embryonic mtDNA is warranted.

SUPPORT: None

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A NOVEL DIAGNOSTIC APPROACH FOR POLYCYSTIC OVARY SYNDROME DIAGNOSIS USING GONADOTROPIN RELEASING HORMONE RECEPTOR AUTOANTIBODY ACTIVITY AND ANTIMULLERIAN HORMONE. Elizabeth A. Weedin, DO, MS,[1] Heather R. Burks, MD,[1] Xichun Yu, MD,[2] Hong Liang Li, MD, PhD,[2] Christopher E. Aston, PhD,[3] David C. Kem, MD,[2] LaTasha B. Craig, MD.[3] [1]University of Oklahoma Health Sciences Center Department of Obstetrics and Gynecology, Oklahoma City, OK; [2]University of Oklahoma Health Sciences Center, Oklahoma Cty, OK; [3]University of Oklahoma Health Sciences Center, Oklahoma City, OK.

OBJECTIVE: Despite being the most common endocrinological disorder of reproductive aged women, polycystic ovary syndrome (PCOS) remains a complex disease of unknown etiology. Patients spend an average of two years of clinical evaluation with at least three health professionals before diagnosis. As PCOS remains a diagnosis of exclusion, there is room for improvement in diagnostic classification. Although the use of Antimullerian hormone (AMH) as a diagnostic test has shown promise, it has limitations. Our laboratory has identifiedvariation in levels of activating autoantibody (AAb) to the second extracellular loop of the gonadotropin-releasing hormone receptor (GnRHR) associated with PCOS in infertile patients. This AAb and its activity level has shown promise as a diagnostic test for PCOS that could be used in conjunction with AMH to provide a direct diagnosis of PCOS. We evaluated the diagnostic capability of GnRHR AAb activity level and its response to a GnRH antagonist, together with age and AMH, to directly discriminate a diagnosis of PCOS using a sample of PCOS patients and unexplained, infertile controls.

DESIGN: Cross-sectional, matched case-control design.

MATERIALS AND METHODS: Sera from 200 patients with PCOS from the Pregnancy in Polycystic Ovary Syndrome II (PPCOS II) trial and from 200 race, parity, age, and body mass index matched ovulatory, unexplained infertile control patients from the Assessment of Multiple Intrauterine Gestations from Ovarian Stimulation (AMIGOS) trial were obtained. GnRHR AAb activity was measured with and without GnRH antagonist (cetrorelix) in all samples using the GeneBLAzer cell-based fluorescence resonance energy transfer (FRET) assay. These activity levels, along with age and AMH levels, were analyzed using logistic regression to develop a prediction model for PCOS. Receiver-operating characteristic (ROC) analyses were used to evaluate the accuracy of prediction of PCOS by this model. This diagnostic algorithm was then applied to a smaller, independent sample of 65 infertile women from an academic infertility practice.

RESULTS: The initial decision point assigned all patients with AMH >13.3 ng/ml as having PCOS. Those with AMH <13.3ng/ml were divided into those above and below 30 years of age; each age group then had its own series of AMH, GnRHR activity and GnRHR activity response decision points. Using ROC analysis, this diagnostic algorithm was estimated to have a sensitivity of 76% and specificity of 87% for PCOS in this sample of infertile women. When applied to the independent sample, the algorithm showed similar sensitivity (73%) and specificity (84%).

CONCLUSIONS: This new diagnostic algorithm incorporating AMH and GnRHR AAb cell activity and response to a GnRH antagonist performs well to diagnose PCOS, with an overall sensitivity of 76% and specificity of 87%; it fills a void in direct diagnosis of PCOS. Additional application studies will aid in identifying feasibility of this testing algorithm with the goal of streamlining and improving efficiency of diagnosis for patients with PCOS.

SUPPORT: University of Oklahoma College of Medicine Alumni Association Grant and the Reproductive Medicine Network (RMN), NICHD.

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POLYCYSTIC OVARY SYNDROME COMORBIDITY PATTERNS DIFFER BETWEEN RACIALLY AND ETHNICALLY DIVERSE PATIENTS. Ky'Era V. Actkins, BS,[1] Melinda Aldrich, PhD,[2] Digna R. Velez Edwards, PhD,[2] Lea K. Davis, PhD.[2] [1]Meharry Medical College Nashville, TN; [2]Vanderbilt University Medical Center, Nashville, TN.

OBJECTIVE: To evaluate the comorbidity patterns of polycystic ovary syndrome (PCOS) in White, African American, Hispanic, and Non-Hispanic women. This study aims to understand which comorbidities are caused by the effects of a PCOS clinical diagnosis or influenced by the genetic risk of the disease.

DESIGN: A case-control study using a hospital electronic health record database and biobank.

MATERIALS AND METHODS: A total of 5,526 PCOS cases between the ages of 11 and 44 were identified using a validated algorithm that required the presence of ICD-9/10 codes for polycystic ovaries or irregular menstruation and hirsutism and excluded any other diagnosis whose symptoms mirrored PCOS characteristics. Women not identified by the algorithm were included as controls (n=394,202). Cases and controls were then stratified based on EHR-reported race and ethnicity. Women who identified as White (n=3,606 cases; 328,194 controls), African American (n=882 cases; 58,165 controls), Hispanic (n=234 cases; 15,291 controls), and Non-Hispanic

(n=4,459 cases; 382,462 controls) were used for this analysis. To determine comorbidity patterns of PCOS diagnosis, a logistic regression model adjusted for median age was performed on PCOS cases and controls for each stratified racial and ethnic group against 1,858 phenotypes in the medical database. To evaluate the effects of genetic susceptibility of PCOS on health outcomes, a logistic regression model adjusted for median age and genetic ancestry was performed on a measurement of PCOS genetic liability, genetic risk scores, and the medical database. Genetic risk scores were generated using summary statistics from a PCOS genome-wide association study[1].

RESULTS: Among Hispanic women almost half of all significant comorbidities were endocrine and metabolic disorders. Dermatologic disorders and genitourinary diseases were the second and third most common comorbidities, respectively. The most common comorbidities for White, African American, and Non-Hispanic patients were also endocrine and metabolic disorders. However, for these three cohorts, genitourinary comorbidities and pregnancy complications comprised the second and third largest comorbidity categories. African American patients had higher rates of polyp of corpus uteri (OR = 5.15, p = 6.04e-09) compared to White patients (OR = 2.70, p = 2.06e-06). Conversely, we found that Hispanic patients had higher odds of having chronic liver disease and cirrhosis (OR = 4.87, p = 1.49e-09) compared to Non-Hispanic patients (OR = 2.61, p = 9.93e-29). We also found that a genetic risk score for PCOS was associated with type 2 diabetes (OR = 1.11, p = 8.75e-08) in addition to polycystic ovaries (OR = 1.11, p = 1.91e-07) and ovarian dysfunction (OR = 1.24, p = 9.18-06) among White women.

CONCLUSIONS: Endocrine and metabolic diseases are the top comorbid conditions experienced by PCOS patients regardless of race or ethnicity. However, different racial and ethnic groups have a greater risk of developing specific PCOS comorbidities. Additionally, females with a greater genetic susceptibility to PCOS share an underlying genetic risk for type 2 diabetes.

References

1. Â Day, Felix, et al. Large-scale genome-wide meta-analysis of polycystic ovary syndrome suggests shared genetic architecture for different diagnosis criteria.Â *PLoS genetics*Â 14.12 (2018): e1007813.

SUPPORT: This study was supported by NIHÂ 5T32GM007628 andÂ U54MD010722.

O-100 2:35 PM Sunday, October 18, 2020

SUBCUTANEOUS ABDOMINAL STEM CELL ADIPOGENESIS PREDICTS METABOLIC IMPROVEMENTS IN NORMAL-WEIGHT POLYCYSTIC OVARY SYNDROME WOMEN.

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OBJECTIVE: Normal-weight polycystic ovary syndrome (PCOS) women have exaggerated subcutaneous (SC) abdominal adipose stem cell (ASC) differentiation into adipocytes that may be programmed. This study examines whether SC abdominal ASC differentiation into adipocytes *in vitro* correlates with endocrine-metabolic functions in normal-weight PCOS women versus age- and body mass index (BMI)-matched normoandrogenic ovulatory (control) women.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Eight normal-weight PCOS women and 8 age- and BMI-matched controls underwent circulating hormone/metabolic determinations, frequently-sampled intravenous glucose tolerance testing, total-body dual-energy x-ray absorptiometry and SC abdominal fat biopsy. PPARγ and *CEBPa* gene expression and lipid content of adipocytes matured *in vitro* were compared between PCOS and control women and correlated with clinical outcomes, including insulin sensitivity (Si), acute insulin responsiveness to glucose (AIRg) and adipose insulin resistance (adipose-IR). Unpaired Student's *t*-tests, two-way ANOVA, Pearson correlation coefficients and partial correlation coefficients adjusting for serum free testosterone (T) levels were performed as appropriate.

RESULTS: PPARγ and *CEBPa* gene expression in ASCs increased to maximal levels by day 12 ($P<0.001$) without a female type effect, when *PPAR*γ levels positively correlated with total body mass in PCOS alone (control, $P=0.097$; PCOS, $P=0.032$). In control ASCs, gene expression positively correlated with fasting serum insulin ($P=0.047$, *PPAR*γ*;* $P=0.006$, *CEBPa*), AIRg ($P=0.023$, *PPAR*γ) and adipose-IR ($P=0.032$, *CEBPa*) and negatively correlated with Si ($P=0.001$, *CEBPa*). In PCOS ASCs, conversely, *CEBPa* gene expression negatively correlated with serum free fatty acid (FFA) ($P=0.002$), adipose-IR ($P=0.033$) and serum free T ($P=0.016$). Moreover, exaggerated lipid content in PCOS ASCs positively correlated with Si ($P=0.041$) and negatively correlated with serum FFA ($P=0.021$). Adjusting for serum free T levels, significant female type differences remained in the correlations of log *CEBPa* gene expression with fasting serum FFA levels ($P=0.010$) and Si ($P=0.010$); and of lipid content on day 12 with adipose-IR ($P=0.034$) and fasting serum FFA levels ($P=0.044$).

CONCLUSIONS: In normal-weight PCOS women compared to age- and BMI-matched controls, exaggerated SC abdominal ASC differentiation into adipocytes *in vitro* accompanies a normal rise in *PPAR*γ and *CEBPa* gene expression and predicts improved insulin sensitivity *in vivo*. The ability of SC abdominal ASCs of normal-weight PCOS to retain their unique cellular and molecular properties of exaggerated SC abdominal ASC differentiation into adipocytes may be programmed in early life by epigenetic events.

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O-101 2:50 PM Sunday, October 18, 2020

AN AMH-BASED SCREENING TOOL IS BOTH SENSITIVE AND SPECIFIC FOR PREDICTING A DIAGNOSIS OF PCOS BY ROTTERDAM CRITERIA.

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OBJECTIVE: To understand whether a polycystic ovary syndrome (PCOS) screening tool using anti-Mullerian Hormone (AMH) in lieu of polycystic ovarian morphology (PCOM) is predictive of patients meeting Rotterdam criteria for PCOS.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: Women with PCOS were diagnosed by ultrasound-based Rotterdam criteria and included 253 subjects from the multisite PPCOS II trial and 111 patients from a tertiary academic centre's multidisciplinary PCOS clinic. Controls included 245 participants in the ovarian aging (OVA) study, a community-based cohort of ovulatory women not seeking treatment for fertility. Received operator curves were used to ascertain the accuracy of AMH thresholds for predicting PCOM. These age-stratified AMH thresholds from women 25-<30, 30-<35, and 35-<40 were used as one of the three criteria for diagnosis of PCOS, in addition to oligomenorrhea (<8 menstrual cycles per year) and biochemical hyperandrogenism (total testosterone >76.5 ng/dL). This modified criteria was applied to all 609 patients; the sensitivity and specificity for diagnosis of PCOS using this AMH-based screening tool was calculated using the Rotterdam criteria as gold standard. All AMH samples were run using an ELISA Ansh Labs AMH assay at a central laboratory, the Ligand Assay and Analysis Core Laboratory at the University of Virginia (UVA).

RESULTS: The optimal thresholds of AMH to predict PCOM were 10ng/dL (ages 25-<30), 6ng/dL (ages 30-<35), and 4.75ng/dL (ages 35-<40). Using these, the screening tool accurately predicted PCOS in 323 out of the 364 patients with diagnosed PCOS by Rotterdam criteria. Conversely, when applied to the control population, it accurately predicted the absence of PCOS in 243 out of 245 patients. This corresponds to a sensitivity of 88.7% and specificity of 99.2%, respectively. Using only oligomenorrhea and hyperandrogenism as diagnostic criteria, the sensitivity decreases to 39.7% (144 out of 364) patients, which is an absolute decrease of 49.1%. We were unable to accurately calculate specificity in this subgroup as our control cohort was ovulatory.

CONCLUSIONS: The PCOS screening tool is both sensitive and specific for predicting a diagnosis of PCOS by Rotterdam criteria. Ultrasonographic assessments of PCOM are subjective, expensive, and invasive. This tool offers a non-invasive, objective alternative to screen patients for PCOS. Further research is necessary to understand how the screening tool would perform prospectively or with a heterogeneous population with varied AMH assays.

References: None

SUPPORT: None

O-102 3:05 PM Sunday, October 18, 2020

POLYCYSTIC OVARY SYNDROME IS ASSOCIATED WITH INCREASED ANEUPLOIDY RATE.

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OBJECTIVE: To determine if aneuploidy rates and average embryonic mitochondrial content scores differ among an infertile population with polycystic ovary syndrome (PCOS) undergoing in vitro fertilization (IVF) with preimplantation genetic testing for aneuploidy (PGT-A) compared to non-PCOS controls. PCOS is the most common cause of ovulatory dysfunction among reproductive aged women. While poor oocyte and embryo quality are associated with increased aneuploidy, little is known about the effect of PCOS on aneuploidy rates or mitochondrial DNA content, which has become increasingly reported along with embryonic ploidy status. Lower mitochondrial scores have been correlated with early blastulation and higher chances of euploidy.

DESIGN: IRB-approved retrospective cohort study.

MATERIALS AND METHODS: Data from all IVF cycles conducted at an academic center from January 2016 to June 2018 was collected. We excluded cycles utilizing donor egg, preimplantation for genetic testing for mutations or structural rearrangements, and cycles without any euploid embryos or reported mitochondrial scores (Igenomix, Los Angeles, CA). PCOS was diagnosed using the Rotterdam criteria. Baseline characteristics and outcome measures were analyzed using chi square/Fisher exact tests for categorical data and two-sample t-tests for continuous variables. Multiple linear regression models were used to examine the association of PCOS with primary outcomes of aneuploidy rate and average mitochondrial score.

RESULTS: Of the 256 subjects included in the analysis, fifty (19.5%) had PCOS. There were no differences in baseline demographic information such as age, parity, or smoking status, while body mass index (BMI) was significantly different between the PCOS and non-PCOS controls. PCOS patients had a statistically significant increased number of oocytes retrieved (19.18 vs 14.36, $p<0.001$), increased number of oocytes fertilized with ICSI (15.34 vs 12.08, $p=0.0004$), increased numbers of 2PN embryos (12.62 vs 9.5, $p=0.0001$), and increased number of blastocysts biopsied (6.12 vs 4.85, $p=0.0039$). There were no differences in fertilization or blastulation rates between the two groups. There were no differences in average mitochondrial content score (23.5 vs 25.02, $p=0.14$), however, there were statistically significant differences in aneuploidy rates among those with and without PCOS (0.49 vs 0.40, $p=0.03$, respectively). We found after controlling for age, BMI, and blastulation rate, women with PCOS have a 9.6% higher aneuploidy rate ($p=0.027$) than those without PCOS. There were no differences in clinical pregnancy rates, live birth rates, or miscarriage rates between the two groups.

CONCLUSIONS: While patients with PCOS have similar fertilization and blastulation rates compared to controls, these women have aneuploidy rates that are significantly higher, by 9.6%. This highlights one aspect of PCOS that impacts fertility success rates and the need for extensive counseling on expected outcomes in those undergoing IVF.

ART LAB: OUTCOME PREDICTORS

O-103 1:50 PM Sunday, October 18, 2020

CLINICAL IMPLEMENTATION OF ALGORITHM-BASED EMBRYO SELECTION USING MULTI-DIMENSIONAL ANALYSIS OF 'BIG DATA' IMPROVES PREGNANCY OUTCOMES IN SINGLE THAWED EUPLOID EMBRYO TRANSFERS (EUPLOID SETS).

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OBJECTIVE: Preimplantation genetic testing for aneuploidy (PGT-A) enables modern assisted reproductive technology treatment centers to better identify and select embryos for transfer. However, even among euploid embryos, morphologic grading remains a significant metric for transfer selection, especially for patients who have >1 euploid embryo available (1,2). Previous work has attempted to determine the accuracy of mathematical models in predicting outcomes using transfer cycles with known clinical results (3). However, there has yet to be a study to evaluate the clinical utilization of an algorithm-based (AB) system for embryo transfer selection. We sought to assess whether AB embryo selection improves clinical outcomes in euploid SETs.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The study included patients who underwent euploid SETs at an academic center from September 2016 to February 2020. Controls included euploid SETs in which a senior embryologist selected the embryo for transfer based on modified Gardner grading (traditional). Cases included euploid SETs in which the embryo was selected using an automated AB approach. Exclusion criteria were euploid SETs from July 2017 to January 2018, in which a mixture of traditional and AB selection were used. The algorithm created a weighted ranking system of each embryonic parameter (expansion, inner cell mass grade, trophectoderm grade) and formulated a composite score. The embryo with the highest score was transferred. Our primary outcome was implantation rate (IR). Secondary outcomes were ongoing pregnancy/live birth rate (OP/LBR), biochemical pregnancy rate (BPR) and clinical loss rate (CLR). Baseline demographics were obtained: age, body mass index (BMI), ovarian reserve testing, obstetric history, endometrial thickness (EnT) and progesterone level (PL) at time of transfer, and embryo grade. Data were analyzed using Student's t-test, chi-squared test, and logistic multivariable generalized estimating equation regression models, with $P<0.05$ considered significant.

RESULTS: 4,521 SETs were performed in the study period and met inclusion criteria (traditional: n=1,119; AB: n=3,402). Patients in the traditional group were older and had a lower BMI, PL, and EnT at time of transfer ($P<0.05$ for all); demographic data was otherwise similar. The IR and OP/LBR were significantly higher in the AB group compared to the traditional group (63.52% vs 56.93%, $P<0.0001$ and 53.13% vs 47.18%, $P=0.006$, respectively). After adjusting for age, BMI, AMH, obstetric history, EnT and PL at time of transfer, and embryo grade, use of the algorithm remained significantly associated with improved IR (OR 1.25, 95% CI 1.07-1.47) and OP/LBR (OR 1.24, 95% CI 1.06-1.45). We saw no differences in BPR or CLR.

CONCLUSIONS: This is the first study to clinically implement AB embryo selection in euploid SETs. Our results demonstrate that utilization of a mathematical model for embryo selection improves clinical outcomes. Future studies implementing the algorithm in prospective, randomized trials are warranted and would better delineate the role of our model in embryo selection.

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SUPPORT: None

O-104 2:05 PM Sunday, October 18, 2020

EUPLOIDY RATES AND PREGNANCY OUTCOMES USING THE *ZYMŌT*™ DEVICE FOR SPERM PREPARATION.

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OBJECTIVE: To compare gradient sperm and *ZyMōt*™ sperm preparation and its impact on euploidy and pregnancy outcomes.

DESIGN: Prospective Cohort study.

MATERIALS AND METHODS: Between April 2019 and April 2020 a total of 1219 embryos were available for analysis for PGT-A from 2825 oocytes fertilized with intracytoplasmic sperm injection. Two methods of sperm preparation are evaluated. A single 90% layer gradient preparation of sperm with a 10 minute centrifugation at 300g followed by a 10 minute wash with a HEPES buffered medium/10 mg per ml of human sera albumin. The second method was using the *ZyMōt*™ 850 μl device where 850 μl of raw semen is

loaded into the devices and covered with 750 μl of HEPES/HSA solution. The device is placed in to a 37◦C incubator for 30 minutes. Removal of 0.5 ml of the HEPES solution completes the preparation. Initial counts and motilities were evaluated before and after the two preparation methods. Embryos were evaluated on day 3 and assisted hatched for via laser ablation. Embryos on day 5 and day 6 with a distinct inner cell mass and multiple cells herniating form the zona pellucida were biopsied for PGS aneuploidy testing. Embryo biopsy consisted of laser removal of 5 to 7 cells from the trophectoderm juxtaposed to the inner cell mass. The biopsied cells were treated according to the reference laboratory protocol for off site aneuploidy screening. Embryos available for testing were vitrified and stored under liquid nitrogen until results were obtained from the reference laboratory.

RESULTS: A significant higher euploidy rate from day 5 embryos was noted with the *ZyMōt*™ prepared sperm as compared to the gradient prepared sperm. A total of 358 day 5 embryos were biopsied with the *ZyMōt*™prepared sperm resulting in 63% euploidy compared to 56% euploidy in 383 embryos from the gradient prepared sperm ($P<0.05$). There was not significant difference in euploidy rates with day 6 embryos in the two subgroups where 51% were euploid from the 245 *ZyMōt*™ embryos and 48% of the 233 embryos from gradient prepared sperm (not significant). There was not significant difference in ongoing pregnancies between the two subgroups, where *ZyMōt*™ prepared sperm resulted in 70% ongoing pregnancies 58% implantation rate as compared to 77% ongoing and 64% implantation with gradient prepared sperm (not signicant).

CONCLUSIONS: This study shows that although there was not a significant difference in pregnancy outcomes, there are higher euploidy rates with the *ZyMōt*™ prepared sperm. Overall resulting in more embryos available for transfer and possibly more available pregnancies. With very little changes in the way sperm is prepared in the ART industry in the past 30 years this study demonstrates the *ZyMōt*™ device provides an alternative to sperm preparation with fewer steps in the process.

O-105 2:20 PM Sunday, October 18, 2020

ACCURATE MEASUREMENT OF SPERM DNA FRAGMENTATION EFFECT ON REPRODUCTIVE OUTCOMES BY CUMULATIVE LIVEBIRTH RATES (CLBR) PER EMBRYO TRANSFERRED AND OOCYTE UTILIZED REVEALS ITS LACK OF RELEVANCE IN OOCYTE DONATION FOR UNSELECTED MALES. Irene Hervas, MSc,[1] Nicolas Garrido, PhD,[1] Rocio Rivera-Egea, PhD,[2] Cristina Gonzalez-Ravina, PhD,[3] David Amoros, PhD,[4] Fernando Quintana, Sr., PhD,[5] Maria Gil Julia, MSc, MRes,[1] Alberto Pacheco, PhD.[6] [1]IVI Foundation - IIS La Fe Biomedical Research Institute Valencia, Spain; [2]IVIRMA Valencia, Valencia, Spain; [3]IVIRMA Sevilla, Sevilla, Spain; [4]IVIRMA Barcelona, Barcelona, Spain; [5]IVIRMA Bilbao, Bilbao, Spain; [6]IVIRMA Madrid, Madrid, Spain.

OBJECTIVE: Info about sperm DNA fragmentation (SDF) effect on clinical outcomes from ovum donation cycles is scarce, and classic measuring of reproductive success using outcomes per embryo transfer is a biased measure, since best embryos are the first transfer choice and does not compute the additional contribution of other embryos within the same cohort. We better addressed this problem studying raw live birth rates (LBR) at first embryo transfer (ET), in all ET (fresh+thawed), and CLBR, per ET, number of embryos replaced (EmbR) and oocytes consumed until reaching a first newborn.

DESIGN: Multicenter retrospective cohort study.

MATERIALS AND METHODS: Patients from IVF/ICSI with donated oocytes (n=819) between Jan 2000-Mar 2019, tested for SDF on ejaculated spermatozoa using TUNEL assay. Groups were established to compare all main outcomes: SDF >15% (H, high) and in 10% SDF ranges: <10%, 10%-20%, 20%-30%, >30%, by X^2 square tests, and CLBR estimated with Kaplan-Meier and Mantel-Cox test, considering the total number of embryo transfers, embryos transferred, and oocytes consumed to obtain the first livebirth.

RESULTS: Characteristics were comparable among groups, and the analysis was conducted from information from of 1903 ET, 2146 embryos and 5039 oocytes. LBR were unaltered by high DNA fragmentation: at 1st ET and in all ET, were 53.6% and 43.2% in men with H while 48.2% and 39.6% respectively, in <15% SDF (low, L). Distributing in groups according to their SDF level, LBR rates were similar ($p>0.05$) 48.7% (<10%), 45.5% (10%-20%), 58.0% (20%-30%) and 61.1% (>30%) at 1st ET, and 39.4% (<10%), 39.2% (10%-20%), 52.0% (20%-30%) and 38.3% (>30%) per all ET performed. CLBR per ET showed in L SDF or H SDF value, 66.7% *vs* 71.5% in the 2nd ET, 75.8% *vs* 80.1% in the 3rd ET, and 89.8% *vs* 82.3% in the 5th ET, without reaching significance, nor it was when compared by the SDF groups. CLBR according to the number of embryos transferred until reaching a newborn considering L or H SDF level was 55.0% *vs* 59.4% with two EmbR and 73.6% *vs* 79.0% with up to four EmbR, resulting in non-significant differences, as when calculated by SDF groups, 57.2% (<10%) and 61.5% (>30%) with two EmbR; 73.5% (<10%) and 83.5% (>30%) with four EmbR. Relative to the number of oocytes required per patient, CLBR were not statistically significant in both analyses. Similar results were found in groups H or L of fragmentation (42.8% *vs* 45.9%, 78.6% *vs* 82.0%, 91.8% *vs* 89.8%) when 5, 10 or 15 oocytes were used respectively. When comparing between SDF groups (<10% *vs* >30%) the rate of newborns was not reduced by high fragmentation at 5 (44.2% *vs* 38.1%), at 10 (79.4% *vs* 87.6%) and at 15 (90.8% *vs* 87.6%) oocytes consumed.

CONCLUSIONS: DNA fragmentation does not negatively affect the live birth rates of unselected patients undergoing an IVF/ICSI cycle with donated oocytes, neither per transfer, nor accumulated per transfer, embryo or oocyte, after the largest and most extensive data analysis done so far.

O-106 2:35 PM Sunday, October 18, 2020

PRESENCE OF ABNORMAL CELL CLEAVAGE, CELL FUSION OR BOTH SEEN DURING EMBRYO DEVELOPMENT ON TIME-LAPSE MICROSCOPY IS NOT PREDICTIVE OF CHROMOSOMAL ANEUPLOIDY. Alice J. Shapiro, M.D.,[1] Lindsay Kroener, MD,[1] Nicholas J. Jackson, PhD, MPH,[1] Zachary Haimowitz, B.S.,[2] Alin Lina Akopians, MD, PhD,[3] Wendy Y. Chang, MD,[3] Carolyn J. Alexander, MD,[3] Shahin Ghadir, MD,[3] Hal Danzer, MD,[3] Mark W. Surrey, MD,[3] Jason A. Barritt, PhD[2] [1]David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA; [2]ART Reproductive Center, Beverly Hills, CA; [3]Southern California Reproductive Center, Beverly Hills, CA.

OBJECTIVE: To determine whether the presence of abnormal cell cleavage, cell fusion or both seen on morphokinetic analysis of preimplantation embryos using time-lapse monitoring (TLM) is predictive of chromosomal aneuploidy when compared to embryos with normal development.

DESIGN: Retrospective cohort study at a large, private fertility center.

MATERIALS AND METHODS: All patients who utilized both the TLM device (Embryoscope®, Vitrolife, Sweden) and preimplantation genetic testing for aneuploidy (PGT-A) at a single IVF center from 1/2018 to 12/2019 were included in the study. Patients using donor oocytes were excluded. Evaluation of embryo development was performed on all embryos from the time of first cell division until 72 hours. Abnormal cell cleavage (AC) was defined as irregular first cleavage of the zygote resulting in more than two daughter cells and/or irregular second cleavage that formed five or more cells instead of four. Cell fusion (CF) was defined as a decrease in number of cells at any time point up until 72 hours. Normal development (ND) was defined as the absence of AC or CF. Trophoectoderm biopsy was performed on day 5, 6, or 7 in blastocysts of good or fair quality. PGT-A was performed using next generation sequencing. All embryos that were sufficient quality for blastocyst biopsy were included in the study. Statistical analyses were conducted using logistic regression with Huber-White standard errors to correct for multiple embryos within a patient.

RESULTS: A total 6,171 embryos were analyzed with TLM and of those, 1,083 embryos from 311 patients developed into blastocysts of sufficient quality to biopsy and were included in the analysis. Of the biopsied blastocysts, 8.1% (87/1,083) had AC, 1.2% (14/1,083) had CF and 0.4% (4/1,083) displayed both AC and CF. The vast majority of embryos, 90.2% (969/1,083), did not have AC or CF. The presence of AC, CF or both did not significantly increase with older age ($p=0.77$). Abnormal development (AC, CF or both) was significantly more likely to be seen in fair-quality compared to good-quality embryos (17.5% v. 5%, $p<0.001$). The aneuploidy rate was not increased in embryos displaying AC (49%), CF (48%) or both (48%) compared to embryos with ND (49%), after controlling for age ($p=0.99$).

CONCLUSIONS: While the presence of early abnormal cell cleavage or cell fusion on TLM is associated with lower quality morphological grade at the blastocyst stage, these markers of abnormal development are not associated with increased aneuploidy. Additional research is needed to assess ongoing pregnancy rates from these embryos to evaluate the clinical significance of AC and CF in early pre-implantation embryo development.

SUPPORT: The research described was supported by NIH/National Center for Advancing Translational Science (NCATS) UCLA CTSI Grant Number UL1TR001881.

O-107 2:50 PM Sunday, October 18, 2020

DOES TOBACCO AFFECT FOLLICULAR AND EMBRYO HEALTH?. David Agudo, PhD,[1] Estefania Castro, Technician,[1] Alberto Pacheco, PhD,[1] Irene Martín Patón, Graduate,[1] María Cruz, PhD,[2] Fernando Bronet, PhD.[1] [1]IVI Madrid Madrid, Spain; [2]IVIRMA Global Headquarters, Madrid, Spain.

OBJECTIVE: The main objective of this study is to compare, between smokers and no smokers egg donors, embryo implantation, embryokinetics times, and apoptosis and necrosis in cumulus cells and follicular fluid cells.

DESIGN: We measured apoptosis and necrosis in the cumulus cells and the follicular fluid cells in these donors using flow cytometry (Anexina V kit, Miltenyi Biotech). We also compared the cumulative implantation rate (until pregnancy with positive fetal heartbeat or until there were no embryos to transfer in case of not getting pregnancy) among the three study groups. In addition, these cycles were incubated in embryoscope, in order to study their cells cleavages times.

MATERIALS AND METHODS: The target population of this study are 216 oocyte donors that meet the requirements established in our oocyte donation program. The oocyte donors, are classified in terms of their tobacco consumption habits. Group I: 79 no smokers, Group II: 82 smokers donors of 1-10 cigarettes per day, Group III: 54 smokers donors of more than 10 cigarettes per day. We perform an ANOVA statistical analysis to analyze the data.

RESULTS: The embryokinetics results showed us that the first cellular events, like second polar body appearance (tPB2) and pronucleus appearance (tPNa), appeared significantly before in the no smoker group ($p<0.05$ and $p=0.036$) as well as the duration of the first and second cell cycle, in this case the duration was significantly longer in no smokers donors ($p=0.012$ and $p=0.032$).

When comparing data of apoptosis and necrosis among the three groups, we found significant differences in necrosis data, being higher in group III (necrosis in cumulus 0.53% and granulosa cells 0.55%), than in group I and II (group I: necrosis in cumulus 0.35% and granulosa cells 0.36%), (group II: necrosis in cumulus 0.23% and granulosa cells 0.33%), with p value of 0.05 and 0.011 respectively.

When we compare the implantation rate among the three groups, we observed how this rate of cumulative implantation is lower in the groups of smokers donors (group II = 54.31% and group III = 55.69%) than in the group of donors who declared themselves no smokers (group I = 65.03%). However, the differences found were not statistically significant, ($p=0.07$), although with a clear tendency towards significance.

CONCLUSIONS: These results could indicate that the smoking habit could reduce the accumulated rates of implantation, although it would be necessary to increase the number of cases in the study in order to clarify the implantation trend or more studies would be necessary to reinforce this conclusion.

A possible biological explanation for the differences founded in implantation rates, could be the higher rate of necrosis found in the cumulus cells and follicular fluid cells, in the smokers donors, which could indicate a toxic follicular environment which could affect the embryonic viability. One of the possible effects of this toxicity, would be the shorter cell cycles founded in smokers donors than in no smokers donors, or the delay in some cellular events, like the meiosis restart.

O-108 3:05 PM Sunday, October 18, 2020

ULTRA LOW OXYGEN EXPOSURE DURING EXTENDED CULTURE OF HUMAN *IN VITRO* EMBRYO SIGNIFICANTLY IMPROVES USABLE BLASTULATION AND CUMULATIVE LIVE BIRTH RATES IN *IN VITRO* FERTILIZATION. Sophie Brouillet, PharmD, PhD,[1] Aneta Andreeva, RESIDENT,[1] Anna Gala, MD,[1] Alice Ferrieres-Hoa, MD,[1] Margaux Anav, MD,[1] Alice Fournier, MD,[1] Vanessa Loup, MD,[1] Noemie Ranisavljevic, M.D., Ph.D.,[2] Samir Hamamah, MD, PhD.[1] [1]Arnaud de Villeneuve Hospital CHU Montpellier, Montpellier, France; [2]CHU and University of Montpellier, Montpellier, France.

OBJECTIVE: Does ultra-low oxygen level during extended culture of human *in vitro* embryos improve IVF outcomes compared to low oxygen level?

DESIGN: A monocentric retrospective cohort study was performed from June 2014 to March 2019. A total of 120 couples were enrolled. The study was approved by local institutional review board (2019_IRB-MTP_09-01). All couples underwent one IVF cycle associated with low oxygen exposure (5%) througout *in vitro* culture (from day 0 to day 6) and then the subsequent IVF cycle associated with low oxygen culture (5%) during early embryo development (from day 0 to day 3) and ultra-low oxygen exposure (2%) during extended embryo culture (from day 3 to day 6). *In vitro* experiments have also been conducted to characterize the impact of oxygen modulation during *in vitro* culture on human embryo development and implantation potential (authorization: 10/04/2018, NOR SSAB1816140S).

MATERIALS AND METHODS: The first objective was to evaluate total and usable blastocyst formation rates in both "5% oxygen exposure" and "2% oxygen exposure" groups during extended culture of human *in vitro* embryos. The secondary objective was to evaluate cumulative implantation, clinical pregnancy and live birth rates obtained after fresh and frozen-thawed morula/blastocyst transfers in both "5% oxygen exposure" and "2% oxygen exposure" groups. The level of expression of numerous key factors in human embryo development and implantation have also been investigated in human embryos donated for the research and cultured under low (5%) or ultra-low (2%) oxygen level during extended embryo culture.

RESULTS: As expected, the maternal age and the total number of IVF cycles were significantly higher in the subsequent IVF attempt associated with "2% oxygen exposure". All other clinical and biological parameters were similar in both groups. The blastocyst formation rate (55% vs. 44%, $p<0.001$) and usable blastocyst formation rate (33% vs. 22%, $p<0.001$) were both significantly higher in the "2% oxygen exposure" group than in "5% oxygen exposure" group during extended embryo culture. There was a statistically insignificant trend in implantation, clinical pregnancy and live birth rates in the "2% oxygen exposure" group compared to the "5% oxygen exposure" group after fresh morula/blastocyst transfers. The cumulative implantation (33% versus 17%, $p<0.05$), clinical pregnancy (37% versus 15%, $p<0.01$), and live birth (23% versus 8%, $p<0.01$) rates were significantly higher in the "2% oxygen exposure" group than in "5% oxygen exposure" group, respectively. Key factors in trophoblast proliferation, survival and invasion were significantly increased in research embryos cultured under 2% of oxygen during extended culture compared to 5%.

CONCLUSIONS: Improved IVF outcomes were obtained in the same couples when ultra-low oxygen exposure (2%) was used compared to low oxygen exposure (5%) during extended embryo culture, in spite of the negative impact of increased maternal age. Ultra-low oxygen exposure may improve blastocyst formation and implantation potential by improving trophoblast implantation ability during IVF.

EARLY PREGNANCY

O-109 1:50 PM Sunday, October 18, 2020

CHRONIC ENDOMETRITIS: WHAT IS THE PREVALENCE AMONG HEALTHY CONTROLS?. Dana B. McQueen, MD, MAS,[1] Kruti P. Maniar, M.D.,[2] Rafael Confino, BS,[2] Lia Bernardi, MD,[1] Mary Ellen Pavone, MD, MSCI.[1] [1]Northwestern Feinberg School of Medicine Chicago, IL; [2]Northwestern University, Chicago, IL.

OBJECTIVE: To evaluate the prevalence of chronic endometritis (CE) in women with unexplained recurrent pregnancy loss (RPL) and healthy controls.

DESIGN: Cohort Study.

MATERIALS AND METHODS: IRB approval was obtained. The RPL group included women with $\geq$ two pregnancy losses, endometrial biopsy (EMB) between 1/2016 and 12/2018, TSH values $<$ 4 mU/L, negative antiphospholipid antibodies and normal uterine anatomy. The control group included volunteers without a history of RPL, infertility, uterine fibroids, polyps, pelvic inflammatory disease or retained pregnancy tissue recruited between 5/2019 and 2/2020. Women 18-50 years of age were included. H&E and CD138 immunohistochemical staining were performed on all endometrial biopsies. A single pathologist blinded to patient history recorded the number of plasma cells per 10 high power fields (HPF) and the presence of endometrial stromal changes (spindling, edema, breakdown, pigment deposition, areas of hypercellularity, and presence of inflammatory cells). Assuming a 3% prevalence of CE in controls and 30% in RPL, 25 controls and 50 women with RPL were needed to detect a difference in the rate of CE with 80% power and alpha of 0.05.

RESULTS: 76 women were included, 50 with RPL and 26 controls. The cohort had a mean age of 34.6 (SD 4.1) years and mean BMI of 26.0 (SD 6.2) kg/m^2. Women with RPL had a mean of 3.1 (SD 0.9) prior pregnancy losses, while controls had no prior pregnancy losses. When the presence of

plasma cells alone was used to define CE, the prevalence among women with RPL was 56% (28/50) with ≥ 1 plasma cell, 44% (22/50) with ≥ 2 plasma cells and 26% (13/50) with ≥ 5 plasma cells by CD138 staining. Using these same criteria, the prevalence of CE among controls would be 31% (8/26) with ≥ 1 plasma cell, 27% (7/26) with ≥ 2 plasma cells and 8% (2/26) with ≥ 5 plasma cells. However, when both endometrial stromal changes and plasma cells were required for CE diagnosis, there were no cases of CE in the control group. Using this definition, the prevalence in the RPL group was 30% (15/50) with ≥1 plasma cells, 28% (14/50) with ≥2 plasma cells and 16% (8/50) with ≥5 plasma cells by CD138 staining, and was statistically significantly higher in women with RPL compared to controls (P=0.0015, 0.0016, and 0.04, respectively).

CONCLUSIONS: Establishing specific diagnostic criteria for CE is necessary for both research and evidence-based treatment guidelines. We demonstrate that while rare plasma cells were found in EMB samples from healthy controls, the presence of plasma cells and endometrial stromal changes was isolated to the RPL cohort. Given that no controls were found to have both plasma cells and endometrial stromal changes, we propose that the definition of CE include 1 or more plasma cells in addition to the presence of endometrial stromal changes. Cases in which endometrial stromal changes are visualized, but no plasma cells are identified by H&E, would benefit from CD138 staining to identify plasma cells. We demonstrate that when using strict criteria to define CE, women with RPL have a significantly higher rate of CE compared to controls. An EMB should be considered as part of the evaluation for RPL.

SUPPORT: Friends of Prentice, Northwestern University

O-110 2:05 PM Sunday, October 18, 2020

MEDICAL VERSUS EXPECTANT MANAGEMENT IN WOMEN WITH INCOMPLETE FIRST-TRIMESTER MISCARRIAGE INITIALLY TREATED WITH MISOPROSTOL: A RANDOMIZED CONTROLLED STUDY. Mahmoud A. Abdelaleem, MD, Mohammed Khairy Ali, MD, Samr Emam, MBBCh, Ahmed M. Abbas, MD. Department of Obstetrics and Gynecology Faculty of Medicine, Assiut University, Assiut, Egypt.

OBJECTIVE: To compare the effectiveness and safety of vaginal misoprostol versus expectant management in women with an incomplete first-trimester miscarriage who had been treated before with misoprostol.

DESIGN: Open labeled, parallel, randomized clinical trial (NCT03148561-clinicaltrial.gov).

MATERIALS AND METHODS: From July 2017 to July 2019, women with a first-trimester miscarriage who had been treated with misoprostol were invited to participate in our study. An incomplete miscarriage was diagnosed when there was a history of passage of tissue and there was heterogeneous material in the uterine cavity with an endometrial thickness of >10 mm by transvaginal ultrasound (TV/US). Eligible women who gave their informed consent were randomized to either group I: misoprostol group received misoprostol 800 μg once dose placed in the posterior vaginal fornix or group II: no intervention group (expectant management). The primary outcome was the number of patients with complete miscarriage at one week. Complete miscarriage is defined as endometrial thickness of <10 mm by TV/US. We calculated the sample size based on our primary outcome (the rate of complete miscarriage). Previous study reported that the success rate of expectant management of incomplete miscarriage after 1 week was 48.5%**.** Using two sided chi-square ($\chi 2$) test with α of 0.05, a total sample size of at least 84 patients in the 2 groups (42 in each arm) will have 80% power to detect a 30% difference between both groups [odds ratio of 3.8] (Epi-info™, CDC, USA).

RESULTS: Eighty-four women were divided equally into two groups; each group included 42 women. Both groups were homogeneous in baseline socio-demographic and obstetric data without statistically significant differences. As regard our primary outcome; we found that the rate of complete miscarriage at one week was significantly higher in misoprostol group than expectant group (29 (69.0%) vs. 7 (16.7%); p=0.000, respectively). There were two patients (4.8%) in group I and 5 patients (11.9%) in group II subjected to surgical evacuation after failed achievement of complete miscarriage at four weeks. The rate of complete miscarriage at two weeks was significantly higher in misoprostol group than expectant group (p=0.000). However; at four weeks; both groups were similar in the rate of complete miscarriage (p= 0.433).

CONCLUSIONS: Vaginal misoprostol seems to be effective in achieving complete uterine evacuation than expectant management in women with incomplete first-trimester miscarriage.

SUPPORT: NONE

O-111 2:20 PM Sunday, October 18, 2020

GNRH ANTAGONISTS INHIBIT TROPHOBLAST INVASION, PROLIFERATION AND OUTGROWTH IN PLACENTA FROM WOMEN WITH ECTOPIC PREGNANCY. Bo Peng, Ph.D.,[1] Lobna Abdellatif, M.Sc.,[2] Paul J. Yong, M.D., Ph.D.,[2] Alexander G. Beristain, Ph.D.,[2] Andrew Horne, MB ChB, Ph.D.,[3] Mohamed Ali Bedaiwy, M.D., Ph.D.[2] [1]American University of the Caribbean, School of Medicine, Cupecoy, Sint Maarten (Dutch part); [2]University of British Columbia, Vancouver, BC, Canada; [3]The University of Edinburgh, Edinburgh, United Kingdom.

OBJECTIVE: Ectopic pregnancy (EP) is a leading cause of maternal morbidity and mortality. Besides surgical intervention, methotrexate (MTX) therapy is the only approved medical treatment for EP. In addition to its side effects, the rate of treatment failure could reach up to 30%. Gonadotropin-releasing hormone (GnRH) and its receptor are abundantly expressed in EP implantation sites. GnRH also has been shown to facilitate implantation by promoting trophoblast invasion. The objective of our study is to investigate the role of GnRH antagonists in inhibiting invasion, proliferation, and outgrowth in a *de novo* primary EP trophoblast cell model and a 3D placental explant model.

DESIGN: *In vitro* primary EP trophoblast cell cultures and *ex vivo* placental explants.

MATERIALS AND METHODS: Placental tissues (n=15) were collected post salpingectomy or salpingostomy, from women with tubal EP. Patients gave written consent to participate in our study. Placental tissues were carefully dissected to remove attached Fallopian tube tissues, then digested with Collagenase-I enzyme to establish *in vitro* primary culture. Villi from the first-trimester eutopic placenta (n=4) were obtained after elective termination of pregnancy and placed in Matrigel-coated culture inserts to establish *ex vivo* placental explants. Primary cultured ectopic cells and eutopic tissue villous explants were subjected to GnRH antagonists Ganirelix or Cetrorelix. The cell invasiveness was examined by a transwell cell invasion assay. Cell proliferation capabilities were evaluated by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay. Explant growth profiles were examined via imaging and measuring the area and length of outgrowth.

RESULTS: Ganirelix significantly inhibited the cell invasiveness of primary trophoblast cells isolated from ectopic placentas at 48h. The cell proliferation of these cells was significantly decreased after Cetrorelix treatment at 72h and 96h. Also, at 48h, Cetrorelix significantly attenuated both the growth area and the length of columns outgrowth from the eutopic placental explants.

CONCLUSIONS: GnRH antagonists attenuate cell invasiveness and proliferation of primary EP trophoblast cells, as well as the outgrowth of villous tissue explants from eutopic placentas. Thus, GnRH antagonists may have the therapeutic potential to treat EP medically.

SUPPORT: This work was supported by a Nelly Auersperg Award from the Women's Health Research Institute to M.A.B.

O-112 2:35 PM Sunday, October 18, 2020

PARENTAL ORIGIN OF EMBRYONIC ANEUPLOIDY IN COUPLES WITH RECURRENT PREGNANCY LOSS. Dana B. McQueen, MD, MAS,[1] Marissa L. Luck, MD,[1] Lydia Hughes, MD,[1] Rachel Ruderman, MD, MPH,[1] Rafael Confino, BS,[1] Melissa K. Maisenbacher, M.S.,[2] Mary Ellen Pavone, MD, MSCI,[1] Lia Bernardi, MD.[1] [1]Northwestern Feinberg School of Medicine Chicago, IL; [2]Natera, San Carlos, CA.

OBJECTIVE: To evaluate the relationship between recurrent pregnancy loss (RPL) and parental origin of embryonic aneuploidy.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Institutional Review Board approval was obtained. All in vitro fertilization (IVF) cycles utilizing preimplantation genetic testing for aneuploidy between 1/2015 and 1/2020 were reviewed. Overall rates of embryonic aneuploidy, as well as rates of maternal and paternal aneuploidy were compared between groups. RPL was defined as three or more pregnancy losses less than 20 weeks gestational size. Continuous variables were compared with a student's t-test and categorical variables with a Chi-square. Assuming an aneuploidy rate of 50%, in order to detect a 10% difference between groups with 80% power and alpha of 0.05, 240 embryos from RPL group and 1200 embryos from non-RPL group were needed.

RESULTS: A total of 453 IVF cycles were included; 62 in women with RPL and 391 in women without RPL. There were no significant differences in maternal age, maternal body mass index (BMI), anti-mullerian hormone (AMH), paternal age, paternal BMI, abnormal semen analysis results, days of stimulation, number of oocytes, number fertilized oocytes or number of blastocysts biopsied between groups (Table). A total of 1720 embryos were analyzed, 275 in women with RPL and 1445 in women without RPL. There was no difference in the rate of embryonic aneuploidy (52.7% vs. 50.9%, P=0.63) or maternal aneuploidy (40.7% vs. 41.4%, P=0.96) between women with and without RPL. There was a significantly higher rate of paternal aneuploidy in women with RPL, 11.6% vs 7.8%, P=0.04. The paternal aneuploidy rate increased with number of prior pregnancy losses, with a rate of 20.5% (18/88) in cycles from women with a history of four or more pregnancy losses.

CONCLUSIONS: Paternal aneuploidy rates were significantly higher in IVF cycles of women with a history of three or more prior pregnancy losses. Further investigation is needed to determine if higher rates of paternal aneuploidy are associated with increased sperm DNA fragmentation. Ultimately, a comprehensive understanding of the male contribution to pregnancy loss is essential in order to effectively identify and treat paternal causes of RPL.

Mean (SD)	RPL (N=62 cycles, 275 embryos)	Not RPL (N=391 cycles, 1445 embryos)	P-value
Maternal Age, yr	36.6 (3.5)	37.5 (3.5)	0.06
BMI, kg/m^2	24.4 (4.1)	25.1 (5.0)	0.30
AMH, ng/mL	3.4 (2.9)	3.0 (2.3)	0.22
Day 3 FSH, mIU/ml	7.4 (2.3)	7.4 (2.2)	1.0
Paternal Age, yr	38.7 (4.9)	39.6 (5.6)	0.23
Paternal BMI, kg/m^2	27.7 (4.3)	27.6 (4.3)	0.87
Abnormal Semen Analysis, % (N)	40.3% (25/62)	52.2% (204/391)	0.11
Oocytes Retrieved	15.8 (8.7)	16.0 (8.3)	0.86
Fertilized Oocytes	9.0 (5.1)	8.8 (5.9)	0.80
Blastocysts biopsied	4.4 (2.9)	3.7 (2.7)	0.06

O-113 2:50 PM Sunday, October 18, 2020

SINGLE NUCLEOTIDE POLYMORPHISM (SNP) ARRAY ANALYSIS OF 63,277 PRODUCTS OF CONCEPTION (POC) SAMPLES: A 10-YEAR LABORATORY EXPERIENCE. Melissa K. Maisenbacher, M.S.,[1] Katrina Merrion, MS,[2] Brynn Levy, M.Sc.(Med)., Ph.D., FACMG,[3] William H. Kutteh, MD, PhD.[4] [1]Natera San Carlos, CA; [2]Natera, Inc., CA; [3]Columbia University, New York, NY; [4]Clinical Professor, Memphis, TN.

OBJECTIVE: To report on the spectrum of findings identified in a large cohort of POC samples using a SNP-based array platform.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: Review of 63,277 consecutive fresh POC samples sent over a 10-year period to a single reference lab. Fresh POC samples were shipped with maternal blood samples to rule out maternal cell contamination (MCC) and determine parental origin of abnormalities. Genotyping was performed using Illumina CytoSNP-12b microarrays with bioinformatics.

RESULTS: Fetal results were obtained on 54,466 of 63,277 samples (86.1%), 8559 (13.5%) had MCC and 252 (0.4%) had incomplete results. From the 54,466 cases with fetal results, 24,483 (44.9%) were euploid and 29,983 (55.1%) were aneuploid. The average maternal age at the time of pregnancy loss was 34.2 years (range 13.6-53.0 years). The average gestational age was 71.8 days (range 11-273 days). The male:female (M:F) ratio of normal results was 1.0:0.98. The M:F ratio of abnormal results was 0.82:1; excluding cases of monosomy X, the M:F ratio of abnormal results was 1:0.99. Abnormal results were categorized as single aneuploidy, multiple aneuploidy, triploidy, deletions/duplications, full paternal uniparental disomy (UPD) and other (Table 1). Monsomy of chromosome 21 and X were the most commonly seen, monosomy 18 was seen in 2 cases, and monosomy of chromosomes 2, 3, 4, 7, 11 and 21 were each seen in a single case. Trisomy of every chromosome was identified with chromosomes 15, 16, 12, 22, and X being the most common representing approximately 2/3 of all single aneuploidy cases.

TABLE 1. Rates of Abnormal Results

Type of Abnormality	Number of Cases	Percentage of Abnormal Cases (%)
Single aneuploidy	22,493	75.0
Multiple aneuploidy	1702	5.7
Triploidy	3981	13.3
Deletions/Duplications	1378	4.6
Full Paternal UPD	188	0.6
Other*	227	0.8
TOTAL	29,984	100

*Includes single UPD, tetraploidy, mosaicism and complex findings.

CONCLUSIONS: Testing of POC samples using traditional karyotyping presents challenges related to cell culture failure, long turnaround times and detection limitations. One study reported a 1:2 M:F ratio due to unidentified MCC and a cell culture failure rate of >20%.[1] SNP microarray analysis of POC samples allows for identification of MCC resulting in an almost 1:1 M:F ratio, a failure rate of <0.5%, and an average turnaround time of 5 business days. Rates of types of abnormalities seen in karyotype compared to SNP array are similar, but SNP array also identifies additional chromosomal causes of pregnancy loss including deletions and duplications down to 1 Mb.[1,2] Using SNP for miscarriage analysis is clinically effective and provides an accurate answer to explain a pregnancy loss and may help direct medical management.

References

1. Menasha et al., Genetics in Med. 2005 Apr;7(4):251-263.
2. Levy et al., Obstet Gynecol. 2014 Aug;124(2 Pt1):202-9.

SUPPORT: Sponsored by Natera, Inc.

O-114 3:05 PM Sunday, October 18, 2020

A BIOCHEMICAL PREGNANCY LOSS AFTER THE FIRST FRESH EMBRYO TRANSFER: CURSE OR BLESSING? Liselotte Gezels, MD, Shari Mackens, MD, Annalisa Racca, MD, Anick De Vos, PhD, Herman Tournaye, MD, PhD, Christophe Blockeel, MD, PhD. Universitair Ziekenhuis Brussel Jette, Belgium.

OBJECTIVE: To evaluate whether subsequent reproductive outcomes differ in patients with a biochemical pregnancy loss (BPL) versus a negative pregnancy test following the first fresh embryo transfer (ET).

DESIGN: A single-center, 9-year (2010-2018), retrospective cohort study.

MATERIALS AND METHODS: Demographic and IVF/ICSI treatment characteristics were collected for both study groups. The outcome of the subsequent ET was retrieved with live birth rate (LBR) as primary endpoint. Secondary endpoints were subsequent ET's early pregnancy loss rate and cumulative LBR taking into account all ETs performed within one year after the first unsuccessful ET, as well as spontaneous conceptions during this time-period. The time to reach an ongoing pregnancy was calculated and compared between both study groups. Two multivariate logistic regression models were applied to correct for potential and relevant confounders a) LBR following the subsequent ET and b) LBR resulting from all ETs and spontaneous conceptions within one year.

RESULTS: Of the 2404 included first fresh single ETs, 2221 resulted in a negative hCG test and 183 in a BPL. Maternal age was the only demographic parameter found to be significantly different between both groups (32.8±4.7 years in the hCG- group vs 32.0±4.6 years in the BPL group, p=0.02). IVF/ICSI treatment cycle characteristics differed between groups in terms of the ET stage (48.8% blastocyst transfer in the hCG- group vs 65.9% in the BPL group, p<0.001) and the number of surplus vitrified embryos (respectively, 1.8±2.2 and 2.1±2.1, p=0.03). Unadjusted analysis of the LBR following the subsequent ET was in favor of the BPL group [35.2% compared to 27.6% in the hCG- group (p=0.05)]. No higher incidence was observed for another BPL or early miscarriage in that subsequent ET cycle (BPL rate of 9.2% in the hCG-group vs 12.8% in the BPL group, p=0.33 and early miscarriage rate of, respectively, 14.6% vs 15.1%, p=0.87). Unadjusted analysis of the LBR taking into account further ETs and spontaneous conceptions within the following year was significantly different and 54.8% in the hCG- group vs 63.3% in the BPL group (p=0.04). The time to reach an ongoing pregnancy was comparable between both groups (19.6±12.5 weeks for the hCG- group

vs 20.9±12.9 weeks for the BPL group, p=0.23). The multivariate logistic regression models correcting for relevant confounders refuted the unadjusted analyses and showed study groups to have similar success rates (respectively, OR 1.41, CI 0.97-2.05, p=0.07 for the LBR after the subsequent ET and OR 1.27, CI 0.90-1.80, p=0.18 for the LBR after one year).

CONCLUSIONS: Patients with a BPL versus a negative pregnancy test following the first fresh ET have comparable subsequent reproductive outcomes. When experiencing a BPL after a first fresh ET, patients can be reassured that they do not seem to have an increased risk of encountering another early pregnancy failure when compared to patients having a negative hCG test and that they have similar chances of reaching a successful pregnancy following the subsequent ET, but also at the timepoint of one year and this within a comparable time window.

LEGAL AND ETHICAL REPRODUCTIVE ISSUES

O-115 1:50 PM Sunday, October 18, 2020

BRINGING INFORMED CONSENT TO THE 21ST CENTURY – THE IMPACT OF AN ONLINE RESOURCE AND CONSENT PROCESS ON FERTILITY PATIENT PERCEPTIONS. Abigail L. Bernard, MD,[1] Ashley K. Barbour, MPhys,[2] Jody L. Madeira, Ph.D., J.D.,[3] Steven R. Lindheim, M.D.,[4] Linnea R. Goodman, MD.[1] [1]University of North Carolina Raleigh, NC; [2]Brody School of Medicine at East Carolina University, Greenville, NC; [3]Professor of Law, Bloomington, IN; [4]Wright State University, Dayton, OH.

OBJECTIVE: To determine if the use of a multimedia electronic (e)-learning resource and e-consent process influences patients' perception of their treatment team and eases the administrative burden.

DESIGN: Prospective randomized controlled trial.

MATERIALS AND METHODS: Patients undergoing their first intrauterine insemination (IUI) or in-vitro fertilization (IVF) cycle were randomized to receive standard fertility counseling and sign paper consents with their physician and nurse team (conventional group) or to receive standard counseling plus access to an interactive multimedia e-learning and e-consent platform (EngagedMD group). Surveys were administered prior to treatment (T1) and at cycle completion (T2) to assess their treatment experience, perception of their treatment team, and the informed consent (IC) process. A therapeutic index (TI) score was generated based on the sum of patients' responses to six questions including how much they agreed or disagreed with statements regarding their physician/nursing team. Additionally, patients were surveyed about their perception of IC in general and their experience with the consent process. The six physicians and four nurses involved in patient care were surveyed regarding their experience during the study. Statistics were performed using the student's t-test and Chi-squared test where appropriate.

RESULTS: Demographics for the 77 patients (42=IVF and 35=IUI) including age, duration of infertility and education level were similar between the conventional and EngagedMD groups. Calculated TI scores revealed no difference at T1 ($p = 0.81$) or T2 ($p = 0.68$) between the conventional and EngagedMD groups. Regarding IC, there was no difference between patients' summed responses in the conventional and EngagedMD groups. Of those that used the online platform, most patients agreed that it was helpful (92.5%), user-friendly (81.4%), and would recommend it to a friend (85.2%). Of those that signed consents online, 25 of 27 (92.5%) patients preferred this over standard paper consents. When rating overall fertility treatment satisfaction on a 1-100 scale, there was no difference between those that used EngagedMD and those that did not (85.2 +/- 21/1 vs. 83.8 +/- 18.5; $p = 0.82$). While none of the physicians surveyed felt that the addition of e-consents aided in patient understanding, all physicians and nurses felt that having e-consents was a valuable addition to the practice and made the process easier.

CONCLUSIONS: The addition of an online learning and consent platform did not significantly impact patients' perception of their treatment team, nor their overall perception of the informed consent process. However, patients and providers using the online consent process agreed that it was a valuable addition to streamline the consent process.

References: none

SUPPORT: none

O-116 2:05 PM Sunday, October 18, 2020

DECISION REGRET AFTER AUTOLOGOUS IN VITRO FERTILIZATION IN WOMEN AGE 42 AND OVER. David Huang, MD, Eleni Greenwood Jaswa, MD, MSc, Marcelle I. Cedars, MD, Heather G. Huddleston, MD. University of California San Francisco Department of Obstetrics and Gynecology, San Francisco, CA.

OBJECTIVE: An increasing number of women greater than or equal to 42 years old choose to pursue autologous IVF (aIVF) despite persistently low success rates in this age group. Few data exist on these patients' reflections on their decision after undergoing aIVF. We aim to describe the level of decision regret in women age 42 and over who underwent aIVF and identify factors associated with moderate/severe regret.

DESIGN: Retrospective cohort survey study.

MATERIALS AND METHODS: Between 2012-2018, 463 women greater than or equal to 42 years old underwent aIVF at a single academic institution. Patients were invited to participate in an online survey that inquired their experience with IVF. The survey contained 38-items, including the validated Decision Regret Scale (DRS) as well as items examining demographics, perceived adequacy of counseling, reproductive outcomes, and impact of IVF on one's relationship, career, and philosophy of life. Our primary outcome was the DRS decision regret score: 0 (no regret), 1-25 (mild regret), and >25 (moderate/severe regret). Demographic and treatment-related variables were compared between patients who demonstrated moderate/severe regret and those with no/mild regret using the Student *t*-test or the chi-square test as appropriate.

RESULTS: Of the 463 eligible participants, 70 (15.1%) obtained at least one live birth from aIVF and 393 (84.9%) did not. The survey was completed by 62 (13.4%) patients; response rate was 37.1% (n=26) in those who obtained a live birth versus 9.2% (n=36) in those who did not. Mean age was 43.1y at time of IVF (range 42-47y), and the elapsed time between survey and last IVF averaged 4.7y (range 1.0-8.1y). Of the 62 respondents, 40.3% (n=25) had no regret, 33.9% (n=21) had mild regret, and 25.8% (n=16) had moderate/severe regret after aIVF. Median DRS score was 7.5 (interquartile range 0-28.75) and the mean was 15.3 (range 0-70). Age at initiating IVF, income, educational attainment, elapsed time from last IVF, and number of aIVF cycles were not associated with higher degree of regret. Having no insurance coverage for IVF was associated with increased regret, though the association did not reach statistical significance (p=0.06). Having no live births was associated with increased regret ($p<0.01$). Among those who were not successful from aIVF, 11.1% (n=4) endorsed no regret, 44.4% (n=16) had mild regret, and 44.4% (n=16) had moderate/severe regret. Of those who failed aIVF but was then successful with donor eggs (n=12), 50.0% (n=6) still reported moderate/severe regret.

CONCLUSIONS: There is a considerable risk of decision regret following aIVF in women age 42 and over. Degree of regret was influenced by insurance coverage for IVF and strongly associated with whether a live birth was achieved. Regret was not eliminated in those who then became successful through donor eggs. Providers should discuss this risk as part of the informed consent. Further data, particularly from those who were unsuccessful, is needed to substantiate these results and identify additional predictors for moderate/severe regret in order to improve patient counseling.

References

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SUPPORT: Not applicable

O-117 2:20 PM Sunday, October 18, 2020

TOP TEN RESEARCH PRIORITIES FOR ETHICS, ACCESS, AND ORGANISATION OF FERTILITY CARE. James M. N. Duffy, DPhil MRes PG HCL MBChB BSc (Hons),[1] Barbara Lynn Collura, MA,[2] Cindy Farquhar, FRANZCOG FRCOG MD MPH,[3] Priority Setting Partnership for Infertility[1]Institute for Women's Health, University College London, Greater London, United Kingdom; [2]RESOLVE: The National Infertility Association, McLean, VA; [3]University of Auckland, Auckland, New Zealand.

OBJECTIVE: To develop the top 10 research priorities for ethics, access, and organization of fertility care.

DESIGN: International consensus development study. Healthcare professionals, people with fertility problems, and others were brought together in an open and transparent process using formal consensus methods advocated by the James Lind Alliance.

MATERIALS AND METHODS: Potential research questions were collated from an initial international survey, a systematic review of clinical practice guidelines, and Cochrane systematic reviews. A rationalized list of confirmed research uncertainties were prioritized in an international survey. Prioritized research uncertainties were discussed during a face-to-face consensus development meeting.

RESULTS: The initial survey was completed by 388 participants, from 40 countries, and 74 potential research questions were submitted. By reviewing 14 clinical practice guidelines and 162 Cochrane systematic reviews a further 19 potential research questions were identified. A rationalized list of 48 confirmed research uncertainties were entered into an interim prioritization survey completed by 317 respondents from 43 countries. The top 10 research priorities for ethics, access, and organization of fertility care were identified during a consensus development meeting involving 41 participants from 11 countries (Table 1).

1 Which public health interventions are effective in preventing infertility?
2 How can the cost of fertility treatment be reduced?
3 How can fertility treatment be made available in lower resource settings?
4 How should the information needs of people with fertility problems be met?
5 What age limit should be applied to women and men seeking fertility treatment?
6 What is the economic burden of infertility?
7 What is the minimum standard of care people with infertility should expect?
8 How should financial conflicts of interest be managed in clinical and research settings?
9 How should social egg freezing be regulated?
10 What are the optimal methods to report long term maternal and offspring outcomes across national and international settings?

Figure 1: Top 10 research priorities for ethics, access, and organization of fertility care

CONCLUSIONS: We anticipate the top 10 research priorities for ethics, access, and organization of fertility care will help research funding organizations and researchers to develop their future research agenda. Healthcare professionals, professional organisations, and patient advocacy groups should champion these research priorities.

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ELECTIVE SINGLE EMBRYO TRANSFER RATES IN THE ERA OF PREIMPLANTATION GENETIC TESTING AND GESTATIONAL CARRIERS: A SART REVIEW.

Bryn Erin Willson, MD, Rebecca Lynne Surrey, MD, MS. UC Davis Health Sacramento, CA.

OBJECTIVE: In recent years, there has been increased utilization of elective single embryo transfer (eSET) as opposed to multiple embryo transfers. Randomized control trials have demonstrated similar pregnancy rates (PR) and live birth rates (LBR) between single and double embryo transfers, however there is a benefit of an overall reduction in multiple gestations, and subsequent neonatal morbidity, with eSET. Additionally, recent advancements in employment of preimplantation genetic testing (PGT) technology has contributed to the success of eSET.

DESIGN: Utilizing the Society for Assisted Reproductive Technology (SART) online database, the goal of this study was to evaluate how often SART-participating clinics utilize eSET with PGT tested embryos created from donor oocytes, specifically with the use of gestational carriers (GC).

MATERIALS AND METHODS: The SART database was queried using 2014, 2015, 2016, and 2017 data with filters "Gestational Carrier" and "PGTA." Donor oocytes cycle characteristics were then reviewed and data recorded including eSET percentage, singleton birth rate, twin birth rate, and higher order multiples birth rate.

RESULTS: In 2017, 1728 recipient cycle starts met criteria. Mean number of embryos transferred 1.3. eSET: 57.1%. Implantation rate 62.7%. Live birth rate 60.3%. Of live births: singleton birth rate 78.9% Twin birth rate 20.3%. Triplets or more 0.8%.Term live birth 78.5%. Preterm 18.1%. Very preterm 3.4%. eSET percentage and multiple birth rate from 2014, 2015, and 2016 are represented in the table below.

CONCLUSIONS: In the setting of improving success rates of assisted reproductive technology, the reproductive endocrinology community has made efforts to decrease the risk of multiples and subsequent neonatal morbidity. A major application of these efforts is to utilize eSET when appropriate. With employment of donor oocytes, PGT, and gestational carriers, eSET rates will likely continue to increase over time.

TABLE 1.

Year	eSET %	Rate of multiples (twin or higher order)	Number of recipient start cycles
2014	44.10%	27.8%	402
2015	47.40%	26.3%	669
2016	51.9%	24.8%	1101
2017	57.10%	21.1%	1728

O-119 2:50 PM Sunday, October 18, 2020

LIABILITY FOR EMBRYO MIX-UPS: LEGAL CASE REVIEW AND RECOMMENDATIONS.

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OBJECTIVE: To discuss recent legal cases of embryo mix-ups to provide recommendations to fertility clinics and reproductive endocrinologists.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: Nexis Uni database and the Public Access to Court Electronic Records portal were used to access case law information and court documents with a focus on lawsuits against reproductive endocrinologists and fertility facilities offering embryo transfer. Emphasis was placed on court decisions, awarded damages, and legal and media coverage related to embryo mix-up events.

RESULTS: A 2018 case of embryo mix-up *Manukyan v CHA Health Systems* resulted in a custody case and a separate suit seeking damages for emotional distress and the $100,000 of legal expenses (1). Claims against the IVF facility included medical malpractice, negligence and intentional infliction of emotional distress (2). In *Andrews v. Keltz* another case of embryo mix-up, all complaints against the reproductive endocrinologist were dismissed, however, the judge ruled the embryologist exhibited negligence and violated the plaintiff's right to informed consent (3). In the case *Hebert v Ochsner*, discrepancies in embryo labeling resulted in the permanent closure of the fertility center (4). A systematic review done by the Center for Disease Control and Prevention found development and implementation of standardized labeling policies and strategies by physicians in the organization to be most effective at reducing patient misidentification due to specimen labeling errors (5).

CONCLUSIONS: When labeling errors and discrepancies in the records of embryo labeling are found, it may be prudent for a fertility clinic to review all patients potentially impacted and provide genetic testing to ensure current parentage prior to embryo implantation. Additionally, establishing a fertility practice as a separate independent business entity such as Limited Liability Company or a Professional Limited Liability Company can protect a physician's personal assets from claims made against the practice. It is advisable for fertility clinics to consider separately insuring embryologists through a stand-alone policy, or to add a rider to the physician's malpractice policy. When faced with a lawsuit with merit, the reproductive endocrinologist should consider an offer to settle for their malpractice insurance policy limit to when damage awards could exceed the policy limit.

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O-120 3:05 PM Sunday, October 18, 2020

HEALTH INSURANCE FOR INFERTILITY SERVICES: IT'S ABOUT WHERE YOU WORK, MORE THAN WHERE YOU LIVE. Nathanael B. Stanley, MA, Tara R. Foti, MPH. University of South Florida Tampa, FL.

OBJECTIVE: The objective of this research is to identify actual uses of existing infertility insurance mandates by people who access infertility services for reproduction, with the purpose of observing the role of employers in the applicability of state-mandated insurance for infertility services.

DESIGN: Accessibility of infertility services are disproportionately experienced by the global public based on sociodemographics such as income, education, race/ethnicity, sexual orientation, and geographic location. Currently, 17 of 50 states have infertility service insurance mandates (National Conference of State Legislatures, 2018), which are assumed to increase accessibility of those services, but no one has critically researched the effect these mandates have on increasing accessibility to those services. An important player in the applicability of this type of insurance is the employer, but current research has not observed the role of employers from both the perspective of patients and organizations that exist to provide financial support for using infertility services.

MATERIALS AND METHODS: Qualitative inquiry consists of 66 interviews with women and men who are U.S. residents age 18-45, as well as 8 expert interviews with organizations. Questions asked in the informal interviews are based on constructs of Social Cognitive Theory (SCT). The selection of these questions reflects the hypothesis that residence, employer, and presence and type of health insurance affect the decisions people make regarding when, how, and to what extent they access infertility services. In SCT, this type of influence on human behavior is referred to as reciprocal causation. Interviews were transcribed verbatim by the PI, and analyzed using MaxQDA using thematic coding. Inter-coder reliability reached at least 85% for all codes.

RESULTS: Results from 66 interviews with women and men in 33 states suggests it is the employer that influences access to any infertility health insurance more than the individual's residence in a state with mandated infertility health insurance. Responses from 8 experts confirm the role of employers in increasing access to infertility services, and express concern about restrictive language within different insurance mandates, knowing their organization's limitations in providing funding to everyone who needs these services to start a family. The majority of participants were currently using infertility services (51.52%), female (92.42%), mean age of 32.7 (*4.09*), mean household income of $155,107, primarily working in healthcare (21.21%), and do not identify with any religion (54.55%). Primary causes of infertility were unexplained (27.3%) and female factor (25.8%), and the majority of people had private health insurance individually or through their employer (87.9%).

CONCLUSIONS: State legislatures can affect reproductive autonomy for residents of other states because of how some employers choose to apply the infertility insurance mandate that exists in their state. It is important to address the effect of public policy qualitatively to truly observe their effectiveness.

HEALTH DISPARITIES

O-121 9:40 AM Monday, October 19, 2020

ASSOCIATION BETWEEN INFERTILITY AND MORTALITY: ANALYSIS OF US CLAIMS DATA. Gayathree Murugappan, MD,[1] Shufeng Li, MS,[2] Ruben J. Alvero, MD,[3] Michael L. Eisenberg, M.D.[4] [1]Stanford University Medical Center, Sunnyvale, CA; [2]Stanford University Medical Center, Stanford, CA; [3]Stanford University, Sunnyvale, CA; [4]Stanford University, Stanford, CA.

OBJECTIVE: To examine the association between female infertility and mortality.

			Infertile	Non-Infertile	aHR (95% CI)
All		N	72,786	3,845,790	
		Deaths (N, %)	13,635 (0.35)	307 (0.42)	1.24 (1.10 -1.38)
Age (years)	<35	N	39,916	2,222,058	
		Deaths	110 (0.28)	4,186 (0.19)	1.31 (1.08 - 1.59)
	≥35	N	32,870	1,623,732	
		Deaths	197 (0.60)	9,449 (0.58)	1.26 (1.10 - 1.46)
MetS Diagnoses	0	N	54,649	3,059,843	
		Deaths	168 (0.31)	7,914 (0.26)	1.24 (1.07 - 1.44)
	≥1	N	18,137	785,947	
		Deaths	139 (0.77)	5,713 (0.73)	1.24 (1.05 - 1.47)
CCI	0	N	55,980	3,104,100	
		Deaths	133 (0.24)	6,966 (0.22)	1.15 (0.97 - 1.37)
	≥1	N	16,806	741,690	
		Deaths	174 (1.04)	6,661 (0.90)	1.20 (1.03 - 1.39)
Follow-up time (years)	<4	N	47,384	2,415,988	
		Deaths	211 (0.45)	9,117 (0.38)	1.09 (0.95 - 1.25)
	≥4	N	25,402	1,429,802	
		Deaths	96 (0.38)	4,518 (0.32)	1.22 (0.99 - 1.50)
Race	Asian	N	7,129	197,821	
		Deaths	12 (0.17)	326 (0.16)	1.20 (0.67 - 2.14)
	Black	N	6,972	364,996	
		Deaths	47 (0.67)	1,803 (0.49)	1.33 (0.996 - 1.78)
	Hispanic	N	9,046	445,851	
		Deaths	18 (0.20)	1,010 (0.23)	0.83 (0.52 - 1.33)
	White	N	40,029	2,365,380	
		Deaths	199 (0.50)	9,037 (0.38)	1.32 (1.14 - 1.52)

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: A total of 72,786 infertile women were identified in the Optum Clinformatics Datamart from 2003-2019 by infertility diagnosis, testing and treatment codes and compared with 3,845,790 non-infertile women seeking routine gynecologic care. Baseline comorbidities were assessed using the presence of ≥ 1 metabolic syndrome (MetS) diagnoses and the Charlson Comorbidity Index (CCI). The primary outcome of all-cause mortality was identified by linkage to Social Security Administration Death Master File outcomes and medical claims. The association of infertility with mortality was examined using Cox proportional hazard regression while adjusting for age, year of evaluation, smoking, number of visits per year, nulliparity, obesity, region of country and race.

RESULTS: Among 16,473,458 person-years of follow up, 13,942 women died. Overall, infertile women had a 24% higher risk of death (aHR 1.24, 95% CI 1.10-1.38) compared to non-infertile women. When stratified by age < 35 or ≥35 years or baseline medical comorbidity, the association between infertility and mortality remained (Table). Risk of death among infertile women did not differ significantly by follow up time. The association was similar for White, Black and Asian women. In contrast, there was no association between infertility and mortality among Hispanic women.

CONCLUSIONS: Infertile women are at increased risk of mortality, reinforcing the disease burden associated with infertility and its potential for longer-term health effects. Longer-term studies are needed to address the time course of this association.

References: None

SUPPORT: None

O-122 9:55 AM Monday, October 19, 2020

NEIGHBORHOOD DISADVANTAGE AND ASSOCIATION WITH OVARIAN RESERVE.

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OBJECTIVE: The purpose of this study was to evaluate the association between neighborhood disadvantage by Area Deprivation Index (ADI), which is a factor-based index measuring neighborhood disadvantage using US Census indicators of education, housing, poverty and employment, and markers of ovarian reserve including antral follicle count (AFC) and anti-Müllerian hormone (AMH).

DESIGN: Cross-sectional cohort study.

MATERIALS AND METHODS: 200 women aged 18-44 with regular menstrual cycles were included. Women who were currently pregnant or who had history of major chronic illness, infertility or ovarian surgery were excluded. Participants' zip codes were used to calculate national ADI percentile using the 2015 University of Wisconsin Neighborhood Atlas. Height and weight were obtained at enrollment to assess body mass index (BMI). AFC was obtained by transvaginal ultrasound. AMH was obtained at the time of participation. Overweight and obese participants (BMI>25) from the 25% most disadvantaged neighborhoods were compared to overweight and obese participants from the 75% least disadvantaged neighborhoods; normal weight participants were similarly compared. One-way ANOVA was used to compare the mean AFC and AMH between groups. Linear regression was used to control for confounding variables including age, race and smoking. Statistical analyses were performed using SPSS Version 25.

RESULTS: Participants had a mean age of 30.92 +/- 6.7 years at enrollment, BMI of 28.28 +/- 7.11, AFC of 27.86 +/- 15.36 and AMH of 2.94 +/- 1.96 ng/mL. There were 48 women who lived in the most disadvantaged neighborhood quartile, of which 75% (n=36) were overweight or obese. There were 145 women who lived in the 75% least disadvantaged neighborhoods, of which 54% (n=79) were overweight or obese. Overweight and obese women from the most disadvantaged neighborhoods had a significantly lower AFC and AMH compared to those from the least disadvantaged neighborhoods and this difference persisted when controlling for age, race and smoking (p=0.028 and p=0.007, respectively). Among normal weight women, there was no statistically significant difference in AFC or AMH when comparing women from the most disadvantaged neighborhoods to those from the least disadvantaged neighborhoods (p=0.227 and p=0.557, respectively).

CONCLUSIONS: Neighborhood disadvantage by ADI is associated with lower AFC and AMH in overweight and obese women, but is not significant in normal weight women. Living in a disadvantaged area may impact ovarian reserve, and this impact may be more pronounced in overweight women, suggesting a role for diet. ADI is a helpful measure of socioeconomic disadvantage and its use can be expanded to fertility medicine. Future studies are needed to explore the relationship between socioeconomic status and ovarian reserve, and to clarify the impact of obesity and diet.

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SUPPORT: **Support:** NIH grant UL1TR000448; Washington University Institute of Clinical and Translational Sciences.

O-123 10:10 AM Monday, October 19, 2020

BLACK RACE RESULTS IN LOWER LIVE BIRTH RATE (LBR) IN FROZEN-THAWED BLASTOCYST TRANSFER CYCLES (FET): AN ANALYSIS OF 7,002 SART FET CYCLES.

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OBJECTIVE: Previous studies of fresh IVF cycles demonstrate lower pregnancy rates in black compared to white women, whereas a small FET study from a single site showed comparable pregnancy rates (1). We examined if racial disparities in IVF pregnancy outcomes persisted in FET cycles on a national level.

DESIGN: Retrospective cohort study with SART data comparing LBR in FET cycles with White, Black, Asian and Hispanic women.

MATERIALS AND METHODS: 12,835 SART FET cycles from 2014-16 were screened and 7,002 were included. Only blastocyst FET cycles with known pregnancy outcome were included. Exclusion criteria included missing race (n=4,668), age >43 years, FSH ≥15 IU/L or other race (n=1,165). Primary outcome was LBR. Secondary outcomes were implantation rate (IR), clinical pregnancy rate (CPR), multiple pregnancy rate (MPR) and clinical loss rate (CLR). Chi square test and one-way ANOVA with post-hoc Tukey were used for categorical and continuous variables, respectively. Multiple logistic regression adjusted for potential confounders including age, BMI, parity, smoking status, uterine or tubal factor diagnosis, prior fresh and frozen IVF cycles, use of PGT and number of embryos transferred. A p-value of 0.05 was considered statistically significant.

RESULTS: The groups differed in age, BMI, parity, smoking status, number of previous fresh or frozen cycles, infertility diagnosis, number of embryos transferred and use of PGT (p<0.01.) LBR was significantly lower in Black versus White and Asian, but not Hispanic groups. IR was significantly lower and CLR higher in Black women compared to all other groups. The adjusted odds of LBR was still lower in Black compared to White women (aOR 0.65 [95% CI 0.51-0.82]) and CLR higher (aOR 1.98 [95% CI 1.40 – 2.80]). There was no significant difference between groups in CPR or MPR (Table 1).

TABLE 1. SELECTED BASELINE AND CYCLE OUTCOMES FOR FET CYCLES

Outcomes	White (n=5055)	Black (n=489)	Asian (n=996)	Hispanic (n=462)	p-value
Age (y ± SD)	$34.4 \pm 3.9_a$	$35.6 \pm 3.8_b$	$35.6 \pm 3.7_b$	$35.2 \pm 4.0_b$	<0.01
No. Embryos transferred (n ± SD)	$1.4 \pm 0.6_a$	$1.6 \pm 0.6_b$	$1.4 \pm 0.6_a$	$1.6 \pm 0.6_b$	<0.01
PGT (%, n)	30.9_a (1561/5055)	18.4_b (90/489)	37.1_c (370/996)	24.9_d (115/462)	<0.01
IR (%, n)	42.3_a (3082/7283)	35.0_b (280/800)	41.8_a (581/1390)	37.8_a (277/733)	<0.01
CPR (%, n)	55.3 (2797/5055)	51.7 (253/489)	55. (549/996)	52.6 (243/462)	0.34
LBR (%, n)	45.9_a (2318/5055)	37.6_b (184/489)	44.7_a (445/996)	$43.3_{a,b}$ (200/462)	<0.01
MPR (%, n)	13.5 (377/2797)	15.0 (38/253)	11.5 (63/549)	17.3 (42/243)	0.15
CLR (%, n)	17.1_a (479/2797)	27.3_b (69/253)	18.9_a (104/549)	17.7_a (43/243)	<0.01

*Subscripts (a-d) indicate significant differences between groups.

CONCLUSIONS: Black race remains an independent predictor of reduced LBR in FET cycles, likely due to higher CLR and lower IR.

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SUPPORT: None.

O-124 10:25 AM Monday, October 19, 2020

PSYCHOBIOLOGICAL, CLINICAL, AND SOCIOCULTURAL FACTORS THAT INFLUENCE AFRICAN AMERICAN WOMEN TO SEEK TREATMENT FOR INFERTILITY: A MIXED METHODS STUDY.

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OBJECTIVE: Studies have shown that African American women in the U.S. have twice the prevalence of infertility (14%) than non-Hispanic White women (7%); yet are less likely to seek initial evaluation for infertility. This study sought to explore the facilitators and barriers affecting treatment seeking among African American women within reproductive endocrinology.

DESIGN: We conducted a convergent parallel mixed methods study that combined quantitative data from a retrospective chart review and semi-structured interviews of African American women seeking treatment at a large infertility clinic in the metropolitan Washington D.C Area between January 2015 and September 2019.

MATERIALS AND METHODS: Extracted variables and interview questions were derived from a systematic review examining treatment seeking for infertility. We analyzed retrospective chart review data using descriptive statistics for a random sample of electronic medical records of African American women. A one-time semi-structured interview was conducted with African American women seeking treatment for infertility. Interview transcripts were transcribed verbatim and underwent attributes, descriptive, and values coding prior to thematic analysis. Joint data displays were used for integration analyses.

RESULTS: The analysis sample included 391 records of African American women patients. The mean age of 35.5 years. Most reported minimal past medical history diagnoses and had experienced infertility symptoms, on average, for 24 months prior to evaluation. The majority (77.2%) experienced primary infertility, 45.6% were of female-factor-only origin, and 75.2% had qualifying insurance. Further, 13 African American women completed interviews. A total of 9 themes emerged: 4 barriers and 5 facilitators to treatment seeking. Barriers to treatment seeking for infertility were low risk perceptions, delayed referral despite clinical disclosure, limited or no knowledge of treatment options, and limited or no disclosure of fertility status to peers. Facilitators were symptoms of fertility distress, failing own lifestyle modifications, finding culturally competent providers, obtaining referral after complex gynecological surgeries, and social media influence. Many of the quantitative and qualitative findings converged, however, the psychological findings diverged showing that although many reported no mental health diagnoses on evaluation, fertility distress and stigma influenced seeking care.

CONCLUSIONS: African American women are often older and wait long periods of time prior to seeking treatment. Many of these delays can be related to knowledge of infertility risk factors and options of treatment. African American women may have many unmet psychological needs related to stigma of race and fertility status. Infertility facilities should consider the diversity and cultural competency of staff when attempting to help improve access to African American women. Additional awareness of infertility and treatment options should be encouraged at the primary care levels as well.

SUPPORT: None

O-125 10:40 AM Monday, October 19, 2020

DOES ETHNICITY IMPACT OOCYTE CRYOPRESERVATION OUTCOMES? NATIONAL TRENDS AND OUTCOMES IN AUTOLOGOUS OOCYTE CRYOPRESERVATION IN THE UNITED STATES.

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OBJECTIVE: To characterize trends, characteristics and outcomes of oocyte cryopreservation (OC) cycles in the United States (U.S.) from 2012-2016, stratified by self-reported race/ethnicity.

DESIGN: Retrospective cohort analysis using the Society for Assisted Reproductive Technology Clinical Outcome Reporting System for cycles completed from 2012-2016.

MATERIALS AND METHODS: OC cycles were separated by race/ethnicity: Non-Hispanic White, Non-Hispanic Black, Asian/Pacific Islander, Hispanic, Other (American Indian, Alaskan Native, or mixed race). Trends in both absolute number of cycles as well as proportion of cycles within each group were calculated. Race/ethnicity was not reported for 47.2% of cycles; multiple imputation was used to account for missing values. Poisson regression models were used to estimate associations between race/ethnicity and oocyte yield and maturity.

RESULTS: Between 2012-2016, there were a total of 29,631 OC cycles. Of the cycles with reported race, the majority, 66.5%, were in White patients, 9.6% were in Asian/Pacific Islander patients, 7.1% were in Black patients, and 4.5% were in Hispanic patients. The total number of OC cycles increased yearly among all ethnic groups; this was most significant for Asian/Pacific Islander patients with an increase from 245 cycles in 2012 to 1,010 cycles in 2016 (p=0.001). Asian/Pacific Islanders also saw the largest increase in proportion of all OC cycles, from 8.4% to 11.4%. Among all cycles, the women were most likely to be under 35 years across ethnic backgrounds, with the exception of Asian/Pacific Islanders, who most commonly performed OC between 35 and 37 years. The majority of cycles were in women with a normal body mass index (BMI) (18.5-24.9 kg/m^2) across races, however Black and Hispanic patients had a disproportionate trend toward a higher BMI. Geographically, in the southern U.S., patients were

predominantly White, Black and Hispanic, while the western U.S. included mostly Asian/Pacific Islander patients. The majority of cycles (79.4%) were in patients who underwent one OC cycle, but Asian/Pacific Islander patients were more likely to do two or more cycles (2: 17.4%, 3 or more: 8.2%) in comparison to other ethnic groups. There was a trend towards higher gonadotropin dosing for Black patients (9.9% required >6,000 IU); however, this was not significant as compared to White patients in the adjusted analysis. After adjusting for age, BMI, stimulation protocol, and gonadotropin dose, predicted oocyte yield and percent maturation was similar across all racial/ethnic groups. Adverse cycle outcomes (e.g. infection, bleeding requiring transfusion, hospitalization) were rare overall.

CONCLUSIONS: Nationally, OC cycles are continuing to increase in number, most often in patients under 35 years, with consistent proportions of patients of different racial/ethnic backgrounds pursuing OC over time. Despite low absolute numbers, trends in cancellation and increased gonadotropin dosing are disproportionately seen for minority ethnic groups in comparison to White patients, particularly among Black and Asian/Pacific Islander patients.

O-126 10:55 AM Monday, October 19, 2020

ULTRASOUND CONFIRMED FIBROID PREVALENCE IN A COHORT OF REPRODUCTIVE AGED LATINX FEMALES: DATA FROM THE ENVIRONMENT, LEIOMYOMAS, LATINAS, AND ADIPOSITY STUDY (ELLAS). Torie C. Plowden, MD, MPH,[1] Anne Waldo, MS,[2] Nicole Contreras-Rodriguez, BS,[3] Felix Valbuena, MD,[4] Lisa M. Neff, MD,[5] Mercedes Carnethon, PhD,[6] Donna D. Baird, Ph.D.,[7] Erica E. Marsh, MD, MSCI, FACOG.[2] [1]Womack Army Medical Center Fort Bragg, NC; [2]University of Michigan, Ann Arbor, MI; [3]Reproductive Endocrinology and Infertility, University of Michigan, Ann Arbor, MI; [4]Community Health and Social Services (CHASS) Center, Detroit, MI; [5]Endocrinology, Metabolism, and Molecular Medicine, Northwestern University, Chicago, IL; [6]Northwestern University, Chicago, IL; [7]NIH, National Institute of Environmental Health Sciences, Research Triangle Park, NC.

OBJECTIVE: Fibroids are thought to be highly prevalent in women by the age of 50 with prevalence being reported as 60-70%. Women of color, specifically African-American women, have consistently been found to have a higher prevalence of fibroids than Caucasian women with prevalence as high as 89% by the age of 50. Less is known about the prevalence of fibroids in other ethnic and racial groups, including the Latina/LatinX community. The purpose of this study was to characterize fibroid prevalence among a cohort of healthy, reproductive age LatinX females from the ELLAS study.

DESIGN: Cross-sectional analysis of data from a prospective longitudinal cohort study.

MATERIALS AND METHODS:Reproductive age women were recruited from southeast Michigan and were enrolled in this study from 2018 – 2020. Inclusion criteria included age 21-50 at the time of enrollment, self-identifying as Latino/Hispanic, female sex at birth, no history of malignancy or health condition requiring chemotherapy or radiation, and ability to understand and read either English or Spanish. All participants completed questionnaires on reproductive health and demographics, including age, country of birth, education history, annual household income, acculturation level, health literacy and insurance status. Presence of fibroids at least 0.5 cm in diameter was documented via transvaginal ultrasound conducted by a single ultrasonographer. Images were reviewed by a blinded ultrasonographer to determine presence and number of fibroids. SAS was used for statistical analysis.

RESULTS: 633 women have enrolled in ELLAS and 561 women have completed the first study visit. Mean age of the participants was 37.4 $\pm$ 6.94 years. Women with fibroids were significantly older than women without fibroids (41.1 $\pm$ 5.54 vs 37.0 $\pm$ 6.96; p <0.001) and fibroid prevalence increased significantly with age from 3% in 21-30 year olds to 17.1% in 46-50 year olds. There were no significant differences in demographics between women with and without fibroids including BMI, gravidity and parity. A total of 53 (9.4%) women had uterine fibroids identified on transvaginal ultrasound and of those, the vast majority (79.2%) had a single uterine fibroid with the remainder having between 2-5 fibroids.

CONCLUSIONS: This is the first prospective study of ultrasound confirmed fibroid prevalence in LatinX females. At the baseline ultrasound, we found that the prevalence of uterine fibroids among this cohort was much lower than reported in the literature for either Caucasian or African-American women – particularly amongst older women. Future research is needed to confirm these findings and understand the biological drivers of this difference in prevalence.

O-127 9:40 AM Monday, October 19, 2020

ENDOMETRIAL THICKNESS FOLLOWING OVARIAN STIMULATION WITH GONADOTROPIN, CLOMIPHENE, OR LETROZOLE FOR UNEXPLAINED INFERTILITY, AND ASSOCIATION WITH TREATMENT OUTCOMES. Alexander M. Quaas, MD, PhD,[1] Sarah Z. Gavrizi, MD,[2] Jennifer D. Peck, PhD,[2] Michael P. Diamond, MD,[3] Karl R. Hansen, MD PhD,.[2] Reproductive Medicine Network[1]University of California San Diego San Diego, CA; [2]University of Oklahoma College of Medicine, Oklahoma City, OK; [3]Augusta University, Augusta, GA.

OBJECTIVE: To determine the ability of endometrial thickness (EMT) to independently predict live birth rates (LBR) after ovarian stimulation with intrauterine insemination (OS-IUI) for unexplained infertility, overall and adjusted for OS regimen

DESIGN: Secondary analysis of the Assessment of Multiple Intrauterine Gestations from Ovarian Stimulation (AMIGOS) trial.

MATERIALS AND METHODS: LBRs were examined graphically by EMT. This distribution informed EMT category cut points (in mm): 3-5, 6-8, 9-12 and $\geq$ 13. Risk ratios (RR) and 95% confidence intervals (CI) were calculated using cluster-weighted generalized estimating equations to account for multiple IUI cycles in the same patient. Confounding by OS regimen, age, ethnicity, body mass index, duration of infertility treatment, and number of follicles $\geq$ 16mm was evaluated, and covariates changing RRs by $\geq$10% retained in adjusted analyses. Crude and adjusted associations between EMT and LBR were examined. Tests for trend were estimated by entering an ordinal variable for EMT into the model using approximate category midpoints as assigned values.

RESULTS: The overall mean EMT in patients with a LB (9.5 mm, 95% CI 8.9-10.0) was significantly higher than in those without LB (8.9, 8.8-9.1; p=0.004). Patients in the gonadotropin arm had a significantly higher mean EMT than those in the other two arms (p<0.0001). Compared to the referent EMT group of 9-12 mm, the unadjusted RR for LB for the EMT groups of $\leq$5 and 6-8 were 0.48 (95% CI 0.22-1.03) and 0.92 (0.69-1.23), respectively, demonstrating non-significant reductions in LBR. The test for trend demonstrated a statistically significant association of EMT and LBR (p=0.03, Table 1). Of all evaluated covariates, only OS regimen changed RRs by >10%, and was therefore included in the final adjusted model. After adjustment, the test for trend for an association between EMT and LBR was no longer significant (p=0.41). Stratified analyses revealed no differences in associations by treatment group.

CONCLUSIONS: LBRs in OS-IUI vary based on EMT measurements, with higher LBRs observed with increasing EMT. When adjusted for OS treatment type, there was no statistically significant association of EMT with LBR. Appreciable live birth rates are seen at all EMTs, even those of $\leq$5 mm, suggesting that OS-IUI cycles should not be canceled for thin endometrium.

TABLE 1. Association between LBR and EMT (n=2459 cycles)

EMT	LB [n (%)]	Cycles [n (%)]	Crude RR (95% CI)	Adjusted RR (95% CI)
$\leq$ 5	7 (3.6)	195 (7.9)	0.48 (0.22-1.03)	0.57 (0.26-1.26)
6-8	74 (7.8)	948 (38.6)	0.92 (0.69-1.23)	1.05 (0.78-1.41)
9-12	107 (9.8)	1088 (44.3)	1.00	1.00
$\geq$ 13	28 (12.3)	228 (9.3)	1.20 (0.81-1.76)	1.09 (0.74-1.59)
p (test for trend)			0.03*	0.41

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SUPPORT: U10HD077680 (KRH)

O-128 9:55 AM Monday, October 19, 2020

INCIDENCE AND ULTRASONOGRAPHIC CHARACTERISTICS OF CESAREAN SCAR NICHES AFTER UTERINE CLOSURE BY DOUBLE-LAYER BARBED SUTURE: A PROSPECTIVE COMPARATIVE STUDY. Franco Alessandri, MD,[1] Simone Ferrero, MD PhD,[2] Michele Altieri, MD,[2] Giulio Evangelisti, MD,[2] Maria Grazia Centurioni, MD,[1] Fabio Barra, MD.[2] [1]IRCCS Ospedale Policlinico San Martino Genoa, Italy; [2]IRCCS Ospedale Policlinico San Martino, Genova, Italy.

OBJECTIVE: To assess the incidence and ultrasonographic characteristics of cesarean scar niches after uterine closure by double-layer barbed suture.

DESIGN: This was a prospective case-control study.

MATERIALS AND METHODS: Women who underwent elective cesarean section at ≥ 38 weeks of gestation were enrolled. Exclusion criteria were a previous cesarean section or uterine surgery. Low transverse hysterotomy was closed either by a double-layer unidirectional barbed suture or by a conventional double-layer smooth suture. The choice of the suture was based on the preference of the surgeon. The first uterine layer was done by continuous unlocked suture, including the endometrial layer and the second layer by continuous unlocked suture imbricating the first. Saline contrast hysterosonography was performed 6 weeks, 6 and 12 months after the surgical procedure. According to the modified Delphi procedure, a niche was defined as an indentation at the site of a Cesarean section with a depth of at least 2 mm. The niche depth was evaluated perpendicular to the uterine wall and was measured as the shortest visible distance between the apex of the niche and the delineation of the endometrium. Postoperative complications were recorded.

RESULTS: The study included 156 women; 94 patients underwent uterine closure by barbed suture and 145 patients by smooth suture. Six weeks after delivery, the residual myometrium thickness (± SD) was significantly higher in the barbed suture group (4.9 ± 1.6 mm) than in the smooth suture group (4.2 ± 1.5 mm; p<0.001). At 6-month follow-up, the incidence of overall niche was significantly lower in the barbed suture group (20.5%, n=17/83 vs 34.1%, n=45/132; p = 0.032). The incidence of complex niche was not different between the two groups (9.6%, n=8 vs. 7.8%, n=10; p=0.595). The mean (± SD) niche depths and largest diameters were 2.5 ± 1.4 mm and 1.9 ± 1.1 mm in the barbed suture group and 3.7 ± 0.7 mm and 2.9 ± 1.0 mm in the smooth suture group (p=0.001 and p=0.002), respectively. At 12-month follow-up, the incidence of niche remained significantly lower in the barbed suture group (21.1%, n=15/76 vs. 30.5%, n=39/118; p=0.042). There was no significant difference in the incidence of postoperative complications between the two groups.

CONCLUSIONS: The use of double-layer barbed suture during cesarean section seems to lead to a low incidence of scar niche formation and reduced size of the niches in patients who have developed them.

O-129 10:10 AM Monday, October 19, 2020

SLOWFLOWHD APPLICATION IN FET CYCLES. Seifeldin Sadek, MD,[1] Tamar Matitashvili, MD,[1] Hadi Ramadan, M.D.,[2] Laurel Stadtmauer, MD, PhD.[1] [1]Jones Institute Norfolk, VA; [2]Eastern Virginia Medical School, Norfolk, VA.

OBJECTIVE: To evaluate endometrial and subendometrial blood flow using SlowflowHD in women undergoing frozen embryo transfers (FET).

DESIGN: A prospective study of 46 women undergoing FET cycles with a normal endometrial cavity and a transfer of a good quality blastocyst.

MATERIALS AND METHODS: Blood flow to the endometrium was measured with the Voluson E10 system by a single examiner at 3 points in the cycle, day 15, Embryo Transfer day (ETD) day, and day of the pregnancy test (ET+11). The endometrial and subendometrial volume and varies indices VI, FI and VFI were measured using the virtual organ computer-aided analysis (VOCAL) imaging program. Using SlowflowHD a histogram analysis was done representing the ratio of the number of color voxels as a percentage. Finally, the S/D and RI were measured in 3 different radial arteries using Pulse Doppler (PD) in SlowflowHD. Continuous data were expressed as mean ±SEM, P values <0.05 was considered statistically significant, independent test for normal distribution and Mann-Whitney test for non-normal distribution.

RESULTS: There were no differences among groups in estradiol levels, progesterone levels, BMI, age, endometrial thickness (ET) and endometrial volume (EV), subendometrial volume. Endometrial and sub-endometrial blood flow increased from day 15 to ET day and trended higher in pregnant patients compared with non-pregnant patients with a significant difference on ET+11. VFI on ETD was 1.5 (pregnant), 1.1 (not pregnant), P=0.7, and ET+11 0.40 (pregnant), 0.057 (not pregnant) P=0.01. Using PD, flow increased in pregnant patients from day 15 to ETD. The percentage of blood flow in the endometrium was highest on day 15 and decreased on ETD and ET+11 in non-pregnant patients. However, there was no decrease in the percentage of blood flow relative to day 15 in pregnant women. Similar trends were seen with the subendometrial blood flow. Resistance to blood flow in small endometrial vessels showed no differences in pregnant and non-pregnant patients.

CONCLUSIONS: SlowflowHD is a new technology that can measure blood flow through the smaller vessels to the endometrium and the spiral arteries. This may represent a novel method to measure endometrial receptivity in a non-invasive way and there may be differences in patients who conceive.

	Pregnancy (yes n=23, no n=23)	Mean	SEM	P value
VI day 15	Yes	2.3	.84	
	No	5.3	3.4	0.4
VI transfer	Yes	9.9	4.4	
	No	5.2	2.2	0.43
VI transfer+11	Yes	**2.4**	**.74**	
	No	**.37**	0.05	0.01
Endometrial slow flow day 15	Yes	30.6	3.7	
	No	41.5	5.1	0.08
Endometrial slow flow transfer	Yes	26.2	4.7	
	No	20.4	3.4	0.3
Endometrial slow flow transfer+11	Yes	33.3	4.0	
	No	21.1	5.9	0.09
Endometrial RI day 15	Yes	0.63	0.06	
	No	0.63	0.09	0.8
Endometrial RI transfer	Yes	0.66	.019	
	No	0.64	0.08	0.3
Endometrial RI transfer + 11	Yes	0.66	.017	
	No	0.65	.023	0.7

SUPPORT: Received loaner Ultrasound from GE Healthcare for study

O-130 10:25 AM Monday, October 19, 2020

OVIDUCTAL PATENCY OF WOMEN AFFECTS SIGNIFICANT INFLUENCES ON CLINICAL OUTCOME OF ART TREATMENT. Aisaku Fukuda, M.D., Ph.D.,[1] Hiroshi Matsumoto, B.S.,[1] Isao Tsuji, M.D., Ph.D.,[1] Yoshiharu Morimoto, M.D., Ph.D.[2] [1]IVF Osaka Clinic, Higashiosaka, Japan; [2]HORAC Grand Front Osaka clinic, Osaka, Japan.

OBJECTIVE: ART was originally invented for tubal factor infertility. It has been widely accepted that major cause of infertility is tubal disorder. Falloposcopic tuboplasty (FT), a novel technology for tubal patency disorders, has been applied as the first choice for tubal patency disorder before ART at our facility. It is obvious that oviduct plays an integral role in reproduction by providing the milieu for not only fertilization and embryo development, but also implantation. However, ART is applied on tubal factor without considering oviductal condition, patent or occluded. Therefore, the relation between ART outcome and oviductal patency was investigated on cleavage and blastocyst transfers on different age groups. Moreover, other conditions such as frozen or fresh ET, endometrial thickness, embryo developmental stages and patient ages as well as with or without FT, were analyzed by multivariate logistic regression analysis.

DESIGN: Retrospective cohort study at private fertility clinic.

MATERIALS AND METHODS: ART outcomes of 537 cycles which received ART after FT or without FT due to bilateral tubal occlusion from Jan. 2011 to Dec. 2019 were retrospectively analyzed. Tubal patency was diagnosed by HSG. The patients with bilateral tubal occlusion received FT to recover their patency for conventional infertility treatment or received ART directly by their choice. ART was performed on 155 cycles (Group A) directly without FT and 382 cycles after FT (Group B). Groups A and

B were subdivided by cleavage stage transfer (Group A-CL, n=212) or single blastocyst transfer (Group-A-BL, n=325). Clinical pregnancy rates (CPR) between ≤39 yo (Young) and ≥40 yo (Old) were compared. Moreover, logistic regression analysis was conducted to investigate which factors are relevant to CPR among cleavage stage or blastocyst transfers, with or without FT, embryo developmental stages, frozen or fresh transfer, endometrial thickness, and patient ages.

RESULTS: CPRs of without FT vs. after FT in Group A-CL and Group A-BL were 14.3% vs. 22.2% per ET (P=0.19) and 35.9% vs. 49.4% (P<0.05), respectively. CPRs of Young vs. Old in Group A-CL and Group A-BL were 16.1% vs. 31.2% (P=0.1), 12.5% vs. 7.1% (P=0.3) and 39.7% vs. 52.5% (P=0.06), 21.1% vs. 31.4% (P=0.42), respectively. Multivariate analysis revealed that receiving FT before ET (P<0.05), embryo stage (P<0.01) and patient age (P<0.01) were the factors associated with higher CPR. The odds of clinical pregnancy for patients who received FT before ET was 1.64 times higher than those without FT after controlling for embryo stage, fresh or frozen ET, endometrial thickness and patient age.

CONCLUSIONS: The present study suggests that tubal patency significantly influences clinical outcomes of ART. Reversal of tubal patency by FT or some other methods may improve implantation via modulation of endometrial condition with various enhancing factors such as cytokines and immunological substances brought by human tubal fluid. Not only ERA, chromic endometritis, endometrial flora and some other related factors, but also restoration of oviductal patency should be included to improve ART outcome.

O-131 10:40 AM Monday, October 19, 2020

PREVALENCE, INCIDENCE AND TRENDS IN ENDOMETRIOSIS DIAGNOSIS BY DIAGNOSTIC MODALITY, PROVIDER TYPE AND RACE. Jacob Christ, MD,[1] Onchee Yu, MS,[2] Renate Schulze-Rath, MD, MSc,[3] Susan D. Reed, MD, MPH, MS.[4] [1]University of Washington Seattle, WA; [2]Kaiser Permanente Washington, Seattle, WA; [3]Bayer AG, Berlin, Germany; [4]University of Washington Seattle, Seattle, WA.

OBJECTIVE: Population based estimates of endometriosis incidence and prevalence are few and vary widely. In a population-based US study we evaluated endometriosis incidence and prevalence and elucidated factors influencing these estimates including diagnostic method and provider type, by race and over time.

DESIGN: Ten-year population based retrospective cohort study.

MATERIALS AND METHODS: Study cohort included women enrollees at Kaiser Permanente Washington, aged 16-60 years, during January 2006-December 2015, who had a uterus, were continuously enrolled for at least 2 years prior to cohort entry and had at least 1 healthcare utilization. Incident endometriosis was identified via ICD-9/ICD-10 diagnosis codes. Incidence rates were age-adjusted by direct standardization to the 2015 study population. Secular trends in incidence overall, by race, by method of diagnosis and by practitioner type were assessed using Poisson regression analyses. Prevalent cases were defined as women with an endometriosis diagnosis prior to 2016. Chart review of women identified with an endometriosis ICD code provided development of a diagnostic algorithm to estimate surgical diagnosis. Imaging on day of diagnosis was used to infer diagnosis by imaging. All others were classified as a clinical diagnosis.

RESULTS: Among 332,056 eligible women who contributed 1,176,329 person-years, 2,863 incident endometriosis cases were identified. Incidence rates declined over the study interval from a high of 30.2 per 10,000 person-years in 2006 to 17.4 in 2015. Incidence rates were similar across races. Among 135,162 women contributed person-time in 2015, 2,521 (1.9%) had an endometriosis diagnosis. Diagnoses were assigned: 45.5% surgically, 5.7% by imaging and 48.8% clinically. Rates of surgically and clinically diagnosed endometriosis decreased over the study interval from 13.4 and 16.1 per 10,000 person-years in 2006 to 7.4 and 8.9 per 10,000 person years in 2015, respectively ($p < 0.001$). Diagnosing provider was: 73.6% obstetrician and gynecologist (OBGYN), 15.7% primary care provider (PCP) and 10.7% "other". Incidence of endometriosis diagnosed by an OBGYN and PCP decreased over the study interval from 22.9 and 5.1 per 10,000 person years in 2006 to 13.1 and 2.5 per 10,000 person years in 2015 ($p < 0.001$). Method of diagnosis and provider type did not differ across races.

CONCLUSIONS: Among a group of non-selected women in the US and without relying on patient self-report, we describe declining rates of endometriosis diagnoses over time and a disease prevalence lower than most previously published estimates (3.3-7.0%). Overall, race did not appear to have a major impact on any outcome. Among our cohort, rates declined uniformly across the main methods of diagnosis and diagnosing provider type. This may suggest that declining rates do not reflect a shift in how endometriosis was diagnosed, rather may be due to a change in management of dysmenorrhea (without assigned endometriosis diagnoses) or less likely, a true decrease in disease burden over time.

SUPPORT: Bayer AG provided financial support for the conduct of the study

O-132 10:55 AM Monday, October 19, 2020

SMALL UTERINE SEPTA: ARE THERE OTHER 3D ULTRASOUND MEASUERMENTS BEYOND SEPTAL LENGTH THAT BETTER CORRELATE TO REPRODUCTIVE OUTCOME? Caterina Exacoustos, MD, PhD,[1] Francesca Conway, MD,[2] Consuelo Russo, MD,[1] Francesco Giuseppe Martire, MD,[1] Terry Siciliano, MD,[3] Martina Cosentino, MD,[1] Carlo Ticconi, MD.[4] [1]University of Rome 'Tor Vergata' Italy; [2]University of Rome 'Tor Vergata', Rome, Italy; [3]Roma, Roma, Italy; [4]Via Edoardo Maragliano 26, Roma, Italy.

OBJECTIVE: Recently different classifications have recently been proposed to define a septate uterus mostly based on septal length, however great discrepancy has been observed between them especially for small septa. With regards to small indentations of the fundus the question is still open on the real reproductive impact of these small defects and the need for surgical treatment. The aim of this study was to propose other parameters based on 3D ultrasound (US) measurements to better classify small cavity indentation less 1cm.

DESIGN: Retrospective study on patients with 3D US diagnosis of a uterine internal fundal indentation, reproductive history of each patient was correlated to the type of uterine anomaly according to different classifications. Indentation length and other 3D US parameters were correlated to reproductive outcome.

MATERIALS AND METHODS: 664 patients with 3D US diagnosis of a uterine internal fundal indentation of ≥ 3mm were classify as septate or arcuate/normal according to the following classifications: Salim (2003), ESHRE/ESGE (2013), ASRM (2016), CUME (2018). We divided the study population in 3 group: patients with uteri with a fundal indentation ≤ 5mm, >5<10mm and ≥ 10mm. The reproductive history of each patient was correlated to the type of uterine anomaly according to the four different classifications in the total population and in the 3 sub groups. High discrepancy between classifications were observed for septal lengths >5<10mm whereas patients with uterine indentation ≤ 5mm and ≥ 10mm showed similarity in type and reproductive outcomes. Small uterine septa of >5<10mm were evaluated with other parameters of cavity indentation the like cavity width, fundal myometrial thickness and indentation angle. These other parameters were correlated to reproductive outcome thus in order to determine which one correlate to fertility problems.

RESULTS: We observed a large discrepancy between the 4 different classifications in diagnosing septate uterus especially in patients with indentation >5<10mm. Of the 664 patients 215 showed a fundal indentation length >5<10mm, of these 136 tried to conceive before our scan: 69(51%) were infertile, 65(48%) had at least one miscarriage, 38(28%) had recurrent abortion(≥2 miscarriages) and 5(4%) at least one delivery. The U Mann Whitney test showed among patients who try to conceive a significant correlation with recurrent abortion and an indentation angle > 128° Infertility was significantly correlated to a cavity width <32mm and a septal length/ fundal myometrial thickness ratio >75%.

CONCLUSIONS: Current classifications don't seem to correlate to each other and with reproductive outcomes. These wide discrepancies between different classifications is more evident in small cavity indentation >5<10mm. For these small uterine septa additional parameters like indentation angle > 128° showed more risk for recurrent miscarriage and cavity width < 32mm and septal length/fundal myometrial thickness ratio > 75% is more correlated to infertility. Further prospective study should verify if these parameters could guide the management of patients with small uterine septa.

O-133 9:40 AM Monday, October 19, 2020

THE ASSOCIATION BETWEEN PRIOR CESAREAN SECTION AND ASSISTED REPRODUCTIVE TECHNOLOGY (ART) OUTCOMES IN WOMEN UNDERGOING AUTOLOGOUS SINGLE THAWED EUPLOID EMBRYO TRANSFER.

Jenna Friedenthal, MD,[1] Dmitry Gounko, MA,[2] Tamar Alkon-Meadows, MD,[2] Carlos Hernandez-Nieto, MD,[2] Joseph A. Lee, BA,[2] Alan B. Copperman, MD,[1] Erkan Buyuk, MD.[1] [1]Icahn School of Medicine at Mount Sinai New York, NY; [2]Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Rates of cesarean section (CS) continue to increase worldwide[1]. Although a CS is often a necessary intervention, it presents increased risk for short and long-term sequelae in mother and infant[2]. Previous work suggests an association between prior CS and reduced fertility in both natural and ART cycles [3-5]. To our knowledge, there is no published research exploring the relationship between a prior CS and subsequent single thawed euploid embryo transfer (euploid SET). The objective of this study was to determine whether prior mode of delivery correlates with subsequent ART outcomes in patients undergoing euploid SET.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All patients undergoing autologous euploid SETs at an academic center with a prior vaginal delivery (VD) or CS from 2012 to 2020 were identified. Cases included patients with 1 prior CS; controls included patients with 1 prior VD. Exclusion criteria included patients with >1 previous live birth and donor/recipient cycles. Our primary outcome was implantation rate (IR); secondary outcomes were ongoing pregnancy/live birth rate (OP/LBR), biochemical pregnancy rate (BPR), and clinical loss rate (CLR). Baseline demographics were obtained: age (at time of retrieval and transfer), body mass index (BMI), obstetric history, endometrial thickness at time of transfer (ETATT), presence of blood in catheter and catheter type as markers of transfer difficulty, embryo grade (Modified Gardner), and day of embryo biopsy for genetic testing. Statistical analysis was performed using Student's t-test, Mann-Whitney U test, and chi-square. Logistic multivariable regression models were used to calculate odds ratios and to adjust for confounders, with $P<0.05$ considered significant.

RESULTS: 551 euploid SETs met inclusion criteria and were included in analysis (VD: n=347; CD: n=204). Patients with a prior CS had a higher BMI (24.50 vs 23.47, p=0.009) than those in the VD cohort; demographic data were otherwise similar. In univariate analysis, IR and OP/LBR were significantly lower in patients with a prior CS compared with VD (58.33% vs 68.01%, P=0.02 and 50.00% vs 59.65%, P=0.03, respectively). After adjusting for age at time of retrieval and transfer, BMI, ETATT, difficulty of transfer, day of biopsy, and embryo grade, prior CS was associated with 41% lower odds of implantation (OR 0.59, CI 0.40-0.88). After adjusting for the same confounders, prior CS was also associated with 38% lower odds of ongoing pregnancy/live birth (OR 0.62, 0.42-0.92). We saw no differences in BPR or CLR.

CONCLUSIONS: This is the first study to demonstrate a significant reduction in IR and OP/LBR associated with a prior CS in patients undergoing euploid SET. Patients who deliver via CS may experience post-CS scarring and subsequent isthmocele formation which may alter the uterine milieu and lead to suboptimal implantation. Patients looking to build families with multiple offspring should be counseled that prior CS appears to be associated with significantly lower success following euploid SET. Our work further stresses the importance on a national level of reducing primary CS rates.

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SUPPORT: None

O-134 9:55 AM Monday, October 19, 2020

EFFECT OF FOLLICULAR PHASE LENGTH ON PREGNANCY OUTCOMES IN NATURAL FROZEN EMBRYO TRANSFER CYCLES.

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OBJECTIVE: To determine whether the length of the follicular phase affects pregnancy outcomes in natural frozen embryo transfer cycles.

DESIGN: Retrospective cohort study performed in an academic hospital setting.

MATERIALS AND METHODS: Patients who underwent their first natural frozen autologous day 5 embryo transfer cycle in our IVF clinic between 01/01/2013 and 12/31/2018 were included. Patients were stratified by length of their follicular phase in that cycle ($\leq$15 days and >15 days). A secondary analysis was performed to analyze only cycles in which a PGT euploid embryo was transferred. Demographic outcomes were collected. The primary outcomes were pregnancy and live birth rates. Logistic regression adjusted *a priori* for patient age and number of embryos transferred was used to estimate the odds ratio with a 95% confidence interval (CI) for pregnancy outcomes.

RESULTS: A total of 2,358 natural frozen embryo transfer cycles met inclusion criteria, including 1,287 cycles in the $\leq$15 day group and 1,071 cycles in the >15 day group. The mean cycle day of the LH surge was 13.1 $\pm$ 1.6 days (range 7-15) in the $\leq$15 day group and 18.8 $\pm$ 3.3 days (range 16-51) in the >15 day group. A diagnosis of oligo-ovulatory infertility was observed in 3.6% of women in the $\leq$15 day group and 9.1% of women in the >15 day group. The mean number of embryos transferred was 1.3 in both groups. The pregnancy rate was similar for patients with a follicular phase length $\leq$15 days (65.4%) and patients with a follicular phase length >15 days (69.0%, OR 1.12; 95% CI 0.94-1.33). In women who achieved pregnancy, there were no significant differences between the $\leq$15 day group and the >15 day group for biochemical pregnancies (15.7% versus 11.4%, OR 0.74; 95% CI 0.55-1.00), miscarriage rate (12.8% versus 11.8%, OR 1.04; 95% CI 0.77-1.42), or live birth rate (69.5% versus 74.6%, OR 1.14; 95% CI 0.91-1.43). In the secondary analysis of the PGT transferred embryos, there were similarly no differences observed between the two groups. The pregnancy rate was 70.0% for women with a follicular phase length $\leq$15 days and 73.8% for women with a follicular phase length >15 days (OR 1.21; 95% CI 0.88-1.66). After achieving a pregnancy, the live birth rate was 58.4% for women in the $\leq$15 day group and 61.2% for women in the >15 day group (OR 1.11; 95% CI 0.83-1.48).

CONCLUSIONS: The length of the follicular phase in patients who underwent a frozen natural embryo transfer did not affect the pregnancy rate. This finding was also observed in euploid embryo transfer cycles. In addition, biochemical, miscarriage, and live birth rates were comparable between both groups. Patients and providers can be reassured that a prolonged follicular phase length in a natural frozen embryo transfer cycle does not affect the pregnancy outcomes in that cycle. We conclude that follicular phase length should not be considered a factor when deciding between a natural or a programmed frozen embryo transfer cycle in ovulatory patients.

SUPPORT: None

O-135 10:10 AM Monday, October 19, 2020

PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY DOES NOT IMPROVE OUTCOME IN YOUNG PATIENTS UNDERGOING IVF TREATMENT: A SART CORS STUDY.

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OBJECTIVE: Preimplantation genetic testing for aneuploidy (PGT-A) is associated with significant improvement in ongoing pregnancy rates per transfer, reduction of multiple pregnancies using elective single embryo transfer (eSET), and reduced miscarriage rates in women > 35 years or older. As these improvements have not been observed in women < 35 years old, we sought to investigate whether offering PGT-A to favorable prognosis young women can be counterproductive and lead to suboptimal pregnancy outcomes.

DESIGN: Retrospective study.

MATERIALS AND METHODS: We analyzed data from 56,773 autologous ART cycles between 2014-2015 reported to the Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS) database. Patients that underwent "freeze-all" with subsequent eSET FET, were included. Comparison was made between FET cycles where the indication for stimulation/freeze-all was (1) to perform blastocyst PGT-A for selecting euploid embryos (study group) versus (2) cycles at risk of ovarian hyperstimulation syndrome (OHSS). OHSS cycles were selected as the control group so that we could compare the outcomes of PGT-A cycles to cycles from good prognosis patients. In the OHSS group, embryos were selected based on morphological criteria and no PGT-A was performed. We assumed that in the PGT-A group, euploid embryos were transferred and embryos with mosaicism or inconclusive results were discarded. Live birth (LBR), clinical pregnancy, and miscarriage rates were compared between PGT-A tested and untested cycles. Multivariable logistic regression was used to estimate adjusted odds ratios (aOR) and 95% confidence intervals (CI) representing the association between PGT-A and selected outcomes (reference group: PGT-A untested). Analyses were stratified by age group (<35 and ≥ 35 years old).

RESULTS: A total of 6,816 FET cycles were selected for analysis. Of those cycles which met inclusion criteria, 2,931 were < 35 and 3,885 were ≥ 35 years old. In the < 35 age group, no difference in LBR was observed between patients who underwent eSET FET with PGT-A tested vs. untested (50.9 % vs. 51.7 %, P= 0.69, aOR 1.03, 95% CI: 0.87-1.21). Additionally, the clinical pregnancy rates (56.0% vs. 56.7%, P=0.71, aOR 1.00, 95% CI:0.85-1.18) and miscarriage rates (8.8% vs. 8.7%, p = 0.88, aOR 0.97, 95% CI:0.72-1.30) were not significantly different between PGT-A tested and untested groups. Among ≥ 35 years old group, no difference was observed between the PGT-A tested and untested groups in LBR (53.8% vs. 49.7%, p=0.15). However after adjusting for potential confounders, PGT-A tested cycles were 1.3 times more likely to have a live birth (95% CI:1.01-1.60)

CONCLUSIONS: Our results are consistent with prior evidence that patients who are ≥ 35 years old, PGT-A leads to a higher chance of LB. The benefits of PGT-A are not reflected in good prognosis patients < 35 years old. However, the observation that PGT-A is not associated with suboptimal pregnancy outcome as compared to good prognosis young patients, justifies its continued use in IVF population when indicated.

O-136 10:25 AM Monday, October 19, 2020

WHEN USING DONOR OOCYTES, DOES EMBRYO STAGE MATTER? AN ANALYSIS OF BLASTOCYST VERSUS CLEAVAGE STAGE EMBRYO TRANSFERS IN A DONOR OOCYTE IN VITRO FERTILIZATION (IVF) MODEL.

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OBJECTIVE: Although studies in autologous oocyte IVF indicate that blastocyst embryo transfer is superior to cleavage stage, the latter are more often performed in poorer prognosis patients, introducing confounding. Oocyte donor IVF with high-quality oocytes offers an ideal model for further inquiry. We investigated if embryo transfer stage has an impact on outcomes in donor oocyte IVF, aiming to identify if any scenario exists in which cleavage transfer is non-inferior to blastocyst.

DESIGN: Retrospective cohort analyzing cycles from a frozen donor oocyte bank, 2008-2015.

MATERIALS AND METHODS: A total of 989 recipients underwent 1189 warming cycles using vitrified donor oocytes resulting in fresh embryo transfer. The association between embryo transfer stage and probability of live birth was investigated using cluster weighted generalized estimating equations, adjusted for recipient age, race, uterine factor infertility, transfer year, and number of day 3 quality cleavage embryos. We further stratified by number of embryos transferred, as double cleavage transfer is often weighed against single blastocyst transfer. Sensitivity analyses were performed restricting to cycles with ≤2 quality cleavage embryos, as in theory these were the cycles where choice between transfer stage was most clinically relevant.

RESULTS: Overall 138 cleavage and 1051 blastocyst embryo transfers were performed. There were no differences in recipient age (mean 40.9 years), race (69.3% White) or body mass index (mean 24.6 kg/m^2) by stage of embryo transfer. Cleavage stage transfers were associated with an adjusted relative risk (aRR) of live birth of 0.76 (95% CI 0.60, 0.89) compared to blastocyst. The association persisted when only including cycles with ≤2 quality cleavage embryos (aRR 0.69, 95% CI 0.55, 0.87) and excluding single cleavage transfers (aRR 0.77, 95% CI 0.63, 0.95), as the latter were the poorest prognosis cycles. After stratifying by number of embryos transferred, the trend toward lower success persisted when comparing the transfer of two cleavage embryos to one blastocyst embryo (Table 1).

TABLE 1. Association between stage/number of embryos transferred and risk of live birth

Transfer Stage	Number Embryos Transferred	N	Risk Ratio of Live Birth (95% CI)	
			Unadjusted	Adjusted
Cleavage	1	21	0.46 (0.20, 1.05)	0.50 (0.22, 1.16)
	2	111	0.86 (0.69, 1.07)	0.89 (0.71, 1.11)
Blastocyst	1	687	1.0 (REF)	1.0 (REF)
	2	359	1.20 (1.09, 1.34)	1.21 (1.07, 1.36)

CONCLUSIONS: Even in a donor oocyte model with presumably excellent oocyte quality, there is a benefit of extended culture and blastocyst stage transfer. The study is limited in its retrospective nature, however, and it is possible that embryos with small differences in quality were more likely subjected to extended culture.

SUPPORT: None

O-137 10:40 AM Monday, October 19, 2020

COMPARISON OF FRESH AND FROZEN EJACULATED SPERM IN DONOR OOCYTE RECIPIENT CYCLES: A PAIRED ANALYSIS UTILIZING SIBLING OOCYTES.

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OBJECTIVE: Use of frozen ejaculated sperm is often necessary for fertilization in IVF-ICSI cycles in patients with non-male factor infertility. Studies assessing outcomes between fresh and frozen sperm have mostly been conducted in patients with male factor infertility or with surgically retrieved spermatozoa. While some studies have shown that frozen and fresh sperm result in similar outcomes, others have found fresh to be superior; however, often these studies have been unable to control for oocyte quality. ART using donor sibling-oocyte recipients (oocytes from the same donor stimulation transferred to two different recipients) offers a unique model that controls to the greatest degree possible for oocyte quality. We sought to determine if fresh and frozen ejaculated sperm are associated with similar pregnancy outcomes by analyzing paired donor egg recipient (DER) cycles using sibling oocytes.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Patients who underwent DER cycles where oocytes from a single controlled ovarian hyperstimulation cycle of a donor were split between two recipients were included. The two recipients of the single donor oocyte cycle were paired and categorized based on type of ejaculated sperm used for ICSI (fresh or frozen sperm) on fresh oocytes and the type of ejaculated sperm used for fresh embryo transfer. Patients with uterine and severe male factor infertility, including surgically retrieved sperm were excluded. Primary outcome was live birth rate. Secondary outcomes were positive pregnancy, implantation and miscarriage rates. Statistical analysis included paired t-tests, and $p<0.05$ was statistically significant.

RESULTS: 1,013 patients who underwent DER cycles between January 2010 and December 2016 were screened for inclusion, of which 408 patients received oocytes from a split donor oocyte cycle. 46 pairs of patients (92 recipients) used discrepant types of ejaculated sperm. The groups were similar for recipient age, gravity, parity, BMI, peak endometrial stripe thickness and number of embryos transferred. Of the frozen sperm samples used, 65.2% were from an anonymous donor and the rest were from the partner. Live birth rates for the fresh sperm group were found to be significantly higher compared to the frozen sperm group (67.3% ± 7.0% vs. 47.8% ± 7.4%, p=0.048). Positive pregnancy rates (76.1% vs. 67.4%, p=0.32), implantation rates (58.0% vs. 44.6% p=0.15) and miscarriage rates (12% vs. 32%, p=0.06) were statistically similar for fresh compared to frozen sperm. In a sub-group analysis, there were no differences in outcomes when fresh sperm was compared separately to partner or donor frozen sperm. There were also no differences in outcomes when comparing partner to donor frozen sperm.

CONCLUSIONS: In this idealized model that controls for oocyte quality to the greatest degree possible by using paired recipients from the same donor from the same stimulation cycle, we found that cycles using frozen sperm resulted in lower live birth rates than those using fresh sperm. These findings suggest that fresh sperm should be preferentially used in non-male factor infertility IVF-ICSI cycles.

O-138 10:55 AM Monday, October 19, 2020

WHAT PREDICTS DESIRE TO PROCEED WITH FERTILITY TREATMENT DURING A PANDEMIC? A RETROSPECTIVE COHORT STUDY FOLLOWING THE COVID-19 SHUTDOWN. Lauren Elizabeth Verrilli, MD, Kellie Woodfield, MD, Joseph M. Letourneau, MD, Erica Johnstone, MD. University of Utah, Salt Lake City, UT.

OBJECTIVE: We sought to identify factors that contributed to proceeding with ART following the COVID-19 shutdown.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients who had planned an IVF cycle or frozen embryo transfer between March 2019 and April 27th, 2020, but had not yet undergone their treatment prior to the COVID-19 shutdown were included in this study. Patient demographics were collected including age, parity, AMH, AFC, history of prior IVF cycles or transfer, and number of frozen blastocysts. Data on gamete source and use of a gestational carrier was included. When IVF was resumed, patient decision to move forward with treatment or delay was recorded. Chi-square tests and Wilcoxon rank sum tests were used to assess the association between proceeding with ART treatment for categorical variables or non-parametrically distributed continuous variables, as appropriate.

RESULTS: A total of 145 patients planning FET and 133 patients planning a fresh cycle were offered the option to restart treatment. In total, 62% of all patients desired to initiate treatment. Of the 133 fresh cycles, 69 (52%) patients proceeded immediately, compared to 104 of the 145 FET cycles (72%). Among the fresh cycles, there was a trend toward older age among those who moved forward (37 vs 35; p=0.05). FET cycles using a gestational carrier were more likely to continue to delay treatment (7% vs 1 % p=0.04).

CONCLUSIONS: The majority of patients whose IVF treatment was delayed with the COVID-19 pandemic shut down desired to resume treatment immediately when able. Those proceeding and delaying were similar with regards to most prognostic factors. Older age, however, showed a trend towards moving forward with a fresh IVF cycle and gestational carrier use was associated with continuing to pause on a transfer. While some patients voiced financial or health related concerns, the majority did not provide concrete reasons why they chose to delay or forgo treatment. Further research is needed to understand the reasons patients choose to proceed with fertility treatment in the setting of a pandemic, including more robust data on financial and personal or family health concerns.

SUPPORT: No financial support

Fresh					
Proceeding			Not Proceeding		
	Median or %	Range	Median or %	Range	P value
Age	37	21-45	35	15-43	0.05
AMH	2.39	0.003-32	2.74	0.61-20.50	0.40
AFC	14	2-75	17	2-150	0.42
Parity	0	0-4	0	0-6	0.55
Prior IVF Cycle	29%		23%		0.47
Prior FET	23%		14%		0.86
# Frozen Blasts	0	0-18	0	0-7	0.45
Donor Egg	7%		6%		0.82
Gestational Carrier	1%		6%		0.15
FET					
Proceeding			Not Proceeding		
	Median or %	Range	Median or %	Range	P value
Age	34	22-45	35	24 - 47	0.17
AMH	3.17	0.34 – 24.6	3.8	0.11 - 15	0.38
AFC	17	0 - 82	18	3 - 70	0.78
Parity	0	0- 3	0	0 - 3	0.60
Prior IVF Cycle	97%		98%		0.88
Prior FET	64%		78%		0.11
# Frozen Blasts	4	0-16	4	0 -12	0.49
Donor Egg	8%		10%		0.69
Gestational Carrier	1%		7%		0.04

MALE REPRODUCTION AND UROLOGY: CLINICAL

O-139 9:40 AM Monday, October 19, 2020

WHAT IS THE OPTIMAL THRESHOLD FOR TOTAL PROGRESSIVE MOTILE SPERM COUNT IN PREDICTING SPONTANEOUS CONCEPTION IN SUBFERTILE COUPLES? Lauren Elizabeth Verrilli, MD,[1] Sorena Keihani, MD,[2] Erica Johnstone, MD,[1] Heidi A. Hanson, PHD, MS,[3] Angela Presson, PhD, MS,[1] Alexander W. Pastuszak, MD, PhD,[2] James Hotaling, MD,[4] Joseph M. Letourneau, MD.[1] [1]University of Utah, Salt Lake City, UT; [2]University of Utah, Salt lake city, UT; [3]University of Utah Health, Salt Lake City, UT; [4]University of Utah School of Medicine Andrology and IVF Laboratories, Salt Lake City, UT.

OBJECTIVE: Total progressive motile sperm count (TPMC) is commonly used in evaluating the male partner in subfertile couples. A TPMC value of >20 million is generally considered normal. We hypothesized that higher TPMC values are associated with more efficient conception rates in subfertile couples. We aimed to find a threshold that is best associated with time to spontaneous conception.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We used longitudinal data from a cohort of subfertile men seen at a single institution from 2002-2017. Demographics and baseline semen parameters, as well as number of children before the first semen analysis (SA) were collected. Couples who used ART or IUI were excluded. Couples were categorized into two cohorts: 1) Male or unexplained infertility: this category included men with a known male factor diagnosis or absence of female factor infertility or 2) those with female factor infertility. Conception data within 5 years of the first SA were collected. We used a log-rank test to select TPMC thresholds associated with earlier time to conception in either cohorts. Cox proportional hazard models were used to compare time to conception across TPMC categories, adjusting for age, BMI, number of previous children and income.

RESULTS: A total of 5126 men with mean age of 32.5±6.5 years were included. Median TPMC was 113.1 M. Overall, 59% of couples were able to conceive spontaneously within 5 years of the male partner's first SA (median time: 27 months, 95% CI: 26–30). Overall, a TPMC threshold of 50 million provided the highest log-rank statistic in predicting earlier time to conception. Those with TPMC>=50 million had 60% increased chances of achieving natural conception within 5 years (HR: 1.60, 95% CI:1.45–1.76, P<0.001) In couples with male factor or unexplained infertility the best TPMC threshold was 70 million and in those with documented female factor infertility the best threshold was 60 million.

CONCLUSIONS: A TPMC threshold of 50 million provides a better prediction for time to spontaneous conception in a large cohort of subfertile men. The optimal threshold can be slightly different depending on the infertility cause at couples' level, however, the clinical significance of these small variations remains unknown.

Hazard ratio for 5-year conception per TPMC dichotomized at threshold for each cohort

	Hazard ratio (95% CI)[1]	p[1]	Hazard ratio (95% CI)[2]	p[2]
Overall cohort				
TPMC≥50 vs. TPMC<50	1.63 (1.50,1.77)	<0.001	1.60 (1.45,1.76)	<0.001
Male factor/unexplained (Cohort 1)				
TPMC≥70 vs. TPMC<70	1.58 (1.45,1.73)	<0.001	1.57 (1.42,1.73)	<0.001
Female factor (Cohort 2)				
TPMC≥6 vs. TPMC<60	1.69 (1.41,2.02)	<0.001	1.52 (1.24,1.85)	<0.001

[1] Unadjusted; [2] Adjusting for male age at SA, median income, and number of children before SA.

O-140 9:55 AM Monday, October 19, 2020

INFLUENCE OF PATERNAL AGE ON ASSISTED REPRODUCTIVE TECHNOLOGY CYCLE AND PERINATAL OUTCOMES. Audrey M. Marsidi, MD,[1] Lauren M. Kipling, MPH,[2] Jennifer F. Kawwass, MD,[1] Akanksha Mehta, M.D., M.S.[3] [1]Emory University School of Medicine, Division of Reproductive Endocrinology and Infertility, Atlanta, GA; [2]Emory University Rollins School of Public Health, Atlanta, GA; [3]1365 Clifton Road NE, Building B, Atlanta, GA.

OBJECTIVE: To characterize paternal age among assisted reproductive technology (ART) cycles performed in the United States, and to evaluate the impact of paternal age on ART cycle and perinatal outcomes.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: We collected data from all fresh, autologous in-*vitro* fertilization (IVF) cycles reported to Society of Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS) in 2017. SART CORS includes data on female demographics, medical and obstetric history, and infertility diagnosis, detailed treatment parameters, and pregnancy outcomes, when applicable. Male partner age became a mandatory field in 2017. Cycles utilizing donor gametes or those with missing and extreme age variables were excluded. Paternal age was categorized into two groups: ≤45 years and ≥46 years, with men aged ≤45 years serving as the reference group for comparison. Primary outcomes of interest were intrauterine pregnancy, live birth (≥20 weeks) and miscarriage (≤20 weeks). Secondary outcomes were full-term live birth (≥37 weeks) among singleton and twin gestations. Modified Poisson regression was performed to determine associations between paternal age and cycle and perinatal outcomes.

RESULTS: Among 77,209 fresh, non-donor IVF cycles, the average paternal age was 37.8 years (± 6.3); average maternal age was 35.5 years (± 4.6). Compared to men ≤45 years, paternal age ≥46 years old was associated with lower likelihood of pregnancy per cycle (aRR 0.81, 95% CI 0.76-0.87) and per transfer (aRR 0.85, 95% CI 0.81-0.90), as well as lower likelihood of live birth per cycle (aRR 0.76, 95% CI 0.72-0.84) and per transfer (aRR 0.82, 95% CI 0.77-0.88), after controlling for maternal age and other confounders. The likelihood of miscarriage was higher among men ≥46 years of age, compared to ≤45 years, including cycles where female partners were <35 years (15.3% vs. 13%), but did not maintain significance in the adjusted analysis.

CONCLUSIONS: Compared to paternal age ≤45 years, paternal age ≥46 is associated with lower likelihood of pregnancy and live birth among couples undergoing IVF. A trend toward increased miscarriage risk was noted as paternal age increased, even for couples where female age was <35. Overall, advanced paternal age negatively impacts reproductive IVF outcomes.

O-141 10:10 AM Monday, October 19, 2020

OPTIMAL TIMING FOR REPEAT SEMEN ANALYSIS DURING MALE INFERTILITY EVALUATION. Nahid Punjani, MD MPH,[1] Gal Wald, BA,[1] Omar Al Hussein Alawamlh, MD,[1] Vanessa L. Dudley, MSHS,[2] Miriam Feliciano, BSc,[2] Philip S. Li, M.D.,[2] Marc Goldstein, M.D.[2] [1]Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY; [2]Center for Male Reproductive Medicine and Microsurgery, Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY.

OBJECTIVE: To assess if the 4-week time period between semen analysis during the work-up of male infertility is optimal, or if an alternative time period may be more desirable.

DESIGN: Retrospective study of prospectively collected data.

MATERIALS AND METHODS: Semen analyses were reviewed between 1997 and 2018 at Weill Cornell in New York City. Included men had two semen analyses completed at our institution, whom had no previous fertility interventions, and had semen analyses completed within 90 days of each other. Men with azoospermia or incomplete data were excluded. We examined Pearson correlation coefficients (*r*) between sperm concentration (million/ml) total sperm count (million), pH, volume (mL), motility (%) and progressive motility (grade 1-4), and morphology (%) for each pair of semen samples and assessed these over weekly time periods.

RESULTS: A total of 1080 semen samples were included for assessment from a total of 540 men. Optimal correlation for volume occurred at weeks 2 (r=0.807), 8 (r=0.802), and 12 (r=0.797). For concentration correlation was maximized at weeks 1 (r=0.950), 4 (r=0.840), and 5 (r=0.798). Total sperm count correlated at weeks 1 (r=0.929), and 2 (r=0.729), and 4 (r=0.806). Motility was maximally correlated at week 1 (r=0.711), 10 (r=0.760) and 13 (r=0.708). Morphology was optimally correlated at week 1 (0.935), 2 (r=0.818) and 10 (r=0.839).

CONCLUSIONS: Historically, repeat semen analysis has been suggested at least four weeks after the initial sample. Our data suggests that this may not be the optimal time. More optimal time periods are within the first two weeks or beyond two months depending on the parameter. These data suggests that the optimal time period for repeat semen analysis should be individualized depending on results of the initial analysis and factors such as recent changes in medications, lifestyle issues such as drug and alcohol abuse, weight change, stress, etc. Further, large studies are required for investigation of this trend.

O-142 10:25 AM Monday, October 19, 2020

ADVANCED MALE PARTNER AGE RESULTS IN LOWER FERTILIZATION AND BLASTULATION RATES IN PATIENTS WHO FAIL TO GENERATE A EUPLOID BLASTOCYST WHEN COMPARED TO PATIENTS WHO ACHIEVE A EUPLOID BLASTOCYST. Haley N. Glatthorn, MD,[1] Brent M. Hanson, MD,[2] Philip J. Cheng, MD,[2] James Hotaling, MD,[3] Richard Thomas Scott, Jr., MD,[2] Jason M. Franasiak, MD, HCLD/ALD.[2] [1]Rutgers Robert Wood Johnson Medical School New Brunswick, NJ; [2]IVI-RMA New Jersey, Basking Ridge, NJ; [3]University of Utah School of Medicine Andrology and IVF Laboratories, Salt Lake City, UT.

OBJECTIVE: Advancing paternal age has been associated with worsened embryology outcomes, but it is unknown whether these effects are more pronounced in patients who ultimately fail to generate a euploid blastocyst. This study investigates the association between increasing paternal age and embryology outcomes in patients who did not generate a euploid embryo for transfer and compares the same outcome measures to couples who produced at least one euploid embryo through in vitro fertilization (IVF).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: This study was performed at a university-affiliated fertility practice from January 2012 to December 2018. Inclusion criteria were specified as couples undergoing a first cycle of IVF using an ejaculated semen sample followed by PGT-A, with fertilization achieved via intracytoplasmic sperm injection (ICSI). Linear regression models were utilized to assess the relationship between paternal age, fertilization rate, and blastulation rate. Fertilization and blastulation rates in patients who failed to achieve a euploid blastocyst were compared to those who met identical inclusion criteria but achieved at least one euploid blastocyst.

RESULTS: 4084 couples failed to generate a euploid blastocyst. Mean male partner age was 37.8 ± 6.4 years and mean female partner age was 35.8 ± 5.1 years. Overall fertilization rate was 79.3% and blastulation rate was 42.6%. After adjusting for female age, male partner age ≥40 within this group resulted in decreased blastulation rates (p=0.03) compared with younger male partner age, but there was no association between male partner age and fertilization rate (p=0.22).

These results were compared to 4368 patients who successfully generated a euploid embryo for transfer. In this group, the median number of euploid embryos produced was 3.0 (IQR 2.0-5.0). Mean male partner age was 37.1 ± 5.5 years and mean female partner age was 34.9 ± 4.0 years. Similar to

observations in couples with no euploid blastocysts, older male partner age (≥40 years) was associated with decreased blastulation (p<0.01), but did not affect fertilization rate (p=0.66). Both fertilization rate (85.0%) and blastulation rate (55.1%) were higher in patients who went on to develop a euploid blastocyst than in patients who did not.

Significantly lower fertilization rates (p<0.01) and blastulation rates (p<0.01) were noted among patients failing to generate a euploid embryo when compared with those who ultimately produced at least one euploid embryo. These findings held true for both younger (<40) and older (≥40) male partners.

CONCLUSIONS: In couples who fail to generate a euploid embryo, increasing paternal age negatively affects the rate of blastocyst formation but does not impact fertilization rate when male partner age of 40 is used as a cutoff. When compared to couples who generated at least one euploid blastocyst, couples who failed to develop a euploid embryo had lower fertilization rates and blastulation rates across all male partner age groups. These findings can be used to guide patient management and set expectations, particularly in the setting of an older male partner.

O-143 10:40 AM Monday, October 19, 2020

SPERM RETRIEVAL RATES AND OUTCOMES IN MEN WITH A HISTORY OF MALIGNANCY. Nahid Punjani, MD MPH,[1] Ryan Flannigan, MD,[2] Kathleen Hart, BSN RN MA,[1] Peter N. Schlegel, M.D.[1] [1]Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY; [2]University of British Columbia, Vancouver, BC, Canada.

OBJECTIVE: To assess sperm retrieval rates and outcomes from a large series of cancer patients undergoing microsurgical testicular sperm extraction (mTESE).

DESIGN: Retrospective study of prospectively collected data.

MATERIALS AND METHODS: mTESE procedures performed by a high-volume surgeon at Weill Cornell between 1995 and 2020 were reviewed. Men with history of malignancy were included. Demographic data included male and partner age. Testicular size was recorded. Sperm retrieval and pregnancy were classified dichotomously, and fertilization rate was evaluated continuously. Treatment including chemotherapy and/or radiation was documented. Adjusted logistic regression models were completed to examine predictors of sperm retrieval.

RESULTS: A total of 177 men with malignancy at the time of mTESE procedure were included. The median male age was 35 (IQR 32-40). Median partner age was 32 (IQR 29-36). Mean FSH levels was 24.7 ± 13.8 IU/mL. A total of 121 men (68.4%) had history of only chemotherapy and 55 men (31.1%) had history of only radiation, 46 men (26.0%) had both and 47 (26.6%) had neither. Sperm retrieval occurred in 86 of 177 men (48.59%). Fertilization rate per injected oocyte was 2.87 ± 4.46. Pregnancy occurred in 62 of 175 men (Table 1), for a total of 35.0%. In the malignancy group, only testis size was marginally associated with sperm retrieval (OR 1.11, 95%CI 1.03-1.19). Testis size was marginally associated with pregnancy in those with malignancy history and with chemotherapy (OR 1.09, 95%CI 1.01-1.18 and OR 1.12, 95%CI 1.02-1.24, respectively).

CONCLUSIONS: Despite a history of malignancy, chemotherapy or radiation therapy, sperm retrieval rates with mTESE are near 50%, and clinical pregnancies occur among 34% of couples. Only testis size had limited associations with sperm retrieval and pregnancy, therefore, limited pre-operative factors exist to determine who will have successful retrievals.

O-144 10:55 AM Monday, October 19, 2020

TELEHEALTH FOR MALE-INFERTILITY IS FEASIBLE AND SAVES PATIENTS' TIME AND MONEY. Alex Zhu, DO,[1] Juan J. Andino, MD, MBA,[1] Zoey Chopra, BA,[2] Stephanie Daignault-Newton, MS,[1] Chad Ellimoottil, MD, MS,[1] James M. Dupree, IV, MD, MPH.[1] [1]Michigan Medicine, Ann Arbor, MI; [2]University of Michigan, Ann Arbor, MI.

OBJECTIVE: There has been a rapid expansion of video visits, a form of telehealth, with the COVID-19 pandemic; however, little is known about the feasibility or benefits of video visits for patients seeking male infertility care. Herein we summarize a single institution's experience using video visits to manage infertility prior to the COVID-19 pandemic. Specifically, we evaluate the number of patients engaging in video visits for the first time, and the patient resources saved by forgoing in-person appointments.

DESIGN: Retrospective case series of patients undergoing video visits for follow-up of male-infertility care.

MATERIALS AND METHODS: We identified all video visits performed at our institution between August 21, 2017 and March 17, 2020. We included men seen for male infertility by a single urologist. We used chart review to collect patient demographic information including age, primary language, race, and occupation. Patients were identified as blue collar versus white collar workers with respect to their engagement in manual labor. We determined whether patients had a prior video visit completed at our institution. We used Google Maps™ to calculate round-trip driving distance and time saved based on patients' city of residence. Driving costs saved were calculated by using American Automobile Association's cost estimate of $0.59/mile. Finally, Glassdoor.com salaries were used to estimate wages lost if taking a half or full day off to attend an in-person clinic visit.

RESULTS: 70 male infertility video visits were completed by 56 patients. Median age of patients was 36 years old (range 20-56), 96% identified preferred language as English, and 78% self-identified as white. There were a total of 49 unique occupations among the 56 men. 32% were blue collar workers and 68% were white collar workers. For 55 of 56 patients, this study period represented their first use of video visits in our health system.

Video visits allowed patients to save a median of 80 miles (interquartile range 46-244) and 97 minutes (IQR 64-250) of travel per visit. This resulted in a median of $47 (IQR 27–144) of driving costs saved per visit. By not having to miss a half or full day of work, patients potentially avoided a median of $102 (IQR $69 – 133) to $205 (IQR $137 – 266) in lost wages, respectively. Total median savings per patient ranged from $149 (half day off) to $252 (full day off). Median salary of our cohort was $51,331.

In total, 70 video visits saved 56 patients 11,646 miles and 12,070 minutes in travel. Total estimated savings to patients was $14,539 (half day off) to $22,206 (full day off).

TABLE 1. Clinical Outcomes by Cancer Treatment

	Cancer (n=177)	Chemotherapy (n=121)	Radiation (n=55)	Both (n=46)
Sperm Retrieved (%)	86 (48.6%)	52 (43.0%)	14 (25.5%)	9 (19.6%)
Pregnancy (%)	62 (35.0%)	38 (31.7%)	9 (16.4%)	6 (13.0%)
Sperm Retrieval (OR, 95%CI)				
Male Age	1.04 (0.99-1.10)	1.02 (0.95-1.09)	1.00 (0.88-1.14)	0.98 (0.85-1.14)
Male FSH	1.01 (0.98-1.03)	0.99 (0.96-1.03)	1.02 (0.97-1.07)	0.97 (0.90-1.05)
Testis Size	**1.11 (1.03-1.19)**	1.08 (0.99-1.18)	1.14 (0.99-1.31)	1.07 (0.90-1.26)
Pregnancy (OR, 95%CI)				
Male Age	**1.08 (1.00-1.16)**	1.05 (0.95-1.16)	0.99 (0.79-1.23)	1.03 (0.82-1.29)
Female Age	0.92 (0.83-1.02)	0.95 (0.84-1.07)	1.06 (0.80-1.39)	1.04 (0.78-1.37)
Male FSH	1.02 (0.99-1.06)	1.01 (0.97-1.05)	1.02 (0.96-1.08)	0.93 (0.82-1.05)
Testis Size	**1.09 (1.01-1.18)**	**1.12 (1.02-1.24)**	1.06 (0.89-1.26)	1.00 (0.81-1.23)

CONCLUSIONS: Video visits are a feasible option for follow-up infertility care and are a patient-centric modality that reduces travel and financial burdens. 98% of patients were first-time video visit users suggesting that men are amenable to using video visits for male infertility care. Calculated cost savings may have underestimated total expenses as we did not account for meals, parking fees and other expenses incurred by traveling for an in-person appointment.

MENTAL HEALTH

O-145 9:40 AM Monday, October 19, 2020

PARENT-CHILD RELATIONSHIP QUALITY AND CHILD PSYCHOLOGICAL ADJUSTMENT IN EGG DONATION FAMILIES: CHILDREN'S PERSPECTIVES AT AGE 5. Susan Imrie, PhD,[■] Joanna Lysons, MSc,[2] Vasanti Jadva, PhD,[2] Susan Golombok, PhD[2] [1]University of Cambridge, Cambridge, United Kingdom; [2]■ ■ ■.

OBJECTIVE: The first phase of this longitudinal study indicated that subtle differences may exist in mother-infant relationship quality between egg donation and IVF families, with egg donation mothers and infants showing less optimal relationship quality. The current study examined parent-child relationship quality and child psychological adjustment from the child's perspective in early childhood.

DESIGN: Forty-nine children born through egg donation (M = 66.96 months, SD = 3.64) and a comparison group of 43 IVF children conceived using the parents' own gametes (M = 66.79 months, SD = 3.80) were compared on a standardized assessment of children's perceptions of their families and themselves. Families were recruited through UK fertility clinics at the first phase of the study, and all were heterosexual two-parent families.

MATERIALS AND METHODS: Families were visited at home by trained researchers. Data collection with children was carried out in a separate room to parents. Children were administered the Berkeley Puppet Interview (BPI; Ablow & Measelle, 1993), an interviewing and coding method used to assess young children's perceptions of their family environment and themselves. The BPI was used to assess children's perceptions of their relationship with their mother and father separately on two scales: warmth/enjoyment, and anger/hostility. The measure was also used to assess children's self-perceptions of their levels of depression, anxiety, and strengths/competencies. Outcomes were examined between family types using independent samples t-tests.

RESULTS: Children conceived through egg donation rated their relationship with their mother as higher in warmth/enjoyment than did children conceived through IVF ($t(62.29) = -2.42$, $p = .02$). This difference was of a medium effect size $d = .55$. No differences were found between groups for children's ratings of their mother's anger/hostility. No differences were found between groups in children's perceptions of their relationship with their father on either the warmth/enjoyment or anger/hostility scale. Neither were there group differences in children's perceptions of their own levels of depression, anxiety or strengths/competencies.

CONCLUSIONS: The findings suggest that children in egg donation families view their family relationships and themselves in a largely similar way to children who are genetically related to both their parents. Where a difference was found, this indicated more positive mother-child relationships in egg donation families, as viewed by children themselves.

SUPPORT: The study was supported by the Wellcome Trust [208013/Z/17/Z]

O-146 9:55 AM Monday, October 19, 2020

SLEEP AND PSYCHOLOGICAL WELL-BEING: IS OBSTRUCTIVE SLEEP APNEA ASSOCIATED WITH DEPRESSION AND ANXIETY IN WOMEN WITH POLYCYSTIC OVARY SYNDROME? Xiaojie P. Zhou, MD,[1] Eleni Greenwood Jaswa, MD, MSc,[2] Nikolaus J. Lenhart, BS,[1] Jamie Corley, BA,[1] Marcelle I. Cedars, MD,[1] Heather G. Huddleston, MD.[2] [1]University of California San Francisco, San Francisco, CA; [2]University of California, San Francisco School of Medicine, San Francisco, CA.

OBJECTIVE: Polycystic ovary syndrome (PCOS) is a common yet complex endocrine disorder in which affected women experience diverse comorbidities, including higher rates of depression and anxiety. Women with PCOS have also been shown to be at risk for obstructive sleep apnea (OSA). In the general population, OSA has been linked to depression and anxiety, with evidence to suggest that treatment of OSA has positive psychological effects. However, relationships between OSA and depression/anxiety have not been well-defined in PCOS. The purpose of this study was to determine whether being high-risk for OSA is associated with elevated depression and anxiety symptoms in women with PCOS.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: All patients seen at a university-based clinic between 2017-2020 with a confirmed PCOS diagnosis by the Rotterdam criteria were included. Participants completed validated questionnaires assessing for OSA (Berlin), depression (Patient Health Questionnaire-9, PHQ-9), and anxiety symptoms (Generalized Anxiety Disorder-7, GAD-7). The Berlin questionnaire consists of 3 categories related to OSA risk. A positive score in 2 or 3 categories is considered high-risk for OSA. Multivariate logistic regression analyses were used to determine the odds of moderate or severe symptoms of depression and anxiety defined by PHQ-9 score $\geq$10 and GAD-7 score $\geq$10 in the high-risk versus low-risk OSA groups. The models were adjusted for age, body mass index (BMI), free testosterone level and insulin resistance as measured by the homeostatic model assessment of insulin resistance (HOMA-IR) score.

RESULTS: A total of 196 women with PCOS were included, of which 37.8% screened high-risk for OSA. The mean age of all participants was 28.1 years (SD 6.1) and mean BMI was 31.0 kg/m^2 (SD 9.1). The high-risk OSA group had a higher mean PHQ-9 score as compared to the low-risk OSA group (12.0 vs. 8.3, p<0.0001), as well as a higher mean GAD-7 score (8.9 vs. 6.1, p=0.0003). Women in the high-risk OSA group had increased odds of moderate or severe depression (OR 3.01, 95% CI 1.66-5.49, p<0.0001) and anxiety (OR 2.81, 95% CI 1.49-5.29, p=0.001). These associations were only slightly attenuated in adjusted models: aOR for moderate or severe depression was 2.489 (95% CI 1.10-5.60, p=0.03) and aOR for moderate or severe anxiety was 2.49 (95% CI 1.05-5.92, p=0.04).

CONCLUSIONS: Among those with PCOS, women at high-risk of OSA experienced elevated levels of depression and anxiety symptoms compared to those at low risk for OSA, independent of the effects of age, BMI, hyperandrogenism and insulin resistance. The complex comorbidities of OSA and psychological conditions in women with PCOS allow for multiple targets of intervention. Routine OSA screening in women with PCOS should be undertaken, particularly in the setting of existing depression and anxiety. Referral for OSA diagnosis and treatment may have added psychological benefits in this population.

O-147 10:10 AM Monday, October 19, 2020

LONG-TERM PSYCHIATRIC ILLNESS IN WOMEN WITH PRIMARY INFERTILITY. Alessandra J. Ainsworth, MD,[1] Emily N. Sadecki, BA,[2] Lauren Kendall Rauchfuss, MD,[1] Amy Weaver, MS,[3] Yulian Zhao, Ph.D.,[4] Elizabeth A. Stewart, MD.[5] [1]Mayo Clinic, Rochester, MN; [2]Mayo Clinic College of Medicine and Science, Rochester, MN; [3]Mayo Clinic Division of Biomedical Statistics and Information, Rochester, MN; [4]Department of Obstetrics and Gynecology, Mayo Clinic, Rochester, MN; [5]Mayo Clinic Department of OB/GYN, Reproductive Endocrinology and Infertility, Rochester, MN.

OBJECTIVE: To evaluate the long-term risk of de novo psychiatric illness in women with a history of primary infertility compared to age-matched referent women.

DESIGN: Population-based retrospective cohort study.

MATERIALS AND METHODS: A random sample of 300 female residents of Olmsted County, MN, diagnosed with primary infertility from 1980-1999 were identified through the Rochester Epidemiology Project (REP) records-linkage system. Medical records were manually reviewed to confirm primary infertility diagnosis and date of diagnosis became the index date. Each woman was 1:1 age-matched (±1 y) to a referent woman residing in the county who had not been diagnosed with primary infertility or undergone hysterectomy prior to the index date. Diagnosis codes for depression, anxiety and bipolar disorder were electronically obtained for each pair using standard REP protocols. Diagnoses made prior to or up to 3 months after the index date were considered prevalent disorders. Each of the psychiatric disorders was evaluated separately; women with a prevalent disorder at index date were excluded from the estimation of risk for the other newly diagnosed disorders (de novo). Cox proportional hazards models were fit to estimate the hazard ratio (HR) and 95% confidence interval to compare the long-term risk between infertility cases and

referents. Live-birth was handled as a time-dependent covariate in Cox models for each outcome.

RESULTS: The mean ± SD age at index date was 29.9 ± 4.6 and 30.0 ± 4.6 for 300 infertility cases and 300 referents, respectively. There was no difference in prevalence of depression, anxiety, and bipolar disorder with 11.7%, 4.3% and 0.3% among infertility cases compared to 10.7%, 3.7%, and 0.7% among referents. The median duration of follow-up after index date was 21.5 years (interquartile range (IQR), 13.0-25.5) and 20.9 years (IQR, 4.9-24.9) for the infertility cases and referents, respectively. The risk of de novo bipolar disorder was 3.6 times higher for women with primary infertility (HR 3.63, 95% CI 0.77-17.09), however, this was not statistically significant as only 10 de novo diagnoses (8 infertility cases and 2 referents) were identified. We did not identify an increased risk of de novo depression (HR 1.07, 95% CI 0.79-1.45) or de novo anxiety (HR 1.25, 95% CI 0.88-1.76). Among women with primary infertility, we found no significant association between live birth and de novo bipolar disorder (HR 0.68, 95% CI 0.16-2.89), depression (HR 1.47, 95% CI 0.91-2.39), or anxiety (HR 1.48, 95% CI 0.88-2.47).

CONCLUSIONS: We found no increased rate of anxiety or depression in women with primary infertility compared to age matched referent women. However, a trend toward higher risk of de novo bipolar disorder was identified. Live birth after diagnosis of primary infertility showed a trend toward decreased incidence of bipolar disorder but increased rates of anxiety and depression. These findings suggest a need for additional studies to evaluate patient characteristics associated with development of de novo bipolar disorder or other psychiatric disorders that may benefit from additional psychiatric evaluation.

SUPPORT: Not applicable.

O-148 10:25 AM Monday, October 19, 2020

SHOULDA, COULDA, WOULDA: COUPLES' DECISIONAL REGRET AND EVALUATIONS REGARDING FERTILITY TREATMENTS SIX YEARS AFTER INITIATION. Colin Johnson, MD, Rachel Cusatis, PhD, Kathryn E. Flynn, PhD, Jay I. Sandlow, MD, Judith Myers, MS, Kate D. Schoyer, MD. Medical College of Wisconsin, Milwaukee, WI.

OBJECTIVE: To assess patients' evaluations about fertility treatments 6 years after their initial consultation with a reproductive specialist.

DESIGN: Longitudinal cohort study using prospectively collected patient-reported data and retrospectively collected clinical data.

MATERIALS AND METHODS: Patients and their partners seeking initial consultation with a reproductive specialist were invited to complete questionnaires prior to their first consultation, at 1 year, and at 6 years. At the 6-year assessment, participants were asked yes/no questions regarding the treatments that they received (Table 1). The Decisional Regret Scale was administered, 5 items assessing regret (0-100), referencing "the decision you made about how to add a child to your family." Medical records were used to ascertain whether each participant achieved a live birth using fertility treatments. Chi-squared tests and independent sample t-tests were used to explore whether gender, a live birth after fertility treatments, or decisional regret scores were associated with responses.

RESULTS: 45 couples and 34 individuals (77 women and 47 men, 80% retention) responded to the 6-year survey. Although 90% of patients were happy with the treatments they chose, 9% of patients wished they had tried more medical treatments, 10% of patients wished they had tried fewer medical treatments, and 5% of patients wished they had tried different medical treatments. There were no significant gender differences in responses. Participants who did not achieve a live birth through fertility treatments were more likely to wish they had tried more treatments (p=0.04) and be less happy with the treatments they chose (p<0.001) compared to those who achieved a live birth. Those who were happy with the treatments they chose had significantly lower decisional regret scores, and the highest regret scores were among those who wished they had tried different treatments (Table 1).

CONCLUSIONS: This longitudinal study provides novel insight into patients' evaluations regarding treatment several years after seeking a fertility consultation. Those who wished they had tried different treatments had the strongest regret. This data is helpful for providers to counsel patients about the impact of treatment decisions on future regret.

SUPPORT: Funding came from R21HD071332 from the National Institute of Child Health and Human Development as well as the Department of Obstetrics and Gynecology at the Medical College of Wisconsin.

O-149 10:40 AM Monday, October 19, 2020

DOES A WEB-BASED APP IMPACT QUALITY OF LIFE MEASURES DURING IN VITRO FERTILIZATION? Caitlin Elizabeth Martin, MD, MS,[1] Michael Lanham, MD,[2] Courtney A. Marsh, MD, MPH,[3] Kenan Omurtag, MD.[1] [1]Washington University School of Medicine, St. Louis, MO; [2]University of Michigan, Ann Arbor, MI; [3]University of Kansas, Overland Park, KS.

OBJECTIVE: To assess whether utilization of a web-based application as an adjunct to assist in medication management during In Vitro Fertilization (IVF) impacts quality of life and anxiety measures during IVF.

DESIGN: A multicentered, randomized controlled trial.

MATERIALS AND METHODS: There were 110 women recruited prior to starting IVF at the time of analysis. Subjects were recruited to assess quality of life during IVF, but were randomized to use a web-based application called "OnTrack" to assist with medication management versus no app with conventional medication management. Women in the application arm were also informed of daily medication changes per clinic protocol. Validated instruments were emailed to patients at three time points: prior to starting IVF (baseline), on day 6 of stimulation and just prior to retrieval. The validated measures included the CART (Concerns of Women Undergoing Assisted Reproductive Technologies) scale, FertiQoL (Fertility Patient Quality of Life) questionnaire and the STAI (Spielberger's State-Trait Anxiety Inventory). University of Michigan Redcap was used for data collection. Statistical analysis was performed in R with package LME4 v1.1-23. Linear mixed models with random intercept by subject were used to control for repeated measures. The data was assessed both together and by study arm to assess if the application use impacted the scores.

RESULTS: A total of 21 (19%) participants reported a history of anxiety. There was a decrease in the total CART score from the baseline to day 6 survey (p=0.004) and pre-retrieval (p=0.132). When comparing the app arm to the control arm, there were lower CART scores at day 6 (p=0.046) and a trend towards lower scores pre-retrieval (p=0.056). There was no significant effect of the application when assessing the FertiQoL scaled score and the STAI scores. When examining both groups together, there was a change in FertiQoL scaled scores from the baseline to pre-retrieval survey

TABLE 1. Independent Sample T-tests of Decisional Regret and Evaluation of Treatment Decisions (n=124)

Statement	Mean Decisional Regret Score if Answered "No"	Mean Decisional Regret Score if Answered "Yes"	p-value
I wish I had tried more medical treatments	9.2	30.5	0.009
I wish I had tried fewer medical treatments	8.4	30.8	0.03
I wish I had tried different medical treatments	9.1	50.0	0.01
I am happy with the medical treatments I chose	44.2	7.5	<0.001

(p=0.011). Lower STAI scores were noted at the pre-retrieval survey compared to baseline (p=0.039). The results were unchanged when controlling for a history of anxiety or history of prior IVF treatment.

CONCLUSIONS: The use of a web-based application to support medication management during IVF did not appear to have much impact on quality of life scores and anxiety measures during IVF. However, when examining the CART score in particular, there was a significant difference in CART scores in the application arm compared to the control arm, which suggests the application may have a positive impact in allaying patient concerns during the IVF process. Medication management during IVF is particularly anxiety-provoking for patients. Patient tools that can improve this component of the IVF experience warrant further study.

University of Michigan Department of Obstetrics & Gynecology

SUPPORT: Michigan Translational Research and Commercialization Program (MTRAC)

O-150 10:55 AM Monday, October 19, 2020

THE EMOTIONAL IMPACT OF THE ASRM GUIDELINES ON FERTILITY PATIENTS DURING THE COVID-19 PANDEMIC. Jenna M. Turocy, M.D.,[1] Alex Robles, M.D.,[1] Daniel Hercz, M.D.,[2] Mary D'Alton, M.D.,[3] Eric J. Forman, M.D.,[1] Zev Williams, M.D., PhD.[1] [1]Columbia University Fertility Center, New York, NY; [2]Jackson Memorial Hospital, Miami, FL; [3]Columbia University Medical Center, New York, NY.

OBJECTIVE: To survey fertility patients' agreement with ASRM recommendations during the COVID-19 pandemic and the emotional impact on them.

DESIGN: An online survey was sent to current fertility patients at a New York City academic fertility practice at the epicenter of the COVID-19 pandemic.

MATERIALS AND METHODS: Patient agreement with the ASRM recommendations during the COVID-19 pandemic and the emotional impact rated on a Likert scale. Ordinal data such as responses rated on a Likert scale were analyzed using Mann-Whitney Wilcoxon testing and responses were compared using Fisher exact or chi-square test as appropriate, with significance at $p<0.05$.

RESULTS: A total of 518 patients completed the survey for a response rate of 17%. Fifty percent of respondents had a cycle canceled due to the COVID-19 pandemic. Of those who had a cycle cancelled, 85% of respondents found it to be moderately to extremely upsetting with 22% rating it to be equivalent to the loss of a child. There was no difference on the emotional impact based on the type of cycle cancelled. Fifty-five percent of patients agreed that diagnostic procedures such as hysterosalpingograms should be cancelled while 36% of patients agreed all fertility cycles should be cancelled (22% unsure, 43% disagreed). Patients were slightly more likely to agree with the ASRM guidelines if they have an upcoming cycle cancelled ($p = 0.041$). Of all respondents 82% would have preferred to have the option to start a treatment cycle in consultation with their doctor.

CONCLUSIONS: Given the severity of the COVID-19 pandemic, the physical, financial and emotional impact of this unprecedented threat cannot be underestimated in our fertility patients.

NUTRITION AND LIFESTYLE

O-151 1:50 PM Monday, October 19, 2020

DOES BMI AFFECT EMBRYONIC MOSAICM? Baruch Abittan, M.D.,[1] Robyn A. Frankel, M.D.,[2] Amber Gamma, MS, CGC,[3] Randi H. Goldman, M.D.[1] [1]Northwell Health Fertility, North Shore University Hospital/Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY; [2]Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY; [3]Northwell Health Division of Medical Genetics, Great Neck, NY.

OBJECTIVE: To examine the association between body mass index (BMI) and embryonic aneuploidy and mosaicism by trophectoderm biopsy and preimplantation genetic testing for aneuploidy (PGT-A).

DESIGN: Retrospective cohort study in an academic fertility center.

MATERIALS AND METHODS: Patients' first fresh autologous stimulation cycles wherein all embryos were biopsied for PGT-A analysis between 2016-2019 were reviewed. BMI (kg/m^2) was recorded prior to cycle start and patients were stratified into World Health Organization BMI categories: underweight (BMI<18.5), normal weight (BMI 18.5-24.9), overweight (BMI 25-29.9), or obesity class I (BMI 30-34.9), II (BMI>35-39.9), or III (BMI>40). PGT-A was performed in a single external laboratory by array comparative genomic hybridization (aCGH) (2016-2017) or next generation sequencing (NGS) (2018-2019, during which mosaicism was additionally reported).

The associations between BMI and rates of euploidy and mosaicism, including low level (LL), high level (HL), whole chromosome, and segmental mosaicism, were determined using forward stepwise multivariable Poisson regressions, controlling *a priori* for age and AMH, and retaining other patient- and cycle-specific variables (e.g., diagnosis) that changed the effect estimates by >10%. For the regression analysis evaluating rate of euploidy, LL mosaic embryos were re-classified as euploid. Regression analyses evaluating rates of mosaicism used data from 2018-2019 only. Relative risks with 95% confidence intervals (RR [CI]) were determined using normal weight as the referent value.

RESULTS: Six-hundred one cycles resulted in 2,992 diagnosed embryos available for analysis. Most patients were of normal weight (N=321) or overweight (N=144), or had class I obesity (N=80). Overall, 21% of patients in the cohort had obesity (BMI >30). The average patient age was 36.0 years, and age and BMI were positively correlated (r=0.2). There was no difference in overall euploid or mosaicism rate stratified by BMI. Compared with normal weight, underweight (RR: 4.1 [1.5-11.3]), overweight (1.6 [1.1-2.5]), and obesity (1.6 [1.1-2.4]) were all associated with significantly higher rates of LL mosaicism (6.3% vs. 20.8%, 10.0%, and 9.1%, respectively). Compared with normal BMI, overweight was associated with lower rates of HL mosaicism (8.1% vs 3.7%, RR: 0.4 [0.2-0.8]) and whole chromosome mosaicism (7.1% vs. 3.7%, RR: 0.5 [0.3-0.9]).

CONCLUSIONS: This is the first study to examine the effect of BMI on embryo mosaicism. Our findings support previous research demonstrating that BMI is not associated with the rate of embryonic euploidy. While the overall rate of mosaicism did not differ among BMI categories, both low and high BMI were associated with increased rates of LL mosaicism compared with normal BMI, and overweight was associated with decreased rates of HL and whole chromosome mosaicism. Though a large proportion of our patient cohort had obesity, further research is needed to clarify the impact of BMI on embryo mosaicism.

O-152 2:05 PM Monday, October 19, 2020

MALE VITAMIN D STATUS AND MALE FACTOR INFERTILITY. Nicole Banks, MD,[1] Fangbai Sun, MPH,[2] Stephen A. Krawetz, PhD,[3] Robert M. Coward, MD,[4] Puneet Masson, MD,[5] JAMES F. SMIH, MD, MS,[6] J. C. Trussell, MD,[7] Nanette Santoro, MD,[8] Heping Zhang, PhD,[2] Anne Z. Steiner, MD, MPH.[9] [1]VCU Health, Richmond, VA; [2]Yale University School of Public Health, New Haven, CT; [3]Wayne State University School of Medicine, Detroit, MI; [4]University of North Carolina, Chapel Hill, NC; [5]Penn Medicine, Philadelphia, PA; [6]University of California, San Francisco, San Francisco, CA; [7]Upstate University Hospital, Syracuse, NY; [8]University of Colorado School of Medicine, Aurora, CO; [9]Duke University, Durham, NC.

OBJECTIVE: To determine the association between 25-hydroxyvitamin D (25OHD) levels in the male partner and fertility outcomes in couples with mild male factor infertility.

DESIGN: Secondary analysis of a randomized, controlled trial.

MATERIALS AND METHODS: Males (n=154) with sperm concentration ≤15 M/ml, motility ≤ 40%, or normal morphology ≤ 4% were eligible. Female partners were ovulatory, ≤ 40 years old, and had documented tubal patency. Men were randomized to a vitamin formulation including vitamin D 2000 IU daily or placebo. Couples attempted to conceive naturally for 3 months and with clomiphene citrate with intrauterine insemination of the female partner in months 4 through 6. Data were analyzed by baseline male 25OHD levels dichotomized at 20 ng/mL. The primary outcome was semen parameters at baseline (semen concentration, motility, morphology, and DNA fragmentation). Secondary outcomes were cumulative pregnancy, miscarriage, and live birth rates. Data were analyzed using Wilcoxon rank-sum test, Chi square, or Fisher's exact test, where appropriate. Multivariable logistic and linear regression models were created to adjust for potential confounders, including male age and race.

RESULTS: Semen parameters and sperm DNA fragmentation were not statistically significantly different in males with vitamin D deficiency compared to males with 25OHD levels ≥ 20 ng/mL (Table 1). Clinical pregnancy and live birth rates did not differ. Male 25OHD level ≥ 20 ng/mL was

associated with a lower pregnancy loss rate (adjusted OR, 0.11; 95% CI, 0.02 to 0.75; P = 0.024).

CONCLUSIONS: Vitamin D deficiency in the male partner is unrelated to semen parameters, pregnancy or live birth rates. Further study is warranted to better characterize the rate of miscarriage in couples with male vitamin D deficiency.

TABLE 1. Semen parameters at baseline by male vitamin D status

Parameters	Vitamin D < 20 ng/mL (n=26)	Vitamin D ≥ 20 ng/mL (n=128)	P value
Sperm concentration (million/ml)	19.0 (11.0-52.0)	19.0 (10.2-38.2)	0.504
Sperm concentration ≤ 15 million/ml	11/26 (42.3%)	52/128 (40.6%)	0.874
Normal morphology (%)	6.5 (4.0-10.0), n=22	5.0 (2.0-8.0), n=94	0.133
Normal morphology ≤ 4%	7/22 (31.8%)	41/94 (43.6%)	0.312
Total motility (%)	44.7 ± 20.2	43.8 ± 16.1	0.908
Total motility ≤ 40%	14/26 (53.8%)	58/128 (45.3%)	0.427
DNA fragmentation (SCSA, DNA fragmentation index) (%)	20.4 (13.6-35.1), n=23	19.7 (14.2-27.9), n=112	0.518
DNA fragmentation > 25%	9/23 (39.1%)	35/112 (31.3%)	0.463

O-153 2:20 PM Monday, October 19, 2020

OBESE WOMEN PRESENT AN INCREASED RISK OF MISCARRIAGE AFTER EUPLOID EMBRYO TRANSFER.

Mauro Cozzolino, MD,[1] Juan A. Garcia-Velasco, MD, PhD,[2] Marcos Meseguer, PhD,[3] Antonio Pellicer, MD,[1] Jose Bellver, MD PhD[4] [1]IVIRMA Foundation, Valencia, Spain; [2]IVI Madrid, Rey Juan Carlos University, Madrid, Spain; [3]IVIRMA Global,Valencia,Spain, Valencia, Spain; [4]IVIRMA Valencia, Valencia, Spain.

OBJECTIVE: To determine whether female body mass index (BMI) is associated with an increased risk of miscarriage after euploid embryo transfer.

DESIGN: Retrospective observational multicenter cohort study.

MATERIALS AND METHODS: We analyzed all the PGT-A cases performed in the seven largest IVI clinics in Spain (Barcelona, Bilbao, Madrid, Málaga, Sevilla, Valencia and Vigo) from January 2016 to April 2019. Patients in whom at least one euploid embryo was transferred after blastocyst stage biopsy were considered. Cases of no embryo survival after vitrification or ovum donation were excluded. We compared clinical and laboratory parameters among BMI groups considering miscarriage rate (total, clinical and biochemical) as the main outcome parameter. The study was approved by the Ethics Committee of the IVIRMA (identification code #1811-FIVI-089-MC). Statistical analysis was performed using chi-square or ANOVA test as required. Logistic regression analysis was also applied to the different BMI categories to control for possible confounders on live birth rates.

RESULTS: Cycles were divided into four BMI groups (kg/m^2): underweight (<18.5, n=155), normal weight (18.5–24.9, n=2,549), overweight (25–29.9, n=591), and obese (≥ 30, n=185). The number of PGT-A cycles per patient was similar among groups. The main PGT-A indication was advanced maternal age. Female age was slightly increased in the overweight group. There were no differences in ovarian stimulation parameters, except for an increased gonadotropin dosage in the overweight and obese groups. Fertilization rate, day of embryo biopsy, technique of chromosomal analysis, number of euploid embryos, number of transferred embryos, and method of endometrial preparation for embryo transfer (modified natural versus hormonally prepared cycles) were similar among BMI groups. Concerning IVF outcomes, implantation rate, pregnancy rate and clinical pregnancy rate showed a non-significant trend to poorer results in obese women. However, miscarriage rates were significantly higher in obese women compared to normal weight women (22.7 % (CI95% 16.7-28.7) vs 15.1% (CI95% 13.6-16.5), p=0.043), especially due to a significant increase in the clinical miscarriage rates. Live birth rates were also reduced in obese women (34.3 % (CI95 27.8-40.7) vs 44.5% (CI95 42.5-46.4), p = 0.034). Only female obesity and day 6 trophectoderm biopsy influenced independently on the reduced live birth rates.

CONCLUSIONS: Obese women present higher miscarriage rates and lower live birth rates than normal weight women after euploid embryo transfer, suggesting other etiologic mechanisms different to aneuploidy.

SUPPORT: No financial support

O-154 2:35 PM Monday, October 19, 2020

THE RELATIONSHIP BETWEEN FEMALE BODY MASS INDEX (BMI) AND EMBRYONIC EUPLOIDY AS DETECTED VIA NEXT GENERATION SEQUENCING BUT (NGS): A STUDY OF 5,703 CYCLES

. Jenna Friedenthal, MD,[1] Dmitry Gounko, MA,[2] Taraneh Gharib Nazem, MD,[2] Joseph A. Lee, BA,[2] Beth McAvey, MD,[1] Alan B. Copperman, MD[1] [1]Icahn School of Medicine at Mount Sinai, New York, NY; [2]Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Women with an elevated BMI (≥25 kg/m^2) have been shown to experience poor reproductive outcomes[1, 2]. Obese patients are at particularly high risk for adverse pregnancy outcomes[3]. Several studies have evaluated the impact of BMI on assisted reproductive technology (ART) outcomes [4, 5]. However, the association between BMI and rate of embryo euploidy as determined by NGS has yet to be fully explored. We sought to assess the impact of BMI on euploid rate (ER) as determined by NGS.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The study included patients at an academic center who underwent in vitro fertilization with intracytoplasmic sperm injection from 2016 to 2020. BMI (kg/m^2) was categorized as follows: underweight (<18.5), normal weight (18.5-24.9), overweight (25-29.9), and obese (≥30). A secondary analysis that compared obese patients with all other BMI categories was also performed. Baseline demographics were obtained: age, AMH, cumulative gonadotropin dose (GND), total number of eggs retrieved, and number of metaphase II (MII) oocytes retrieved. Our primary outcome was ER as diagnosed by NGS. Secondary outcomes were maturation rate (MR), fertilization rate (FR), blastulation rate (BR), and biopsied blastocyst rate (BBR). Data were analyzed using ANOVA, Kruskall-Wallis test, chi-square, and logistic multivariate generalized estimating equation (GEE) regression models to adjust for confounders, with P<0.05 considered significant.

RESULTS: 4,067 patients underwent 5,703 cycles during the study time period and were included in analysis. Overweight (n=1,267 cycles) and obese (n=660 cycles) patients were older, had lower average AMH levels, required higher cumulative GND, and had significantly fewer total oocytes and MII oocytes retrieved than patients with a low (n=210 cycles) or normal (n=3,566 cycles) BMI (P< 0.05 for all).

After adjusting for age, AMH, cumulative GND, and number of oocytes retrieved, overweight patients demonstrated a slightly higher BR (OR 1.02, CI 1.01-1.03) compared to patients with normal weight; however, we found no association between BMI and ER, MR, FR, or BBR (P>0.05 for all). Additionally, when comparing obese patients with all other BMI groups, after adjusting for confounders, we found no association between obesity and ER (OR 1.01, CI 0.98-1.04). There was also no association between obesity and MR (OR 0.99, CI 0.98-1.01), FR (OR 0.99, CI 0.98-1.01), BR (OR 1.01, CI 0.99-1.03), or BBR (OR 1.00, CI 0.98-1.01).

CONCLUSIONS: In the largest study to date evaluating the association between BMI and rate of embryonic euploidy as diagnosed by NGS, our results demonstrated that BMI is not predictive of euploid rate. In particular, obesity does not appear to result in increased risk of embryonic aneuploidy. Although mouse models have suggested potentially deleterious effects of abnormal metabolites from obesity on oocyte quality, spindle formation, and chromosome alignment, our findings suggest that the detrimental effect of elevated BMI on pregnancy and ART outcomes may be the result of non-genomic, endocrine, uterine, or an unspecified alternative etiology.

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SUPPORT: None

O-155 2:50 PM Monday, October 19, 2020

TIME-RESTRICTED FEEDING OF NORMAL DIET INCREASES BODY WEIGHT AND IMPAIRS THE DEVELOPMENTAL COMPETENCE OF OOCYTES AFTER IVF IN FEMALE MICE.

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OBJECTIVE: Previous studies have revealed that time-restricted feeding (tRF) reprograms clock gene transcription in peripheral tissues, especially in the liver and influences metabolic pathways in numerous organs, resulting in the changes in the phenotypes associated with metabolic diseases that are characterized in obese male mice. However, the impact of temporally restricted food access on females especially reproductive capabilities has not been fully evaluated so far. Here, we investigated reproductive function of mice fed normal diet either ad libitum or under tRF.

DESIGN: Experimental animal study.

MATERIALS AND METHODS: Mice were fed normal diet (29.9% protein, 11.6% fat, 58.5% carbohydrates) either ad libitum or under tRF for 11 weeks. They were allowed food access between ZT15.5 (3.5 hr after lights off) and ZT24 (just before lights on) under tRF. Comparisons of total calorie intake, body weight and average feeding speed during the period over which food access was allowed were made between the mice fed ad libitum and under tRF (n=140). Diurnal pattern of mRNA levels of *Per2* and *Cry1*, core circadian suppressor genes in the liver were compared between ad libitum and tRF. The numbers and cytoplasmic reactive oxygen species (ROS) levels of oocytes retrieved after ovarian hyperstimulation and blastulation rates after IVF were compared between ad libitum and tRF (n=53).

RESULTS: Total calorie intake of tRF mice was significantly lower than ad libitum (817.6 $\pm$ 43.9kcal vs 866.0 $\pm$ 31.8kcal, $p<0.01$). However, mice fed under tRF was significantly heavier than ad libitum (22.9 $\pm$ 1.5g vs 21.7 $\pm$ 1.3g, $p<0.01$). Feeding speed of mice fed under tRF and ad libitum was 1.25 $\pm$ 0.72 kcal/h and 0.48 $\pm$ 0.36 kcal/h, respectively ($p<0.01$). The oscillation of *Per2* and *Cry1* mRNA levels was jumped in tRF mice as compared to ad libitum. The number of oocytes retrieved from the mice fed under tRF was similar to ad libitum (21.0 $\pm$ 3.3 vs 23.3 $\pm$ 2.6, $p=0.58$). However, the ROS level of oocytes retrieved from the mice fed tRF was significantly higher than ad libitum ($p<0.01$). The blastulation rate of fertilized ova from mice fed under tRF was significantly lower than ad libitum (73.4% vs 89.0%, $p<0.01$).

CONCLUSIONS: As previously reported in the studies of male obese mice, time-restricted feeding increased the peak to trough ratio of mRNA levels of hepatic clock genes. However, body weight was significantly increased by tRF as compared to ad libitum though total calorie intake was small. Oocyte developmental competence was also impaired by tRF. According to several reports, eating fast is associated with postprandial high blood glucose levels that could engender cytoplasmic ROS. It is suggested that eating fast forced by time-restricted feeding is harmful to reproductive function and ROS production in the ooplasm is underlying this impairment.

SUPPORT: Part of this work was supported by a grant from the Japan Society for the Promotion of Science (20K09674 to SH).

O-156 3:05 PM Monday, October 19, 2020

PRE-CONCEPTION RISK PREDICTION INDEX FOR SEVERE MATERNAL MORBIDITY AMONG INFERTILE WOMEN.

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OBJECTIVE: Infertile women who become pregnant are at increased risk of severe maternal morbidity (SMM), defined by the CDC as indicators of a life-threatening complication. The degree to which age and medical comorbidities compound the risk of SMM among infertile women is unknown. Our goal was to create a pre-conception risk prediction index for SMM among infertile women.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: We identified births among infertile women $\leq$ 45 years of age using the Optum® insurance claims database from 2012-2017. Infertile women were identified using infertility diagnosis, testing, or treatment codes and fertility drug dispensing codes. The primary outcome was SMM, identified as any indicator from the CDC Index except blood transfusion alone, which can overestimate true cases. Comorbidities were selected from prior literature. Multivariable logistic regression was performed on all comorbidities significant in bivariate analyses while adjusting for education, race/ethnicity and delivery year. A risk score was then created for each comorbidity in the index. Discrimination of the index was assessed with an ROC curve.

RESULTS: Among 46,161 births, the overall rate of SMM was 2.4% (n=1,120). The highest risk comorbidities were bleeding disorders and pulmonary hypertension, followed by chronic renal and cardiac disease (Table). HIV, substance abuse, and PCOS were not significant. The AUC for the comorbidity index was 0.72.

CONCLUSIONS: We created an index to predict the likelihood that individual comorbidities in an infertile woman would lead to SMM. The discrimination of the index was good based on ROC curves. Our goal after further validation is to develop an open-access online calculator to individualize SMM risk prediction for infertile patients during pre-conception counseling.

Risk Factor	Incidence of SMM, n (%)	aRR (95% CI)	Risk Score
Bleeding Disorder	309 (10.25)	5.15 (4.33-6.13)	7
Pulmonary Hypertension	10 (20.83)	5.04 (2.01-12.59)	7
Chronic Renal Disease	68 (6.22)	1.96 (1.43-2.68)	3
Cardiac Disease	242 (6.11)	2.04 (1.67-2.50)	3
Anemia	401 (4.43)	1.56 (1.33-1.83)	2
Asthma	148 (4.11)	1.60 (1.29-1.99)	2
Hypertension	184 (5.76)	1.55 (1.24-1.94)	2
Age $\geq$ 40 Years	197 (3.28)	1.37 (1.13-1.67)	1
Neuromuscular Disease	234 (3.79)	1.31 (1.08-1.59)	1
Uterine Fibroids	180 (3.84)	1.39 (1.13-1.71)	1
Gastrointestinal Disease	180 (3.93)	1.26 (1.02-1.56)	1
Prior Cesarean Delivery	116 (3.87)	1.13 (0.87-1.47)	NS
Prior Uterine Surgery (Non-Cesarean)	101 (4.50)	1.20 (0.92-1.58)	NS
Connective Tissue Disease	33 (4.11)	0.69 (0.44-1.08)	NS
Endometriosis	82 (3.02)	1.02 (0.77-1.35)	NS
Thyroid Disease	126 (3.21)	1.11 (0.86-1.43)	NS
Mental Health Disorder	309 (3.18)	1.14 (0.96-1.35)	NS
Diabetes Mellitus	94 (4.14)	1.13 (0.86-1.48)	NS

PEDIATRIC AND ADOLESCENT GYNECOLOGY

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UNDERSTANDING THE INFLUENCE OF GENDER IDENTITY AND SEXUAL ORIENTATION ON THE FUTURE PARENTING DESIRES OF TRANSGENDER AND NON-BINARY ADOLESCENTS IN COMPARISON TO THEIR CISGENDER SIBLINGS.

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OBJECTIVE: To assess the influence of gender identity and sexual orientation on the attitudes of transgender and non-binary (TNB) adolescents and their cisgender siblings toward future parenting options and intentions.

DESIGN: This study used a multiphase mixed methods design through integration of cross-sectional quantitative data with qualitative data sequentially collected in 2017-2018.

MATERIALS AND METHODS: TNB adolescents and their cisgender siblings participated in a one-time, one-on-one semi-structured interview and survey. Interview data was coded to develop themes that then guided analysis of the survey data. To assess the fertility attitudes of TNB and their cisgender siblings, a modified version of the Transgender Youth Fertility Attitudes Questionnaire (TYFAQ) was utilized. Possible answers to the TYFAQ survey included "agree," "maybe," or "disagree." Outcomes were treated as ordinal and associations were analyzed using the Mann-Whitney U test.

RESULTS: A total of 40 participants were included in the analysis (29 TNB adolescents, 11 cisgender siblings). Four major themes were noted when comparing the two groups: 1) the role of gender identity and gender dysphoria 2) desire for future economic and social stability 3) perceived personal reproductive potential 4) future partner's gamete compatibility. TNB adolescents were more likely to say they would consider adoption someday (93% vs 54%, p = .0068). Cisgender adolescents were more likely than TNB adolescents to say it is important to have biological children (65.5% vs 27%, p = 0.05). Cisgender boys were more likely to feel pressured by their family to have biological children than their transmasculine TNB peers (20% vs 0%, = 0.04). In comparing heterosexual adolescents to those who identify as lesbian, gay, bisexual, or queer (LGBQ), heterosexual adolescents were more likely to say it is important to have biological children in the future (77% vs 18%, p=0.0023). Among TNB adolescents, those currently using gender-affirming hormones were less likely to think their feelings about children might change in the future (p = 0.029). TNB adolescents with a prior diagnosis of gender dysphoria were more likely to say they wanted to have kids someday (71% vs 37%, p = 0.003) and less likely to say their family would be sad if they did not have biological children (0% vs 25%, p = 0.03). TNB adolescents who endorsed parental support were more likely to say it is not important to have biological children in the future (72% vs 25%, p = 0.05), and those that that do not participate in a support group were more likely to say their parents would be disappointed if they did not have biological children (25% vs 0%, p = 0.003).

CONCLUSIONS: Sexual orientation and gender identity are important factors to consider when assessing an adolescent's desire for future family building. TGN youth, on average, express lower desires for biological children when compared to their cisgender siblings, which is influenced by their experience with dysphoria and perception of community support. These factors should be considered when counseling adolescents on their future fertility and family building options.

O-158 2:05 PM Monday, October 19, 2020

CIRCULATING INFLAMMATORY MARKERS AND ENDOMETRIOSIS PAIN SYMPTOMS AMONG ADOLESCENTS AND YOUNG ADULT WOMEN. Amy L. Shafrir, Sc.D.,[1] Britani Wallace, MPH,[2] Allison F. Vitonis, M.S.,[2] Kathryn L. Terry, Sc.D.,[2] Stacey A. Missmer, ScD[3] [1]Boston Children's Hospital and Boston Center for Endometriosis, Boston, MA; [2]Brigham and Women's Hospital, Boston, MA; [3]College of Human Medicine, Michigan State University, Grand Rapids, MI.

OBJECTIVE: Endometriosis is characterized by immune dysregulation. Limited research, particularly among adolescents and young adults (AYA), has investigated the association between circulating inflammatory markers and endometriosis-related pain symptoms.

DESIGN: Cross-sectional analysis of circulating inflammatory markers from 264 laparoscopically-confirmed endometriosis participants and 275 population-based controls from the Women's Health Study: from Adolescence to Adulthood, a cohort of primarily AYA women.

MATERIALS AND METHODS: Participants completed the World Endometriosis Research Foundation (WERF) Endometriosis Phenome and Biobanking Harmonization Project (EPHect) clinical questionnaire including items on presence and severity of dysmenorrhea and acyclic pelvic pain. Using multiplex microarrays, we measured interleukin (IL)-1β, -6, -8, -10, -16, tumor necrosis factor (TNF) α, monocyte chemotactic protein (MCP)-1, -4, chemokine ligand (CCL) 17, and Interferon gamma-induced protein (IP) 10 in plasma samples collected and processed using the WERF EPHect standards. We used linear regression to compute age-adjusted geometric mean (GM) marker levels with 95% confidence intervals (95%CI) for presence and severity of dysmenorrhea or acyclic pain among endometriosis cases and controls. We assessed effect modification by case status using the Wald test statistic.

RESULTS: More severe dysmenorrhea was associated with lower IL-8 levels among both endometriosis cases and controls [cases: IL-8 GM_{severe}=4.02 (95%CI=3.78-4.27) pg/ml vs. GM_{mild}=5.24 (95% CI=3.96-6.93) pg/ml, P_{trend}=0.01; controls: GM_{severe}=2.93 (2.63-3.27) pg/ml vs. GM_{mild}=3.64 (3.26-4.06) pg/ml, P_{trend}=0.007; $P_{interaction}$ (P_{int})= 0.15]. MCP-4 levels were lower among cases with severe [GM_{severe}=75.9 (68.9-83.6) pg/ml] compared to mild dysmenorrhea [GM_{mild}=108 (69.3-168] pg/ml, P_{trend}=0.03], but no trend was observed among controls (P_{int}=0.06). TNFα and IL-8 levels were lower among controls who ever experienced acyclic pain compared to never [TNFα GM_{ever}=5.98 (5.53-6.47) pg/ml vs. GM_{never}=6.62 (6.37-6.88) pg/ml, P=0.03; IL-8 GM_{ever}=2.87 (2.57-3.22) pg/ml vs. GM_{never}=3.61 (3.41-3.81) pg/ml, P<0.001], with no association observed for cases (TNFα P_{int}=0.13; IL-8 P_{int}<0.001). MCP-1 levels were higher among endometriosis cases with acyclic pain [MCP-1 GM_{ever}=139 (131-148) pg/ml vs. GM_{never}=123 (113-134) pg/ml; P=0.03] but not among controls (P_{int}=0.03) and decreased with increasing acyclic pelvic pain severity for cases but not controls (cases: P_{trend}=0.02, P_{int}=0.07). Among cases, MCP-4 levels decreased with increasing acyclic pain severity (P_{trend}=0.04), whereas IL-1β levels increased with increasing acyclic pain severity (P_{trend}=0.05) with no effect modification by case status (P_{int}>0.12).

CONCLUSIONS: Among AYA participants, IL-1β, -8, MCP-1, -4, and TNFα were associated with the presence and severity of dysmenorrhea and acyclic pelvic pain, with differential associations by case status for IL-8, MCP-1, and MCP-4. No associations were observed for IL-6, -10, -16, CCL-17, or IP-10.

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IDENTIFYING BEST FIT IMPLEMENTATION STRATEGIES FOR IMPROVING FERTILITY CARE FOR ADOLESCENT AND YOUNG ADULT (AYA) CANCER SURVIVORS. Anna Dornisch, BS, Emily Yang, BS, Jamie Gruspe, MPH, Bonnie N. Kaiser, PhD MPH, Teresa Helsten, MD, Paula Aristizabal, MD MAS, Hui-Chun I. Su, MD MSCE. University of California San Diego La Jolla, CA.

OBJECTIVE: Oncofertility care remains under-implemented with limited tools to scale up effective implementation strategies. Guided by the Consolidated Framework for Implementation Research (CFIR), the objective was to systematically assess factors that influence implementation of oncofertility care and map strategies, particularly electronic health record (EHR) enabled ones, that fit adult and pediatric oncology care contexts.

DESIGN: Sequential mixed methods study.

MATERIALS AND METHODS: Using purposeful sampling, we recruited healthcare providers (HCPs) and female AYA cancer survivors from a comprehensive cancer center and a freestanding children's hospital. Participants underwent semi-structured interviews and focus groups based on CFIR. Thematic analysis was used to develop inductive codes and CFIR provided deductive codes to characterize barriers and facilitators to oncofertility care and implementation strategies. Two coders independently coded each transcript with a third coder resolving discrepancies by consensus. Developed strategies were evaluated quantitatively by HCPs for acceptability, appropriateness and feasibility. Score range for each measure was 1-5; higher scores indicate more acceptability, appropriateness and feasibility.

RESULTS: We recruited 19 oncology and fertility HCPs and 9 AYA survivors. We identified barriers and facilitators to fertility care in the CFIR domains of individual, inner setting, outer setting and process, allowing us to conceptualize oncofertility care in three necessary stages: oncofertility needs screen, referral and fertility preservation counseling. To fit an adult and pediatric contexts, five implementation strategies were mapped: fertility needs screen using a Best Practice Advisory (BPA), fertility referral order, televideo fertility counseling, provider audit & feedback (A&F) and a provider educational session. Mean acceptability, appropriateness and feasibility scores across strategies were high (Table). Six additional strategies were designed but did not fit our contexts.

	BPA	A&F	Educational Session
Appropriateness Score Mean (95% CI)	4.4 (4.1, 4.7)	4.0 (3.5, 4.6)	4.7 (4.5, 4.9)
Acceptability Score Mean (95% CI)	4.4 (4.0, 4.7)	4.0 (3.4, 4.6)	4.7 (4.5, 5.0)
Feasibility Score Mean (95% CI)	4.4 (4.2, 4.7)	4.2 (3.7, 4.6)	4.7 (4.5, 4.9)

CONCLUSIONS: Access to oncofertility care remains a challenge for young cancer patients, in part due to unaddressed barriers and facilitators across clinical settings. An implementation science approach systematically assessed oncofertility care, mapped strategies and explored their acceptability, appropriateness and feasibility, providing a theory-based approach and scalable EHR tools to support wider dissemination.

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SERUM MICRORNA'S AS DIAGNOSTIC BIOMARKERS OF ENDOMETRIOSIS IN ADOLESCENT FEMALES. Alla Vash-Margita, MD, Ramanaiah Mamillapalli, PhD, Tran C. Dang, BS, Luisa M. Coraluzzi, BSN, Hugh S. Taylor, MD. Yale University School of Medicine New Haven, CT.

OBJECTIVE: The prevalence of endometriosis in adolescent girls with chronic pelvic pain reaches 75%. Despite this high prevalence, diagnosis of endometriosis in adolescent females remains delayed. Laparoscopy has diagnostic and therapeutic benefits, but major surgery may not be acceptable to young patients. The search for noninvasive biomarkers is ongoing. Recently serum microRNA's have been shown to have diagnostic value in adult women. This study assessed levels of several microRNA's in young women as potential marker of endometriosis.

DESIGN: This was a prospective study evaluating adolescent subjects with a clinical suspicion for endometriosis.

MATERIALS AND METHODS: Female subjects ages 14-25 were seen at the Pediatric/Adolescent Gynecology or Reproductive Endocrinology Clinics for evaluation of chronic pelvic pain and screened for endometriosis under an approved IRB protocol. Subjects with surgically proven endometriosis or imaging suggestive of the disease were assigned to the endometriosis group. Subjects who underwent laparoscopy with no endometriosis were assigned to the control group. Serum was collected from blood samples, and miRNAs were extracted. Expression levels of six microRNAs, miR-125b-5p, miR-150-5p, miR-342-3p, miR-451a, Let-7b, and miR-3613-5p were determined using quantitative real-time polymerase chain reaction (qRT-PCR), and normalized to U6 levels. A student t test was used to compare the clinical characteristics of subjects in the endometriosis and control groups. The fold-change of miRNAs of endometriosis and control groups were compared using Mann-Whitney U test. Logistic regression and receiver operating characteristic (ROC) analysis were performed to determine the diagnostic power of the combination of these six miRNAs.

RESULTS: Subjects (N=27) who were diagnosed by laparoscopy as well as imaging were divided into the endometriosis (N=19) or control (N=8) groups. Of those with endometriosis, fourteen subjects had biopsy proven pelvic endometriosis and in five subjects endometriosis was diagnosed based on imaging (endometrioma). Demographics (age, BMI, ethnicity) between endometriosis and control groups were not statistically significant. The mean age of subjects was 16.6 and 17.3 years, and BMI 24.1 and 28.2 kg/m^2 for the endometriosis and control groups, respectively. The vast majority of subjects with endometriosis were Caucasian (68.4%) and had stage I-II disease (78.6%). qRT-PCR results showed increased levels of miR-125b-5p, miR-150-5p, miR-Let-7b, miR-342-3p and miR-451a, while miR-3613-5p was decreased. Logistic regression analysis of this training set showed that a combination of all six microRNAs resulted in the highest AUC (1.00, p=0.004).

CONCLUSIONS: Endometriosis in girls and young women is highly prevalent yet under-diagnosed. A highly sensitive and specific diagnostic test will have great clinical significance in adolescent females with pelvic pain and suspicion of endometriosis. This study demonstrated that a combination of microRNAs, if validated, can be used as an effective diagnostic tool for endometriosis in adolescent females.

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TURNER SYNDROME: UNDERSTANDING INDIVIDUALIZED MEDICAL RISKS DETERMINED BY KARYOTYPE SUBGROUP. Vaishnavi Purusothaman, MD, MA,[1] Victoria W. Fitz, MD, MSCR,[1] Jennifer R. Law, MD, MSCR,[1] Emma M. Rosen, MSPH,[2] Mary Peavey, MD[1] [1]University of North Carolina, Chapel Hill, NC; [2]UNC Gillings School of Public Health, Chapel Hill, NC.

OBJECTIVE: Turner Syndrome (TS) is the most common sex chromosome abnormality in females and is associated with several phenotypic conditions with a high risk of subsequent comorbidity. Numerous karyotypes are associated with TS, including 45X and 45X/46XX, but there is limited data regarding the relationship between karyotype and phenotype in TS. In this retrospective cohort, we aim to characterize the prevalence of congenital malformations and acquired diseases by karyotype. This information will allow clinicians to provide individualized counseling to women with TS based on their specific risks.

DESIGN: Retrospective cohort of patients presenting to the University of North Carolina Turner Syndrome Clinic from April 2014 to January 2020.

MATERIALS AND METHODS: Patients were categorized into four exposure groups by karyotype: 45X, 45X/46 XX, miscellaneous karyotypes with no Y chromosome material, and miscellaneous karyotypes with Y chromosome material. Clinical information and laboratory results, including prevalence of structural cardiac anomalies, structural renal anomalies, autoimmune thyroid disease, hypertension, dyslipidemia, celiac disease, renal dysfunction, growth failure, hearing loss, and being overweight or obese were collected from chart abstraction. Descriptive statistics were performed using SAS and prevalence of each outcome was reported. Fisher's exact test was used to compare the prevalence of each outcome between the groups.

RESULTS: A total of 105 patients were identified and categorized into four groups: group 1 (45X, n=38), group 2 (45X/46 XX, n=13), group 3 (miscellaneous with no Y chromosome material, n=43), and group 4 (miscellaneous with Y chromosome material, n=11). The median age at last visit was 13 (range 1-24). Structural renal and cardiac anomalies were most prevalent in the 45X group, with a prevalence 51.4% (P<0.01) and 66.7% (P=0.02), respectively. Growth failure was least common in patients with 45X/46XX (46.2%), compared to those with 45X (79%), miscellaneous karyotype with Y chromosome material (100%), and miscellaneous karyotype without Y chromosome material (79.1%; P<0.05). The prevalence of dyslipidemia, being overweight or obese, hypertension, liver dysfunction, and hearing loss was similar in all groups. No patients in our cohort developed glucose intolerance (median age 15), and only two patients developed renal dysfunction (median age 14). Similarly, very few patients in the group developed autoimmune thyroid disease (17/102) and celiac disease (6/96).

CONCLUSIONS: Medical comorbidities vary depending on karyotype and mosaicism. The 45X karyotype was associated with a more severe structural phenotype, with a higher prevalence of congenital anomalies and growth failure. Notably, there was no difference in the metabolic phenotype between the karyotype groups in our cohort. Providers should be aware of these individual differences when caring for women with TS.

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PREDICTIVE FACTORS FOR FERTILITY PRESERVATION IN PEDIATRIC PATIENTS WITH PLANNED GONADOTOXIC TREATMENT. Glory E. Mgboji, BS,[1] Christina N. Mitchell, MD,[2] Mindy S. Christianson, MD[2] [1]Johns Hopkins University School of Medicine, Baltimore, MD; [2]Johns Hopkins Medical Institutions, Lutherville, MD.

OBJECTIVE: To characterize a female pediatric patient population seen for fertility preservation consultation at an academic center and to identify demographic and clinical factors associated with receiving fertility preservation treatment (FPT).

DESIGN: Retrospective chart analysis.

MATERIALS AND METHODS: We performed an analysis of female pediatric patients seen for fertility preservation consultation at an academic fertility center between 2005-2019. Fisher exact tests were used to compare fertility preservation status based on demographic and clinical factors. Logistic regression models were constructed to calculate odds ratios with 95% confidence intervals describing factors associated with fertility preservation.

RESULTS: In the study period, 106 females ages 3-21 were seen for consultation with a mean age of 16.6 years. Diagnoses included: hematologic malignancies (41.5%), gynecologic malignancies (9.4%), non-malignant hematologic disease (14.2%), other malignancies (31.1%), and non-malignant conditions (3.8%). Of all patients, 64.2% pursued fertility preservation with treatments including oocyte cryopreservation (35.8%) and ovarian tissue cryopreservation (23.6%). Patients who underwent gonadotoxic therapy prior to consultation had a lower odds of receiving FPT (OR= 0.24, 95% CI 0.10-0.55). Age, race, diagnosis, time elapsed from diagnosis, and median household income were not significantly associated with odds of FPT.

CONCLUSIONS: Pediatric patients who received prior chemotherapy had a lower odds of pursuing FPT. This finding emphasizes the need for early intervention in patients facing gonadotoxic therapies. Additional studies

are needed to further investigate the implications of these data and to explore the barriers to early interventions for FPT in these patients.

PRACTICE MANAGEMENT

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COST-EFFECTIVENESS ANALYSIS OF THE ORIGINATOR RECOMBINANT HUMAN FOLLICLE-STIMULATING HORMONE (R-HFSH) AND URINARY HIGHLY PURIFIED MENOPAUSAL GONADOTROPIN (HMG) BASED ON DATA FROM A LARGE GERMAN REGISTRY. Klaus F. Bühler, MD,[1] Robert Fischer, MD,[2] Edel Falla, MSc,[3] Jeroen Luyten, PhD,[4] Claudia Roeder, PhD,[5] Boyang Bian, PhD,[6] Wilma Bilger, PhD,[7] Monica Lispi, MSc,[8] Thomas M. D'Hooghe, MD, PhD[9] [1]Department of Gynaecology, Jena-University Hospital-Friedrich Schiller University, Jena, Germany; [2]MVZ Fertility Center Hamburg GmbH, Hamburg, Germany; [3]IQVIA, London, United Kingdom; [4]KU Leuven (University of Leuven), Leuven, Belgium; [5]Pharma Value Consulting, Oberwil, Switzerland; [6]EMD Serono, Inc, Billerica, MA; [7]Merck Serono GmbH, Darmstadt, Germany; [8]Merck KGaA, Darmstadt, Germany; [9]Merck Healthcare KGaA, Darmstadt, Germany.

OBJECTIVE: Recombinant human follicle-stimulating hormone (r-hFSH) and urinary highly purified menopausal gonadotropin (hMG) are two treatment options in assisted reproductive technology (ART). We used outcomes from the real-world setting in Germany (RecDate) to compare the costs per live birth for r-hFSH and hMG.

DESIGN: Cost-effectiveness analysis.

MATERIALS AND METHODS: All women in the RecDate registry undergoing ART for the first time, receiving either r-hFSH or hMG between 2007 and 2012, were included. Total dose of FSH used, pregnancy and live birth rates (adjusted for age, body mass index, infertility type, gonadotropin-releasing hormone [GnRH] protocol, year and in-vitro fertilisation centre using propensity score weighting) were extracted. Costs for oocyte retrieval, embryo transfer, pregnancy and live birth were obtained from publicly available German sources. These clinical outcomes and costs were integrated in a decision-tree model developed to consider up to three treatment cycles (each comprising one fresh and related freeze-thaw transfers). The model was used to compare cumulative live birth rates and the cost per live birth for the two treatments.

RESULTS: Effectiveness data were identified from 48,437 cycles in 28,641 women across 71 centres. r-hFSH was associated with higher cumulative live birth rates per patient compared with hMG after the first treatment cycle and after up to three consecutive treatment cycles (Table). The lower total costs for the first cycle and for up to two or three consecutive cycles in the r-hFSH group were driven by lower medication costs and better reproductive outcomes, translating into a lower cost per live birth compared with hMG for all cycles (Table).

CONCLUSIONS: In a large German registry (RecDate), r-hFSH was associated with higher cumulative live birth rates and lower total costs per patient compared with hMG. The lower cost per live birth for r-hFSH indicated that r-hFSH may offer better economic efficiency than hMG.

SUPPORT: **Funding**: Merck KGaA, Darmstadt, Germany

O-164 2:05 PM Monday, October 19, 2020

SOCIAL MEDIA IN THE TIME OF COVID-19: AN EVALUATION OF SOCIETY FOR ASSISTED REPRODUCTIVE TECHNOLOGY (SART) MEMBER CLINICS. Miriam A. Andrusier, M.P.H.,[1] Seth J. Barishansky, M.D., M.S.,[2] Elizabeth A. Dilday, M.D.,[3] Angela K. Lawson, Ph.D.,[4] Luis R. Hoyos, M.D.[5] [1]SUNY Downstate Health Sciences University, Brooklyn, NY; [2]The George Washington University School of Medicine and Health Sciences, Washington, DC; [3]Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, University of California, Los Angeles, Los Angeles, CA; [4]Northwestern University Feinberg School of Medicine, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Chicago, IL; [5]UCLA, Los Angeles, CA.

OBJECTIVE: To evaluate the available COVID-19 content in regard to fertility care on the social media (SM) platforms from Society for Assisted Reproductive Technology (SART) member clinics.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: From March 17-30/2020, following the release of the first American Society for Reproductive Medicine (ASRM) COVID-19 recommendations, SART member clinics' SM platforms including Facebook and Twitter were examined. The presence of information on COVID-19, its pregnancy implications, acknowledgement of and compliance with ASRM recommendations, mention of Centers for Disease Control and Prevention (CDC) risk mitigation strategies and local health department guidelines, as well as advertisement for telehealth and availability of mental health resources were queried. Websites were categorized by practice size ($<$500 vs. $\geq$500 cycles/year), type (academic vs. private) and degree of statewide COVID-19 burden based on CDC surveillance data (low: 0-1000; high: $\geq$1000 diagnosed cases). Group differences were evaluated using χ^2.

RESULTS: SM accounts were available from 84% (315/375) of SART member clinics and were more common among private compared to academic clinics [96% (274/286) vs. 46% (41/89), respectively, P$<$0.05]. No difference was found in the presence of COVID-19 posts when comparing private and academic clinics [80% (220/274) vs. 78% (32/41), respectively, P=0.68]. Private clinics were more likely to post individualized recommendations rather than ASRM recommendations, and to advertise the use of telehealth [34% (93/274) vs. 7% (3/41) and 64% (174/274) vs. 46% (19/41), respectively, P$<$0.05, all values]. There was no difference in the advertisement of mental health resources on SM [31% (86/274) vs. 44% (18/41), respectively, P=0.15]. Larger compared to smaller clinics were more likely to provide information on COVID-19, its pregnancy implications, and to acknowledge ASRM recommendations, CDC risk mitigation strategies and local health department guidelines on SM [86% (112/130) vs. 76% (140/185); 49% (64/130) vs. 34% (62/185); 49% (64/130) vs. 34% (62/185); 59% (77/130) vs. 42% (77/185) and 33% (43/130) vs. 22% (40/185), respectively, P$<$0.05, all values]. Larger clinics were also more likely to advertise telehealth and mental health resources on SM [71% (92/130) vs. 55% (101/

TABLE. Cumulative live birth rates and costs per complete treatment cycles 1–3 (fresh and frozen embryo transfers) with r-hFSH and hMG (2007–2012)

	Treatment cycle 1 (n=28,641)			Treatment cycle 1 and 2 (n=7,296)			Treatment cycle 1, 2 and 3 (n=1,783)		
	r-hFSH	hMG	Difference	r-hFSH	hMG	Difference	r-hFSH	hMG	Difference
Live birth (%)	24.9	22.4	2.5	41.7	37.7	4.0	51.5	47.0	4.5
Medication costs (€)*	972	1,072	-99	1,703	1,904	-201	2,270	2,571	-302
Total costs (€)†	9,547	9,579	−32	14,790	15,017	−226	17,324	17,757	−433
Cost per live birth (€)	38,341	42,763		35,449	39,845		33,630	37,753	

* Gonal-f and Menogon HP/Menopur, based on the total dose (IU) and duration of controlled ovarian stimulation. † r-hFSH/hMG acquisition, IVF preparation, oocyte retrieval, embryo transfer, pregnancy and live birth costs.

185) and 42% (54/130) vs. 27% (50/185), respectively, P<0.05, all values]. Clinics in high COVID-19 burden states were less likely to follow ASRM recommendations compared to clinics in low burden states [36% (56/154) vs. 50% (80/161), respectively, P<0.05].

CONCLUSIONS: Use of SM accounts for dissemination of COVID-19 related information was common among SART member clinics with SM presence. However, academic clinics were less likely to have any, and when they did, less likely to offer telehealth, possibly hindering care for their patients. Conversely, larger clinics were more likely to provide pertinent information and advertise telehealth and mental health resources. Private, smaller and high COVID-19 burden clinics were less likely to report compliance with ASRM recommendations.

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TRAITS OF PATIENTS SEEN VIA TELEMEDICINE VERSUS IN-PERSON FOR NEW PATIENT VISITS IN A FERTILITY PRACTICE. Vinita M. Alexander, MD,[1] Allison Schelble, MD,[1] Kenan Omurtag, MD[2] [1]Washington University in St. Louis, St. Louis, MO; [2]Washington University School of Medicine, St. Louis, MO.

OBJECTIVE: Integration of telemedicine (TM) into reproductive endocrinology and infertility (REI) is quickly occurring due to changes in the practice environment and recently, COVID19. However, no US studies have investigated telemedicine's impact on REI practices. This study aimed to evaluate differences in demographics, time to treatment initiation, clinical outcomes, and dropout rates between patients using telemedicine relative to in-person (IP) visits.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All new patients seen via TM (between June 2017 to February 2020) at an academic practice were compared with control new IP visits (seen in 2019). The following were evaluated for each new patient encounter by visit type (TM or IP): demographics, cancellation, distance to clinic, infertility diagnosis, duration of infertility, time to treatment initiation, number of clinic-contacts (i.e. number of e-messages or phone calls from patient) prior to treatment start, and dropout rate. We performed t-test analysis by group for continuous independent variables and Chi-square analyses by group for categorical independent variables. Binary logistic regression analysis was performed to estimate the odds of initiating treatment in the TM group.

RESULTS: Seventy-one patients were identified in the TM group, and 71 followed in the IP group. The average age of the IP and TM groups was similar, at 33.5 ± 5.0 and 33.2 ± 5.2, respectively (p=0.723). There were no differences between groups in the following: BMI (p=0.723), area deprivation index (p=0.235), and treatment recommended (e.g. ovulation induction, IVF, surgery, etc.) (p=0.475). There were no differences between the TM and IP groups in: treatment dropout rates (p=0.075), cancellation rates (p=0.379), time to treatment initiation (mean 74.82 days in TM group; 77.5 days in IP group; p = 0.315), or number of times the patient contacted the clinic prior to treatment start (p=0.153). Of those who became pregnant, time to positive pregnancy test was not significantly different between the TM (n=11, mean 176.4 days) and IP groups (n=19, mean 226.45 days) (p=0.368). Compared to IP patients, TM patients were significantly more likely to live further away (mean 223.6 miles vs 69.28 miles, p = 0.006) and have a longer duration of infertility (mean 41.9 months vs 19.49 months, p = 0.006). The lengths of TM appointments were significantly shorter than IP visits (mean 56.3 ± 9.1 minutes vs 59.3 ± 4.6 minutes, p < 0.001) and much less likely to contain documentation of height or weight (p=0.001). In the TM group, age and distance from clinic were not significantly associated with likelihood of dropping out of treatment (p=0.467).

CONCLUSIONS: Telemedicine appears to be of particular interest to patients who live further from clinics and have longer durations of infertility, and it could help reduce visit times. Patients seen in person and via telemedicine are equally likely to pursue treatment. Telemedicine consultation for new-patient visits is feasible in REI practice and is especially useful in areas with limited access to fertility specialists and beyond in a post-COVID landscape.

O-166 2:35 PM Monday, October 19, 2020

MAKING IT (NET)WORK: A SOCIAL NETWORK ANALYSIS OF "FERTILITY" ON TWITTER BEFORE AND DURING THE COVID-19 PANDEMIC. Meghan Brooke Smith, MD,[1] Jennifer K. Blakemore, MD,[2] Jacqueline Ho, MD MS,[1] James A. Grifo, MD, PhD[2] [1]University of Southern California, Los Angeles, CA; [2]NYU Langone Prelude Fertility Center, New York, NY.

OBJECTIVE: To characterize activity, text sentiment, and online community characteristics regarding "fertility" on Twitter (TW) before and during the COVID-19 pandemic using social network analysis (SNA).

DESIGN: Cross sectional study.

MATERIALS AND METHODS: SNA uses graph theory to understand structure, flow, content, and relationships of networks among individuals. SNA was performed using NodeXL, a software platform that performs social network and content analysis. The search term "fertility" on TW was investigated during the weeks of February 20-27th, 2020 (Pre-COVID) and April 29th-May 6th, 2020 (during-COVID). User demographics, tweet content, and characteristics of the network were collected and analyzed during these time periods. These included: # users (vertices); edges (connections, defined as unique and total); self-loops (tweet without connection to another user); connected components (groups of users communicating back and forth frequently); maximum vertices in a connected component (largest group size); maximum and average geodesic distance (number of tweets to connect two users in the network); graph density; positive and negative sentiment tweets; top 5 hashtags; and top 5 word pairs. Statistical analyses included a z-ratio for comparison of proportions, with p<0.05 considered significant.

RESULTS: There were 1426 unique users and 401 groups in the pre-COVID data compared to 1492 unique users and 453 groups in the during –COVID data. There was no difference in the number of total connections [96.8% (1381/1426) vs 96.0% (1433/1492), p=0.25] or self-loops [20.0% (286/1426) vs 22.1% (329/1492), p=0.19]before and during the COVID-19 pandemic. The percentage of unique connections per user decreased during COVID-19 [91.6% (1381/1508) pre-COVID vs 83.3% (1433/1720) during COVID, p<0.0002]. The average and maximum distance between users in the community increased during COVID (maximum: 5 pre-COVID, 8 during-COVID; average 1.95 pre-COVID, 2.43 during-COVID). The percentage of positive sentiments per total number of tweets increased during COVID [58.1% pre-COVID (773/1331) vs 64.3% (1198/1863) during-COVID, p<0.0004]. The overall character of the TW fertility social network remained constant at both time points with a broadcast "spoke and out wheel" shape. The top 5 hashtags changed during COVID to include COVID19. The top word pairs changed from "family, hereditary; parents, children" to "fertility, treatment; healthcare, decisions."

CONCLUSIONS: Despite the challenge to the fertility community amidst COVID19, overall TW sentiment regarding fertility was more positive during than before the pandemic. Top hashtags/word pairs changed to reflect the emergence of COVID and the unique healthcare decision making challenges faced. While the character, # of users, and total connections remained constant, unique connections and distance between users changed to reflect more self-broadcasting and less tight connections. Given no change in network structure where time at home could have led to increased social media (SM) use, further study is needed to leverage SM in these situations.

References: None

SUPPORT: None

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PATIENT PREFERENCES FOR FOLLOW-UP OF GENDER AFFIRMING HORMONE THERAPY. Erin Inman, MD,[1] Daria Stelmak, BS,[1] Emily K. Kobernik, MPH, MS,[1] Juan J. Andino, MD, MBA,[2] Daphna Stroumsa, MD, MPH, MSc,[1] Molly B. Moravek, MD, MPH,[1] John F. Randolph, Jr., MD[1] [1]University of Michigan, Ann Arbor, MI; [2]Michigan Medicine, Ann Arbor, MI.

OBJECTIVE: Approximately 1.4 million people in USA identify as transgender and a large portion (78%) of these will seek out gender-affirming hormonal therapy (HT). Given ongoing discussions about who should provide

HT, our objective was to characterize patient preferences about which providers they seek for HT care and how follow-up can be provided.

DESIGN: Prospective cross-sectional survey.

MATERIALS AND METHODS: Between May to October 2019 a survey was administered at a Midwest tertiary medical center's outpatient clinics prior to implementation of telemedicine. Adult patients 18 years or older initiating or continuing gender affirming hormone therapy were included. The 38-item survey included questions on demographics, barriers to care, and preference for HT follow-up care. All physicians were reproductive endocrinology and infertility physicians or general obstetrician-gynecologists specialized in gender-affirming care. Interest for telemedicine was measured using a likert scale (1, strongly not interested to 5, strongly interested). Bivariate analysis was performed to compare demographic characteristics and survey responses across patient interest in telemedicine. Multivariable logistic regression was used to identify patient factors independently associated with interest in telemedicine.

RESULTS: Among 111 patients, 70.3% (n = 78) self-identified as transgender, 5.4% (n = 6) as gender queer, non-binary, or gender-nonconforming, 17.1% (n =19) as female, and 7.2% (n = 8) as male. Regarding follow-up for HT care, 63.1% (n=70) preferred an in-person visit with a specialist followed by 21.6% (n = 24) video visit with their specialist. Only 15.3% (n = 17) of patients preferred follow-up with a primary care provider (PCP). 29% (n=31) reported that they would never feel comfortable transitioning care, and the most common concern patients had in transitioning care to their PCP was the expertise of the provider (64.0%, n = 71).

Notably, 52.3% (n = 58) of patients were interested in a video visit (4 or 5 on a Likert scale). Factors associated with interest in telemedicine included identifying as a transgender man (OR 3.94, 95% CI [1.24-12.53]), minority race/ethnicity (OR 6.71 [1.79- 25.17]), no need to travel (OR 3.34, [1.14-9.85]), no concerns about video visits (OR 14.66, [4.34-49.56]), and concern about their PCP offering a broad range of gender services (OR 8.63, [2.41-29.67]). Age, income, education, and insurance providers were not significantly different among patients interested in telemedicine and those who were not interested.

41% of patients (n=46) had no concerns regarding the use of video visits for follow-up. The most common concern chosen by patients was a preference for in-person communication (50.5%, n=56).

CONCLUSIONS: Patients presenting for HT follow-up prefer continued care with a specialist as opposed to a PCP. Prior to implementation, a majority of patients were interested in telemedicine. As such, video visits are a feasible way for specialists to offer continued management of gender affirming HT to their patients.

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SURVEY OF CURRENT PRACTICE AND SATISFACTION OF SREI MEMBERS: AN SREI COMMITTEE REPORT. Laurel Stadtmauer, MD, PhD,[1] Paula Amato, MD,[2] Seifeldin Sadek, MD,[1] Elizabeth A. McGee, MD,[3] Brooke Rossi, MD,[4] Bradley S. Hurst, M.D.[5] [1]Jones Institute, Norfolk, VA; [2]Oregon Health & Science University, Portland, OR; [3]University of Vermont Larner College of Medicine, Burlington, VT; [4]Ohio State University Medical College, Columbus, OH; [5]Carolinas Medical Center Atrium Health, Charlotte, NC.

OBJECTIVE: To identify the current practice and satisfaction of reproductive endocrinologists in the U.S.

DESIGN: Cross-sectional survey.

MATERIALS AND METHODS: Cross-sectional survey including 37 questions assessing practice patterns/metrics, compensation, and physician satisfaction. Survey invitations were emailed 3 times in the 4th quarter of 2019 to 982 full members of Society for Reproductive Endocrinology and infertility (SREI). This survey was exempt from IRB approval as it was voluntary and anonymous. Results were compared to a similar SREI survey sent to SREI members in 2014 published by Barnhart et al. in 2016. Continuous data were expressed as mean ±SD.

RESULTS: 314 individuals responded (32%): 48% women and 51% men, a 10% increase in women compared to 2014. 78% were Caucasian, median age range was 51-60 years, and the median years of practice 18 years.

Respondents worked a mean of 51 hours per week. 43% work in academia, 40% in private groups, 12% corporate or hospital owned practice, and 5% solo practice, which represents a 6% increase in the proportion of corporate practices from the prior survey; 29% have left academics a to join a private practice, while only 8% have left private practice for an academic position.

The mean practice size was 7.6 ±5.2, increased from 5.5 in 2014. 66% expect to add more physicians within five years. A mean of 617 ±914 fresh IVF cycles were performed annually, compared to 470 previously. Surgery volume varies widely, with the mean number of major and minor cases at 19.9±41.7, and 21.1 ±47.9, respectively, per practice.

The mean reported compensation was $493,118.18 ±93813.60 up from $400,512 in 2014 with a median salary of $400,000. 39% are salaried, for 41% compensation is revenue-based and the remainder receive compensation based on a combination of factors. 66% feel that their compensation is fair, and 13% are considering leaving their position due to compensation. 31% were equity partners (down from 44%), and 27% report that their practice offers partnership in a mean of 3.1 years.

35% felt very positive about the current state of the specialty of REI, and 42% felt somewhat positive. 78% had a positive professional morale, decreased from 85% in 2014. 68% report that patient interaction is the most satisfying part of their job, and the least satisfactory is work schedule for 48%. 91% would again choose REI as a career.

CONCLUSIONS: Based on the 2019 SREI membership survey, the morale in our sub-specialty remains high. It is a predominately middle-aged Caucasian specialty, but the number of female physicians has increased. Average compensation has increased compared to 2014, and the number of IVF cycles performed per group has increased. The number of REI's in academic practice remained stable compared to 2014.

Acknowledgment: The authors would like to thank the SREI Board of Directors and Members for supporting this report.

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SUPPORT: None

PROCEDURES AND TECHNIQUES

O-169 1:50 PM Monday, October 19, 2020

SAFETY EVALUATION OF A NOVEL PROGESTERONE VAGINAL RING (PVR) IN LUTEAL PHASE SUPPORT: SARA TRIAL RESULTS. Laurel Stadtmauer, MD, PhD,[1] Vicki L. Schnell, MD,[2] John K. Park, MD,[3] Cristin C. Slater, MD,[4] Eric D. Foster, PhD,[5] Sarah A. Grover, MBBS,[5] Patrick W. Heiser, PhD[5] [1]Jones Institute, Norfolk, VA; [2]Center of Reproductive Medicine, Houston, TX; [3]Carolina Conceptions, Raleigh, NC; [4]Idaho Center for Reproductive Medicine, Boise, ID; [5]Ferring Pharmaceuticals, Inc, Parsippany, NJ.

OBJECTIVE: To assess the safety and tolerability of the PVR after implementation of manufacturing enhancements via comparison to the similarly designed pivotal phase 3 trial which established the safety and efficacy of once-weekly PVR relative to daily 8% progesterone vaginal gel (Stadtmauer 2013).

DESIGN: Prospective, open-label, single-arm, multi-center trial.

MATERIALS AND METHODS: Women aged 18-34 years old with body mass index $\leq$38 kg/m^2 and diagnosed with tubal, idiopathic, male factor, ovulatory dysfunction, or endometriosis-linked infertility underwent ovarian stimulation with highly purified human menotropin (HP-hMG) at a fixed dose of 225 IU/day, followed by adjustments according to individual response in a standardized long agonist protocol. Weekly administration of the PVR started the day after oocyte retrieval (OR) followed by fresh blastocyst transfer according to ASRM guidelines (2017) and continued for up to 10 weeks. The primary endpoint was the cumulative rate of any spontaneous abortion, defined as two positive β-hCG tests but followed by observation of any empty intrauterine gestational sac or one without a fetal heartbeat or absence of viable fetuses up to 12 weeks after OR.

RESULTS: Across 14 U.S. trial sites, 254 evaluable subjects were treated with PVR. Mean subject age was 30.8 years, BMI 26.5 kg/m^2, AMH 2.8 ng/mL, and FSH 7.0 mIU/mL. Adverse events (AEs) occurring in $\geq$5% of the population included nausea (8.7%) and headache (5.1%). Incidence of predefined vaginal/cervical AEs of special interest was low (2.0%), comprised of 6 events of vaginal bleeding, 3 events of vulvovaginal pain, and 1 event of cervix disorder. Fresh embryo transfer after IVF/ICSI was performed in 243 (95.7%) of the 254 exposed subjects. The mean number of oocytes retrieved/subject was 11.3, resulting in 4.3 day 5 blastocysts and 3.0 good quality day 5 blastocysts. Biochemical abortion rates were 10.3%. The

primary objective was met, with a cumulative spontaneous abortion rate of 7.4% with upper bound of the 95% confidence interval (CI; 4.4%, 11.5%) below the predefined threshold of 15.0% set based upon the observed 10.0% rate (CI 7.6%, 12.8%) in the pivotal trial (Stadtmauer 2013). Clinical pregnancy rates were 43.2% at 10 weeks post OR.

CONCLUSIONS: This trial established a safety bridge between PVR produced via enhanced manufacturing processes and the legacy PVR based upon a rate of spontaneous abortion comparable to that observed in the pivotal phase 3 trial. Weekly administration of the PVR was well-tolerated with good pregnancy outcomes associated with its use in conjunction with HP-hMG stimulation. Based upon demonstrated safety and efficacy coupled with more convenient dosing than existing therapeutics, PVR offers an important option for luteal phase supplementation.

References: Stadtmauer, L., Silverberg, K.M., Ginsburg, E.S., Weiss, H., Howard, B. Progesterone vaginal ring versus vaginal gel for luteal support with in vitro fertilization: a randomized comparative study. Fertil Steril. 2013;99:1543-1549.

SUPPORT: Ferring Pharmaceuticals, Inc. Parsippany, NJ

O-170 2:05 PM Monday, October 19, 2020

SECOND GENERATION ARTIFICIAL INTELLIGENCE TECHNOLOGY FOR PREIMPLANTATION GENETIC TESTING (PGT) IMPROVES PREGNANCY OUTCOMES IN SINGLE THAWED EUPLOID EMBRYO TRANSFER CYCLES (STEET).

Julia Buldo-Licciardi, M.D.,[1] Mike Large, Ph.D.,[2] David H. McCulloh, Ph.D.,[3] Caroline McCaffrey, PhD,[4] James A. Grifo, MD, PhD[5] [1]Hackensack University Medical Center, Hackensack, NJ; [2]CooperSurgical, Houston, TX; [3]NYU Langone Fertility Center, New York, NY; [4]NYU Langone School of Medicine, New York, NY; [5]NYU Langone Prelude Fertility Center, New York, NY.

OBJECTIVE: To evaluate whether the use of artificial intelligence technology in PGT (PGTai) improves STEET pregnancy outcomes.

DESIGN: Retrospective cohort study in single university-based fertility center.

MATERIALS AND METHODS: Three next generation sequencing (NGS) platforms were compared in analyzing trophectoderm biopsies: standard NGS, NGS with first generation artificial intelligence (PGTai 1.0^{SM} Technology Platform) and NGS with second generation artificial intelligence (PGTai 2.0^{SM} Technology Platform). PGTai 2.0 utilizes proprietary low-pass SNP calling mechanisms to confirm or reject non-diploid copy number regions of interest. Outcomes included rates of implantation, clinical pregnancy, biochemical pregnancy, spontaneous abortion and ongoing pregnancy and/or live birth (OP/LBR). OP/LBR was defined as pregnancies greater than 20 weeks over total number of STEETs. Significant differences were calculated using chi-squared test.

RESULTS: The OP/LBR was significantly higher in the PGTai 2.0 group compared to standard NGS (128/182 (70.3%) vs. 328/529 (62.0%)). PGTai 2.0 vs. NGS showed increased implantation rates (151/182 (82.9%) vs. 415/529 (78.4%)) and clinical pregnancy rates (141/182 (77.4%) vs. 379/529 (71.6%)), but the differences did not reach significance. PGTai 2.0 vs. NGS decreased biochemical pregnancy rates (7/151 (4.63%) vs. 36/416 (8.6%)) and spontaneous abortion rates (16/141 (11.3%) vs. 47/329 (12.4%)), but these differences did not reach significance. Outcomes in the PGTai 1.0 group were similar to standard NGS.

CONCLUSIONS: The goal of PGT is to increase live birth rates per retrieval and PGT using second-generation artificial intelligence technology with NGS significantly improves pregnancy outcomes over standard NGS and PGTai 1.0. Larger scale analysis will determine if this next generation of PGTai provides improved diagnostic precision by decreasing the percentage of false positive results, which may narrow the number of embryos diagnosed as mosaic.

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O-171 2:20 PM Monday, October 19, 2020

USE OF FROZEN DONOR OOCYTES ARE ASSOCIATED WITH A DECREASED LIVEBIRTH RATE COMPARED TO FRESH DONOR OOCYTES: A SART DATABASE ANALYSIS.

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OBJECTIVE: To evaluate the pregnancy and perinatal outcomes of embryos derived from fresh and frozen donor oocytes.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The SART database was used to identify all donor oocyte cycles that resulted in a fresh embryo transfer during 2014 and 2015. Gestational carrier cycles were excluded. Generalized linear regression models were used to compare pregnancy and perinatal outcomes of pregnancies after fresh embryo transfer of embryos that were derived from fresh compared to frozen donor oocytes. Models were adjusted for the following factors: maternal age, BMI, current smoking status, parity, infertility diagnosis, prior IVF attempt, ICSI, assisted hatching, number of embryos transferred, multiple gestation and fetal heart reduction. Live birth rate was the primary outcome. Secondary outcomes include miscarriage rate and birthweight.

RESULTS: There were 14,972 embryo transfer cycles analyzed; 11,482 cycles (76.7%) utilized embryos derived from fresh and 3,490 cycles (23.3%) utilized embryos derived from frozen donor oocytes. The mean ages of oocyte donors and intended parent recipients were 26.3 years (±SD 3.6) and 41.4 years (±SD 5.4) respectively. On initial comparison of embryos derived from fresh and frozen donor oocytes, the live birth rate was 41% and 42% respectively. However, once the data was adjusted for the above factors, a significant decrease in live birth was observed with embryos derived from frozen donor oocytes (aRR 0.85, 95% CI 0.8-0.89). A significant increase in biochemical pregnancy loss was noted with embryos derived from frozen donor oocytes (5.6 [fresh] vs 8.6% [frozen], aRR 1.29, 95%CI 1.08-1.53). There was no difference in the proportion of clinical miscarriage between the two groups (12.6 vs 17.4%, aRR 1.06, 95%CI 0.95-1.19). Additionally, there was no difference in low birthweight (32.9 [fresh] vs 29.5% [frozen], aRR 0.98, 95%CI 0.89-1.07) or large for gestational age infants (4.6 vs 6.2%, aRR 1.27, 95%CI 0.96-1.69) between the two groups. This remained true when singletons were analyzed separately for both low birthweight (11.8 vs 12.6%, aRR 1.17, 95%CI 0.93-1.46) and large for gestational age (7.8 vs 9.4%, aRR 1.25, 95%CI 0.94-1.65).

CONCLUSIONS: The use of frozen donor oocytes has become an increasingly popular option in recent years for patients electing to use donor egg. This study, reassuringly, does not suggest a difference in birthweight between fresh and frozen donor oocytes. However, these results do indicate an increased risk for biochemical pregnancy loss and a decrease in live birth rate with frozen donor oocytes. This finding deserves further research in order to optimize the use of frozen donor oocytes in clinical practice.

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FIRST REGISTERED PILOT TRIAL TO VALIDATE THE SAFETY AND EFFECTIVENESS OF MATERNAL SPINDLE TRANSFER TO OVERCOME INFERTILITY ASSOCIATED WITH POOR OOCYTE QUALITY.

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OBJECTIVE: Poor quality oocytes frequently fail to fertilise or produce embryos that arrest during their first days of culture *in vitro*. Oocyte cytoplasmic dysfunctions (including, but not limited to mitochondria) have

been indicated as a major cause of this problem. Since maternal spindle transfer (MST) allows replacement of the entire cytoplasm of an affected oocyte, it holds promise for the enhancement of embryonic development. Recent studies in the mouse and in human oocytes donated for research have confirmed the technical feasibility of MST and provided reassurance concerning safety. Here we present results from the first registered pilot trial aiming to reveal whether MST has potential to overcome infertility caused by poor oocyte quality.

DESIGN: This pilot trial (ISRCTN 11455145) was restricted to 25 patients, selected based on their multiple previous failed IVF attempts, in each case associated with massive embryo development arrest. Female age over 40y/o and severe male factor were exclusion criteria. Procedures were authorized by the National Authority of Assisted Reproduction (437/23.9.2016) and approved by the Hospital's IRB. Informed consent was obtained from patients and donors to conduct all procedures and follow-up the children born.

MATERIALS AND METHODS: The meiotic spindle from patient's oocytes was isolated in a minimal cytoplasmic volume and transferred to a previously enucleated donor oocyte. MST oocytes were inseminated by ICSI and cultured up to 6 days in a time-lapse incubator. Good morphology blastocysts underwent biopsy, aneuploidy testing and analysis of mitochondrial DNA (*mtDNA*) carryover levels. SNPs analysis and DNA fingerprints were used to confirm the origin of the nuclear genome and mtDNA in biopsied samples, amniotic fluid and somatic tissues of resulting children.

RESULTS: A total of 25 MST cycles were performed in patients with an average age of 37.1 y/o and a mean number of previous failed IVF attempts of 5.7 (min 3 and max 11). The mean number of MII oocytes used for MST per patient was 4.4. MST was applied successfully in 113 of 123 oocytes (91.9%) used. Normal fertilization was confirmed in 76.1% (86/113) of injected oocytes and 52 of these developed into good quality blastocysts (60.5%). Genetic screening revealed 50% (26/52) of embryo biopsy specimens to be euploid and mtDNA carryover levels <1%. In 16/25 cases, at least one euploid blastocyst of good morphology was obtained. Thus far, single blastocyst transfers were performed in 9 patients, resulting in 6 clinical pregnancies (66.7%). Two patients have delivered a healthy child and 3 more pregnancies are ongoing. Genetic analyses of the biopsied cells, amniotic fluid and samples collected after birth (blood, urine, saliva, cord blood, placenta) confirmed the parentage of the children and the origin of the donated mtDNA. Follow-up studies are being performed on the children born.

CONCLUSIONS: Given the difficult reproductive history of the patients, results are encouraging. However, more carefully controlled pilot trials and follow-up studies are needed to provide more insights into the efficacy of MST to overcome infertility.

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ONLY SEGMENTAL OR MOSAIC ANEUPLOID EMBRYOS AVAILABLE FOR TRANSFER: A RARE PHENOMENON IN PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) CYCLES USING TARGETED NEXT GENERATION SEQUENCING (NGS).

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OBJECTIVE: Use of next generation sequencing (NGS) for preimplantation genetic testing for aneuploidy (PGT-A) improves resolution for detecting segmental aneuploidy (SEG) and mosaicism (MOS). However, these additional categories create difficult management decisions when the only available embryo for transfer falls into one of these categories. With this in mind, this study sought to investigate: 1) how often the only available embryo carries a SEG or MOS diagnosis, and 2) whether this risk is modified by age and the number of embryos tested in a cohort.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: All cycles at a single center utilizing targeted NGS-based PGT-A between July 2016 and December 2019 were included in the analysis. Each embryo's PGT-A result was placed into 1 of 4 categories: 1) aneuploid (at least 1 whole chromosome aneuploidy present), 2) SEG (no whole chromosome aneuploidy, but deletion or duplication present), 3) MOS (no whole chromosome aneuploidy or segmental present, but mosaic range diagnosis present), and 4) euploid (no abnormalities). Only euploid, SEG, and MOS embryos were considered eligible for transfer. The percentage (%) of cycles in which the only eligible embryo for transfer carried a SEG or MOS diagnosis was then calculated for the entire study population, according to female age, and according to the number of embryos in a given cohort. The relationship between female age and each diagnostic category was also evaluated using logistic regression.

RESULTS: A total of 7,220 retrieval cohorts resulting in 34,717 embryos were evaluated. The overall prevalence of aneuploidy, SEG, and MOS per embryo were 29.4%, 7.3%, and 3.3% respectively. Female age was strongly associated with the presence of whole chromosome aneuploidy ($p<0.0001$). The older the female subjects' age the lower were the SEG or MOS results rate ($p<0.001$). The number of cycles in which the only available embryo contained a SEG or MOS was 2.5 and 1.2 percent respectively across the entire cohort. The risk was similar across all ages and never exceeded 7.2 and 2.5 percent respectively in any age year. The percent of SEG only or MOS only cycles decreased as number of embryos in the cohort increased and was <1% when at least 5 embryos were available for testing.

CONCLUSIONS: Few PGT-A cycles analyzed by NGS result in a scenario where the only available embryo for transfer carries a SEG or MOS diagnosis. This low risk is consistent across all age groups and in our cohort female age was inversely associated with risk of SEG or MOS diagnosis. These findings are relevant in guiding pre-cycle PGT-A counseling and expectations.

O-174 3:05 PM Monday, October 19, 2020

ENHANCING CELL INJECTION SYSTEMS BY REAL TIME CONFIRMATION OF CYTOPLASMIC PENETRATION.

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OBJECTIVE: Visual assessment of true cell penetration with a microinjection pipette is not always feasible due to cloudy solutions, adjacent cells, and light microscopy wavelength limitations. This is especially true for microinjection in bovine oocytes and zygotes due to their cytoplasmic opacity. We hypothesized that an increase in electrical resistance upon bovine zygote plasmatic membrane piercing can serve as a real-time tool to confirm cell penetration and embryo viability.

DESIGN: Experimental study.

MATERIALS AND METHODS: In the first part of the study, the minimal electrical resistance increase (minΔR [MΩ]) that occurs when penetrating visually viable zygotes (compared to non-viable ones) was determined. Bovine zygotes were produced by in vitro fertilization. Electrical resistance of the microinjection pipette tip was measured continuously throughout the procedure. ROC analysis was performed. In the second part of the study, the ability of the minΔR [MΩ] (identified in the first part of the study) to predict cell penetration and viability was tested by the microinjection of in vitro transcribed (IVT) mRNA coding for the fluorescent 'mCherry' nuclear protein into zygotes. Cleavage embryos showing nuclear fluorescence 20 hours post injection were considered viable.

RESULTS: ROC analysis showed minΔR $>$ 4 MΩ to identify visually viable embryos (n=67) versus non-viable ones (n=15) (97% sensitivity, 100% specificity, AUC 0.99 (CI 0.95 – 1.00)). In the second part of the study, 11 zygotes had minΔR $>$ 4 MΩ at the time of IVT mRNA injection. Seven of them (64%) cleaved and showed positive nuclear fluorescence 20 hours post injection. Eight zygotes had minΔR $\leq$ 4 MΩ and none of them (0%) showed nuclear fluorescence 20 hours post injection.

CONCLUSIONS: When attempting cytoplasmic zygote microinjection, electrical resistance increase can serve as a reliable tool to confirm successful cell penetration and embryo viability, independent of optical visualization. This technology can potentially be integrated into a manual or robotic cell injection system.

O-175 1:50 PM Monday, October 19, 2020

MANUFACTURING OOCYTES THROUGH SOMATIC CELL NUCLEAR TRANSFER. Aysha Trout, B.A., Philip Xie, B.S., Robert Setton, M.D., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: Somatic cell haploidization in a project of neogametogenesis is normally monitored by the sole extrusion of a pseudo-polar body. Here we determined whether an earlier identification of a meiotic-like spindle after somatic cell nuclear transfer (SCNT) enhances the likelihood of successful haploidization.

DESIGN: Constructs were observed for meiotic-like spindle identification at least 2 hours after SCNT. Oocytes with either negative (NS) or positive (PS) spindle were inseminated, together with an unmanipulated control. Embryo development and molecular karyotype were assessed between the two cohorts.

MATERIALS AND METHODS: Metaphase II oocytes from B6D2F1 mice were exposed to cytochalasin B, and under Oosight™ visualization, meiotic spindles and polar bodies were removed. A single *cumulus* cell was fused with the resulting ooplast using Sendai virus. Reconstituted oocytes were assessed for the presence of a newly formed meiotic-like spindle and inseminated by piezo-ICSI. Piezo-ICSI of unmanipulated oocytes served as control. Successful haploidization was confirmed by the extrusion of a pseudo-polar body at the time fertilization, and time-lapse imaging was used to monitor preimplantation development. Whole genome sequencing of resulting blastocysts determined ploidy.

RESULTS: Out of 320 oocytes that underwent SCNT, 186 (58%) displayed a meiotic-like spindle at least 2 hours later, while the remaining did not (42%). Control oocytes (n=49), 92 NS oocytes, and all 186 PS oocytes underwent piezo-ICSI insemination. NS and PS groups, although at a lower rate than the control (86%, $P<0.0001$), survived at a comparable rate of 63% and 52%, respectively. Of the surviving NS oocytes, only 10% showed successful haploidization by extrusion of a pseudo-polar body, while 55% of PS oocytes haploidized ($P<0.00001$). The control oocytes fertilized at a superior rate of 74% compared to the experimental groups ($P<0.00001$); however, between the two experimental cohorts, NS oocytes fertilized at a rate of 7%, while PS oocytes fertilized at a significantly higher rate of 53% ($P<0.00001$). Lastly, although at lower rates than the control (81%, $P<0.0001$), NS and PS oocytes developed to blastocysts at comparable rates of 50% and 27%, respectively. DNA sequencing of trophectoderm biopsies (4-8 cells) from 2 NS blastocysts and 6 PS blastocysts showed that both NS blastocysts (100%) and 4 PS (67%) blastocysts were euploid.

CONCLUSIONS: The assessment of a meiotic-like spindle after SCNT demonstrated a higher proportion of haploidized and fertilized oocytes. In both cohorts, we were able to observe a full preimplantation development morphokinetically comparable to the control and proved to be euploid. Once the reproducibility and safety of this technique are demonstrated, it may be applied in humans to generate oocytes for women of advanced maternal age or with exhausted ovarian reserve.

O-176 2:05 PM Monday, October 19, 2020

DEVELOPMENT OF A NOVEL TECHNIQUE TO EDIT THE GENOME OF THE MALE GAMETE. June Wang, B.A., Philip Xie, B.S., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: Editing the genome at the gamete level may prevent the creation of mosaic embryos. For spermatozoa, this is a challenge due to the unique compaction of their DNA. Our aim is to identify whether an ooplasm-mediated technique can promote editing of the mouse spermatozoa genome.

DESIGN: To facilitate decondensation of the male genome, enucleated oocytes were injected with individual spermatozoa (haploid ICSI, or h-ICSI), creating pseudo-blastocysts containing only the male genome. Gene editing was performed via injection of a CRISPR solution designed to knock out the *Tyr* gene to create an albino phenotype. A control group was produced through standard ICSI with the same CRISPR solution (diploid ICSI, or d-ICSI), following the established approach for heritable genome editing. Gene editing success was analyzed in the resulting embryos and compared between groups. An initial assessment of mosaicism was conducted on h-ICSI embryos.

MATERIALS AND METHODS: Metaphase II oocytes were retrieved from superovulated B6D2F1 mice and divided into two groups: h-ICSI and d-ICSI. Oocytes for h-ICSI were enucleated and given 2 hours to rest. Both groups then underwent piezo-actuated ICSI with a solution of pre-complexed Cas9 and *Tyr* knockout gRNA. Embryos were incubated for 24 hours, and then cryopreserved. DNA was extracted, and a 423-bp region around the CRISPR target site was amplified. CRISPR activity was analyzed by the T7E1 assay. To assess mosaicism, additional h-ICSI embryos were cultured and disaggregated into blastomeres before freezing. DNA was analyzed by Illumina sequencing.

RESULTS: Of 96 oocytes, 57 underwent d-ICSI as the control group and 31 underwent h-ICSI. Overall, 75% (43/57) of d-ICSI embryos survived after ICSI, 70% (30/43) developed to the 2-cell stage, and 36% (10/28) contained gene modification at the target site. Of the h-ICSI group, 74% (23/31) survived after sperm injection, 43% (10/23) progressed to the 2-cell stage, and 29% (2/7) had confirmed gene editing. A significant difference ($P < 0.05$) was seen only for the rate of development. Of the 8 h-ICSI embryos evaluated for mosaicism, 6 demonstrated gene modification. Of these, half were mosaic, while the remaining 3/6 uniformly had the albino gene knocked out.

CONCLUSIONS: We propose a haploid ICSI technique that allows successful editing of the spermatozoa genome at a comparable rate to the standard diploid ICSI approach. Once our editing technique is optimized, individual pseudo-blastomeres of h-ICSI embryos can be used as the male gamete to inseminate oocytes. If reproduced successfully in humans, our model may address the inheritance of paternal monogenic disorders.

References: None

SUPPORT: None

O-177 2:20 PM Monday, October 19, 2020

A NON-HUMAN PRIMATE MODEL OF OVARIAN ISCHEMIA AND REPERFUSION REVEALS PHYSIOLOGICAL HYPOXIA IN THE PRIMORDIAL FOLLICLES. Adam J. Krieg, Ph.D., Melinda J. Murphy, B.S., Alison Ting, Ph.D. Oregon National Primate Research Center, Beaverton, OR.

OBJECTIVE: During ovarian transplantation, the tissue undergoes both ischemia and reoxygenation, which can result in oxidative damage to the remaining follicle pool. In order to optimize fertility preservation techniques, it is essential to determine the native levels of oxygen (O2) in the ovary, particularly the primordial follicle. Using an ischemia and reperfusion model in nonhuman primates, our studies would have direct applicability to human fertility studies.

DESIGN: Basic science study using non-human primates (rhesus macaques) to measure O2 dynamics in the primate ovary exposed to ischemia and reperfusion.

MATERIALS AND METHODS: The ovaries of ten juvenile female rhesus macaque (1-1.5 years of age) were exposed by laparotomy and the O2 level of the tissue ovarian cortex (1.0-2mm from surface) was measured using an O2 sensor equipped with a microprobe. One random ovary in each animal was exposed to ischemic (ovarian vessel clamping; 20 min) and reperfusion (unclamping; 5-20 min) conditions. Tissue O2 in the ovary underwent ischemia-reperfusion (I/R) was measured throughout the procedure. The vessel of the contralateral ovary was unclamped and serveds as control (CTRL). Bromodeoxyuridine (BrdU) was injected in each animal to label growing follicles. Five animals were also injected with pimonidazole in order to label hypoxic tissues in the ischemic and control ovaries, and underwent bilateral oophorectomy 24 hours later. The remaining five animals underwent oophorectomy 18 days after surgery to measure longer term follicle damage. Formalin-fixed and paraffin-embedded ovaries were processed for immunohistochemical detection of BrdU, pimonidazole, and the hypoxia marker gene CA-IX. Mean O2 concentrations at discrete timepoints were compared by One-Way ANOVA using Tukey's test for multiple comparisons.

RESULTS: The baseline O2 concentration of juvenile rhesus ovarian cortex was equivalent to $5.6 \pm 2.3\%$ (atmospheric O2 is $\sim$20.9%). After 5 minutes of ischemia, oxygen dropped to $1.7 \pm 1.5\%$ ($P = 0.014$); and remained low ($1.4 \pm 1.7\%$, $P = 0.027$). After 5 minutes of reoxygenation, O2 returned to baseline ($6.6 \pm 3.9\%$, $P = 0.96$). IHC detection of pimonidazole and CA-IX revealed robust pimonidazole uptake and CA-IX expression in the

primordial follicles of both control and ischemic ovaries, with expansion of staining to the medullar and stromal cells in ischemia. BrdU was detected in growing follicles in all ovaries, with little change due to ischemia and reoxygenation.

CONCLUSIONS: The oxygen concentration of the juvenile rhesus ovary is approximately 5% O2, equivalent to many other tissues. However, the robust pimonidazole and CA-IX staining of the oocyte and granulosa cells suggest that the local environment of the primordial follicle experiences physiological hypoxia (<1.5% O2). Similar levels of BrdU uptake in CTRL and I/R ovaries suggest short-term follicle growth (in secondary and antral follicles) was not affected by O2 fluctuation. The maintenance of physiological hypoxia could be an important consideration for maintaining follicle quiescence and oocyte quality during fertility preservation procedures.

SUPPORT: This work was supported byÂ R21HD094983 (AJK and AT) andÂ P51OD011092 (ONPRC)

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SURVIVIN-SODIUM IODIDE SYMPORTER REPORTER AS A NON-INVASIVE DIAGNOSTIC MARKER TO DIFFERENTIATE BETWEEN UTERINE LEIOMYOSARCOMA VERSUS LEIOMYOMA.

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OBJECTIVE: The aim of this study is to evaluate the use of Survivin-Sodium iodide symporter (Ad-SUR-NIS) as a reporter gene to differentiate between uterine leiomyoma (LM) and uterine leiomyosarcoma (LMS) by positron emission tomography (PET) imaging.

DESIGN: Laboratory research studies using LMS and LM animal models.

MATERIALS AND METHODS: 28 Adult female nu/nu Nude mice, 6-8 weeks of age, weighing between 20-25 g, were used. A total of $2x10^7$ cells of LMS or LM cells were inoculated subcutaneously into the right flank. One week after inoculation with visible and palpable tumors, the mice were transfected via retro-orbital with Ad-SUR-NIS ($1x10^9$ PFU/mouse) or PBS (control). 24 hours after Ad-SUR-NIS injection, 14 animals were submitted to PET/CT scanning using $NaBF_4^{18}$ as a radiotracer to assess the expression of NIS reporter gene. For safety evaluation, 14 animals were euthanized after 24 hours of the Ad-SUR-NIS transfection. Tumors and organs (brain, liver, kidney, spleen, lung, ovary, uterus and heart) were collected and histopathologic analysis was performed by a pathologist.

RESULTS: 5 minutes after the $NaBF_4^{18}$ administration, the PET/CT scan images showed an increased radiotracer uptake attributable to Ad-SUR-NIS on the LMS tumors when compared to LM. Presumably, due to the overexpression of NIS in LMS in contrast to LM. The nature of the tumor masses (LMS vs LM) were confirmed histologically. 24 hours after the Ad-SUR-NIS or PBS transfection LM and LMS tumors along with the organs, were collected. H&E-stained sections were examined histologically and compared to the PBS group. No pathological changes were found in any of these tissues after Ad-SUR-NIS transfection.

CONCLUSIONS: Ad-SUR-NIS PET reporter is a promising imaging biomarker which differentiates uterine LMS from LM using $NaBF_4^{18}$ as a radiotracer. This new diagnostic method can provide a much-needed tool in clinical practices to effectively triage women with suspicious uterine masses.

SUPPORT: POC- University of Illinois at Chicago

O-179 2:50 PM Monday, October 19, 2020

OVARIAN AGING AND REPRODUCTIVE SENESCENCE IN MOUSE MODEL OF MITOCHONDRIAL DYSFUNCTION.

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OBJECTIVE: To evaluate the mechanisms of female reproductive aging and senescence induced by mitochondrial dysfunction in mice.

DESIGN: Prospective cohort design study. 13 female mice with mitochondrial dysfunction (mtDNA-depleter) and 13 wild-type (WT) female mice were studied at three time points in their reproductive life cycle: 4-6, 8-10, and 11-12 months of age.

MATERIALS AND METHODS: A transgenic mouse model with an inducible gene for mitochondrial dysfunction (mtDNA-depleter) was previously created by our lab. All protocols were approved by our institutional IACUC. At each of the three time points, reproductive markers were assessed, including estrous cyclicity, plasma anti-Mullerian hormone (AMH), ovarian follicles, estrogen receptor staining, and uterine and vaginal atrophy. Breeding experiments were performed to assess fertility. Differences between the mtDNA-depleter and WT groups were evaluated by independent two-sample t-test.

RESULTS: Twenty-six female mice were studied from 4 to 12 months of age. The estrous cycles in 4-6-month mtDNA-depleter mice were prolonged, 9.4 days (n = 7), versus 5.3 days in WT (n = 9), p-value of 0.021. By 11-12 months, both groups had prolonged estrous cycles consistent with physiologic aging. AMH levels in 4-6-month mtDNA-depleter mice were decreased, 84 (n = 4), versus 114 ng/mL in WT (n = 5), p-value of 0.013. AMH was reduced in older mice at 8-10 and 11-12 months, but there were no significant differences between groups. Looking at the data collectively for all three time points, there were fewer tertiary (early antral, antral, or pre-ovulatory) follicles in mtDNA-depleter mice than in WT, 3.5 versus 4.9 per cut section, respectively (p-value of 0.039). There were fewer corpora lutea in mtDNA-depleter mice than in WT, 0.90 versus 1.7 per cut section, respectively (p-value of 0.027). Collectively, average uterine weight in mtDNA-depleter mice was lower, 62.2, versus 92.3 mg in WT mice, p-value of 0.0028. Vaginal epithelium in 4-6-month mtDNA-depleter mice was thinner, 98 μm (n = 4), versus 200 μm in WT mice (n = 4), p-value of 0.035. In breeding experiments, mtDNA-depleter mice at age 3 and 5 months did not produce litters. Estrogen receptor levels were reduced in mtDNA-depleter mouse ovary relative to WT, evident from both immunofluorescence and semi-quantitative PCR analysis.

CONCLUSIONS: Mitochondrial dysfunction in mice is associated with premature reproductive aging and senescence, as evidenced by early onset of prolonged estrous cycles, diminished ovarian reserve, uterine and vaginal atrophy, and sterility. Mitochondrial dysfunction is also associated with premature estrogen receptor down-regulation in the mouse ovary.

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SUPPORT: UAB Department of Obstetrics and Gynecology

O-180 3:05 PM Monday, October 19, 2020

INVESTIGATION OF APOPTOSIS AND FOLLICLE ACTIVATION BY PROTEOMICS IN AN EXPERIMENTAL MODEL OF CYCLOPHOSPHAMIDE-INDUCED FOLLICLE DEPLETION IN OVARIAN CULTURE.

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OBJECTIVE: The mechanisms of primordial follicle depletion (PrFD) and infertility following cyclophosphamide (CPA) treatment remain unclear. This study investigated mechanisms of CPA-induced PrFD focusing on apoptosis and follicle over-activation and associated protein profile changes.

DESIGN: Experimental controlled study using a mouse ovarian culture model.

MATERIALS AND METHODS: Ovaries (n=24) from B6CBA/F1 postnatal day-4 mouse were cultured according to O'Brien *et al* [1]. The ovaries were randomly assigned to CPA-treated group (5 μM 4-hydroperoxyCPA) or control. Ovaries were analyzed 24, 48 or 72 h after treatment. Follicle density on histology (counted number of follicles/area) was estimated for primordial follicle density (PFD) and growing follicle density (GFD). Apoptosis was assessed by a qualitative analysis of TUNEL assay at 24 h. Mass spectrometry-based proteomics analysis was performed at 24 h (4 ovaries/group), followed by gene ontology analysis on PANTHER for protein class, molecular function, biological process and pathways.

RESULTS: In CPA-treated ovaries, PFD showed a marked progressive reduction and a lower PFD was found at all timepoints compared to controls. At 72 h, PFD decreased by 82.4% from 401.4±266.7 follicles/mm^2 at 24 h in the CPA-treated group, whereas it decreased by 25.2% from 673.2±231.9 follicles/mm^2 at 24 h in control. On the contrary, GFD was higher in CPA-treated ovaries than in controls at all timepoints. At 24 h, 109.8±63.8 follicles/mm^2 were counted in CPA-treated group vs 61.8±1.6 follicles/mm^2 in

control. These numbers increased around 50% in both groups at 48 h. However, from 48 h to 72 h, a GFD reduction of 15.1% was observed in CPA-treated ovaries vs a further GFD increment of 34.5% in controls.

The TUNEL assay revealed positive stained oocytes in primordial follicles and granulosa cells of growing follicles in CPA-treated ovaries but this was not observed in controls.

The proteomics analysis identified 9531 proteins. Of those, 9018 were common to both groups, 245 were found only in CPA-treated group and 268 only in control. Comparing to control, CPA-treatment increased proteins related to defense/immunity, nuclei acid binding, translation regulation, intercellular signal and cell proliferation, such as transmembrane proteins, immunoglobulins, DNA helicase. Additionally, proteins related to transporter and transfer/carrier decreased in CPA-treated group. In pathways, apoptosis, B and T cell activation were only involved in CPA-treated group, while PI3K was only in control.

CONCLUSIONS: The preliminary findings indicated a reduced PFD and an increased GFD in CPA-treated ovaries, suggesting that both apoptosis and follicle over-activation may be involved in the PrFD. The GFD decrease at 72 h suggested that activated follicles were damaged by CPA in longer culture. The TUNEL assay revealed direct damage to oocytes in CPA-treated ovaries. The proteomics analysis supported these findings, as apoptosis related proteins were increased in CPA-treated ovaries whereas proteins related to maintenance of primordial follicle dormancy were only identified in control.

References

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ART LAB: TECHNOLOGY

O-181 9:40 AM Tuesday, October 20, 2020

OPENING THE BLACK BOX: RELATION BETWEEN AI PREDICTED EMBRYO IMPLANTATION AND TRADITIONAL MORPHOKINETIC AND MORPHOLOGICAL ANNOTATIONS. Jørgen Berntsen, M.Sc., Jens Rimestad, M.Sc., Jacob Theilgaard Lassen, M.Sc., Mikkel Fly Kragh, PhD. Vitrolife A/S Viby, Denmark.

OBJECTIVE: Is there a correlation between predictions from an artificial intelligence (AI) model trained solely on fetal heart beat outcome and time-lapse parameters annotated by embryologists?

DESIGN: A deep neural network was trained on clinical outcome from 98,583 embryos with either known fetal heart beat (n=12,432) or that were discarded (n=86,151). The data were obtained from 18 different clinics from 2011 to 2019. All embryos were incubated for at least 4 days. In addition, a data set with 17,249 embryos were used for test. Correlation of score predictions with manually labelled morphokinetic and morphological parameters on the test data were assessed.

MATERIALS AND METHODS: Videos in the test data with annotations by embryologist were analysed for parameters including direct cleavage (DC), tB, ICM and TE. DC annotations include DC from 1 to 3 (DC1-3), DC from 2 to 5 (DC2-5) and absence of DC (no-DC). Annotations of tB was grouped into 5 intervals ranging from <100, 100-105, 105-110, 110-115, >115 hours post insemination. Wilcoxon sum rank test was used to test significant differences between scores and manual annotations. The trained AI outputs a score between 1 and 9.9, increasing with the likelihood of implantation.

RESULTS: The trained AI was tested on a data set (n=17,249) that had not been used during training. For embryos showing DC1-3, DC2-5 or no-DC (n=6,049), the average scores were 3.48, 4.04, 5.50, respectively. The scores were significantly different between all groups ($p<0.0001$). Embryos from these 3 groups that reached the blastocyst stage (n=2,434) showed average scores of 6.41, 6.31, 7.39, for DC1-3, DC2-5 and no-DC, respectively. The scores in the no-DC group were significantly different from both DC1-3 and DC2-5 ($p<0.0001$). However, there was no significant difference between DC1-3 and DC2-5 ($p=0.71$). This maybe due to that DC1-3 and DC2-5 only included 161 and 159 embryos, respectively.

For the tB groups (n=2,447) the average scores were 8.64, 8.05, 7.27, 6.56 and 5.59 for the intervals <100, 100-105, 105-110, 110-115, >115, respectively. For the different groups of ICM grades (n=1,636) the average scores were A=8.51, B=7.55 and C=5.56, respectively. For the different groups of TE grades (n=1,636) the average scores were A=8.75, B=7.71 and C=5.70, respectively. For tB, TE and ICM there were significant differences for the scores between all groups ($p<0.0001$).

CONCLUSIONS: AI output correlated with standard morphokinetic and morphological parameters such as direct cleavages (DC), time to blastocyst (tB), inner cell mass (ICM) and trophectoderm (TE).

Our results suggest that the AI score reflects parameters known to correlate with implantation. However, this does not imply that the AI directly estimates these parameters. As the AI is trained directly on the entire video sequence it likely identifies features of embryo development that human analysis may not recognize.

SUPPORT: The work was partly funded by the Innovation Fund Denmark (IFD) under File No. 7039-00068B.

O-182 9:55 AM Tuesday, October 20, 2020

COMPARISON OF PRONUCLEAR (PN) NUMBER OBSERVATIONS BASED ON EMBRYOLOGIST'S EXPERIENCE AND DETECTION BY ARTIFICAL INTELLIGENCE (AI) TRAINED WITH DEEP LEARNING TECHNOLOGY. Hiroyuki Watanabe, M.S.,[1] Noritaka Fukunaga, Ph.D.,[1] Sho Sanami, Ph.D.,[2] Hiroya Kitasaka, Ph.D.,[1] Yuji Tsuzuki, M.S.,[2] Yuta Kida, M.S.,[1] Seiji Takeda, M.S.,[2] Fumiya Kondo, M.S.,[1] Sho Takeda, B.S.,[1] Yoshimasa Asada, M.D., Ph.D.[1] [1]Asada Ladies Clinic, Nagoya, Japan; [2]Dai Nippon Printing Co., Ltd., Tokyo, Japan.

OBJECTIVE: Gamete and embryo evaluation in human IVF programs are critical skills that are developed through formal followed by actual experience over many years in a laboratory. Whilst the aim is to ensure consistency in evaluation between embryologists in any one laboratory, it is a major challenge to ensure and maintain high accuracy across operators.

Therefore, we have developed an automatic PN number detection system utilizing deep learning technology to provide an effective system for clinical use. In this study, the accuracy of PN number detection assessed by AI was compared with that assessed by junior, intermediate, and senior embryologists in order to indicate the effectiveness of the AI generated system vs. human assessment.

DESIGN: Training data, for constructing the AI for automatic PN number detection, consisted of 70-80 images before and after pronucleus formation of one fertilized embryo were captured by a time-lapse incubator. Using these 70-80 images as one set, 300 sets of each 0PN, 1PN, 2PN, 3PN embryos were inputted into the AI algorithm. For comparison of data from embryologists, we selected three junior embryologists on the first day of work, three intermediate embryologists with three years of experience, and three senior embryologists with more than six years of experience.

MATERIALS AND METHODS: For testing data to evaluate accuracy of the AI algorithm, we used a total of 40 time-lapse videos including 0,1,2,3 PN embryos in which the PN numbers were decided by different embryologists.

For the test data set, the PN number of each embryo was judged by each junior, intermediate, senior embryologist, and the AI. The correct answer rates were then compared.

RESULTS: The correct answer rates for 0PN were 70.0% (junior), 96.7% (intermediate), 100% (senior) and 100% by AI. The correct answer rates for 1PN were 66.7% (junior), 85.2% (intermediate), 88.9% (senior) and 66.7% by AI. The correct answer rates for 2PN were 81.8% (junior), 97.0% (intermediate), 100% (senior) and 81.8% by AI. The correct answer rates for 3PN were 63.3% (junior), 96.7% (intermediate), 90.0% (senior) and 70.0% by AI.

CONCLUSIONS: Whilst the accuracy of the AI was higher in some of the assessments (e.g. junior on 1 and 3 PNs and that of intermediate on 0 PN), it was not consistent with assessments by seniors. For the AI to be clinically useful it should have not only higher accuracy across all users but also be stable across different PN states. We are therefore continuing to improve the AI to have a higher accuracy for PN number detection by introducing into the algorithm, Z-axis multi-sliced images.

References: none

SUPPORT: none

O-183 10:10 AM Tuesday, October 20, 2020

NONINVASIVE DETECTION OF BLASTOCYST PLOIDY (EUPLOID VS. ANEUPLOID) USING ARTIFICIAL INTELLIGENCE (AI) WITH DEEP LEARNING METHODS. Josue Barnes, B.S.,[1] Jonas Malmsten, D.P.S.,[1] Qiansheng Zhan, Ph.D.,[1] Iman Hajirasouliha, Ph.D.,[1] Olivier Elemento, Ph.D.,[1] Jose Sierra, Ph.D.,[2] Nikica Zaninovic, Ph.D.,[1] Zev Rosenwaks, M.D.[3] [1]Weill Cornell Medicine, New York, NY; [2]QED Analytics LLC, Princeton, NJ; [3]The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: The current method of preimplantation genetic testing for aneuploidy (PGT-A) involves invasive trophectoderm (TE) biopsy. Although PGT-A has improved the success rate per embryo transfer, it has notable limitations. These include the cost of sequencing, mosaicism, the skill required to biopsy TE cells, and the fact that only a select number of blastocysts (BLs) can be tested. Embryologists rely on morphological assessment and clinical information to select BLs for PGT-A. The development of noninvasive methods of embryo screening, as an alternative to PGT-A, is essential. We propose an embryo selection method that leverages the power of deep learning classification methods trained on spatial and temporal information stored in time-lapse images (TLM) that capture embryo development along with clinical parameters; this method can be used to select embryos for PGT-A and to predict embryo ploidy (euploid vs. aneuploid) without a biopsy.

DESIGN: In our study, we used a retrospective dataset consisting of 10,872 embryos of known ploidy status (euploid or aneuploid) to train and validate several deep learning models.

MATERIALS AND METHODS: We developed deep learning models for embryo image analysis based on pre-trained ResNet18. The models utilized images of human embryos captured using time-lapse microscopy (EmbryoScope™) at 110 hours post-ICSI and known PGT-A results (aneuploid n = 6,443; euploid n = 4,429) as ground truth labels. The developed models use several clinical features, including maternal age, morphokinetics, BL grade, and BL score. Using an 80/20 training-validation split of the data, performances were measured by validation accuracy and the AUC. Class activation mapping (CAM) was employed to identify which areas within embryo images were used to predict ploidy.

RESULTS: Several models were trained and validated, each with varying features.

Model	Features	AUC	Accuracy
A	Image	0.6214	62.87%
B	Image, Age	0.7293	68.06%
C	Image, Morphokinetics	0.6094	62.55%
D	Image, BL Score	0.6901	64.07%
E	Image, BL Grade	0.6876	65.51%
F	Image Age, Morphokinetics	0.7341	68.29%
G	**Image, Age, BL Score**	**0.7558**	**70.23%**
H	Image, Age, BL Grade	0.7595	69.54%
I	**Image, Age, Morphokinetics, BL Score**	**0.7614**	**69.68%**
J	Image, Age, Morphokinetics, BL Grade	0.756	69.03%

CONCLUSIONS: The implementation of deep learning image analysis permits a more objective assessment of BLs and, with the addition of oocyte age, morphokinetics, and BL grade or score, improves the model's ability to predict embryo ploidy in a noninvasive manner. CAM results from BL images suggest that the model focuses on the presence and absence of cavitation to predict embryo ploidy at 110 hours.

O-184 10:25 AM Tuesday, October 20, 2020

EMBRYOLOGY LAB-ON-A-CHIP: AUTOMATED OOCYTE DENUDATION MICROFLUIDIC DEVICE. Amir Mokhtare, M.S.,[1] Philip Xie, B.S.,[2] Alireza Abbaspourrad, Ph.D.,[1] Zev Rosenwaks, M.D.,[2] Gianpiero D. Palermo, M.D., Ph.D.[2] [1]Cornell University, Ithaca, NY; [2]The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To develop an automated microfluidic device to perform cumulus cell (CC) removal prior to intracytoplasmic sperm injection (ICSI) in a controlled microenvironment aimed at minimizing mechanical stress to the oocytes.

DESIGN: We developed a semi-automated oocyte denudation microfluidic chip (ODMC) modulated by microcontrollers and operated by a graphical user interface (GUI). The device consists of a 2-layer microchannel with a channel width of 200 μm. The bottom layer is etched with bas-relief structures to create chaotic mixing within microchannels. To assess mechanical stress on the oocytes, microfluidic profiles and shear stress present in manual pipetting (MP) and ODMC were quantified by computational fluid dynamics (CFD) simulations. Denudation efficiency was defined as the percentage of complete removal of CCs. ICSI was performed on oocytes processed by ODMC and compared to those obtained from MP to assess the oocyte developmental potential.

MATERIALS AND METHODS: The COCs were retrieved from superovulated B6D2F1 mice and individually dissected. ODMCs were fabricated from polydimethylsiloxane by planar photolithography and installed with inlet and outlet reservoirs that moderated the flow of denudation medium within the system. Individual COCs were loaded in the ODMC and denuded by chaotic mixing created by the bas-relief structures. The GUI visualized the denudation process in real-time and released denuded oocytes at the operator's discretion. Denuded oocytes by MP or ODMC were inseminated by piezo-actuated ICSI. Embryo developmental parameters were assessed in a time-lapse incubator.

RESULTS: Murine COCs were processed by our novel ODMC with optimized geometry and operating parameters including oscillating frequency, flow rate, and density of bas-relief structures. Orchestrated oscillating frequency and flow rate were able to tumble the COCs to allow interaction with bas-relief structures to strip off CC evenly. CFD simulation indicated that the maximum shear stress imposed on COCs was 40% less in ODMC with comparable denudation efficiency being at 95% for ODMC and 91% of MP without oocyte damage. Piezo-actuated ICSI was performed on 50 oocytes processed by MP or ODMC, and yielded comparable post-ICSI survival (82% vs. 84%), fertilization (90% vs. 90%), and blastulation rates (80% vs. 81%), with comparable morphokinetic development.

CONCLUSIONS: This device validated the potential of a fully automated embryology laboratory on a chip for ICSI without compromising oocyte developmental competence. Once the operation parameters are optimized for human gamete manipulation, this device can significantly reduce time and labor while providing optimal quality control and minimizing inter- and intra-operator variability. In conjunction with artificial intelligence, additional modules for different tasks can be fully automated such as maturity recognition, robotic ICSI, and embryo evaluation.

SUPPORT: None

O-185 10:40 AM Tuesday, October 20, 2020

FLUORESCENCE LIFETIME IMAGING MICROSCOPY (FLIM) DETECTS DIFFERENCES IN METABOLIC SIGNATURES BETWEEN EUPLOID AND ANEUPLOID HUMAN BLASTOCYSTS. Jaimin S. Shah, M.D.,[1] Marta Venturas, M.Sc.,[2] Tim H. Sanchez, Ph.D.,[3] Alan S. Penzias, M.D.,[1] Dan Needleman, Ph.D.,[2] Denny Sakkas, PhD[4] [1]Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA; [2]Harvard University, Cambridge, MA; [3]None; [4]Boston IVF, Waltham, MA.

OBJECTIVE: To determine whether non-invasive imaging via FLIM can detect metabolic differences in discarded human blastocysts with known ploidy status.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: We studied 150 discarded human blastocysts that had been biopsied and vitrified on day 5 or 6 with Gardner morphology Grade A or B in a University affiliated private IVF laboratory. PGT-A deemed 17 blastocysts as euploid and 133 as aneuploid. A comparison was made between euploid embryos and all aneuploid embryos as a group then by specific chromosomal abnormality (any monosomy/trisomy [n=85], chaotic [n=30], triploidy [n=12], or autosomal monosomy [n=6]). Embryos were warmed, cultured for 2 hours and imaged via FLIM to analyze their metabolic signatures. Embryo metabolic state was assessed using FLIM to measure autofluorescence of NADH and FAD. Eight metabolic parameters were obtained from each blastocyst (4 for NADH and 4 for FAD): short (T_1) and long (T_2) fluorescence lifetime, fluorescence intensity (I), and fraction of the molecule engaged with enzyme (F). The redox ratio (Intensity of NADH)/(Intensity of FAD) was also calculated for each

embryo. Multilevel models were used for analysis with $p < .05$ showing significance.

RESULTS: The mean (± SD) patient ages in years for the euploid and aneuploid groups were 36.4 ± 4.7 and 36.8 ± 3.9, respectively. Our data showed a number of statistically significant metabolic differences when comparing euploid versus aneuploid embryos. Comparing euploid versus all combined aneuploid embryos demonstrated significant metabolic differences in NADH-*F* ($p < .03$) and FAD-*I* ($p < .01$). Furthermore, comparing euploid versus the grouped chromosomal aneuploidies, NADH-*F* ($p < .05$), FAD-*I* ($p < .01$), and redox ratio ($p < .04$) showed significant metabolic differences.

CONCLUSIONS: FLIM has identified significant metabolic differences between euploid and aneuploid embryos. These findings provide preliminary evidence that FLIM may be a useful non-invasive clinical tool. Additional data is required to elucidate the true directional relationship between ploidy status and metabolism. Further studies are planned to determine if metabolic signatures via FLIM can assist in clinical embryo selection.

SUPPORT: Supported by the Blavatnik Biomedical Accelerator Grant at Harvard University. Becker and Hickl GmbH and Boston Electronics sponsored research with the loaning of equipment for FLIM.

O-186 10:55 AM Tuesday, October 20, 2020

IT TAKES TWO TO DOUBLE WITNESS: EVALUATING THE REAL TIME REQUIRED FOR MANUAL VERSUS ELECTRONIC DOUBLE WITNESSING IN THE *IN VITRO* FERTILIZATION (IVF) LABORATORY.

Rebecca Holmes, PhD, HCLD,[1] Kelly A. Wirka, MS, TS (AAB),[2] Brooke Hayward, SM, MBA,[2] Allison B. Catherino, PhD,[2] Jason E. Swain, PhD, HCLD[3] [1]CCRM Boston, Newton, MA; [2]EMD Serono, Inc. (a business of Merck KGaA, Darmstadt, Germany), Rockland, MA; [3]CCRM IVF Network, Lone Tree, CO.

OBJECTIVE: To examine, via head-to-head comparison with manual double witnessing, the impact of an electronic witnessing system (EWS) on double-witnessing procedures in an IVF laboratory, and to assess the time required to double witness procedures, including the interruption time required for the second witness.

DESIGN: Noninterventional, longitudinal study over 3 months.

MATERIALS AND METHODS: Three procedures of varying complexity levels – intracytoplasmic sperm injection (ICSI), Day 3 embryo assessment, and embryo transfer (fresh or frozen) – were double witnessed both manually and electronically during 2 weeks each month. This study was determined exempt from Institutional Review Board review by Western IRB, USA. Five embryologists in a single IVF laboratory double witnessed procedures manually (performer), second witnessed by a second person (witness), and using an EWS (Gidget®, Genea Biomedx, Sydney, AUS). Time was tracked for all sessions, including the interruption time when the second witness was kept away from an initial task. Study procedures occurred over 6 independent weeks, selected *a priori* to capture different workloads and staff availability. To address potential bias, the sequence of witnessing sessions was alternated.

RESULTS: Overall, 76.6% (49/64) of ICSIs, 44.4% (32/72) of embryo assessments, 100% (2/2) of fresh embryo transfers, and 93.9% (31/33) of frozen embryo transfers (FETs) underwent double witnessing manually and using the EWS. Witnessing of 114 procedures, including 342 witnessing times (114 EWS, 114 manual, and 114 interruptions to witnessers), were analyzed. For the performer, EWS reduced the mean (standard deviation) time to witness by 29.7 (38.8) seconds per ICSI, 16.8 (26.5) seconds for Day 3 embryo assessment, 27.0 (19.8) seconds per fresh embryo transfer, and 18.5 (15.0) seconds per FET. Overall, EWS saved the performer 25.3 seconds per procedure compared with manual witnessing ($p<0.0001$; 95% confidence interval –36.70, –13.84). When accounting for the second witness interruption time required for manual double witnessing, EWS reduced the total times (performer's waiting and witnesser's interruption) by 91.5 (23.58) seconds per ICSI, 62.0 (18.86) seconds for Day 3 embryo assessment, 58.3 (18.86) seconds per fresh embryo transfer, and 59.4 (13.31) seconds per FET. The time saved did not differ by embryologist, sequence of double witnessing, or period of data collection, indicating that time savings were independent of workload and staff availability.

CONCLUSIONS: Electronic witnessing can significantly reduce the overall time required for double witnessing by 3.1- to 5.2-fold. For the first time, these data represent a fair comparison between manual double witnessing and an EWS, as they account for the second witness interruption time. An EWS may help to improve laboratory efficiency and workflow by minimizing interruptions, which have long been underestimated in today's complex IVF laboratory practice.

SUPPORT: Study sponsored by EMD Serono, Inc., Rockland, MA, USA (a business of Merck KGaA, Darmstadt, Germany).

ENDOMETRIOSIS

O-187 9:40 AM Tuesday, October 20, 2020

EFFICACY AND SAFETY OF RELUGOLIX COMBINATION THERAPY IN WOMEN WITH ENDOMETRIOSIS-ASSOCIATED PAIN: PHASE 3 RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY (SPIRIT 2).

Sawsan As-Sanie, MD, MPH,[1] Christian M. Becker, MD,[2] Neil Johnson, MD,[3] Bruce Arthur Lessey, MD, PhD,[4] Mauricio S. Abrao, MD,[5] Eric L. Brown, MD,[6] Krzysztof Wilk, MD,[7] Juan Camilo Arjona Ferreira, MD,[8] Vandana Mathur, MD, FASN,[9] Yulan Li, PhD,[8] Qurratul Ann Warsi, MD, MAS,[8] Rachel B. Wagman, MD,[8] Linda C. Giudice, MD, PhD[10] [1]University of Michigan Medical Center, Ann Arbor, MI; [2]University of Oxford, Oxford, United Kingdom; [3]Robinson Research Institute, University of Adelaide, Australia; [4]Wake Forest Baptist Health, NC; [5]Gynecologic Division, BP - A Beneficencia Portuguesa de Sao Paulo, Sao Paulo, Brazil; [6]Medi-Sense, Inc., Atlanta, GA; [7]Boni Fratres Hospital Obstetrics and Gynecology Department Katowice, Katowice, Poland; [8]Myovant Sciences, Inc., Brisbane, CA; [9]MathurConsulting, Woodside, Woodside, CA; [10]University of California, San Francisco, San Francisco, CA.

OBJECTIVE: To evaluate the efficacy and safety of treatment with Relugolix combination therapy (Rel-CT; relugolix 40 mg [an oral gonadotropin-releasing hormone receptor antagonist], estradiol 1 mg, norethindrone acetate 0.5 mg) compared with placebo in women with endometriosis-associated pain. SPIRIT 2 is the first of two identical pivotal phase 3 studies assessing Rel-CT that have been completed.

DESIGN: Multinational, phase 3, randomized, double-blind, placebo-controlled study.

MATERIALS AND METHODS: Premenopausal women (age 18-50 years) with surgically diagnosed endometriosis (EM) and a history of moderate to severe dysmenorrhea (DYS) and non-menstrual pelvic pain (NMPP) were randomized 1:1:1 to 24 weeks of treatment with daily Rel-CT, delayed Rel-CT (relugolix 40 mg monotherapy for 12 weeks followed by Rel-CT for 12 weeks), or placebo. Co-primary endpoints were the comparison between Rel-CT and placebo on the proportion of DYS and NMPP responders at Week 24, based on daily Numerical Rating Scale (NRS) scores (0=no pain, 10=worst pain imaginable). A responder was a woman who achieved a predefined, clinically meaningful reduction from baseline in NRS score (2.8 for DYS and 2.1 for NMPP) with no increase in analgesic use. Secondary endpoints included change from baseline in EHP-30 pain domain scores and opioid use. Safety assessments included adverse events and bone mineral density (BMD) changes by dual-energy X-ray absorptiometry.

RESULTS: A total of 623 patients were randomized and 507 (81%) completed the study. Both co-primary endpoints were met: the proportion of DYS responders was 75.2% with Rel-CT vs 30.4% with placebo, and for NMPP was 66.0% vs 42.6%, respectively (both $p<0.0001$). In the delayed Rel-CT group, the DYS and NMPP responder rates were 72.8% and 52.9%, respectively. At baseline, mean NRS for DYS and NMPP for Rel-CT were 7.2 (severe) and 5.9 (moderate), decreasing to 1.7 (mild) and 2.9 (mild) at Week 24, and equating to 75.1% and 49.2% reduction from baseline in DYS and NMPP, respectively. Patients receiving Rel-CT vs placebo had significant improvements in daily functioning as measured by the EHP-30 pain domain score (–32.2 vs –19.9, $p<0.0001$) and more were opioid-free (82% vs 66.2%, $p<0.0001$) at Week 24. Adverse event incidence was overall comparable between Rel-CT and placebo. Mean percent change from baseline to Week 24 in lumbar spine BMD was –0.78% vs 0.02%, respectively, in the Rel-CT and placebo groups and –1.92% in the delayed Rel-CT group.

CONCLUSIONS: Once-daily oral Rel-CT significantly reduced DYS and NMPP in women with surgically confirmed EM and reduced pain-related functional limitations, while reducing the need for opioids. Rel-CT was associated with minimal BMD loss and was generally well tolerated.

SUPPORT: Myovant Sciences Inc.

O-188 9:55 AM Tuesday, October 20, 2020

QUINAGOLIDE VAGINAL RING FOR ENDOMETRIOSIS: RESULTS FROM THE CLINICAL PHASE 1 PROGRAM. Yu Bagger, MD, Joan-Carles Arce, MD, PhD. Ferring Pharmaceuticals Copenhagen, Denmark.

OBJECTIVE: To describe the pharmacokinetics (PK) and safety as well as changes in reproductive hormone levels, menstrual cyclicity and endometrial histology of several intravaginal doses of quinagolide, a non-ergot, selective dopamine receptor 2 agonist, being developed for the management of endometriosis.

DESIGN: Analysis of the three clinical phase 1 trials including 134 female healthy volunteers. Trial 1 was randomized, placebo-controlled and single-blind. Trial 2 was randomized, placebo-controlled and double-blind. Trial 3 was randomized and double-blind.

MATERIALS AND METHODS: Trial 1 investigated the PK of quinagolide at a single dose of 25, 50 and 75 μg intravaginal tablets and after repeated dosing (5 days) of 75 μg intravaginal and oral tablets. Trial 2 investigated the PK of quinagolide vaginal rings designed for extended release for up to 35 days with target release rates of 4.5, 9 and 13.5 μg/day. Trial 3 investigated the PK, reproductive hormone levels, menstrual cyclicity and endometrial histology with the use of quinagolide vaginal rings with target release rates of 4.5 and 13.5 μg/day, administered for two consecutive menstrual cycles. Safety was evaluated in all trials.

RESULTS: In Trial 1, intravaginal administration of 75 μg quinagolide tablets for 5 days led to maximum concentration (C_{max}) and area under the curve (AUC) values that were approximately 1.6-fold and 5-fold higher, respectively, than oral administration. Intravaginal administration circumvented first-pass metabolism. Median time to reach maximum concentration (t_{max}) was 8.5 hours with intravaginal versus 0.8 hours for oral administration. In Trial 2, quinagolide vaginal ring administration resulted in a median t_{max} of 36-48 hours across release rates. The plasma concentration of quinagolide initially increased in a dose-proportional manner to peak and then declined; trough levels remained 1-10 pg/mL for all release rates for up to 35 days. In Trial 3, repeated administration of quinagolide vaginal rings for two consecutive menstrual cycles showed consistent C_{max} and AUC between cycles for each release rate and no apparent accumulation. Furthermore, quinagolide vaginal ring had no impact on serum FSH, LH, estradiol and progesterone levels in the early follicular or mid-luteal phases. Ovulation was not affected, with confirmed presence of corpus luteum in 93% of the women after two cycles. There were no changes in menstrual cycle duration (median 25.5-28.0 days), bleeding duration (median 4.0-5.0 days), or mid-luteal phase endometrial histology (all secretory) with quinagolide vaginal ring at any of the release rates. Quinagolide vaginal rings were well tolerated. There was no apparent effect of dose or release rate on the adverse event frequency.

CONCLUSIONS: Intravaginal administration of quinagolide has a higher bioavailability than oral administration. The vaginal rings provide adequate plasma concentrations of quinagolide throughout an entire menstrual cycle lasting up to 35 days. Quinagolide vaginal rings are well tolerated and do not alter reproductive hormone levels, menstrual cyclicity or endometrial histology.

SUPPORT: Ferring Pharmaceuticals

O-189 10:10 AM Tuesday, October 20, 2020

ENDOMETRIOSIS STROMAL CELLS INDUCE BONE MARROW MESENCHYMAL STEM CELLS DIFFERENTIATION AND PD-1 EXPRESSION THROUGH PARACRINE SIGNALING. Ramanaiah Mamillapalli, PhD, Chen Peng, MD, PhD, Shutaro Habata, MD, PhD, Hugh S. Taylor, M.D. Yale University School of Medicine, New Haven, CT.

OBJECTIVE: Endometriosis is an estrogen-dependent, inflammatory disorder characterized by the growth of endometrial cells as lesions outside the uterus. Bone marrow-derived cells (BMDCs) engraft into these lesions and promote their growth. The interactions between BMDCs and resident cells in lesions are still poorly characterized. Specifically, the ability of endometrial stromal cells to induce specific cell-type differentiation of BMDCs has not been investigated. Here we investigate the role of paracrine communication in BMDC differentiation.

DESIGN: Endometrial biopsies were collected from 20 women with and 15 without endometriosis identified by laparoscopy and histologically verified; stromal cells were isolated and cultured. BMDCs were co-culturing with stromal cells to determine if endometrial cells from endometriosis affected BMDC differentiation. A murine model of endometriosis was created and the lesions were collected after 12 weeks. Western blot, qRT-PCR and immunochemical techniques were performed to measure the gene and protein expression.

MATERIALS AND METHODS: Primary endometrial stromal cells were cultured from endometrial biopsies and used for co-culture experiments with BMDCs. Total RNA and protein were extracted from cell cultures using Trizol reagent and used for qRT-PCR and western blot to analyze the gene and protein expression, respectively. Endometriosis was induced in 9-week-old female C57BL/6 mice by suturing donor uterine sections to the walls of the peritoneal cavity. A Sham control group was also created using no uterine tissue. After 12 weeks, all mice were euthanized and lesions were collected. Tissue sections from lesions were subjected to immunochemical studies for localization of T-cells as well as BMDCs that express PD-1.

RESULTS: *In-vitro* studies demonstrated that both mRNA and protein levels of vimentin (stromal cell marker), cytokeratin (epithelial cell marker) and *PD-1* (T-cell marker) were significantly increased in BMDCs co-cultured with primary stromal cells from endometriosis (ENDO) patients compared to stromal cells from normal endometrium (CNTL). Significant increases in mRNA expression for all three markers (3, 7 and 2.5 fold, respectively; $p<0.05$) were observed after 1, 3 and 6 days of co-cultures. In our *in vivo* endometriosis model we confirmed the localization of T-cells in endometriotic lesions using IHC. A 15 fold increase of PD-1 protein levels in lesions was confirmed in GFP BMDCs engrafted into endometriotic lesions. The number of GFP labeled cells that are engrafted into lesions as well as the number of BMDCs that express PD-1 were significantly higher ($p<0.05$) in endometriosis compared to controls.

CONCLUSIONS: In endometriosis local paracrine factors promote BMDCs cell differentiation into stromal, epithelial cells and immune cells. Further, stromal cells from endometriosis specifically lead to upregulation of PD-1 in bone marrow derived T-cells engrafted into endometriotic lesions, potentially suppressing immune mediated endometriosis rejection. Therapeutics to target and inhibit PD-1 may be helpful in treating endometriosis.

SUPPORT: This work was supported by the Endometriosis Foundation of America AWD0003567

O-190 10:25 AM Tuesday, October 20, 2020

ESTRADIOL IS ASSOCIATED WITH DECREASED CARDIOVASCULAR RISK COMPARED TO ETHINYLESTRADIOL WHEN CONTAINED IN COMBINED HORMONAL PREPARATIONS: IMPLICATIONS FOR THE DEVELOPMENT OF NEW ENDOMETRIOSIS THERAPIES. Sophia von Stockum, PhD, Clare Barnett, MBBS (Hons), MPH, Anja Bauerfeind, PhD, Klaas Heinemann, MD, PhD, MBA. ZEG Berlin GmbH Berlin, Germany.

OBJECTIVE: Combined estrogen-progestin preparations have a long history in women's health and are currently used for multiple indications, including the treatment of endometriosis-related symptoms. Empirically, estradiol (E2) and its ester, estradiol valerate (E2Val) carry a reduced cardiovascular risk due to their reduced impact on the hepatic system compared to the most-widely used estrogen ethinylestradiol (EE). However, robust comparative studies in pre-menopausal women are limited. A new hormonal product containing E2 in combination with the progestin norethindrone acetate (NETA) and the gonadotropin-releasing hormone receptor antagonist, relugolix, has been developed for the treatment of uterine fibroids and endometriosis. This analysis tries to quantify the cardiovascular risk of E2/E2Val-NETA in pre-menopausal women.

DESIGN: A pooled analysis of four large cohort studies assessing the risk of cardiovascular events in users of combined oral contraceptives (COCs).

MATERIALS AND METHODS: Data regarding users of COCs containing either E2/E2Val or EE$\leq$30μg were retrieved from four large prospective, controlled, observational, cohort studies in 14 European countries, US and Canada. Baseline characteristics, including reproductive, contraceptive and medical history, were summarized using descriptive statistics. Propensity score sub-classification was applied to balance baseline parameters between cohorts and time-to-event analysis of venous and arterial thromboembolic events was carried out based on the extended Cox model to calculate crude and adjusted hazard ratios (HR) including 95%-confidence intervals (CI).

RESULTS: The analysis was based on 210,000 women, who contributed 470,000 women years of exposure. The observed prevalence of prognostic factors at baseline showed typical features of US and European COC users. However, the mean age in the E2/E2Val cohort was higher compared to the EE $\leq 30\mu g$ cohort (31.7 years $\pm$9.76 and 26.1 years $\pm$7.89, respectively). A time-to-event analysis of the VTE data was carried out based on the extended Cox model. Validity of the model was demonstrated by the standardized differences summarized over strata as weighted average yielded upon PS subclassification, which were consistently <0.25 and mostly <0.1. A comparison between cohorts showed a decreased risk of venous thromboembolism in users of COCs containing E2/E2Val vs users of COCs containing EE $\leq 30\mu g$; adjusted hazard ratio: 0.49 (95% CI, 0.28-0.84). A risk reduction in the E2/E2Val cohort was also observed with regards to arterial thromboembolic events; adjusted hazard ratio: 0.26 (95% CI, 0.08-0.83).

CONCLUSIONS: Data presents a solid safety assessment of combined hormonal preparations in over 200,000 pre-menopausal women and shows a decreased cardiovascular risk of E2/E2Val when compared to low-dose EE. This provides reassurance for current users of E2/E2Val-containing COCs and opens new perspectives for the development of safe and effective endometriosis treatments, such as the recently developed product containing E2/NETA, in combination with relugolix.

SUPPORT: This analysis was supported by a grant from Myovant Sciences. Dataset is owned by ZEG Berlin GmbH.

O-191 10:40 AM Tuesday, October 20, 2020

HOW SHOULD WE MANAGE WOMEN WITH MILD, MODERATE, AND SEVERE ENDOMETRIOSIS IN LIGHT OF UNCERTAINTY ABOUT THE EFFECTIVENESS AND SAFETY OF LAPAROSCOPIC SURGERY? A COCHRANE REVIEW UPDATE TO INFORM FUTURE DEBATE AND CLINICAL PRACTICE.

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OBJECTIVE: Limited evidence regarding the surgical management of mild, moderate, and severe endometriosis is driving the substantial variation in clinical practice and differences in patient outcomes. We prepared a Cochrane review evaluating the effectiveness and safety of laparoscopic surgery for endometriosis.

DESIGN: Cochrane systematic review informing the development of clinical practice and research recommendations.

MATERIALS AND METHODS: Randomised trials evaluating laparoscopic surgery for endometriosis were included. Selection of studies, assessment of trial quality, and extraction of relevant data were performed independently by two researchers. We calculated the summary estimates and 95% confidence intervals using a random effects model.

RESULTS: Fourteen randomised trials, reporting data from 1381 women with endometriosis, were included. Laparoscopic surgery improved pregnancy rates when compared with diagnostic laparoscopy (OR 1.91; 95% CI 1.24, 2.95). Laparoscopic surgery improved overall pain, measured 12 months following surgery, when compared with diagnostic laparoscopy (MD 1.65; 95% CI 1.11, 2.19). There was no difference in reported adverse events (OR 0.95; 95% CI 0.06, 16.31). When comparing laparoscopic ablation with laparoscopic excision there was poor reporting of outcome data. When comparing conservative laparoscopic surgery with radical laparoscopic surgery in women with deep endometriosis infiltrating the rectum there was no difference in reported quality of life. Radical laparoscopic surgery was associated with more adverse events, including rectal lumen stenosis (OR 0.09; 95% CI 0.00, 1.79).

CONCLUSIONS: Laparoscopic surgery should be routinely offered to women with mild to moderate endometriosis. There is uncertainty regarding the most appropriate laparoscopic method to excise or destroy endometriotic deposits. Further research is required to evaluate the role of laparoscopic surgery in the management of severe endometriosis. Clinicians, professional societies, and patient advocacy groups should champion the routine access to laparoscopic surgery for women with mild to moderate endometriosis.

O-192 10:55 AM Tuesday, October 20, 2020

INCREASED CELLULAR SENESCENCE IN DEEP INFILTRATING ENDOMETRIOSIS.

Helena Malvezzi, MSc,[1] Camila Hernandes, PhD,[1] Bruna C. de Azevedo, PhD,[1] Carla A. Piccinato, PhD,[1] Juliana Meola, PhD,[2] Sérgio Podgaec, M.D. PhD.[1] [1]Albert Einstein Hospital, São Paulo, Brazil; [2]Universidade de São Paulo, Ribeirão Preto, Brazil.

OBJECTIVE: Endometriosis is characterized by increased inflammatory process and to be apoptosis resistant. Senescence cells are apoptosis resistant and present the senescence associated secretory phenotype (SASP). Cellular senescence is an irreversible suspension of cell proliferation process, responsible for controlling tissue growth. In endometriosis, senescence cells would be regulating cell cycle block which would favor disease maintenance and progression.

DESIGN: A cross-sectional study with biopsies of deep infiltrating endometriotic lesions and ectopic endometrium from women with (n=27) and control endometrium from women without endometriosis (n=19) in both cycle phase (secretory and proliferative).

MATERIALS AND METHODS: Biopsy tissues were prepared for senescence markers (p16 and Lamin b1) detection using immunohistochemistry technique followed by histometry to calculate antibody positive areas in the tissue. For tissue IL-17A detection, multiplex assay was used. Wilcoxon test was used for pared samples and gamma generalized linear models to evaluate groups relationship. Alfa lower than 0.05 was considered significant.

RESULTS: Deep infiltrating lesion from secretory and proliferative phase had 4.4 ($p<0.001$) and 2.82 ($p<0.001$) times more p16 expression than secretory eutopic endometrium. Also, proliferative eutopic endometrium had 3.05 ($p<0.002$) times more p16 expression than secretory eutopic endometrium. Although no difference between cycle phases was detected, lesions had less lamin b1 expression compared to eutopic endometrium ($p=0.016$). Higher concentration of IL-17A was found in the proliferative phase of the lesions ($p=0.014$) compared to proliferative eutopic endometrium and in the secretory phase of the eutopic endometrium ($p=0.014$) compared to control endometrium. IL-17A increases p16 expression in 1.04 times ($p=0.029$).

CONCLUSIONS: Deep infiltrating lesions presents more senescence markers than eutopic endometrium, as the increase in p16 expression and the depletion in lamin b1 expression. The p16 protein plays a critical role in regulating cell senescence, being a potent inhibitor of cell proliferation and lamin b1 is associated with maintaining the structure of the nuclear membrane during cell cycle processes. Our results suggest that IL-17A increases p16 expression and as there were more IL-17A and p16 in lesions compared to eutopic endometrium, we believe that IL-17A could be favoring p16 expression in deep infiltrating lesions and thus maintaining an inflammatory and senescent environment. This environment, in addition to providing a basal state of inflammation, may be causing more cells to enter senescence, favoring disease maintenance.

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O-193 9:40 AM Tuesday, October 20, 2020

COPY NUMBER LOSSES IN SPECIFIC REGIONS OF COMMON VARIATION ARE SIGNIFICANTLY MORE PREVALENT IN INFERTILITY PATIENTS COMPARED WITH A POPULATION OF DEMONSTRATED FERTILITY AND LOW FETAL WASTAGE.

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OBJECTIVE: Chromosomal microarray analysis (CMA) is a valuable standard of care for assessment of individuals with developmental disabilities and other pathological states. However, interpretation of incident copy number variants (CNV) is highly dependent upon use of prevalence data from "normal" populations. Infertility which is present in up to 15% of any population is known to be genetically heterogeneous, however such patients would typically appear in CNV databases in the "normal" population and relevant findings may go unsuspected.

DESIGN: We performed bioinformatic analysis of the variation observed in 539 consecutive women receiving services at a major US Infertility practice for the presence of potentially relevant CNV relating to their underlying condition or unsuspected genetic risks. We compared these to a population of 79 women with exceptional fertility (grand multiparas) as demonstrated by 5 or more uncomplicated term deliveries with no clinically apparent reproductive losses.

MATERIALS AND METHODS: CNV were assessed with an FDA approved CMA (Affymetrix, CytoscanDX). CNV association analysis of the entire databases of CNV segments in the "infertile" and "grand multipara" cohorts was undertaken with ParseCNV program (http://parsecnv.sourceforge.net/).

RESULTS: A typically wide range of CNV and runs of homozygosity (ROH) was observed, with many overlapping known common regions of variation and the majority predicted to be likely benign. Potential impactful rare gene findings have been reported elsewhere, including two well described recurrent pathogenic CNV observed in 3 patients each, and an appreciable number of deletions encompassing all or part of genes for known over 40 autosomal recessive conditions suggesting CNV analysis would add positively to expanded carrier screening programs.

A striking presence of genomic deletions in three regions in the "infertile" cohort (6-18%), none of which were observed in any of the "grand multiparas" (p value range: 0.02-$\leq$0.000005) We used one-sided Fisher's exact test to test for enrichment of either deletion or duplication CNVs between the "infertile" case subjects and the comparison individuals. These differential CNVs all occurred in regions of common well-known CNV of gene families on chromosomes (chr) 7, 14, and 11 (typically 12-40% prevalence range for regions; Database of Genomic Variants [DGV]; http://dgv.tcag.ca/). There was no difference in the relative occurrence of any duplications or ROH.

CONCLUSIONS: Deletions significantly differential in prevalence between these groups were observed in several regions of very common known CNV, which may have plausible link to key theories on reproductive success and evolution. The variants observed on the first two regions (chr7 & 14) involved variant transcripts of the T-cell receptor-g and -a respectively. On chromosome 11 the deletions involved the 52N1 and 52N5 families of olfactory receptor genes. Both the immune response and olfactory perceptions have been suggested to be involved with the evolution of eutherian mammalian reproduction and fertility in humans.

SUPPORT: Predictive Laboratories, Inc.

O-194 9:55 AM Tuesday, October 20, 2020

INFERTILITY AND RISK OF PREMATURE MORTALITY: A PROSPECTIVE COHORT STUDY.

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OBJECTIVE: To prospectively investigate the association between infertility and risk of premature mortality (before age 70 years).

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: We followed 103,748 women participating in the Nurses' Health Study II who attempted conception and who were free of cardiovascular disease (CVD), type 2 diabetes, and cancer at enrollment in 1989. Biennial questionnaires updated information on infertility status (defined as attempting conception for at least 12 months), pregnancies, lifestyle characteristics, and several health-related outcomes. Hazard ratios (HR) and 95% confidence intervals (CI) for the associations of infertility and underlying reasons for infertility with the risk of premature mortality were estimated using Cox proportional hazards models, adjusting for race/ethnicity, and time-varying age, body mass index, oral contraceptive use, hormone replacement use, aspirin use, family history of CVD, cigarette smoking status, physical activity, and diet quality.

RESULTS: During 28 years of follow-up, 32,464 women (31%) reported infertility and 2,327 women died before age 70, including 1,065 deaths caused by cancer and 211 by CVD. Women who experienced infertility were 20% (95% CI: 10%, 31%) more likely to die prematurely from any cause during follow-up than women who never reported infertility. This relation was largely driven by deaths from cancer (HR, 1.19; 95% CI: 1.05, 1.35). The association between infertility and all-cause mortality was stronger among women who first experienced infertility early in their reproductive life. The HR (95% CI) for all-cause mortality for women first experiencing infertility before age 26y, between ages 26 and 30y, and after age 30y were, respectively, 1.21 (1.07, 1.37), 1.19 (1.07, 1.32), and 1.08 (0.91, 1.28).

CONCLUSIONS: Our findings suggest that a history of infertility may be associated with a greater risk of premature mortality, particularly among women first experiencing infertility before age 30y. Future research is needed to confirm these novel finding.

O-195 10:10 AM Tuesday, October 20, 2020

EVALUATING THE RISK OF UNEXPLAINED INFERTILITY IN WOMEN WITH RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS.

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OBJECTIVE: The presence of infertility among women with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) remains unclear. To date, there have been no large-scale studies assessing this risk. Using a large population database, our primary objective was to examine if the risk of unexplained infertility in women of reproductive age with RA and SLE is different compared to women without these diseases. A subgroup analysis sought to assess the effects of age, ethnicity, and insurance status on this risk.

DESIGN: Cross-sectional analysis of a large healthcare database

MATERIALS AND METHODS: This study used Explorys, Inc (IBM Watson Health) a large population health database which aggregates de-identified patient data from a variety of electronic health records in multiple health systems across the United States. As such, this work is IRB exempt. This is a cross-sectional analysis that utilized data in excess of 72 million patients from the Explorys, Inc database as of February 12, 2020. We used this platform to collect data points such demographic information, diagnostic codes, laboratory studies, and drug prescriptions. Only women with unexplained infertility were included in this analysis. We identified women between 18 and 45 years of age with a diagnosis of infertility and a diagnosis of RA or SLE. A control group of women with infertility and without RA or SLE were included for comparison. Chi-squared test was used for categorical variables with $p<0.05$ being considered significant.

RESULTS: The distribution of patients for both diseases is outlined in table 1. Women with a diagnosis of RA were noted to have a higher risk of unexplained infertility ($p<0.0001$, OR 2.7, 95% CI of 2.5-3.0). Women with a diagnosis of SLE were also noted to have a higher risk of unexplained infertility ($p<0.0001$, OR 2.1, 95% CI of 1.8-2.3). Subgroup analysis indicated Asian women with RA did not have an increased risk of infertility. The presence of RA was associated with a higher risk of unexplained infertility for all other age, insurance, and ethnicity groups. SLE was associated with a higher risk for unexplained infertility for all subgroups.

TABLE 1.

	Infertility Present (n)	Infertility Absent (n)
RA	440	47750
No RA	41350	12311690
	Infertility Present (n)	Infertility Absent (n)
SLE	347	48700
No SLE	42330	12489710

CONCLUSIONS: Women with a diagnosis of RA or SLE have a higher risk of unexplained infertility compared to women who did not have RA or SLE. Future studies will elucidate the mitigating effects of ethnicity among RA patients and insurance status among SLE patients.

SUPPORT: None

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CHARACTERIZATION OF PITUITARY AND OVARIAN HORMONE CONCENTRATIONS DURING TREATMENT WITH RELUGOLIX COMBINATION THERAPY.

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OBJECTIVE: To characterize the effects of Relugolix combination therapy (Rel-CT; relugolix 40 mg, estradiol [E2] 1 mg, norethindrone acetate 0.5 mg) on pituitary (luteinizing hormone [LH] and follicle-stimulating hormone [FSH]) and ovarian (E2 and progesterone [P]) hormone concentrations, follicular growth, and endometrial thickness.

DESIGN: An open-label, single-cohort study. Healthy, premenopausal, ovulatory women (n=70) received oral administration of Rel-CT once daily for 84 days.

MATERIALS AND METHODS: Blood samples for determination of LH, FSH, E2 and P serum concentrations were collected every 3 (±1) days during the treatment and post-treatment periods. LH, FSH and P were quantified using a validated, enzyme-linked immunosorbent assay. E2 serum concentrations were quantified using a validated liquid chromatography-tandem mass spectrometry method. The size of the dominant follicle and endometrial thickness were measured by transvaginal ultrasound performed every 3 (±1) days during the treatment and post-treatment periods.

RESULTS: Relugolix, an orally active, potent, non-peptide gonadotropin-releasing hormone (GnRH) receptor antagonist, blocks endogenous GnRH from binding to GnRH receptors, preventing the release of LH and FSH from the anterior pituitary gland. Reduction in FSH minimizes follicular growth and development, with consequently lower production of E2. In the absence of an LH surge, and ovulation, the corpus luteum does not develop, resulting in decreased production of P. In the current study, during treatment with Rel-CT, mean LH concentrations were below 1.0 U/L, and FSH concentrations were suppressed, being maintained between 2 and 3 U/L, with an absence of pre-ovulatory peaks. Follicular growth was diminished, with a mean dominant follicle size consistently at approximately 6 mm. Mean (median) E2 concentrations were maintained between 32.6 and 44.5 pg/mL (30.6 and 40.1 pg/mL), comparable to concentrations in the early follicular phase of the menstrual cycle, as a result of profound suppression of ovarian E2 production and exogenous administration of E2 as part of Rel-CT. Endometrial proliferation was markedly suppressed, with mean endometrial thickness between 4 and 5 mm. Mean P concentrations remained between 1 and 1.3 nmol/L, with individual concentrations below 5 nmol/L (corresponding to 1.57 ng/mL), reflecting an absence of luteal activity. Over 84 days, Rel-CT inhibited ovulation in 100% of women.

CONCLUSIONS: Rel-CT consistently suppressed pituitary and ovarian hormone concentrations, follicular growth and endometrial thickness. The reduction in systemic E2 and progesterone concentrations is expected to minimize hormone-induced growth and proliferation of uterine fibroids and endometriosis lesions, resulting in an improvement of disease-related symptoms without adverse consequences related to a hypoestrogenic state.

SUPPORT: Myovant Sciences Inc.

O-197 10:40 AM Tuesday, October 20, 2020

CELL-LEVEL EXPRESSION OF SARS-COV-2 CELL ENTRY FACTORS IN HUMAN ENDOMETRIUM DURING THE PRECONCEPTION PERIOD.

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OBJECTIVE: ACE2 enzyme serves as SARS-CoV-2 human receptor through binding of the viral S protein and subsequent trimming of S protein between S1 and S2 units by host serine proteases as TMPRSS2, CTSB or CTSL. Here, we aim to investigate the expression of the different cell entry proteins involved in SARS-CoV-2 infection in the different cell types of the human endometrium throughout the menstrual cycle using single-cell RNA-seq (scRNAseq).

DESIGN: Gene expression patterns for SARS-CoV-2 entry molecules were analyzed by scRNAseq in a total of 73,181 endometrial single cells obtained from endometrial biopsies from 19 reproductive-age women across the full menstrual cycle (Fluidigm C1: 2,149 cells) and 10 women from the same cohort (10x: 71,032 cells). For two women, both C1 and 10x data were collected as anchors for comparison.

MATERIALS AND METHODS: After tissue dissociation, single cell capture was performed on Fluidigm C1 system (n= 2,149 cells) or Chromium 10x system (Chromium Next GEM Chip G, 10x Genomics) (n= 71,032 cells) followed by reverse-transcription, cDNA generation and library construction. Barcoded libraries were sequenced in pair-end reads on Nextseq (Illumina) for the C1 dataset or Novaseq (Illumina) for the 10x dataset . Data pre-processing, quality filtering, and statistical analyses were performed using custom Python, R, and Java scripts.

RESULTS: Expression analysis across the menstrual cycle showed no significant expression of *ACE2* in stromal or unciliated epithelial cells in any cycle phase. *TMPRSS2* was expressed more highly in glandular epithelial cells during the early proliferative phase and towards the end of the cycle. Interestingly, expression of *CTSB* and *CTSL* was observed in both stromal and epithelial cells across all phases of the menstrual cycle, with *CTSB* the more abundant of the two. All four genes were simultaneously expressed in less than 0.7% of glandular epithelial cells.

Expression analysis during the secretory phase did not detect significant expression of *ACE2* (less than 2% of epithelial or stromal cells). *TMPRSS2* showed mild expression in about 12% of unciliated epithelial cells. In contrast, *CTSB* and *CTSL*were highly expressed in ∼80% and ∼40% of cells during the mid-late secretory phase, aligning with what we detected via Fluidigm. In addition, while *CTSB* was highly expressed in both epithelial and stromal cells, *CTSL* was more highly expressed in stromal cells across the menstrual cycle.

CONCLUSIONS: Percentages of endometrial cells expressing *ACE2, TMPRSS2, CTSB,* or *CTSL* were <2%, ∼12%, ∼80%, and ∼40%, respectively, with <0.7% of cells expressing all four. This finding implies low efficiency of SARS-CoV-2 infection in the endometrium before embryo implantation, providing information to assess preconception endometrial infection risk in COVID-19 asymptomatic carriers.

FV & WW contributed equally.

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HIGH PREVALENCE OF MEASLES NON-IMMUNITY IN REPRODUCTIVE AGE WOMEN.

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OBJECTIVE: To determine if the percentage of reproductive age women who are immune to measles is at or above the level required for herd immunity (95%) and to evaluate the patient characteristics and demographics that correlate with measles non-immunity.

DESIGN: Retrospective case control.

MATERIALS AND METHODS: A retrospective chart review of women seeking preconception and fertility care who underwent serum testing for measles, rubella, and/or varicella immunity between March 1, 2018 and May 1, 2020 were included in the analysis. Serum tests resulted as either immune, non-immune, or equivocal, as determined by serum IgG titer levels for the respective diseases. Women with equivocal results underwent further testing to quantitate titers and determine immunity. Equivocal results that did not have follow up testing were excluded from the final analysis. Clinical characteristics were collected on the women including age, BMI, parity, race, and ethnicity. Students t test and chi square tests were used for continuous and categorical outcomes. Multivariable logistic regression was performed to control for confounding. A post hoc power analysis was performed.

RESULTS: 3,255 women were included in the study. Of the 1,396 women tested for measles antibodies (n=1396), 20.1% were considered non-immune

and 79.9% were immune. Of the 2,654 women tested for rubella antibodies, only 3.5% were non-immune, while 93.7% were immune and 2.8% were equivocal. Of those tested for varicella (n=3023), 7.5% were non-immune, 89.2% were immune and 3.2% were equivocal. Women who were considered non-immune to measles were younger and had a higher body mass index (BMI) after adjusting for confounders. More specifically, women born after 1984 and obese women were more likely to be measles non-immune.

	Immune	Non-Immune	P-Value
Age (mean years +- SD)	35.5 ± 4.31	34.9 ± 4.49	0.035
Birth Year <1985	82.4% (n=612)	17.6% (n=131)	0.016
Birth Year >/=1985	77.2% (n=504)	22.8% (n=149)	
BMI (mean kg/m^2 +- SD)	26.4 ± 6.59	27.7 ± 7.28	0.009
Non-obese (BMI <30)	81.1% (n=215)	18.9% (n=71)	0.028
Obese (BMI >/=30)	75.2% (n=976)	24.8% (n=248)	

CONCLUSIONS: Among women seeking preconception and fertility care, the seroprevalence of measles immunity is only 79.9%, which is significantly lower than that required for herd immunity (95%). Interestingly, low IgG titers for measles are associated with a younger age and higher BMI. Additional testing to correlate IgG titers with clinical immunity needs to be performed. In the meantime, and given this high prevalence, measles immunity should be included in the preconception evaluation.

FERTILITY PRESERVATION

O-199 9:40 AM Tuesday, October 20, 2020

MAJORITY OF WOMEN UNDERGOING ELECTIVE OOCYTE CRYOPRESERVATION DO NOT ATTAIN OPTIMAL NUMBER OF OOCYTES CRYOPRESERVED FOR REASONABLE LIKELIHOOD OF FUTURE LIVE BIRTH. Amy Wijekoon, MD, Heather G. Huddleston, MD, Marcelle I. Cedars, MD, Eleni Greenwood Jaswa, MD, MSc. University of California San Francisco San Francisco, CA.

OBJECTIVE: This study aimed to evaluate the frequency with which women undergoing planned oocyte cryopreservation (OC) ultimately banked an optimal quantity of eggs.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Subjects included 999 women undergoing planned OC between January 2012 and February 2020. The primary outcome of optimal number of oocytes cryopreserved (OOC) was defined as ≥80% probability of at least one live birth (LB) using a published model accounting for age (Goldman et al., 2017). Baseline factors were compared between those with and without OOC using Student's t-test, Mann-Whitney U-test, and Chi squared test as appropriate. Logistic regression modeling identified predictors for achieving OOC, controlling for age, race, antral follicle count (AFC), anti-mullerian hormone (AMH), insurance status, and total cycles.

RESULTS: 415 women undergoing planned OC (42%) achieved OOC after an average of 1.5 cycles. The majority of women ≤35 years achieved OOC (63%); however, few women ages 39-40 years, and no women ≥41 years, achieved OOC (Table 1). Based on median oocytes frozen, the majority of women ≤38 years achieved >50% probability of at least one LB; however, at >38 years, women achieved much lower chances of LB (Table 1). Average age (34 v 37 years, p<0.001), AFC (12 v 7, p<0.01), AMH (3.1 v 1.5 ng/mL, p<0.01), and total number of cycles (1.5 v 1.4, p=0.01) differed between the cohorts that did and did not achieve OOC, respectively. In the multivariate logistic regression, age (aOR 0.69, p<0.001), AFC (aOR 1.05, p<0.01), AMH (aOR 1.50, p<0.01), total number of cycles (aOR 2.15, p<0.01), and Asian (aOR 0.54, p=0.01) or other non-White (aOR 0.60, p=0.02) race were independent predictors of the primary outcome. Insurance coverage was not associated with odds of achieving OOC.

CONCLUSIONS: The majority of women (58%) who undergo planned OC do not bank sufficient eggs to yield an 80% chance of LB. Ovarian reserve markers and age predicted failure to achieve OOC and should be weighed when counseling. Asian/other non-white races had lower adjusted odds of achieving OOC compared to white race patients. Future studies should investigate the cause of these racial differences in planned OC outcomes.

TABLE 1. Cycle outcomes by age group

	Age (years) at first planned OC								
	≤35	36	37	38	39	40	41	42	≥43
n	*472*	*140*	*131*	*98*	*63*	*39*	*30*	*15*	*11*
Optimal # oocytes for 80% probability of one LB	14	18	23	27	32	44	55	70	>100
Median # oocytes frozen	**17**	**16**	**15**	**14**	**12**	**11**	**16**	**11**	**9**
Probability of one LB *%*	*86*	*77*	*65*	*56*	*45*	*33*	*36*	*22*	*12*
# of patients who achieved OOC	**298**	**64**	**31**	**16**	**5**	**1**	**0**	**0**	**0**
%	*63*	*46*	*24*	*16*	*7*	*3*	*0*	*0*	*0*
Mean # cycles to achieve OOC	**1.4**	**1.7**	**1.6**	**1.5**	**1.8**	**4**	-	-	-
SD	*0.7*	*0.9*	*0.8*	*0.7*	*0.8*	*0*			
Mean # cycles in those who did not achieve OOC	**1.3**	**1.4**	**1.5**	**1.4**	**1.4**	**1.4**	**1.6**	**1.8**	**2.1**
SD	*0.7*	*0.7*	*0.8*	*0.7*	*0.7*	*1.1*	*0.9*	*1.4*	*1.0*

References: Goldman RH, Racowsky C, Farland LV, Munné S, Ribustello L, Fox JH. Predicting the likelihood of live birth for elective oocyte cryopreservation: a counseling tool for physicians and patients. *Hum Reprod*. 2017;32(4):853-859.

SUPPORT: None

O-200 9:55 AM Tuesday, October 20, 2020

PLANNED OOCYTE CYROPRESERVATION – 10-15 YEAR FOLLOW-UP: RETURN RATES AND CYCLE OUTCOMES. Jennifer K. Blakemore, MD,[1] James A. Grifo, MD, PhD,[2] Shannon Devore, MD,[1] Brooke Hodes-Wertz, MD, MPH,[3] Alan S. Berkeley, MD[4] [1]NYU Langone School of Medicine, New York, NY; [2]NYU Langone Prelude Fertility Center, New York, NY; [3]NYU Langone Prelude Fertility Center, New York, NJ; [4]New York University School of Medicine, New York, NY.

OBJECTIVE: Planned oocyte cryopreservation (POC) has increased exponentially since the experimental label on egg freezing was lifted in 2012[1]. Given the relatively recent change, many questions remain concerning long term oocyte utilization. Our objective was to evaluate the outcomes of POC patients most likely to have a final disposition.

DESIGN: Retrospective cohort study of all patients who underwent at least one cycle of POC between 1/2005 and 12/2009.

MATERIALS AND METHODS: All patients who underwent POC in the study time-period were reviewed. Patients who 1) only had a POC consult, 2) started a cycle but did not get retrieved or 3) underwent OC for medical indications were excluded. Primary outcome was disposition of oocytes at 10-15 years. Secondary outcomes included thaw types, lab outcomes and live-birth (LB) rates. **Outcomes/variables treated per patient.**

RESULTS: 231 pts with 280 cycles were included. The mean age at 1st retrieval was 38.2 years (range 23-45), with 90% of patients between of 35-42 years. Utilization of POC consistently increased over the 5 years. A total of 3250 oocytes were retrieved, with an average of 10 M2/retrieval. To date, 88 patients (38.1%) have thawed their oocytes, 109 (47.2%) remain in storage, 27 (11.7%) discarded and 7 (3.0%) transported elsewhere. The return rate (patients who thawed oocytes) was similar by SART age group: 40.0% in <35, 44.1% in 35-37, 36.3% in 38-40, 33.3% in 41-42, and 25.0% in >42 year olds. The mean age of discarding oocytes was 47.4 years (range 40-57) with rates by SART age group: 6.7% in <35, 8.8% in 35-37, 12.4% in 38-40, 14.8% in 41-42, and 25.0% in >42 years old. Rates of continued storage were also similar by SART age group: 46.7% in >35, 44.1% in 35-37, 48.7% in 38-40, 48.2% in 41-42, and 50.0% in >42 year olds. Of the 88 patients who thawed oocytes, the mean age at time of thaw was 43.9 years (range 38-50) with mean of 5.9 years frozen (range 1-12). 9 patients (10.2%) thawed for secondary infertility. 62.5% of patients created embryos with a partner, 37.5% with donor sperm. On average, 14.3 oocytes were thawed/patient, with 74.2% survival (range 0-100%) and an mean fertilization rate of 68.8% of surviving oocytes. 39/88 patients (44.3%)

planned a fresh transfer (ET). 36/39 had at least 1 embryo for fresh ET and 11 patients had a total of 14 babies. 49/88 patients (55.7%) planned for PGT-A with a mean of 4.2 embryos biopsied (range 0-14) and euploidy rate of 28.9%. 17 patients (34.7%) had all aneuploidy or no embryos biopsied. 24 patients underwent a total of 36 single euploid ET with 18 LBs from 16 patients. Notably, 8 PGT-A patients have a euploid embryo but no ET yet which will affect the future cumulative pregnancy rate. Overall, 80 thaw patients had a final outcome: 20 had nothing for ET (arrested/aneuploid); of the 60 who had at least one ET, 27 had a total of 32 babies - for a LB rate of 33.8%.

CONCLUSIONS: This is the first study to report actual final outcomes useful for patient counseling: a utilization rate of 38.1% and a "no use" rate of 58.9% similar across age groups. Further studies with larger cohorts are needed. Whether newer patients are epidemiologically the same as this cohort remains to be seen.

References

1. Cobo A, Garcia-Velasco JA, Coello A, Domingo J, Pellicer A, Remohi J. Oocyte vitrification as an efficient option for elective fertility preservation. Fertility and Sterility. 2016; 105:755-764.

SUPPORT: None.

O-201 10:10 AM Tuesday, October 20, 2020

PREDICTING THE PROBABILITY OF HAVING ONE EUPLOID BLASTOCYST IN ELECTIVE OOCYTE CRYOPRESERVATION CYCLES: A COUNSELING RESOURSE.

Patrizia Rubino, MS,[1] Luca Pagliardini, Bs,[2] Eric Urcia, MS,[3] Charlotte Khoury, MS,[4] John Wilcox, MD, FACOG,[1] Bradford Kolb, MD, FACOG,[1] Jeffrey R. Nelson, DO FACOOG,[1] John M. Norian, MD FACOG,[1] Robert Boostanfar, MD FACOG,[3] Daniel A. Potter, MD FACOG,[4] Tih Tan, MS[1] [1]HRC Pasadena, Pasadena, CA; [2]IRCCS San Raffaele Scientific Institute, Milano, Italy; [3]HRC Encino, Encino, CA; [4]HRC Newport Beach, Newport Beach, CA.

OBJECTIVE: Women selecting elective fertility preservation (EFP) often ask about the 'ideal' number of oocytes to store for future use. As preimplatation genetic testing (PGT) becomes more popular, many couples may request PGT for their egg thaw cycles. However, current predictive models do not take PGT into consideration, when considering the number of oocytes needed to freeze for a succesful outcome. The purpose of the present study was to provide an evidence-based tool to counsel patients on the ideal number of oocytes to freeze in order to have at least one euploid blastocyst. Additional analyses on frozen egg donor cycles is also provided.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The data from 186 cycles (Jan 2017 to Dec 2018) with vitrified/warmed oocytes were retrospectively analyzed. Only cycles with PGT performed on all available blastocysts were included. A sensitivity analysis on the probability to obtain at least one euploid blastocyst (positive result) in relation to the number of thawed oocytes was conducted. Patients were categorized into four groups according to their age at freezing: egg donors (n=52), < 36 (n=54), between 36 and 39 (n=50), >39 (n=30). All donors were from an in-house program. The sliding window method was used to calculate the probability of a positive result for different numbers of thawed oocytes. The dimension of the window was 5 oocytes and was centered on the number of thawed oocytes to test.

RESULTS: The mean age of the women was 33.0 ± 6.6 (min: 23; max: 47). The minimum number of thawed oocytes was 1 while the maximum was 65 (median [IQR]: 11 [7-17]). A total of 2832 oocytes were thawed, 2464 survived (87.0%) 1783 fertilized (72.3%) and 777 (43.6%) reached the blastocyst stage (blastulation rate for fresh cycles in the same study period: 62.5% p<0.01). The number of thawed oocytes needed to obtain 90% probability of a positive result for donors and women with age <36 was 9 and 12, respectively. For the other age groups no number of thawed oocytes guaranteed a 90% probability of a positive result. The threshold to reach the positive result with a probability of 80% was also evaluated: 5, 11 and 14 oocytes were needed, respectively, for the donor, <36 and 36-39 age groups. The group with age >39 did not reach a 80% probability of a positive result with any number of thawed oocytes. Finally, the best result achievable for each age groups was analyzed: for donors a probability of 100% required 11 oocytes, for the <36 group a probability of 100% required 12 oocytes, for the 36-39 group a probability of 89% required 15 oocytes and for the >39 group a probability of 60% required 15 oocytes.

CONCLUSIONS: The number of oocytes needed to obtain at least 1 euploid blastocyst in PGT cycles with frozen oocytes was higher than the number that the models predicts for fresh oocytes (1). In agreement with previous studies (2), our cryopreserved oocytes showed a significantly lower blastulation rate compared with our fresh oocytes possibly explaining our findings. Data on PGT in egg frozen cycles are minimal in the literature and our results may be used to provide counseling for women desiring EFP.

References

1. A Novel Predictive Model to Estimate the Number of Mature Oocytes Required for Obtaining at Least One Euploid Blastocyst for Transfer in Couples UndergoingÂ in vitroÂ Fertilization/Intracytoplasmic Sperm Injection: The ART Calculator

Sandro C. Esteves,Â José F. Carvalho,Â Fabiola C. Bento, andÂ Jonathan Santos, The POSEIDON Group

Front Endocrinol (Lausanne). 2019; 10: 99.

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2. Â Â Â Â Long-term Cryopreservation of Human Oocytes Does Not Increase Embryonic Aneuploidy

Kara N GoldmanÂ ,Â Yael KramerÂ ,Â Brooke Hodes-WertzÂ ,Â Nicole NoyesÂ ,Â Caroline McCaffreyÂ ,Â Jamie A GrifoÂ

Fertil Steril 2015 Mar;103(3):662-8.

SUPPORT: none

O-202 10:25 AM Tuesday, October 20, 2020

SOCIO-DEMOGRAPHIC DISPARITIES IN UTILIZATION OF FERTILITY SERVICES AMONG REPRODUCTIVE AGE WOMEN DIAGNOSED WITH CANCER IN THE US: A SECONDARY ANALYSIS OF THE 2011-2017 NATIONAL SURVEY FOR FAMILY GROWTH (NSFG).

Paxton E. Voigt, BA,[1] Jesse Benjamin Persily, BA,[2] Sameer Thakker, BA,[1] Jennifer K. Blakemore, MD,[3] Frederick L. Licciardi, M.D.,[4] Bobby B. Najari, MD MSc[2] [1]NYU Langone School of Medicine, New York, NY; [2]New York University School of Medicine, New York, NY; [3]NYU Langone Prelude Fertility Center, New York, NY; [4]NYU Langone Health, New York, NY.

OBJECTIVE: Previous studies have shown disparities in access to fertility services (FS) in women diagnosed with cancer on local and regional levels[1]. We sought to investigate the relationship between socio-demographic factors and use of FS on a national level among reproductive age women diagnosed with cancer in the US.

DESIGN: Secondary analysis of the 2011-2017 waves of the NSFG.

MATERIALS AND METHODS: We used the provided sample weights and the complex sample analysis required by the NSFG survey design. All women who indicated a cancer diagnosis were included. Women who sought FS before their cancer diagnosis were excluded. Women who sought FS any time after their cancer diagnosis were compared to women who never sought FS after their diagnosis. Comparisons included demographic and healthcare utilization characteristics. Statistical analyses included multivariate logistic regression, with $p < 0.05$ considered statistically significant.

RESULTS: 580 respondents reported a history of cancer. 35 (6.03%) accessed FS before their cancer diagnosis and were excluded from analysis, leaving 545 women included for analysis. The average age of the sample population was 35.1 years old. 76% identified as Non-Hispanic White, 11.3% as Hispanic, 8.1% as Black and 4.6% as Non-Hispanic Other. The average income was 256.8% of the poverty level. The majority of respondents self-identified as Protestants (53.8%), followed by non-religious (23.5%). Additionally, the majority were married (43.9%) and had at least attended some college (61.5%). 43 women (7.41%) accessed FS after their cancer diagnosis and 502 (86.6%) never accessed FS. Using the NSFG sample weights, this equates to a population of 161,500.7 and 1,811,955.3, respectively. In multivariate analysis, socioeconomic status, marital status, and race were found to be statistically significant predictors for utilizing FS following a cancer diagnosis. Women of higher socioeconomic status were more likely to pursue FS (OR 1.00, CI 0.91-1.09, p< 0.001). Women who were married were more likely than those who were divorced, separated (OR 0.18, CI 0.07-0.049, p < 0.001) or never married (OR 0.16, CI 1.03-1.10, p<0.001) to pursue FS. Hispanic (OR 0.185, CI 0.013-2.547 p=0.015) and Non-Hispanic Other (OR 0.323, CI 0.056-1.868, p<0.015) were less likely to utilize FS. Age (p=0.943), religion (p=0.137) and education (p=0.814) were not found to be statistically significant predictors of accessing FS. Interestingly, having insurance (p=0.380), having a usual place to access healthcare (p=0.700) and good self-perceived health status (p=0.907) were not statistically significant predictors of FS use.

CONCLUSIONS: In this nationally representative cohort of reproductive age women diagnosed with cancer, there were socioeconomic and racial differences between those who did and did not utilize FS. This difference did not

appear to be due to insurance coverage or access to healthcare. While expanding insurance coverage is necessary to ensure equal FS opportunity to all, further studies are needed to ensure socioeconomic and racial disparities are addressed.

References: Letourneau, J.M., et al., *Racial, socioeconomic, and demographic disparities in access to fertility preservation in young women diagnosed with cancer.* Cancer, 2012. 118(18): p. 4579-88.

O-203 10:40 AM Tuesday, October 20, 2020

THE USE OF OOCYTE CRYOPRESERVATION (OC) FOR FERTILITY PRESERVATION (FP) IN GIRLS WITH SEX CHROMOSOME DISORDERS (SCD): A CASE SERIES DESCRIBING OUTCOMES.

Rachel A. Martel, BA,[1] Jennifer K. Blakemore, MD,[2] Mary Elizabeth Fino, MD[2] [1]NYU Grossman School of Medicine, Manhattan, NY; [2]NYU Langone Prelude Fertility Center, New York, NY.

OBJECTIVE: Women with SCD, such as Turner Syndrome, will likely experience an accelerated decline of ovarian reserve[1], and may therefore pursue FP with OC in adolescence or young adulthood (AYA). We sought to characterize the outcomes of AYA patients with SCD after consultation.

DESIGN: Retrospective case series of all AYA (<25 years) patients (pts) with SCD seen for OC consultation at a university based fertility center from 2011-2019.

MATERIALS AND METHODS: All AYA pts seen for consult in the study time period were reviewed. Only those with a SCD were included. Primary outcomes were pt age, SCD, number who attempted OC, number of FP cycles attempted, and cycle outcomes. Statistics included multiple logistic regression with $p<0.05$ considered significant.

RESULTS: 22 pts were included for analysis: 16 with Turner Syndrome (TS), 5 with Turner Syndrome Mosaicism (TSM) and 1 with 47XXX. Median age at consult was 14 (range 8-21). 14 (64%) pts elected for OC: 8 TS, 5 TSM, and 1 47XXX who pursued a total of 31 OC cycles. Reasons for not undergoing OC after consult included lack of menarche or elevated FSH. Table 1 shows cycle outcomes. Of the 14 pts who attempted OC, 10 underwent retrieval and 9 had oocytes successfully frozen. 7 pts (50%) underwent >1 cycle and 6 (43%) had ≥1 cancellation. 3/3 pts who pursued cycles after 1st cancellation never got to retrieval. Looking at potential clinical predictors: age, SCD type, and FSH at cycle start did not predict ability to freeze M2s or cycle cancellation. Notably, there was a wide range of FSH, with only 1 pt with a high level and 4 with an FSH <1mIU/mL. Of the AMH data available, all pts >1ng/mL froze M2s. Only pt #10 returned after OC: at age 21 with a partner, and attempted 4 cycles of ovulation induction and 2 cycles of IVF. All 6 cycles were cancelled for low response, and her oocytes remain frozen.

CONCLUSIONS: AYA pts with SCD have a high risk of poor response and cycle cancelation but the majority froze M2s. OC offers an important option to have genetic offspring but setting expectations is important. A larger sample size is needed to evaluate possible clinical predictors of success.

References: 1. Oktay K, Bedoschi G, Berkowitz K, et al. Fertility preservation in women with Turner syndrome: a comprehensive review and practical guidelines. *Journal of Pediatric and Adolescent Gynecology.* 2016;*29*(5): 409-416.

SUPPORT: none

O-204 10:55 AM Tuesday, October 20, 2020

OOCYTE CRYOPRESERVATION VERSUS OVARIAN TISSUE CRYOPRESERVATION AS FERTILITY PRESERVATION FOR ADULT WOMEN UNDERGOING GONADOTOXIC THERAPY: A COST-EFFECTIVENESS ANALYSIS.

Esther H. Chung, MD,[1] Stephanie L. Lim, MD,[1] Haley A. Moss, MD, MBA,[2] Kelly S. Acharya, MD[3] [1]Duke University Medical Center, Durham, NC; [2]Division of Gynecologic Oncology, Duke University Medical Center, Durham, NC; [3]Division of Reproductive Endocrinology and Infertility, Duke University Medical Center, Durham, NC.

OBJECTIVE: Until recently, fertility preservation for adult women facing cancer diagnoses and gonadotoxic therapy was limited to mature oocyte cryopreservation (OC) or embryo cryopreservation. In December 2019, the American Society for Reproductive Medicine designated ovarian tissue cryopreservation (OTC) as no longer experimental. While indications for and the populations opting for each of these treatments often differ, the choice between OC or OTC (or both) will arise as OTC becomes more commonplace. This study's objective was to compare the cost-effectiveness of OC versus OTC for fertility preservation in adult oncofertility patients. No such cost analysis has been performed in this population to date.

DESIGN: Cost-effectiveness study.

MATERIALS AND METHODS: A decision analytic cost-effectiveness model was designed from the payer perspective to compare two strategies: (1) mature oocyte cryopreservation (OC); (2) ovarian tissue cryopreservation (OTC). All clinical costs and probabilities were abstracted from the literature. The cost of each strategy was calculated as average payer costs and included costs of oocyte cryopreservation prior to chemotherapy, thaw and fertilization cycles, frozen embryo transfers, laparoscopic oophorectomy, tissue processing, and robotic transplantation, among others. Effectiveness was quantified as the percentage of patients who achieved a live birth, with secondary effectiveness as the percentage of patients who achieved a clinical pregnancy. Incremental cost-effectiveness ratios (ICERs) were determined to establish cost-effectiveness, and sensitivity analyses were run to assess for variations in costs and clinical probabilities.

RESULTS: The base case cost of each strategy was: OC $16,588 and OTC $10,032. OC had an effectiveness of 1.6% and OTC an effectiveness of 1.0% at achieving a live birth. OC was more costly but more effective than OTC, with an ICER of $1,163,954 per additional live birth when compared to OTC. In the secondary analysis, OC had an ICER of $1,434,989 per additional clinical pregnancy compared to OTC. In a sensitivity analysis of utilization of cryopreserved oocytes or ovarian tissue, OC is less expensive and more effective when the utilization rate is 63% or higher. In another sensitivity analysis of the cost of oocyte cryopreservation prior to chemotherapy, OC is less expensive and more effective when the cost is less than $8,100.

CONCLUSIONS: Given current pricing and utilization rates, OC is more effective but markedly more costly than OTC, with an ICER of $1,163,954 per additional live birth. However, OC becomes cost-saving with increased utilization or when the cost of oocyte cryopreservation prior to chemotherapy is much lower than the current average cost. These findings indicate that lowering the high entry cost of OC and increasing its utilization can significantly impact its overall cost-effectiveness.

SUPPORT: None

TABLE 1. OC cycle outcomes in AYA patients with SCD.

Pt ID	Age (yrs) at 1st Cycle	SCD	E2 (pg/mL) / FSH (mIU/mL) at 1st cycle	AMH (ng/mL)	No. OC Attempts	No. Retrievals	Total Oocytes Retrieved / Frozen	M2 / M1 / GV Oocytes Frzn
1	13	TS	38/5.2	2.99	1	1	14 / 14	12 / 2 / 0
2	14	TSM	41/0.4	<0.16	1	1	4 / 4	2 / 1 / 1
3	14	TS	27/4.5	2.08	1	1	21 / 21	16 / 3 / 2
4	14	TSM	23/20.6	0.03	3	0	0	0
5	15	TSM	23/3.9	na	2	0	0	0
6	15	TSM	30/0.2	na	1	1	15 / 15	15 / 0 / 0
7	15	TS	109/1.8	<0.003	1	0	0	0
8	16	TS	<20/0.5	1.63	3	2	19 / 18	8 / 6 / 4
9	16	47XXX	44/3.3	1.04	2	2	22 / 18	15 / 1 / 2
10	17	TS	49/1.1	na	9	4	3 / 3	0 / 3 / 0
11	18	TS	35/<0.1	na	2	0	0	0
12	21	TS	80/6.5	2.6	1	1	22 / 21	16 / 13 / 2
13	21	TSM	21/9.3	<0.03	3	2	2 / 0	0
14	21	TS	42/5.4	5.34	1	1	19 / 19	14 / 0 / 5
Mean	Median 15.5				2.2	1.1	Median 9 / 9	6.8 / 1.4 / 1.4

O-205 9:40 AM Tuesday, October 20, 2020

QUALITY-OF-LIFE IMPROVEMENT WITH RELUGOLIX COMBINATION THERAPY IN PATIENTS WITH HEAVY MENSTRUAL BLEEDING ASSOCIATED WITH UTERINE FIBROIDS: RESULTS FROM THE LIBERTY PHASE 3 PROGRAM. Ayman Al-Hendy, MD, PhD,[1] Elizabeth A. Stewart, MD,[2] Roberta Venturella, MD, PhD,[3] Alfred Poindexter III, MD,[4] Claudio Villarroel, MD,[5] Jennifer Kang, MS, MPH,[6] Rachel B. Wagman, MD,[7] Elke Hunsche, PhD,[8] Andrea S. Lukes, MD, MHSc[9] [1]Department of Surgery, University of Illinois at Chicago, Chicago, IL; [2]Mayo Clinic Department of OB/GYN, Reproductive Endocrinology and Infertility, Rochester, MN; [3]Magna Graecia University of Catanzaro, Catanzaro, Italy; [4]Advances In Health, Houston, TX; [5]Institute for Mother and Child Research (IDIMI), Faculty of Medicine, University of Chile, Santiago, Chile; [6]Myovant Sciences, Inc., Brisbane, CA; [7]Myovant Sciences Inc., Brisbane, CA; [8]Myovant Sciences GmbH, Basel, Switzerland; [9]Carolina Women's Research and Wellness Center, Durham, NC.

OBJECTIVE: To evaluate the effect of Relugolix combination therapy (Rel-CT) on Quality of Life (QoL) using the Uterine Fibroid Symptom Health-Related QoL (UFS-QoL) questionnaire, an instrument developed to assess symptom severity (SS) and health-related QoL (HRQoL) in women with uterine fibroids (UF).

DESIGN: LIBERTY 1 and LIBERTY 2 were Phase 3, multinational, randomized, double-blind, placebo-controlled studies that evaluated the effect of Rel-CT (once-daily relugolix 40 mg, estradiol 1 mg, norethindrone acetate 0.5 mg) on heavy menstrual bleeding (HMB). Since UF-associated symptoms frequently impact women's daily activities and emotional wellbeing, assessments of SS, overall HRQoL as well as HrQoL subscales were secondary endpoints in the studies.

MATERIALS AND METHODS: Patients completed the UFS-QoL at baseline, Week 12, and Week 24. Changes from baseline to Week 24 in the UFS-QoL SS and HRQoL scale scores and HRQoL subscale scores (activities, concern, energy/mood, control, self-consciousness, sexual function) were assessed in pooled data from LIBERTY 1 and 2. Least-squares mean changes in UFS-QoL SS scale and HRQoL (sub)scale scores were compared between the Rel-CT and placebo groups, using a repeated measures mixed-effects model, with treatment, visit, region, baseline menstrual blood loss (MBL) volume, and treatment by visit interaction as fixed effects. Higher UFS-QoL SS scores reflect more severe symptoms; higher HRQoL (sub) scores indicate better QoL. Contribution of changes in subscale scores to the HRQoL total score change was also assessed.

RESULTS: In total, 253 patients were randomized to Rel-CT and 256 patients to placebo (modified intent-to-treat population). At baseline, mean (SD) MBL volume was 243 (183) and 215 (127) mL, respectively, and mean (SD) UF volume 73 (127) and 73 (123) cm^3, respectively; 48% vs 54% of patients on Rel-CT vs placebo were African American. UFS-QoL SS was reduced with Rel-CT from a mean (SE) of 57.0 (1.4) at baseline to 22.4 (1.6) at Week 24, compared with placebo from 59.6 (1.4) at baseline to 46.9 (1.6) at Week 24; the between-treatment difference (Rel-CT vs placebo) in change scores (–21.4) was statistically significant ($p<0.0001$). Total HRQoL improved significantly ($p<0.0001$) with Rel-CT vs placebo (difference: 24.5): from 38.3 (1.4) at baseline to 76.6 (1.7) at Week 24 with Rel-CT compared with placebo from 35.7 (1.4) at baseline to 48.2 (1.7) at Week 24. All HRQoL subscales improved significantly ($p<0.0001$) with Rel-CT vs placebo, with between-treatment differences: concern 34.9; control 17.9; activities 28.2; energy/mood 21.0; self-consciousness 22.5; sexual function 17.2. Changes in all subscales contributed to improvement in total HRQoL score, with the activities and concern subscales having the largest impact.

CONCLUSIONS: Improvements in MBL, pain, and anemia observed with Rel-CT are associated with significant reductions in symptom severity and improvements in QoL for women with HMB associated with UF. Rel-CT improved many different aspects of QoL, including daily activities, emotional wellbeing, and sexual life.

SUPPORT: Myovant Sciences Inc.

O-206 9:55 AM Tuesday, October 20, 2020

RELUGOLIX COMBINATION THERAPY SIGNIFICANTLY REDUCED MENSTRUAL BLOOD LOSS WITH FIRST TREATMENT CYCLE IN WOMEN WITH HEAVY MENSTRUAL BLEEDING ASSOCIATED WITH UTERINE FIBROIDS: RESULTS FROM THE LIBERTY PHASE 3 PROGRAM. Roberta Venturella, MD, PhD,[1] Ayman Al-Hendy, MD, PhD,[2] Andrea S. Lukes, MD, MHSc,[3] Jennifer Kang, MS, MPH,[4] Laura McKain, MD,[4] Elizabeth A. Stewart, MD[5] [1]Magna Graecia University of Catanzaro, Catanzaro, Italy; [2]Department of Surgery, University of Illinois at Chicago, Chicago, IL; [3]Carolina Women's Research and Wellness Center, Durham, NC; [4]Myovant Sciences, Inc., Brisbane, CA; [5]Mayo Clinic Department of OB/GYN, Reproductive Endocrinology and Infertility, Rochester, MN.

OBJECTIVE: To evaluate the time to treatment response with once-daily Relugolix combination therapy (Rel-CT), assessed by decrease in menstrual blood loss (MBL) volume observed in the Phase 3 LIBERTY studies.

DESIGN: LIBERTY 1 and LIBERTY 2 were multinational, randomized, double-blind, placebo-controlled studies that evaluated effect of Rel-CT (relugolix 40 mg [an oral gonadotropin-releasing hormone receptor antagonist], estradiol 1 mg, norethindrone acetate 0.5 mg) on heavy menstrual bleeding associated with uterine fibroids (UF). Reduction in MBL volume was a predefined secondary endpoint.

MATERIALS AND METHODS: Premenopausal women (age 18–50 years) with ultrasound-confirmed UF and MBL $\geq$80 mL per cycle (assessed by the alkaline hematin method) were randomized 1:1:1 to Rel-CT (n=254), Delayed Rel-CT (relugolix 40 mg monotherapy for 12 weeks followed by Rel-CT for 12 weeks, n=259), or placebo (n=257) for 24 weeks. Treatment response was assessed by measurement of MBL volume using monthly collections of feminine products and subsequent alkaline hematin extraction. The primary endpoint was defined as an MBL volume <80 mL and a reduction in MBL volume $\geq$50% from baseline. Pooled results from the LIBERTY 1 and 2 studies in the modified intent-to-treat population for Rel-CT (n=253) and placebo (n=256) groups are presented. No notable differences were observed between Rel-CT and Delayed Rel-CT groups. The mean percent changes in MBL volumes from baseline were compared using the mixed-effects model, and responder rates were compared using the stratified Cochran–Mantel–Haenszel test.

RESULTS: The enrolled women had a mean age of 42.1 years, mean body mass index of 31.5 kg/m^2, mean uterine volume of 408 cm^3, and mean largest fibroid volume of 78 cm^3. Mean (standard deviation) baseline MBL volume was 228.8 (154.3) mL. Approximately half of patients were Black or African American; 76% were from North America. In the Rel-CT group, a significantly greater mean percent reduction of 52.4% in MBL volume was observed in the first menstrual cycle compared with 14.7% for placebo ($p<0.0001$). By the second menstrual cycle, the reduction in MBL volume was 80.2% with Rel-CT compared with 11.6% for placebo ($p<0.0001$). The improvement was sustained through end of the study (24 weeks), at which point the observed mean reduction in MBL volume in the Rel-CT group was 84.7%, with a treatment difference from placebo of 65.2% ($p<0.0001$). Moreover, 72.3% of women met the primary endpoint by reaching both an MBL volume <80 mL and a reduction in MBL of at least 50% from baseline. The differences in the proportion of patients meeting the primary endpoint were statistically significant and clinically meaningful between the pooled Rel-CT and placebo groups from the Week 4 visit through to the end of the treatment period at Week 24 ($p<0.0001$).

CONCLUSIONS: A rapid clinical response, evidenced by significant reduction in MBL volume, was observed in patients treated with once-daily Rel-CT. This improvement in MBL was significant and clinically meaningful compared with placebo and was maintained throughout the treatment period.

SUPPORT: Myovant Sciences Inc.

O-207 10:10 AM Tuesday, October 20, 2020

RECTAL VERSUS SUBLINGUAL MISOPROSTOL IN DECREASING BLOOD LOSS DURING ABDOMINAL MYOMECTOMY: A RANDOMIZED CLINICAL TRIAL. Ahmed M. Abbas, MD, Sara M. Tolba, MBBCh, Ahmed M. Abdelmagied, MD, Tarek Farghaly, MD, Ahmed Nasr, MD. Department of Obstetrics and Gynecology Faculty of Medicine, Assiut University, Assiut, Egypt.

OBJECTIVE: The current study aims to compare the effectiveness of rectally administered PGE1 synthetic analogue (misoprostol) 400 mcg versus sublingual administered misoprostol before abdominal myomectomy to decrease blood loss during the operation.

DESIGN: Randomized, single-blind, clinical study(Clinicaltrials.Gov:NCT02716142).

MATERIALS AND METHODS: The current study was conducted between March 2017 and December 2019. The study included women with

documented uterine fibroids on pelvic imaging, age between 18 and 50 years, pre-operative hemoglobin >8 g/dl, with five or less symptomatic subserous or intramural fibroids and the uterine size less than 24 weeks pregnancy. Sample size was calculated based on a study stated that the mean blood loss with rectal misoprostol was 574±194.8 ml. Using two sided chi-square (x2) test with alpha error of 0.05, a total sample size of at least 58 patients (29 in each arm) will have 80% power to detect 25% difference in mean blood loss with sublingual misoprostol intake. Women were randomized to (group A) received 400 mcg misoprostol (2 tablets) rectally one hour before the operation, and group (B) received 400 mcg misoprostol sublingual at the same time. The primary outcome was the mean amount of intraoperative blood loss. Chi^2-test was used to compare the nominal data of the study groups while student t-test was used to compare the quantitative data of the groups.

RESULTS: The study included 60 patients (30 in each arm). Both groups had no statistical significant differences as regarding the baseline or clinical data. The mean amount of blood loss in rectal group was 247.44 ± 106.04 ml vs. 256.17 ± 116.27 ml in the sublingual group (p=0.06). No difference between both groups regarding the change of hemoglobin level and hematocrit value pre- and post-operatively (p>0.05). similarly, no difference between both groups regarding the duration of surgery (p=0.9) and the need for post-operative blood transfusion (p=0.08). Both groups were similar regarding the rate of adverse effects (p=0.97). Fever and chills were the most common observed adverse effects.

CONCLUSIONS: Both rectal and sublingual misoprostol 400 mcg are equally effective in decrease the blood loss during abdominal myomectomy with quiet similar adverse effects.

SUPPORT: None

O-208 10:25 AM Tuesday, October 20, 2020

A NOMOGRAM PREDICTING THE LIKELIHOOD OF INCOMPLETE REMOVAL OF SUBMUCOUS MYOMAS IN PATIENTS UNDERGOING HYSTEROSCOPIC MYOMECTOMY.

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OBJECTIVE: To develop a nomogram predicting the likelihood of incomplete removal of submucous myomas in patients undergoing hysteroscopic myomectomy.

DESIGN: Data on 571 consecutive patients who underwent hysteroscopic myomectomy for submucous myomas were prospectively collected. Patients who underwent hysteroscopic procedures in an earlier period formed the training cohort (n=424) for nomogram development, and those who underwent procedure thereafter formed the validation cohort (n=147) to confirm the model's performance. This study was registered in clinicaltrials.gov (NCT04400942).

MATERIALS AND METHODS: Before hysteroscopy, patients underwent a transvaginal ultrasound to evaluate the presence and characteristics of myomas. Pre and intraoperative variables associated with incomplete myoma resection in the training cohort were evaluated by univariate logistic regression analysis. Beta-coefficients of significant variables in derivation set were used to generate the nomogram, which was based on proportionally converting each regression coefficient in logistic regression to a 0-100-point scale. The predictive performance of the nomogram was measured by concordance index (C index) and calibration with 1000 bootstrap samples to decrease the overfit bias. The receiver operating characteristic curve was analyzed to calculate the optimal cutoff value by maximizing the Youden index for identifying procedures at a high risk of incomplete myoma resection.

RESULTS: Out of 424 hysteroscopic procedures in the training cohort, there were 49 (11.6%) incomplete myoma resection. 17.7% of the procedures were performed by surgical fellows, 58.0% by consultants, and 24.3% by consultants expert in hysteroscopic surgery. The following variables (odds ratio; 95% CI) were independently associated to incomplete myoma resection: procedure performed by fellows (5.228; 2.395-11.414), largest diameter of myoma ≥4 cm (4.410; 1.464-13.287), intramural myoma extension ≥75% (3.982; 1.725-9.194), uterine volume ≥50 cm^3 (3.562; 1.473-8.616), number of myomas >2 (3.514; 1.294-10.252), concomitant presence of adenomyosis (2.951; 1.179-7.389), previous laparotomic or laparoscopic myomectomy (2.624; 1.006-6.844). No significant association was found for: uterine myoma topography, extension of myoma base, previous 3-month hormonal therapy, menstrual cycle phase, previous vaginal delivery or cesarean section, concomitant presence of ≥1 endometrial polyp. The nomogram deriving from significant variables was characterized by a C index (95% CI) of 0.81 (0.78-0.85) and 0.80 (0.75-0.86) in predicting the incomplete myoma resection in the training and validation cohorts, respectively, and had well-fitted calibration curves. By identifying a cutoff value of 77, the positive and negative predictive values of the nomogram were 81.2% (76.2%-83.4%) and 88.9% (83.6%-95.2%) for the training cohort, and 84.6% (79.7%-88.4%) and 90.2% (86.0%-95.7%) for the validation cohort.

CONCLUSIONS: This nomogram may support clinicians by identifying patients at high risk of incomplete hysteroscopic myoma resection.

O-209 10:40 AM Tuesday, October 20, 2020

COLLAGENASE *CLOSTRIDIUM HISTOLYTICUM*-TREATED UTERINE FIBROIDS SHOW REDUCTION OF TISSUE STIFFNESS AND CELL PROLIFERATION, AND INDUCTION OF CELL DEATH THROUGH AUTOPHAGY AND NECROPTOSIS, AND ALTERATION OF HIPPO SIGNALING.

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OBJECTIVE: Uterine fibroids are prevalent collagen-rich fibrotic tumors, with limited therapeutic options. Collagens in fibroids contribute to an increased mechanical stiffness of extracellular matrix (ECM) with activation of mechanotransduction, thus promoting the fibrotic process. YAP is a transcriptional effector of Hippo signaling that acts as a sensor to regulate a wide range of physical and mechanical stresses, including stiffness of ECM. In a soft matrix, YAP becomes phosphorylated and degraded in the cytoplasm, preventing the YAP-mediated transcription of genes involved in cell growth and fibrosis. Collagenase *Clostridium histolyticum* (CCH) is used to treat fibrotic conditions, such as Dupuytren's contracture and Peyronie's disease. Here, we tested the hypothesis that degradation of collagens by CCH would alter stiffness of ECM leading to changes in markers of cell growth, cell death and Hippo signaling.

DESIGN: Analysis of fibroid tissues from a Phase 1 clinical trial (NCT02889848) after injection of CCH. A fixed dose (1.16 mg) of CCH was injected in 3 fibroids and tissues were harvested at 24-48 h. Nine additional fibroids (n=3 per dose) were injected with increasing doses of CCH at 0.05 mg/cm^3 (dose 1), 0.1 mg/cm^3 (dose 2), and 0.2 mg/cm^3 (dose 3), and harvested at 60-90 days. Non-injected control fibroids were harvested at the same timepoints.

MATERIALS AND METHODS: Mechanical stiffness was quantified with unconfined rheometry. Markers for cell proliferation (PCNA), autophagy (LC3B), necroptosis (RIPK3), and Hippo signaling (phosphorylated YAP or p-YAP) were quantified with immunofluorescence staining and ImageJ software. Two-tailed t-test was used for data analysis. Statistical significance was defined as $p<0.05$.

RESULTS: Fibroid tissues varied in stiffness but overall stiffness of CCH-injected tissues was reduced by 26% and 32% compared to controls at the early and late time points, respectively, and 47% at the two highest doses. The cell proliferation marker PCNA was increased at 24-48 h ($p<0.05$), after CCH injection, but was decreased in fibroids (5 of 6) after 60 days at high doses (0.1 and 0.2 mg/cm^3) ($p<0.05$). There was an increase in the autophagy marker, LC3B ($p<0.05$), and the necroptosis marker, RIPK3 ($p<0.05$), among 55% (6 of 11) and 36% (4 of 11) CCH-treated fibroids, respectively, suggesting the activation of autophagic and necroptotic cell death. Changes in Hippo signaling factors were assessed, specifically phosphorylated YAP (p-YAP), the transcriptionally inactive form of YAP. Notably, p-YAP was increased, particularly at the highest dose of CCH (2 of 3) ($p<0.05$).

CONCLUSIONS: The injection of collagenase led to a reduction of tissue stiffness and markers of cell growth at the highest doses. These changes were accompanied by increased staining for markers of cell death via autophagy and necroptosis and alteration of Hippo signaling. The reduction in PCNA staining accompanied by an increase in p-YAP suggests that CCH-treatment could lead to a reduction in fibroid growth. Though preliminary, these data suggest that CCH might represent a new approach to reduce fibroid growth.

SUPPORT: Ines Mandl Research Foundation (to MSI) and Howard W. and Georgeanna Seegar Jones Endowment (to JHS).

O-210 10:55 AM Tuesday, October 20, 2020

PRO-INFLAMMATORY AND IMMUNOSUPPRESSIVE ENVIRONMENT CONTRIBUTES TO THE DEVELOPMENT AND PROGRESSION OF UTERINE FIBROIDS. Hoda Elkafas, B. Pharm, MSc,[1] Maria Victoria Bariani, Ph.D.,[1] Mohamed Ali, BPharm, MSc,[1] Lauren Prusinski Fernung, M.D., Ph.D.,[2] Balasubashini Muralimanohara, Ph.Dm,[3] Hailian Shen, MD/PhD,[3] Tom Boyer, Ph.D.,[3] Qiwei Yang, PhD,[1] Ayman Al-Hendy, MD, PhD,[1] Nahed Ismail, MD, Ph.D.[4] [1]University of Illinois at Chicago, Chicago, IL; [2]Medical College of Georgia at Augusta University, Augusta, GA; [3]University of Texas Health Science Center at San Antonio, San Antonio, TX; [4]University of Illinois at Chicago, CHICAGO, IL.

OBJECTIVE: Uterine fibroids (UFs) are the most common benign tumors in reproductive-age women. Previous studies suggested that UFs originate from a single deregulated myometrial stem cell (MMSC) that converts to a UF-initiating cell (UFSC). However, the mechanism underlying UF development after this conversion remains unknown. It is well known that chronic inflammation predisposes to tumor development and progression, but the contribution of an inflammatory microenvironment to the natural history of UFs remains elusive. This work aimed to analyze the immune/inflammatory signaling and the immune checkpoint axis in UFSCs and UF tissues.

DESIGN: Laboratory research studies using human myometrium and UF tissues, primary cells, and stem cells (SCs).

MATERIALS AND METHODS: Tissue microarrays (TMA) comprising 7 patient-matched samples of UF and adjacent myometrium (MM) tissues, derived from consented women undergoing surgical intervention at UT Health San Antonio, were used for immunohistochemical analysis. Fresh UF and adjacent myometrium (MM) tissues were collected via the University of Illinois Medical Center at Chicago from consented women and subjected to primary and SCs isolation (n=3), using dual Stro-1 and CD44 surface markers. MM and UF primary and SCs were cultured under their specific conditions. Conditioned media from these cells were collected, concentrated, and subjected to secreted cytokine profiling using a 65-plexHuman Cytokine/Chemokine Discovery assay. Ingenuity Pathway Analysis (IPA) was used to establish perturbed gene networks, including those linked to the inflammatory pathway. Two-tailed unpaired Student's t-test was used to assess any statistically significant differences ($P < 0.05$).

RESULTS: IHC-TMA staining showed a significant upregulation of transcription factor NFkB and downstream pro-inflammatory cytokines; IL-1β, TNFα, INFg, and Thymic stromal lymphoprotein (TSLP) in UFs compared to adjacent MM tissues ($P<0.05$). These cytokines play a crucial role in the activation of T cells and antigen-presenting cells in the tumor microenvironment. Notably, the expression of immune check-point PDL-1 protein was increased in UFs compared to MM tissues ($p<0.05$). Further, the levels of neutrophils and dendritic cells growth factors (GM-CSF and G-CSF), CX3CL1 (a pro-inflammatory chemokine that promotes NK cells cytotoxicity and their secretion of IFNg), IL-1α/ IL-9 (T cell growth factor), and FGF-2 (fibroblast growth factor) were significantly higher in conditioned media from UFSCs compared to the ones from MMSCs ($p<0.05$). Also, primary UF cells secreted higher levels of G-CSF, INF-g, IL-12P70, CCL11, and stem cell factor (SCF) than MM primary cells ($p<0.05$).

CONCLUSIONS: Our results suggest, for the first time, that UFs and UFSCs exhibited a pro-inflammatory and pro-tumorigenic phenotype that promotes stem cell proliferation as well as the generation of an immunosuppressive tumor microenvironment; two key events that contribute to the development and progression of UF. Targeting these immunomodulatory molecules could provide a novel non-hormonal therapy for uterine fibroids

SUPPORT: ES028615 (AA), R01 HD094378 (AA), R01 HD094380 (AA), U54 MD007602 (AA)

MENOPAUSE AND PRIMARY OVARIAN INSUFFICIENCY

O-211 1:50 PM Tuesday, October 20, 2020

FORECASTING EARLY ONSET DIMINSHED OVARIAN RESERVE FOR YOUNG REPRODUCTIVE AGE WOMEN. Blair R. McCallie, BS, Mary E. Haywood, PhD, Michelle M. Denomme Tignanelli, PhD, Rachel Makloski, RN, William B. Schoolcraft, MD, Mandy G. Katz-Jaffe, PhD. Colorado Center for Reproductive Medicine Lone Tree, CO.

OBJECTIVE: Diminished ovarian reserve (DOR) is a condition where the number or quality of oocytes is compromised, significantly impacting a woman's reproductive potential. While this is expected as women reach their fifth decade, about 10% of younger women (<35 years) will be diagnosed with premature DOR. With the causes of early-onset DOR being largely unknown, the objective of this study was to investigate the biological networks associated with DOR in young women and the subsequent molecular impact on preimplantation embryos.

DESIGN: Research study.

MATERIALS AND METHODS: Whole peripheral blood was collected from patients with consent and IRB approval: young women presenting with diminished ovarian reserve (DOR; n=40) and age-matched young women with normal ovarian reserve (CONT; n=40). A diagnosis of young DOR was defined as maternal age $\leq$34 years (range 27-34), antral follicle count <10 and AMH <1.0 (ng/ml). Maternal exome sequencing (Illumina NovaSEQ 6000; GATK4 analysis aligned to the hg38 reference genome with BWA-MEM) identified exclusive DOR variants using Ingenuity Pathway Analysis (Qiagen). Sequencing validation was performed with Taqman SNP Genotyping Assays (Applied Biosystems). Global methylome sequencing (n=6 individual blastocysts) was performed using the Methyl-Maxi-Seq platform (Zymo Research) with Bismark software for bisulfite sequencing alignment and statistical analysis utilizing the Student T-test ($P<0.05$). Transcriptome sequencing (n=12 individual blastocysts) was performed on the HiSeq 4000 (Illumina) and reads were mapped to the human genome using gSNAP with ANOVA in R used to quantify statistical significance ($P<0.05$).

RESULTS: Exome sequencing revealed 730 significant DNA variants across the genome that were observed exclusively in the young DOR patients ($P<0.01$). Bioinformatic analysis revealed a significant impact to the Glucocorticoid receptor (GR) signaling pathway ($P<0.01$). Each young DOR female had an average of 6.2 deleterious DNA variants within the GR signaling pathway. Successful validation included gene members of the GR signaling pathway (*AGT*, *KRT6A*, *KRT19*, *NCOA2*, *TAF1*) and key ovarian genes (*AHRR*, *CCDC8*, *IGFBP5*, *LRRC17*, *PCDH11X*, *PDGFD*). Additional stratification based on patient age resulted in a cut-off at 31 years for young DOR discrimination. Embryonic global methylome sequencing resulted in only a very small number of total CpG sites with methylation alterations (1,775; 0.015% of total) in the DOR group ($P\leq0.05$). Additionally, there was no co-localization between these limited number of altered CpG sites and significant variants, genes or pathways. RNA sequencing also resulted in no biologically significant transcription changes between DOR blastocysts and controls ($P\leq0.05$).

CONCLUSIONS: GR signaling DNA variants were observed in women with early-onset DOR potentially compromising oocyte production and quality. Utilization of a targeted SNP assay in forecasting premature DOR for young reproductive-age women may allow for earlier identification and clinical intervention, giving them greater chances of creating a family with their own oocytes.

SUPPORT: None

O-212 2:05 PM Tuesday, October 20, 2020

DOES A DIAGNOSIS OF UNEXPLAINED INFERTILITY IMPACT AGE AT MENOPAUSE? LONG TERM FOLLOW-UP FROM FASTT. Denis A. Vaughan, MD,[1] Marlene B. Goldman, ScD,[2] June L. Fung, PhD,[2] Katherine G. Koniares, MD,[3] Carleigh B. Nesbit, DO,[4] Thomas L. Toth, MD,[5] Richard H. Reindollar, MD[2] [1]Beth Israel Deaconess Medical Center, Boston, MA; [2]Geisel School of Medicine at Dartmouth, Hanover, NH; [3]Tufts Medical Center, Boston, MA; [4]Dartmouth Hitchcock Medical Center, Lebanon, NH; [5]Boston IVF, Waltham, MA.

OBJECTIVE: To investigate age at menopause in women who were enrolled in a large randomized controlled trial (RCT, FASTT[1]).

DESIGN: Long term follow up of RCT participants.

MATERIALS AND METHODS: Between March 2019 and February 2020, a telephone survey was administered to women who had been enrolled in FASTT, an RCT that investigated time to conception and cost effectiveness of treatment for unexplained infertility in women aged 21-39 years. The survey included a smoking history with a heavy smoking history defined as at least 5 pack years. Statistical analyses were performed using SAS v 9.2. Categorical variables were compared between groups using chi-square and Fisher's exact tests and continuous variables with two-sample t-tests and analysis of variance where appropriate, with $P<0.05$ as significant. The National Health and Nutrition Examination Survey (NHANES, 2017-2018 cycle) data for women age 40-56 years was used to compare data from the current study to the general population.

RESULTS: Of the 503 women originally enrolled in FASTT, 311 (61.8%) were contacted of whom 286 (56.9%) consented to participate in the survey. Mean age and day 3 FSH at enrollment in FASTT was 33.1 ± 3.2 years and 6.8 ± 2.2 mIU/ml for those who participated in the follow up survey. Mean age at follow-up was 49.5 ± 3.4 years with 253 (89.4%) Caucasian. 82 women (29.3%) reported no longer having menses at follow up with 54 (19.3%) confirming that they have not had a spontaneous menstrual period in ≥12 months with a mean age at spontaneous menopause of 48.8 years ± 3.6 years. In NHANES, 179/785 (22.8%) women reported not having regular menses for the prior 12 months secondary to menopause. Mean ± SD of age of menopause was 47.6 ± 4.4 years which was not significantly different from the present study (P=0.07). 17 women (6.1%) had undergone a hysterectomy and 3 (1.1%) had undergone a bilateral salpingo-oopherectomy. 35 women (18.5%) who had delivered a live birth during FASTT had gone through menopause at follow up compared to 19 (20.9%) of those who did not (P=0.64). 48 women (18.3%) who had at least one live birth were post-menopausal at follow up compared to 6 (35.3%) of those who had never had a live birth (P=0.11). Of those women who were post-menopausal, there was no significant difference in age at menopause between those who had never had a live birth (49.5 ± 3.6) compared those who had at least one live birth (48.7 ± 3.6 years). Neither a history of ever smoking nor a history of heavy smoking impacted the mean age at spontaneous menopause compared to those who never smoked (48.1 ± 4.8 and 47.9 ± 5.5 vs 49.0 ± 3.2 years, P=0.56, P=0.59 respectively). Controlling for age at enrollment of FASTT, day 3 FSH at enrollment was not significantly different between those who had undergone spontaneous menopause compared to those who had not at the time of follow-up. (7.3 ± 2.2 vs 6.6 ± 2.1 mIU/mL, P=0.53).

CONCLUSIONS: Being diagnosed with unexplained infertility did not increase the risk for earlier menopause in this follow up study compared to U.S. women. A higher day 3 FSH at enrollment in FASTT or being a current or former smoker were not independent risk factors for earlier menopause.

References

1. Â Reindollar RH, Regan MM, Neumann PJ, et al. A randomized clinical trial to evaluate optimal treatment for unexplained infertility: the fast track and standard treatment (FASTT) trial.Â *Fertil Steril*Â (available online June 16, 2009). https://doi.org/10.1016/j.fertnstert.2009.04.022.

SUPPORT: None

O-213 2:20 PM Tuesday, October 20, 2020

GRAVIDITY, PARITY, BREASTFEEDING AND AMH: FINDINGS FROM THE OVARIAN AGING AND RESERVE STUDY (SOAR). Emma Giuliani, MD,[1] Anne Waldo, MS,[1] Lia Bernardi, MD,[2] Mercedes Carnethon, PhD,[2] Lisa M. Neff, MD,[2] Erica E. Marsh, MD, MSCI, FACOG[1] [1]University of Michigan, Ann Arbor, MI; [2]Northwestern University, Chicago, IL.

OBJECTIVE: Very few studies on anti-mullerian hormone (AMH), the most commonly used serum biomarker of ovarian reserve in women, have been conducted in young, healthy women of non-European race, and factors affecting its levels are still largely unknown. The objective of this analysis was to investigate whether gravidity, parity and breastfeeding are associated with AMH levels in reproductive aged African American women (AAW).

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: The Study of Ovarian Aging and Reserve (SOAR) leveraged an existing NIEHS study cohort of AAW aged 23-34 years. Anthropometric measurements, health information and serum AMH levels (picoAMH assay - Ansh Labs, Webster, TX) were analyzed. Multivariable linear regression models adjusted for age, age^2, BMI, current hormonal contraception use, and history of irregular menstrual cycles were used to estimate the effect of gravidity, parity and breastfeeding on AMH levels (SAS 9.4 - Cary, NC).

RESULTS: A total of 1,646 women with a mean age of 29.2±3.4yo, mean BMI of 33.7±9.6 Kg/m^2, and median AMH value of 4.1 ng/mL (IRQ 2.3-6.7) were included, of which 449 (26.6%) were nulligravidae, 206 (12.2%) had been pregnant but never given birth, and 1,034 (61.2%) had at least one live birth. Mean gravidity was 3.1±2.0 and parity was 2.1±1.3. Mean age at first pregnancy was 19.9±3.6yo, while mean years since last pregnancy and last birth were 4.4±3.7 and 5.1±3.8, respectively. A history of breastfeeding was reported in 38.7% of women with an average cumulative breastfeeding time for all children per woman of 5.4±8.7 months. In adjusted models, history of pregnancy was inversely associated with lnAMH (-0.13, 95% CI -0.24 to -0.03, p=0.01). No significant association was seen between AMH levels and number of pregnancies among women who were ever pregnant, number of livebirths among parous women, history of breastfeeding, or cumulative breastfeeding time in parous women.

CONCLUSIONS: In this large cohort of AAW, a population that is largely underrepresented in the ovarian reserve literature, history of pregnancy was inversely associated with AMH. The finding of lower AMH levels in women with at least one proven pregnancy is consistent with previous studies that have demonstrated that higher AMH levels are associated with certain conditions that may lead to infertility, such as polycystic ovarian syndrome. A better understanding of how factors related to previous pregnancies influence AMH levels in women of different backgrounds will improve physician interpretation of ovarian reserve testing and patients' counseling.

O-214 2:35 PM Tuesday, October 20, 2020

ASSOCIATION BETWEEN OVARIAN RESERVE AND MENSTRUAL CYCLE LENGTH. Benjamin S. Harris, MD, MPH,[1] Anne Z. Steiner, MD, MPH,[2] Anne Marie Jukic, PhD[3] [1]Division of Reproductive Endocrinology and Infertility, Duke University Medical Center, Durham, NC; [2]Duke University, Durham, NC; [3]National Institute of Environmental Health Sciences, Durham, NC.

OBJECTIVE: To determine the association between anti-Müllerian hormone (AMH) levels and menstrual cycle length.

DESIGN: Secondary analysis of a prospective time-to-conceive cohort study.

MATERIALS AND METHODS: We used data from Time to Conceive (TTC), a prospective time-to-pregnancy study of women, aged 30 to 44. Participants completed up to 4 months of daily diaries while attempting to conceive. Conception cycles were excluded. Ovulation was determined by ovulation predictor kit, cervical mucus, or basal body temperature records. Serum was analyzed for AMH (Ultrasensitive AMH ELISA, Ansh Labs). AMH levels were examined in two ways: continuous linear variable, and four categories. We examined continuous menstrual cycle length with linear mixed models, and short cycles (<25 days), long cycles (35+ days), short follicular phase (≤10 days), and long follicular phase (18+ days) with marginal models and GEE, adjusting for, age, race, body mass index, education, and cycle of blood draw.

RESULTS: There were 3,179 menstrual cycles from 689 women included in the analysis. Results presented in Table. Compared with an AMH level of 1.6-3.4 ng/mL, AMH level <1.6 ng/mL was associated both with cycles that were about one day shorter and with 1.5 times the odds of short cycles . An AMH level >8 ng/mL was associated both with cycles that were 2.5 days

TABLE. Association of Categorical AMH with Change in Menstrual Cycle Length, Long and Short Cycles, and Follicular Phase

	Menstrual Cycle Length	Long Cycles (>35 days)	Short Cycles (<25 days)	Follicular Phase Length	Long Follicular Phase (≥18 days)	Short Follicular Phase(≤ 10 days)
AMH (ng/mL)	Adjusted Cycle Length (in days) (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted Cycle Length(in days) (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)
<1.6	**-0.994 (-1.47, 0.519)**	**0.587 (0.289,1.193)**	**1.46 (1.04, 2.06)**	**-1.69 (-3.39, 0.013)**	**0.405 (0.239,0.687)**	**1.29 (0.753, 2.24)**
1.6 – 3.4	**REFERENCE**					
>3.4-8	**1.29 (0.841, 1.76)**	**2.42 (1.38, 4.24)**	**0.463 (0.298, 0.718)**	**0.469 (-1.13,2.07)**	**1.24 (0.806,1.88)**	**0.669 (0.342, 1.31)**
>8	**2.46 (1.79, 3.12)**	**5.69 (2.91, 11.1)**	**0.296 (0.142, 0.617)**	**4.75 (2.59, 6.91)**	**2.33 (1.42,3.83)**	**0.328 (0.098, 1.10)**

longer and with over 5 times the odds of long cycles. When evaluating follicular phase length, an AMH of >8 ng/mL was associated both with follicular phases that were 4.8 days longer and with over 2.3 times the odds of being long. However, there was no statistically significant association between AMH and short follicular phase.

CONCLUSIONS: Among women age 30-44 attempting to conceive naturally, increasing levels of AMH are associated with longer menstrual cycles and follicular phase lengths, respectively. Findings support the biological impact of ovarian reserve on cycle length and ovulation timing.

O-215 2:50 PM Tuesday, October 20, 2020

INFLUENCE OF ARTHRITIS AND TREATMENTS ON OVARIAN RESERVE: A PROSPECTIVE STUDY. Vinita M. Alexander, MD,[1] Jillian Ashley-Martin, PhD,[1] Joan Riley, PhD, HCLD,[1] Amber R. Cooper, MD,[2] Valerie Ratts, MD,[1] Emily S. Jungheim, MD, MSCI[3] [1]Washington University in St. Louis, St. Louis, MO; [2]Vios Fertility Institute St Louis, St. Louis, MO; [3]Northwestern Feinberg School of Medicine, Chicago, IL.

OBJECTIVE: Women with autoimmune disease may experience an accelerated loss of ovarian function due to the disease itself and the disease treatments. We examined serum levels of Anti-Mullerian hormone (AMH) in patients with arthritis and the influence of five arthritic drug regimens (no medications, methotrexate, TNFα-antagonist, a combination of the two, or other regimens containing steroids, hydroxychloroquine, etc.) on AMH level.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Serum AMH levels were measured using Elecsys® AMH immunoassay at two time points (T_0 and T_1) in 129 premenopausal women (age 18 to 45) with a diagnosis of Rheumatoid Arthritis, Spondyloarthritis, or Juvenile Idiopathic Arthritis. AMH levels at T_0 in arthritis patients were compared to an existing control population of healthy females age 18 to 44 without infertility (n=200). Participating women provided information on sociodemographic characteristics (age, race, body mass index, smoking history) and medical history (current and past treatment regimens for arthritis, disease severity measures, obstetric history, and inability to conceive after 12 months of trying) at baseline and follow-up.

Association between sociodemographic characteristics and diminished ovarian reserve (DOR, AMH < 1.1 ng/mL) was quantified using univariate logistic regression. To identify women with highest rates of ovarian reserve loss over time, percent change in AMH per year was dichotomized at the 75th percentile. Univariate and multivariable logistic regression was carried out to identify sociodemographic and clinical variables associated with the highest annual percent decrease in AMH (>75th percentile, or > 28% change in AMH per year).

RESULTS: Median time between T_0 and T_1 was 1.7 years. At time T_0, mean (standard deviation) AMH in the arthritis population (2.00 ± 2.18) was significantly lower than in the control population (2.52 ± 5.98) ($p < 0.001$)). At T_0, 59 women met criteria for DOR. At highest risk for DOR were women with history of sterilization (OR 2.30, 95% CI: 1.00-5.25), or over age 35 (OR 8.24, 95% CI: 1.40-41.47). Women over age 35 (OR 4.75, 95%CI: 1.50-15.09) or who sought care for infertility (OR 3.02, 95% CI: 1.12-8.12) were at increased odds of having the highest annual percentage loss in ovarian reserve. After controlling for age, compared to those on no medications, patients on these regimens were less likely to be in the highest quartile of ovarian loss: methotrexate alone (OR 0.07, 95%CI: 0.01-0.61) and methotrexate plus TNFα-antagonists (OR 0.09, 95%CI: 0.11-0.79).

CONCLUSIONS: This is the first study to prospectively describe AMH in a large cohort of premenopausal women with arthritis with mean follow-up of over one year. We found AMH levels in women with arthritis are lower than in healthy controls, and those with accelerated loss in AMH are more likely to be over 35 or report a history of difficulty conceiving. Odds of a high rate of ovarian reserve loss are lower with long-term methotrexate compared to other drug regimens or no medications. Our findings suggest long-term methotrexate use is not harmful to ovarian reserve as measured by AMH.

O-216 3:05 PM Tuesday, October 20, 2020

ENDOCRINE EFFECTS OF INTRAOVARIAN INJECTION OF PLATELET-RICH PLASMA (PRP) IN WOMEN WITH PREMATURE OVARIAN AGING. David H. Barad, MD, MS,[1] David F. Albertini, PhD, MS,[1] Norbert Gleicher, MD[2] [1]Center for Human Reproduction, New York, NY; [2]Center for Human Reproduction, Foundation for Reproductive Medicine, Rockefeller University, Medical University Vienna, New York, NY.

OBJECTIVE: Since PRP treatments have been without prior validation quickly entering IVF practice, to investigate short-term effects of PRP treatments in a formal study format.

DESIGN: Prospective registered studies: NCT04275700 and NCT3542708.

MATERIALS AND METHODS: Premature ovarian failure (POF), also called primary ovarian insufficiency (POI) is characterized by amenorrhea and FSH >40.0mIU/mL. Affected women may, however, still have sporadic menses and may even occasionally achieve spontaneous pregnancy. In contrast, premature ovarian aging (POA), also called occult primary ovarian insufficiency (oPOI), represents a milder form of ovarian insufficiency, characterized by abnormally high FSH (though below 40.0mIU/mL) and abnormally low age-specific AMH. During 2018-2020, 51 women with a diagnosis of POF/POI or POA/oPOI presented to our center for PRP treatments, 20 with POF/POI (PPR#1; age, 34.1 ±5.0 years) and 31 with POA/oPOI (PRP#2, 39.7 ± 6.3 years). To qualify for PRP treatment, patients must have failed a maximal ovarian stimulation with gonadotropins (600IU/day) after at least 6 weeks of pre-supplementation with DHEA (75mg/day) and CoQ10. (800-1,000mg/day. PRP was prepared from patients' bloods using the RegenLab™ USA PRP preparation system (New York, N.Y). The supernatant was withdrawn, and 2.5 ccs of patient plasma was used to re-suspend platelets. Under intravenous sedation and ultrasound control 0.70 cc of PRP was injected subcapsular into ovaries at 7 different sites. In PRP#1, injections were given into only 1 by computer randomly selected ovary, with the 2ndovary serving as control; in PRP#2, both ovaries were injected. Patients were followed with vaginal ultrasounds and estradiol (E) and FSH determinations in blood every 3 days for 12 days, and then weekly, for up to 12 weeks. Since study recruitment is still incomplete, we here only report endocrine changes over the first 60 days following PRP injection without regard to randomization.

RESULTS: FSH was 184.9 ± 58.4 mIU/mL (PRP#1) and 60.5 ± 47.8 mIU/mL (PRP#2). PRP#I over first 60 days revealed no changes in E or FSH levels although 4/20 (20%) demonstrated follicle growth on ultrasound. PRP#2 patients actually revealed a significant fall in E and rise in FSH over the first 30 days, though then followed up with a rise in E (P= 0.007) and drop in FSH (P= 0.038).

CONCLUSIONS: These observations are to our knowledge the first time-controlled hormonal observations in women with POF/POI and POA/oPOI following intraovarian PRP treatments. Not unexpectedly, they demonstrate different hormonal response patterns between the 2 study groups, though both patient populations appear to develop a hormonal response to PRP. Three ongoing PRP trials in different populations should reveal further clinical outcome data.

SUPPORT: Intramural funds from The Center for Human Reproduction and grants from The Foundation for Reproductive Medicine.

LGBTQ

O-217 1:50 PM Tuesday, October 20, 2020

HOW DOES QUALITY OF LIFE IMPACT TRANSGENDER PATIENTS' INTEREST IN FERTILITY COUNSELING AND PRESERVATION? Hillary Pearson, M.D.,[1] Alixandra Domney, M.D., M.P.H.,[1] Aren Skolnick, DO,[2] Randi H. Goldman, M.D.,[3] Christine Mullin, M.D.[3] [1]Department of OBGYN, North Shore University Hospital/Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY; [2]Department of Endocrinology/Diabetes and Metabolism, North Shore University Hospital/Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Manhassett, NY; [3]Northwell Health Fertility, North Shore University Hospital/Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: Transgender patients face unique challenges in the medical setting, which may lead to poorer quality of life (QOL). Fertility counseling is a critical component of care for transgender individuals. This study aims to investigate if an association exists between QOL and transgender patients' interest regarding their fertility and fertility counseling.

DESIGN: Lifestyle survey.

MATERIALS AND METHODS: Adult transgender patients at a single academic medical center from 2019-2020 were surveyed using the validated Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System. This questionnaire is traditionally used for patients with chronic conditions to quantitatively assess subcategories of QOL,

including social (SWB), functional, emotional, sexual, and financial well-being (FiWB). The questionnaire was specifically adapted to assess QOL parameters of transgender patients and approved for use. Composite scores may range from 37-106, with higher scores indicating better QOL. T-tests were used to compare composite scores between patients who felt that their QOL influenced their interest in fertility versus those who did not.

RESULTS: Of 47 patients surveyed, 43 completed FACIT in its entirety. Most patients (30/47, 63.8%) reported that they were never offered fertility counseling. Of the 17 patients who were offered counseling, 6 discussed fertility with their doctor once, 8 twice, and 3 discussed options $\geq$3 times.

Fifty-eight percent (25/43) of patients felt that at least one QOL subcategory either positively or negatively influenced their feelings towards fertility. The average QOL score for these patients was not different than the average score for those who felt that their interest in fertility was unaffected by any subcategory (76.2 vs. 77.3, NS). The mean composite QOL score for patients whose interest in fertility was positively affected by at least one subcategory was significantly higher than that of patients who did not feel that any QOL subcategory positively affected their interest (84.3 vs. 67.5 respectively, p=0.009). FiWB was reported to most negatively impact level of interest in fertility (60%), while SWB was reported to most positively impact their level of interest (66.7%). Most patients did not feel that any QOL subcategory influenced their fertility interest.

CONCLUSIONS: Despite increased access to care, the majority of transgender patients surveyed were not offered fertility counseling, and the most commonly selected QOL subcategory that participants felt negatively impacted their interest in fertility was FiWB. We as a field have the unique opportunity to support transgender individuals by providing education regarding fertility planning and building biologically linked families.

SUPPORT: None.

O-218 2:05 PM Tuesday, October 20, 2020

IS THE MID-LUTEAL PROGESTERONE CHECK AN EXAMPLE OF MEDICALIZATION IN THE TREATMENT OF SAME-SEX FEMALE COUPLES UNDERGOING DONOR SPERM INTRAUTERINE INSEMINATION?

Jenna Friedenthal, MD,[1] Joseph A. Lee, BA,[2] Noah Copperman, BS,[2] Daniel E. Stein, MD,[1] Tanmoy Mukherjee, MD,[1] Alan B. Copperman, MD[1] [1]Icahn School of Medicine at Mount Sinai, New York, NY; [2]Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Evaluation of mid-luteal progesterone (MLP) is frequently performed in order to assess evidence of ovulation. While some researchers have demonstrated a positive association between MLP and live birth [1], others have demonstrated no difference in MLP between fertile and non-fertile cycles [2, 3]. Several studies have evaluated MLP in ovulation induction (OI) cycles within heterosexual couples [4, 5], yet, data regarding the clinical value of MLP in same-sex female couples is limited. It has been suggested that medicalization, the process by which human conditions and problems come to be defined and treated as medical conditions, adds to healthcare costs while not impacting treatment. Our study aimed to evaluate whether MLP in same-sex female couples is associated with changes in outcomes in natural cycles using donor sperm intrauterine insemination (DIUI).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: This was a retrospective study of all same-sex female couples undergoing DIUI from 2004 to 2020. Cases included all patients who had evaluation of MLP. Controls included all patients without MLP testing. MLP was obtained approximately 7 days after ovulation. Medicated cycles for OI were excluded. Our primary outcome was implantation rate (IR); secondary outcomes were ongoing pregnancy/live birth rate (OP/LBR), biochemical pregnancy rate (BCPR), and clinical loss rate (CLR). Baseline demographics were obtained: patient age, body mass index (BMI), day 3 follicle stimulating hormone (D3FSH), gravidity, parity, and endometrial thickness (EnT) at time of ovulation. Statistical analysis was performed using student t-test, Mann-Whitney U test for skewed data, and chi-square. Logistic multivariable generalized estimating equation (GEE) regression models age were used to calculate odds ratios and to adjust for potential confounders, with P<0.05 considered significant.

RESULTS: 660 patients met inclusion criteria and were included in the study; 47 underwent assessment of MLP and 613 did not undergo MLP assessment. There were no differences in demographics between the groups. The mean MLP in those assessed was 10.78ng/mL. Of those in the MLP group, 17/47 (36.17%) subsequently received supplemental progesterone; 14 received vaginal progesterone, while 3 utilized oral progesterone. In an unadjusted analysis, there were no significant differences in clinical outcomes between the groups. After adjusting for age, BMI, D3FSH, and EnT at time of ovulation, having mid-luteal progesterone evaluated did not predict IR (OR 3.65, 0.49-27.34, p=0.21) or OP/LBR (OR 3.83, CI 0.46-31.71, p = 0.21). No differences in BCPR or CLR were observed.

CONCLUSIONS: Our results demonstrate that MLP assessment does not appear to be associated with clinical outcomes in same-sex female couples undergoing natural cycles with DIUI. Our findings suggest that clinicians may reconsider the evaluation of the MLP within same-sex female couples who use DIUI, as it does not appear to enhance treatment outcome. Larger, prospective studies may further delineate the cost-benefit analysis of MLP assessment in this patient cohort.

SUPPORT: None

O-219 2:20 PM Tuesday, October 20, 2020

DECISION REGRET FOLLOWING FERTILITY PRESERVATION FOR THE TRANSGENDER INDIVIDUAL COMPARED TO THE CISGENDER WOMAN.

Viji Sundaram, MD,[1] Brett Stark, MD,[1] Eleni Greenwood Jaswa, MD, MSc,[2] Evelyn Mok-Lin, MD[3] [1]University of California, San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA; [2]University of California San Francisco, San Francisco, CA; [3]REI UCSF, Center for Reproductive Health, San Francisco, CA.

OBJECTIVE: 1) To determine differences in depression, anxiety, body image, quality-of-life (QOL), and decision regret scale (DRS) score in trans individuals who undergo fertility preservation (FP) compared to those who do not; 2) to determine if DRS score following FP varies between transgender individuals and cis-gender women.

DESIGN: Cross Sectional Cohort.

MATERIALS AND METHODS: All transgender individuals, both birth-assigned males and females, presenting for initial consultation for FP at the University of California, San Francisco between January 2016 to November 2019 were retrospectively contacted for study participation. Those desiring participation completed a web-based survey including questions on demographics, partner information, decision satisfaction, and the following standardized scales: Beck Depression Inventory II (BDI-II), Hospital Anxiety & Depression Scale (HADS), Body Image Scale for Transsexuals (BIS), Satisfaction with Life Scale (SLS), Short Form Health Survey (SF-36), and DRS. Cis-gender women, who underwent elective oocyte cryopreservation at the same institution, were recruited from 2012 to 2016 and completed an online survey with demographics and DRS scores. Data analysis was performed with descriptive statistics; chi-square test for comparison of categorical variables; Wilcoxon rank-sum (Mann-Whitney) test for comparison of continuous variables.

RESULTS: 32 birth-assigned (BA) females and 28 BA-males were identified for inclusion and contacted for survey completion. 16 (50%) BA-females and 13 (46%) BA-males completed the survey. 10 BA-females and 12 BA-males underwent FP. Of the 7 trans people (6 BA-females & 1 BA-male) that elected not to undergo FP, common reasons for declining were: need to be off gender-affirming therapy (5/7, 71%), not desiring biological children (3/7, 43%), and fear of ultrasound (2/7, 29%). 503 surveys were distributed to cis-gender women with 201 women (41%) responding. Transgender patients undergoing FP were significantly younger (27.8 years) than cis-gender patients (36.1 years, p<0.01); more likely to have a partner [trans n=11 (50%), cis n=55 (26%), p<0.01]; and more likely married [trans 5 (23%), cis n=4 (2%), p=0.001]. BDI-II, HADS Anxiety, BIS, SLS, SF-36, and DRS scores were not significantly different between trans individuals who underwent FP and those who did not. Median DRS score for all trans people undergoing FP was 7.5 (mean 12.3, SD 14.5), consistent with mild regret from a score of 1-25, while median for cis-gender women was 0 (mean 10.1, SD 15.0, p=0.31). BA-females and BA-males undergoing FP reported DRS median scores 5 (mean 9, p=0.89) and 7.5 (mean 15, p=0.20), respectively, both of which were not significantly different from cis-gender women nor from each other (p=0.43).

CONCLUSIONS: Transgender individuals seek FP earlier in life and are more likely partnered or married at time of FP compared to cis-gender women. Depression, anxiety, body image, and QOL are not significantly different between trans people who undergo FP and those who do not. Gender does not appear to have an effect in decision regret following FP.

O-220 2:35 PM Tuesday, October 20, 2020

THE EFFECT OF ESTROGEN THERAPY ON SPERMATOGENESIS IN TRANSGENDER WOMEN. Annika Sinha, MD, Cecile A. Ferrando, MD, MPH. Cleveland Clinic Foundation Cleveland, OH.

OBJECTIVE: To describe the histopathology parameters of orchiectomy specimens obtained from transgender women following gender-affirming surgery who have used gender-affirming hormone therapy (GAHT).

DESIGN: This is a retrospective cohort study of all transgender women (individuals assigned male at birth who identify as female) who underwent orchiectomy with or without vaginoplasty at a tertiary referral center between December 2015 and March 2020.

MATERIALS AND METHODS: Patients were identified by their Current Procedural Terminology codes for orchiectomy. Once identified, the electronic medical record was queried for demographic and peri-operative data and pathology records were reviewed. The following pathology parameters were recorded: testicular volume, testicular weight, presence of spermatogenesis (active vs reduced), maturation arrest, testicular atrophy, hyalinization, scarring/fibrosis, Sertoli cell and Lydig cell phenotypes. Patients were grouped into one of 3 categories describing duration of GAHT use: 0-3 years, 3-5 years, >5 years. Descriptive statistics were performed and comparisons between outcomes (demographic data and pathology parameters) were made between the GAHT groups.

RESULTS: Eighty-five (N=85) patients underwent orchiectomy during the study period with 85.9% (73) undergoing concurrent vaginoplasty. Mean age and BMI of the cohort were 39 (16) years and 28.4 (5.4) kg/m2. There were no differences between the GAHT groups with the following exception: patients using GAHT 3-5 and >5 years were more likely to be using GAHT compared to those on it 0-3 years (100% vs 100% vs 83.3% GAHT use, p=0.007). Also, while this was not statistically significant, patients in the 3-5 and >5 year groups were also more likely to smoke marijuana (26.3% vs 21.2% vs 4.2%, p=0.09). Mean testicular weight and volume across the cohort were 60.1 (24.9) gms and 65.5 (41.1) cm3. Spermatogenesis was present in 28.2% (24) of specimens with active spermatogenesis noted in 8.2% (7). Hyalinization, scarring/fibrosis and atrophy were present in 28.2% (24), 20% (17), 25.9% (22) of specimens, respectively. There were no differences in pathology parameters across the GAHT groups. Testicular weight and volume were not associated with any differences in pathology parameters. Additionally, age was not associated with testicular weight or volume or pathology parameters with the exception of the following: when patients where categorized as either $<$ 40 years of age (n=48) versus $>$ 40 years of age (n=37), patients who were older were more likely to have hyalinization (43.2% vs 16.7%, p = 0.01) as well as atrophy (40.5% vs 14.6%, p = 0.007).

CONCLUSIONS: Duration of GAHT is not associated with any differences in orchiectomy pathology parameters in patients undergoing gender-affirming surgery. The use of GAHT appears to be associated with a reduction in fertility potential in many patients; however, some patients may still have some potential based on the parameters observed in this study.

O-221 2:50 PM Tuesday, October 20, 2020

INITIAL EVALUATION OF SAFETY AND EFFICACY OF ADMINISTRATION OF ESTRADIOL (E2) BY SUBCUTANEOUS (SC) INJECTIONS TO MALE-TO-FEMALE (MTF) TRANSGENDER PATIENTS. Jennifer A. LaBudde, MD, Wendy Y. Craig, PhD, Daniel I. Spratt, MD. Maine Medical Center Portland, ME.

OBJECTIVE: The primary aim of this study was to determine if SC injection of E2 valerate could produce serum E2 levels within our clinic's target therapeutic range for MTF patients (75-200 pg/mL) without causing significant adverse effects. Secondary aims were to assess: 1) if SC E2 can suppress serum total testosterone (T) levels (<50 ng/dL) as effectively as oral (PO) E2 , 2) if SC administration has less of a hepatic effect than PO, 3) if serum E2 levels remain within the target range between weekly injections and 4) if SC E2 is acceptable to patients.

DESIGN: Retrospective chart review of MTF patients treated in Maine Medical Center Reproductive Endocrinology clinic.

MATERIALS AND METHODS: All charts of MTF patients seen from 2011-2020 were reviewed. Patients were allowed to choose PO, SC or transdermal (TD) administration. Inclusion criteria were age 18-79 years, PO or SC E2 therapy, and serum E2 and T levels measured by LabCorp (Calabasas CA). E2 valerate was injected SC using a 5/8' 25g needle. 17β-E2 was administered orally. Serum E2, T, estrone (E1), and sex hormone binding globulin (SHBG) levels and fasting lipid panels were measured in SC and PO patients and values compared by Mann Whitney U test. Peak and nadir serum E2 concentrations were measured in a subgroup of SC patients. Serum sex steroid concentrations were measured by liquid chromatography/mass spectrometry. Local and systemic adverse effects were assessed by history and physical exam. The study was approved by the Maine Medical Center IRB.

RESULTS: 102 charts were reviewed. Of 65 patients who were offered PO, TD or SC therapy (the SC option became available in May 2017), 23 choose SC. 61 patients were included in the final analysis, 23 in the SC group and 38 in the PO group. Median dose of E2 for the PO group was 4 mg/day [full range=1-12]; for SC E2 it was 4 mg/week [full range=2-6]. For the SC and PO groups the median E2 were 155.5 [75-291] (n=18) and 122 [76-208] pg/mL (n=38) respectively. Median and range of serum T levels in the SC and PO groups were 16 [4.5-82] (n=14) and 13 [4.8-515] (n=38) ng/dL respectively. E1 serum levels in the SC and PO groups were 49.0 [31.0-104.0] (n=10) and 495 [198-926] (n=12) pg/mL (p=0.003). SHBG and lipid levels did not vary significantly between the two groups (not shown). In a subgroup of SC patients, the median serum E2 decreased from 212 [158-245] to 112 [87-150] pg/mL from the day after to the day before an injection (n=12). 22/23 patients in the SC group chose to continue this method, 0/23 patients experienced a systemic reaction and 1/23 experienced a local site reaction.

CONCLUSIONS: These preliminary data suggest that SC E2 injection is a safe and effective option for administration of E2 that appears to be well accepted by patients. It is well absorbed with minimal adverse effects and suppresses serum T levels as effectively as PO E2. SC E2 has less hepatic effect as reflected by serum E1 levels (but not SHBG or lipids in this small sample size). Serum E2 levels decrease between weekly injections and additional studies are required to refine dosing to maintain E2 values within the target range. Additional pharmacodynamic studies are also indicated.

O-222 3:05 PM Tuesday, October 20, 2020

A SURVEY STUDY OF THE LARGEST SERIES OF GAY AND BISEXUAL MEN PURSUING PARENTHOOD. Philip J. Cheng, MD,[1] Mark Leondires, M.D.,[2] Brent M. Hanson, MD,[1] Daniel J. Kaser, MD,[1] James Hotaling, MD[3] [1]IVI-RMA New Jersey, Basking Ridge, NJ; [2]Reproductive Medicine Associates of Connecticut, Norwalk, CT; [3]University of Utah School of Medicine Andrology and IVF Laboratories, Salt Lake City, UT.

OBJECTIVE: An increasing number of gay and bisexual men (GBM) are becoming parents. There is a lack of data to help GBM navigate this complex process. The aim of this study is to assess the needs and unique challenges of GBM who are interested in paternity with a focus on those who want to have biologically-linked children.

DESIGN: IRB-approved web-based questionnaire.

MATERIALS AND METHODS: Between April 2019 and May 2020, GBM were invited to participate in an online, anonymous survey through a high-volume fertility center and Facebook groups focused on GBM interested in parenthood. We used a standardized questionnaire with 26 multiple choice and Likert scale questions that focused on family building preferences, sperm source, egg donor and surrogate characteristics, access to care, legal issues, and financial burden.

RESULTS: 110 men who identified as gay (107, 97.3%) or bisexual (3, 2.7%) completed the questionnaire. The median age was 35 years (IQR 33-40) and the majority of respondents were in a relationship (103, 93.6%) and highly educated, with 69 men (62.7%) earning a post-graduate degree.

A subset of 85 men (77.3%) with an interest in biological parenthood were analyzed separately. The majority of respondents (67, 78.8%) desired more than one child and 54 (63.5%) used or plan to use sperm from both partners. While 83.6% of the 55 men who had pursued fertility services felt that the staff addressed their needs as a GBM, many of them had to travel to another state or country for services (40, 47.2%) and 23 (27.0%) men reported that these services were illegal for GBM where they lived. Only 8 (9.4%) men reported having insurance coverage for any costs associated with assisted reproductive technology and/or surrogacy. Accordingly, the majority of men (62, 72.9%) reported that financial issues were significant considerations in their family building decisions.

CONCLUSIONS: We have created a standardized survey tool to assess the needs of GBM, which can facilitate an individualized approach to treatment and measure access and barriers to care. The majority of gay and bisexual men surveyed want to pursue biological parenthood. These men face unique reproductive challenges, including impaired access to fertility care due to

legal and financial obstacles. Based on this survey, providers should be aware of educational levels, financial costs, and a common desire for two genetically-related intended fathers.

SUPPORT: None

OVARIAN STIMULATION

O-223 1:50 PM Tuesday, October 20, 2020

DIFFERENTIAL OVARIAN RESPONSE TO GONADOTROPIN PREPARATIONS DESPITE SIMILAR OVARIAN RESERVE: MENOPUR IN GNRH (GONADOTROPIN RELEASING HORMONE) ANTAGONIST SINGLE EMBRYO TRANSFER - HIGH RESPONDER (MEGASET-HR) TRIAL ANALYSIS. Andrew F. Khair, PhD, MBA, Eric D. Foster, PhD, Anshul Sinha, B.Tech, Okan Umit Elci, PhD, Gaurang S. Daftary, MD, MBA, Patrick W. Heiser, PhD. Ferring Pharmaceuticals Inc, Parsippany, NJ.

OBJECTIVE: Assess possible interactions between treatment group [highly-purified human menopausal gonadotropin (HP-hMG) or recombinant follicle stimulation hormone (r-FSH)] and ovarian reserve as indicated by baseline levels of anti-Müllerian Hormone (AMH) on the number of oocytes retrieved.

DESIGN: Post-hoc analysis of a randomized, open-label, assessor-blind, non-inferiority trial conducted at 31 U.S. trials sites.

MATERIALS AND METHODS: 620 ovulatory women aged 21-35y with BMI 18-30 kg/m2 and serum anti-Müllerian hormone (AMH) $\geq$5 ng/mL were randomized 1:1 to a 150 IU start dose of HP-hMG (N=311) or rFSH (N=309) in a GnRH antagonist cycle with dose adjustments based upon response from day 6 onward. Human chorionic gonadotropin (hCG) was used to trigger oocyte maturation (GnRH agonist if at high risk of ovarian hyperstimulation syndrome [OHSS]). Central laboratory serum hormone measurements were measured at baseline and stimulation days: 6, day of/after trigger. Fresh transfer of a single blastocyst was performed in hCG-triggered cycles; all embryos were frozen if the risk of OHSS was high. Live births resulting from all fresh and any frozen transfers occurring within 6 months of randomization were collected. A normal regression model was used to explore interactions between treatment group and baseline AMH on the number of oocytes retrieved.

RESULTS: Demographics across treatment arms were similar (mean patient age: 30 years for both; HP-hMG, rFSH mean [SD] BMI: 24.4 [3.3], 24.3 [3.4] kg/m2; AMH: 7.8 [3.6], 7.5 [2.4] ng/mL; antral follicle count: 30.5 [15.5], 31.0 [12.2]). The average number of oocytes per patient in the rFSH arm (22.2 [11.54]) was significantly higher than in the HP-hMG arm (15.1 [10.12]) as were serum estradiol levels at stimulation days 6 and trigger and OHSS rates, described previously.[1] Cumulative live birth rates were similar between treatment groups at 51.5% and 50.6% in rFSH and HP-hMG arms respectively. A positive effect of baseline AMH levels on the number of oocytes retrieved was identified and differed statistically by treatment group (p value=0.032); subjects with higher baseline level of AMH had a larger ovarian response to rFSH versus HP-hMG. For every 1.6 ng/ml (11.1 pmol/L) increase in baseline AMH, rFSH stimulation results in one extra oocyte versus HP-hMG in predicted high-responders.

CONCLUSIONS: Increasing baseline AMH was associated with higher oocyte yields but no difference in cumulative live birth rates in rFSH vs HP-hMG treated patients, with an accompanying increase in OHSS rates also observed in the rFSH arm. This unexpectedly exaggerated ovarian response, which is positively correlated with increasing ovarian reserve based upon the well-established biomarker AMH, highlights a key distinction between the gonadotropin preparations evaluated, creating opportunities for further optimization of stimulation.

References

1. Witz CA, et al. Fert Steril May 2020, in press PMID: 32416978.

SUPPORT: Ferring Pharmaceuticals, Inc., Parsippany, NJ

O-224 2:05 PM Tuesday, October 20, 2020

SERUM GONADOTROPIN ASSOCIATION WITH LIVE BIRTH IN HIGH-RESPONDERS UNDERGOING OVARIAN STIMULATION: MENOPUR IN GONADOTROPIN RELEASING HORMONE (GNRH) ANTAGONIST SINGLE EMBRYO TRANSFER - HIGH RESPONDER (MEGASET-HR) TRIAL ANALYSIS. Sarah A. Grover, MBBS, Eric D. Foster, PhD, Anshul Sinha, B.Tech, Okan Umit Elci, PhD, Gaurang S. Daftary, MD, MBA, Patrick W. Heiser, PhD. Ferring Pharmaceuticals Inc, Parsippany, NJ.

OBJECTIVE: To explore possible relationships between live birth rate (LBR) and age, endocrine variables [baseline anti-Müllerian hormone (AMH); Stimulation days 1, 6, day of/after trigger estradiol, progesterone, human chorionic gonadotropin (hCG), luteinizing hormone, and follicle stimulating hormone (FSH)] after controlled ovarian stimulation of predicted high-responders with either highly-purified menopausal gonadotropin (HP-hMG) or recombinant FSH (rFSH).

DESIGN: Post-hoc analyses of a randomized, open-label, assessor-blind, non-inferiority trial conducted at 31 U.S. trial sites.

MATERIALS AND METHODS: Ovulatory women aged 21-35 years with BMI 18-30 kg/m^2 and serum AMH $\geq$5 ng/mL (N=620) were randomized 1:1 to a 150 IU start dose of HP-hMG or rFSH in a GnRH antagonist cycle; dose revision was allowed from Day 6 onward based upon response. Serum hormone parameters at baseline and during stimulation were assessed by central laboratory. HCG was used to trigger oocyte maturation (GnRH agonist if at high risk of ovarian hyperstimulation syndrome) followed by mandatory single blastocyst transfer. Live birth outcomes resulting from all fresh and any frozen transfers occurring within 6 months of randomization were collected. Full efficacy and safety outcomes were presented previously.[1] Logistic regression was performed to separately identify relationships between each factor (per visit, as appropriate) and the cumulative live birth rate. Interaction effects of the factors with the treatment group (HP-hMG, rFSH) were investigated. Results were reported as odds ratio (OR) and 95% confidence intervals (CI) with corresponding p-values: **OR (CI; p-value)**.

RESULTS: Serum hCG on the last day of stimulation in HP-hMG treated subjects had a significant effect on the probability of live birth: **1.38 (1.00, 1.89; 0.048)**. For every 1 mIU/mL increase in hCG, the odds of live birth increased by 38%. hCG could not be detected in the serum of rFSH treated subjects. A significant serum FSH interaction by treatment group was identified on Day 6. For every 1 IU/mL increase in serum FSH the odds ratio of live birth was reduced by 13% in rFSH treated compared to HP-hMG treated subjects: **0.87 (0.77,0.98; 0.020)**. No other significant treatment interactions on live birth were found in the time points/factors evaluated.

CONCLUSIONS: The present analyses suggest that hCG derived from HP-hMG contributes positively to the likelihood of live birth when used in ovarian stimulation of predicted-high responders, creating an opportunity to target a serum hCG threshold through HP-hMG dosing. Moreover, the negative association of serum FSH levels in rFSH treated relative to HP-hMG treated subjects on stimulation day 6 following a fixed dose of 150 IU, could be explained by FSH isoform differences or hCG modulation early in the cycle. Further studies are required to confirm these findings and to provide mechanistic insight.

References

1. Witz CA, et al. Fert Steril May 2020, in press PMID: 32416978.

SUPPORT: Ferring Pharmaceuticals, Inc., Parsippany, NJ

O-225 2:20 PM Tuesday, October 20, 2020

FRESH VERSUS FROZEN EUPLOID BLASTOCYST TRANSFER OUTCOMES IN PREDICTED HIGH-RESPONDERS: MENOPUR IN GNRH (GONADOTROPIN RELEASING HORMONE) ANTAGONIST SINGLE EMBRYO TRANSFER - HIGH RESPONDER (MEGASET-HR) TRIAL ANALYSIS. Patrick W. Heiser, PhD,[1] Jack L. Crain, MD,[2] Lauren Johnson, MD, MSCE,[2] Jennifer L. Patrick, MS, PhD,[2] Eric D. Foster, PhD,[1] Anshul Sinha, B.Tech,[1] Okan Umit Elci, PhD,[1] Gaurang S. Daftary, MD, MBA[1] [1]Ferring Pharmaceuticals, Inc, Parsippany, NJ; [2]Reproductive Endocrinology Associates of Charlotte, Charlotte, NC.

OBJECTIVE: To evaluate the impact of blastocyst ploidy on fresh and frozen transfer outcomes in predicted high-responders.

DESIGN: Post-hoc assessment of a randomized, open-label, assessor-blind, non-inferiority trial conducted at 31 U.S. centers.

MATERIALS AND METHODS: 620 ovulatory women aged 21-35y with BMI 18-30 kg/m^2 and serum anti-Müllerian hormone (AMH) $\geq$5 ng/mL (N=620) were randomized 1:1 to a 150 IU start dose of HP-hMG or rFSH in a GnRH antagonist cycle, with dose adjustments based upon response from day 6 onward. Human chorionic gonadotropin (hCG) was used to trigger oocyte maturation (GnRH agonist if at high risk of ovarian hyperstimulation syndrome [OHSS]). Day 5 trophectoderm biopsies were performed

for preimplantation genetic testing (PGT) by real-time polymerase chain reaction analysis. Fresh transfer of a single, best quality blastocyst selected by morphology was performed in hCG-triggered cycles; all embryos were frozen if the risk of OHSS was high. PGT results were only available to guide blastocyst selection for frozen transfers. Live births resulting from all fresh and any frozen transfers occurring within 6 months of randomization were collected, allowing for comparisons of single euploid blastocyst transfer outcomes in different transfer settings via logistic regression. To eliminate the confounding variable of a prior failed transfer in the trial, only outcomes from subjects' first transfer were considered. Full efficacy and safety outcomes were presented previously.[1]

RESULTS: There was no evidence of a difference between fresh and frozen transfer live birth rates for first trial transfer, even after normalization based on karyotype.

CONCLUSIONS: The novel MEGASET-HR trial design provides an opportunity to compare outcomes in morphologically-selected fresh vs euploid frozen transfer cycles. Use of PGT for embryo selection in frozen transfer cycles did not improve live birth rates in predicted high-responders $\leq$35 years of age. Importantly, euploid blastocyst outcomes were higher in fresh versus frozen transfer, questioning an emerging U.S. practice trend favoring freeze-all cycles in high-responders.

Live Birth n/N (%)			Live Birth n/N (%)	p-value*
First transfer, fresh	198/389 (50.9%)	First transfer, frozen, euploid	52/106 (49.06%)	0.899
First transfer, fresh, euploid	157/261 (60.15%)	First transfer, frozen, euploid	52/106 (49.06%)	0.104

* p-values based on treatment-adjusted logistic regression model.

References: 1. Witz CA, et al. Fert Steril May 2020, in press PMID: 32416978.

SUPPORT: Ferring Pharmaceuticals, Inc., Parsippany, NJ

O-226 2:35 PM Tuesday, October 20, 2020

EFFECT OF HOSPITAL VOLUME ON THE INCIDENCE OF MAJOR COMPLICATIONS IN PATIENTS HOSPITALIZED WITH OVARIAN HYPERSTIMULATION SYNDROME.

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OBJECTIVE: A relationship between higher hospital volume and improved outcomes has been established for many medical conditions and surgical procedures. However, it has not been previously studied with regards to ovarian hyperstimulation syndrome (OHSS). This study aimed to elucidate the association between hospital volume and OHSS-related complications in hospitalized patients.

DESIGN: A retrospective analysis of the National inpatient Sample from January 2001 to December 2011.

MATERIALS AND METHODS: Patients hospitalized with OHSS were included. International Classification of Disease 9th edition codes were used to examine incidence of major complications. Major complications were defined by the presence of ICD-9 codes for hypotension, shock or systemic inflammatory response syndrome, hemorrhage, coagulopathy, venous or arterial thromboembolism, pulmonary embolism, stroke, cerebral edema, myocardial infarction, pericardial effusion, pneumonia, respiratory failure, pulmonary edema, ovarian torsion, or ileus/small bowel obstruction. Annualized hospital volume was defined as the average number of patients with OHSS treated by a given hospital per year: low-volume (average 1 case/year), mid-volume (average $>$1 but $<$3.5 cases/year), and high-volume (average $\geq$3.5 cases/year, *i.e.* the top-decile). Characteristics and major complication rates related to hospital treatment volume were assessed with multivariable analysis.

RESULTS: There were 11,968 cases of OHSS treated at 735 hospitals; 2,441 (20.4%) patients were treated at low-volume centers, 5,078 (42.4%) at mid-volume centers, and 4,449 (37.2%) at high-volume centers. Of the entire cohort, 1,625 (13.7%) patients experienced a major complication during hospitalization. Patients treated at high-volume centers had lower rates of major OHSS-related complications (low-volume 15.6%, mid-volume 15.2%, and high-volume 11.0%; $P<0.001$). On multivariable analysis, treatment at a high-volume center was independently associated with a nearly 20% lower rate of major OHSS-related complications (adjusted-odds ratio 0.82, 95% confidence interval 0.70-0.97, $P=0.021$).

CONCLUSIONS: Major complications were common among patients admitted to the hospital with OHSS. Our study suggests that higher hospital volume may be associated with improved outcomes in OHSS.

SUPPORT: Ensign Endowment for Gynecologic Cancer Research

O-227 2:50 PM Tuesday, October 20, 2020

PROLONGING FOLLICULAR STIMULATION TO OPTIMIZE OOCYTE YIELD DOES NOT COMPROMISE IMPLANTATION POTENTIAL OF SCREENED EMBRYOS.

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OBJECTIVE: The number of oocytes retrieved following stimulation is an independent predictor of in vitro fertilization (IVF) cycle outcome. During fresh IVF cycles, oocyte maturation trigger (OMT) must be carefully timed in order to simultaneously optimize oocyte development and endometrial receptivity, which is based on the timing of luteinization. However, with the increased utilization of freeze-all cycles, reproductive endocrinologists have shifted the focus of stimulation to maximizing oocyte yield. The potential benefits of this strategy must be weighed against potential negative impacts, including hyperstimulation syndrome and impaired oocyte quality. Prior work has shown that delayed administration of OMT does not negatively impact the oocyte maturation rate, fertilization rate, and euploid rate[1]. Studies to date have not yet evaluated associated clinical pregnancy outcomes. Our goal was to determine whether delayed OMT is associated with IVF outcomes following single thawed euploid embryo transfer (euploid SET).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The study included patients who underwent euploid SET in GnRH-antagonist IVF cycles from 2016 to 2019. IVF cycles were divided into two groups: (1) administration of OMT in the presence of at least 2 follicles 18mm in diameter, and (2)delayed OMT despite the presence of at least 2 18mm follicles . Preimplantation genetic testing for aneuploidy (PGT-A) was performed using next generation sequencing (NGS). Primary outcome was implantation rate (IR). Secondary outcomes included ongoing pregnancy/live birth rate (OP/LBR) and clinical loss rate (CLR). Cycles involving transfer of $>$1 screened embryo or unscreened embryos were excluded. Statistical analysis was performed using T-tests, Wilcoxon two-sample T-test (non-parametric), and a logistic regression analysis with a generalized estimation equation to control for confounders with $p<0.05$ considered significant.

RESULTS: 2,701 euploid SETs were performed during the study period. Among these, 2,132 were from cycles in which OMT was administered in the presence of $\geq$2 mature follicles, and 569 were from cycles in which OMT was delayed despite the presence $\geq$2 mature follicles. Univariate analysis demonstrated differences in patient age and peak estradiol. In an unadjusted analysis, there was a significant difference in IR between patients who were triggered when 2 mature follicles were visualized vs delayed OMT (61.12% vs 66.26%, P=0.02). However, after adjusting for confounders, there were no significant differences in IR (OR 0.72, 95% CI 0.48-1.08), OP/LBR (OR 0.75, 95% CI 0.51-1.10), or CLR (OR 0.80, 95% CI 0.38-1.71).

CONCLUSIONS: In the largest study to date evaluating the impact of delayed OMT during controlled ovarian stimulation cycles, our results demonstrated no association between delay in OMT and IR, OP/LBR, or CLR. Patients can be reassured that prolonging stimulation to optimize oocyte yield does not negatively impact cycle outcome. Prospective studies are needed to more definitively understand the optimal timing of trigger administration.

References

1. Chang, S., et al.,Â *Does extending controlled ovarian hyperstimulation during a GnRH antagonist protocol in vitro fertilization cycle affect oocyte quality?*Â Fertility and Sterility, 2019.Â 112(3): p. e217.

SUPPORT: None

O-228 3:05 PM Tuesday, October 20, 2020

DOES THE TIMING OF CABERGOLINE ADMINISTRATION IMPACT RATES OF OHSS?

Eryn Sarah Rubenfeld, M.D., Daniel Dahan, NA, Yehuda Dahan, NA, Michael H. Dahan, M.D. McGill University, Montreal, QC, Canada.

OBJECTIVE: To investigate whether the timing of dopamine agonist (either at the time of trigger or on the day of oocyte collection) impacts the rates, symptomatology or severity of ovarian hyperstimulation syndrome (OHSS) in a group with GnRH-agonist triggering.

DESIGN: A retrospective cohort study of 285 patients undergoing IVF treatment at the McGill University Health Center (MUHC) between June 1st, 2011 and December 31st, 2019.

MATERIALS AND METHODS: 285 patients who were at high risk of OHSS based on peak serum estradiol (E2) levels > 3,500 pg/mL (the equivalent of approximately 13,000 pmol/L) or stimulation of at least 17 follicles were divided into two groups. Both groups were on the GnRH-antagonist protocol, had final oocyte maturation triggered using a GnRH-agonist and received cabergoline 0.5mg orally daily for 7 days. 101 subjects initiated Cabergoline at the time of trigger (Trig), while 184 patients started on the day of oocyte retrieval (Retriev). Statistical analysis was performed with Analysis of Variance (ANOVA) or chi-squared (X^2) testing where appropriate. Data is presented as mean±SD or %. The Navot criteria for OHSS were used. A power analysis suggested an 82% power to detect the observed differences with an alpha error of 5%.

RESULTS: Both groups were of similar ages (p=0.72), basal serum FSH levels (p=0.11) and rates of PCOS (p=0.57). Trig appeared to be at slightly higher risk of OHSS based on a statistically higher antral follicle count (20.2±4.2 vs. 19.0±4.3; p=0.02), higher number of stimulated follicles >10mm at trigger (25.7±7.0 vs. 22.8±8.3, p=0.003) and higher peak serum E2 (17325±2542 vs. 14822±3098; p=0.0001). Other stimulation parameters including FSH dose were similar. The Trig group had lower rates of mild and moderate OHSS (24% vs. 36%; p=0.045). Neither group had any patients develop severe OHSS. Fewer patients in Trig presented with pelvic free fluid (13% vs. 23%; p=0.03). In the subgroup of patients who had blood drawn (N=181), the Trig subjects showed less hemoconcentration (hemoglobin 12.6 vs. 13.5; p=0.0001, albumin 30.4 vs. 29.5; p=0.0001 and potassium 3.9 vs. 4.2; p=0.0002). There were no differences in the number of subjects presenting with discomfort or bloating (p=0.7). No patients in Trig reported weight gain, compared to 2 patients in Retriev.

CONCLUSIONS: Our findings suggest a potential benefit to prescribing Cabergoline to start on the day of GnRH agonist trigger for patients who are at risk of OHSS, as opposed to waiting until the day of oocyte collection. Our study is the first one to look specifically at whether the timing of cabergoline administration affects the rates and severity of OHSS. Larger, prospective studies in women receiving hCG should confirm these findings.

SUPPORT: None

MALE REPRODUCTION AND UROLOGY: RESEARCH

O-229 1:50 PM Tuesday, October 20, 2020

FUNCTIONAL AND TAXONOMIC DYSBIOSIS OF THE GUT, URINE, AND SEMEN MICROBIOME IN MALE INFERTILITY.

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OBJECTIVE: The microbiome refers to the unique community of microbes present in nearly every niche in the human body, but the role of the genitourinary and gastrointestinal microbiomes in the pathogenesis of male infertility remains poorly understood. To test the hypothesis that the microbiome is associated with idiopathic male infertility, we explored the gut, urine, and semen microbiomes of infertile men and compared these to paternity-proven fertile controls using both marker-based gene sequencing and shotgun metagenomics.

DESIGN: We prospectively enrolled 25 men with primary infertility and 12 paternity-proven controls. We collected semen, midstream urine, and rectal swab specimens and positive/negative experimental controls.

MATERIALS AND METHODS: We performed a detailed history and physical exam, comprehensive semen testing, hormonal profiling, and 16S ribosomal RNA (rRNA) gene sequencing for quantitative taxonomic analysis at strain resolution. Using shotgun metagenomics, we then compared molecular functional pathway expression differences between fertile and infertile men.

RESULTS: We identified a diverse semen microbiome similar to urine but distinct from the rectal microbiome. Infertile men harbored decreased rectal *Anaerococcus* and increased seminal *Aerococcus* compared to fertile controls. *Prevotella* was inversely associated with sperm concentration, and *Pseudomonas* was directly associated with total motile sperm count. Several anaerobes were highly overrepresented in infertile, but not fertile, men with a varicocele. Oxidative stress and leukocytospermia were associated with only subtle differences in the microbiome. Vasectomy appeared to alter the seminal microbiome, suggesting a testicular or epididymal contribution. Metagenomics data from infertile men revealed significant differences in the S-adenosyl-L-methionine (SAM) cycle, which is involved in DNA methylation, antioxidant production, and polyamine synthesis and may play a multifaceted role in the pathogenesis of infertility.

CONCLUSIONS: This pilot study represents the first comprehensive investigation into the microbiome in male infertility and provides proof-of-principle for future mechanistic studies to explore causality and design future diagnostic and therapeutic strategies for men with this complex, costly, and emotionally debilitating disease.

O-230 2:05 PM Tuesday, October 20, 2020

INCREASING PATERNAL AGE IS NEGATIVELY ASSOCIATED WITH DONOR OOCYTE RECIPIENT SUCCESS: A PAIRED ANALYSIS UTILIZING SIBLING OOCYTES.

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OBJECTIVE: Compared to maternal age, there is a less robust understanding of the effects of paternal age on pregnancy outcomes. Some studies have shown that increasing paternal age has a negative effect on assisted reproductive outcomes, while others have shown no clear association. However, many of these studies have been unable to adequately control for oocyte quality, which affects embryo quality and IVF success rates. ART using sibling-oocyte recipients (oocytes from the same donor stimulation transferred to two different recipients) offers a unique model that controls to the greatest degree possible for oocyte quality. We sought to determine if increasing paternal age has an adverse effect on implantation and pregnancy rates by analyzing outcomes in sibling-oocyte recipients.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients who underwent donor egg recipient (DER) cycles in which oocytes from a single controlled ovarian hyperstimulation cycle were split between two recipients were included. The two recipients of the single-donor oocyte cycle were paired and categorized based on paternal age of donor sperm (group A: <45 years old; group B: >45 years old). Patients with uterine factor and severe male factor infertility, including the use of surgically retrieved sperm, were excluded. The primary outcome was implantation rate. Secondary outcomes were positive pregnancy, live birth, and miscarriage rates. Statistical analysis included paired t-tests, and $p<0.05$ was deemed statistically significant.

RESULTS: A total of 1,013 patients who underwent DER cycles between January 2010 and December 2016 were screened for inclusion, of which 408 patients had received oocytes from a split donor oocyte cycle. There were 87 pairs of patients (174 recipients) who received sperm from men with discrepant age based on the pre-specified groups. The mean age was 39.8 years old for group A and 49.5 years old for group B. The groups were similar for gravity, parity, body mass index, number of embryos transferred, peak endometrial stripe, and prior uterine surgery. The implantation rates were found to be significantly higher in group A compared to group B (62.6% ± 4.6% vs. 47.7% ± 4.7%, p=0.026). Likewise, the positive pregnancy rates (82.8% ± 4.1% vs. 66.7% ± 5.1%, p=0.005) and live birth rates (66.7% ± 5.1% vs. 51.7% ± 5.4%, p=0.03) were significantly higher in group A, the younger age group. Miscarriage rates were similar for groups A and B (19.3% ± 5.5% vs. 25.0% ± 6.1%, p=0.44).

CONCLUSIONS: In this idealized model that controls to the greatest degree possible for oocyte quality by using paired recipients from the same

donor from the same stimulation cycle, we found that increasing paternal age had a negative effect on implantation, positive pregnancy, and live birth rates.

O-231 2:20 PM Tuesday, October 20, 2020

POST-MORTEM EXAMINATION OF THE EFFECTS OF SEVERE ACUTE RESPIRATORY SYNDROME (SARS) ASSOCIATED CORONAVIRUS (SARS-COV) ON TESTIS. Justin K. Achua, MS, Kevin Y. Chu, MD, Himanshu Arora, PhD, Oleksii Lakymenko, MD, Oleksandr N. Kryvenko, MD, Ranjith Ramasamy, M.D. University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: The coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 quickly grew into a global pandemic. The virus has been known to impact the respiratory system; however, the extent of impact on testicular tissue remains unknown. It has been found that COVID-19 binds to angiotensin converting enzyme (ACE) 2 receptors, and since ACE2 expression is high in the testes we believe COVID-19 may be prevalent in testes tissue.

DESIGN: In the present study, we analyzed the pathological changes within the testes of three patients who died of COVID-19 pneumonia and sepsis.

MATERIALS AND METHODS: In the present study, autopsy collection was done according to the University of Miami protocol. Testes tissue we collected from COVID-19 positive men (n=3) as well as COVID-19 negative men (n=3) to be used as controls. Tissue was formalin fixed and paraffin embedded. Samples were sectioned to 5-micron sections and stained with hematoxylin and eosin (H&E) as well as subjected to various fluorescently labeled antibodies to specifically differentiate cells or fluorescently labeled COVID RNA hybridization strands within the testes tissue. Fluorescent-labeled tissue slides were imaged on a quantitative pathology scope with various zoom levels allowing for comprehensive qualitative and quantitative imaging.

RESULTS: Among pathological examination of H&E stained slides from COVID-19 positive men, one case demonstrated increased inflammation and leukocyte infiltration, as well as occasional seminiferous tubules comprised of only Sertoli cells. The other 2 showed no abnormal change. These 2 cases had no leukocyte or macrophage infiltration, no inflammation, no abnormal basement membrane thickening, or changes to spermatogenesis. There was little to no difference between the two COVID-19 positive cases and COVID-19 negative controls. Sectioned slides from both COVID-19 positive as well as COVID-19 negative men are currently undergoing fluorescent labeled antibody staining for COVID RNA with results pending.

CONCLUSIONS: This study suggests that, despite the increase in ACE2 receptor presence in testes tissue and the SARS-CoV-2 virus' propensity to bind to said receptor, the male reproductive tract may not be targets of COVID-19 infection in all men. Whether COVID-19 RNA is detected in testes tissue remains to be evaluated.

O-232 2:35 PM Tuesday, October 20, 2020

TOP TEN PRIORITIES FOR MALE INFERTILITY RESEARCH. James M. N. Duffy, DPhil MRes PG HCL MBChB BSc (Hons),[1] Cindy Farquhar, FRANZCOG FRCOG MD MPH,[2] Priority Setting Partnership for Infertility. [1]Institute for Women's Health, University College London, Greater London, United Kingdom; [2]University of Auckland, Auckland, New Zealand.

OBJECTIVE: To develop the top 10 research priorities for male infertility.

DESIGN: International consensus development study. Healthcare professionals, men with fertility problems, and others were brought together in an open and transparent process using formal consensus methods advocated by the James Lind Alliance.

MATERIALS AND METHODS: Potential research questions were collated from an initial international survey, a systematic review of male infertility guidelines, and Cochrane systematic reviews. A rationalized list of confirmed research uncertainties were prioritized in an international survey. Prioritized research uncertainties were discussed during a face-to-face consensus development meeting.

RESULTS: The initial survey was completed by 388 participants, from 40 countries, and 107 potential research questions were submitted. By reviewing five clinical practice guidelines and four Cochrane systematic reviews a further 18 potential research questions were identified. A rationalized list of 34 confirmed research uncertainties were entered into an interim prioritization survey completed by 317 respondents from 43 countries. The top 10 research priorities for male infertility were identified during a consensus development meeting involving 41 participants from 11 countries (Table 1).

TABLE 1. Top 10 research priorities for male infertility.

1	Are sperm tests other than bulk parameters useful in evaluating male fertility? If so, which?
2	What is the emotional and psychological impact of male infertility? Can addressing it improve outcomes?
3	Do environmental factors cause male infertility? If so, which?
4	Does treating specific causes of male infertility improve outcomes?
5	Can we improve surgical sperm extraction outcomes by using endocrine stimulation protocols?
6	What modifiable risk factors cause male infertility?
7	Does treating modifiable risk factors improve outcomes?
8	What co-morbidities are associated with infertility?
9	Does treating co-morbidities improve outcomes?
10	Are nutraceuticals useful in improving male reproductive potential? If so, which?

CONCLUSIONS: We anticipate the top 10 research priorities for male infertility will help research funding organizations and researchers to develop their future research agenda. Healthcare professionals, professional organisations and patient advocacy groups should champion the research priorities to highlight the many unanswered questions which need to be addressed in order to improve the outcomes of men with fertility problems.

References: Graham L, Illingworth BJG, Showell M, Vercoe M, Crosbie EJ, Gingel LJ, Farquhar CM, Horne AW, Prior M, Stephenson JM, Magee LA, Duffy JMN. Research priority setting in women's health: A systematic review. *BJOG: An International Journal of Obstetrics & Gynaecology* 2020; 127(6): 694-700.

SUPPORT: The study was funded by the Auckland Medical Research Foundation, Catalyst Fund, Royal Society of New Zealand, and Maurice and Phyllis Paykel Trust.

O-233 2:50 PM Tuesday, October 20, 2020

THRESHOLDS FOR TESTICULAR SIZE DISCREPANCY IN FERTILE MEN WITH AND WITHOUT VARICOCELE. William T. Berg, MD,[1] Gabriella J. Avellino, MA, MD,[1] Kathleen Hwang, MD,[2] Mark Sigman, MD[1] [1]Brown University, Providence, RI; [2]University Pittsburgh, Urology, Pittsburgh, PA.

OBJECTIVE: The difference in testicular sizes between right and left testes is often utilized to determine the effect of pathology such as varicoceles on testicular growth. Furthermore, the normal testicular size differential in adult fertile men is currently unknown. We sought to characterize the testicular size distribution in fertile men with and without clinical varicoceles.

DESIGN: Cross-sectional retrospective cohort study.

MATERIALS AND METHODS: Records from men presenting for vasectomy consultation were evaluated. Men with a history of a solitary testicle, testicular torsion, or infertility were excluded. Only those men who fathered children were included. Testicular volume was measured using a modified Takihara orchidometer. The modified orchidometers were created using an ellipse formula and 3-D printing to make larger rings up to 60 cc to allow for measurements of testes beyond the original orchidometer ring size, which went up to only 34 cc. Testicular size measurement and the presence or absence of varicocele was determined by clinical exam by three fellowship trained male infertility specialists. Testicular size distribution and differential means were calculated. Reference ranges and differences in testicular size were calculated to include 95% of the patients. Comparisons were then made between those with and without varicoceles. Parametric statistics were used for normally distributed data (testicular sizes) while non parametric tests of significance were used for non-normally distributed data (difference s in testicular size).

RESULTS: Out of 3,235 men, 618 met inclusion criteria. In fertile men without a varicocele, the mean left testis volume was 31.4 cc (95% population range 17.5 – 48.6 cc) and the mean right testis volume was 32.5 cc (95 % population range 17.5 – 55.0 cc). Testicular size was greater on the right than on the left in 88% of men. A varicocele was present in 17.7% of patients. The presence of a varicocele was associated with decreased testicular size on both the left (31.4 cc vs 27.9 cc, $p<0.01$) and the right (32.5 cc vs 30.5 cc, $p=0.03$). In patients whose right testicle was larger than or equal to

the left testicle, the mean size discrepancy was 2.0 cc vs 3.2 cc in those without a varicocele compared to those with a varicocele ($p<0.001$). The mean percentage size discrepancy between right and left testicles in these patients was 5.8%. vs 10.3% ($p < 0.001$). In addition, 95% of these patients had a difference in testis volume of less than or equal to 8 cc and a percent difference in testicular size of less than or equal to 23%.

CONCLUSIONS: In fertile men, the normal reference limits for left testicular volume is approximately 17 cc to 50 cc. In addition, the normal upper reference range threshold for the difference in testicular size in fertile men without varicocele is 8 ml or 23%. This is the first study to date to establish population means and normal ranges for a cohort of fertile men without varicocele. In patients with a varicocele, testicular size can be expected to decrease accordingly. These reference ranges will serve as important guides when assessing male fertility status.

O-234 3:05 PM Tuesday, October 20, 2020

EVALUATION OF SERUM 17-HYDROXYPROGESTERONE AS PREDICTOR OF SEMEN PARAMETER IMPROVEMENT IN MEN UNDERGOING MEDICAL TREATMENT FOR INFERTILITY.

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OBJECTIVE: To identify infertile men with testosterone deficiency (TD) who will respond with semen parameters improvement to medical therapy with clomiphene citrate (CC) and human chorionic gonadotropin (hCG).

DESIGN: Prospective cohort study from July 2018 to January 2020.

MATERIALS AND METHODS: We included men with impaired semen parameters and TD. Men received either CC or CC/hCG if history of testosterone use. We assessed demographic information, serum testosterone (T), 17-hydroxyprogesterone (17-OHP) - maker of intratesticular testosterone (ITT), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and semen parameters before and after therapy. Semen quality upgrading was based on assisted reproduction eligibility: in vitro fertilization (< 5 million), intrauterine insemination (IUI) (5-9 million), and natural pregnancy (> 9 million). Variables were compared using the U Mann Whitney or Wilcoxon rank test.

RESULTS: 31 men were included. Median follow-up was 3.7 [3.3 – 5.1] months. 16 men upgraded semen quality. 6/10 men with initial total motile sperm count (TMSC) of 0 had motile sperm after treatment, and 11/20 men with TMSC < 5 upgraded semen quality into the range of IUI / natural pregnancy. Low 17-OHP was the only factor that predicted semen quality upgrading. Men with 17-OHP ≤ 55ng/dL upgraded semen quality along with improving hormones, whereas men with 17-OHP > 55ng/dL did not upgrade semen quality. (Table 1)

CONCLUSIONS: Medical therapy for infertile men with TD resulted in the improvement of sperm concentration, TMSC, T and 17-OHP. Semen quality upgrading appears to be more significant in patients with low 17-OHP, suggesting that ITT can be used as a biomarker to predict semen parameters improvement.

SUPPORT: None

PROFESSIONAL DEVELOPMENT

O-235 1:50 PM Tuesday, October 20, 2020

DO OUTCOMES OF EMBRYO TRANSFERS DIFFER WHEN COMPLETED BY REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY (REI) FELLOWS VERSUS FACULTY? AN 11-YEAR RETROSPECTIVE REVIEW.

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OBJECTIVE: To compare the clinical pregnancy rate (CPR) and live birth rate (LBR) of embryo transfers performed by REI fellows versus faculty physicians.

DESIGN: Retrospective cohort analysis.

MATERIALS AND METHODS: All patients who underwent an embryo transfer (ET) at Mayo Clinic Rochester from 1/2009 - 1/2020 were identified. Only patients who denied research access to their records were excluded. First-year fellow ETs occurred only after completion of 30 mock transfers under faculty supervision. The primary outcomes, CPR and LBR, were evaluated based on fitting generalized linear regression models assuming a binomial distribution and the logit link function, with fellow/faculty as a random effect, and adjusted for patient age, autologous or donor oocyte, fresh or frozen embryo, and the number of embryos transferred.

RESULTS: Fifteen fellows completed 1,236 (39.9%) of 3,100 total transfers during the study period. A comparison of all fellow versus faculty transfers showed no statistically significant difference in the CPR or the LBR (Table 1). This was also true when differentiating between autologous and donor oocyte transfers. When outcomes were stratified by fellowship year (FY1, FY2, FY3), the CPR (43.6% vs. 43.3% vs. 44.8%, p=0.92) and LBR (38.4% vs. 38.7% vs. 36.0%, p = 0.92) were similar. Eleven fellows completed at least 30 ETs in their FY1. Comparing each fellow's initial 30 ETs to all future FY1 ETs found that the CPR (48.2% vs. 40.6%, p=0.018) and LBR (45.0% vs. 34.5%, p=0.001) were both significantly higher among the initial transfers. One explanation may be that fellows were more likely to transfer at least 2 embryos during their first 30 ETs as compared to subsequent transfers (60.6% vs. 45.7%, p<0.001).

CONCLUSIONS: To date, this is the largest and most extensively controlled study of outcomes of embryo transfers performed by REI fellows versus faculty physicians. We found no differences in clinical outcomes between fellow and faculty transfers. First-year fellows who were appropriately trained had success rates equal to more experienced fellows, even among their first 30 transfers. These data demonstrate that allowing fellows to perform live ETs would not have a detrimental effect on clinical outcomes.

TABLE 1. Comparison of hormones levels and semen parameters at baseline and follow-up according to baseline 17-OHP (ng/dL).

	17-OHP > 55			17-OHP ≤ 55		
	Baseline (n = 12)	Follow-up (n = 12)	p-value	Baseline (n = 19)	Follow-up (n = 19)	p-value
Hormones						
17-OHP	82 [69 - 106.8]	102.5 [64.5 – 134]	0.209	27 [19 - 35]	86 [55 – 125]	**< 0.001**
T (ng/dL)	359.6 [224 3 - 406.3]	474.5 [374 - 617.5]	**0.019**	165 [120 – 248]	350 [301 - 671.7]	**< 0.001**
FSH (mIU/mL)	8.2 [3.4 - 23.7]	13 [3.4 - 22.8]	0.241	4.1 [3 - 8.8]	6 [2.1 - 16.5]	0.052
LH (mIU/mL)	5.1 [3.2 - 5.8]	5.5 [3.5 - 7.4]	0.173	3 [1 - 6.4]	4.1 [1.8 - 8.6]	0.074
Semen Parameters						
Volume	2.8 [2 – 3]	3 [2 - 3.4]	0.678	2 [1.5 – 4]	2.6 [1.8 - 3.1]	0.365
Concentration	2.9 [0.2 - 10.1]	8.5 [1.8 – 15]	0.169	0.7 [0 – 10]	9.3 [0.7 – 20]	**0.004**
Motility	0.31 [0.10 - 0.57]	0.39 [0.06 - 0.52]	0.102	0.10 [0.00 - 0.60]	0.50 [0.20 - 0.56]	0.265
TMSC	1.3 [0.03 - 16.5]	10.6 [0.7 - 21.6]	0.139	0.3 [0 – 9]	7.7 [0.1 – 25]	**0.049**
TMSC category						
< 5	7 (58.3%)	4 (33.3%)		13 (68.4%)	5 (26.3%)	
5 – 9	1 (8.3%)	0		2 (10.5%)	5 (26.3%)	
> 9	4 (33.3%)	8 (66.7%)	0.059	4 (21.1%)	9 (47.4)	**0.008**

Median [IQ 25-75].

TABLE 1. Comparison of Outcomes of ETs Performed by REI Fellows vs. Faculty, Overall and Stratified by Autologous vs. Donor Oocyte

Outcome	Fellows	Faculty	p
CPR			
Overall	43.7% (540/1236)	41.3% (770/1864)	0.28
Autologous	43.7% (495/1132)	40.8% (665/1628)	0.26
Donor Oocyte	43.3% (45/104)	44.5% (105/236)	0.78
LBR[†]			
Overall	38.2% (435/1139)	36.2% (602/1665)	0.38
Autologous	38.2% (396/1038)	35.6% (514/1446)	0.36
Donor Oocyte	38.6% (39/101)	40.2% (88/219)	0.78

[†]Analysis of the LBR was restricted to the 2,084 transfers performed prior to 3/22/2019.

O-236 2:05 PM Tuesday, October 20, 2020

EVALUATING TRENDS IN AUTHORSHIP BY GENDER WITHIN *FERTILITY AND STERILITY*, 2005-2019. Chelsea Henshaw, MD, Jaden R. Kohn, MD, MPH, Melissa McHale, MD, Kristin Darwin, MD, Holly Rankin, MD, Shari M. Lawson, MD, MBA. Johns Hopkins University School of Medicine Department of GYN/OB, Baltimore, MD.

OBJECTIVE: To examine trends in academic mentorship in Reproductive Endocrinology and Infertility research by assessing the genders of first and last authors of publications in *Fertility and Sterility*.

DESIGN: A bibliometric analysis of *Fertility and Sterility*.

MATERIALS AND METHODS: This study included case series, original research, and systematic reviews from *Fertility and Sterility* from 2005-2019. Data was obtained from *Fertility and Sterility* through Web of Science. The genders of the first and last author were determined using a validated gender-inference algorithm to assign gender to the corresponding first name. For first names with less than 70% gender assignment accuracy, gender identities were confirmed using internet searches of the individual and/or name. Cochrane-Armitage test and linear regression were used.

RESULTS: Gender of first and last authors was identified for 6,692 of 7,754 publications in *Fertility and Sterility* from 2005-2019.

A woman fulfilled the first author position of 40.5% of publications from 2005-2019, which slightly increased to 48.8% from 2010-2019. Women were the last authors of only 21.9% of all publications from 2005-2009, with an increase to 30.8% from 2010-2019 ($p<.05$).

Women were both the first author and last author of 11.5% of all publications from 2005-2009, however this percentage has increased to 19.7% over the past decade and a half ($p<.05$). Men as a first and last author pairing for publications decreased from 49% in 2005-2009 to 36% of all publications in 2010-2019 ($p<.05$).

Overall from 2005-2019, a publication is 2.74 times more likely to have a female first author and male last author pair versus a male first author with a female last author pair. However, over time this gap has decreased.

CONCLUSIONS: Over the past nearly two decades, dramatic changes can be seen when evaluating the author gender trends of publications in *Fertility and Sterility*. This suggests an increase in representation of women as leaders in the field of Reproductive Endocrinology and Infertility. Although these advances are commendable, gender equity in this field of academia has not yet been reached.

Genders of first- and last- author pairs in *Fertility & Sterility, 2005-2019*

Year	Both male authors	Both female authors	First author female, Last author male	First author male, Last author female
2005	56	11	24	9
2006	52	10	24	14
2007	50	11	29	10
2008	50	11	29	10
2009	47	13	30	10
2010	43	16	29	11
2011	40	15	35	10
2012	36	19	31	13
2013	33	21	33	13
2014	35	20	32	14
2015	37	19	32	13
2016	30	20	37	13
2017	35	19	32	14
2018	32	26	32	9
2019	30	19	38	13

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EXPERIENCE EQUALS EXPERTISE: OUTCOMES OF LIVE EMBRYO TRANSFERS (ET) BY REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY (REI) FELLOWS (FEL) COMPARED TO ATTENDING (ATT) PHYSICIANS. Jacquelyn Shaw, MD,[1] Carlos M. Parra, MD,[2] Jennifer K. Blakemore, MD,[1] Mary Elizabeth Fino, MD,[1] Frederick L. Licciardi, M.D.[2] [1]NYU Langone Prelude Fertility Center, New York, NY; [2]NYU Langone Health, New York, NY.

OBJECTIVE: Live embryo transfer is arguably the most important skill learned in REI fellowship, yet approximately half of 3rd year fellows perform <10 ETs prior to graduation.[1] Some educators believe ETs performed by trainees reduce pregnancy rates.[2] Our center employs a thorough ET education with vast live ET training. Our objective was to examine if ET outcomes differ by FEL and ATT REI physicians.

DESIGN: Retrospective cohort study of all ETs at a large urban university based fertility center from 7/2015-3/2020.

MATERIALS AND METHODS: Our center completes >500 ETs annually, with FELs directly involved from year one. All ETs are direct and ultrasound (US) guided. FELs perform the US for all ATT ETs throughout fellowship. FELs complete 50 IUIs and perform 10 supervised, US guided IUIs with ET catheter before initiating supervised live ET. FEL ETs were identified and compared to those performed by ATT. The primary outcome was clinical pregnancy (CP) rate per euploid ET. Secondary outcomes evaluated livebirth/ongoing pregnancy (LB/OP) and spontaneous abortion (SAB) rates in all types of ET and by FEL year. Statistical analysis was performed using Chi-square and, with $p<0.05$ considered significant.

RESULTS: 5534 total ETs were completed, with 252 (5%) performed by 4 clinical FEL. FEL performed 17% (42) fresh, 71% (179) frozen, 11% (28) donor egg, and 59% (149) euploid ETs, at similar rates compared to ATT ($p=0.17$). 26% (66) of ETs were performed by a 1st year, 28% (70) by a 2nd year, and 46% (115) a 3rd year FEL, with no difference in ET type ($p=0.25$). For euploid ETs performed by FEL compared to ATT physicians (respectively), the CP [68% (101/148) vs. 69% (2360/3413)], biochemical [12% (18/148) vs. 9% (300/3413)], and ectopic [0.7% (1/148) vs. 0.3% (11/3413)] rates were statistically the same ($p=0.37$). Euploid LB/OP rates (60% vs. 59%) and SAB rates (3% vs. 7%) were the same ($p=0.26$). For all ETs, the CP [65% (163/251) vs. 62% (3172/5082)], biochemical [11% (28/251) vs. 10% (501/5082)], and ectopic [0.4% (1/251) vs. 0.3% (16/5082)] rates were statistically similar ($p=0.55$), as were the LB/OP rates (53% vs 52%) and SAB rates (8% vs 8%) ($p=0.89$). Analysis of individual FEL year compared to ATT or other FEL years produced similar results with no statistical difference ($p=0.64$). The 1st 10 FEL ETs (40 total) resulted in slightly lower but not statistically different CP (63%) and LB (48%) rates, with higher biochemical (13%) and SAB (15%) rates ($p=0.31$-0.93). To ensure FEL clinical proficiency, defined as no more than 10% different from the 65% ATT CP rate with 95% confidence, an a priori power analysis approach determined that the minimum number of FEL live ETs needed is 45.

CONCLUSIONS: ETs performed by REI FELs produce the same clinical pregnancy and livebirth rates as ATT physicians, without increased rates of biochemical pregnancies, ectopic pregnancies or miscarriages. Live ETs are essential to fellowship training, can be taught effectively with hands-on experience, and can be performed without compromising patient outcomes. We suggest a well-defined educational pathway for FELs to gain proficiency with a goal of 45 live ET during fellowship.

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O-238 2:35 PM Tuesday, October 20, 2020

FERTILITY PRESERVATION AND INFERTILITY TREATMENT IN MEDICAL TRAINING: AN ASSESSMENT OF RESIDENCY PROGRAM DIRECTORS' ATTITUDES ACROSS SPECIALTIES IN THE UNITED STATES. Megan B. Huynh, BS candidate,[1] Ange Wang, MD,[2] Lusine Aghajanova, MD PhD[3] [1]Georgetown University, Washington, DC; [2]Stanford University School of Medicine, Stanford, DC; [3]Stanford University, Stanford, CA.

OBJECTIVE: To assess knowledge and support of residency program directors (PDs) in the United States towards the reproductive needs of their residents.

DESIGN: Cross-sectional survey.

MATERIALS AND METHODS: An online survey emailed to residency PDs of various medical specialties in the US.

RESULTS: Respondents included 299 PDs, with the most represented specialties being Emergency Medicine (11.0%), Obstetrics & Gynecology (9.7%), and Family Medicine (9.0%). The most common lengths of parental leave were 6-8 weeks of maternity leave (30.4%) and less than two weeks of paternity leave (33.1%). The majority of PDs lacked knowledge of their program's specific fertility insurance policies; 57.2% did not know about coverage for infertility treatment and 68.6% reported not knowing coverage for fertility preservation. 52.2% of PDs surveyed were unaware if any of their residents were facing infertility or recurrent pregnancy loss. PDs reported offering fertility-related support in the forms of moral support (68.2%), time off for appointments (65.2%), and insurance coverage (36.1%). 56.2% of PDs felt that their personal level of support was aligned with their programs'. Regarding fertility preservation, the majority of PDs (66.2%) reported never having a resident express interest to them; main resources available to residents included moral support (59.2%) and time off for appointments (48.5%). Similar to infertility treatment policy, the majority of program directors (55.9%) felt that their personal level of support was aligned with their program's for fertility preservation. Most respondents felt it was important to increase resources for residents interested in infertility treatment and fertility preservation and believed the best ways to do so were increasing their own personal awareness of individual needs (47.5%), establishing official policies on fertility treatment (34.1%), and financial support (33.4%). PDs reported that time (32.1%) and costs (24.8%) were the primary barriers that prohibited residents from seeking treatment for fertility-related issues. Stratification of results by PDs in surgical and non-surgical specialties, as well as by gender, revealed differences in support level and knowledge. Surgical specialty PDs emphasized more the need for increased resources for their residents' fertility needs, and male PDs generally appeared less knowledgeable about their residents' fertility issues.

CONCLUSIONS: The study found wide variance regarding residency PDs' personal knowledge and levels of support for their residents' fertility needs. The majority of PDs were unaware of fertility issues that their residents may be going through but were commonly ready to offer moral support and time off for any fertility-related issues. While many PDs felt that their personal level of support was aligned with their program's, they also felt that it would be important to improve resources for their residents, through increasing their own awareness of these issues, creating policies related to fertility treatment, and providing financial support for the treatment.

O-239 2:50 PM Tuesday, October 20, 2020

IMPROVING RESIDENT EDUCATION AND MASTERY IN REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY FOR THE GENERALIST OB/GYN: A SURVEY-BASED STUDY. Emma V. Gilmore, MD,[1] Jennifer K. Blakemore, MD,[1] Susan Maxwell, MD,[2] Shannon Devore, MD[1] [1]NYU Langone School of Medicine, New York, NY; [2]Northwell Health, New York, NY.

OBJECTIVE: Exposure to Reproductive Endocrinology and Infertility (REI) varies widely among OB/Gyn residencies, with most depending on a single 3-4 week rotation. At our institution, residents provide care to an underserved infertility population through ovulation induction (OI). However, the system was not optimized for education, so a new PGY2-directed monitoring service was created in 2018. Our objective was to evaluate the new system in regard to REI education within a generalist training framework.

DESIGN: Anonymous quantitative and qualitative IRB-approved survey of residents at a large urban academic center.

MATERIALS AND METHODS: In brief, the new system, designed to supplement the REI rotation, assigned residents to a 2-hour daily monitoring session, 5 days/week, twice during their PGY2 year, for transvaginal ultrasounds (TVUS), evaluation and counseling of patients undergoing OI. Presentations were made via telephone to a remote REI fellow who reviewed the ultrasound and precepted their plan. One year after the program was introduced, all residents who participated in the new OI curriculum (participants, n=10) as well as those trainees who partook in the old REI curriculum without the monitoring addition (controls, n=17) were included and surveyed.

A 23-question survey was created and vetted by 2 REI-trained physicians to evaluate knowledge, TVUS skills, confidence gained, and educational experience. Quantitative data are reported as %; qualitative data as unedited free text. Statistical analysis included unpaired t-tests for continuous variables where appropriate, with $p<0.05$ considered significant.

RESULTS: 8 participants and 14 controls responded, for a response rate of 91.6%. Most participants (62.5%) strongly agreed that they acquired REI knowledge and skills, compared to 7.1% of controls. Subjects rated their confidence with TVUS pre/post their experience (scale 0-100). Participants reported a statistically significant confidence increase of 28-Pre to 82-Post compared to controls of 58-Pre to 63-Post (t -3.02, $p<0.03$). Subjects were asked if they would feel confident implementing 3 cycles of OI prior REI referral and 87.5% of participants strongly agreed compared to 78.5% of controls. All participants (100%) agreed that the curriculum helped achieve their educational objectives, and that a remote REI preceptor was helpful and informative. The same trends were observed in a sub-group analysis of subjects with or without subspecialty interests. Overall, subjects enjoyed the curriculum with two reporting "the curriculum is fantastic and the junior residents know so much more than I do!" and "even as a chief this year I gained so much experience and knowledge helping my junior residents ... This is a truly valuable resident education experience!"

CONCLUSIONS: This curriculum intervention provided residents with increased confidence in REI knowledge, enhanced education, and skill acquisition. A remote REI preceptor was helpful and could be implemented in programs even without on-site sub-specialists. Further study is needed to determine if this system can be applied to other programs.

O-240 3:05 PM Tuesday, October 20, 2020

AGE AND INFERTILITY: AN OPPORTUNITY FOR IMPROVING MEDICAL EDUCATION. Kathryn Smith, B.S.,[1] Anne P. Hutchinson, M.D.,[2] Elaine O. Cheung, PhD,[3] Jessica L. Thomas, A.M.,[1] Patricia I. Moreno, PhD,[3] Veronika Elisabeth Grote, B.S.,[3] Kara N. Goldman, M.D.,[2] Neil Jordan, PhD,[4] Eve C. Feinberg, M.D.[2] [1]Northwestern University Feinberg School of Medicine, Chicago, IL; [2]Northwestern University Feinberg School of Medicine, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Chicago, IL; [3]Northwestern University Feinberg School of Medicine, Department of Medical Social Sciences, Chicago, IL; [4]Northwestern University Feinberg School of Medicine, Department of Psychiatry and Behavioral Sciences, Mental Health Services & Policy Program, Chicago, IL.

OBJECTIVE: Assess female physicians' knowledge about age and fertility.

DESIGN: Survey followed by qualitative semi-structured interviews in a subset of participants.

MATERIALS AND METHODS: Eligibility survey links were presented at a Women in Medicine conference and on Facebook physician mom groups. Questions assessed knowledge of age-related fertility decline and respondents' experiences with infertility and assisted reproductive technology (ART).

Qualitative interviews were conducted in a subset of 10 respondents who fulfilled eligibility criteria: graduation from medical school 1999-2019, current job in academic medicine. Interviews were conducted in-person or remotely over video conference using a semi-structured interview guide. Open-ended questions assessed participants' knowledge of age-related fertility decline, sources of education, and recommendations for physician education in fertility and family planning. All transcripts were qualitatively coded by two research team members using Dedoose.

RESULTS: Of the 44 survey respondents (mean age 34.5y, SD 5.4), 31 were attendings, 2 were fellows, 10 were residents, and 1 left medicine. Ten (9 attendings and 1 fellow) were invited to complete qualitative interviews (age 34.4 ± 2.1).

All 44 respondents correctly identified peak fertility as <30y and that egg quality declines as women age. Eighty percent (35/44) correctly identified that fertility begins to decline in the early 30s. Twenty percent (9/44) incorrectly believed that fertility begins to decline between ages 35 and 39.

Almost half of women surveyed (21/44) experienced infertility, and 12 (27.3%) used in vitro fertilization to conceive. Fifteen women considered oocyte vitrification, 7 sought consultation with a reproductive endocrinologist, 4 completed an oocyte vitrification cycle, and 2 were actively engaged in fertility preservation.

All 10 women who underwent qualitative interviews expressed that preclinical medical education on age-related fertility decline was insufficient. Instead, participants reported learning about fertility through witnessing the infertility experiences of patients (n=3), family/friends (n=4), and/or their own struggles (n=4). To improve medical education regarding fertility and family planning, 9 of 10 recommended having frank discussions with trainees on fertility, family planning considerations, and their available options (e.g., parental leave, fertility preservation benefits, infertility coverage) specific to pursuing a career in medicine.

CONCLUSIONS: A survey revealed high rates of fertility knowledge but high ART utilization among female physicians due to delayed childbearing. Qualitative interviews revealed informal education through the experiences of patients, peers, or personal experience. Medical school provides an ideal gender-inclusive environment for more structured education on age-related fertility decline. Female physicians voiced a desire for transparent discussions of access to fertility care and family planning options during residency.

SUPPORT: This research was funded by the 2019 ASRM Research Grant, awarded to Eve Feinberg, M.D. and Elaine Cheung, Ph.D. (co-PI's),Â Northwestern University.

REGENERATIVE MEDICINE AND STEM CELLS

O-241 9:40 AM Wednesday, October 21, 2020

THE EMBRYONIC DEVELOPMENTAL COMPETENCE OF RECONSTRUCTED ZYGOTES USING A CLONED MALE GAMETE. Philip Xie, B.S., Aysha Trout, B.A., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To test the feasibility of ooplast-mediated male genome replication as a source of male gametes to generate full preimplantation embryos.

DESIGN: Through injection into an enucleated oocyte, we generated identical copies of male genomes. The resulting androgenetic pseudo-blastomeres were used as male gametes and fused to artificially activated oocytes to generate zygotes. Full embryonic development was assessed in a time-lapse system in comparison to control ICSI conceptuses.

MATERIALS AND METHODS: Metaphase II (MII) oocytes from B6D2F1 mice were exposed to cytochalasin B, enucleated under Oosight™ visualization, and then injected with individual sperm heads from the same strain. The resulting pseudo-blastomeres containing copies of male genomes were exposed to DNA polymerase inhibitor and fused to chemically activated oocytes. Control conceptuses were generated by piezo-actuated ICSI. The resulting embryonic development was observed up to 96h.

RESULTS: The enucleation of 30 oocytes yielded the same number of ooplasts. They were subsequently injected with individual spermatozoa resulting in a 73% survival rate, and all developed a single male pronucleus. Following 16h in culture, 21 (95%) androgenetic constructs cleaved to the 2-cell stage, yielding 42 male pseudo-blastomeres. Each pseudo-blastomere was then fused with 42 chemically activated oocytes, and 39 successfully fused (93%) into reconstituted biparental zygotes. Thirty-five unmanipulated oocytes were injected with sperm heads, resulting in 30 control embryos (86%). Both control and experimental zygotes were then cultured in a time-lapse incubator and monitored for full preimplantation development. The control zygotes developed into 2-cell (87%), 4-cell (83%), morula (80%), and blastocyst (80%) embryos, while comparable cleavage parameters were obtained in the experimental embryos (90%, 87%, 85%, and 77%, respectively), without noticeable morphokinetic impairment.

CONCLUSIONS: These results support the feasibility of generating multiple copies of male gametes from a single spermatozoon. Once embryo implantation and the health of the offspring are confirmed, this technique has potential for use in replicating scarce male gametes, allowing pre-fertilization genetic screening for heterozygous conditions, and in conjunction with heritable genomic editing.

SUPPORT: None

O-242 9:55 AM Wednesday, October 21, 2020

MALE NEOGAMETOGENESIS TO GENERATE FULLY DEVELOPED PREIMPLANTATION EMBRYOS. Sherina Lawrence, B.S., Philip Xie, B.S., Mounia Haddad, M.D., Allison C. Petrini, M.D., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To assess the feasibility of haploidizing epiblast-like cells (EpiLCs) derived from male mouse embryonic stem cells (mESCs) to generate full preimplantation embryos.

DESIGN: Male mESCs were propagated and differentiated in a novel 3D culture system by the direct spherification technique. After 3 days of exposure to differentiating medium, EpiLCs, confirmed by specific biomarkers and synchronized at G1, were fused with intact oocytes following activation and completion of biparental haploidization. Full preimplantation development of the zygotes was assessed by time-lapse imaging and compared to control ICSI conceptuses.

MATERIALS AND METHODS: Male mESCs were suspended in base spherification solution and encapsulated by exposure to sodium alginate. Each sphere containing approximately $6.0x10^5$ cells, with diameter ranging from 8 to 10 mm, was bathed in medium supplied with activin A, bFGF, and KSR. Differentiated EpiLCs were isolated by trypsinization to assess OCT4 and Nanog expression. An additional 1.5 μM aphidicolin was supplied to the media 24 h before fusing with oocytes. Individual EpiLCs treated by Sendai virus were injected in the perivitelline space of an oocyte. Resulting oocytes displaying 2 spindle complexes were activated by 10 μM calcium ionophore. Control embryos were generated by piezo-actuated ICSI. Embryonic developmental morphokinetic parameters were detected through time-lapse imaging.

RESULTS: Male mESCs, engulfed in 4 spheres and plunged in differentiating medium, aggregated into embryoid bodies with a mean diameter of 250 μm. After isolation by mechanically breaching the spheres followed by trypsinization, cells showed a positive expression of OCT4 (>90%) and a decreased Nanog positivity (<40%), confirming differentiation to EpiLCs. Sendai virus–mediated cell fusion was performed on 80 oocytes, with a 100% fusion rate. A total of 49 oocytes displayed biparental spindle complexes (61.3%). After oocyte activation, 37 zygotes extruded the second polar body alongside a third pseudo polar body (from the haploidized EpiLCs), and developed 2 pronuclei (75.5%). After 96 h in a time-lapse incubator, the control embryos developed into 2-cell (86.7%), 4-cell (83.3%), morula (83.3%) and blastocyst (83.3%) embryos. Meanwhile, embryos in the experimental group developed into 2-cell embryos at a lower rate (69.4%, $P < 0.001$). Further developments into 4-cell (49.0%), morula (32.7%) and blastocyst (32.7%) embryos were also lower in zygotes obtained from biparental haploidization ($P < 0.00001$).

CONCLUSIONS: Neogametogenesis was accomplished by differentiating mESCs to EpiLCs in a novel 3D culture system. Zygotes obtained from biparental haploidization yielded full preimplantation development to expanded/hatching blastocysts. Despite a lower rate of blastocysts development, embryo morphokinetic characteristics were comparable to the control ICSI conceptuses. Once the ability to generate healthy pups is confirmed, this model may represent an ideal option to treat men with germ cell aplasia or spermatogenic arrest.

O-243 10:10 AM Wednesday, October 21, 2020

SAFETY AND TOXICOLOGY STUDY AFTER INTRA-OVARIAN ENGRAFTMENT OF HUMAN BONE MARROW MESENCHYMAL STEM CELL IN CHEMOTHERAPY INDUCED POI MOUSE MODEL. Hang-Soo Park, PhD,[1] Rishi Man Chugh, PhD,[1] Amro Elsharoud, MD,[1] Mara Ulin, MD,[1] Sahar Esfandyari, DVM,[1] Lale Bakir, MD,[1] Alshimaa Aboalsoud, MD - Ph D,[2] Ayman Al-Hendy, MD, PhD[1] [1]The University of Illinois College of Medicine, Chicago, IL; [2]Faculty of medicine, Tanta university, Egypt, Tanta, Egypt.

OBJECTIVE: Primary ovarian insufficiency (POI) refers to the ovarian loss of function under the age of 40 years and lead those patients to

amenorrhea and infertility. Our previous study showed that transplantation of human bone marrow-derived mesenchymal stem cells (hBM-MSC) in chemotherapy-induced POI mouse ovary can reverse POI through correction of serum hormonal levels, promote follicular generation in the ovary, increase in granulosa cells population, and achieve pregnancy. According to this research, BM-MSC is a promising cell source to treat POI patients, however, there are still concerns about the potential risks of stem cell engraftment due to the route of administration. For further clinical application using allogenic hBM-MSC in POI, these reproductive, developmental and toxicity concerns should be addressed. Understanding the distribution of engrafted hBM-MSC in an animal model will explain how hBM-MSC interacts in the host animal and ensures the safety of allogenic hBM-MSC intra-ovarian transplantation.

DESIGN: We hypothesize that engrafted hBM-MSC remain in the ovary and do not distribute to any other organs.

MATERIALS AND METHODS: In this study, we induced POI in C57/BL6 mice by chemotherapy. We then engrafted hBM-MSCs (500,000 cells/ovary) by direct intra-ovarian injection. 2 weeks and 4 weeks after MSC treatment, we sacrificed the mice and collected the major organs to analyze the presence of human-specific ALU repeat in genomic DNA (10 animals/group). We also analyzed the transmission of human DNA with fetus genomic DNA (8 fetuses/ group). Moreover, we traced engrafted hBM-MSC using whole body cryo-imaging.

RESULTS: We found that human genes representing engrafted hBM-MSC were detected only in mouse ovaries and not in any of the major organs such as the heart, lungs, and liver. We also found that human DNA was not transmitted into the fetus during development. Pups delivered by the hBM-MSC treated mice had no abnormal morphology and developed normally.

CONCLUSIONS: Our data revealed that engrafted hBM-MSC via intra-ovarian injection was not migrated into other organs. Engrafted cells stayed in targeted organs after 2 weeks and 4 weeks. hBM-MSCs engraftment does not affect fetuses or pups development. Our study demonstrates the safety data for allogenic hBM-MSC transplantation as POI therapy for future translations research and clinical trials.

SUPPORT: This study supported by Startup package at UIC

O-244 10:25 AM Wednesday, October 21, 2020

BONE MARROW-DERIVED MESENCHYMAL STEM CELLS UPREGULATE ENDOMETRIAL STROMAL CELL MIGRATION BUT NOT PROLIFERATION. Qingshi Zhao, PhD, Yahaira Naaldijk, PhD, Oleta A. Sandiford, BS, Nicole M. Marchetto, MD, MPH, Nataki C. Douglas, MD, PhD, Pranela Rameshwar, PhD, Sara S. Morelli, MD, PhD. Rutgers New Jersey Medical School Newark, NJ.

OBJECTIVE: Cyclic regeneration of the endometrium is crucial for successful reproduction. Bone marrow-derived mesenchymal stem cells (BM-MSC) traffic to the endometrium and have been implicated in endometrial regeneration and repair of the menstrual "wound". Precise mechanisms are unknown, but likely occur via paracrine action, since the BM-MSC secretome contains growth factors and cytokines that promote wound healing in other tissues. Our objective was to test the hypothesis that the BM-MSC secretome upregulates human endometrial stromal cell (HESC) migration and proliferation, and activates genes involved in cell motility and survival.

DESIGN: Laboratory in vitro studies utilizing telomerase-immortalized HESC cell line (T-HESC) and mesenchymal stem cells (MSC) cultured from the bone marrow aspirate of a healthy female donor.

MATERIALS AND METHODS: Flow cytometry was performed to confirm BM-MSC phenotype. Conditioned medium (CM) was collected from BM-MSC after 24h of monolayer culture. T-HESC were then cultured for 24h in BM-MSC CM or phenol red-free DMEM + 10% charcoal-stripped FBS as control. We determined the effect of the BM-MSC secretome on T-HESC expression of *CCL2,* a chemokine that enhances HESC survival and motility, and *BCL2*, a cell survival gene. Total RNA was extracted from T-HESC and qRT-PCR was performed using 18S rRNA to normalize. For migration assays, a scratch was made through a confluent T-HESC monolayer and wound area was measured at 0, 8, and 24h using ImageJ software. Percent wound closure was calculated from a mean of 5 wound area measurements per well. To assess T-HESC proliferation, immunohistochemistry was performed using a specific anti-Ki67 antibody. The percentage of T-HESC expressing Ki67 was calculated in 10 high power fields per experiment. All experiments were performed three times in duplicate or triplicate. Mann-Whitney test was used for analysis of nonparametric data and unpaired t-test for parametric data, with $p<0.05$ considered significant.

RESULTS: Flow cytometry demonstrated that BM-MSC expressed MSC markers CD29, CD44, CD73 and CD90, and lacked expression of the hematopoietic marker CD45. The BM-MSC secretome upregulated T-HESC expression of *CCL2* mRNA by 13.5±1.7-fold (median±IQR, $p<0.0001$), but did not change expression of *BCL2* mRNA (0.9 ± 0.1-fold, $p=0.6$). Exposure to the BM-MSC secretome increased T-HESC migration (% wound closure) at 8h (16.9±4.3% CM vs. 10.3±3.1% control [mean±SD], $p=0.002$) and at 24h (68.4±4.8% CM vs. 48.5±14.5% control, $p=0.001$). T-HESC proliferation was unchanged after exposure to BM-MSC CM for 24h; the percentage of T-HESC expressing Ki67 was 47.8±4.4% in CM and 45.4±0.9% in controls (mean±SD, $p=0.3$).

CONCLUSIONS: The BM-MSC secretome upregulates endometrial stromal cell migration, a cellular process required for endometrial regeneration and repair. Increased expression of *CCL2* mRNA in T-HESC implicates a novel mechanism by which BM-MSC may mediate HESC motility. These findings support a role for BM-MSC in supporting physiologic endometrial regeneration, and imply a potential role for BM-MSC in promoting endometrial repair after injury.

O-245 10:40 AM Wednesday, October 21, 2020

SINGLE CELL TRANSCRIPTOME ANALYSIS IDENTIFIES PUTATIVE CELL SURFACE MARKERS OF HUMAN SPERMATOGONIAL STEM CELLS. Sarah Munyoki, B.A.,[1] Adrienne N. Shami, B.S.,[2] Xianing Zheng, B.S.,[2] Qianyi Ma, Ph.D.,[2] Meena Sukhwani, Ph.D,[3] Sue Hammoud, Ph.D.,[2] Jun Z. Li, Ph.D.,[2] Kyle Orwig, Ph.D.[4] [1]University of Pittsburgh School of Medicine, Pittsburgh, PA; [2]University of Michigan, Ann Arbor, MI; [3]Magee-Womens Research Institute, Pittsburgh, PA; [4]University of Pittsburgh, Pittsburgh, PA.

OBJECTIVE: Identify the protein markers of human and monkey spermatogonial stem cells (SSCs) and the signaling pathways regulating their self-renewal and proliferation, to facilitate the development of SSC-based therapies for the treatment of male infertility.

DESIGN: We performed high throughput, unbiased, single-cell RNA-sequencing of normal adult primate testicular tissue. Clustering analysis coupled with the evaluation of expression patterns identified potential marker genes of primate stem/progenitor spermatogonia. The expression of these candidate markers on human testicular tissue was evaluated by immunostaining techniques. SSC transplantation was used to determine the candidate markers that may be utilized to sort and enrich human SSCs for downstream clinical applications.

MATERIALS AND METHODS: We performed drop-seq single cell RNA sequencing of 5 human and 4 rhesus macaque healthy adult donor testicular tissue, generating ~13,560 and 20,242 single cell transcriptomes respectively. Principal component analysis (PCA) dimensionality reduction and T-distributed Stochastic Neighbor Embedding (tsne)/ Uniform Manifold Approximation and Projection(UMAP) unsupervised clustering analysis partitioned the primate cells into transcriptionally distinct populations, representing the known primate testicular cell types. Differential expression analysis identified marker genes of the undifferentiated spermatogonia cell populations, that were validated by immunoflourescence techniques. Fluorescence activated cell sorting (FACS) and human to nude mouse xenotransplantation was used to evaluate SSC colonization activity.

RESULTS: Our transcriptome data identified CDK17, MAGEB2, MORC1, TCF3, PIWIL4, GPX1,DNAJB6, FMR1 and TSPAN33 as candidate markers genes of primate stem/progenitor spermatogonia. These genes exhibited unambiguous staining of cells on the basement membrane of human seminiferous tubules and demonstrated overlapping expression with human undifferentiated spermatogonia UCHL1, and more limited overlap with the differentiation marker cKIT. Colometric staining revealed that expression of these markers is mainly restricted to Adark and Apale spermatogonia which are thought to represent the SSC population in primate testes. Flow cytometry analysis of cell surface proteins TSPAN33 and PLPPR3 found that ~3% and ~1.5% of human testicular cells express these proteins respectively. When FACS sorted TSPAN33+, TSPAN33- or PLPPR3+,PLPPR3- and unsorted control fractions were xenotransplantated into infertile recipient mice, we observed significant enrichment of SSC colonization activity in the TSPAN33+ and PLPPR3+ fractions.

CONCLUSIONS: We have identified putative marker genes of primate stem/progenitor spermatogonia. These genes are implicated in WNT, Hedgehog, FGF, BMP, MAP2K/AKT signaling as well as metabolism that may be important in regulating primate SSC growth dynamics in vivo and/or in vitro. Our transcriptome data may reveal markers/niche signaling pathways that can be exploited to isolate and enrich primate SSCs and expand them in vitro.

SUPPORT: Magee womens Research Institute (MWRI) T32 fellowship in reproductive sciences

O-246 10:55 AM Wednesday, October 21, 2020

CHROMATIN ACCESSIBILITY, TRANSCRIPTIONAL NETWORKS, AND FATTY ACID (FA) SYNTHESIS DURING ADIPOGENESIS IN SUBCUTANEOUS (SC) ADIPOSE STEM CELLS (ASCS) OF POLYCYSTIC OVARY SYNDROME (PCOS) WOMEN.

Gregorio D. Chazenbalk, Ph.D.,[1] Smriti Sanchita, B.S.,[2] Karen L. Leung, B.S.,[1] Catherine T. Pham, B.S.,[1] Tristan R. Grogan, M.S.,[1] Xinmin Li, Ph.D.,[1] Xiangming Ding, Ph.D.,[1] Matteo Pellegrini, Ph.D.,[1] Marco Morselli, Ph.D.,[1] Lucia Carbone, Ph.D.,[3] Brett Davis, M.S.,[3] Mariam Okhovat, Ph.D.,[4] Phillip A. Dumesic, M.D., Ph.D.,[5] Kevin J. Williams, Ph.D.,[1] Daniel A. Dumesic, M.D.[1] [1]UCLA, Los Angeles, CA; [2]UCLA, Los Angeles, CA, India; [3]OHSU, Portland, OR; [4]Oregon Health and Science University, Portland, OR; [5]Dana-Farber Cancer Institute, Boston, CA.

OBJECTIVE: To examine dynamic changes of chromatin accessibility, transcriptional regulation, and total vs. *de novo* fatty acid (FA) synthesis in subcutaneous (SC) adipose stem cells (ASCs) of normal-weight PCOS women vs. age- and BMI-matched controls.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: SC abdominal ASCs were obtained from 3 non-Hispanic Caucasian normal-weight PCOS women who had previously shown higher *PPARg* and *CEBPα* mRNA expression in newly-formed adipocytes compared to age- and BMI-matched controls. ASCs were cultured in adipogenic medium for 0-12 days. Chromatin and RNA were isolated at days 0, 3, 7 and 12 for Assay Transposase Accessible Chromatin (ATAC)- and RNA-sequencing (RNA-seq). Accessible regions and enriched transcription factor (TF) binding motifs were identified from ATAC-seq using MACS2 and Homer (Hypergeometric Optimization of Motif EnRichment), respectively. Differentially expressed genes identified from RNA-seq were filtered for significance ($p_{adj}<0.05$) and fold-change (>2-fold); gene ontology (GO) functions and canonical pathways were determined using Ingenuity Pathway Analysis, and gene set enrichment analysis (GSEA) was used to identify enriched cellular processes. A subset of ASCs were exposed to adipogenic medium containing ^{13}C-glucose 48 hours before cell harvest at days 7 and 12 to analyze *de novo* FA synthesis. Different FAs were detected by high pressure liquid chromatograph-mass spectrometry and quantified with Fatty Acid Source Analysis. Paired and unpaired t-test were used for statistical analyses.

RESULTS: PCOS cells showed a substantial shift in chromatin accessibility between days 0 and 12, when less accessible chromatin at day 0 became more accessible than control cells by day 12. In correspondence of open chromatin, binding motifs for crucial adipogenic TFs FRA1, ATF3, BATF, FRA2, JUNB, AP-1 and FOSL2 were significantly enriched at days 0, 3 and 12. RNA-seq indicated adipogenic genes (*PPARγ, CEBPα, ADIPOQ, AGPAT2, FABP4, LPL, PLIN1*; 2-6 fold changes) were upregulated in PCOS cells, while lipid oxidation and FA β-oxidation ($z>2$, $p<0.05$) were upregulated GO functions at days 3, 7, and 12. In parallel, up-regulated pathways in PCOS included oxidative phosphorylation and cholesterol biosynthesis at days 3, 7, and 12. GSEA confirmed significantly increased transcripts related to oxidative phosphorylation, peroxisome activity and adipogenesis at days 3, 7, and 12 in PCOS cells ($p_{adj}<0.05$). *De novo* FA synthesis was 30% of total FA content. During adipocyte formation at day 7, total and *de novo* synthesis of myristic, palmitic, palmitoleic, and oleic acid increased in ASCs of both female types (day 7 to 12, $p<0.02$), but were significantly greater in PCOS than control cells at day 12 ($p<0.05$).

CONCLUSIONS: ASCs of PCOS women exhibit dynamic changes in chromatin accessibility during adipogenesis, with little accessibility at day 0 to enhanced accessibility by day 12. These developmental programming events may enhance transcriptional activation of crucial adipogenic genes and pathways, promoting greater FA production and fat storage in mature adipocytes.

THIRD PARTY REPRODUCTION

O-247 9:40 AM Wednesday, October 21, 2020

INTRACERVICAL INSEMINATION AND INTRAUTERINE INSEMINATION FOR DONOR SPERM TREATMENT IN THE NATURAL CYCLE: A RANDOMIZED CONTROLLED TRIAL.

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OBJECTIVE: Both ICI and IUI in the natural cycle are performed as first line treatments in women who are eligible for donor sperm treatment. IUI is more costly than ICI, due to the involvement of sperm processing. The aim of this study was to determine if six cycles of ICI are non-inferior to six cycles of IUI in donor sperm treatment in terms of ongoing pregnancy.

DESIGN: We performed a multicenter, non-blinded, non-inferiority randomized controlled trial in six fertility clinics in the Netherlands and Belgium. Based on our retrospective cohort study we assumed a live birth rate of 40% after six cycles of IUI. To assess a non-inferiority margin of 12%, we needed to include 416 women.

MATERIALS AND METHODS: All women scheduled for donor sperm treatment were eligible, regardless of the indication for treatment. Women were allocated to receive either ICI or IUI in a natural cycle during six cycles within a time horizon of eight months. Eligible women were informed about the study by their doctor or by a dedicated research nurse. After written informed consent women were randomized using a central password protected Internet-based randomization program.

In ICI cycles, one insemination was performed with unprocessed semen by straw or by cervical cap within 24 hours after the LH surge in urine or blood. In IUI cycles, one intra-uterine insemination was performed with processed semen one day after the LH surge in urine or blood.

The primary outcome was conception within eight months after randomisation leading to a live birth. Secondary outcomes were multiple pregnancy, miscarriage and time to ongoing pregnancy.

We calculated relative risks (RR) and risk difference (RD) and 95% CI. We analysed the data both on an intention to treat and a per protocol basis. The per protocol analysis was limited to women who were treated according to the study protocol, who did not switch treatment and who had either become pregnant or completed six treatment cycles in case of treatment failure.

RESULTS: Between June 2014 and February 2019, we included 421 women, of whom 211 women were randomly allocated to ICI and 210 to IUI. Women's age was on average 34 years (SD $\pm$ 4) in both groups. Ongoing pregnancy occurred in 52 women (25%) in the ICI group and 82 women (39%) in the IUI group (RR 0.63, 95% CI: 0.47 to 0.84). Live birth rate occurred in 51 women (25%) in the ICI group and 81 women (39%) in the IUI group (RR 0.63, 95% CI: 0.47 to 0.84)). ICI was inferior to IUI; the left boundary of the 95% confidence interval was minus 0.24 and crossed the pre-set absolute difference of 12% (RD of -0.14, 95% CI: -0.18 to -0.30).

In the per protocol analysis ongoing pregnancy occurred in 50 women (39%) in the ICI group and 80 women (56%) in the IUI group (RR 0.69, 95% CI: 0.53 to 0.90). Live birth rate occurred in 49 women (38%) in the ICI group and 80 women (56%) in the IUI group (RR 0.68, 95% CI: 0.52 to 0.88). The time to pregnancy was longer in the ICI group compared to the IUI group after six cycles (HR 0.58, 95% CI: 0.41-0.82).

CONCLUSIONS: In women undergoing donor sperm treatment in a natural cycle, ICI results in lower ongoing pregnancy rates than IUI. Therefore, IUI should be the preferred treatment.

SUPPORT: This trial received funding from the Dutch Organisation for Health Research and Development (ZonMw).

O-248 9:55 AM Wednesday, October 21, 2020

JUST OVER ONE-THIRD OF PATIENTS INTERESTED IN EMBRYO DONATION COMPLETE EMBRYO DONATION. Olivia Carpinello, MD,[1] B. Mitchell Bodily, MD,[2] Samad Jahandideh, PhD,[3] Morine Cebert, Ph.D., RN,[4] Joshua C. Combs, MD,[5] Micah J. Hill, DO,[5] Alan H. DeCherney, MD,[6] Kate Devine, MD[3] [1]Program in Reproductive Endocrinology and Gynecology, NICHD, NIH, Bethesda, MD; [2]Uniformed Services University, Bethesda, MD; [3]Shady Grove Fertility, Washington D.C., DC; [4]University of Pennsylvania & Philadelphia VA Medical Center, Philadelphia, PA; [5]Walter Reed National Military Medical Center, Bethesda, MD; [6]Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD.

OBJECTIVE: To describe one infertility center's experience with embryo donation, which has recently become an option for family building.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Patients at a single infertility practice who expressed interest in embryo donation from 2015-January 2020 were referred to the practice's embryo donation team. Criteria for embryo donation included: embryos vitrified onsite at blastocyst stage on day 5 or 6, egg age <40 years, sperm age <50 years, PGT-M/SR excluded, PGT-A euploid permitted. Embryos were accepted if associated clinical data indicated ≥40-45% odds of live birth, assuming no recipient uterine factor. Patient characteristics were assessed using descriptive statistics, and comparisons were made between those who completed donation and those who did not to determine if certain characteristics were associated with likelihood to complete donation. To determine the differences between the groups, independent samples T tests were performed, and proportions were compared with Chi-square.

RESULTS: 438 patients expressed interest in donating supernumerary embryos. On average, initial donation inquiry occurred 5 years from the patient's initial visit. Mean age at donation inquiry was 40.7 years. 89.3% of all patients had either a live birth or ongoing pregnancy from ART, with a mean of 1.2 live births from ART. The majority of patients interested in embryo donation were Caucasian (70.1%). Nine (2.1%) were in same-sex relationships and 28 (6.4%) were single females. 49 patients (11.2%) used donor sperm and 185 (42.2%) used donor eggs for embryo creation. Ultimately, 173 (39.5% of those who expressed interest) completed embryo donation. There was no statistically significant difference in the use of donor gametes between those who donated and those who did not (13.9% versus 9.2% for donor sperm and 48.0% versus 39.0% for donor egg). There was no difference in mean age at inquiry, gravidity, parity, patient ethnicity, infertility diagnosis, or relationship status between those who donated and those who did not. Caucasians, black or African Americans, and Asians made up 68.0%, 10.1% and 10.1%, respectively, of those who completed donation. A mean of 2.9 supernumerary embryos were donated.

CONCLUSIONS: Just over one third of patients who expressed interest completed embryo donation. There are likely complex social, cultural, psychological, and ethical components to embryo donation. These data show that, ultimately, the majority of interested patients choose not to donate. A surprisingly large number of patients interested in donating embryos (42.2%), and of those who ultimately donated (48.0%), utilized donor eggs in embryo creation. These numbers are much higher than the approximate 10% of IVF cycles which utilize donor egg within the practice. It is possible that these patients have a less genetically-centered definition, and experience, of family, which makes them more inclined both to use donor eggs and to donate embryos. It is also possible that donor egg recipients are more likely to have a desire to "give back" and to donate embryos in order to help others achieve parenthood.

O-249 10:10 AM Wednesday, October 21, 2020

HEALTHCARE PROVIDER PREFERENCES RELATED TO DISTRIBUTION OF GAMETE DONOR MEDICAL HISTORY UPDATES. Lauren Isley, MS, CGC, Pamela Callum, MS, CGC. Generate Life Sciences Los Angeles, CA.

OBJECTIVE: Personal and family medical history is collected from gamete donors during their initial eligibility assessment for participation in a donor program. This medical information captures only a short period of time given that donors are required to be young and healthy at the time of donation. New diagnoses in a gamete donor, a family member or a donor-conceived individual could significantly impact the health management of other donor-conceived offspring. Thus, the ASRM Ethics Committee recently published recommendations for donor programs (1) to encourage donors and recipients to provide medical updates and (2) to develop policies which outline the mechanisms for collecting and distributing updates. Numerous stakeholders including recipients, donors, donor-conceived individuals, and all of their healthcare providers, can benefit from an exchange of long-term health information. The Ethics Committee recommendation does not include specific guidance as to how often, by what method, and to whom new medical information should be distributed. This study investigated reproductive medicine providers' experience with and preferences for receiving updated medical information on gamete donors.

DESIGN: An online survey was developed and distributed by the ASRM Genetic Counselor Special Interest Group to all members of the Nursing, Legal, Mental Health, and Reproductive Managers professional groups.

MATERIALS AND METHODS: Not applicable.

RESULTS: A total of 57 responses were received and included members of all of the professional groups surveyed. The majority of respondents were mental health professionals, followed by nurses/nurse managers and practice administrators. Forty percent of respondents indicated they are unaware of the terms under which the gamete providers they work with will notify them or their patients of significant new medical information. The majority (65%) would prefer the gamete facility provides updates to both the clinic and the recipient. Twenty-four percent of respondents prefer to receive updates by email, followed by a letter (21%) or an online portal (21%). The majority of respondents (72%) wanted notified of high risks to the donor's offspring (i.e. donor is a carrier of an X-linked condition and 50% of males will be affected) and 63% also desired updates which confer a low risk to the offspring (i.e. donor is a carrier for an autosomal recessive condition; offspring will not be affected unless recipient is also a carrier). Nearly half (47%) indicated they want to receive updated medical information on gamete donors for an indefinite period of time.

CONCLUSIONS: There are currently multiple models of managing new medical information involving gamete donors. It is important that healthcare providers and recipients are aware of the terms under which updated medical information may be actively communicated to them by their gamete providers. This study aids gamete providers in understanding the preferences and expectations of reproductive providers as stakeholders in these communications and can inform their policy development.

References: Interests, obligations, and rights in gamete and embryo donation: an Ethics Committee opinion. Ethics Committee of the American Society for Reproductive Medicine. Fertil Steril.Â 2019 Apr;111(4):664-670.

O-250 10:25 AM Wednesday, October 21, 2020

REPRODUCTIVE OUTCOMES OF WOMEN 40 AND OLDER UNDERGOING IVF WITH DONOR SPERM. Pietro Bortoletto, MD, Stephanie Willson, MD, Phillip A. Romanski, MD, Owen Davis, M.D., Zev Rosenwaks, M.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To determine if women ≥ 40 years old without a male partner utilizing donor sperm have the same reproductive outcomes as those with a male partner who utilize their partners sperm.

DESIGN: Retrospective cohort study conducted at a university-affiliated center.

MATERIALS AND METHODS: We included women ages 40 years and older undergoing their first COH cycle at our center followed by a fresh cleavage (day 3) or blastocyst (day 5) embryo transfer (ET). Patients were divided into two groups based on the ejaculated sperm source utilized: Donor sperm or partner sperm. Live birth rate was the primary outcome. Pregnancy rate was the secondary outcome. Multivariable logistic regression was performed with adjustment for age, developmental stage of embryo, and number of embryos transferred. Odds ratios (OR) with 95% confidence intervals (CI) for pregnancy & live birth were estimated. Statistical significance was denoted by $p<0.05$.

RESULTS: A total of 3,910 cycles in women ≥ 40 years were analyzed, of which 307 utilized donor sperm and 3,603 utilized their partners sperm to conceive. In the univariate analysis, patients utilizing donor sperm were found to have similar pregnancy rates as those utilizing their partners sperm (41.0 versus 39.8%, OR: 0.95, 95% CI: 0.75-1.20). After adjusting for age, number of embryos transferred, and developmental stage of embryos, the model estimates did not vary (aOR: 1.22, 95% CI: 0.95-1.56). Similarly, the univariate analysis for live birth did not demonstrate a difference between groups (19.2 versus 17.8%, OR: 0.91, 95% CI: 0.67-1.22). However, after

similar adjustment for confounders, the use of donor sperm was associated with statistically significant increased odds of live birth (aOR: 1.38, 95% CI: 1.01-1.88).

CONCLUSIONS: Women ≥ 40 years old who are unpartnered or in same sex relationships can be counseled that their odds of a live birth are slightly better than women in heterosexual relationships utilizing their partners sperm. These findings serve to further refine and individualize counseling regarding expected IVF outcome for women in this age group and social scenario.

O-251 10:40 AM Wednesday, October 21, 2020

ASSOCIATION OF OBSTETRIC AND NEONATAL OUTCOMES WITH GESTATIONAL CARRIER GUIDELINE ADHERENCE. Brett Stark, MD,[1] Amy Kaing, MD,[2] Kate Swanson, MD,[2] Evelyn Mok-Lin, MD[3] [1]University of California, San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA; [2]University of California San Francisco, San Francisco, CA; [3]REI UCSF, Center for Reproductive Health, San Francisco, CA.

OBJECTIVE: To assess whether criteria described by American Society for Reproductive Medicine (ASRM) guidelines for gestational carriers and additionally non-described factors are associated with an increase in poor obstetric and or neonatal outcomes.

DESIGN: This is a cross-sectional study of births from gestational carrier pregnancies at a single institution in San Francisco, California between 2008 and 2019.

MATERIALS AND METHODS: Violations of ASRM guidelines include age <21 or >45 years, nulliparity, prior stillbirth, tobacco or percutaneous drug use, >5 prior deliveries, >3 prior cesarean delivery (CD), major comorbidities or mental health conditions, BMI >35, and short interval pregnancy (<12 months). The primary outcomes were clinical pregnancy, biochemical pregnancy, preterm delivery, term delivery, and pregnancy complications. Associations were analyzed using Fisher's exact test, Chi-squared test as appropriate, and multivariate logistic regression.

RESULTS: A total of 194 gestational carriers were included in this analysis. Among gestational carriers, Twenty-five percent (50/194) did not meet ASRM criteria, with BMI >35 (38%) and age (mostly >45 or <21) (36%) being the most common criteria violated. Seventy-six percent of carrier pregnancies (148/194) were mediated through a Surrogacy Agency. Surrogates presenting from agencies were more likely to adhere to ASRM guidelines (OR 3.02, 95% CI 1.49 – 6.13, p= .002). After categorizing the gestational carriers into complete guideline adherence versus any guideline non-adherence groups, we found that complete adherence to ASRM Guidelines did not alter rates of antepartum complications, intrapartum complications, and postpartum complications. Those in the non-adherence cohort were found to have significantly increased risk of spontaneous abortion (OR 4.89, 95% CI 2.04-12.4, p= .001). In a multivariate logistic regression adjusting for each ASRM guideline factor, age >45 (aOR 3.98, 95% CI 1.22-15.00,p=0.005) and BMI > 35 (aOR 4.89, 95% CI 1.59-15.00, p=0.005) were notable predictors of spontaneous abortion in non-guideline adherent gestation carrier pregnancies. Whether adherent or non-adherent to guidelines, gestational carriers with a history of a prior spontaneous abortion were more likely to experience a biochemical pregnancy (OR 3.2, 95% CI 1.2 – 8.4, p=0.018), and those with a history of prior preterm birth were more likely to experience a spontaneous abortion (OR 3.19, 95% CI 1.1-9.2, p=0.031).

CONCLUSIONS: Nearly one in four gestational carrier pregnancies in this cohort did not meet ASRM guidelines. Guidelines are less likely to be followed when a gestational carrier is found through means other than an agency. Non-adherence to ASRM guidelines was associated with an almost 5-fold increase in odds of spontaneous abortion. In both guideline adherent and non-adherent gestational carriers, history of prior spontaneous abortion as well as history of prior preterm birth are significantly associated with poorer pregnancy outcomes; thus, are important historical factors to rigorously account for when making carrier selection.

O-252 10:55 AM Wednesday, October 21, 2020

FAMILIES CREATED THROUGH EGG DONATION: PARENTAL PSYCHOLOGICAL HEALTH IN EARLY CHILDHOOD. Joanna Lysons, MSc, Susan Imrie, PhD, Vasanti Jadva, PhD, Susan Golombok, PhD. University of Cambridge, Cambridge, United Kingdom.

OBJECTIVE: This study examined mothers' and fathers' psychological health in families who had conceived a child using egg donation (ED). Data are reported from phase two of a longitudinal study, when children were aged five.

DESIGN: Cross-sectional design using standardized questionnaires.

MATERIALS AND METHODS: Questionnaire data were obtained from 66 families who had a child through egg donation, and a comparison group of 46 families who had a child through IVF with own-gametes. The average ages of mothers were 47.06 years (ED) and 42.24 years (IVF); fathers' average ages were 48.08 years (ED) and 45.11 years (IVF). Questionnaires assessing parental psychological health (Trait Anxiety Index, Edinburgh Depression Scale), stress associated with parenting (Parenting Stress Index), marital quality (Golombok Rust Inventory of Marital State), social support (Multidimensional Scale of Perceived Social Support) and resilience (Brief Resilience Scale) were completed by mothers and fathers. Independent-samples t-tests and Mann-Whitney U-tests were used to analyse the data.

RESULTS: Preliminary results found that mothers and fathers in both groups scored within the normal range for all questionnaire measures of psychological health. No significant differences were found between ED and IVF mothers in reported levels of anxiety, depression or resilience. ED mothers reported significantly lower couple relationship quality than IVF mothers ($t(93) = 2.97$, $p = .004$). However, when mother's age was controlled for, the test was no longer significant. ED mothers reported significantly higher parenting stress than IVF mothers ($U = 1070.5$, $p = .02$) and significantly lower levels of perceived social support than IVF mothers ($U = 1037$, $p = .007$). No significant differences were found between ED and IVF fathers in reported levels of couple relationship quality, perceived social support or resilience. ED fathers reported significantly higher levels of parenting stress ($U = 766.5$, $p = .01$), anxiety ($t(88.95) = 2.45$, $p = .016$) and depression ($U = 798.5$, $p = .03$) than IVF fathers. However, group differences in depression were no longer significant after controlling for father's age.

CONCLUSIONS: Egg donation parents appear to be functioning within the normal range with regards to parental psychological health. However, egg donation mothers reported lower couple relationship quality, higher parenting stress and lower social support, and egg donation fathers experienced greater parenting stress, anxiety and depression, relative to their IVF counterparts. It is notable that ED mothers' lower couple relationship quality and ED fathers' higher levels of depression appear to be related to the older age of egg donation parents, rather than their use of egg donation *per se*. Possible explanations for the differences in psychological health between the ED and IVF parents will be discussed.

SUPPORT: This study was funded by the Wellcome Trust (grant 208013/Z/17/Z)

REPRODUCTIVE IMMUNOLOGY

O-253 9:40 AM Wednesday, October 21, 2020

HIGH-SENSITIVITY C-REACTIVE PROTEIN (HS-CRP) LEVEL AND PREGNANCY OUTCOMES IN WOMEN WITH UNEXPLAINED INFERTILITY UNDERGOING OVARIAN STIMULATION WITH INTRAUTERINE INSEMINATION (OS-IUI) IN A MULTICENTER TRIAL. Sarah Z. Gavrizi, MD,[1] Sushila Arya, MD,[1] Jennifer D. Peck, PhD,[1] Jennifer F. Knudtson, MD,[2] Karl R. Hansen, MD PhD,[1] Reproductive Medicine Network. [1]University of Oklahoma College of Medicine, Oklahoma City, OK; [2]University of Texas Health Science Center San Antonio, San Antonio, TX.

OBJECTIVE: To determine if chronic inflammation, as assessed by basal hs-CRP level, was associated with pregnancy outcomes in women with unexplained infertility undergoing OS-IUI.

DESIGN: Secondary analysis of a prospective, randomized, multicenter clinical trial investigating pregnancy, live-birth, and multiple pregnancy rates following ovarian stimulation-intrauterine insemination treatments, the Assessment of Multiple Intrauterine Gestations from Ovarian Stimulation (AMIGOS) trial.

MATERIALS AND METHODS: Of the 900 AMIGOS participants, 778 were available for analysis after excluding patients with hsCRP levels ≥10 indicative of infection, ectopic pregnancies and those missing pregnancy outcome or baseline hs-CRP serum measures. Hs-CRP concentration was evaluated using two definitions: first by hs-CRP categories of < 2mg/L and 2 - 9.9 mg/L as previously defined in the literature, and second, by tertiles (tertile 1 ≤ 0.725 mg/L, tertile 2 0.725 to 2.42 mg/L, and tertile 3 > 2.42 mg/L)[1] . Risk ratios (RR) and 95% confidence intervals for the outcomes of live birth, clinical pregnancy, and pregnancy loss were estimated using modified

Poisson regression models with robust standard errors.Adjustment for covariates were examined in multivariable models. No covariate evaluated (age, duration of infertility, BMI, history of pregnancy loss, race, ethnicity, income, and treatment group) met the a priori criteria for confounding (>10% change in RR upon inclusion (or removal from) the model), and therefore were not retained in the final model.

RESULTS: Elevated hs-CRP levels (2 to 9.9 mg/L) were observed in 39% (95% CI 35.5-42.4) of study participants. We found no relationship between baseline hs-CRP level and live birth or clinical pregnancy outcomes. Risk of pregnancy loss was greater in patients with hs-CRP levels in the middle (RR 1.72, 95% CI 1.05-2.83) and upper tertiles (RR 1.56, 95% CI 0.93-2.61) compared those in the lowest tertile, although the confidence interval for the upper tertile included the null value. Collapsing the two upper tertiles under an assumption of homogeneous patterns of risk suggested greater risk of pregnancy loss for hsCRP >0.725 (RR 1.64, 95% CI 1.03-2.60). However, when evaluated using cutpoints reflecting inflammation, hs-CRP level of 2 to 9.9 mg/L was not associated with a significant increase in pregnancy loss compared to <2 mg/L.

CONCLUSIONS: Basal hs-CRP was not associated with live birth or clinical pregnancy outcomes in women with unexplained infertility undergoing OS-IUI. However, hs-CRP >0.725 mg/L was associated with an increased risk of pregnancy loss. Additional studies are needed to refine hs-CRP cutpoints associated with increased risk of pregnancy loss.

References

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SUPPORT: The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD): U10 HD077680, U10 HD39005, U10 HD38992, U10 HD27049, U10 HD38998, U10 HD055942, HD055944, U10 HD055936, and U10HD055925. Research made possible by the funding by American Recovery and Reinvestment Act. Content is solely the responsibility of the authors and does not necessarily represent the official views of the NICHD or NIH.

O-254 9:55 AM Wednesday, October 21, 2020

PD-1 RECEPTOR AND LIGANDS ARE CONCENTRATED IN THE EXOSOME FRACTION OF HUMAN OVARIAN FOLLICULAR FLUID.

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OBJECTIVE: We have found that membrane bound and soluble variants of PD-1 and ligands are expressed by permanent constituent cell types of the human ovary and fallopian tube. We hypothesize that PD-1 signaling controls both immunomodulatory and non-immunomodulatory events in the ovary and tube. During our first evaluation of cell-free human follicular fluid (hFF), we detected full-length PD-1 receptor and also full-length ligands PD-L1 and -L2. Because secreted variants of PD-1 and ligands are produced by alternative splicing, it was unclear why full-length proteins were detectable in cell-free hFF. Here we have tested two hypotheses: first, that full-length proteins are packaged in exosomes in HFF, and second, that both immune and non-immune cells participate in *bona fide* PD-1 receptor:ligand interactions in the ovary and tube. Because initial evaluation of the reproductive tracts of Pd-l1 knockout mice revealed alterations in ovarian (corpus luteum) vasculature, we evaluated receptor:ligand interactions within human ovarian and tubal vasculature.

DESIGN: Biochemical assessments of human ovary and fallopian tube tissue specimens and hFF collected during *in vitro* fertilization treatment cycles.

MATERIALS AND METHODS: Immunostaining and western blots were performed using de-identified human ovary and tubal specimens and hFF. Cells were removed from hFF *via* centrifugation, followed by optionally processing using an exosome isolation kit to produce exosome-enriched and -depleted fractions. To detect receptor:ligand interactions *in situ*, proximity ligation analysis (PLA) was performed. Negative controls were performed where primary antibodies were omitted. Statistical difference of comparisons between groups was conducted using Welch’s two sample t-test. P-values <0.05 were considered statistically significant.

RESULTS: PD-1 and ligands are present in several ovarian and tubal cell types. These include oocytes, granulosa cells, cells of the CL, ovarian and tubal vasculature, and the tubal lumen. Further, soluble proteins are present in hFF at bioactive levels that can control T cell PD-1 activation and IFNγ production. Western blots of exosome and non-exosome hFF fractions show that receptor and ligands are mostly concentrated in the exosome fraction. Immunostaining showed that PD-L1 and PD-L2 were expressed prominently in the smooth muscle layers of arterioles and venules, and also in these layers of larger hilar ovarian vessels. PLA analysis supported direct PD-1:PD-L1 interactions within blood vessels and between other ovarian and tubal cell types.

CONCLUSIONS: PD-1 ligands are expressed throughout human ovarian vasculature, and *bona fide* receptor-ligand interactions (membrane-bound and/or soluble) are supported by PLA analysis. hFF exosomes were found to contain bioactive full-length PD-1 and ligands, suggesting that exosomal delivery of these proteins may modulate immune responses and regulate vascular development during ovulation and at other times during follicular development.

O-255 10:10 AM Wednesday, October 21, 2020

DO ENDOMETRIAL NATURAL KILLER AND REGULATORY T CELLS DIFFER IN INFERTILE AND CLINICAL PREGNANCY PATIENTS? AN ANALYSIS IN PATIENTS UNDERGOING FROZEN EMBRYO TRANSFER CYCLES.

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OBJECTIVE: To characterize proportional presence and phenotypic changes in endometrial and peripheral blood natural killer (NK) and regulatory T cells (Tregs) during frozen embryo transfer (FET) cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Endometrial tissue was collected from patients with recurrent pregnancy loss or history of implantation failure undergoing frozen embryo transfer cycles as part of an ERA biopsy or endometrial scratch. Endometrial NK (eNK) and Treg cell density was compared based on pregnancy status in the subsequent frozen embryo transfer cycle.

Peripheral blood was also collected from a separate cohort of patients undergoing frozen embryo transfer cycles. There were three time points for blood collection: 1) follicular phase, 2) day of the embryo transfer, and 3) day of quantitative serum β-hCG analysis. Peripheral blood Treg cell phenotype and density were compared based on timing of the blood draw and then stratified by the presence/absence of a clinical pregnancy.

RESULTS: A total of 33 luteal phase endometrial tissue samples were analyzed. There were more endometrial Tregs, similar eNK cells and a trend toward lower CD 16+ eNK in women with an ongoing clinical pregnancy compared to non-pregnant women. There were no differences in eNK and Treg density in natural “scratch cycles” vs programmed cycles or in non-receptive vs receptive endometrium (ERA cycles). 35 patients were enrolled in the peripheral blood analysis portion of the study. In the pregnant group, peripheral blood Tregs were elevated on the day of serum β- hCG time point when compared to the non-pregnant group.

CONCLUSIONS: Higher levels of endometrial Tregs and lower levels of CD16+ eNK cells are positive prognostic factors for infertile women prior to frozen embryo transfer. Our work on phenotypic and proportional analyses of endometrial immune cells may complement the endometrial receptivity assay in predicting improved pregnancy rates in patients with implantation failure.

O-256 10:25 AM Wednesday, October 21, 2020

DOES TESTING FOR IMMUNOLOGICAL MARKERS IN REPEATED IMPLANTATION FAILURE HAS A SIGNIFICANCE IN PROGNOSTICATING OUTCOMES OF FRESH NON DONOR IN VITRO FERTILIZATION CYCLES? - A PROSPECTIVE OBSERVATIONAL STUDY.

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OBJECTIVE: The purpose of study is to compare the various immunological markers (Pro Inflammatory markers -IL-6, IL-17,IFN γ and Anti-Inflammatory markers -IL-4,IL-10, Anti-cardiolipin antibody IgG and IgM, Lac, anti-beta2 glycoprotein) in serum of women with implantation failure with that of the women with successful implantation during IVF cycle and establishing the correlation between different immunological markers and implantation failure.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: IVF was performed using flexible antagonist stimulation protocol. Inclusion criteria were:. Age 25- 35 years, History of one or more previously failed IVF/ICSI cycle, Fresh non donor IVF cycles, BMI 23 -29 kg/m2, AMH > 2ng/ml, FSH <9IU, AFC >8, Normal uterine cavity. Embryo transfer was done on day 2/3/5.Participants were divided into controls(40 patients) and cases(40 patients) groups after testing for serum β hCG on day-16. Cases included women with one or more implantation failure who were found serum β hCG negative. Control group included women with positive serum βhCG. Blood sample of 2-3ml for each immunological marker was drawn . A highly sensitive sandwich ELISA kit was employed for the estimation of serum levels of IL-4, IL-6, IFN-γ, IL-10, IL-17, and LAC, aCL, β2 GP.

Data analysis was carried out using STATA version 12.0. Descriptive statistics such as mean, standard deviation and range values were calculated for normally distributed data with comparison of mean values tested using Student-t independent test. Bi-variate correlation analysis between optical density and concentration of IL-markers were performed. To assess significant risk factors for implantation failure, univariate and multivariate logistic regression analysis were carried out. Adjusted odds ratio with 95% confidence interval was presented. For all statistical tests a two-sided probability of P <0.05 was considered for statistical significance.

RESULTS: Baseline characteristics were matched between study and the control group. There was a significant increase in the pro-inflammatory markers (IL-17 and IFN-γ) in the study group when compared with the control group. ($p < 0.0001$). However the anti-inflammatory markers among both the groups were comparable with no statistical difference. The ratio of the pro-inflammatory /anti-inflammatory markers was detected and there was significant increase in the following ratios in the study group. IL-17/IL-4, IL-17/IL-10, IFN-γ/IL-4, IFN-γ/IL-10 ($p<0.0001$). Antiphospholipid antibodies were not detected in both groups. The distribution of embryo transfer day was statistically significant ($p<0.03$) and this was found to be a confounding factor. The adjusted odds ratio for day of embryo transfer was 10.1 (95% CI 2.30 – 44.34).

CONCLUSIONS: Immunological imbalance is associated with implantation failure in IVF cycles. Defining the evidence-based immunological studies is essential for the appropriate evaluation and prognostication of couples with implantation failure which may lead to newer treatment modalities.

SUPPORT: Institutional Research Grant

O-257 10:40 AM Wednesday, October 21, 2020

CH50 COMPLEMENT PATHWAY ADJUST BY ANTI MÜLLERIAN HORMONE LEVELS AT INFERTILITY PATIENTS.

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OBJECTIVE: To evaluate the importance of immunological screening (Ch50, C3, C4), to determine the correlation between ovarian reserve and complement pathway.

DESIGN: A prospective study with patients with infertility diagnosis who undergoing to IVF from January 2019-May 2020.

MATERIALS AND METHODS: We study 40 patients with normal distribution: we took basal blood samples (day 1-3 of menstrual cycle), measuring complement pathway: CH50 (CAE) , C3 (mg/dl) , C4 (mg/dl); to evaluate ovarian status. We quantify Anti Müllerian hormone (ng/dl) Multivariate analysis was performed with version 12, JMP ® for a comparison analyses a Spearman correlation test was achieved with a significant result ($P < 0.005$).

RESULTS: 40 female age from 28-48 years (mean=37.87 years), the value of CH50 65-268 CAE (mean=153.2 CAE), C3 13.9- 183mg/dl (mean=128.52 mg/dl), C4 11.5-106 mg/dl (mean=29.86 mg/dl), AMH 0.10-3.9 ng/dl (mean=1.32ng/dl). Multivariate analysis comparison was performed with significant results: AMH with age (Spearman correlation -0.6; P 0.001) and AMH with CH50 (Spearman correlation -0.4; P 0.0129), rest not significant. (Table 1).

Variable	Variables	Spearman	Prob > $\lvert\rho\rvert$	
CH50 (CAE 63-145)	Age	0.2641	0.1042	+++
C3 (mg/dl 83-193)	Age	0.0993	0.5476	+
C3 (mg/dl 83-193)	CH50 (CAE 63-145)	0.2458	0.1314	++
C4 (mg/dl 15-57)	Age	0.2038	0.2132	++
C4 (mg/dl 15-57)	CH50 (CAE 63-145)	0.0035	0.9829	
C4 (mg/dl 15-57)	C3 (mg/dl 83-193)	0.229	0.1608	++
AMH	Age	-0.5065	0.001	———
AMH	CH50 (CAE 63-145)	-0.3946	0.0129	——
AMH	C3 (mg/dl 83-193)	-0.2352	0.1494	–
AMH	C4 (mg/dl 15-57)	0.0938	0.5699	+

CONCLUSIONS: Anti Müllerian hormone levels correlates inversely with age and the increase of CH50 levels negatively correlate with AMH. The combination of AMH with CH50 levels, could be a marker of deficient response at this complement pathway. Nevertheless, we need further investigation to value the immune system in infertility patients.

O-258 10:55 AM Wednesday, October 21, 2020

INTRAUTERINE ADMINISTRATION OF PERIPHERAL BLOOD MONONUCLEAR CELLS INCREASES CLINICAL PREGNANCY RATES IN FROZEN-THAWED EMBRYO TRANSFER CYCLES OF PATIENTS WITH IMPLANTATION FAILURE.

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OBJECTIVE: Intrauterine administration of peripheral blood mononuclear cells (PBMC) has been proposed to improve implantation rates in women with implantation failure. Our aim was to observe the effects of intrauterine administration of maternal and paternal PBMC on clinical pregnancy rate (CPR) of patients who received frozen-thawed embryo transfer (FET).

DESIGN: Retrospective cohort study from January 2019 to January 2020.

MATERIALS AND METHODS: Patients who had not experienced successful pregnancy despite one or more IVF-ET sessions were enrolled in this study (n=66).

Based on the patient's treatment preferences, maternal and paternal PBMC were freshly isolated from each couples and then administered to the intrauterine cavity of that patient. FET was performed and the success of implantation in the group of patients with two or more implantation failure ($n = 28$) was compared with that in the control groups of patients with one implantation failure ($n = 38$).

RESULTS: Pregnancy rate per transfer was evaluated in only 59 patients. A beneficial effect of endometrium immunomodulation was observed in FET cycles of all the patients with 28 pregnancies obtained after intrauterine insemination of maternal and paternal activated PBMC.

Baseline clinical parameters, number and quality of embryos transferred were comparable in the two groups.

CPR were significantly higher in the RIF group compared to control groups (50 % vs 36, 8%; respectively p< .0,5)

CONCLUSIONS: Intrauterine administration of maternal and paternal PBMC improves CPR, in FET cycles of all patients. The treatment improves

significantly the pregnancy outcomes much more for women with two or more implantation failure.

IVF OUTCOME PREDICTORS 2

O-259 9:40 AM Wednesday, October 21, 2020

THE EFFECT OF OBESITY ON EUPLOIDY RATES IN WOMEN UNDERGOING IN VITRO FERTILIZATION (IVF) WITH PREIMPLANTATION GENETIC TESTING (PGT). Stephanie M. Hallisey, MD,[1] Reeva B. Makhijani, MD,[2] Jeffrey Thorne, MD,[3] Prachi N. Godiwala, MD,[2] John Nulsen, MD,[2] Claudio A. Benadiva, MD,[2] Daniel R. Grow, MD,[2] Lawrence Engmann, MD[2] [1]University of Connecticut Health Center, Center for Assisted Reproductive Services, Farmington, CT; [2]Center for Advanced Reproductive Services, University of Connecticut School of Medicine, Farmington, CT; [3]RMA of Philadelphia, King of Prussia, PA.

OBJECTIVE: Elevated body mass index (BMI) is associated with a higher risk of miscarriage and lower probability of live birth following IVF (1-3). The etiology underlying these disparities is currently unclear. It is plausible that obesity may be associated with higher rates of aneuploidy, which could result in worsened pregnancy outcomes, although this has not been previously studied. Thus, we examined the impact of BMI on euploidy rates in IVF cycles with PGT.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: This study included women aged ≤45 years who underwent IVF with PGT from 1/2013 to 2/2018 at a single academic fertility center. 533 cycles were divided into 3 cohorts according to BMI: 1) Normal: 18.5-24.9; 2) Overweight: 25-29.9; and 3) Obese: ≥30. The primary outcome was euploidy rate. Secondary outcomes included number of oocytes, fertilization rate, blastocyst development rate, number of blastocysts biopsied, and livebirth rate. Chi-Square and one-way ANOVA with post hoc Tukey tests were used for categorical and continuous variables respectively. Multiple linear regression analysis was performed to control for age, AMH, number of oocytes retrieved, blastocyte development rate, and number of blastocysts biopsied. A two-sided p-value of 0.05 was considered statistically significant.

RESULTS: Obese women were significantly older and had a lower blastocyst development rate than women with normal BMI. There was no difference in AMH, oocytes retrieved, fertilization rate, or embryos biopsied between BMI cohorts. There was no significant difference in euploidy rate between BMI cohorts (Table 1), which persisted after controlling for potential confounders. There were no differences in livebirth rate between normal weight (91/145; 62.8%), overweight (44/70; 62.9%) and obese (35/48; 72.9%) patients who underwent a subsequent transfer (p=0.41).

TABLE 1. IVF Outcomes by BMI Cohort in Patients Undergoing IVF with PGT

	BMI Cohorts			
Outcome (mean ± SEM)	Normal (n=301)	Overweight (n=118)	Obese (n=116)	P Value
Age (years)	37.4 ± 0.2[a]	37.9 ± 0.4[a,b]	38.5 ± 0.3[b]	0.03
AMH (ng/dl)	2.8 ± 0.2	3.1 ± 0.5	2.5 ± 0.3	0.42
Oocytes Retrieved (n)	14.1 ± 0.5	15.5 ± 0.8	14.2 ± 0.9	0.33
Fertilization Rate (%)	75.2 ± 1.0	71.3 ± 1.9	75.9 ± 1.5	0.09
Blastocyst Development Rate (%)	58.7 ± 2.0[a]	57.0 ± 3.3[a,b]	48.6 ± 2.3[b]	0.02
Blastocysts Biopsied (n)	4.6 ± 0.2	4.6 ± 0.3	3.8 ± 0.3	0.12
Euploid Rate (% ±)	33.5 ± 1.8	31.7 ± 2.9	33.7 ± 3.0	0.85

[a,b]Cohorts with different letters indicate significant differences between groups.

CONCLUSIONS: There was no significant difference in euploidy rates between BMI cohorts in women undergoing IVF with PGT. These findings suggest that the association between elevated BMI and unfavorable pregnancy outcomes may not be related to increased oocyte aneuploidy.

References: 1. Rieenberg V, Sobaleva S, Ahmad A, Oteng-Ntim E, Bolton V, Khalaf Y, Braude P, El-Toukhy T. Influence of BMI on risk of miscarriage after single blastocyst transfer. Human Reproduction 2011;26(10):2642-2650.

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O-260 9:55 AM Wednesday, October 21, 2020

ADHERENCE TO ASRM SINGLE EMBRYO TRANSFER GUIDELINES IN FAVORABLE-PROGNOSIS PATIENTS UNDER 35 YEARS: A SART STUDY. Julian A. Gingold, MD, PhD,[1] Michelle Kappy, MD,[1] Rachel S. Gerber, MD,[1] Michelle Goodman, BS,[1] Melissa Fazzari, PhD,[1] Harry Lieman, MD,[1] Manvinder Singh, MD,[1] Staci E. Pollack, MD, MS,[2] Sangita K. Jindal, Ph.D.[1] [1]Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY; [2]Albert Einstein College of Medicine, Bronx, NY.

OBJECTIVE: To measure adherence with 2013 ASRM guidelines recommending elective single embryo transfer (eSET) in favorable-prognosis patients.

DESIGN: Retrospective cohort from SART national patient registry.

MATERIALS AND METHODS: Inclusion criteria were IVF cycles from 2014-2016 in patients <35 years undergoing their first autologous fresh embryo transfer. Each cycle must have generated at least two blastocyst embryos, with at least one 3BB-grade or better transferred fresh. Cycles from PGT embryos and recurrent pregnancy loss patients were excluded.

Summaries of eSET and non-eSET live birth rate (LBR), gestational age at delivery, and birth weight were computed. Differences between groups were presented along with 95% confidence intervals. P-values were generated based on chi-square tests or t-tests, as appropriate.

RESULTS: The cohort included 28,311 favorable-prognosis fresh blastocyst transfers, of which 15,643 (55%) underwent eSET. Non-eSETs typically transferred two (n=12,609 (99.5%)), and rarely 3 (n=57) or 4 (n=2), blastocysts.

Age, BMI, parity, max FSH and AMH were clinically comparable between eSETs and non-eSETs. The infertility etiologies of non-eSETs were less likely than eSETs to be unexplained (1967 (15.5%) vs 3229 (20.6%)) and more likely to be male factor (5,287 (41.7%) vs 6,033 (30.6%)) (all p<0.001).

Multiple pregnancy, preterm delivery and birth weight <2500g were far more common in non-eSET than eSET births. However, LBR from non-eSET was also higher than from eSET cycles (Table 1, all p <0.001).

TABLE 1.

Cycle outcomes	Non-eSET (n=12668)	eSET (n=15643)	Absolute difference eSET vs. non-eSET (95% CI)
Clinical pregnancy, n (%)*	8698 (68.7%)	9436 (60.3%)	-8.5 (-9.6,-7.3)
Live birth, n (%)*	7809 (61.6%)	8254 (52.7%)	-8.9 (-10.0,-7.7)
Multiple pregnancy, n (%)*	3538 (27.9%)	147 (0.9%)	-27.0 (-27.8,-26.2)
Number of live births	11,443	8,403	
*Singleton**, n (%)*	4271 (37.3%)	8107 (96.4%)	59.2 (58.2,60.2)
*Twin**, n (%)*	6886 (60.2%)	290 (3.5%)	-56.0 (-57.0,-55.0)
*Triplet**, n (%)*	282 (2.6%)	6 (<.1%)	-2.4 (-2.7,-2.1)
*Quadruplet**, n (%)*	4 (<.1%)	0 (<.1%)	NS
*Delivery at <37 weeks** GA, n (%)*	3545(28.0%)	1603 (10.3%)	-17.7 (-18.7,-16.8)
*Birth weight (g)**, mean (SD)*	2795 (750)	3224 (697)	429 (409,449)
*Birth weight <2500g**, n (%)*	4642 (42.0%)	895 (10.6%)	-31.4 (-32.5,-30.3)

All p<0.001 except as noted with NS (not significant).
* Per embryo transfer. ** Per live birth.

CONCLUSIONS: There was widespread non-adherence with 2013 ASRM embryo transfer guidelines in favorable-prognosis patients. Despite slightly improved LBRs with non-eSET, the dramatically increased multiple pregnancy rates, preterm births and low birth weights should strongly discourage this practice.

References: 1. Criteria for Number of Embryos to Transfer: A Committee Opinion. Fertil Steril. 2013;99(1):44–6.
SUPPORT: None

O-261 10:10 AM Wednesday, October 21, 2020

LESS IS MORE: SART CORS STUDY COMPARING OBSTETRICAL AND NEONATAL OUTCOMES WHEN TRANSFERRING 1 VERSUS ≥2 PGT-A EMBRYOS.

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OBJECTIVE: To compare obstetrical and neonatal outcomes following single embryo transfer (SET) versus (vs.) multiple embryo transfer (MET) from frozen-thawed embryo transfer cycles (FET) of autologous pre-implantation genetic tested for aneuploidy (PGT-A) embryos.

DESIGN: Retrospective cohort study from the SART CORS national database.

MATERIALS AND METHODS: Cycle data were obtained from the SART CORS database for all autologous FET cycles of PGT-A embryos between 2014-2016. The primary outcomes measured were live birth rate (LBR) and multiple pregnancy rate (MPR). Secondary outcome measures included rates of preterm delivery (<37 weeks, <34 weeks, and <28 weeks), low birth weight (LBW, <2500g) and very LBW (<1500g). Outcomes were compared between SET and MET groups using chi-square tests, with statistical significance defined as $p<0.05$.

RESULTS: There were 14,408 SET and 2,501 MET cycles. There were no clinically significant differences between groups in terms of age, BMI, parity, infertility diagnosis, or AMH levels. In the MET group, >99% transferred 2 embryos, and only 16 cycles reported 3 embryos transferred. While the LBR was greater with MET compared with SET (66.3% vs. 54.9%), the MPR was dramatically greater (46.8% vs. 1.7%) (Table 1). Preterm delivery (PTD) rates at <37 weeks (31.4% vs. 9.9%), <34 weeks and <28 weeks were significantly elevated in MET compared with SET cycles. Compared with SET, MET cycles were also associated with significantly higher rates of LBW (35.8% vs. 8.1%) and very LBW (5.6% vs. 1.3%) (Table 1).

CONCLUSIONS: Nearly half of the pregnancies resulting from PGT-A tested METs are multiples. Compared to SETs, METs are associated with significantly higher rates of neonatal morbidity, including PTD and LBW. Transfer of more than one PGT-A embryo should be strongly discouraged and patients should be counseled on the significant potential for adverse outcomes.

TABLE 1. Autologous FET PGT-A cycles*

Pregnancy and neonatal outcomes**	≥2 embryos transferred (n=2501)	Single embryo transferred (n=14,408)
Clinical pregnancies***	1876 (75%)	9180 (63.7%)
Live birth rate***	1658 (66.3%)	7907 (54.9%)
Multiple pregnancy rate***	776 (46.8%)	137 (1.7%)
Number of infants born	2448	8045
Singleton	882 (36.0%)	7770 (96.6%)
Twin	1524 (62.3%)	272 (3.4%)
Triplet	42 (1.7%)	3(<.1%)
Gestational age at delivery < 37 weeks	787 (31.4%)	1419 (9.9%)
Gestational age at delivery < 34 weeks	226 (9.0%)	312 (2.2%)
Gestational age at delivery < 28 weeks	30 (1.2%)	38 (0.3%)
Birth weight at delivery <2500g	877 (35.8%)	650 (8.1%)
Birth weight at delivery <1500g	136 (5.6%)	104 (1.3%)

*All comparisons are statistically significant with $p<0.001$.
**All data summarized as n (%).
***Per embryo transfer.

References: None.
SUPPORT: None.

O-262 10:25 AM Wednesday, October 21, 2020

ART TREATMENT HAS MINIMAL EFFECT ON COST OF HOSPITAL CARE IN CHILDREN TO AGE 4.

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OBJECTIVE: To compare the cost of hospital care for children to age 4 among ART-treated, subfertile, and fertile women.

DESIGN: Retrospective evaluation of linked ART, birth certificate, and hospital data in Massachusetts.

MATERIALS AND METHODS: Cost of hospital care through age 4 was evaluated for singleton children born in Massachusetts between July 1, 2004 and December 31, 2012 to women ≥ 18 years of age with private insurance at delivery, born at ≥ 23 weeks gestational age (GA) who survived birth hospitalization to age 4. Data were obtained by linking ART deliveries from the Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS) to the Pregnancy to Early Life Longitudinal (PELL) data system, which links birth certificates to hospital discharge records for mothers and infants in Massachusetts. We included hospitalizations, observational stays, and emergency room visits of children born to mothers of fertile (those without ART, other infertility treatments, or indicators of infertility), unassisted subfertile (UF: those without ART who had indicators of infertility and did not require any assistance with reproduction), non-ART medically assisted reproduction (MAR, required non-ART assistance with reproduction) and ART (deliveries linked to SART CORS). Costs prior to first discharge home from the birth hospitalization have been previously reported and were excluded. Outliers, or costs that were below the 1st or above the 99th percentile were recoded to 1st and 99th percentile, respectively. Multivariable gamma regression models comparing the ART, subfertile, and fertile groups were adjusted for age, race, education, chronic diabetes and hypertension, gestational diabetes and hypertension, low birthweight, prematurity, parity, gender, year of birth, and method of delivery. Costs are expressed in 2017 US Dollars. Statistical significance was noted where $P<0.05$.

RESULTS: There were 158,506 fertile, 3,168 UF, 1,912 MAR, and 6,667 ART children. Adjusted least square mean costs of care (± SE) without recoding top values were \$4,259 (±356), \$4,894 (±428), \$4,448 (±400), 4,005 (±341) respectively with only the unassisted subfertile group higher than the fertile ($P<0.01$) and the ART significantly lower than fertile ($P=0.0012$). When the 99th percentile was recoded, the adjusted costs were \$4,176 (±337), \$4,309 (±364), \$4,666 (±406), \$4,187 (±345) respectively with the MAR group having higher costs than the fertile group ($P=0.0007$). When selecting only those children born at <37 weeks GA only the MAR (\$6,799) group had higher average cost than the fertile group (\$6,116) ($P=0.0027$).

CONCLUSIONS: ART-treatment had minimal effect on cost of hospital care in children to age 4. Costs were increased slightly for children born to subfertile women.

SUPPORT: NIH RO1HD67270

O-263 10:40 AM Wednesday, October 21, 2020

CLOMIPHENE CITRATE EXPOSURE DOES NOT ADVERSELY AFFECT CLINICAL OUTCOMES IN SINGLE, EUPLOID FET CYCLES.

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OBJECTIVE: Clomiphene citrate (CC) is a selective estrogen receptor modulator utilized for OI and COH. Pharmacologically, CC has a half-life of 5 days; yet, it can be excreted after 6 weeks after initial administration[1]. CC is known to have antioestrogenic side effects which had been associated to a reduction in implantation rates for patients who undergo fresh IVF cycles[2]. However, evidence is scarce about the effect of CC on implantation potential in FET cycles. One study showed that patients who undergo a FET within 90 days after CC treatment had lower pregnancy rates compared with FET cycles that occur after 90 days of CC treatment [3]. Conversely,

another study did not find lower implantation rates in patients who undergo FET cycles, regardless of the time of CC administration [4]. To date, no study has analyzed CC exposure and subsequent transfer of euploid embryos. The objective of this study is to analyze implantation rates in patients exposed to CC prior to a single, euploid FET cycle.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: The study included patients who underwent a single, euploid FET from 2016 to 2020. PGT-A was performed by NGS. Cohorts were segregated in 2 groups according to duration between the last day of CC administration and FET day (Group 1: $\leq$90 days, Group 2: patients unexposed to CC or when exposure elapsed $>$ 90 days). Patients with genetic translocations, uterine factor, hydrosalpinx and RPL diagnosis were excluded from the analysis. Demographic characteristics and IVF outcomes were assessed. Comparative statistics and an adjusted multivariate analysis with a GEE framework were used for analysis. A sample size of 355 FET cycles per group was calculated to have an 80% power to detect a difference of 10% on implantation rates (α=0.05).

RESULTS: 433 FET cycles in which patients were exposed to CC within 90 days (Group 1) were compared with 5723 control cycles (Group 2). AMH levels were different among groups (3.5± 4 vs 3.5±3, p=0.02). The remaining demographic characteristics, including endometrial thickness at ET, were comparable among groups. Clinical pregnancy rate (CPR) (67.2% vs 61.4%, p=0.01) and ongoing pregnancy rate (OPR) (57.7% vs 51.5%, p=0.01) were significantly different among groups. No differences were found in implantation or clinical pregnancy loss (CPL) rates among groups. After adjusting for age, BMI, AMH, endometrial thickness at ET, embryo quality, and day of biopsy, there was no association with CC exposure and lower odds of implantation (OR 1.12,CI 95% 0.8-1.4,p=0.36), CPR (OR 1.21,CI 95% 0.9-1.5,p=0.09), OPR (OR 1.18,CI 95% 0.9-1.4,p=0.12), or higher odds of CPL (OR 0.96,CI 95% 0.6-1.3,p=0.85), when compared with controls. On a sensitivity analysis we also found no association within shorter CC exposure times (30 & 60 days) and IVF outcomes.

CONCLUSIONS: Although CC is a safe oral agent for ovarian stimulation, unfavorable effects on endometrial thickness are possible and could result in implantation failure during fresh IVF cycles. However, our study demonstrated no association between exposure to CC and adverse effect on IVF outcomes in patients undergoing a single, euploid FET cycle.t

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SUPPORT: None

O-264 10:55 AM Wednesday, October 21, 2020

SIMILAR PERINATAL OUTCOMES IN CHILDREN BORN AFTER FRESH OR FROZEN EMBRYO TRANSFER USING DONATED OOCYTES.

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OBJECTIVE: Singletons born after fresh embryo transfer (ET) are associated with higher rates of preterm birth and low birthweight, while frozen embryo transfers (FET) seem to convey a higher risk of large for gestational age. However, studies comparing these outcomes using autologous oocytes are unable to adequately disentangle the potential effect of embryo vitrification from the possible consequences on endometrial receptivity caused by ovarian stimulation/preparation, prior to ET. Hence, the oocyte donation (OD) model is optimal for this differentiation and, so far, information available regarding neonatal outcomes is limited to either small and/or heterogeneous studies.

DESIGN: We performed a multicenter retrospective cohort study including 5848 singletons born between 2009 and February 2020 following OD and single blastocyst transfer, subdivided into fresh ET and FET groups.

MATERIALS AND METHODS: Patients with a first singleton livebirth after single blastocyst transfer were compared using multivariable regression analysis to account for potential confounding. The primary outcome was birthweight. Secondary outcomes were low birth weight (below 2500g and 1500g), birthweight z-scores, small/large for gestational age, prematurity, neonatal morbidity (Apgar scores and need for neonatal intensive care) and maternal morbidity (gestational hypertensive disorders, diabetes and cesarean delivery). The control variables included were female recipient/donor age, body mass index and smoking status, sperm source, endometrial thickness and preparation technique (natural or artificial cycle), serum estradiol and progesterone levels, and newborn gender. Continuous outcomes are presented with medians and interquartile ranges (IQRs) while dichotomous outcomes are shown using percentages and 95% confidence intervals (CIs).

RESULTS: There was no significant difference between the fresh ET and FET groups in terms of birthweight (3215 g, IQR [2900g, 3540 g]; versus 3200.0g, IQR [2860g, 3500 g]) and birthweight z-scores (0.03, IQR [-0.67, 0.73]; versus 0.1, IQR [-0.59, 0.71]), in both the unadjusted and confounder-adjusted models. However, artificial endometrial preparation was associated with a higher birthweight (3220 g, IQR [2900g, 3540 g]; versus 3105 g, IQR [2800g, 3450 g]) and birthweight z-scores (0.06, IQR [-0.63, 0.74]; versus -0.13, IQR [-0.73, 0.59]), even following confounder adjustment.

The premature birth rates ($<$37weeks) were, respectively, 9.9% (8.9%-10.8%) and 11.2% (9.8%-12.6%) for fresh ET and FET, while the very premature birth rates ($<$32 weeks) were 1.4% (1.0%-1.8%) and 1.9% (1.3%-2.5%), with no significant difference, even following confounder adjustment. There were also no statistically significant differences in other neonatal outcomes and maternal morbidity.

CONCLUSIONS: Perinatal outcomes did not seem to be affected by the embryo vitrification process in an OD model. Other factors may contribute to the hindered perinatal outcomes described, particularly the potential effect ovarian stimulation and endometrial preparation may have on endometrial receptivity.

SUPPORT: None.

P-01 4:30 PM Saturday, October 17, 2020

STATE INSURANCE MANDATES AND TRENDS IN PREIMPLANTATION GENETIC TESTING (PGT) UTILIZATION IN THE UNITED STATES.

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OBJECTIVE: To assess associations between insurance mandates for fertility care and PGT utilization over time

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: Fresh, autologous IVF cycles from the 2007-2016 SART registry were analyzed in two periods due to changes in SART cycle definitions in 2013. Frozen, cancelled, and banking cycles were excluded. Cycles were categorized by level of insurance coverage mandated in the state they were performed as follows: comprehensive, partial, or no coverage. State census data were used to determine the population of reproductive age women and median household income. Log binomial regression was used to analyze change in proportion of PGT cycles over time relative to mandate type.

RESULTS: 875,567 cycles were included. The majority of IVF cycles occurred in states with no coverage. Per capita, IVF cycles were performed at higher rates in comprehensive coverage states (336 per 100,000 women in 2016) followed by partial (186) and no (142) coverage. For PGT cycles, comprehensive coverage states had the highest use per capita (98), followed by no (53) and partial coverage (34). However, beginning in 2009, the proportion of IVF cycles using PGT was actually highest in no coverage states. Median household income decreased with decreasing insurance coverage.

Between 2007-2013, there was a minimal, yet statistically significant yearly increase in the rate of PGT use (β= 0.05, SE= 0.003, $p<0.0001$). For partial and comprehensive coverage states, this increase was lower compared to no coverage states ($p<0.0001$). Between 2014-2016, there was a substantial increase in the use of PGT (β = 0.43, SE=0.005, $p<0.0001$). This rise was more substantial in partial coverage states (β = 0.11, SE= 0.03, $p<0.0001$).

CONCLUSIONS: This is the first study to examine the association between state mandated insurance coverage and PGT use. Across both time periods, there was a strong association between state mandate and PGT use. Additionally, PGT utilization increased substantially after 2013, corresponding to the publication of several influential papers on PGT. These trends may also be attributed in part to changes in SART definitions, state-level economics, PGT costs, and socioeconomic characteristics of women accessing IVF.

SUPPORT: The Center for Administrative Data Research is supported in part by the Washington University Institute of Clinical and Translational Sciences grant UL1 TR002345 from the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health (NIH) and Grant Number R24 HS19455 through the Agency for Healthcare Research and Quality (AHRQ).

P-02 4:30 PM Saturday, October 17, 2020

REDUCED WAITING TIMES AND IMPROVED EFFICIENCY FOR COUPLES ACCESSING PUBLIC, OUTPATIENT FERTILITY CLINICS IN THE NATIONAL MATERNITY HOSPITAL, DUBLIN, IRELAND.

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OBJECTIVE: In Ireland there are difficulties accessing public outpatient services across all specialties. With a population of just under 5 million, it is estimated that there were 550,000 patients on waiting lists for first hospital outpatient visits at the end of 2019. Fertility services are particularly poorly resourced.

Fertility is very time sensitive, with the biggest prognosticator in terms of the success of assisted reproduction treatment being female age. Long wait times are therefore detrimental for these patients and international comparisons show that Irish patients are older when they access fertility treatment.

We noticed that there was a very poor attendance rate at our public infertility clinics, possibly exacerbated by the long wait time for an appointment. The aim of this study was to implement a new appointment strategy to address these unacceptably long waiting times and to reduce the "did not attend" (DNA) rate.

Ultimately reducing the number of clinic appointments per patient and reduced waiting time to treatment and pregnancy.

DESIGN: Retrospective comparative study

MATERIALS AND METHODS: Prior to 2019, referral letters from family doctors were triaged by hospital nursing staff. Patients were sent an appointment slot and asked to complete specific fertility investigations (hormone profile and semen analysis) at the hospital prior to their scheduled appointment.

From March 2019, all patients were asked to complete and return a lifestyle and medical history questionnaire and to have the required tests performed at the hospital. Only then was an outpatient appointment slot was scheduled.

The outcome of all referrals received between March and August 2019 (new system) was compared with that of patients referred between March and August 2018 (old system).

RESULTS: A total of 185 patient files were reviewed – n 78 (2018); 107 (2019)

Post implementation of the new system, the DNA (did not attend) rate was reduced from 32% to just 2%. Less than half of those initially referred (39%) returned the questionnaire and completed the required investigations therefore receiving an appointment.

For those who were given an appointment in 2019, the waiting time averaged 52 days compared to 178 previously. The total number of clinic visits needed to complete the basic work up reduced from two to one.

Disappointingly, it took, on average, 189 days to complete the basic investigations. However this is compared to almost a year (326 days) in 2018. The rate limiting factor contributing to this was the waiting time for a pelvic ultrasound, with the average wait being 120 days after initial consultation.

Period	1							2		
Year	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Total cycles	81512	82920	82776	83402	83894	82215	77364	92074	100318	109092
% of total cycles using PGT	4.9	4.6	4.4	4.6	5.2	5.4	6.4	17.4	25.7	33.7
% change in % PGT	-	-7.3	-4.5	5.9	11.7	3.8	18.7	-	47.1	31.4
% PGT – no coverage	4.8	4.7	4.6	5.1	5.8	5.9	6.9	19.4	28.5	37.0
% PGT – partial coverage	3.5	2.9	2.2	2.3	2.1	1.9	4.2	6.9	12.3	18.4
% PGT – comprehensive coverage	5.6	4.8	4.5	4.2	4.6	5.2	5.8	15.4	21.9	29.1

Almost one third of the women attending our clinic fell into the 35 – 39 age group category. Such a wait is not acceptable at this age.

CONCLUSIONS: By ensuring patients complete their basic investigations before they receive an appointment, we have drastically reduced waiting times and the DNA rate.

Now more than ever in this post COVID-19 era, we should aim to be streamlined and cost effective, prioritising our patients access to outpatient care. This approach could be adopted by other clinical services in Ireland to reduce clinic waiting times.

P-03 4:30 PM Saturday, October 17, 2020

CONSIDERING LOCATION IN ACCESS TO INFERTILITY SERVICES. Nathanael B. Stanley, MA University of South Florida, Tampa, FL.

OBJECTIVE: The objective of this research is to observe aspects of location in reference to the use of infertility services by U.S. residents, with the purpose of identifying instances of interstate and international travel related to accessing infertility services, and the locations of CDC reporting ART clinics in relation to population and birth density.

DESIGN: Place, location, and travel are important factors to consider when discussing accessibility of specialized healthcare, such as infertility services. The ability to observe differences in the locations of clinics is informative, but geographic proximity to a clinic does not equate to increased access to infertility services. Medicine in the United States is a business, so geographic spread of ART clinics will undoubtedly follow population density. When reviewing different national surveys available that include questions about residence and infertility services, such as the Society for Assisted Reproductive Technology (SART) and the National Survey of Family Growth (NSFG), the surveys did not ask the right questions that would give insight into the influence of location hypothesized to be influential, such as the type of employment (employment status, part time, full time, state in which people work) and whether people travel for services (*where* and *how far* people go to access infertility services).

MATERIALS AND METHODS: This research uses a survey instrument developed by the PI, and spatial analysis of 2017 CDC-reporting ART clinics in relation to population and birth density in the United States. The survey instrument includes questions about: employment, travel intentions and reasons, and state of residence. Frequency statistics calculated using SAS 9.4 will show variations in answers. Spatial analysis consists of geocoding CDC-reporting ART clinics, and comparing their location with population and birth density data at the Census Tract level. In order to identify spatial clustering of clinics, an Optimized Hot-Spot analysis of 2017 ART clinics was conducted in ArcPro 2.5.

RESULTS: Survey results from 134 persons in 33 states using infertility services reveal the majority of people accessing infertility services accessed those services in their same state of residence (88.3%), most people have not and are not considering traveling out of state (90.3%) or out of country (82.7%) to access infertility services. There were 440 ART clinics reporting data to the CDC in 2017. Optimized Hot Spot analysis revealed 147 output features statistically significant based on an FDR correction for multiple testing and spatial dependence, and those areas overlapped with the largest population and birth density census tracts.

CONCLUSIONS: Based on survey results, it does not appear that interstate or international travel for infertility services occur with high frequency for U.S. citizens. Spatial analyses revealed distinct spatial patterns regarding the location of CDC-reporting ART clinics and population and birth densities. Based on the nature of medicine in the United States as a business, it makes logical sense that ART clinics exist in areas with high population.

P-04 4:30 PM Saturday, October 17, 2020

EMERGENCY DEPARTMENT UTILIZATION FOR OVARIAN TORSION IN THE UNITED STATES (2006-2016). Jessie-Joyce Kue, MSCR,[1] Charley Jiang, MS,[1] Emma Giuliani, MD,[2] Chelsea N. Fortin, MD,[2] Erica E. Marsh, MD, MSCI, FACOG[2] [1]MD/MSCR candidate, Ann Arbor, MI; [2]University of Michigan, Ann Arbor, MI.

OBJECTIVE: Ovarian torsion (OT), a condition in which the ovary twists on its vascular and lymphatic support, can compromise the blood supply and lead to edema, ischemia, and eventually necrosis of the ovary. OT is a gynecologic emergency that requires prompt intervention. Although it is mainly diagnosed in the Emergency Department (ED), little is known about the utilization of EDs for this condition. The purpose of this study was to characterize use of United States (US) EDs for adult ovarian torsion patients.

DESIGN: Retrospective analysis of national database

MATERIALS AND METHODS: Data were extracted from the Nationwide Emergency Department Sample (NEDS), developed by the Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality. ICD-9 and ICD-10 codes were used to identify women aged 18-65 years who were seen in the ED with a primary diagnosis of OT between 2006-2016. Other variables analyzed include payer type, income quartile by zip code, region, hospital teaching status, and hospital location. Descriptive statistics regarding ED utilization were obtained using SAS 9.4.

RESULTS: From 2006 to 2016, the number of ED visits for OT among 18 – 65-year olds increased from 2,791 to 4,420 ($p< 0.0001$). Approximately one-third of these visits were comprised of women aged 26 – 44 years. More than half of all ED visits were paid for by private insurance (56.6%), followed by Medicaid (20.3%) as the next largest payer. 31.5% of visits occurred in large metropolitan areas. Metropolitan teaching hospitals experienced a notable increase in ED visits for OT over the study period, during which time visits for OT doubled from 1,263 to 2,695. Conversely, the number of visits remained at about 1,662 cases per year at metropolitan non-teaching and non-metropolitan hospitals. ED charges for OT nearly quadrupled over the study period. The average charge for OT patients in 2006 was $5,134 and in 2016 was $19,012 – an average annual increase of 14.4% compared to an annual increase of 8.5% for all other diagnoses in age matched women. Hospital admission rates declined over the study period from 76% in 2006 to 38% in 2016 ($p< 0.01$).

CONCLUSIONS: The overall utilization of the ED for ovarian torsion increased significantly during the 11-year study period, despite a significant decrease in admission rates. Given that OT is considered a surgical emergency, this decrease in admission rate is quite surprising. The majority of patients were insured by private insurance, and metropolitan teaching hospitals saw a significant increase of OT cases from 2006 to 2016. Furthermore, the cost of ED visits for OT increased dramatically, with ED charges climbing from $5,000 to almost $20,000. Future studies are needed to elucidate the drivers behind the decrease in admissions for torsion.

P-05 4:30 PM Saturday, October 17, 2020

THE COST OF INFERTILITY (COIN) STUDY: ASSOCIATIONS WITH INCOME & BURDEN OF TREATMENT. Viji Sundaram, MD,[1] Jerrine R. Morris, MD, MPH,[1] Jake Anderson, MBA,[2] Martha Noel, MD[1] [1]University of California, San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA; [2]FertilityIQ, San Francisco, CA.

OBJECTIVE: (1) To conduct an analysis in a national cohort of patients pursuing in vitro fertilization (IVF) to determine significant predictors for total out-of-pocket (OOP) cost; (2) To evaluate to what degree total OOP costs are determined by income; (3) To characterize how patients finance the cost of IVF

DESIGN: Cross Sectional Cohort

MATERIALS AND METHODS: In collaboration with a national fertility education company (FertilityIQ), a recruitment email was sent to all registered users of FertilityIQ who had undergone at least 1 cycle of IVF. Survey participants completed a web-based, anonymous, self-reported survey including questions regarding demographics, reproductive and IVF history, insurance information, financial details, opinions on legislation, and a standard Decision Regret Scale (DRS). Survey questions were created through an iterative process and revised to incorporate changes following pilot delivery to 10% of FertilityIQ users. Data analysis was performed with descriptive statistics; univariate logistic regression for dichotomous outcomes; and one-way analysis of variance (ANOVA) with pairwise comparisons using the Bonferroni adjustment for categorical outcomes.

RESULTS: Recruitment emails were distributed to 4,326 registered FertilityIQ users, with 1,568 people (36%) opening the email & 337 (8%) completing the survey. 66% of respondents were $\leq$34 years of age, and 85% were white. 40% had a household income of <$100,000, with 43% spending $25-70,000 on their total IVF care. Significant univariate predictors of total OOP cost included: education, income, insurance fertility coverage, length of time trying to conceive, use of an egg donor or gestational carrier, total egg retrievals and embryo transfers, and time spent on IVF. Patients with an annual household income of >$250k spent significantly more (median $55k) on their IVF care then patients making less (median $32,500, $p<0.01$), while families with an income of <$100k to $250k spent similar amounts. Of families making <$150k, 21-29% reported spending >50% of their disposable income on IVF. Common sources of funding for IVF regardless of income, included borrowing money, payment with credit cards, and delaying regular savings contributions. Those in lower-income groups relied on outside funding sources more than in higher-income groups,

including borrowing money, paying with credit cards, delaying home-buying, and delaying further education.

CONCLUSIONS: Funding for IVF creates a significant burden on families, even with incomes up to $250k. Patients making <$100,000 are able to fund IVF care through many different methods.

P-06 4:30 PM Saturday, October 17, 2020

ACCESS TO ART CARE AT A UNIVERSITY SATELLITE CLINIC: OUTCOME ANALYSIS OF PREGNANCY RATES, INCLUDING SINGLETON LIVE BIRTH RATES. Estefania Santamaria Flores, MD, MPH,[1] John Yeh, MD,[2] Shaila V. Chauhan, MD[3] [1]University of Massachusetts Medical School, Worcester, MA; [2]UMass, Worcester, MA; [3]U MassMedical School, Worcester, MA.

OBJECTIVE: The development of satellite clinics has improved the access of ART services to infertile patients. Little has been published about the pregnancy rates of such centers in comparison to the main centers with which they are connected. We investigated the first embryo transfer and subsequent embryo transfer outcomes in women cared for at our satellite center and compared these to rates of the main ART center and national data to better understand the utility of satellite clinics to improve access.

DESIGN: Retrospective, comparative cohort. This study was approved by the University of Massachusetts Institutional Review Board (#14573).

MATERIALS AND METHODS: All women ages 23 to 45 undergoing ART procedures in 2017 and 2018 at UMass Memorial Medical Center's infertility clinic were included. The patients had their ovulation induction managed at the satellite clinic and had their oocyte retrieval, embryo culture and embryo transfers at the main ART center. Positive pregnancy tests, clinical pregnancies, miscarriage rates, and live birth rates were calculated. The cases were divided into the following age groups: < 35, 35-37, 38-40, 41-42, and > 42. Using data published by the Society for Reproductive Technology Clinic Outcome Reporting System, we compared these rates to those of the affiliated main center and national data. The Student's t-test was used and $p < 0.05$ was considered statistically significant.

RESULTS: In 2017, 66 first embryo transfers and 28 subsequent embryo transfers were completed. Women < age 35 had a higher first embryo transfer singleton birth rate at our satellite clinic compared to the main center and national rates (61.2 % vs. 30.8 % vs. 35.4 %, respectively; $p < 0.05$). In 2018, 66 first embryo transfers and 34 subsequent embryo transfers were completed. For 2018, women < age 35 undergoing subsequent embryo transfers at our satellite clinic had higher live birth rates (70 % vs. 48.3 % vs. 47.1 %, respectively; $p < 0.05$). Analysis for all other categories for 2017 and 2018 demonstrated no other statistically significant differences when compared to both main center and national data.

CONCLUSIONS: Increased access to ART care was achieved by having our satellite clinic. We found that for women < age 35, there was a higher first embryo transfer singleton birth rate for 2017 and a higher subsequent embryo transfer live birth rate for 2018. No other statistically significant differences were noted for other categories for either year. These findings highlight the ability of satellite clinics to provide access to ART services and the continued need for quality improvement measures at satellite clinics to mirror the rates of their associated main centers.

P-07 4:30 PM Saturday, October 17, 2020

THE COST OF INFERTILITY (COIN) STUDY: MODELING DECISION REGRET. Viji Sundaram, MD,[1] Jerrine R. Morris, MD, MPH,[1] Jake Anderson, MBA,[2] Martha Noel, MD[1] [1]University of California, San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA; [2]FertilityIQ, San Francisco, CA.

OBJECTIVE: To determine how much out-of-pocket (OOP) cost of in vitro fertilization (IVF) influences decision regret.

DESIGN: Cross Sectional Cohort

MATERIALS AND METHODS: In collaboration with a national fertility education company (FertilityIQ), a recruitment email was sent to all registered users of FertilityIQ who had undergone at least 1 cycle of IVF. Survey participants completed a web-based, anonymous, self-reported survey including questions regarding demographics, reproductive and IVF history, insurance information, financial details, opinions on legislation, and a standard Decision Regret Scale (DRS). Survey questions were created through an iterative process and revised to incorporate changes following pilot delivery to 10% of FertilityIQ users. Data analysis was performed with descriptive statistics; univariate logistic regression for dichotomous outcomes; Spearman's rank correlation; and one-way analysis of variance (ANOVA) with pairwise comparisons using the Bonferroni adjustment for categorical outcomes.

RESULTS: Recruitment emails were distributed to 4,326 registered FertilityIQ users, with 1,568 people (36%) opening the email & 337 (8%) completing the survey. 66% of respondents were ≤34 years of age, and 85% were white. 40% had a household income of <$100,000, with 43% spending $25-70,000 on their total IVF care. Mean DRS score in all survey participants was 25.4, consistent with moderate to severe regret. 3 out of 4 women had some degree of regret after undergoing IVF. Significant univariate predictors of moderate to severe regret included: total years spent on IVF (OR1.12, CI 1.02-1.24), if respondents had a live birth (OR 0.12, CI 0.06-0.25), number of live births using IVF (0.62, CI 0.47-0.81), and OOP costs of IVF treatment (OR 1.15, CI 1.04-1.28). The relationship between DRS score and total OOP cost was examined with a significant positive correlation noted (rho 0.127, $p=0.02$). Mean DRS scores reveal a significantly higher level of regret in those who did not have a live birth (41.74) following IVF compared to those who did (16.78, $p<0.0001$), which persisted regardless of total OOP cost spent on IVF.

CONCLUSIONS: Funding for IVF creates a significant burden on families, even with incomes up to $250k. Despite the large financial burden, regret around pursuing IVF is not associated with amount of money spent but entirely dependent on if a couple has a live birth.

P-08 4:30 PM Saturday, October 17, 2020

FINANCIAL ASSISTANCE OPPORTUNITIES FOR INFERTILITY TREATMENTS: MALE FACTOR INFERTILITY IS OFTEN FORGOTTEN. Darren J. Bryk, MD,[1] Sarah C. Vij, MD[2] [1]Cleveland Clinic, Cleveland, OH; [2]Cleveland Clinic Foundation, Cleveland, OH.

OBJECTIVE: Financial assistance opportunities (FAOs), in the form of grants and donated or discounted services or medications, can relieve the significant burden of fertility treatment costs on infertile couples. We analyzed the characteristics of fertility FAOs and hypothesized that FAOs for male factor infertility (MFI) would be less prevalent than those for female factor infertility (FFI).

DESIGN: Google search was performed for fertility FAO websites. Websites of all FAOs were then reviewed.

MATERIALS AND METHODS: Google search was performed and many aggregating websites that list fertility FAOs were found; cofertility.com had the most extensive list with links to each FAO's website. The websites for all FAOs found on cofertility.com were thoroughly reviewed. Those that only support adoption, that do not have a functioning website, or that have limited details listed on the website were excluded. Primary endpoint was evidence of financial support based on gender.

RESULTS: Eighty-six FAOs were reviewed. All 86 (100%) primarily support FFI; 72 include financial assistance for or discounted ART and intrauterine insemination (IUI), 16 for fertility preservation and egg cryopreservation, 4 for egg donation and 13 for fertility medications. None of the reviewed FAOs focus solely on MFI. MFI is mentioned in 27/86 (31.4%) of the FAOs; of these, 19 FAOs support ART or IUI related to MFI with 6 specifically noting surgical sperm retrieval or other procedures for MFI. Sperm cryopreservation and medications for MFI is supported by 5 and 4 FAOs, respectively. Among the entire cohort, specific populations that have dedicated FAOs are those in military (active duty, reserve or veteran) with 21/86 (24.4%) FAOs and current or prior-treated patients with cancer with 11/86 (12.8%) FAOs. Of the FAOs dedicated to military personnel, 7/21 (33.3%) include support for MFI. Of the FAOs dedicated to patients with a history of cancer, 5/11 (45.5%) include support for MFI. With regard to the type of financial assistance, 29/86 (33.7%) provide discounted or free fertility treatments or medications, 36/86 (41.9%) provide monetary grants (range $250 – $41,500) for fertility treatments, 1/86 (1.2%) FAO provides free fertility treatment and a monetary grant, 18/86 (20.9%) do not specify the type of assistance, and 1/86 (1.2%) provide a warranty if the IVF cycle is unsuccessful.

CONCLUSIONS: Couples with infertility due to a male factor have fewer opportunities for grants and discounted fertility treatments than do couples with FFI in the US. Further financial support may alleviate some of the burden on this subset of infertile patients.

SUPPORT: none

P-09 4:30 PM Saturday, October 17, 2020

ASSESSING TRANSPARENCY OF COSTS OF SPERM CRYOPRESERVATION ACROSS THE UNITED STATES. Johnny S. Su, BA,[1] Nicholas J. Farber, MD,[2] Yida Cai, BA,[1] Johnathan Doolittle, MD,[2] Sajal Gupta, MD,[3] Ashok Agarwal, PhD,[3] Sarah C. Vij, MD[2] [1]Case Western Reserve University School of Medicine, Cleveland, OH; [2]Glickman Urological and Kidney Institute, Cleveland Clinic, Cleveland, OH; [3]American Center for Reproductive Medicine, Cleveland Clinic, Cleveland, OH.

OBJECTIVE: The objectives of our study are to assess the average cost of sperm cryopreservation and to determine the transparency in costs reported online in the U.S.

DESIGN: In March of 2020, we queried the Food and Drug Administration's Human Cell and Tissue Establishment Registration for facilities that have a registration to store semen products. Duplicate entries and those with no websites were excluded.

MATERIALS AND METHODS: Each facility was searched online for pricing data on sperm cryopreservation. Facilities were categorized by census region and facility type. Fisher's exact test and one-way analysis of variance were performed to compare online transparency and cost among different groups.

RESULTS: A total of 542 facilities were included, with only 96 facilities (17.7%) have any pricing information on sperm cryopreservation online. Of these, 16.7% (16/96) had price listings that were a part of fertility packages such as intrauterine insemination or in vitro fertilization. 12.5% (12) report transferring semen samples to another facility for long-term storage. 15.6% (15) charge their storage fee per client, while only 2.1% (2) charge by the number of semen specimens stored. 28.1% (27) offer storage plans longer than one year at reduced rates. Table 1 demonstrates the national cost of sperm cryopreservation. Online price transparency was different among the U.S. census regions: Northeast (21.2%), South (11.9%), Midwest (25.5%), and West (17.1%) (p=0.04). By facility type, 71.4% of biobanks had pricing information online compared to 34.5% of academic hospitals, 40% of non-university affiliated hospitals, and 6.3% of private practices (p<0.01). The Northeast had the highest annual storage fee (mean US$478) compared to the South ($443), the Midwest ($307), and the West ($395) (p=0.03). There were no differences in annual storage fee by facility type or in initial fee across groups.

CONCLUSIONS: Costs transparency of sperm cryopreservation is poor across the U.S., with less than one-fifth of registered facilities displaying any cost information online. The annual cost of storing sperm is highest in the Northeast, which could be attributed to differences in laboratory techniques, demographic patterns, or IVF insurance coverage. Achieving effective cost transparency can promote consumer decision-making and decrease the barrier for men seeking fertility preservation.

TABLE 1. National cost of sperm cryopreservation (in USD)

	Mean	Median	SD	# Reporting
Initial bank	389.12	350	225.06	80
Free storage (months)	9.5	12	4	14
Repeat bank	271.14	260	69.20	28
Storage - 1 month	46.87	48.00	11.24	23
Storage - 1 year	396.43	385.00	180.68	67
Thawing fees	170.98	150.00	143.69	29
Specimen retrieval	53.08	45.00	77.8	26
Infectious disease testing	171.22	140.00	58	9

P-10 4:30 PM Saturday, October 17, 2020

RURAL LOCALE PROTECTIVE FOR ETHNICALLY AND RACIALLY DIVERSE WOMEN AT RISK FOR GESTATIONAL DIABETES MELLITUS IN THE PACIFIC NORTHWEST. Kelsie Clausen, MA, OMSII,[1] Kathaleen Briggs Early, PhD, RDN, CDE,[1] David Gothard, MS,[1] Lizzie Lamb, MPH,[1] Laurene Enns, MA,[1] Esther Park-Hwang, MD, MBA[2] [1]Pacific Northwest University of Health Sciences, Yakima, WA; [2]MultiCare Health System, Tacoma, WA.

OBJECTIVE: Pregnancy-related complications like gestational diabetes mellitus (GDM) lead to adverse outcomes and increased chronic disease risk for both mother and fetus. Women living in rural and medically underserved communities are at especially high risk due to the inverse association of health outcomes with the social determinants of health and high rates of obesity. Prevalence of GDM in rural and non-rural areas has not been not been previously evaluated, and with co-morbidities leading to lifelong health implications, it is imperative to identify disparities to mitigate them. Our primary aim was to determine if there is a significant difference in GDM prevalence between rural and non-rural communities, and if there are certain variables that contribute as predictors for GDM risk.

DESIGN: This research is a retrospective, case-control study of the Center for Disease Control's (CDC) Pregnancy Risk Assessment and Monitoring System (PRAMS), years 2012-2015, Phase 7.

MATERIALS AND METHODS: We used SPSS v25.0 software to analyze data from PRAMS for AK, OR, and WA including birth certificate and core 7 questionnaire variables. The sample was weighted to be reflective of a population of 450,294.8 persons. Univariate analysis was performed to identify variables that were significantly different in rural or non-rural areas using a p-value threshold of 0.05. The significant variables were accounted for in a multivariable logistic regression model for GDM outcome to determine the additive influence of rural locale after adjustment for potentially confounding significant factors. Commonly known confounding risk factors, such as advanced maternal age, obesity, socioeconomic status, macrosomia, and caesarean section were controlled for in the model. Outcome measures were evaluated by adjusted odds ratios with 95% confidence intervals and tested for equivalence to 1.

RESULTS: Overall, rural locale was not significantly different than urban for GDM, but indicated a slightly increased odds ratio (p=0.690). Hispanic race was significant for increased prevalence in rural locations (p<0.001) and decreased risk of GDM (p=0.024). Combined, being Hispanic and having rural locale did not increase GDM risk (p=0.329). Additionally, the Kessner index, describing adequacy of prenatal care, was higher in rural locales and a predictor for decreased odds of GDM, though p=0.310. Post-hoc analysis revealed rural locale was significant for *reducing* risk for GDM among non-white women (aOR=0.562). Also, despite white race as a protective factor in general (p<0.001), white women were at increased risk of GDM in rural locations (p=0.031).

CONCLUSIONS: Overall, there was no difference in GDM prevalence between rural or non-rural areas of AK, OR and WA. White maternal race was a protective factor, but for non-white women, rural residence adds a significant protective influence on GDM risk. Several aspects could account for this, including social support practices, the quality and type of occupation, nutritional intake, or physical activity.

SUPPORT: None.

P-11 4:30 PM Saturday, October 17, 2020

BARRIERS TO FAMILY BUILDING AND IMPACT ON CAREER TRAJECTORY FOR WOMEN IN MEDICINE. Anne P. Hutchinson, M.D.,[1] Kathryn Smith, B.S.,[2] Elaine O. Cheung, PhD,[3] Patricia I. Moreno, PhD,[3] Neil Jordan, PhD,[4] Kara N. Goldman, M.D.,[1] Jessica L. Thomas, A.M.,[2] Veronika Elisabeth Grote, B.S.,[3] Eve C. Feinberg, M.D.[1] [1]Northwestern University Feinberg School of Medicine, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Chicago, IL; [2]Northwestern University Feinberg School of Medicine, Chicago, IL; [3]Northwestern University Feinberg School of Medicine, Department of Medical Social Sciences, Chicago, IL; [4]Northwestern University Feinberg School of Medicine, Department of Psychiatry and Behavioral Sciences, Mental Health Services & Policy Program, Chicago, IL.

OBJECTIVE: Explore female physicians' perceptions and experiences of fertility, pregnancy, and parenthood in academic medicine, and their impact on family planning and career trajectory.

DESIGN: Qualitative semi-structured interview study

MATERIALS AND METHODS: Qualitative interviews were conducted in person or remotely over video conference using a semi-structured interview guide. The interviewer asked open-ended questions to elicit participants' knowledge, experiences and concerns as related to partnership, family planning, fertility, pregnancy and parenthood, and whether these factors had impacted participants' career paths. All interview transcripts were qualitatively coded by two members of the research team in Dedoose.

RESULTS: 10 female physicians in academic medicine (age M = 34.4, SD: 2.1, range: 28-38) completed qualitative interviews: 9 attending physicians, and 1 fellow.

All 10 women expressed frustration that leave, childcare, and fertility benefits were not openly discussed. The 4 women with children reported that they relied on peer mentorship, as opposed to Human Resources transparency, to navigate the process. Among the 6 women without children, 5 lacked information about their institution's parental leave policies.

Nine of 10 women interviewed reported delaying childbearing (range: 0.5-6 years). Among the women who delayed childbearing, 7 cited barriers in the training/work environment (lack of time, lack of flexibility in schedules, financial strain) as their primary reason for delay, and 2 cited the lack of a partner.

Six of 10 women reported frustration with their lack of schedule flexibility, and 7 of 10 perceived lack of peer support for parental leave, fertility, or childcare needs.

Nine of 10 women reported that they would decrease their clinical time to allow for additional flexibility with childbearing. Two would consider changing specialties or leaving medicine completely to accommodate childbearing and parenthood.

These stressors were notably diminished in women who selected their career paths with flexibility for childbearing in mind (e.g., hospital medicine) or were in divisions composed of predominantly young female physicians. These stressors were also diminished in women who reported having additional support for family and parenthood outside of the workplace (e.g., financial and/or childcare support provided by romantic partners and other family). While all participants agreed that their partner should share in parenting responsibilities, 8 reported that they would not expect their partner to make any changes to their career paths to facilitate family life.

CONCLUSIONS: This study identified several important barriers to female physicians interested in parenthood while pursuing careers in academic medicine. Young female physicians are bearing the brunt of the stressors of parenthood, and without proper social and institutional support they are at increased risk for burnout, turnover, or departure from medicine. These findings reinforce the importance of clear-cut, supportive policies and ongoing dialogue about these issues and available resources.

POSTER SESSION: ART LAB: BASIC

P-12 4:30 PM Saturday, October 17, 2020

HUMID VS DRY CULTURE: DOES RELATIVE HUMIDITY AFFECT THE MORPHOKINETICS OF *IN VITRO* CULTURED EMBRYOS?. María de los Ángeles Valera, PhD Student,[1] Carmela Albert, PhD,[2] Lorena Bori, M.Sc,[2] Lucia Alegre, PhD,[2] Thamara Viloria, PhD,[2] Marcos Meseguer, PhD[2] [1]IVIRMA Global; IVI Foundation, Valencia, Spain; [2]IVIRMA Global, Valencia, Spain.

OBJECTIVE: The aim of this study is to compare the timing of the main development events of embryos cultured in humid (HC) or dry conditions (DC) in a time-lapse system (TLM) incubator.

DESIGN: In this retrospective study we analysed the morphokinetics of 7014 embryos belonging to 832 ICSI treatments performed during two consecutive years, from autologous (n=393) or ovum donation programs (n=439). Embryos were cultured in an incubator equipped with time-lapse monitoring system, in dry (3281 embryos) or humid conditions (n=3149). Timing of the main development events of each embryo were annotated and compared between the two study groups.

MATERIALS AND METHODS: Stimulation, oocyte pickup and fertilization were performed according to the standard procedures of the clinic. Fertilized oocytes were cultured in a Geri incubator (Genea Biomedx, Australia). This incubator has 6 separated chambers for individual patients, 3 of them operating with dry environment, and 3 adapted for culture in a high relative humidity atmosphere. Embryo cohorts were randomly assigned to DC or HC. Embryo development was monitored using Assess 2.0 TLM software from Geri and the main morphokinetic parameters were automatically annotated and compared between those incubated in dry vs humid conditions. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) in search for significant differences between the two groups.

RESULTS: Morphokinetic parameters were compared between all embryos cultured in HC and DC, as well as only good morphology blastocysts and only transferred embryos. Significant differences ($p \leq 0,05$) were found in the mean values of **tPNf** (23,350h in HC vs 23,591h in DC), **t2** (26,809h in HC vs 27,149h in DC), **tM** (85,958h in HC vs 86,904h in DC) and **tEB** (114,727h in HC vs 113,805h in DC), being all except the latter lower in embryos cultured in HC. When comparing only good morphology blastocysts, **tPNf** (22,821h vs 23,165h), **t2** (25,569h vs 25,843h) and **tM** (85,226h vs 86,573h, $p \leq 0,001$) remained being significantly lower in HC, as well as **tSC** (98,499h vs 99,187h), but no significant difference was found in tEB. However, when comparing only transferred embryos (n=394), no significant differences in tPNf nor t2 were found, although **tM** remained significantly lower in HC (83,424h vs 86,020h in DC, p=0,002). Later developmental events occurred faster in transferred embryos cultured in HC than DC: **tSB** (95,806h vs 97,249h, p=0,042), **tB** (101,870h vs 103,662h, p=0,05) and **tEB** (108,086h vs 109,851h, p= 0,012), in contrast with the observed in the whole set.

CONCLUSIONS: Embryos cultured in HC had a slightly faster development than those cultured in DC, being the time to reach morulae stage the most affected parameter, which has been previously related with higher embryo quality and implantation potential (Goodman *et al*, 2016). These findings are consistent with previously published results (Albert *et al,* 2020) where embryos cultured in HC had higher ongoing pregnancy rates than those cultured in DC.

References: Albert, C.Â *et al,Â* in-press.Â *The effect of high humidity by using single step culture media on continuous embryo monitoring incubator.* Manuscript submitted for publication, ESHRE Congress 2020.

Goodmann, L. R.,Â *et alÂ* (2016).Â *Does the addition of time-lapse morphokinetics in the selection of embryos for transfer improve pregnancy rates? A randomized controlled trial.Â* Fertil Steril;105(2):275-85.e10.

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P-13 4:30 PM Saturday, October 17, 2020

HOW LOW CAN YOU GO WITH OXYGEN CONCENTRATION?. Rachel Blair Danis, MD,[1] Jesse L. Stone, MS,[2] Jacqueline Ho, MD MS,[1] Trenton Place, DO, PhD,[1] Lynda K. McGinnis, PhD,[1] Ali Ahmady, PhD[3] [1]University of Southern California, Los Angeles, CA; [2]USC Fertility, Los Angeles, CA; [3]Keck School of Medicine, University of Southern California, Los Angeles, CA.

OBJECTIVE: The concentration of oxygen in the female reproductive tract gradually decreases from 5-7% in the fallopian tube to 2% in the uterus. A reduction in oxygen from atmospheric to physiologic levels improves cell number, decreases DNA fragmentation, and induces less oxidative stress on the blastocyst. However, studies investigating benefits of ultralow oxygen concentrations *in vitro* have shown inconsistent findings[2,4–8]. We sought to determine if culturing from single-cell stage embryos at various ultralow oxygen concentrations improved embryo development in the mouse model.

DESIGN: Basic science

MATERIALS AND METHODS: Cryopreserved single-cell stage mouse embryos ($B_6C_3F_1$ X $B_6D_2F_1$ strain; Embryotech, Haverhill, MA) were thawed and randomly divided into 5 oxygen treatment arms: 0.7-0.8% (n=173), 1.5% (n=176), 2% (n=166), 3% (n=171), and 5% (n=171, control arm). Embryos were cultured to the blastocyst stage in groups of 6 in 25μl droplets of Continuous Single Culture Complete (CSCC, Irvine Scientific) in an incubator (Heracell 150i) at 8% CO_2 and a pH of 7.3. Embryo development was evaluated by quantifying cell number over a 5-day period. Chi square test and logistic regressions were used to test associations where appropriate. A p-value of <0.05 was considered statistically significant.

RESULTS: Mouse embryos cultured at ultralow oxygen concentrations of 1.5%, 2%, and 3% had similarly high rates of blastocyst development, whereas those cultured at 0.7-0.8% had the lowest rate of blastocyst development (Table). Compared to cleavage-stage embryos cultured at 5%, mouse embryos cultured at 2% and 3% oxygen concentrations were more likely to become blastocysts, (OR 4.1 and OR 3.7, $p<0.05$, respectively), and those cultured at 0.7-0.8% were least likely to develop into blastocysts (OR 0.2, 95% CI 0.12-0.34, $p <0.001$; Table).

CONCLUSIONS: We demonstrated a unimodal distribution for optimal oxygen concentrations *in vitro*. Too low, 0.7-0.8%, resulted in poor blastulation, and the standard 5% did not improve embryo development. Oxygen concentrations at 2% and 3% resulted in optimal blastocyst development.

TABLE. Mouse embryo development at ultralow oxygen concentrations

Oxygen Tension	0.7-0.8%	1.50%	2%	3%	5%
Number of single-cell embryos on Day 1*	173	176	166	171	171
Number of cleavage* (%)	171 (98.8)	176 (100)	156 (94.0)	163 (95.3)	170 (99.4)
Number of blastocyst* (%)	94 (54.3)	159 (90.3)	150 (90.4)	156 (91.2)	146 (85.4)
Odds ratio of a cleavage stage mouse becoming a blastocyst	0.20*	1.5	4.1*	3.7*	1.0 (ref)

Logistic regression used; *significance $p<0.05$

These findings shed light on the potential benefit of ultralow oxygen concentration, particularly at 2-3%.

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SUPPORT: None

P-14 4:30 PM Saturday, October 17, 2020

REALISTIC MEASUREMENT OF THE EFFECT OF SPERM DNA FRAGMENTATION ON REPRODUCTIVE OUTCOMES BY CUMULATIVE LIVEBIRTH RATES (CLBR) PER EMBRYO REPLACED AND OOCYTE EMPLOYED REVEALS ITS LACK OF RELEVANCE IN UNSELECTED MALES USING OWN OOCYTES. Irene Hervas, MSc,[1] Nicolas Garrido, PhD,[1] Rocio Rivera-Egea, PhD,[2] Cristina Gonzalez-Ravina, PhD,[3] David Amoros, PhD,[4] Fernando Quintana, Sr., PhD,[5] Maria Gil Julia, MSc, MRes,[1] Alberto Pacheco, PhD[6] [1]IVI Foundation - IIS La Fe Biomedical Research Institute, Valencia, Spain; [2]IVIRMA Valencia, Valencia, Spain; [3]IVIRMA Sevilla, Sevilla, Spain; [4]IVIRMA Barcelona, Barcelona, Spain; [5]IVIRMA Bilbao, Bilbao, Spain; [6]IVIRMA Madrid, Madrid, Spain.

OBJECTIVE: Sperm DNA fragmentation (SDF) effect on reproductive outcomes has been extensively studied and contradictory conclusions have been reached so far, probably caused by an inappropriate way of measuring reproductive success influenced by sperm biomarkers. Using clinical outcomes per embryo transfer is a biased measure of the impact of SDF on the embryonic cohort, since does not consider the surplus contribution of other cohort embryos and the best are firstly selected.We addressed this problem by studying raw live birth rates (LBR) at first embryo transfer (ET), in all ET (fresh + thawed), and CLBR, per ET, number of embryos replaced (EmbR) and oocytes consumed until reaching a first live, better assessing its actual effect.

DESIGN: Retrospective cohort multicenter study.

MATERIALS AND METHODS: Patients undergoing IVF/ICSIs with autologous oocytes (n=1055) from Jan 2000-Mar 2019, tested for SDF on ejaculated spermatozoa using TUNEL assay. Analysis groups were established to compare all main outcomes: SDF >15% (H, high) and in 10% SDF ranges: <10%, 10%-20%, 20%-30%, >30%, by X^2 square tests, and CLBR estimated with Kaplan-Meier and Mantel-Cox test, considering the total number of embryo transfers, embryos transferred, and oocytes needed to obtain the first livebirth.

RESULTS: 2759 embryo transfers were considered, and a total of 2469 embryos and 5657 consumed oocytes had been including. Overall population characteristics were comparable. No difference in LBR was shown neither at first embryo transfer nor in all, with high/low (L) SDF 41.9% vs 38.2% and 39.9% vs 36.5% respectively. LBR rates considering 10% SDF ranges were comparable in first and in all transfers. CLBR per ET performed showed non-significant differences between H or L fragmentation groups: 40.7% vs 46.9% (1st), 59.1% vs 66.4% (2nd), 69.9% vs 77.0% (3rd) and 86.7% vs 100.0% (5th). If compared by 10% SDF ranges, CLBR of the group with the lowest (<10%) SDF versus the highest (>30%) were 41.1% vs 38.9%, 59.0% vs 71.8% and 68.1% vs 78.8% with the first three ET respectively. Cumulative LBR according to the number of EmbR were similar (L vs H): for 2 EmbR (48.0% *vs* 54.3%) and 4 EmbR (67.5% *vs* 74.0%), as they were comparing CLBR by SDF groups, being 49.0% (<10%) and 53.3% (>30%) CLBR with 2 EmbR, or when up to 4 embryos were replaced, 66.0% (<10%) and 81.3% (>30%). CLBR per number of oocytes consumed was comparable in L group (43.3%, 67.3% and 81.9%), and in H group (46.0%, 68.35% and 87.3%) for 5, 10 or 15 oocytes used respectively. By SDF groups, CLBR was analogous, f.i. in <10% *vs* >30% groups: 43.5% *vs* 49.2% at 5 oocytes, 68.3% *vs* 77.4% at 10 oocytes, and 81.6% *vs* 88.7% at 15 oocytes consumed.

CONCLUSIONS: DNA fragmentation does not negatively affect the live birth rates of unselected patients undergoing an IVF-ICSI cycle with their own oocytes, neither per transfer, nor accumulated per transfer, embryo or oocyte, after the largest and most extensive data analysis done so far.

P-15 4:30 PM Saturday, October 17, 2020

EFFECT OF PENTOXIFYLLINE SUPPLEMENTATION ROUTINELY ADDED TO SPERM SUSPENSIONS IMMEDIATELY BEFORE INTRACYTOPLASMIC SPERM INJECTION. Rita C. S. Figueira, Ph.D.,[1] Sidney Verza, Jr., B.Sc.,[1] Vanessa C. F. Moreno, B.Sc.,[1] Sandro C. Esteves, M.D., Ph.D.[2] [1]Androfert, Campinas, Brazil; [2]ANDROFERT & University of Campinas (UNICAMP), Campinas, Brazil.

OBJECTIVE: Effects of PTX indiscriminate use have not been properly studied, and concerns exist of possible embryotoxicity. We investigated the clinical utility of routine PTX-sperm supplementation on the fertilizing ability and embryo development.

DESIGN: Prospective cohort study

MATERIALS AND METHODS: In the study group, 10μL of a commercially available PTX (20mg/mL; Vascer, União Qumica, Brazil) was added 1:1 v/v to the sperm suspension and this preparation was immediately transferred to a PVP drop in an ICSI dish. Motile sperm, preferentially those exhibiting hyperactivation, were selected to injection. Blastocysts were subjected to trophectodermal biopsy and comprehensive chromosomal screening. Statistical analysis was performed using Student T-test, Chi-square and multiple regression models. The primary endpoint was 2PN fertilization rates (FRs) and the secondary endpoints were embryonic outcomes.

RESULTS: In study periods 1 (July/18 - April/19, Control) and 2 (May/19 - December/19, PTX), 141 and 178 couples were subjected to 232 and 244 ICSI cycles without and with PTX supplementation, respectively. Demographic data were similar between control and PTX groups. PTX increased

FRs in the overall populations and subgroups, including azoospermic men, with a more pronounced effect when ICSI was carried out with testicular sperm. No apparent toxic effect was noticed concerning the rates of blastocyst formation and euploidy. Table 1 presents a summary of the results. Multiple regression models showed a significant and independent increment on fertilization ability when sperm samples derived from non-male factor cycles were PTX-incubated (β=6.01, p=0.03).

	Fertilization rate			Blastocyst rate			Blastocyst euploidy rate		
Cycles	PTX	Control	P	PTX	Control	p	PTX	Control	p
All	74.4	68.1	<0.001	49.6	49.3	0.88	40.8	40.9	0.97
Non-male factor	78.1	70.0	<0.001	52.8	54.0	0.64	39.1	40.1	0.84
Male factor	69.4	64.1	0.05	44.7	39.0	0.11	43.9	44.0	0.98
Azoospermia	65.6	52.1	0.01	35.5	33.7	0.79	50.0	41.7	0.65
Testicular sperm	63.6	46.5	0.005	32.0	32.1	0.99	43.8	42.9	0.96

CONCLUSIONS: Our findings indicate that the routine use of PTX enhances sperm fertilizing ability without compromising embryo development and genetic competence. Beside its positive effect on intracellular cyclic AMP concentrations, other mechanisms might be involved. The observed beneficial effect of PTX in our cohort warrants further investigation to confirm its efficiency and safety.

P-16 4:30 PM Saturday, October 17, 2020

SEPARATION OF NON-APOPTOTIC SPERM VIA MAGNETIC ACTIVATED CELL SORTING BEFORE INTRACYTOPLASMIC SPERM INJECTION IN AUTOLOGOUS OOCYTES INCREASED CUMULATIVE LIVE BIRTH RATES WITH LIMITED CLINICAL IMPACT. Maria Gil Julia, MSc, MRes,[1] Fernando Quintana, Sr., PhD,[2] David Amoros, PhD,[3] Alberto Pacheco, PhD,[4] Cristina Gonzalez-Ravina, PhD,[5] Rocio Rivera-Egea, PhD,[6] Irene Hervas, MSc,[1] Nicolas Garrido, PhD[1] [1]IVI Foundation - IIS La Fe Biomedical Research Institute, Valencia, Spain; [2]IVIRMA Bilbao, Bilbao, Spain; [3]IVIRMA Barcelona, Barcelona, Spain; [4]IVIRMA Madrid, Madrid, Spain; [5]IVIRMA Sevilla, Sevilla, Spain; [6]IVIRMA Valencia, Valencia, Spain.

OBJECTIVE: The benefit of using magnetic activated cell sorting (MACS) to select annexin V negative, non-apoptotic sperm before intracytoplasmic sperm injection (ICSI) has been a matter of controversy. One reason might be the bias caused by embryo selection in each transfer and measuring success only on the first attempt. The aim of this study is to retrospectively evaluate MACS when using autologous oocytes, measuring success by cumulative rates per embryo transferred and oocyte consumed until a first child is born, overcoming the classical limitations.

DESIGN: Multi-center retrospective observational cohort study.

MATERIALS AND METHODS: Data was extracted from the results of ICSI cycles with autologous oocytes (Jan 2008-Feb 2020) which used semen samples processed by standard preparation protocols (control) or the standard procedure plus an added MACS step. Descriptive variables were compared by t-tests and gestational outcomes per embryo transfer (ET) and, in case of live birth rates (LBR) also per cycle, by Fisher's exact test. Kaplan-Meier (K-M) estimates reported cumulative LBR (CLBR) per ET and metaphase II oocyte (MII) in both groups. Mantel-Cox tests were performed to compare the plotted curves for each group. The threshold for statistical significance was set at p-value<0.05.

RESULTS: Overall cycle and patients characteristics were similar between groups.

When computed per ET, MACS group (n=2802 transfers) had a 46.9% biochemical pregnancy rate, a 39.7% clinical pregnancy rate and a 32.4% ongoing pregnancy rate, while the control group (n=60503) showed 45.4%, 38.7% and 31.8% respectively. None of these differences were statistically significant.

In terms of LBR, MACS group showed a 29.3% LBR per ET and a 38.8% per cycle (n=2115 cycles). The control group exhibited a 29.2% LBR per ET and 37.4% per cycle (n=60503). Neither of the comparisons were statistically significant.

CLBR per ET was 63.6% (60.1, 66.8) for two transfers, 80.6% (75.5, 84.6) for three in the MACS group, whereas the control group presented a rate of 59.6% (58.9, 60.4), 72.3% (71.2, 73.3) respectively.

CLBR per embryos transferred was 21.5% (19.4, 23.6) for one embryo, 55.5% (52.6, 58.2) for two, 65.4% (62.0, 68.5) for three and 83.3% (78.9, 86.7) for four, while the control group's CLBR was 15.0% (14.7, 15.4), 49.1% (48.6, 49.7), 58.0% (57.3, 58.7) and 73.3% (72.5, 74.1). Both CLBR measures displayed K-M curves with a statistically significant difference.

If computed per MII used, control group showed a CLBR of 13.1% (12.8, 13.5) for five MII, 39.8% (39.2, 40.4) for ten and 62.7% (62.00, 63.4) for fifteen, while the MACS group had a CLBR of 11.0% (9.6, 12.4), 36.6% (33.9, 39.1) and 59.8% (56.3, 63.0). K-M curves had a statistically significant difference.

CONCLUSIONS: Considering the largest sample size for this type of studies yet, the findings suggest that the separation of annexin V negative non-apoptotic sperm through MACS prior to ICSI using their own oocytes decreases the number of embryos needed to achieve the first live birth, but not the oocytes. However, the overall clinical relevance remains low.

P-17 4:30 PM Saturday, October 17, 2020

OOCYTE IN VITRO MATURATION DOES NOT ADVERSELY AFFECT THE PROGRESSION OF THE FIRST MEIOTIC DIVISION. Marga Esbert, PhD,[1] Cristina Garcia, MSc,[1] Georgina Cutts, MSc,[2] Evelin Lara-Molina, MD,[1] Emre Seli, MD,[3] Agustin Ballesteros, MD,[1] Nicolas Garrido, PhD,[4] Mariona Quera, MSc,[1] Richard Thomas Scott, Jr., MD,[3] Dagan Wells, PhD,[2] Elpida Fragouli, PhD[2] [1]IVI RMA Barcelona, Barcelona, Spain; [2]JUNO GENETICS, Oxford, United Kingdom; [3]IVI RMA New Jersey, Basking Ridge, NJ; [4]IVI Foundation - IIS La Fe Biomedical Research Institut, Valencia, Spain.

OBJECTIVE: Immature oocytes account for 15% of all oocytes collected and are usually discarded during IVF. There is little information on the aneuploidy frequency of *in vitro* matured (IVM) oocytes derived from young fertile women, and a standardized protocol enabling effective IVM is lacking. Our study aimed to: 1. Assess whether the addition of autologous cumulus cells (CCs) improves IVM rates; 2. Perform a comprehensive analysis of aneuploidy frequency and type in oocytes cultured in the presence or absence of autologous cumulus cells (CCs) during IVM.

DESIGN: This is a prospective randomized study including 390 oocytes [116 metaphase II (MII) and 274 immature oocytes] from 91 donors undergoing ovarian stimulation in one clinic between March-July 2019. The immature oocytes underwent IVM in the presence (n=137) or absence of CCs (n=137) according to a randomization plan. The MII oocytes served as a control for the IVM groups.

MATERIALS AND METHODS: Oocyte donors (mean age 25.57 $\pm$ 4.47) had a normal karyotype and did not have fertility problems. Biopsy of the 1st polar body (PB) was performed directly after denudation for MII oocytes, or after IVM for immature ones. IVM took place in a time-lapse incubator until 1st PB extrusion, or for 50 hours. CC suspension (1ul) was added to the culture well of 137 of the immature oocytes. The cytogenetics of oocytes and their 1st PBs was examined via a well-validated next generation sequencing (NGS) strategy. Our sample size calculation indicated that 74 MII were required per group (with an Alpha risk of 5%, a Beta risk of 20%) to reach statistical significance.

RESULTS: CC co-culture did not enhance IVM rates. Overall, 62.77% of oocytes co-cultured with CCs matured to MII, compared with 71.53% of oocytes cultured without CCs. A significantly higher number of mature MII oocyte-PB pairs (86.28%) yielded NGS results, compared to the IVM pairs (77.90%, P = 0.01). Reciprocal results between oocyte and their 1st PBs were obtained for most (77.84%) of the samples. A similar euploidy rate was observed for the MII oocytes (81.97%), and the IVM oocytes cultured in the presence (80.00%) or absence (85.42%) of CCs. Abnormalities resulting from loss or gain of whole chromosomes or of individual chromatids occurred at a similar rate for MII and IVM oocytes.

CONCLUSIONS: Our data suggest that CC supplementation does not enhance IVM. The IVM process does not seem to affect the accuracy of the first meiotic division and there were no statistical differences observed in the various types of meiotic error. Since DNA degradation is one of the principle reasons for failure of NGS analyses, the lower proportion of IVM oocytes/PBs that yielded results during this study may indicate reduced DNA integrity following IVM, a possibility that warrants further investigation. To our knowledge, this is the largest study employing NGS to provide a definitive insight into the chromosome constitution of IVM oocytes.

P-18 4:30 PM Saturday, October 17, 2020

ASSESSING THE CLINICAL VIABILITY OF MICRO 3PN ZYGOTES. Albert Li, BA,[1] Rose Marie Roth, MSc, TS(ABB), CLT (NYS),[1] Richard Slifkin, BA, TS(ABB), CLT(NYS),[1] Christine Briton-Jones, PhD, HCLD,[1] Joseph A. Lee, BA,[1] Daniel E. Stein, MD,[2] Alan B. Copperman, MD[2] [1]Reproductive Medicine Associates of New York, New York, NY; [2]Icahn School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: Following intracytoplasmic sperm injection (ICSI) of an oocyte in vitro, fertilization is evaluated using morphological assessment and count of pronuclei (PN). Normal fertilization is characterized by the appearance of 2 PN, observed 13-19 hours post-ICSI. Occasionally, a 3rd "micro" PN can be observed in the zygote. This finding has traditionally been interpreted by embryologists to be an abnormality that is consistent with embryonic aneuploidy, including triploidy [1,4]. Reproductive biologists have demonstrated that the appearance of a 3rd micro PN following injection of a single spermatozoon can result from the retention of the second polar body, oocyte meiotic failure, or sperm abnormalities [2, 3]. Embryos resulting from tri-pronucleated zygotes have also been found to be euploid, perhaps due to self-correction during subsequent cell division [4]. This study aims to evaluate the clinical viability of micro 3PN zygotes by assessing rates of embryo ploidy and frozen embryo transfer (FET) outcomes.

DESIGN: Retrospective

MATERIALS AND METHODS: Micro 3PN zygotes were identified from patients who underwent IVF with ICSI and pre-implantation genetic testing for aneuploidy (PGT-A). On day 3 of development, embryos underwent laser assisted hatching to breach the zona pellucida. At the blastocyst stage of development (day 5, 6 or 7), a trophectoderm biopsy was performed on any embryo(s) that met biopsy criteria ($\geq$5 trophectoderm cells herniating, $\geq$grade "C" inner cell mass and trophectoderm). Samples of biopsied trophectoderm were sent to a commercial laboratory for genetic analysis using a next generation sequencing method. Embryos were vitrified post-biopsy, and euploid embryos were subsequently thawed for FET.

RESULTS: A total of 107 micro 3PN zygotes were evaluated between March 2018 and January 2020. After culturing to the blastocyst stage,16.8% (n=18) of the embryos were biopsied, and 72.2% (n=13) of those displayed diverse types of aneuploidy, although triploid embryos were not found. A euploid rate of 27.8% (n=5) was detected, with 60% (n=3) of those transferred in a FET cycle. A clinical pregnancy rate of 66.7% (n=2) was achieved. One patient reported a livebirth and the other pregnancy is currently ongoing.

CONCLUSIONS: This study demonstrates the reproductive potential of micro 3PN zygotes within an IVF setting. Although there is a high rate of embryonic aneuploidy in micro 3PN-derived blastocysts, our study shows a proportion of these embryos are euploid, can be selected for embryo transfer, and lead to a positive pregnancy outcome. We suggest extending culture of micro 3PN zygotes due to their capability of having a normal genetic profile. With the validation of genetic screening, patients can be assured that normal pregnancies can be sourced from micro 3PN zygotes.

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SUPPORT: None

P-19 4:30 PM Saturday, October 17, 2020

EFFECTS OF A23187 AND IONOMYCIN ON OOCYTE ACTIVATION IN PATIENTS WITH PREVIOUS TOTAL FERTILIZATION FAILURE OR SEVERE OLIGO-ASTHENO-TERATOZOOSPERMIA: A 9-YEAR RETROSPECTIVE STUDY. Lei Jia, Master,[1] Shujing He, MM,[2] Wenlong Su, MS,[3] Cong Fang, PHD, MD[4] [1]Reproductive Medicine Research Center, Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; [2]The Sixth Affiliated hospital of Sun Yat-Sen University, Guangzhou, China; [3]Sixth Affiliated hospital of Sun Yat-Sen University, Guangzhou, China; [4]The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: To assess effects of the applications of Ca^{2+} ionophore A23187 and Ionomycin on fertilization rate, embryonic developmental potential and clinical outcomes in patients with a history of total failed fertilization/lower fertilization rate or severe oligo-astheno-teratozoospermia.

DESIGN: A 9-year retrospective study was conducted with clinical-based data at Reproductive Medicine Research Center of the Sixth Affiliated Hospital of Sun Yat-sen University from May 2010 to December 2019.

MATERIALS AND METHODS: The indications for assisted oocyte activation (AOA) in our center were: (1) patients with total failed fertilization (0%)/lower fertilization rate (fertilization rate <33.3%) in previous ICSI cycles (at least three mature oocytes on the day of oocyte retrieval); or (2) severe oligo-astheno-teratozoospermia including globozoospermia, cryopreserved micro-dissection testicular sperm extraction (MD-TESE) and cryopreserved rare human spermatozoa. The AOA procedure was performed as follows: the oocytes were exposed to either the ready-to-use A23187 solution (GM508, Cult-Active, Gynemed) or 10μM ionomycin (407952,Sigma-Aldrich) after ICSI. All patients were categorized into two groups: A23187-AOA group and Ionomycin-AOA group. And each group was divided into two subgroups according to origin (ejaculated or testicular sperm). Statistical analyses were performed by SPSS 22.0 with the chi-square test, Yates' correction, or Fisher's exact probabilities accordingly when comparing frequencies or proportions. P <0.05 were considered to be statistically significant.

RESULTS: A total of 65 patients whose oocytes were exposed to either the A23187-(n=39) or Ionomycin-AOA (n=26) protocol were included in the final analysis. Significantly higher 2PN fertilization rate (55.0% vs. 43.3%, P<0.01), 2PN cleavage rate (97.4% vs. 90.4%, P<0.05) and blastocyst formation rate (69.1% vs. 45.2%, P<0.05) were observed in Ionomycin-AOA group compared with those in A23187-AOA group. In ejaculated spermatozoa subgroup, 2PN cleavage rate (97.1% vs. 85.8%, P<0.05) and rate of D3 transferable embryos (92.6% vs. 73.6%, P<0.01) in Ionomycin-AOA group were higher than those in A23187-AOA group; In testicular spermatozoa subgroup, the 2PN fertilization rate(55.4% vs.37.7%, P<0.05), blastocyst formation rate(93.3% vs.20.0%,P<0.01) and cumulative clinical pregnancy rate(66.7% vs.10.0%, P<0.05) in Ionomycin-AOA group were higher than those in A23187-AOA group. A total of 20 healthy neonates were delivered in 65 patients and 9 pregnancies were ongoing. None of congenital anomalies (birth defects) was found in fetuses following AOA.

CONCLUSIONS: Ionomycin may be superior to A23187 for improving fertilization rate and embryonic developmental potential. And compared with A23187, Ionomycin provides better clinical outcomes for patients with testicular-origin severe oligo-astheno-teratozoospermia.

SUPPORT: Found Program: Medical Scientific Technology Research Foundation of Guangdong Province of China (A2020226); National Natural Science Foundation of China (81801449)

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INCREASED BLASTOCYST EUPLOID RATE USING A NOVEL SINGLE-STEP CULTURE MEDIUM. Rebecca Holmes, PhD, HCLD,[1] Rebecca Kile, MS,[2] Courtney Grimm, MS,[2] William B. Schoolcraft, MD,[2] Jason E. Swain, PhD, HCLD,[3] Rebecca L. Krisher, PhD[4] [1]CCRM Boston, Newton, MA; [2]Colorado Center for Reproductive Medicine, Lone Tree, CO; [3]CCRM IVF Network, Lone Tree, CO; [4]CCRM Colorado, Lone Tree, CO.

OBJECTIVE: The objective of this study was to compare the impact of a novel single-step culture medium versus a commercial sequential media on cycle outcomes following sibling oocyte splits.

DESIGN: Prospective randomized trial using sibling oocytes.

MATERIALS AND METHODS: All procedures were conducted at a single IVF center and all PGT-A results were from a single genetics lab. After ICSI all injected oocytes were evenly and randomly distributed between two dishes containing either a novel single-step medium (CCRM Single Step) or a commercial sequential media (Sage media, Cooper Surgical). All media were supplemented with the same lot of 10% SPS protein and cultured under oil in the same benchtop incubator under oil using ~6% CO_2, 5% O_2. All embryos were treated identically except for the culture medium used. In phase 1, media were exchanged following 24h, 72h and 120h of culture for both the sequential and single-step media. In Phase 2 the single step medium was exchanged at 72h, while the sequential media was changed at 24h, 72h and 120h. Data were analyzed using Fisher's Exact Test

RESULTS: In Phase 1, more good quality blastocysts (GQB) were obtained on day 5 and in total with the single step medium. This resulted in a significantly increased blastocyst rate of 10% and an increased euploid/2PN of 5% for single step medium compared to sequential.

In Phase 2, GQB on D5 was again higher in the single step medium, although overall GQB percentage was similar in both media systems. However, overall blastocyst development was lower in single-step. The percentage of euploid embryos/2pn remained higher in the single step medium

PHASE 1	# 2PN	%D5 GQBL/2PN	%Total GQBL/2PN	% Total BL/2PN	euploid/ 2PN
SAGE CM/BM	164	21%	47%	57%$_a$	28.5%
Single Step	191	29%	51%	67%$_b$	33.8%
PHASE 2					
SAGE CM/BM	99	18%	46%	57%	26.0%
Single Step	111	25%	46%	50%	32.9%

CONCLUSIONS: A novel single-step medium performed as well as, if not better than, a commercial sequential media. In phase 1, using the same number of media exchanges, the single step media outperformed the sequential media, suggesting superiority of the media formulation to meet the developmental needs of the preimplantation embryos. Fewer media exchanges were performed in Phase 2 with the single step medium to reduce handling and test if this might further improve outcomes. While still yielding higher good quality D5 blastocyst rates, reduced handling using the single step medium did not further enhance outcomes, suggesting that embryo handling/media exchanges were not a significantly detrimental factor. In our hands, this single step medium results in more D5 blastocysts, more blastocysts available for biopsy, and more euploid embryos - ultimately benefiting the patient.

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ASSISTED HATCHING (AH) IN COLLAPSED BLASTOCYSTS IS ABLE TO RESTORE THE IMPLANTATION RATES: A RETROSPECTIVE STUDY. Alberto Tejera, PhD,[1] Lucia Alegre, PhD,[1] Amparo Mifsud, PhD,[1] Jose Maria De los Santos, PhD,[1] Marga Esbert, PhD,[2] Marcos Meseguer, PhD[1] [1]IVIRMA Global, Valencia, Spain; [2]IVI RMA Barcelona, Barcelona, Spain.

OBJECTIVE: Blastocyst contraction has been extensively described by Time-Lapse monitoring systems, affecting approximately 20% of the embryos, decreasing their implantation potential to 10% (Scorio et al. 2020). Our objective is to demonstrate whether performing AH for those collapsed blastocysts (CB) may help to restore their implantation potential. To demonstrate our hypothesis we calculated the implantation rate as well as pregnancy rate (PR) of CB with AH comparing these results to those blastocysts with collapse but without AH.

DESIGN: Retrospective Cohort Study.

MATERIALS AND METHODS: We analyzed 208 blastocyst from oocyte donation program during one consecutive year(January 2019-January 2020) that were distributed in two groups**:** the control group (107 CB without AH) and the study group (101 CB with AH). All blastocysts included in the study were cultured in a time-lapse system to identify the collapse episode ($\geq$50% of the surface of the trofoctoderm separated from the zona pellucida), being verified the collapse through the Embryo Viewer^{TM} or Asses 2.0 workstations. Both study and control group were formed by frozen blastocyst where the collapse episode was retrospectively identified before warming. AH was achieved in the study group through laser (eliminating one quarter part of the zona pellucida). All embryos were incubated for 3-4 hours before being transferred. Pregnancy and implantation rates were analyzed and compared in both groups by X^2 test and regression logistic analysis(RLA) was performed considering body mass index, maternal age, blastocyst vitrification day(D5 vs D6) and blastocyst morphology as confounding factors to weight the effect of AH on ongoing pregnancy rate(OPR).

RESULTS: Considering cases with known implantation, after applying AH in the collapsed blastocysts(101) resulted higher pregnancy rates(PR) compared to those without AH(107): 54.5% vs 40.6% for PR with p=0.049; 45.5% vs 31.7% for clinical pregnancy rate(CPR) with p= 0.043 and 35.6% vs 20.8% for OPR with p=0.019. When we only selected SET cases (177) the benefits were equally effective for CB with AH (84) compared to CB without AH(93), getting higher OPR (34.5% vs 17.2% p=0.008). The blastocysts were categorized by morphology (ASEBIR) into A, B or C. After performing a RLA , AH presented an odds ratio of 3.23 (CI95% 1.491-6.979) for OPR (p=0.003).

CONCLUSIONS: Our findings support the use of AH for CB to improve up to three times the OPR. Maybe the strong contractions suffered by the blastocysts during the embryo development imply a waste of energy necessary for the implantation process. This behaviour would explain the decreased of the implantation of those embryos without AH. Performing AH in CB could recover the implantation capacity impaired by the collapse. Also irrespective of either blastocyst morphology or vitrification day a benefit was observed and quantified after carrying out AH.

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A REDESIGN OF THE PROTEX TO HARVEST FREE OXYGEN SPECIES APPEARS TO IMPROVE OVERALL SEMEN PARAMETERS. Samuel D. Prien, PhD,[1] Melissa Sillivent, M.S.,[2] Lindsay L. Penrose, PhD[1] [1]Texas Tech University Health Sciences Center, Lubbock, TX; [2]Texas Tech University, Lubbock, TX.

OBJECTIVE: Previous research from this laboratory has demonstrated that semen quality, both physiological and biochemical, can be improved via a simple redesign of the semen collection cup. The redesign termed the Device for Improved Semen Collection (DISC – trade name ProteX), maintains a stable environment during and after collection, preventing cell shock and preserving cell function. However, the original design did nothing to prevent DNA fragmentation. Recently the system underwent a redesign incorporating a proprietary method to harvest free oxygen radicals, an identified cause of DNA fragmentation. The object of this study was to determine the effects of the redesign on all cellular functions.

DESIGN: Lab-based study of standard semen parameters

MATERIALS AND METHODS: In these initial studies, frozen bovine semen was thawed and processed similarly to an IUI sample to yield a final 6 mL sample containing approximately 20 million cells/mL. Two milliliters of the cell suspension was then transferred to a standard specimen cup (SSC), the original ProteX device (PRO), or the redesigned system (Pro+), and the sample maintained on a benchtop at room temperature. At times 0, 1, 3, 6, 9, 24, and 48 hrs, the samples were briefly vortexed, and aliquots used to prepare slides for semen analysis, acrosome reactions, and DNA fragmentation. Semen analyses were performed on a Hamilton Thorn IVOS unit, and acrosome and DNA fragmentation determined using standard techniques. Resulting data were analyzed using ANOVA with repeated measures.

RESULTS: As expected, all semen analysis parameters decreased over time ($P < 0.001$). However, cells stored in the Pro and Pro+ maintained significantly higher cellular activity for all semen parameters when compared to the SSC after as little as 6 hrs ($P < 0.005$). This difference can be seen easily at 48 hrs were the Pro and Pro+ maintained over 20% of the initial motility and rapid cells while the SSC had dropped to 7% and 1%,

respectively ($P < 0.001$). Further, while the motility and rapid cells were similar between the Pro and Pro+, other semen parameters, such as linearity and straightness, indicated the cell stored in the Pro+ possessed better overall activity than in the Pro ($P < 0.01$). Acrosome and DNA fragmentation data are pending.

CONCLUSIONS: The ProteX semen collection system continues to be a superior collection system for andrology samples than a standard specimen cup. Further, the redesigned ProteX appears to provide additional protection to overall sample quality, which should result in healthier cells for all ART procedures.

SUPPORT: The Innovation HUB at Texas Tech University and Reproductive Solutions Inc.

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VOLATILE ORGANIC COMPOUND PROFILE OF MINERAL OIL AFFECTS EMBRYO DEVELOPMENT.

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OBJECTIVE: A high quality mineral oil overlay is an essential component of a successful in vitro embryo culture system. Mineral oils may contain impurities and by-products from manufacturing such as volatile organic compounds (VOCs) that have the potential to leach into culture medium and disrupt embryo development. The aim of this study was to investigate the VOC content of four commercial oils, and to assess whether oil VOC content affects mouse embryo development and developmental kinetics.

DESIGN: Research study

MATERIALS AND METHODS: Mouse embryos (ND4, 4-8 wks) were produced by in vitro maturation (IVM) and fertilization (IVF). Zygotes were cultured in an EmbryoScope (Vitrolife) under one of four commercial oils: Vitrolife Ovoil, Life Global Paraffin Oil (LGPO), Sage Oil for Tissue Culture, or Spectrum USP Mineral Oil (four replicates, n=48/oil). Spectrum and LGPO were also tested in individual embryo culture in 2uL drops (four replicates, n=69 and 67, respectively). Triplicate samples of the four oils were analyzed using gas chromatography-mass spectroscopy (GC-MS) to assess relative VOC content.

RESULTS: There were no significant differences in embryo developmental kinetics due to type of oil overlay at any of the time points examined (pronuclear fade, first cleavage, morula compaction, appearance of the blastocoel, blastocyst, expansion, and hatching). There were also no differences in embryonic development to first cleavage, blastocyst, or hatching blastocyst in the Embryoscope. In microdrop culture, however, there were significant differences in development to blastocyst at 96 hours of culture (LGPO=13±6%, Spectrum=65.6±26%; p=0.028) and to hatching blastocyst at 112 hours of culture (LGPO=7.8±9.7%, Spectrum=50±27%, p=0.045). The GC-MS results showed four distinct VOC profiles by brand. VOC levels were significantly higher in LGPO for heptadecane (LGPO=9.8x106 ±2.9x106, Spectrum=2.8x106±1x105; p=0.0288) and for decane (LGPO=2.6x107±2.1x106, Spectrum=8.8x106±2.7x106, p=0.00013). Tetradecane, undecane, and dodecane were found in LGPO but were not detectable in Spectrum.

CONCLUSIONS: Although the four oils tested had distinct VOC profiles, there were no differences in development or developmental kinetics data for embryos cultured in the EmbryoScope under each oil. There were, however, significant developmental differences for single embryo culture in microdrops under LGPO and Spectrum oils, suggesting that this may be a more sensitive assay for assessing oil toxicity. Heptadecane, decane, tetradecane, undecane, and dodecane content of LGPO oil may be responsible for the significantly reduced development observed in microdrop culture. Oil containing elevated levels of these VOCs should be avoided for human embryo culture.

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STRONTIUM-INDUCED OOCYTE ACTIVATION IN NON-MALE FACTOR ICSI CYCLES AND ADVANCED MATERNAL AGE.

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OBJECTIVE: Abnormal calcium (Ca2+) oscillations in aged oocytes may adversely affect fertilization and subsequent embryonic development. Strontium (Sr2+) induces Ca2+ oscillations via the InsP3 receptor and PLCζ activation. However, unlike the sperm factor and calcium ionophore induced Ca2+ oscillations, Sr2+ does not require putative maternal machinery. We investigated the role of Sr2+ for artificial oocyte activation (AOA) in aged oocytes among non-male factor infertility couples undergoing assisted reproduction technology (ART).

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: This study included infertility couples with non-male factor infertility and advanced maternal age (40 years and over) with at least one previous non-AOA failed ICSI cycle. Ovarian stimulation and laboratory protocols were similar between non-AOA and the Sr2+-AOA, except for the use of AOA. In the study group (Sr2+-AOA cycles) all injected oocytes were stimulated using 10 mM SrCl (Sigma-Aldrich, St Louis, MO, USA) for 60 min, immediately after ICSI. The zygotes were cultured up to the blastocyst stage, and the resulting embryos were subjected to trophectoderm biopsy for preimplantation genetic testing for aneuploidies using next-generation sequencing. Comparisons between Sr2+-AOA and previous non-AOA cycles were performed using the paired Student's t-test. The primary endpoint was 2PN fertilization rates and the secondary endpoints were embryonic outcomes. Statistical analyses also included generalized linear and binary logistic regression models.

RESULTS: Between September 2019 and March 2020, we performed 18 Sr2+-AOA cycles in 13 couples who have undergone an average of 1.9 previous failed ICSI without AOA (range 1–6 cycles). The 2PN fertilization rate after Sr2+-mediated AOA was significantly higher than that of the routine non-AOA ICSI procedure (81.0% vs. 67.1%, p=0.04). Adjusted linear regression models showed that fertilization rates were significantly and independently associated with Sr2+-AOA (β=19.85, p=0.007). Sr2+-mediated AOA had no negative impact on blastocyst formation rate (30.9% vs. 34.5%, p=0.67) and on the likelihood of having at least one euploid blastocyst for transfer (OR=1.46, 95% IC: 0.26-8.27).

CONCLUSIONS: Age-related oocyte activation defects might adversely impact fertilization rates by ICSI, thus affecting the number of resulting embryos. Our results suggest that Sr2+-mediated AOA improves fertilization rates in aged oocytes, probably related to a sperm-independent activation. Our data corroborate previous studies on the safe utilization of Sr2+ on gametes and embryos cultured to the blastocyst stage. However, large-scale studies are warranted to evaluate the effectiveness of Sr2+-mediated AOA on pregnancy outcomes.

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MIGRATION SPEED OF NUCLEOLAR PRECURSOR BODIES IN PRONUCLEI: A NOVEL PARAMETER FOR PREDICTING LIVE BIRTH.

Taketo Inoue, Ph.D.,[1] Sayumi Taguchi, M.S.,[1] Mikiko Uemura, Ph.D.,[2] Yoshiko Tsujimoto, M.S.,[1] Kazunori Miyazaki, Ph.D., M.D.,[1] Yoshiki Yamashita, Ph.D., M.D.[1] [1]Umeda Fertility Clinic, Osaka, Japan; [2]Kansai University of Welfare Science, Kashiwara, Japan.

OBJECTIVE: Nucleolus precursor bodies (NPBs) are dynamic and the characteristic NPB pattern changes within a short time during the syngamy process on time-lapse imaging. However, the relationship between NPB migration speed and human IVF outcomes remains unclear.

DESIGN: Migration of 262 NPBs from 47 zygotes (12 patients) were prospectively analyzed after ICSI, and embryonic development was observed until blastocyst (blastocyst: $n = 25$; arrest: $n = 22$). The relationship between NPB migration and pregnancy was retrospectively analyzed from live birth/ongoing pregnancy (> 22 wks) (LB/OP, $n = 30$) and negative clinical pregnancy patients ($n = 30$) in frozen-thawed single ICSI-derived blastocyst transfer cycles. The zygotes were cultured in a time-lapse incubator (Geri+; CO_2; 6% O_2, 5% at 37°C and 80±20% humidity), and images were recorded every 5 min.

MATERIALS AND METHODS: The mPN and fPN were identified by appearance location in a zygote (fPN appearance: just below polar bodies). The central coordinates of mPN, fPN, and 2–5 NPBs/PN were measured by motion capture software. The migration distance of NPBs between two sequential images was calculated as the standard of central coordinates of PN, and then the migration speed of NPBs was calculated thereafter. A univariate logistic analysis was used to analyze the relationship among blastocyst development and 25 factors including time of cleavage and cleavage interval from termination of ICSI to day 3. Subsequently, multivariate logistic analysis was used to analyze the relationship among the blastulation and

migration speed of NPBs in factors that were $P < 0.15$ after univariate logistic analysis. Receiver operating characteristic curve analysis was used to calculate the cutoff values of blastocyst development and LB/OP.

RESULTS: The migration speed of NPBs was significantly faster in the blastocyst developed group than in the arrested group (mPN: $P < 0.001$; fPN: $P = 0.024$). The timing of blastocyst formation was correlated with the migration speed of NPBs in mPN ($rs = -0.633$, $P < 0.001$). In the arrested group, 68.2% embryos were arrested until day 3. The blastulation was related to the migration speed of NPBs in mPN and fPN, tPNf, tPNf-tPNa, t2, t3-t2, and t3-tPNf ($P < 0.05$) in a univariate logistic analysis, while the factor associated with blastocyst development was the migration speed of NPBs in mPN (OR: 5.14, 95%CI: 1.20–21.90, $P = 0.027$) in multivariate logistic analysis. As regards blastocyst development, the cutoff value of the migration speed of NPB in mPN was 3.70 μm/h (AUC: 0.81, 95%CI: 0.68–0.95). Compared to the negative clinical pregnancy patients, the migration speed of NPBs in LB/OG patients was significantly faster (mPN: $P < 0.001$; fPN: $P = 0.045$). As regards LB/OP, the cutoff value of the migration speed of NPB in mPN was 4.56 μm/h (AUC: 0.75, 95%CI: 0.63–0.88). The LB/OP rate in $\geqq$ cutoff value was significantly higher than that in $<$ cutoff value groups (75.0% vs. 33.3%, $P = 0.002$).

CONCLUSIONS: The migration speed of NPBs is a novel predictor of human embryo development and clinical outcomes.

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IS THERE A CLINICAL IMPACT OF BLASTOCYST SHRINKAGE PRIOR TO VITRIFICATION?. Kana Murakami, M.S., Hiroya Kitasaka, Ph.D., Tomokuni Yoshimura, B.S., Noritaka Fukunaga, Ph.D., Yoshimasa Asada, M.D., Ph.D. Asada Ladies Clinic, Nagoya, Japan.

OBJECTIVE: Blastocyst vitrification is an essential technique when carrying out preimplantation genetic testing (PGT) due to the time it takes to receive the results of the biopsy. An important point for blastocyst vitrification is to confirm that penetration of the equilibration solution is sufficient and this can be observed by the shrinkage and re-expansion of the blastocyst. It can however be difficult to observe re-expansion of a shrunken blastocyst just before vitrification. Shrunken blastocysts may have exceeded an optimal time in the equilibration solution and there are some concerns about the negative effects of the cryoprotectant. In this study, we examined the impact on blastocysts that had shrunken just before vitrification on subsequent clinical performance.

DESIGN: Retrospective study.

MATERIALS AND METHODS: We examined 11247 cycles in which vitrification–warming single embryo transfer was performed from 2013 to 2018. The blastocysts (graded $\geq$3BB) were vitrified on day 5 or day 6. First, we compared the clinical performance with shrunken blastocysts just before vitrification (S group) and non-shrunken blastocysts (N-S group). Secondly, we compared the rate of re-expansion with the S group and N-S group after 4h warming.

RESULTS: The patient age in these the groups was similar (S group 34.9$\pm$3.7; N-S group 34.7$\pm$3.8). The pregnancy rate of the S group (36.3%,53/146) was significantly lower (P<0.05) than that of N-S group (45.8%,5055/11034). The miscarriage rate of the S group (35.8%,19/53) was significantly higher(P<0.05) than that of N-S group (21.9%,1106/5055). The rate of S group's re-expansion after warming (79.5%,116/146) was significantly lower (P<0.05) than N-S group (91.9%,10142/11034). The pregnancy rate of blastocysts in the S group with re-expansion (44.0%,51/116) was the same as that of N-S group (47.8%,4848/10142). The miscarriage rates in these same groups was similar (S group 35.3%,18/51; N-S group 21.8%,1057/4848). However, the pregnancy rate of blastocysts in the S group which did not re-expand (6.7%,2/30) was significantly lower(P<0.05) than N-S group (23.2%,207/892).

CONCLUSIONS: In view of the significantly lower pregnancy rate of S group blastocysts, we conclude that there was an impact on blastocysts that had shrunken just before vitrification on subsequent clinical performance. In addition, the rate of re-expansion in S group blastocysts after warming was also significantly lower. It is possible that there was a negative impact on blastocyst shrinkage caused by the cryoprotectant. As a next step, we need to examine the time change of shrunken blastocyst in equilibration solution, so that the vitrification method may be improved leading to a higher clinical performance.

SUPPORT: None.

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MORPHOKINETICS OF MORULA STAGE EMBRYO FAIL TO PREDICT BLASTOCYST FORMATION AND BLASTOCYST QUALITY. Nabil Sayme, Dr. med,[1] Thomas Krebs, Dipl.-Biol,[1] Dieter H. A. Maas, Prof. Dr. med.,[1] Marija Kljajic, Master of Biology Science[2] [1]Team Kinderwunch Hannover, Hannover, Germany; [2]Saarland University Medical Center, Homburg, Germany.

OBJECTIVE: In the last decade, the introduction of time-lapse technology enables almost continuous monitoring of embryo development. This technology generates comprehensive information regarding morphology and kinetics of embryo development and facilitates observation of dynamic, and often transient, events occurring between static observation periods. Together, these have been defined as 'morphokinetic' variables. Although for the past five years, there has been a rapid rise in the use of 'morphokinetic' variables, some disagreement concerning widely applied of this method into an embryo selection model is still present.

DESIGN: In the present study, cell cycle duration is calculated using time-lapse, according to a single cell division. The injection time of ICSI was designated as "time zero" (t0), and computer software was used to calculate the time frame between the injection and the moment of pronuclei disappearance (tPNf), as well as the time frame between injection and compaction process of morula (tM). Besides the mentioned time frames, the software also calculated the cleavage interval from the moment when PN disappear (tPNf) to the moment when morula is reached as well as the cleavage interval (t2M) from the two-cell stage to the morula and from the four-cell stage to the morula (t4M). Obtained results of those embryo cycle duration were later associated with the embryo capability to forming a blastocyst as well as with blastocyst quality.

MATERIALS AND METHODS: A total of 87 blastocysts from 20 patients undergoing an antagonist cycle for ICSI treatment between November 2019 and December 2019 were evaluated. All blastocysts were cultured in Embryoscope™ according to the manufacturer's specifications (Vitrolife, Sweden). The Gardner and Schoolcraft scoring system was used to describe blastocyst quality. Correlations between the data were calculated using logistic regression analysis. Statistical significance was defined as p<0.05. All statistical analyses were performed using SAS software.

RESULTS: Morphokinetic data showed that the time of pronuclei disappearance (tPNf) was significantly different (p<0.01) in successfully formed blastocysts (21.36 $\pm$2.23) versus arrested or non-blastulating embryos (22.80$\pm$2.27). Furthermore, this parameter as well significantly affect blastocyst quality (p<0.05). On the other hand, the time necessary for the compaction process/fully reached morula stage (tM) between embryos which successfully reached the blastocyst stage and those embryos that did not, were not statistically significant (tM: p>0.05).

Neither cleavage intervals (t2M) from the two-cell stage to morula, and from the four-cell stage to morula (t4M) did not show a significant impact on blastocyst formation. What is more, blastocyst quality neither was affected by presented morphokinetic (tM; t2M; t4M) parameters.

CONCLUSIONS: Obtained results as we believe are helpful for a better understanding of the association between embryo morphokinetic parameters and blastocyst development and potentially can be incorporated into an embryo classification model.

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QUALITY CONTROL VIA ASSESSMENT OF CONSISTENCY IN EMBRYOLOGY AND CLINICAL ENDPOINTS BETWEEN MULTIPLE LABS USING A SINGLE DONOR EGG BANK. Jason E. Swain, PhD, HCLD,[1] Rebecca L. Krisher, PhD,[2] William B. Schoolcraft, MD[2] [1]CCRM IVF Network, Lone Tree, CO; [2]CCRM Colorado, Lone Tree, CO.

OBJECTIVE: Quality control is an essential component of a quality management program for an IVF laboratory. Instrumental in this process is performing routine monitoring to ensure measured outcomes are falling within acceptable standards and established ranges. It can be difficult to identify causative factors within a single lab due to variation in the infertile patient population, especially when laboratory volume is low. Having a series of related laboratories utilizing the same culture system and standardized protocols with regular peer group comparisons can offer a benefit in quickly

identifying and isolating possible issues within the IVF culture system or differences in clinical practices. This troubleshooting can be further improved via examination of a control, fertile population using oocyte donors.

DESIGN: Retrospective data analysis

MATERIALS AND METHODS: Data was collected over a 2 year period from frozen donor oocyte warms performed in 8 clinical IVF laboratories utilizing the same donor egg bank. Oocyte cryosurvival, fertilization and blastocyst conversion rates were compared. Additionally, rates of blastocyst aneuploidy and pregnancy rate were determined. Means and SEMs were calculated for each laboratory and also combined to help establish a higher acceptable threshold for future quality improvement. Differences were compared using one way ANOVA and Bonferroni pairwise comparisons

RESULTS: Comparison of laboratories demonstrated consistency between locations. One laboratory had significantly lower cryosurvival than two other labs (p=0.004). All other labs had similar oocyte survival upon warming. There were no differences in fertilization per survived oocyte or blastocyst conversion rates per fertilized zygote between labs. Rates of blastocyst aneuploidy were also similar between labs. No significant difference in number of embryos transferred per recipient between locations was apparent, and resulting pregnancy rates were comparable (p=0.25). Per thawed egg, there was a trend (p=0.099) for one laboratory to have reduced total blastocyst development compared to three others. Combining data from all laboratories yielded an overall mean and SEM for each endpoint assessment (Survival: 90.3±0.8%, Fert: 80.1±1.2%, Total GQB: 50.5±1.7%, Total Blast: 65.7±1.6%, Euploid rate: 67.7±2.3%, Ongoing CPR: 75.7±4.2%).

CONCLUSIONS: Having the ability to compare outcomes between related IVF laboratories utilizing identical products and similar protocols provides a powerful model for ongoing quality control assessment. Examining outcomes from a donor oocyte population from a single donor egg bank can further improve this quality control approach. Having more data and points of comparison from a control patient population within an IVF laboratory peer group can help quickly identify issues within the lab and provide insight as to whether they may be related to lab consumables, local embryology technique or clinical approaches. This model, along with consistent periodic review, provides the ability to implement corrective action in a timely fashion.

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BENEFITS OF DAY 7 BLASTOCYST CULTURE?: A COMPARISON OF CONVERSION AND EUPLOIDY RATES BETWEEN RELATED IVF LABORATORIES WITH DIFFERENT VOLUMES. Jason E. Swain, PhD, HCLD,[1] William B. Schoolcraft, MD,[2] Rebecca L. Krisher, PhD[2]
[1]CCRM IVF Network, Lone Tree, CO; [2]CCRM Colorado, Lone Tree, CO.

OBJECTIVE: Traditional culture systems grow embryos for up to 6 days to the blastocyst stage. The assumption is that after this point, the potential for good quality and/or euploid blastocyst development is minimal. However, several studies have shown that blastocysts with the ability to support live birth can develop in vitro on Day 7. Day 7 culture may be a source of additional embryos for patients to further increase their reproductive potential following IVF and may vary based on size of the IVF program due to differences lab procedure timings. The objective of this study was to compare rates of Day 7 blastocyst development and resulting euploid rates between related IVF labs of differing sizes.

DESIGN: Retrospective analysis

MATERIALS AND METHODS: Embryos from all patients undergoing PGT-A over the same 2 year time period in 11 related IVF programs were cultured to Day 6 and blastocysts of grade 3BB or better were cryopreserved. In an effort to balance desire for additional embryos with laboratory logistic and impact on incubator capacity, any patient undergoing PGT-A with no blastocysts on day 5/6 or who had remaining morulae or early stage blastocysts by day 6, were kept in culture for one additional day to determine if additional good quality blastocysts were available on day 7. Good quality embryos were biopsied for PGT-A and frozen. Data were analyzed using pairwise comparisons and regression analysis

RESULTS: Each laboratory was able to cryopreserve day 7 blastocysts. The number of blastocysts and resulting euploid rate varied by location. No correlation was apparent between number of retrievals and percentage of day 7 blastocysts, R^2=0.003.

CONCLUSIONS: Culturing blastocysts to day 7 in select patients is a feasible approach to increase the number of additional euploid embryos available for transfer, while balancing the impact of laboratory workflow and resources. In a related network of labs using similar protocols, no correlation was apparent between day 7 blastocyst development and cycle volume, indicating that both large and small programs can benefit from this approach. However, it should be noted that larger laboratories with many procedures that go later in the day or who may not be able to be as strict on procedure timings may potentially find more blastocysts on day 7 than smaller labs.

SUPPORT: None

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TRANSFER STRATEGY OF OBTAINING FEWER THAN 3 EGGS IN IVF CYCLE. Tingting Li, Doctor
Reproductive Medicine Research Center, Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: To explore the strategy of embryo transfer with ≤3 eggs in IVF cycles.

DESIGN: A retrospective study

MATERIALS AND METHODS: A retrospective study was conducted with clinic-based data in the Reproductive Medicine Centre of the Sixth Affiliated Hospital of Sun Yat-sen University from Jan 2017 to Apr 2019. A total of 1 600 cycles were divided into 3 groups: fresh D3 embryo transfer (Group 1, *n*=615), frozen D3 embryo transfer (Group 2, *n*=525), frozen blastocyst transfer (Group 3, *n*=460). We compared the general character of patients and clinical outcomes among the 3 groups.

RESULTS: There were no significantly differences found in age, AMH, and basal FSH among the 3 groups, Biochemical pregnancy, clinical pregnancy and live birth rates (38.2% *vs.* 29.3%, 34.5% *vs.* 25.9%, 18.2% *vs.* 11.2%) were significantly higher in group 1 than those in group 2. These differences were statistically significant. When patients canceled fresh embryo transfer due to various reasons, better biochemical pregnancy, clinical pregnancy and live birth rates were achieved in group 3 than group 2 (36.7% *vs.* 29.3%, 33.4% *vs.* 25.9%, 13.7% *vs.* 11.2%). These differences were also statistically significant. Through multivariate regression analysis, after controlling for potential confounding factors such as age, AMH and embryo transfer grade, the live birth rate of group 1 was still significantly higher than that of group 2 (OR=1.906(1.272-2.857), P=0.002, and the live birth rate of group 3 was still significantly higher than that of group 2 (OR = 3.388 (1.876-6.118), P = 0.000)

Lab #	1	2	3	4	5	6	7	8	9	10	11
# of Retrievals	3197	1831	1359	1089	1075	732	680	623	588	353	131
Avg. female Age	37.5	36.4	36.5	36.7	36.8	36.5	36.9	37.5	36.7	36.1	37.0
% Day 7 Blastocyst Rate	4.7^{a}	5.0^{ac}	2.9^{b}	4.0^{d}	3.5^{d}	2.5^{b}	5.9^{e}	5.6^{ce}	5.0^{ac}	5.5^{c}	2.8^{b}
% D7 Euploid Rate	37.2^{ad}	44.5^{ab}	56.2^{c}	46.9^{ab}	44.1^{ab}	51.7^{bc}	41.0^{a}	36.3^{ad}	59.6^{b}	30.1^{d}	20.1^{e}

different superscripts between columns, within the same row, indicate significant difference, p<0.05

	Biochemical pregnancy	Clinical pregnancy	Live birth
Fresh D3 (n=615)	235 (38.2)	212 (34.5)	112 (18.2)
Frozen D3 (n=525)	154 (29.3)	136 (25.9)	59 (11.2)
χ^2	9.931	9.801	10.802
Crude OR, P	1.490 (1.162-1.910)	1.505 (1.164-1.945)	1.759 (1.252-2.470)
	P=0.002	P=0.002	P=0.001
Adjusted OR, P	1.457 (1.085-1.956)	1.596 (1.184-2.153)	2.059 (1.387-3.058)
	P=0.012	P=0.002	P=0.000
Frozen blastocyst (n=460)	169(36.7)	154(33.4)	63 (13.7)
Frozen D3 (n=525)	154(29.3)	136(25.9)	59 (11.2)
χ^2	6.101	6.770	1.365
Crude OR, P	1.399(1.071-1.827)	1.439(1.093-1.895)	1.253(0.858-1.832)
	P=0.014	P=0.009	P=0.243
Adjusted OR, P	2.147(1.444-3.192)	2.319(1.532-3.508)	3.271(1.859-5.756)
	P=0.000	P=0.000	P=0.000

CONCLUSIONS: In patients with no more than 3 oocytes retrieved, fresh D3 embryo transfer achieves optimal pregnancy and live birth rate. If frozen embryo transfer is performed, blastocyst transfer is recommended.

SUPPORT: NoÂ financial support.

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HOW TO OPTIMIZE CULTURE MEDIA OSMOLALITY IN IVF TREATMENTS. Renata de Lima Bossi, PhD, Brenda Campos Villa Pinto, BSc, Marcos Sampaio, MD PhD, Marco Tulio Vaintraub, MD MSc, Selmo Geber. Professor, ORIGEN, Belo Horizonte, Brazil.

OBJECTIVE: Study aim was compare osmolality in sequential and single step culture media, covered with two types of oil mineral and paraffin, in two types of incubators, dry and humid.

DESIGN: A prospective observational study was performed from March to November 2019. For each incubator, humid water jacket (Forma 4130, Thermo Scientific) and dry bench top (G185, K-Systems), both trigas, a total of 30 dishes were prepared with sequential (Cleavage Medium, Cook) and single step media (CSCM, Irvine Scientific), covered with paraffin oil (Ovoil, Vitrolife). Another 30 dishes were prepared as mentioned above, covered with mineral oil (Light Mineral Oil, Irvine Scientific). Statistical analysis was performed using ANOVA.

MATERIALS AND METHODS: Twenty 35x10 millimeters dishes (Falcon), at a time, were prepared in a laminar flow hood at room temperature, using 25 microliter droplets of CSCM and Cleavage Medium. Ten were covered with 3,0 mL mineral oil and ten with paraffin oil. Half of the dishes were incubated in a dry incubator and another half in a humid. Osmolality (mOsm/kg) was measured using osmometer (Advanced Instruments) on day 1, 3, 5 and 7, one drop per day.

RESULTS: Humid incubator is better for maintaining the osmolality of culture media, regardless of the type of oil used. CSCM has lowest levels of osmolality on day 1 when compared to Cleavage (263 X 286, p<0.0001) and maintained statistically lowest levels of osmolality on day 3, 5 and 7. In humid incubator, both culture media using paraffin or mineral oil, had similar osmolality on day 3 (269 X 270, P=0.391 for CSCM; 293 X 292, P=0.759 for Cleavage) , day 5 (270 X 271 P=0.978 for CSCM; 292 X 293 P=0.914 for Cleavage) and day 7 (271 X 271 P=0.999 for CSCM; 294 X 292 P=0.624 for Cleavage). Paraffin oil provided greater protection against evaporation, maintaining lower levels of osmolality, in a dry incubator, for CSCM media in D3 (281 x 284, P<0.001), D5 (287 x 293, P<0.001) e D7 (298 x 304, P<0.001). No significant difference was observed for Cleavage osmolality on day 3 and 5 (304 X 306, P=0.213) (314 X 314, P=1.0) comparing two types of oil, in a dry incubator. On day 7 paraffin oil is better to maintain osmolality (322 X 325, P=0.003).

CONCLUSIONS: Our study demonstrated that combination of humid incubator and paraffin oil are better for maintaining osmolality level of single step media, which can improve continuous and undisturbed embryonic culture. Comparing humid versus dry benchtop incubators, using different types of oils and culture media, is necessary for better IVF results.

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PREDICTION OF IMPLANTATION RATE IN SINGLE EUPLOID FROZEN-THAWED BLASTOCYST TRANSFER CYCLES BY CULTURE TIME AND/OR RE-EXPANSION RATE AFTER TROPHECTODERM BIOPSY. Vasileios Stolakis, MSc, PhD, MLS (ASCP)CM Kofinas Fertility Group, New York, NY.

OBJECTIVE: To examine whether the culture time and/or re-expansion rate after trophectoderm (TE) biopsy can predict implantation rate in single euploid frozen-thawed blastocyst transfer (seFET) cycles.

DESIGN: Retrospective cohort study in a private assisted reproductive technology (ART) program.

MATERIALS AND METHODS: In this retrospective cohort study 397 blastocysts (Day-5 and -6) from 344 patients (35.8 ± 4.2 years of age) were characterized as euploid after preimplantation genetic screening by array comparative genomic hybridization or next generation sequencing. The TE biopsies and the (seFET) cycles were performed at the Kofinas Fertility Group ART clinic from January 2016 to January 2020. All aneuploidy screenings were authorized by patients after consultation. The euploid blastocysts of all participants were divided in two groups: (i) those that were cultured for 1-4 h after TE biopsy (Cultured Group; CG, n=184) and (ii) those that were cryopreserved immediately after TE biopsy (Non-Cultured Group; NCG, n=213). In addition, the CG was further divided in two subgroups based on the re-expansion rate after TE biopsy in relation to the initial blastocoel expansion rate; these subgroups were either: (i) partially re-expanded (pRE) blastocysts (blastocoel formation, but not full re-expansion) or (ii) fully re-expanded, hatching or completely hatched blastocysts (fRE). Implantation rate was assessed in the examined groups and subgroups.

RESULTS: No significant difference was detected in the overall implantation rate between the two examined groups, CG and NCG (70% *vs* 69%, respectively) and between the two subgroups of the CG group, pRE and fRE (70% *vs* 71%, respectively). In contrast, Day-5 euploid blastocysts that belong to the pRE subgroup demonstrated a significantly higher implantation rate compared to Day-6 euploid blastocysts belonging to the same subgroup (78% *vs* 52%, respectively, $p<0.01$). Most importantly, euploid blastocysts cultured for ≤2h after biopsy belonging to the fRE subgroup were characterized by a significantly higher implantation rate when compared with euploid blastocysts cultured for more than 2h after biopsy belonging to the pRE subgroup (83% *vs* 54% respectively, $p<0.05$).

CONCLUSIONS: Implantation rate in seFET cycles can be improved by selecting blastocysts that are able to achieve full re-expansion when cultured for ≤2h after TE biopsy, instead of blastocysts that are cultured for >2h after TE biopsy and they have only partially re-expanded. Further studies are required in order to shed more light on the optimal culture time and/or re-expansion rate after TE biopsy.

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EMBRYONIC CHROMOSOMAL CHANGES AND EMBRYONIC MORPHOLOGY: WHAT IS THEIR RELATIONSHIP TO THE CHOICE OF THE BEST EMBRYO. Mariana Moraes Piccolomini, MS,[1] Edson G. Lo Turco, PhD,[2] Lucas Yamakami, MD,[3] Helio Sato, PhD,[3] Fernando Prado Ferreira, MD, PhD,[3] Renato Tomioka, MD,[3] Orcar Duarte, MD[4] [1]Senior Embryologist, São Paulo, Brazil; [2]IonMedicine - Precision Medicine, Sao Paulo, Brazil; [3]Clinical Chief, São Paulo, Brazil; [4]Clinical Chief in Lab For Life Laboratory, São Paulo, Brazil.

OBJECTIVE: The embryonic morphology is an important factor while evaluating embryonic potential. With the advances in the field of genetic analysis techniques, it is known that the decision to transfer an euploid embryo is related to higher pregnancy rates. However, genetic evaluation is an invasive exam, which does not occur with the morphology evaluation, which can be considered an advantage. Nonetheless, it is not yet known whether it is possible to associate embryonic quality with euploidy, and the literature are very controversial. Because of this, we aimed to evaluate the effects of embryo quality on the aneuploidy.

DESIGN: Prospective study.

MATERIALS AND METHODS: Data from 1037 blastocysts were collected that were cultivated in continuous culture medium in incubators at 37oC, CO_2 8%, and O_2 5%. The blastocyst morphology was classified by SART criteria and the best quality embryos (3-6; A and B) were denominated top-quality embryos. The blastocysts were biopsied, and the cells were sending to PGT-A, subsequently being cryopreserved. According to the results, the embryos were separated into three groups: >75% aneuploidy (G1), between 74,9%-24,9% aneuploidy (G2), and <25% aneuploidy (G3). 320 couples undergoing *in vitro* fertilization in 2019 agreed to participate in the study. The female partners underwent controlled ovarian stimulation and had their oocytes recovered and subsequently inseminated. The fertilized embryos were cultivated in the group with the CSCM (Irvine) culture medium. In the stage of the blastocyst, they were biopsied and the preimplantation genetic diagnosis was performed by next-generation sequencing. Besides that, the embryos were evaluated for their quality through the morphological assessment.

RESULTS: Considering the morphologic variables, the G3 group (<25% aneuploidy) presented a significant ($p<0.01$) higher rate of top-quality embryos (55.1%±39.1%) when compared with the G1 group (35.9%± 41.9%). No significant difference was found when compared to the G3 group with the G2 group (46.4%±40.0%), and the G2 group with the G1 group, concerning the rate of top-quality embryos. These results show that embryos with better morphology assessment end up being euploid, which would allow the association of morphology evaluation with the embryo genetics status. However, this study has the same weakness that other blastocysts morphological studies, the evaluation always can be influenced by the observer, in addition to the possible loss of events due to time of analysis.

CONCLUSIONS: Because of this, further studies are necessary to establish whether it is safe to predict ploidy through embryo morphological analysis, also with the support of new technologies such as time-lapse. However, this study shows the relation between blastocyst aneuploidy and embryo quality on day 5/6. Our results are close to the routine of the vast majority of laboratories in the world, which do not have the resources of time-lapse technology, and It is possible to think of a joint strategy that allows the association of the morphological analysis to choose the better embryos to do the biopsy.

References: No reference

SUPPORT: Non

P-34 4:30 PM Saturday, October 17, 2020

MITOCHONDRIAL SUPPORT OF EMBRYOS FROM WOMEN OF ADVANCED MATERNAL AGE DURING ART. Rebecca Kile, MS, Deirdre M. Logsdon, MS, Catherine Nathanson, BS, Sue McCormick, BS, William B. Schoolcraft, MD, Rebecca L. Krisher, PhD Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: The supplementation of MitoTempo and mitoquinol (MTQ) in mouse embryo culture results in better quality blastocysts by supporting mitochondrial function. Women of advanced maternal age have reduced oocyte quality due in part to dysfunctional mitochondria. The aim of this study was to determine the effect of supplementation of mitochondrially targeted antioxidants (MTQ) during human embryo culture for women of advanced maternal age (≥35 yr).

DESIGN: Prospective clinical trial with sibling embryos.

MATERIALS AND METHODS:: After oocyte retrieval, cumulus oocyte complexes (COC) were denuded of cumulus cells. Mature oocytes (MII) were fertilized by ICSI and randomly allocated into sequential culture medium, 2/3 to control and 1/3 to medium with MTQ. Zygotes were moved into second step medium on day 3 and cultured for 5-7 days, at which time good quality blastocysts were biopsied for PGT-A and vitrified. MTQ was present throughout the culture period.

RESULTS: A total of 11 patients with advanced maternal age (AMA) (average age 39.4 yr, range 35-46) were included in this study. Post ICSI, 143 presumptive zygotes were placed in control medium and 66 in medium supplemented with MTQ. Normal fertilization, determined by presence of 2 pronuclei (2PN), was 83% in control and 91% in MTQ ($p=0.11$). There were no differences between control and MTQ treatment in D5 (control, 18%; MTQ, 20%) or total (control, 48%; MTQ, 45%) good quality blastocyst (≥grade 3BB) development (per 2PN), or total blastocyst development (control, 63%; MTQ, 62%). There was also no difference in the percentage of euploid blastocysts (control, 33%; MTQ, 30). To date, four euploid blastocysts from the control treatment and one from the MTQ treatment have been transferred individually to a total of 5 patients, all resulting in ongoing pregnancies with fetal heart beat.

CONCLUSIONS: In this preliminary study, we did not note any improvement in good quality or euploid blastocyst development due to inclusion of MTQ in the culture media. Both treatments resulted in an equal percentage of transferrable euploid embryos per oocyte injected with sperm. One embryo has been transferred after MTQ treatment, resulting in a healthy ongoing pregnancy. These data suggest that MTQ treatment of human embryos in culture is safe, although at this point it does not appear to be effective in increasing blastocyst development for women of AMA. However, further research is required to determine if there are any positive effects of MTQ treatment on implantation and/or pregnancy loss that are not yet evident from this initial trial.

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IN-VITRO FERTILIZATION TECHNIQUES COULD INCREASE MONOZYGOTIC TWINS RATE IN SINGLE EMBRYO TRANSFERS. Sofia Ana Dominici, Gynecologist, Estefania Navall, Gynecologist, Valentina Torres Monserrat, Embryologist, Maria Cecilia Delpiccolo, Embryologist, Nicolas Carizza, Gynecologist, Trinidad Leiva, Gynecologist, Maria Noelia Lardizabal, Embryologist, Ariadna Sol Ruiz, Gynecologist, Carlos Carizza, Medical Director Fertya, Rosario, Argentina.

OBJECTIVE: The objective of this study is to determine monozygotic twins rate in single embryo transfer of IVF cycles and analyze the associated factors of this event.

DESIGN: A retrospective analysis of blastocyst single embryo transfer in fresh and freeze-thaw cycles of all patients enrolled in IVF treatments in Fertya, since October 2015 until March 2019. Patients were divided in two groups: Group 1 (G1), 442 fresh blastocysts single embryo transfer, and Group 2 (G2), 597 freeze-thaw blastocysts single embryo transfer. The main outcomes studied were clinical pregnancy, multiple pregnancy and live birth rates for each group. The second outcome analyzed was the incidence on monozygotic twins pregnancy with the use of high complexity laboratory techniques and patients age.

MATERIALS AND METHODS: Embryos obtained in fresh IVF cycles were grown until day five or six in K-System® G-185 or Thermo Fisher Scientific® Heracell 150i incubators with Sage® or Global Total® mediums and then vitrified and warmed with Kitazato® Kits. Blastocysts were vitrified only when full expansion with a blastocele >50% of the embryo was observed. Blastocyst's morphology was assessed using Istanbul Consensus scoring. Chi square independence test and Fisher's exact test were used to compare the results of the two groups, statistical difference represented by a $p<.05$.

RESULTS: We observed that in fresh blastocyst single embryo transfers our clinical results are clinical pregnancy rate 38,23 % (169/442), multiple pregnancy rate 3,55 % (6/169) and live birth rate 34,61 % (153/442). Analyzing single blastocyst freeze-thaw transfers there were no statistical differences compare to G1, clinical pregnancy rate 37,02 % (221/597), multiple pregnancy rate 3,62 % (8/221) and live birth rate 31,65 % (189/597). *Analyzing only monozygotic twin pregnancies, abortion rate was 42,86 % and live birth rate 50 % (6 produced two births and 2 a single birth).*

Monozygotic twin pregnancy occurred only in under 35 years old patients. When analyzing the techniques used in the laboratory, in 57,0 % of the multiple pregnancies assisted hatching with laser was performed previous to embryo transfer and, when comparing the employed culture media, 50 % was cultured in GLOBAL TOTAL ® and 50% in SAGE ®. When carrying out hypothesis contrast over the twin rate in comparison to the values of spontaneous monozygotic twins pregnancies of the general population of 0,4 %, a value of p<0,0001 was obtained.

CONCLUSIONS: Our blastocyst single embryo transfer in IVF cycles shows an increase in monozygotic twins rate in comparison to the general population. All our cases occurred in women ≤35 years old. When considering laboratory high complexity techniques employed, neither vitrification, culture media nor the assisted hatching technique seem to affect the rate of twins. However, the main limitation of this work is the low number of cases analyzed.

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COMPARISON OF EMBRYO MORPHOKINETICS FOLLOWING ASSISTED SPERM FUSION INSEMINATION AND RESCUE INTRACYTOPLASMIC SPERM INJECTION. Shota Hatakeyama, Master,[1] Yasuyuki Araki, Ph.D.,[2] Yasuhisa Araki, Ph.D.,[2] Shirei Ohgi, M.D.,[1] Atsushi Yanaihara, M.D.[1] [1]Yanaihara Women's Clinic, Kamakura, Japan; [2]Gunma Paz University, Takasaki, Japan.

OBJECTIVE: In a previous study, assisted sperm fusion insemination (ASFI), which is a fertilization method using a single motile sperm without breaking the oocyte membrane, yielded fertilization rates and blastocyst formation rates similar to those obtained by rescue intracytoplasmic sperm injection (ICSI) (1). In this study, we assessed embryo development following ASFI and rescue ICSI via a time-lapse system.

DESIGN: A retrospective observational study using a time-lapse system was used to monitor 33 blastocysts from 25 patients undergoing ASFI (N=13 blastocysts) or rescue ICSI (N=20 blastocysts) between April 2019 and March 2020.

MATERIALS AND METHODS: Three hours after conventional in vitro fertilization, all inseminated oocytes were denuded of cumulus cells and the presence of the second polar body was confirmed. Oocytes with a single polar body were incubated for another 3 hours. Oocytes exhibiting only one polar body were defined as unfertilized oocytes and used for ASFI or rescue ICSI. Rescue ICSI was performed following conventional ICSI procedures. For ASFI, a motile sperm bound to the zona pellucida was collected using an injection needle and this sperm was pressed onto the membrane of an unfertilized oocyte for 30 seconds. Following fertilization, the oocytes were cultured and imaged using a time-lapse system.

RESULTS: The mean and standard deviation of ages of the women in the ASFI and rescue ICSI groups were 37.3±4.0 and 35.3±4.4 years, respectively, which was not significantly different (p>0.05). The ASFI and rescue ICSI groups showed no statistical difference in the time of pronuclei appearance (4.8±1.1 vs. 5.2±1.2 hours), pronuclear fading (20.9±2.3 vs. 21.1±2.3 hours), formation of eight-cell stage (54.4±7.4 vs. 56.7±8.1 hours), initiation of blastulation (92.1±8.1 vs. 95.4±7.1 hours), and full blastulation (100.6±7.9 vs. 104.1±7.9 hours).

CONCLUSIONS: This observational study showed that there were no differences in the morphokinetic parameters of embryo development between ASFI and rescue ICSI. For more general applications, further studies using a larger number of patients are necessary.

References: 1. Hatakeyama S, Araki Y, Ohgi S, Yanaihara A. Fertilization with human sperm bound to zona pellucida by pressing onto the oocyte membrane. Hum Cell. 2020; https://doi.org/10.1007/s13577-020-00348-4

P-37 4:30 PM Saturday, October 17, 2020

THE OOCYTE MATURATION FAILURE AND EMBRYO ARREST: A RETROSPECTIVE STUDY IN THE THIRTEEN-YEAR PERIOD. Lada Diachenko, MSc, Pavlo Mazur, MSc, Dmytro O. Mykytenko, MD, DSc, Valery Zukin, MD, PhD Clinic of Reproductive Medicine "Nadiya", Kyiv, Ukraine.

OBJECTIVE: Oocyte maturation and embryo arrest are well-known cases in clinical practice but this issue is still not sufficiently analyzed. According to investigations on animal models more than 35 genes have been found to be associated with abnormal early embryonic development. It has already been confirmed that five human genes, such as TUBB8, TLE6, PATL2, PADI6 and KHDC3L, have the similar functions. According to the Istanbul consensus, arrested embryos are those that have not cleaved during a 24-h period. There is a group of patients for whom the embryo arrest is a stable problem and recurs in subsequent IVF cycles. Patients with inability to obtain mature, morphologically normal egg that can be fertilized are rarer.The aim of the study was to evaluate the frequency of embryo arrest and oocyte maturation arrest within patients under 37 years of age.

DESIGN: Retrospective study.

MATERIALS AND METHODS: Cycles of 6015 patients in the thirteen-year period (2006-2018) were analyzed in this retrospective study. Only patients under 37 years of age, who underwent routine stimulation protocols, were included in the investigation. The embryo and oocyte maturation arrest group included patients who did not receive any blastocysts during all their stimulations.

RESULTS: The analysis showed that the group with embryo and oocyte maturation arrest reached to 3.34 % (n =201). Additionally two groups of poor (n=851) and good responders (n=5164) were assessed. It was shown that the percentage of patients with embryo and oocyte maturation arrest in the group of good responders was 1.8% (n=92) compared with the poor responders group – 12.8% (n=109). This study included a group of patients from only one IVF clinic. For clearer understanding of this issue there is a need of similar analysis among different groups within different populations. According to our assumptions, the results may be the same.

CONCLUSIONS: It is important to analyze other populations for more accurate evaluation of embryo and oocyte maturation arrest frequency. Moreover, it is crucial to assess the genetic background of such conditions. The identification of new genes that play a key role in early embryonic development will allow to create a new genetic screening panel.

POSTER SESSION: ART LAB: OUTCOME PREDICTORS

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BIRTH OF HEALTHY BABIES FROM BLASTOCYSTS DERIVED FROM MONO-PRONUCLEAR ZYGOTES FOLLOWING INTRACYTOPLASMIC SPERM INJECTION. Haruhisa Tsuji, M.S., Hiroya Kitasaka, Ph.D., Noritaka Fukunaga, Ph.D., Yoshimasa Asada, M.D., Ph.D. Asada Ladies Clinic, Nagoya, Japan.

OBJECTIVE: We have previously reported that 80.7% of 1PN zygotes derived from IVF or ICSI had a biparental chromosome, and some of these developed to the blastocyst stage (Tokoro et al. ASRM 2013). However, it has also been demonstrated that all embryos derived from 1PN-ICSI zygotes are chromosomally abnormal and these zygotes should be discarded, though 1PN zygotes derived from IVF(1PN-IVF) could be used for reproductive purposes (Mateo et al. Fertil Steril. 2013; 99: 897-902). In addition, it has been reported that zygotes derived from 1PN-ICSI produced blastocysts but did not lead to pregnancies (Igashira et al. ASRM 2016). In this study, we examined mono-pronuclear zygotes derived after ICSI (1PN-ICSI) can develop normally and result in a healthy live birth.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: This was a retrospective study including 2482 ART patients treated in 2814 cycles and where 3618 zygotes formed 1PN after ICSI. The time period was 72 months (January 2013 to December 2018). Patients seeking infertility treatment in a well-established private IVF clinic. Blastocyst rates, clinical pregnancy and miscarriage rates after a single blastocyst embryo transfer following the culture of 1PN-ICSI zygotes were compared with data on 1PN-IVF or normal 2PN zygotes during the same time period. Furthermore, follow up information was obtained on the health status of live births derived from 1PN-ICSI zygotes. Statistical significance was determined using the chi-square test (level of P<0.05).

RESULTS: The formation rate of 1PN-ICSI was 2.8%(3618/127728), significantly lower (P<0.05) than 1PN-IVF (4.6%; 1044/22799). The blastocyst rate of 1PN-ICSI zygotes (14.8%; 525/3547) was significantly lower (P<0.05) compared to 1PN-IVF zygotes (26.5%; 274/1035) or normal 2PN (62.0%, 22420/36189) . The clinical pregnancy rate of 1PN-ICSI transferred zygotes (24.4%; 53/217) was significantly lower (P<0.05) compared to 1PN-IVF transferred zygotes(36.6%; 41/112) or normal transferred zygotes from 2PN (40.2%; 4802/11947). However, the miscarriage rates were not significantly different (respectively, 30.2%, 34.1% and 23.3%) 21 healthy newborns were obtained from the successful pregnancies after embryo transfer of 1PN-ICSI blastocysts.

CONCLUSIONS: These results suggest that not all 1PN-ICSI zygotes are abnormal, and these can result in a viable pregnancy and healthy live birth. Continued culture to blastocyst of 1PN-ICSI zygotes should be carried out in order to further assess their potential for transfer.

SUPPORT: None.

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ALL TWIN PREGNANCIES ARE NOT THE SAME: EFFECT OF MATERNAL PARITY ON OUTCOMES OF TWIN PREGNANCIES CONCEIVED SPONTANEOUSLY VERSUS WITH ASSISTED REPRODUCTIVE TECHNOLOGY. Rachel S. Mandelbaum, MD, Meghan Brooke Smith, MD, Brittany L. Klooster, MD, Rachel Blair Danis, MD, Lynda K. McGinnis, PhD, Jacqueline Ho, MD MS, Kristen Bendikson, MD, Richard J. Paulson, MD, MS University of Southern California, Los Angeles, CA.

OBJECTIVE: Multiple gestations are a leading cause of preterm birth and neonatal morbidity, and reducing rates of multiple gestation with assisted reproductive technology (ART) has been a key focus over the past decade. Previous literature has suggested that parity may affect outcomes in multiple gestations, however this has not been studied with regards to the ART population.[1] Therefore, this study sought to evaluate the effect of maternal parity on neonatal outcomes of twin pregnancies conceived spontaneously versus with ART.

DESIGN: A retrospective populational study using Centers for Disease Control and Prevention (CDC) National Center for Health Statistics (NCHS) Natality database, which is derived from the birth certificates of United States residents.

MATERIALS AND METHODS: Data for all twin gestations between 2016 and 2018 was extracted. Pregnancies affected by hypertensive disorders, pre-eclampsia, gestational or pre-gestational diabetes, or a history of preterm birth were excluded. Cases were stratified by the use of ART, and pregnancies in which the use of ART was unknown or not recorded were also excluded. Primary outcomes included gestational age at delivery, birth weight, and NICU admission. Student's t-test was used for continuous variables and chi squared test for dichotomous variables.

RESULTS: A total of 268,710 twin gestations met criteria for inclusion in the study, 22,677 (8.4%) of which were conceived via ART. 64,547 (24.0%) women overall were primiparous; there were 9,146 (38.7%) primiparous women with ART twin pregnancies compared to 55,762 (22.7%) primiparous women with spontaneously conceived twin pregnancies. Average gestational age and birthweight at delivery was 34.8 $\pm$ 3.8 weeks and 2,265.0 $\pm$ 657.3 grams, respectively, for primiparous women compared to 35.4 $\pm$ 3.1 weeks and 2,407.1 $\pm$ 604.5 grams, respectively, for multiparous women ($P<0.001$, both). Rates of NICU admission were significantly higher among twin neonates born to primiparous women compared to multiparous women (40.1% vs. 33.8%, $P<0.001$). Among ART pregnancies in particular, gestational age at delivery, birthweight, and NICU admission rates were similar to that of the overall cohort. Gestational age at delivery and birthweight remained significantly higher and NICU admission rates significantly lower in multiparous women with ART twin pregnancies compared to primiparous women ($P<0.001$, all). Average age of women with ART pregnancies was significantly higher than those with spontaneously conceived pregnancies ($P<0.001$).

CONCLUSIONS: Outcomes of twin gestations are improved in multiparous women compared to primiparous women in both ART and spontaneously conceived pregnancies, including higher birth weight and gestational age at delivery with lower rates of NICU admission. Counseling women about the risk of multiple gestation and associated neonatal morbidity with ART must include consideration of prior parity.

References: 1. James S, Gil KM, Myers NA, Stewart J. Effect of parity on gestational age at delivery in multiple gestation pregnancies. *J Perinatol.* 2009;29(1):13-19.

P-40 4:30 PM Saturday, October 17, 2020

EFFECT OF CO-INCUBATION OF SPERMATOZOA WITH HUMAN ENDOMETRIAL CELLS ON ASSISTED REPRODUCTION OUTCOMES. Rumiana Ganeva, MSc, Dimitar Parvanov, PhD, Ivaylo Rangelov, MSc, Silviya Gogeva, MSc, Georgi Stamenov, MD/PhD Nadezhda Women's Health Hospital, Sofia, Bulgaria.

OBJECTIVE: To evaluate the effect of the co-incubation of spermatozoa with human endometrial cells prior ICSI on the assisted reproduction outcomes (fertilisation rate, proportion of high quality embryos, implantation rate and live birth rate) in couples with unexplained infertility.

DESIGN: Prospective.

MATERIALS AND METHODS: 110 couples fulfilled the inclusion criteria of unexplained infertility and males with normozoospermia or teratozoospermia. All patients have signed written informed consent. Couples were randomly allocated to study group (n=55) and control group (n=55).

After liquefaction all fresh semen samples were washed and were subjected to swim up. Semen samples from the study group were co-incubated for 2 hours with endometrial cell culture, obtained from their partners' endometrial biopsy. All patients underwent standard ICSI protocol. Embryo transfer was performed in 42 couples of the control group and on 40 couples in the co-incubation group.

Main outcomes were fertilisation rate, proportion of high quality embryos, implantation rate and live birth rate. Statistical analyses were performed using SPSS v21. $P>0.005$ was considered significant.

RESULTS: The study group and the control group were comparable in terms of female age, male age, count of unsuccessful IVF cycles, oocyte count and oocyte quality. There were no significant differences in the fertilisation rate (78$\pm$9% vs. 80$\pm$8%, $p>0.05$) and the proportion of high quality embryos (62$\pm$12% vs. 65$\pm$9%, $p>0.05$) between the co-incubation group and the control group. However, the implantation rate after sperm co-incubation with human endometrial cells was significantly higher when compared to the control group (46% vs. 33%, $p<0.05$). The live birth rate of the successfully implanted embryos was also significantly higher in the co-incubation group in comparison to the control group (95% vs. 40%, $p=0.003$).

CONCLUSIONS: Co-incubation of spermatozoa with endometrial cell culture has no effect on fertilisation rate and proportion of high quality embryos, but leads to higher implantation rate and live birth rate in comparison to conventionally prepared semen for ICSI. These results indicate that couples with unexplained infertility can benefit from sperm co-incubation with endometrial cells before performing ICSI.

P-41 4:30 PM Saturday, October 17, 2020

OVERVIEW OF 2018 U.S. ASSISTED REPRODUCTIVE TECHNOLOGY (ART) TREATMENT OUTCOMES AND CONTRIBUTION OF ART TO MULTIPLE BIRTHS AND PRETERM BIRTHS IN THE UNITED STATES. Saswati Sunderam, M.A PhD,[1] Dmitry M. Kissin, MD, MPH,[1] Yujia Zhang, PhD,[1] Amy Jewett, MPH,[1] Sheree L. Boulet, DrPH,[2] Lee Warner, PhD,[3] Charlan D. Kroelinger, PHD,[3] Wanda D. Barfield, MD[3] [1]Centers for Disease Control and Prevention, Chamblee, GA; [2]Emory University School of Medicine, Atlanta, GA; [3]Centers for Disease Control and Prevention, Atlanta, GA.

OBJECTIVE: To assess national and state-specific ART utilization and outcomes and the contribution of ART to multiple births and prematurity.

DESIGN: Population-based cross-sectional analysis

MATERIALS AND METHODS: Data for ART procedures and birth outcomes in 2018 were obtained from CDC's National ART Surveillance System (reporting years 2017 and 2018). Data for all infants born in the U.S. were obtained from 2018 CDC's National Vital Statistics System. The number of ART procedures performed per million women 15-44 years of age (ART utilization); rates of single embryo transfers (SET) among women <35 years, 35-37 years, >37 years; rates of preterm (<37 weeks gestation) and multiple births among ART-conceived infants and all infants; and proportions of U.S. multiple births and preterm births that are ART-conceived were calculated for 50 States, District of Columbia, and Puerto Rico, classified by mother's state of residence. The proportion of infants who were small for gestational age (SGA) (born at <10th percentile of birthweight for gestational age) was calculated for singleton births (22–44 weeks gestation) for ART and all infants.

RESULTS: Among 3,813,136 infants born in the U.S. in 2018, 2.0% (74,926) were conceived with ART (range: 0.4% in Puerto Rico to 5.1% in Massachusetts). ART utilization ranged from 484 (Puerto Rico) to 7,438 (Massachusetts) procedures per million women aged 15-44 years. The national SET rate among women <35 years was 74.1% (range: 28.2% in Puerto Rico to 89.5% in Delaware). The national SET rates among women 35-37 years and >37 years were 72.8% (range: 30.6% in Puerto Rico to 93.7% in Delaware) and 66.4% (range: 27.1% in Puerto Rico to 85.3% in Delaware), respectively. The rates of infants that are

multiple births and preterm births were 21.4% and 26.1% among ART infants versus 3.3% and 10.0% among all infants, respectively. Nationally, the proportion of U.S. multiples and preterm infants that are ART-conceived was 12.5% and 5.1%, respectively. The percentage of ART-conceived singletons that were SGA was 7.3%; the corresponding percentage among all singletons was 9.4%.

CONCLUSIONS: In the U.S., a higher proportion of ART-conceived infants are multiples or were born preterm compared to all infants. Wide variations were observed among states and territories in the rates of ART utilization and SET. Greater utilization of SET, where appropriate, could reduce the contribution of ART to multiple births and preterm births. Rates of SGA for singletons were lower among ART-conceived infants compared with all infants, possibly indicating better health behaviors and care among ART patients.

SUPPORT: None.

P-42 4:30 PM Saturday, October 17, 2020

IMPACT OF ENDOMETRIAL PATTERN ON LIVE BIRTH RATE AND SUBSEQUENT DEVELOPMENT OF HYPERTENSIVE DISORDERS OF PREGNANCY.

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OBJECTIVE: Recent studies suggest that FET cycles are associated with a higher incidence of hypertensive disorders of pregnancy (HTN). In FET cycles, endometrial thickness and pattern have been used as indicators of endometrial receptivity, although the ability of these measures to predict clinical pregnancy rate (CPR), live birth rate (LBR), and pregnancy complications remains unclear. The current study examines the influence of endometrial pattern (EP) and thickness on CPR, LBR, and HTN.

DESIGN: Prospective cohort study

MATERIALS AND METHODS: A total of 257 consecutive FET cycles in women aged 24-40 years were assessed at a single academic center. Cycles using donor egg-derived embryos, PGT embryos and natural thaw were excluded. EP was classified as one of three types: EP-A (Trilaminar), EP-B (Intermediate), or EP-C (Homogenous). EP and thickness were assessed prior to progesterone start. A multivariate regression model was used to assess the relationship between endometrial pattern. We adjusted for age at embryo cryopreservation, BMI, estradiol (E2) level, days on oral estradiol, and number of embryos transferred and thickness with CPR, LBR, HTN, birth weight, and gestational age at delivery.

RESULTS: There were no significant differences in patient age between the different pattern groups. EP-A was positively associated with CPR and LBR, while EP-C negatively correlated with these outcomes ($p<0.05$). Endometrial thickness was associated with CPR ($p<0.05$). The multivariate regression model showed: Odds of CPR were 2 times greater (95% CI [1.6, 6.1]) with EP-A than C. The odds of LB were 3 times greater (95% CI [1.3, 5.0]) with pattern A than with C. EP was a predictor of ongoing pregnancy with nearly half of pregnancies with +hCG in the pattern C not resulting in a live-birth (LB). Women with endometrial pattern C who did have a LB were significantly more likely to develop HTN ($p<0.05$) compared to women with EP-A (OR 4.8 (95% CI [1.4, 16.2])). No other factors in our model were associated with HTN. EP was not related to birth weight, gestational age at delivery, or multiple gestation.

Pattern Type	# patients	Avg. Age	+hCG (%)	CP (%)	LB (%)	HTN*
A	118	33.7	78.8	64.4	52.5	20.7
B	78	34.8	73.1	55.1	47.4	30.3
C	61	34.4	60.7	41.0	31.1	50

*HTN data available for 109 subjects: (EP-A n=58; EP-B n=33; EP-C n=18)

CONCLUSIONS: EP may serve as a biomarker of endometrial receptivity. Trilaminar EP (Type A) independently predicts CPR and LBR in FET cycles, with a 3-fold increase odds of LB. Abnormal EP (i.e. Type C) increases the risk of HTN, which may be linked to poor implantation. Further studies are needed to understand the mechanism by which endometrial pattern contributes to a healthy pregnancy.

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IMPACT OF OVARIAN STIMULATION AND IN VITRO FERTILIZATION ON LIPID PROFILE OF MICE BLASTOCYSTS.

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OBJECTIVE: To evaluate the impact of ovarian stimulation (OS) and OS plus in vitro fertilization (IVF) procedure on lipid profile of mice blastocysts by comparing the lipid profile of blastocysts originated from natural mating with or without previous superovulation and blastocysts from oocytes of superovulated females subject to IVF.

DESIGN: Experimental study.

MATERIALS AND METHODS: Blastocysts were recovered from C57BL/6J females (8 weeks) that were mated with males after confirmation of the estrous cycle (natural in vivo control group - N) or after superovulation with 5 UI equine chorionic gonadotropin followed by 5UI human chorionic gonadotropin (superovulation in vivo control group – S). For the IVF group (IVF), oocytes collected from superovulated females were inseminated with $1x10^6$ sptz/ml and cultivated for 96 hours in continuous culture media *(KSOM, Cosmo bio co., LTD)* incubated at 37°C with 5% CO_2. Blastocysts of each group were individually fixed in methanol/water. Lipids of 9 blastocysts per group were extracted using *One Step Methanol* protocol. Individual samples containing the lipid extracts of blastocysts were then diluted and flow injected into the triple quadrupole spectrometer equipped with an electrospray ion source. Lipids were analyzed using the multiple reaction monitoring profiling (*MRM*-profiling) method and values of relative intensities of ions detected in each group were compared using univariate (one-way ANOVA, volcano plot) and multivariate analysis (PCA, PLS-DA, hierarchical cluster analysis).

RESULTS: One-way ANOVA (p-value ≤ 0.05) showed that 95 out of the 125 lipids were differently expressed among the three groups. The top five important features identified by partial least square discriminant analysis (PLS-DA) variables of importance (VIP) scores (>1.32) were free fatty acid C28:0, sphingomyelin (SM d18:1/14:0), phosphatidylserine PS(20:4), phosphatidylcholine PCo(36:5), and phosphatidylethanolamine PE(14:1), all of which were more abundant in the IVF group, followed by S and N, respectively. This pattern was observed in all top 50 features selected by PLS-DA VIP (>1). PCA and heatmaps generated by hierarchical cluster analysis suggested that IVF was further separated from the other groups. This was confirmed by two by two-group analysis using volcano plot (p-value ≤ 0.05, fold change ≥ 1.5) that detected 15, 57, and 99 significant features between N vs. S, IVF vs. S, and IVF vs. N, respectively.

CONCLUSIONS: While ovarian stimulation alone promotes some alterations in lipid profile of in vivo originated blastocysts when compared with in vivo blastocysts from natural cycles, mainly on phosphatidylcholines, IVF process using oocytes from superovulated mice was responsible for more extensive changes observed on the lipid profile of the studied blastocysts, related to overall increased abundances in the relative concentration of specific membrane phospholipids and fatty acids.

CNPq (process n. 305173/2019-7), Trial registration number: CEUA-FMRP/USP-107/2017.

SUPPORT: Coordenação de Aperfeiçoamento de Pessoal de Nvel Superior (CAPES) – process n. Â 88887.371487/2019-00; Fundação de Apoio ao Ensino, Pesquisa e Assistência do Hospital das Clnicas da FMRP – USP (FAEPA); Invitra Assisted Reproductive Technologies LTDA.

P-44 4:30 PM Saturday, October 17, 2020

METABOLIC IMAGING OF CUMULUS CELLS AND EMBRYO OUTCOME.

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OBJECTIVE: Bidirectional metabolic cooperativity between the human oocyte and its surrounding cumulus cells is essential for successful

development. However, the relationship between cumulus cell metabolism and oocyte viability is not well established. Our aim was to determine whether non-invasive metabolic imaging of cumulus cells mitochondrial function is associated with the clinical outcome of the corresponding oocyte.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: Cumulus cell clusters (n=458 from 177 patients, mean age 36.7y) were dissected from cumulus oocyte complexes prior to assisted reproduction technique treatment. Morphology of embryos was assessed on day 3. Grades were stratified as excellent (n=89), good (n=79), fair (n=43) and poor morphology (n=62). Clinical outcomes of the corresponding oocytes were tracked. Embryos were transferred on day 3 or 5, either fresh (n=48 and 10) or after warming (n=7 and 20). Cumulus cell metabolism was assessed non-invasively using fluorescence lifetime imaging microscopy (FLIM) to measure the autofluorescence of NADH and FAD+, two key metabolites in cellular respiration and glycolysis. This approach enabled quantitative information to be obtained on concentrations of these coenzymes and on metabolite enzyme engagement. Overall a single FLIM measurement provides a total of 8 metabolic parameters (4 for NADH and 4 for FAD+). An additional parameter, the Redox Ratio can also be acquired (NADH intensity / FAD+ intensity). We used multilevel models to investigate the association of cumulus cell metabolic parameters with day 3 embryo morphology and clinical outcome.

RESULTS: Of the cumulus samples analyzed, 62 corresponded to embryos that did not implant, and 23 led to a clinical pregnancy. We found significant associations between cumulus cell FAD+ fraction bound to enzyme (p =0.02) and FAD+ short lifetime (p <0.001) and the clinical outcome of the corresponding embryo. There were no significant associations between cumulus metabolic parameters and embryo quality assessed at day 3.

CONCLUSIONS: Cumulus cell metabolic parameters are significantly associated with embryo outcome, although not with day 3 embryo quality. These findings suggest that metabolism and morphology provide complementary information. We are working to develop an embryo selection algorithm using machine learning based approaches that combines cumulus cell metabolic data, patient clinical characteristics (age, BMI, AMH levels), and morphological assessment of embryo quality.

SUPPORT: NIH RO1 (5R01HD092550-02).Â Becker and Hickl GmbH, and Boston Electronics sponsored research with the loaning of equipment for FLIM.

P-45 4:30 PM Saturday, October 17, 2020

SUPERIOR SPERM SELECTION? MICROFLUIDIC SPERM SORTING IMPROVES EUPLOID EMBRYO ONGOING PREGNANCY RATE COMPARED TO DENSITY GRADIENT CENTRIFUGATION.

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OBJECTIVE: Euploid embryo pregnancy failures are frustrating for clinicians and patients alike and remain a poorly understood aspect of infertility. Novel sperm selection techniques using microfluidic sorting devices are reported to improve embryo quality and pregnancy outcomes, though existing data is limited by small sample size. This study aims to compare euploid embryo ongoing pregnancy rates from embryos generated with the use of microfluidic sperm sorting (MSS) versus standard density gradient centrifugation (DGC).

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: All IVF/PGT-A cycles resulting in embryo biopsy between January and October 2019 at a large, multicenter, private practice were included in analysis. Our center transitioned to use of MSS devices for all IVF cycles mid-way through this time period. PGT-A cycles were divided into two cohorts based on sperm preparation technique prior to ICSI: MSS (n = 167 cycles) and DGC (n = 167 cycles). Primary outcome was ongoing pregnancy rate following euploid embryo transfer. Secondary outcomes included fertilization rate, biopsiable blastocyst rate, and euploidy rate. Statistical analysis included two-tailed Student's t-test for continuous variables and Chi-square test for categorical variables, with $p < 0.05$ defining statistical significance.

RESULTS: Demographics, including oocyte age, body mass index, and baseline sperm parameters, were similar between MSS and DGC cohorts with the exception of AMH: mean 2.5 ng/mL in MSS versus 3.4 ng/mL in DGC, p=0.01. Euploid embryo transfers following MSS demonstrated higher ongoing pregnancy rate (86.1%) compared to DGC (70.8%), p=0.02 (Table 1). Fertilization, biopsiable blastocyst and euploidy rates were equivalent in MSS and DGC groups. Of note, MSS resulted in a trend towards greater percentage of Day 7 biopsies (5.1%) versus DCG (2.6%).

TABLE 1. MSS versus DGC Primary & Secondary Outcomes

	Microfluidic Sperm Sorting (MSS)	Density Gradient Centrifugation (DGC)	P-value
Fertilization Rate (%)	69.7	71.5	0.38
Biopsiable Blastocyst Rate (%)	54.8	51.2	0.17
Euploidy Rate (%)	47.4	50.2	0.45
Pregnancy Rate (%)	80.9	82.3	0.85
Ongoing Pregnancy Rate (%)	86.1	70.8	0.02
Biochemical Pregnancy Rate (%)	22.2	16.7	0.16
Clinical Miscarriage Rate (%)	5.6	10.4	0.4

CONCLUSIONS: Despite equivalent fertilization, embryo progression, and euploidy rates, microfluidic sperm sorting results in a higher ongoing pregnancy rate following euploid embryo transfer compared to standard density gradient centrifugation. Our findings may be explained by the lower DNA fragmentation and hence improved embryo quality of resultant embryos.

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STAGE OF TRANSFERRED BLASTOCYST MAY AFFECT PREGNANCY OUTCOMES WHEN TIMED WITH ENDOMETRIAL RECEPTIVITY ASSAY (ERA).

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OBJECTIVE: ERAs have become popular tests in fertility patients with recurrent implantation failure and is used to personalize the timing of the transfer of embryos based on endometrial receptivity. Our study was performed to determine if blastocyst (BL) stage, at time of transfer, influences pregnancy outcomes when transferred based on ERA recommendations.

DESIGN: We performed a retrospective analysis of 200 single, euploid frozen embryo transfers (FETs) from patients who underwent ERA testing between 2018-2020. FET cycles were divided into groups based on stage of BL post thaw, early BL (B) (n=68), expanded BL (ExB) (n=56), hatching BL (HB) (n=42), and fully hatched BL (fHB) (n=34). Differences in implantation rates (IR), ongoing pregnancy rates (PR), and biochemical rates (BR) were statistically compared between groups.

MATERIALS AND METHODS: Between January 2018 and February 2020, 200 ERA timed, single euploid FETs were performed. Cycles that resulted in the transfer of two embryos or non-tested embryos were excluded. Pictures of embryos taken post thaw, 2+ hours before transfer, were analyzed and cycles were divided into 4 groups based on BL stage post thaw.

Group I – (B), 0% hatching out of zona
Group II – (ExB), <25% hatching out of zona
Group III – (HB), ≥25% hatching out of zona
Group IV – (fHB), embryo fully hatched out zona

Results were analyzed by Chi square analysis. A P value of $<.05$ was considered statistically significant.

RESULTS: The synchronization between the developing embryo and endometrium is essential for successful pregnancy. Transfers were divided into groups of B, ExB, HB, and fHB, achieving IR of 44%, 71%, 55%, and 50%, respectively, and PR were as follows, 35%, 50%, 38%, 24% (Table 1).

ExB did have significantly higher IR than B ($p<0.001$). ExB also had significantly higher PR compared to fHB ($p<0.05$). There was no significant difference in BR among groups.

TABLE 1.

Blastocyst Stage	FETs #	Implantation Rate # (%)	Pregnancy Rate # (%)	Biochemical Rate # (%)
B (Group I)	68	30 (44)[a]	24 (35)	4 (6)
ExB (Group II)	56	40 (71)[a]	28 (50)[b]	5 (9)
HB(Group III)	42	23 (55)	16 (38)	5 (12)
fHB(Group IV)	34	17 (50)	8 (24)[b]	4 (12)

[a] Group II implantation rate significantly different than group I. [b] Group II pregnancy rate significantly different than group IV

CONCLUSIONS: The transfer of an ExB based on ERA timing was associated with higher IR and PR compared to other BL stages. Personalized medicine has been promoted with individualized stimulation protocols and ERAs, which have improved results through identification of the optimal "window of implantation". The embryo remains another major factor and success can further be improved by personalizing embryo transfers based on BL stage at time of transfer. Further investigation is required to confirm these initial findings.

References: None

SUPPORT: None

P-47 4:30 PM Saturday, October 17, 2020

THE EFFECT OF EMBRYO CATHETER-LOADING TECHNIQUE ON PREGNANCY AND IMPLANTATION RATES IN FROZEN EMBRYO TRANSFER CYCLES.

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OBJECTIVE: The purpose of the study was to compare the implantation and clinical pregnancy rate when using a medium-only catheter loading technique versus an air-fluid method in frozen embryo transfer (FET) cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: 113 women undergoing FET were included in our study. Group 1 (n=70) had FET done between 6/1/19 and 9/30/19 using an air-fluid technique of embryo loading. Group 2 (n=43) had FET done between 1/1/20 and 4/30/20, when a fluid-only method was implemented.

In Group 1, loading was done by filling the catheter with 15-20μL of medium and then aspirating 10μL air followed by 5-10μL of medium containing embryo(s). Loading was completed by adding 10μL of air at the tip of the catheter.

In Group 2, loading was performed by filling the catheter with 15-20μL of medium followed by an additional 5-10μL containing embryo(s), without air.

In both groups the catheter was flushed with 1ml of Global Total (Cooper-Surgical, Denmark) prior to loading and embryos were aspirated in Embry-oGlue (Vitrolife, Sweden).

Embryo transfer technique was identical in both groups and was standardized among physicians based on current ASRM practice guidelines.

Data was analyzed using unpaired Student's t-test to compare quantitative variables and chi square test for qualitative variables.

RESULTS: No statistical difference was detected between the groups with regard to age, body mass index, diagnosis, FET and ovarian stimulation cycle characteristics, number and quality of embryos transferred (all P >0.05).

113 FETs resulted in 59 positive pregnancy test results and 49 clinical pregnancies - defined as documented intrauterine gestational sac with fetal pole and positive fetal heartbeat on ultrasound.

There was no statistical difference between Group 1 and Group 2 in clinical pregnancy (45.7% vs 39.5% P=0.38) and implantation rate (55.7% vs 46.5% P= 0.35).

CONCLUSIONS: No difference was found between groups with respect to implantation and clinical pregnancy rates.

We conducted this study to gain more insight into potential differences between two techniques, as only 2 prospective trials with similar sample size, conducted in fresh cycles, were reported more than 20 years ago. Even though no significant difference in pregnancy rate was demonstrated at that time, routine use of air brackets is still controversial. While it may offer some psychological comfort to the doctor, as the echogenic air droplet makes it easier to visualize the procedure on ultrasound, there exists a theoretical assumption that reactive oxygen species may cause damage to the embryo, given the fact that the introduction of air is non-physiologic.

Currently, no studies have utilized a sample size large enough to demonstrate a statistical difference between methods. Additionally, transfer guidelines and advances in ART techniques have changed dramatically since the earliest reports. We intend to increase our sample size to achieve sufficient statistical power.

SUPPORT: None

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MICROFLUIDIC DEVICE-BASED SEMEN PREPARATION INFLUENCES EUPLOIDY RATES OF HUMAN BLASTOCYSTS.

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OBJECTIVE: The study has been conducted to assess preimplantation development of human embryos following ICSI with two different sperm separation techniques. Zymot, a microfluidic sperm separation device (MFSS), which was based on motility within a micro-environment, and density gradient centrifugation (DGS) which was based on centrifugal force. The study was carried out between 2018 and 2019.

DESIGN: Retrospective

MATERIALS AND METHODS: A total of 371 ART-cycles were included in the study. Semen samples from patients with severe male pathology, TESE, MESA, and donor semen were excluded. Fresh ejaculated specimens from consenting men were collected for standard semen analysis in accordance with WHO 2015 guidelines. DGC (Control Group, n=220) and MFSS (Treatment Group, n=151) were used to isolate motile spermatozoa based on cell motility and fluid dynamics. 1802 blastocysts were biopsied and analyzed to determine ploidy status . Patient characteristics such as male and female age, number of retrieved oocytes, number of embryos were comparable between control and treatment groups. All oocytes were inseminated by ICSI and cultured following standard embryo culture protocols. Trophectoderm biopsies were performed on Day 5 or 6 of development and screened for euploidy using NGS. Experimental end points of the study were fertilization, blastocyst conversion and euploidy rates of preimplantation embryos. Ch-square and regression analyses were used to compare treatments and to identify factors affecting ploidy status of blastocysts.

RESULTS: Fertilization and blastocyst conversion rates were comparable between the sperm prep methods tested. Regression analysis of the factors influencing the ploidy status of the blastocysts indicated that use of MFSS method, ZyMot increases the number of euploid embryos by 0.44/cycle, controlling for other known characteristics of patient sets (p: 0.05 *).

Semen Prep Method	ICSI Cycles (N)	ICSI Oocyte (n)	Fertilization %	Blastocysts Biopsied (%)	Euploid Blastocyst (%)
DGS	220	2058	1667 (81.0)	1050 (51.0)	620 (59.0)
MFSS	151	1419	1078 (76.0)	752 (53.0)	474 (63.0) *

CONCLUSIONS: This study suggests that the use MFSS for sperm preparation for ICSI ccyles could improve the number of euploid embryos, modestly. Although the morphology and DNA integrity were not assessed in this study directly, widely reported improvements in these aspects by the MFSS may explain the improvements in PGT-A outcomes. The findings of our study should to be considered in the light of some limitations, such as a modest sample size and absence of morphology and DNA integrity data. These need to be addressed in future studies to provide a more complete assessment of the treatments.

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SORT-TERM *IN VITRO* MATURATION (IVM) CULTURE OF CUMULUS-OOCYTE COMPLEXES IMPROVES SUBSEQUENT EMBRYONIC DEVELOPMENT IN STIMULATED CYCLES. Ya-Nan Shi, PhD,[1] Yi Zhou, Master,[2] Lei Jia, Master,[1] Yingying Liu, Master,[1] Cong Fang, PHD, MD,[3] Xiao-yan Liang, M.D., Ph.D.[3] [1]Laboratory of Reproductive Endocrinology, The Research Center of Reproductive Medicine, The 6th Affiliated Hospital, Sun Yat-Sen University, Guangzhou, China; [2]492459979@qq.com, Guangzhou, China; [3]The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: To determine the effect of short-term culture in IVM medium on oocyte maturation, subsequent embryonic development and the clinical outcome.

DESIGN: A prospective study was conducted under the following background. Current standard stimulation protocols use gonadotropins (recombinant or hMG) combined with LHRH agonists to prevent the problem of premature ovulation with the aim of obtaining an average of 10–15 mature oocytes per retrieval. However, it is quite often containing some immature oocytes retrieved with mature oocytes even after triggering of LH surge. Practically those immature oocytes retrieved were discarded. Insemination is performed normally after approximately 41 h of HCG injection. Therefore, there is a few hours (3-5 h) after oocyte retrieval before insemination in fertilization medium (FM). We do not know whether or not FM is suitable for final oocyte maturation.

MATERIALS AND METHODS: Forty-five infertile women under 35 years of age were enrolled in this study. All the patients underwent autologous intracytoplasmic sperm injection (ICSI) cycles with more than 2 cycles failed previously. GnRH antagonist protocol was used for controlled ovarian hyperstimulation. Twelve patients were enrolled in the treated group, the COCs were cultured in balanced IVM medium (IVM Kit, SAGE, Coopersurgical, USA) immediately after retrieval for 4 hours in 5% CO_2, 5% O_2, 90% N_2at 37°C incubator before ICSI. Those thirty-there untreated patients underwent conventional ICSI with a similar duration of incubation in FM before ICSI. The oocyte maturation rate was compared in the two groups, and subsequent fertilization rate, early embryonic development and the pregnancy rate were also determined.

RESULTS: The maturation rate was 72.1%(98/136) and 69.8%(233/334) in treated and untreated groups. The fertilization rate, usable embryo rate, good quality embryo rate, blastocyst formation rate as well as biochemical and clinical pregnancy rate were 72.4%(71/98) vs 69.1%(161/233), 78.9%(56/71) vs 59.0%(95/161) (P<0.1), 52.1%(37/71) vs 33.5%(54/161) (P<0.1), 60.6%(20/33) vs 57.9%(22/38), 57.1%(4/7) vs 35.7%(10/28) and 42.9%(3/7) vs 35.7%(10/28) respectively.

CONCLUSIONS: Short-term IVM culture of COCs remarkably improves the usable embryo rate and good quality embryo rate, subsequently could obtain higher proportion of good quality embryos for transfer, thereby improves pregnancy rate.

SUPPORT: This project was supported by the National Key R&D Program of China (2017YFC1001604, 2017YFC1001601), and Chinese National Natural Science Foundation (81801449).

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EFFECT OF RE-EXPANSION IN FROZEN-THAWED EMBRYO TRANSFERS ON PREGNANCY OUTCOMES. Kathryn D. Coyne, MD, Mabel Lee, MD, Lauren Alexis Palavos, BS, James Hamrick, BS, Brooke A. Belvin, BS, Rachel S. Weinerman, MD, Rebecca Flyckt, MD, James H. Liu, M.D., Sung Tae Kim, PhD, HCLD University Hospitals Fertility Center/Case Western Reserve University, Beachwood, OH.

OBJECTIVE: To evaluate the effect of blastocyst re-expansion on frozen-thawed embryos at time of transfer on pregnancy outcomes.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients undergoing frozen-thawed embryo transfer (FET) from January 2017 to March 2020 in our center were included. Following a standard FET protocol, vitrified blastocysts were re-warmed on the day of ET and images of the thawed embryo were taken prior to transfer. Images were reviewed by at least two embryologists and the degree of expansion at least 1 hour post thaw at time of FETs was documented and included: 1) fully re-expanded 2) partially re-expanded 3) non re-expanded. Primary outcomes included: high quality embryo, defined by minimum grades of B for both trophectoderm and inner cell mass by Gardner's blastocyst grading scale; pregnancy; clinical pregnancy; miscarriage; and, ongoing pregnancy and live birth. Statistical analyses were done using ANOVA for continuous data and Chi Square for dichotomous outcomes.

RESULTS: A total of 645 single FET cycles were analyzed in the study. There were 301 fully re-expanded (46.7%), 274 partially re-expanded (42.4%), and 70 non re-expanded (10.9%) embryos at the time of transfer. The mean age, BMI, and endometrial thickness was not significantly different between the groups (p=NS). There was a significantly higher rate of embryo quality (56.8% and 58.0% vs. 44.3%; p=0.034), pregnancy rate (68.4% and 68.2% vs. 55.7%; p=0.048), clinical pregnancy rate (62.1% and 62.8% vs. 55.7%; p=0.030), and ongoing or live birth rate (50.2% and 51.8% vs. 38.6%; p=0.048) in frozen-thawed embryos that were fully or partially expanded at the time of transfer versus non re-expanded, respectively. No difference was noted in miscarriage rate between the groups (10.6%, 10.9%, 10.0%; p=0.9). The majority of thawed embryos were at least partially re-expanded (89.1%). The non re-expanded group has fewer high quality embryos (56.8% and 58.0% vs. 44.3%; p=0.034). When the high quality embryos were analyzed alone, there were no significant differences (p=NS) in pregnancy rates (70.2% vs. 72.5% vs. 64.5%), clinical pregnancy rates (64.9% vs. 67.5% vs. 54.8%), ongoing or live birth rates (52.6% vs. 58.8% vs. 41.9%) or miscarriage rate (10.0% vs. 8.8% vs. 12.9%) between the fully, partially, and non re-expanded groups, respectively.

CONCLUSIONS: Transferring a non-re-expanded blastocyst, as compared to a fully or partially expanded blastocyst, at the time of FET is associated with a lower ongoing pregnancy and live birth rate in our study. However, embryo quality appears to have a greater effect on pregnancy outcomes than re-expansion, as there were no differences in outcomes between the groups when considering only high-quality blastocysts.

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EFFECTS OF CULTURE TIME ON PREGNANCY OUTCOME OF FROZEN-THAWED D5 BLASTOCYST. Junxia Liu, MD,[redacted] Guoning Huang, M.D[2] [1]ChongQing Health Center for Women and Children; [2][redacted].

OBJECTIVE: To explore the effect of culture time on pregnancy outcome of frozen-thawed D5 blastocysts, and to optimize the blastocyst transfer strategy.

DESIGN: A retrospective cohort study.

MATERIALS AND METHODS: A retrospective cohort study of 1576(age<38) frozen-thawed high quality blastocyst transfer cycles vitrified on day 5, were divided into 2 ~ 4 h (group A, n = 677) and 16 ~ 20 h (group B, n = 899) according to culture time after thawed.

RESULTS: The implantation rate (64.58%), clinical pregnancy rate (77.99%) and ongoing pregnancy rate (71.79%) in group A were higher than those in group B (51.35%, 67.96%, 58.39%), the difference was statistically significant ($P = 0.000$). The early miscarriage rate in group A (6.44%) was lower than that in group B (11.13%, $P = 0.000$).

CONCLUSIONS: D5 thawed blastocysts cultured for 2~4 hours had better pregnancy outcomes.

SUPPORT: NO

P-52

WITHDRAWN

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IS THE BIGGEST IMPACT ON CLINICAL IVF OUTCOMES OBTAINED BY IMPLEMENTATION OF CONTINUOUS MEDIA, TIME-LAPSE INCUBATOR OR BOTH?. Teija Peura, PhD,[1] Andrew Murray, MSc,[2] Natalie Hesketh, MSc,[2] Sarah Dalati, PhD,[2] Mark Bowman, MB BS PhD,[2] Steven J. McArthur, BSc[2] [1]Genea Biomedx, Sydney, NSW, Australia; [2]Genea, Sydney, NSW, Australia.

OBJECTIVE: The objective of this work was to explore which change has the biggest impact on clinical IVF outcomes; implementation of continuous media, timelapse incubator or a combination of the two.

DESIGN: Separate prospective sibling oocyte studies were conducted to compare embryo culture in continuous medium vs. sequential media, and in timelapse incubator vs. benchtop incubator. Subsequently a change in embryo culture system was introduced across a chain of clinics and retrospective comparative data of outcomes of old (sequential + benchtop) vs. new (continuous media + timelapse) system were collated and analysed. Altogether 970 and 42,892 embryos were included in prospective and retrospective studies, respectively, between 2014-2019.

MATERIALS AND METHODS: Patients with min. 2 or 1 fertilised oocytes were included in prospective and retrospective studies, respectively. Embryos were culture in Gems® Cleavage and Blastocyst Medium or Geri Medium (Genea Biomedx) in Geri® incubator, or in MINC™ benchtop (Cook Medical) or Geri® timelapse incubator (Genea Biomedx) in Gems Sequential media. Retrospective follow-up included patients with comparable ages, fertilisation methods (IVF vs ICSI) and PGT prevalence and outcomes. Cumulative pregnancy outcomes were collated over a two-year period.

RESULTS: No statistical differences in grade 1 or 2 utilisable blastocysts by Day 5 or 6 (26.9 vs. 26.2%) or cumulative live births/on-going pregnancies for 112 patients (16 vs. 21) were observed between sequential vs. continuous media in prospective media studies. The tendency for more embryos being vitrified at Day 5 for PGT in continuous media group resulted in more cryo-PGT transfers in that group despite comparable euploidy outcomes between groups. In incubator studies, the corresponding embryo development rates were significantly higher (43.3 vs. 27.5%, $p<0.001$) in Geri incubator compared to MINC benchtop. In addition, more embryos reached grade 1 or 2 by day 5 in Geri than in MINC (93% vs. 76%). Cumulative live births/ongoing pregnancies for 80 patients were also higher in Geri than in MINC (14 vs. 25, $p<0.05$). In retrospective follow-up, the combination of Geri continuous media + Geri timelapse incubator led to significantly higher embryo development (38.7 vs. 29.1%, $p<0.001$) and cumulative live births/ongoing pregnancies (30.3 vs. 34.1%, $p<0.001$) than Gems sequential media + MINC benchtop. Overall, data from >42,000 embryos showed statistically highly improved ($p<0.00001$) outcomes both in utilisable embryo development as well cumulative pregnancy rates. Although groups were balanced for PGT cases, the overall increase in NGS PGS over the years with associated embryo manipulations and impact on patient cohorts could have been expected to have a negative impact on outcomes under the new, later adopted system. However, the new system still proved superior.

CONCLUSIONS: Although both the change into continuous media and timelapse incubation separately had some positive impacts on outcomes, the true benefits emerged more clearly when the two were combined.

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IS THERE A DIFFERENCE IN IVF DEVELOPMENTAL OUTCOMES BETWEEN OOCYTES RETRIEVED IN ROOM TEMPERATURE OOCYTE COLLECTION MEDIUM OR MEDIUM MAINTAINED AT 37oC?. Sarah Dolisca, MD,[1] Karissa C. Hammer, MD,[2] Stylianos Vagios, MD,[2] Jennifer Hsu, MD,[2] Caitlin Sacha, MD,[2] Irene Souter, MD,[2] Manoj Kumar Kanakasabapathy, MS,[3] Prudhvi Thirumalaraju, BS,[3] Charles L. Bormann, PhD,[2] Hadi Shafiee, PhD[3] [1]Brigham and Women's Hospital, Boston, MA; [2]Massachusetts General Hospital, Harvard Medical School, Boston, MA; [3]Brigham and Women's Hospital, Harvard Medical School, Boston, MA.

OBJECTIVE: Analyzing the impact of collection medium temperature during egg retrievals on IVF outcomes using convolutional neural networks (CNN) and preimplantation genetic testing for aneuploidy (PGT-A)

DESIGN: A retrospective review of 206 IVF-ICSI cycles at a single institution between 2016-2019 comparing oocyte retrieval medium at room temperature to medium at 37oC. The percentage of normally fertilized MII oocytes (2PN) was measured 16-18 hours post-insemination (hpi). A CNN model trained to classify images of embryos at 113 hpi compared D5 embryo development. A trained CNN predicted the implantation potential of PGT-A embryos calculated the average implantation potential for each embryo imaged per cycle.

MATERIALS AND METHODS: Using a dataset comprised of 1971 embryos cultured and imaged in the EmbryoScope comparisons were made after varying the temperature management of collection tube media between two cohorts: 1) room temperature and 2) 37oC. Comparisons were made regarding the percentage of normal fertilization (2PN), D5 embryo development, average implantation potential for each embryo, percentage of euploid blastocysts per cycle, and average number of euploid embryos per cycle.

RESULTS: Room temperature and 37oC treatment groups were comparable by age (36.5, 37.5 years, respectively), and all cycles had at least one blastocyst available for PGT-A (room temperature N=32, 37oC N=173).

Both groups were comparable for rate of normal fertilization, 76.9% for room temperature and 77.9% for 37oC ($p=0.711$). There were no differences in D5 embryo development between the two groups, 55.5% room temperature and 60.7% at 37oC ($p=0.122$). Similarly, there were no significant differences in percentage of high quality D5 blastocyst development between the two groups, 31.1% at room temperature and 33.0% at 37oC ($p=0.544$).

The average implantation potential for each embryo imaged was comparable between the two treatment groups at 41.0% per embryo for room temperature and 43.0% per embryo at 37oC ($p=0.189$). The percentage of euploid embryos per cycle were similar as well, 35.8% at room temperature and 42.1% at 37oC ($p=0.335$). No differences were observed between the average number of euploid embryos per cycle: 1.4 at room temperature and 1.7 at 37oC ($p=0.308$).

CONCLUSIONS: Patients who underwent oocyte retrieval with collection tube medium warmed to 37oC had comparable outcomes to those at room temperature. These findings suggest that room temperature collection tube medium is equally efficacious for IVF procedures.

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SUPPORT: This work was partially supported by the Brigham Precision Medicine Developmental Award (Brigham Precision Medicine Program, Brigham and Women's Hospital), Partners Innovation Discovery Grant (Partners Healthcare), R01AI118502, and R01AI138800.

P-55 4:30 PM Saturday, October 17, 2020

THE EFFECTS OF TEMPERATURE VARIATION TREATMENTS ON MOUSE EMBRYO MORPHOKINETICS AND METABOLISM.

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OBJECTIVE: This study aimed to evaluate the effects of temperature variation treatments on mouse embryo morphokinetics and metabolism.

DESIGN: Prospective study.

MATERIALS AND METHODS: Frozen-thawed hybrid B6C3F1 x B6D2F1 mouse embryos (N=161) were cultured in time-lapse system incubators under 3 temperature variation treatments: Treatment 1 (T1) at 37°C during the day and 35.5°C during the night, Treatment 2 (T2) at 38.5°C during the day and 37°C during the night and Control (C) with constant 37°C. For this study, 3 time-lapse system incubators were used (one for each study group), temperature was changed in the set-up function every 12 hours (9am and 9pm) and embryo culture was performed at 6% CO_2, in dry atmosphere. Experiments terminated at 9am of Day 5 (96 hours post-thaw) and culture media was collected individually for metabolomics. The following morphokinetics events were annotated: first cleavage (t2), division to 3-cells (t3), 4-cells (t4), 5-cells (t5) and 8-cells (t8), start of blastulation (tSB), full blastocyst (tEB) and hatching of the blastocyst (tHB). All the time points were normalized to pronuclear fading (tPNf). Based on the pre-compaction time points annotated it was calculated the duration of the second (ECC2) and third cell cycle (ECC3), as well as, the synchronicity of the second (s2) and third cell cycle (s3). With blastocyst time points it was also calculated the duration of blastulation (dB). The Targeted Metabolomics was performed with a HPLC coupled with an Amino Acid Analyzer. The amino acids library (23 metabolites) was based on the dynamic metabolism of a developing mouse embryo, from zygote to blastocyst stage.

RESULTS: Considering the morphokinetics variables (N=161 blastocysts) it was found statistical differences for the variables: t2, t3, t4, ECC2, t5, t8, tSB, tB, tHB, with the embryos from T1 (low temperature) group consistently showing a lower rate of development when compared to both T2 and C group. On the other hand, the rate of development of T2 (high temperature) group was very similar to the control group, with no statistical differences for all variables between these 2 study groups. The individual metabolomics of culture media (N=81 samples) showed that the amino acids L-histidine, ammonium chloride, valine, L-ornithine, tryptophan, L-alpha-aminoapidic acid, L-threonine, L-aspartic acid, L-isoleucine, cystine, L-methionine, L-alanine, glutamic acid, phenylalanine and serine were highly expressed in the T1 (low temperature) group, indicating a more stressed metabolism, while both T2 and C group showed a low expression of the same metabolites.

CONCLUSIONS: In summary, considering normal metabolism and morphokinetics events throughout embryonic development, culturing embryos at 37°C during the day and 35.5°C during the night (T1) showed negative effects, such as low rate of development and stressed metabolism. In contrast, the second temperature variation treatment with 38.5°C during the day and 37°C during the night (T2) seemed to be as efficient as the control group for *in vitro* mouse embryo culture.

SUPPORT: This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nvel Superior – Brasil (CAPES) – Finance Code 001.

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AMH IS NOT ASSOCIATED WITH HIGH-GRADE EMBRYO QUALITY AS ASSESSED BY DAY 3 AND DAY 5 MORPHOLOGY.

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OBJECTIVE: The purpose of this study was to determine if there is a correlation between AMH and the quality of day 3 and day 5 embryos in patients undergoing fresh IVF cycles.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: All fresh IVF cycles at a single academic center in 2016 were evaluated. Patients with an AMH level documented within one year prior to stimulation who proceeded to retrieval were included in our analysis. Patients without AMH levels drawn before stimulation were excluded. Experimental perimeters included age, BMI, #eggs retrieved, #mature eggs, # fertilized embryos (2pn), #day 3 blasts, and # day 5 blasts. A morphological grading system was used to determine the quality of day 3 and day 5 embryos. Criteria for high quality day 3 (HQD3) embryos were: 7-10 cells, <10% fragmentation, and no fragmentation or scattered fragmentation. For high quality day 5 blastocysts (HQD5) criteria were: 1) presence of a blastocyst that is expanding, fully expanded, or hatching with 2) an inner cell mass that is loosely grouped with several cells or tightly packed with many cells, and 3) the trophectoderm described as containing few cells forming loose epithelium or many cells forming a cohesive epithelium, and the absence of necrotic cells. Multiple linear regression analysis was performed to assess if embryo quality, (defined as #HQD3/#2pn or #HQD5/#2pn) is associated with AMH level, controlling for patient's age and BMI. Significance was determined at a p-value of 0.05.

RESULTS: 292 cycles met inclusion criteria and were analyzed. Higher AMH levels were associated with significantly younger patients (r^2=0.09, $p<0.001$) and significantly more oocytes retrieved (r^2= 0.13, $p<0.001$). After controlling for age and BMI, there was no significant relationship between AMH level and embryo quality as defined by the study's parameters for percentage of high quality Day 3 and Day 5 embryos.

CONCLUSIONS: In our study, we did not find AMH to be a predictor of embryo quality. This information is important when counseling patients on the utility of AMH. While AMH levels predict the number of oocytes retrieved during an IVF cycle, it may not predict the quality of embryos, which is an important distinction for patients and clinicians.

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SUPPORT: None

P-57 4:30 PM Saturday, October 17, 2020

HEALTHY BABIES CAN ALSO BE OBTAINED FROM BLASTOCYSTS WITH DIRECT CLEAVAGE.

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OBJECTIVE: Direct cleavage (DC) of an embryo has been reported to decrease blastocyst formation, but if such an embryo does go to blastocyst, viability can be similar to normally dividing one.However, whilst there are some reports of live births from DC embryos, there is still unsufficient clarity on the relationship between DC and outcome. Therefore we compared the prognosis of normally dividing and DC embryos in blastocyst transfer.

DESIGN: This was a retrospective analysis of embryos that were cultured in time-lapse incubators between December 2016 and December 2018 and then a single frozen-thawed blastocyst was replaced.

MATERIALS AND METHODS: Part 1: After confirming the 2 pronuclei, we targeted 1177 embryos that had been cultured at time lapse for up to 7 days and were frozen in blastocysts (Blast3 ≦, not including CC) and

transferred by singly.The pregnancy and miscarriage rates were compared for three groups: normally dividing embryos (normal division group, n=933), Abnormal direct cleavage at the first division (DC1 group, n=164) and Abnormal direct cleavage at the second division (DC2 group, n=80).Part 2: We compared the prognosis of the three groups in 176 cases. We examined the average body weight (37-41 weeks of term birth), male-female ratio, birth defect rate, preterm birth rate, Caesarean section rate, and average apgar score.Statistical significance was analyzed by Ryan method and Steel-Dwass test multiple comparisons.

RESULTS: Part 1: The pregnancy rate was 49.0% (457/933), 35.4% (58/164), and 48.8% (39/80) in the normal division group, DC1 group, and DC2 group, DC1 group was significantly lower than that in the normal division group. ($p < 0.05$)The miscarriage rates were 19.9% (91/457), 20.7% (12/58), and 25.6% (10/39), respectively, showing no difference.Part 2: Average body weights were 3141.6 ± 486.6 ($n = 130$), 3097.3 ± 331.9 ($n = 17$), 2823.3 ± 468.6 ($n = 10$) in the normal divided, DC1, and DC2 group, respectively. Male-female ratio (male / female) was 1.20 (79/66), 1.25 (10/8), 1.75 (7/4), congenital anomaly rate was 2.7% (4/147), 0% (0/18), 0 % (0/18), premature birth rate was 9.2% (12/143), 5.9% (1/18), 10.0% (1/11), Caesarean section rate (Caesarean section / total) was 32.6% (47/144) , 27.8% (5/18), 45.5% (5/11), and the average apgar score was 8.4 ($n = 114$), 8.0 ($n = 15$), 7.9 ($n = 11$), showing no difference between the 3 groups.

CONCLUSIONS: The DC1 embryo had a lower pregnancy rate than the normal dividing embryo, but the miscarriage rate was not different between the DC1 embryo and the normal dividing embryo. DC2 embryos were not different from normal division embryos in terms of pregnancy and abortion rate. From the prognosis of childbirth, it was suggested that both DC1 and DC2 embryos may have the same results as normal dividing embryos.These results demonstrate that the pregnancy rate of blastocysts from DC1 embryos was lower, however if the blastocyst stage is reached in DC1 and DC2 embryos replacement should be considered if there are no other blastocysts available.

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THE COMPARABLE BIRTH OUTCOME OF YOUNGER AND OLDER PATIENTS. IS THIS POSSIBLE?. Oscar Perez, Ph.D.,[1] Hannalie Adriaanse, BS,[1] Gabriella Navarrete, BS,[1] Breanna Tilley, MSc,[1] Linda Lay, BS,[1] Lucille M. Little, BS,[1] Jessica Kozlowski, B.S.,[1] Ravi Gada, MD,[2] Laura Lawrence, MD,[2] Karen Lee, M.D.,[2] Mika R. Thomas, MD,[2] Samuel J. Chantilis, MD[2] [1]Dallas Fertility Center, Dallas, TX; [2]Dallas-Fort Worth Fertility Associates, Dallas, TX.

OBJECTIVE: Women of advanced age (≥ 41 years old) are an expanding reproductive age group; however, it is well known that fertility is remarkably reduced with the increasing age of women using assisted reproductive technologies (ART). Technology tools such as preimplantation genetic testing (PGT) offer the possibility to combine ART procedures for selecting embryos with higher implantation potential. The objective of this study was to compare the implantation rate and birth outcome of patients ≤ 34 years old (younger patients) and patients 41-44 years old (older patients) that underwent frozen embryo transfer (FET).

DESIGN: Data were prospectively collected over four years for all patients (n=1299) undergoing FET.

MATERIALS AND METHODS: Patients using autologous oocytes who underwent primary and secondary FET's from January 2016 to August 2019 were divided into four groups. Younger patients with PGT (n=393), younger patients without PGT (n=775), older patients with PGT (n=85), and older patients without PGT (n=46). The FET's were a combination of primary and secondary transfers. For patients with a primary frozen embryo transfer, the rates were 55% for the younger and 56% for the older patient groups. Vitrified blastocysts were thawed using rapid warm™ Blast (Vitrolife) and cultured in G2™ (Vitrolife) plus 20% protein for one hour and then transferred to the transfer dish containing hyaluronan for at least 3 hours before the embryo transfer. Chi-square analysis was applied to detect differences in the clinical and birth endpoints.

RESULTS: As expected, differences were observed in the implantation rates between younger patients and older patients with FET without PGT treatments. Similarly, the birth outcomes in patients without PGT treatment showed the same result. The implantation rates and birth outcomes for FET and PGT procedures are summarized in the table 1.

CONCLUSIONS: Data from this study suggest that implantation rate and birth outcome when offering FET and PGT are increased in older patients. These outcomes were constant for over four years. Patients between 41 and 44 years old who have euploid frozen embryos can obtain similar high implantation and birth outcomes when compared with younger patients in the ≤ 32 years old group.

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PROGNOSTIC VALUE OF OOCYTE QUALITY IN *IN VITRO FERTILIZATION* OUTCOMES: A SYSTEMATIC REVIEW. Nicole Mercado Fischer, MPH,[1] Ha Vi Nguyen, MD,[2] Bhuchitra Singh, MD, MPH, MS,[3] Valerie L. Baker, MD,[4] James Segars, MD[3] [1]Johns Hopkins University School of Medicine, Division of Reproductive Endocrinology and Infertility, Baltimore, MD; [2]Johns Hopkins School of Medicine, Baltimore, MD; [3]Johns Hopkins University School of Medicine, Baltimore, MD; [4]10751 Falls Road, Lutherville, MD.

OBJECTIVE: The development of an objective and accurate test to assess human oocyte quality remains an important goal of reproductive medicine. The aim of this study was to survey and critically assess current methodological innovations used to test oocyte quality that have prognostic value in predicting *in-vitro* fertilization (IVF) outcomes.

DESIGN: Systematic review.

MATERIALS AND METHODS: Following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, we surveyed published literature between January 1st, 2010 and December 31st, 2019 using PubMed, Scopus, and Embase databases. Two reviewers screened for English-language articles regarding the predictive value of oocyte quality markers for IVF outcomes of interest including fertilization rate, embryo quality, implantation rate, pregnancy, continued pregnancy, and live birth rate. Articles that did not mention oocytes, or focused on non-human subjects, oocyte aging, oocyte maturation, embryo quality markers, oocyte quality interventions, or specific clinical diagnoses (endometriosis and polycystic ovarian syndrome) were deemed outside the scope of this analysis and excluded.

RESULTS: Twenty-seven relevant articles were identified, including 19 prospective and 8 retrospective cohort studies (n=3,472 patients). We identified three general approaches for oocyte quality assessment: morphological evaluation by embryologist (12 papers), genomics and proteomics (13 papers), and artificial intelligence classification systems using oocyte images (2 papers). Morphologic assessment, while a mainstay of clinical practice, did not show a consistent pattern of strong predictive value in IVF outcomes (7 papers in favor of its predictive value, 5 against). A considerable proportion of genomic and proteomic articles identified potentially promising biomarkers that may predict pregnancy and live birth rates (12 in favor, 1 against). Artificial intelligence is a more recent and rapidly growing method which minimizes subjectivity while potentially improving predictive ability (2 in favor).

CONCLUSIONS: Modern oocyte quality assessment research largely entails morphological evaluation, genomics/proteomics, and artificial

TABLE 1. Implantation rate and birth outcome in younger (≤ 34 years old) and older patients (41-44 years old).

	Implantation Rate n (%)		Birth Outcome n (%)	
Age Group	FET and Non-PGT	FET and PGT	FET and Non-PGT	FET and PGT
≤ 34 Years Old	549/976 [a] 56%	276/438 [a] 63%	376/775 [a] 49%	211/393 [a] 54%
41-44 Years Old	24/69 [b] 35%	61/97 [a] 63%	12/46 [b] 26%	47/85 [a] 55%

The numbers within columns with different superscripts indicate significant differences ($P<0.05$).

intelligence to predict reproductive success. Contemporary reproductive scientists, embryologists, and clinicians should be familiar with these strategies, which have the potential to move the field forward with substantial improvement in predicting patient reproductive outcomes and identifying potential targets for future therapies. Although there remains a lack of consensus on optimal methods, artificial intelligence and genomics demonstrate promise in improving understanding of oocyte quality assessment and prognostication.

References: None.

SUPPORT: None.

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ASSOCIATION OF MITOSCORE AND TIME TO BLASTULATION: EVALUATION AS PREDICTORS OF REPRODUCTIVE OUTCOMES AFTER SINGLE FROZEN EMBRYO TRANSFER. Janet Bruno-Gaston, MD, Luwam A. Ghidei, MD, Yadav Ghanshyam, MD, Chellakkan Selvanesan Blesson, PhD, William Gibbons, MD Baylor College of Medicine, Houston, TX.

OBJECTIVE: Evaluate the correlation of mitoscore and time to blastulation (TTB) among euploid embryos and its predictive value on reproductive outcomes

DESIGN: Single-center retrospective cohort study

MATERIALS AND METHODS: We performed a retrospective chart review of patients who underwent IVF with ICSI and pre-implantation genetic testing for aneuploidy (PGT-A) with mitoscore (Igenomix) from 10/2017 to 12/2019. Embryos were cultured in a time-lapse incubator and timing to blastulation (TTB) was recorded. Medical records were reviewed for patient demographics and FET cycle characteristics. The primary outcome was to assess correlation of mitoscore and TTB. Secondary outcomes included implantation and ongoing pregnancy, defined as cardiac activity on ultrasound at 10wks gestation or later. Spearman correlation analysis was performed to assess association of mitoscore and TTB, and a $p < 0.05$ was considered statistically significant. Statistical analyses were done between patient groups using t-test or Mann-Whitney U test. Logistic regression was applied to assess predictors of implantation and pregnancy.

RESULTS: We identified 137 patients with 465 embryos and 145 frozen embryo transfers (FET). We found an overall implantation rate of 68.3% (n=99) and ongoing pregnancy rate of 53.7% (n=78). A significant correlation between Mitoscore and TTB ranking were found among all embryos (ρ=0.54, p< .0001, 95%CI 0.47-0.60). This positive correlation persisted amongst patients with implantation (ρ=0.52, p<0.001, 95% CI 0.36-0.65) and no implantation (ρ=0.44, p<0.002, 95% CI 0.17-0.65) following single FET. We noted no differences in mitoscore or TTB among patients with or without implantation (Mitoscore p=0.61, 95%CI -2.31 to 1.43: TTB p=0.41, 95%CI -3.77-1.55) or ongoing pregnancy (Mitoscore p=0.28, 95%CI -2.66-7.60: TTB p=0.92, 95%CI -2.29-2.52). Logistic regression of demographics, FET cycle characteristics, mitoscore and TTB revealed no predictors of implantation. Factors including age, BMI, parity, endometrial thickness, and FET protocol were not different between implanted vs. non-implanted groups.

CONCLUSIONS: Mitoscore and TTB are correlated amongst euploid embryos. However, neither was found to be an independent predictor of implantation. Continued efforts to refine embryo selection outside of ploidy status may help address implantation failure following single euploid FET.

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OFFSPRING GENDER RATIO AFTER SPERM CO-INCUBATION WITH ENDOMETRIAL CELLS PRIOR IVF. Rumiana Ganeva, MSc, Dimitar Parvanov, PhD, Kristina Nikolova, MSc, Georgi Stamenov Stamenov, MD/PhD Nadezhda Women's Health Hospital, Sofia, Bulgaria.

OBJECTIVE: To observe and compare the offspring gender ratio in couples who had co-incubation of spermatozoa with human endometrial cells prior IVF and patients with conventionally performed IVF.

DESIGN: Observational.

MATERIALS AND METHODS: Data on the offspring gender of 106 couples who had sperm co-incubation with the partners' endometrial cells prior IVF (study group) and 104 couples who reached labour after conventional IVF (control group) was recorded.

Cells obtained from endometrial biopsies were cultivated in DMEM F12 10% FBS for 48 hours at 37oC and 5%CO_2. On the day of the follicular punction washed semen was incubated for 2 hours with the confluent endometrial cells followed by conventional IVF protocol.

Statistical analysis was performed by Chi-square test using SPSS v.21. P<0.05 was considered significant.

RESULTS: The conventional IVF group and the sperm co-incubation group were comparable in age, BMI, oocyte quality and number of unsuccessful ART procedures.

The female to male ratio in the conventional IVF group was 1:1.08 (female:male) with 48.1% females and 51.9% males.

Live births after sperm co-incubation with endometrial cells prior IVF resulted in significantly more female than male babies (63.2% vs. 36.8%, respectively, p<0.05) with gender ratio 1.71:1 (female:male).

When the gender ratios were compared between the two groups, female proportion was significantly higher in the co-incubation group in comparison to the control group (p<0.05).

CONCLUSIONS: Our data show that spermatozoa co-incubated with endometrial cells prior IVF skews the sex ratio of the offspring to favor females. This observation suggests that co-incubation of spermatozoa with endometrial cell culture may lead to preferential hyperactivation of human spermatozoa bearing X chromosome. More studies are needed to analyze the effect of the endometrial cell culture on spermatozoa.

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EXCESSIVE TRIMMING OF CUMULUS CELLS IS ASSOCIATED WITH LOWER FERTILIZATION RATES AFTER CONVENTIONAL INSEMINATION. Carlos A. Guerrero, Ph.D., Jennifer A. Rodriguez, B.Sc., Daniel Skora, M.D., Rebecca A. Chilvers, M.D., Satin S. Patel, M.D., Jerald S. Goldstein, M.D. Fertility Specialists of Texas, Frisco, TX.

OBJECTIVE: Trimming of cumulus cells during the oocyte retrieval procedure is a common practice. The objective of this study was to evaluate the effect of excessive trimming of cumulus cells on normal and abnormal fertilization rates after conventional insemination.

DESIGN: Retrospective analysis of data collected from January 2018 through January 2020. Patients were divided into two treatment groups based on different levels of cumulus cell trimming after follicular aspiration: A) minimal trimming (most layers of cells remain) and B) excessive trimming (few layers of cells remain). Laboratory end points were analyzed using t-test and Chi-square test as appropriate.

MATERIALS AND METHODS: Patients ≤35 years old undergoing IVF with conventional insemination (n=291) were used in this study. Oocytes

TABLE 1. Effect of cumulus cell trimming on fertilization and blastocyst rates.

Cumulus Cell Trimming Level	# of Patients	Avg. # Mature Oocytes	Normal Fertilization Rate (%)	Abnormal Fertilization Rate (%)	Blastocyst Rate (%)
Minimal Trimming	120	14.1[a]	1291/1613 (80%)[a]	139/1613 (8.6%)[a]	881/1291 (68%)[a]
Excessive Trimming	171	14.4[a]	1841/2589 (71%)[b]	287/2589 (11.1%)[b]	1230/1841 (67%)[a]

[a,b] Different superscripts within columns indicate significant differences (P<0.05)

were trimmed using two 25g needles immediately after follicular aspiration. Oocytes were then inseminated with 150 m/ml motile sperm 4-6 hours post oocyte retrieval and cultured overnight in P-1 medium. Fertilization was assessed 17-19 hours post insemination. Zygotes were cultured in sequential G-1/G-2 media under 6% CO_2, 5% O_2 and 89% N_2 at 37.1℃. Patients with abnormal semen parameters based on WHO 5th Edition guidelines were excluded from this study.

RESULTS: There was a higher normal fertilization rate when oocytes were minimally trimmed during the oocyte retrieval procedure. In addition, abnormal fertilization increased when cumulus cells were trimmed excessively (Table 1). No difference was noted between treatment groups for patient age, average number of mature oocytes and blastocyst rate.

CONCLUSIONS: These findings suggest that cumulus cells should be minimally trimmed during the oocyte retrieval procedure to increase normal fertilization rates and reduce the number of oocytes fertilized abnormally.

SUPPORT: None.

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EMBRYO CULTURE WITH SEQUENTIAL VS SINGLE STEP MEDIA: EFFECT ON EUPLOID RATES?. Krishna Mantravadi, Sr., MBBS, PGDHOM, Masters in clinical embryology, Gayathri Gedela, Master in Clinical Embryology, Durga Gedela Rao, Sr., MRCOG, Sandeep Karunakaran, Sr., MS, PGDHM, PGDMLE Oasis fertility, Hyderabad, India.

OBJECTIVE: The aim of this study was to see whether the mode of embryo culture based on the kind of media use (Sequential Vs Single step media) had an effect on the euploidy rate

DESIGN: Retrospective Case Control Comparative Study. Private Fertility Clinic

MATERIALS AND METHODS: Patients who have opted to go for Pre-Implantation Genetic Testing for Aneuploidy (PGT-A) for selection of embryos were included in the study (May 2014 - January 2020) (n=335). The total number of embryos biopsied was 1323 embryos

All the biopsies and tubing were performed by one operator and the embryos were cultured in the bench top incubator with low oxygen culture condition. All things being constant, the only variable was the media used for culturing the embryos. Sequential media was from COOK Medicals & Single step media was from Cooper Surgicals, Origio. The patients were divided into 2 groups: Group A (n=167): Sequential Media, Group B (n=168): Single Step Media. All the oocytes were subjected to ICSI. They were cultured till Blastocyst and on Day 5 TE biopsy was done and frozen as per our clinics standard operating protocols. The biopsied samples were sent for PGT-A testing, done by next generation sequencing (NGS). The euploidy rate was calculated in both the groups. Study groups were further sub classified based on age of women (<37 years - young age & >37 years - advanced maternal age) and euploidy rates were assessed. This was done to eliminate bias from age.

RESULTS: The mean embryo euploidy rate was calculated in both the groups (Group A) 35.30% and (Group B) 36/6%.

Euploid rates based on age stratification were:

Group A - Younger women had euploidy of 39.74% Vs Older women 27.2 %

Group B - Younger women had euploidy of 40 % Vs Older women 28 %

Choice of culture media does not seem to affect the euploid status of the embryos. We did an age stratification to rule out age related decrease in the euploidy status. Advanced maternal age with either sequential or single step media did not seem to affect the euploid rates of the embryos.

CONCLUSIONS: Sequential or Single step culture media in the embryo culture system do not seem to have an effect on the policy status of an embryo. Based on the data from this study we can opt to use any system of media for embryo culture.

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IMPACT OF BLASTOCYST MORPHOLOGY GRADING ON PREDICTING IMPLANTATION OF EUPLOID EMBRYOS IN GESTATIONAL CARRIERS. Jordana Mashiach Friedler, MD MHA,[1] Michal Dviri, MD,[2] Anjila Roumia, MD,[3] Noga Fuchs Weizman, MD,[1] Shira Baram, MD,[1] Clifford Lawrence Librach, MD[1] [1]CReATe Fertility Centre, Toronto, ON, Canada; [2]University of Toronto, Toronto, ON, Canada; [3]CReATe fertility centre, Toronto, ON, Canada.

OBJECTIVE: Our study aimed to investigate the correlation between static morphology of euploid embryos and pregnancy outcome in the optimal setting of sFET to a Gestational carrier (GC).

DESIGN: Retrospective cohort study. We reviewed all the single FET using euploid embryos and GCs at CReATe fertility center, Toronto Canada between Jan 2017 and Mar 2019. Mosaic embryo transfers were excluded. Only GC were included to eliminate other factors that may impact implantation.

MATERIALS AND METHODS: Blastocysts were graded immediately before TE biopsy according to the degree of expansion and ICM and TE morphology. using a modified SART method. The grading was as follows: ICM A-round/oval, tightly packed/compacted cells; B- not oval, partly spread and some tight cells; C-small/few cells and loosely group; D-seldom scattered cells, no visible cohesion, empty and degenerating. TE: A-many highly compacted cells, cohesive epithelium; B- few, slightly larger cells, continuous epithelium; C-less, larger cells, no continuous epithelium; D-very few cells, around 2-5 cells, degenerating. All embryologists are trained in order to minimize inter-observer variability in embryo grading, and standardize their biopsy technique. All PGT samples were analyzed using standard NGS methodology and reported as euploid, aneuploid or mosaic. The GCs have all had at least one successful pregnancy of their own, and went through an evaluation that included a medical assessment, lab testing and anatomical investigation of their uterus via pelvic ultrasound and sonohysterography. All FET were preformed using a HRT primed protocol of estrogen either PO, trans-dermal or both. After achieving a sufficient endometrial thickness of at least 7mm, progesterone, either IM or vaginal was added and timed with the embryo transfer. Ongoing pregnancy (OGP) is defined as a pregnancy passed 12 weeks gestation. Implantation was regarded as all patients that had either biochemical pregnancies, early miscarriages and OGP or Live birth.

RESULTS: 319 euploid embryo transfers to GCs were identified. The following data was collected: age at OPU, type of HRT preparation and endometrial thickness at day of Progesterone initiation. We compared pregnancy and implantation rates in groups according to ICM grade , TE grade and built a three tier system in which AA,AB,BA were regarded -GOOD; CA,CB,AC,AB were regarded FAIR; CC, DA, DB, DD, AD, BD, CD were regarded POOR - P>0.05 . Implantation and pregnancy rates of the euploid embryos were similar in all groups regardless of the morphology grading.

CONCLUSIONS: In euploid embryos morphologic grading of ICM or TE alone or in combination was not found to be a predictor of implantation or pregnancy. Therefore, other strategies for prioritization of euploid embryos should be explored to help prioritize embryos and maximize pregnancy rates per transfer.

P-65 4:30 PM Saturday, October 17, 2020

EFFECT OF LASER-ASSISTED HATCHING ON CLINICAL AND NEONATAL OUTCOMES IN PATIENTS UNDERGOING SINGLE VITRIFIED-WARMED BLASTOCYST TRANSFERS. Yuji Endo, Ph.D,[1] Yoshitaka Fujii, Ph.D,[2] Shingo Mitsuhata, M.S.,[2] Momoko Hayashi, B.Sc.,[2] Hiroaki Motoyama, MD.[3] [1]Chief Embryologist, Kurashiki, Japan; [2]Embryologist, Kurashiki, Japan; [3]Chief doctor, Kurashiki, Japan.

OBJECTIVE: The American Society for Reproductive Medicine recommends minimal use of assisted hatching (AH) procedures for all patients undergoing *in vitro* fertilization (IVF), due to poor live-birth data and increased risk of multiple pregnancies (1). However, it can still be disputable considering that no comparison was made between various techniques of AH, different stages of embryo, and types of cycle. Thus, there is a clash of viewpoints in term of AH effectiveness. Furthermore, very few follow-up studies of newborns after AH have been reported. This study aims to determine the effect of laser-AH on clinical and neonatal outcomes in patients undergoing IVF using single vitrified-warmed blastocyst transfers.

DESIGN: A retrospective, observational study.

MATERIALS AND METHODS: During June 2014 and March 2018, a total of 453 warmed blastocyst transfer cycles, including 279 patients (mean age = 34.0±3.9) were analyzed; of which, 231 cycles were treated by laser-AH and 222 cycles with no treatment were used as control. The day 5 blastocyst before vitrification that was expanded and had a good quality was enrolled in this study. During blastocyst warming, multiple laser beams cut off a small section of the zona pellucida (ZP) area where empty perivitelline space was found. After an overnight culture, a re-expanded blastocyst that had survived was transferred and followed up until the delivery of a

newborn. The primary outcome was live-birth rate. Secondary outcomes were completely hatched rate, clinical pregnancy rate, and neonatal outcomes, including the average gestational weeks, birth weight, malformation rate, and twin-birth rate.

RESULTS: Following overnight culture, the completely hatched rate was significantly higher in AH treatment group than in the nontreatment control group (90% versus 3%, respectively, P<0.01). The quality of the transferred blastocysts was comparable between the two groups. However, statistically, AH group had a significantly higher clinical pregnancy (49% versus 37%, P<0.01) and live-birth delivery (42% versus 27%, P<0.01) rates compared to the control group. Neonatal data were collected from 84 babies in the AH group and 55 babies in the control group. No differences were observed between both groups with respect to the average gestational weeks (39±1.6 weeks vs. 38±3.5 weeks), birth weight (3029±411 g vs. 3003±702 g), and malformation (0% vs. 2%) in newborns, respectively (P>0.05). All of them were single live births.

CONCLUSIONS: The laser-AH treatment increased live-birth rate after the transfer of a vitrified-warmed blastocyst and had no adverse effects on neonatal outcomes. The warmed blastocyst with partially removed ZP encouraged the hatching processes without cell trapping and slitting. The laser-AH did not increase the risks of multiple pregnancies after single blastocyst transfer; however, the low number of outcomes limits this interpretation. Our findings are consistent with the findings of Alteri et al. (2) who systematically evaluated the AH results of all available publications.

References:
1. Fertil Steril. 2014;102:348-51.
2. J Assist Reprod Genet. 2018;35:367-91.

SUPPORT: Not applicant.

P-66 4:30 PM Saturday, October 17, 2020

SHORT ABSTINENCE IS A GOOD STRATEGY FOR TREATING VERY SEVERE OLIGOASTHENOTERATOSPERMIC (OAT) COUPLES.

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OBJECTIVE: Sexual abstinence is considered one of the several factors that influence sperm quality. Recent studies show that a shortening could be beneficial mostly in OAT patients. The present study has the objective to study the efficiency of a second semen sample produced after a short abstinence in severe OAT infertile patients.

DESIGN: retrospective study. 127 cycles performed at our University Hospital Infertility Center (May 2014 - May 2018) were divided into two groups:

Group 1 (Study Group): 75 cycles. Very severe OAT patients with the following characteristics on the day of treatment:

1) count < 0.2x106/ml, without progressive motility;
2) count > 0.2x106/ml, and no total or progressive motility;
3) 0% normal morphology.

Two samples were requested.

Group 0 (Control Group): 52 cycles. Normospermic or light OAT patients programmed for treatment the same day of at least one couple of Group 1.

Semen parameters and outcomes were compared between Groups.

MATERIALS AND METHODS: Group 1: 75 cycles (59 fresh, 16 with thawed oocytes), Group 0: 52 cycles (43 fresh, 9 with thawed oocytes). Ovulation was induced with r-hCG administered 36h before oocytes retrieval. Oocytes cryopreservation were carried out by vitrification/warming. ICSI was utilized as insemination technique for all oocytes.

RESULTS: women's mean age Group 1 (36.96±3.95) and Group 0 (37.4±3.92) and men's mean age Group 1 (40.57±5.49) and Group 0 (40.56±5.41) were not significantly different ($P = .834$, $P = .954$ respectively). Conventional semen parameters were compared between sample of Group 0 vs 1° sample of Group 1. All parameters, excluding volume, resulted significantly different (*P<.001)*. The same comparison was done between 1° and 2° sample of Group 1. Significant differences were found between volume, total and progressive motility ($P < 0.001$).

The percentage of utilization of Group 1 semen samples for ICSI was as follows: 1° sample (6/70) 8.6%; 1°+2° samples (18/70) 25.7%; 2° sample (46/70) 65.7%.

A total of 383 oocytes (321 fresh and 62 thawed) were inseminated.

Fertilization, pregnancy rate/transfer, implantation and miscarriage rates were 63% and 86% ($P<.001$), 34.8% and 30.6% ($P = .78$), 23.3% and 17.5 ($P = .35$), 25% and 20.0% ($P = .002$) in Group 1 and Group 0 respectively.

CONCLUSIONS: Results show that short abstinence in severe OAT patients allows us to obtain sperms with better motility to be used for ICSI. The request of a second semen sample in couples with extreme semen parameters is a valid and simple strategy that helps to obtain the same probability of pregnancy compared to a Control Group. Furthermore, it allows us to utilize fresh sperms avoiding to resort to cryopreserved reserve or testicular surgery.

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GDF9 IN DAY 3 EMBRYO CULTURE MEDIUM IS A STRONG PREDICTOR OF EMBRYO QUALITY.

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OBJECTIVE: To explore the whether the concentration of GDF9 in Day 3 culture medium can be used as non-invasive biomarker for predicting embryo quality.

DESIGN: Prospective study.

MATERIALS AND METHODS: A total of 70 patients who obtained at least 2 transferable and 2 untransferable embryos with 6-12 blastomeres at Day 3 were enrolled into the present study. Four spent culture medium corresponding to the 2 good quality embryos and 2 bad quality embryos from each patient were collected. The concentration of GDF9 in embryo culture medium was quantified by ELISA. Statistical analyses defined correlations between GDF9 concentration and embryo quality.

RESULTS: Good-quality embryos exhibited a significantly lower concentration of GDF9 compared with bad-quality embryos, suggesting that GDF9 in culture medium is an objective marker for embryo quality assessments. The GDF9 concentration in the medium increased with the increasing of embryo fragmentation. The receiver operating

characteristic curve for good-quality embryos by GDF9 concentration in the culture medium had an area under the curve of 0.785, and using a threshold of 796.5 pg/ml, sensitivity and specificity values were 61.31 and 89.47 %, respectively.

CONCLUSIONS: The determination of GDF9 concentration in the culture medium can be used to predict good-quality embryos.

SUPPORT: No

P-68 4:30 PM Saturday, October 17, 2020

COMPARABLE PREGNANCY OUTCOMES BETWEEN HIGH-SCORE BLASTOCYSTS WITH LOWER EXPANSION GRADE ON DAY 5 AND HIGHER EXPANSION GRADE ON DAY 6: AN ANALYSIS OF 1751 FROZEN-THAWED CYCLES.

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OBJECTIVE: To identify blastulation and expansion grade predictive of pregnancy and live births outcomes with high-score blastocysts in frozen-thawed transfer cycles.

DESIGN: A retrospective study was conducted with clinic-based data in the Reproductive Medicine Centre of the Sixth Affiliated Hospital of Sun Yat-sen University from February 2014 to April 2020.

MATERIALS AND METHODS: High-score blastocysts frozen on day 5 (grade 3AA, 3AB, 3BA or 3BB) or day 6 (grade ≥4 and neither C grades in the evaluations of ICM nor TE) using vitrification-freezing protocol were included. Endometrial preparation was carried out with natural cycle, hormone replacement cycle or controlled ovarian hyperstimulation cycle accordingly. Progesterone administration was commenced when the thickness of endometrium reached 8 mm or more. Single embryo was transferred on day 5 after ovulation or progesterone supplementation. Difference in baseline characteristics, characteristics of embryo transfer cycles and clinical outcomes between two groups were assessed. Statistical analyses were performed stratified by age and anti-Müllerian hormone (AMH).

RESULTS: A total of 617 blastocysts in day 5 group and 1134 blastocysts in day 6 group were assessed. As a whole, patients in day 5 group were

younger than patients in day 6 group (34.22 versus 34.73, P = 0.041). No significant differences were observed in characteristics of transfer cycles, clinical pregnancy rate and live birth rate between groups. Stratified analyses showed that the biochemical pregnancy rate and clinical pregnancy rate were higher in day 5 group for patients aged below 30 years (60.6% versus 43.8%, P = 0.001 and 55.8% versus 38.2%, P < 0.001, respectively) when basic patient demographics were comparable, while rates of miscarriage, ongoing pregnancy and live birth were similar between groups. No significant differences were found in pregnancy outcomes for patients in other subgroups (31 to 35 years, 36 to 40 years, > 40 years). Stratified by AMH (< 1.1 ng/ml or ≥1.1 ng/ml), pregnancy outcomes were all comparable between day 5 group and day 6 group.

CONCLUSIONS: In frozen-thawed transfer cycles, the pregnancy potential of high-score blastocysts with lower expansion grade on day 5 and higher expansion grade on day 6 are comparable for patients aged above 30 years.

SUPPORT: Supported by the National Natural Science Foundation of China [grant number 81871214] and National Key R&D Program of China [grant number 2017YFC1001603]

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EFFECT OF TROPHECTODERM GRADE OF BLASTOCYST AT EMBRYO TRANSFER ON PREGNANCY OUTCOMES.

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OBJECTIVE: To evaluate the effect of trophectoderm vs. inner cell mass grade of blastocyst at time of embryo transfer on pregnancy outcomes.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients undergoing both fresh and frozen-thawed single embryo transfer (ET) from January 2017 to March 2020 in our center were included. Following a standard FET protocol, vitrified blastocysts were rewarmed on the day of ET and images of the thawed embryo were taken prior to transfer. Similarly, images of fresh embryos prior to transfer were taken. These images were reviewed by at least two embryologists and each were assigned a grade by Gardner's blastocyst grading scale. High quality grades were defined as A or B grades. Fair quality grades were defined as C grades. Groups for analysis included blastocysts with both high quality inner cell mass and trophectoderm grades (group A), blastocysts with high quality inner cell mass grade and fair trophectoderm grade (group B), and blastocysts with fair quality inner cell mass grade and high trophectoderm grade (group C). Primary outcomes included: pregnancy, clinical pregnancy, miscarriage, and ongoing pregnancy and live birth. Statistical analyses were done using ANOVA for continuous data and Chi Square for dichotomous outcomes.

RESULTS: A total of 531 fresh and frozen single ET cycles were analyzed in the study. There were 384 group A embryos, 129 group B embryos, and 18 group C embryos. The mean age, BMI, and endometrial thickness was not significantly different between the groups (p=NS). There were no significant differences in pregnancy rates (70.1% vs. 69.0% vs. 66.7%; p=NS), clinical pregnancy rates (63.3% vs. 59.7% vs. 61.1%; p=NS), ongoing or live birth rates (53.4% vs. 48.8% vs. 38.9%; p=NS) or miscarriage rate (8.6% vs. 10.1% vs. 22.2%; p=NS) between group A, B, and C, respectively. The majority of transferred embryos were of high quality inner cell mass and trophectoderm grades (72.3%).

CONCLUSIONS: There appears to be no difference in pregnancy outcomes when comparing high quality inner cell mass grade with fair quality trophectoderm grade vs. fair quality inner cell mass quality and high quality trophectoderm grade. Thus, this study demonstrates that the grade of trophectoderm does not have a greater impact than that of the inner cell mass on pregnancy outcomes, as had been hypothesized and shown in other studies. Further, embryos with both fair inner cell mass and trophectoderm grades have potential for good pregnancy outcomes. Morphology evaluation is subjective and dependent on embryologist assessment; therefore, each center should perform their own data analysis in order to establish a morphology standard for embryo selection for transfer.

P-70 4:30 PM Saturday, October 17, 2020

IS IT POSSIBLE TO PREDICT THE RESULT FOR THE TUNEL ASSAY FROM A ROUTINE SPERMOGRAM ANALYSIS?.

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OBJECTIVE: to investigate the spermogram parameters which might have an association with sperm DNA fragmentation.

DESIGN: cross-sectional study.

MATERIALS AND METHODS: This study was performed between December 2013 and December 2019. Routine spermograms and sperm DNA fragmentation tests (TUNEL) were performed in 600 samples by the same observer in a Fertility Center in Buenos Aires. Spermogram parameters were recorded according to WHO guidelines. The dependent variable was the TUNEL test, which was confronted to the rest of the spermogram parameters. To estimate the predictive value for the TUNEL test we used the multiple linear regression analysis. Statistical analysis was performed with Stata 12, considering p <0.05 as a significant value.

RESULTS: The parameters associated with the possibility of predicting the TUNEL test result were: patient's age (more than 45 years old), semen volume, percentage of progressive motility and total sperm retrieved in the swim up. The model showed a significant difference (test F <0,0001) and the variables included had a p < 0.05 value.

CONCLUSIONS: There is an association between some spermogram parameters and the TUNEL test. These parameters were: patient's age, semen volume, percentage of progressive motility and total sperm retrieved in the swim up. This mathematical model is particularly suited to this data set, but with a high predictive value. These results cannot be taken properly exhaustive, but as an hypothesis generator for future studies and perhaps councelor when requesting a TUNEL test. A larger sample study is required to validate these findings.

SUPPORT: None

P-71 4:30 PM Saturday, October 17, 2020

REPRODUCTIVE & PERINATAL OUTCOMES OF FRESH VERSUS FROZEN TESTICULAR SPERM IN NON-OBSTRUCTIVE AZOOSPERMIA MEN.

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OBJECTIVE: To investigate Reproductive & Perinatal Outcomes of Fresh or Frozen-thawed surgically retrieved sperms (SRS) in Non-Obstructive Azoospermia (NOA) individuals

DESIGN: Retrospective data Analysis of (n=108) patients undergoing SRS during January 2013 to June 2019.The study group was divided into two groups, Fresh SRS (n=60) and Frozen SRS (n=48) in our private IVF clinic.

MATERIALS AND METHODS: **Study Design and Duration-**Retrospective data Analysis of (n=108) patients undergoing SRS during January 2013 to June 2019.The study group was divided into two groups, Fresh SRS (n=60) and Frozen SRS (n=48) in our private IVF clinic.

Inclusion-Couples undergoing Assisted Reproductive Technique (ART) cycles where the women were < 37 years old and male partners had NOA and had a successful retrieval of sperm, were included. Only self-gamete cycles were considered.

Exclusion –Advanced maternal age (>38yrs), People with no sperm retrieval, People who did not have viable sperms after freezing and thawing.

Women underwent controlled ovarian stimulation and oocyte retrieval (OPU) as per our clinic's standard operating procedure (SOP). Male partner's

underwent SRS and testicular sperms were either used for ICSI if done at OPU or frozen and thawed for use in subsequent cycles as per SOP. Embryos cultured till blastocyst stage and freeze all policy was adopted. Couples underwent Frozen embryos transfers with two blastocysts and reproductive outcomes were evaluated.

Primary Outcome- Blastocyst Rate (BR), Implantation Rate (IR), Live Birth Rate (LBR).

Secondary Outcome-Fertilization Rate (FR), Miscarriage Rate (MR), Clinical Pregnancy Rate (CPR), Perinatal Outcomes.

RESULTS: The Reproductive outcome for Fresh and Frozen Surgically Retrieved Sperms, respectively were, **Fertilization Rate** was 92.72 % v/s 92.74 % (p value 0.9968)

Blastocyst Rate was 46.74 % v/s 35.57 % (p value 0.2444)

Implantation Rate was 43.97 % v/s 47.27 %(p value 0.7334)

Clinical Pregnancy Rate was 59.67 % v/s 73.33 % (p value 0.1390)

Live Birth Rate was 45.16 % v/s 63.33 % (p value 0.0612)

Miscarriage Rate was 4.84 % v/s 3.33 % (p value 0.6978)

Perinatal Outcomes

Both study groups had comparable perinatal outcomes with no concerning trends.

Congenital anomalies - Only One baby from fresh SRS had Anglemans syndrome.

There isn't a marked difference in the outcomes between Fresh or Frozen SRS. Freezing testicular sperms doesn't seem to alter reproductive and perinatal outcomes.

CONCLUSIONS: Frozen Testicular Sperm seem to offer comparable outcomes with Fresh Testicular sperms in ART cycles. All trial attempts for sperm retrieval should be backed up with cryopreservation.

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IMPACT OF SEMEN PARAMETERS IN INTRACYTOPLASMIC SPERM INJECTION (ICSI) OUTCOME IN FRESH OVODONATION PROGRAM. Maria Cecilia, Delpiccolo, Embryologist, Valentina Torres, Monserrat, Embryologist, Maria Noelia, Lardizabal, Embryologist, Nicolas Carizza, Gynecologist, Trinidad Leiva, Gynecologist, Estefania Navall, Gynecologist, Sofia Ana, Dominici, Gynecologist, Ariadna Sol Ruiz, Gynecologist, Carlos Carizza, Medical Director Fertya, Rosario, Argentina.

OBJECTIVE: The main objective of this study is to analyze the relationship between semen parameters and fertilization, blastulation and implantation rate in donated fresh oocytes.

DESIGN: A retrospective study comparing results obtained in fertilization, blastulation and implantation rates using fresh oocytes from young and healthy donors microinjected in the period 2017-2018. We included a total of 98 patients in the analysis, who received at least five fresh oocytes from our egg bank undergoing ICSI treatment using their partners´semen samples. Considering a successful treatment those whose fertilization rate were $\geq$70% and blastulation rate were $\geq$40%, we defined different groups of treatments (successful vs. unsuccessful, regarding fertilization or blastulation rates) and analyzed the semen parameters according to WHO (World Health Organization) within groups. We also evaluated if implantation rate was related to semen quality obtained in a previous semen analysis.

MATERIALS AND METHODS: Embryos obtained from fresh oocyte cycles of ICSI in our private clinic were incubated in K-System® G-185 incubator or ThermoFisher Scientific® Heracell 150i incubator with Sage® Medium or Global Total® Medium. Semen samples were washed and prepared using density gradient Irvine® media. The different semen parameters were previously analyzed using the software computer-aided sperm analysis (CASA) Ivos II™ Hamilton Thorn® and the Halosperm® technique to evaluate the sperm DNA damage. The Chi square independence test and Fisher's exact test was used to compare groups regarding implantation, blastulation, fertilization (2PN) rates and the different semen parameters previously analyzed in the seminogram. Statistical difference was represented by a $p<.05$.

RESULTS: Our results show that there is no statistical difference in sperm concentration between groups, considering both fertilization rates (p-value= .118) or blastulation rates (p-value= .815). The same results were obtained for sperm morphology related to successful fertilization (p-value= .459), and blastulation (p-value= .970). No relationship was obtained between DNA fragmentation and successful fertilization (p-value= .566) or blastulation (p-value= .385). An interesting result was obtained for spermatozoa motility, which shows a statistical difference in total motility related to successful fertilization rate (p-value= .039) but no difference to blastulation rate (p-value= .872). In addition, we analyzed if there was a relationship with altered seminograms values (semen analysis which shows at least one altered parameter) and implantation rate, the result showed no statistical difference (p-value= .858).

CONCLUSIONS: Analyzing different covariates we only found statistical difference in favor of total sperm motility and successful fertility rate but no statistical difference in blastulation rate. Based on our results, we can conclude that semen quality seems not to be decisive or determinant for the success of the fertilization, blastulation and implantation rate using oocytes of healthy and young patients in ICSI treatments.

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EFFECT OF CULTURE MEDIUM ON BLASTOCYST DEVELOPMENT. Deepti Tiwari, MS,[1] Caroline McCaffrey, PhD,[1] Roberto Olivares, BS TS,[1] Barry Witt, MD[2] [1]NYU Langone School of Medicine, New York, NY; [2]Greenwich Fertility and IVF Center, Greenwich, CT.

OBJECTIVE: To compare a commercial medium with our established medium in the IVF lab in terms of blastocyst formation, utilization and development.

DESIGN: Medium I was assessed for performance alongside our standard culture Medium G in a pilot sibling oocyte study. Having confirmed successful performance of Medium I a prospective comparison of both media was undertaken to compare development of thawed donor eggs. Chosen KPIs for comparison were Blastocyst Formation (BFR), Blastocyst Utilization (BUR) rates and BUR on Day 5.

MATERIALS AND METHODS: In the sibling oocyte comparison a total of 19 patients were selected based on sufficient numbers of eggs to split (N = 12). On Day 1 following fertilization check zygotes displaying 2PN from sibling oocytes were split between Media I and G, both supplemented with 10% protein supplement and equilibrated in conditions yielding manufacturers' recommended pH values. Embryo assessment was conducted on days 5, 6 and 7. Trophectoderm biopsy and subsequent blastocyst vitrification was carried out on good quality blastocysts on Days 5 through 7 as appropriate.

In the second phase of the study thawed donor eggs were placed in either Medium I or Medium G immediately following ICSI and cultured through day 7. All other culture conditions such as incubator conditions, culture dishes, culture drop volume, oil overlay etc were maintained constant in all stages of the comparison.

RESULTS: In the sibling oocyte study 19 patients yielding a total of 218 x 2PN were separated into 2 groups for culture in medium I or G. BFRs of 64% (51/80) vs 55% (72/131) (p = 0.94), BURs of 56% (45/80) vs 47% (62/131) (p = 1.0) and EU of 21% (17/ 80) vs 17% (23/131) (p = 0.83) were achieved in Medium I & G respectively. There was no significant difference in % blastocysts that developed to usable blastocysts on Day 5 in Medium I (33%) when compared to Medium G (23%) despite a trend suggesting that Media I supported a higher Day 5 blastocyst development.

The table below shows the results for the thawed donor eggs.

	Medium I	Medium G	Sig
Egg thaw N cycles	7	6	
Fert rate (2pn / # ICSI'd)	35/43 (81%)	30/49 (61%)	0.04 (Sig)
BFR (# Blast/ # ICSI'd)	23/43 (54%)	20/49 (41%)	0.30 NSD
BUR Day 5 (Usable Blasts/ # ICSI'd)	11/43 (26%)	6/49 (12%)	0.11 NSD
BUR Total (Usable Blasts / # ICSI'd)	17/43 (40%)	17/49 (35%)	0.67 NSD

CONCLUSIONS: Both culture media supported a similar proportion of blastocyst formation and utilization. Although there was no significant difference in BFR, BUR or BUR on day 5 between the 2 media this allowed the lab to maintain redundancy with culture conditions should an emergency arise with a single supply chain. In addition, it provides an extra level of QC in the lab with a media comparison

SUPPORT: No Financial support.

P-74 4:30 PM Saturday, October 17, 2020

EFFECT OF MEDIA CHANGE PARADIGMS ON THE EFFICACY OF A SINGLE STEP CULTURE MEDIUM. Rebecca Holmes, PhD, HCLD,[1] Jason E. Swain, PhD, HCLD,[2] William B. Schoolcraft, MD,[3] Rebecca L. Krisher, PhD[4] [1]CCRM Boston, Newton, MA; [2]CCRM IVF Network, Lone Tree, CO; [3]Colorado Center for Reproductive Medicine, Lone Tree, CO; [4]CCRM Colorado, Lone Tree, CO.

OBJECTIVE: Sequential and single step culture media are both popular choices embryo culture. The objective of this study was to compare the impact of sequential versus single step culture media on outcomes following different media exchange paradigms.

DESIGN: Prospective randomized trial using sibling oocytes.

MATERIALS AND METHODS: All procedures were conducted at a single IVF center and all PGT-A results were from a single genetics lab. Our objective was to study the impact of the culture medium itself so all other variables were controlled for. After ICSI, sibling oocytes were randomly allocated between two dishes containing either an in-house formulated sequential media or a single-step media (CSCM-NX, Irvine Scientific). All media were supplemented with the same lot of 10% SPS protein and cultured in a K systems G210 incubator under 4 mL oil with ~ 6% CO2 and 5% O_2. In phase I, media was exchanged following 24h (PN check), 72h (D3) and 120h (D5) of culture. In Phase II media was only exchanged at 72h. Data were analyzed using Fisher's Exact Test

RESULTS: In phase 1 with media changes on days 1, 3 and 5, although not statistically significant more blastocysts were observed in the single-step media on day 5, 6 and 7, including good quality blastocysts. However a higher aneuploidy rate was observed in the single step medium resulting overall in no more usable blastocysts. In phase II with a single media change on D3, the sequential system yielded more euploid blastocysts compared to the single step medium.

	Phase I		Phase II	
Media type	Sequential	Single step	Sequential	Single step
# patients	13	13	26	26
# oocytes	60	64	178	192
fert rate	86.7	82.8	85.4	82.8
%day 5 blasts	46.2	62.3	58.6	57.2
% day 7 blasts	61.5	73.6	70.4	71.7
% ≥3BB day 5	23.1	32.1	28.9	31.4
% ≥3BB day 7	46.15	56.60	46.7	50.9
% Euploid blast	54.17	43.33	59.6_a	45.3_b

CONCLUSIONS: A 10% increase in usable blastocysts was observed in the single-step medium when refreshed every 48. However PGT-A revealed a >10% decrease in euploid blastocysts in the single-step medium resulting in no overall difference in the percentage of transferable euploid embryos per zygote. When media refresh was done on day 3 only, there was no significant difference in usable blastocysts between the media systems. However, a significant decrease in the percentage of euploid blastocysts was observed using the single-step medium.

In our hands, this single-step media with multiple media changes results in more blastocysts available for biopsy, but did not result in more euploid blastocyst available for transfer. With a single media change there was no advantage in blastocyst development while reduced euploidy persisted. This data suggests that embryo ploidy can be affected by culture medium and sequential media is preferred based on the two media tested here.

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SINGLE-LAYER DENSITY GRADIENT CENTRIFUGATION IS A SIMPLE AND EFFECTIVE SPERM PREPARATION APPROACH IN DECREASING THE INCIDENCE OF THE CONTAMINATION ORIGINATED IN THE POTENTIAL PATHOGENS IN HUMAN SPERM SAMPLES DURING IVF PRACTICE. Yongrui Du, Ph.D. Tianjin Central Hospital of Gynecology Obstetrics, Tianjin, China.

OBJECTIVE: The aim of this study was the evaluation of single-layer density gradient centrifugation, compared with swim-up step, on decreasing the occurrence of the embryo contamination from purified sperm pellets in couples undergoing conventional IVF.

DESIGN: a retrospective cohort study

MATERIALS AND METHODS: Patients less than 45 years of age who participated in a fresh IVF-ET cycle from January 2017 to May 2020 were included in this study. Poor responders with less than three mature oocytes were excluded. Patients were requested to abstain for three days sexually. G-IVF medium (GIM) was used in combination with Single-layer density-gradient centrifugation (SDGC) or swim-up (SUP) methods for sperm preparation. A total of 2565 fresh conventional IVF cycles were grouped according to methods used for sperm preparation and retrospectively analyzed (SDGC, n=997; SUP, n=1568) differences in the incidence of bacterial embryo contamination originated in purified sperm pellets and some key performance indicators (fertilization rate, good quality embryo rate, and pregnancy rate).

RESULTS: With SDGC, we identified no patient's embryos contaminated (0/997) from purified sperm pellets during conventional IVF. With swim-up, we identified 14 (14/1568) patients' embryos bacterial contaminated. Total fertilization rates were not statistically different between the SDGC and SUP groups (86.7% vs. 83.1%, respectively, p=0.248); while significant differences were found in 2PN fertilization rate (75.8% vs. 63.5%, p=0.045), and good embryos rates (47.1% vs. 41.9%, p=0.028).

CONCLUSIONS: Centrifugation through single-layer density gradient centrifugation efficiently diminished the bacterial contamination if strict aseptic techniques were also used.

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INCREASING THE AMOUNT OF LEARNING DATA FOR DEEP LEARNING IS EFFECTIVE IN IMPROVING THE AUTOMATIC PRONUCLEUS NUMBER DETECTION SYSTEM FOR HUMAN EMBRYOS. Hiroya Kitasaka, Ph.D.,[1] Noritaka Fukunaga, Ph.D.,[1] Sho Sanami, Ph.D.,[2] Hiroyuki Watanabe, M.S.,[1] Yuji Tsuzuki, M.S.,[2] Yuta Kida, M.S.,[1] Seiji Takeda, M.S.,[2] Fumiya Kondo, M.S.,[1] Sho Takeda, B.S.,[1] Yoshimasa Asada, M.D., Ph.D.[1] [1]Asada Ladies Clinic, Nagoya, Japan; [2]Dai Nippon Printing Co., Ltd., Tokyo, Japan.

OBJECTIVE: Deep Learning (DL) technology is a set of machine learning techniques to train artificial neural networks, which are systems that mimic interactions of human nerve cells. By using a neural network with multiple layers, it is possible to learn features included in data and to obtain capability to recognize images. We have already reported the development of the first automatic system to detect pronuclear number for human embryos by using DL technology. However, the detection accuracy was low in 1PN and 3PN human embryos. In this study, we examined whether the detection accuracy could be improved by increasing the amount of training data of 1,3PN embryos.

DESIGN: Prospective study using DL technology. The pronuclear number detection algorithm was constructed by using neural networks.

MATERIALS AND METHODS: Embryo images for the training data were acquired by a time-lapse incubator of the fertilization phenomena from ICSI oocytes. The captured interval was 15 minutes over 18 hours, and 32152 images taken over the time period were used. The same embryos (n=983) were used for comparison of two networks trained with different amounts of training data. A network was trained with 0PN: 14652, 1PN: 469, 2PN: 15788, 3PN: 154 images from time-lapse images in which the embryologist had visually determined the pronuclear number. Another network was trained with same number of 0PN and 2PN images and with an increased number of 1PN: 990 and 3PN: 722 images. The pronuclear number detection rates were then compared.

RESULTS: The detection rate of the pronuclear number before the increase in number of training data vs. after the increase was 100% vs 98.1% for 0PN, 29.2% vs 53.6% for 1PN, 95.0 vs 89.9% for 2PN and 0% vs 21.9% for 3PN. By increasing the amount of training data, 1PN detection rate was higher and the detection rate for 3PN was significantly improved (P <0.01, Fisher's exact test).

CONCLUSIONS: By increasing the amount of training data we have demonstrated that the accuracy of automatic pronucleus detection can be improved for 1PN and 3PN embryos. By exposing DL technology to increasingly larger amounts of data improved performance of the automatic system can be obtained. This can be usefully applied for automation of tasks such as

evaluating human pronuclear oocytes and hence it can be a powerful support tool for embryologists.

References: none.

SUPPORT: none.

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AUTOMATED IDENTIFICATION OF DEGRADED AREAS WITHIN BLASTOCYSTS BY MEANS OF ARTIFICIAL VISION.

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OBJECTIVE: to assess an artificial vision system's capabilities to identify degraded areas within blastocysts in an automated fashion, and based on information extracted from single blastocysts' micrographs.

DESIGN: prospective analysis of blastocysts' micrographs retrospectively obtained from two IVF clinics.

MATERIALS AND METHODS: images of degenerated blastocysts were retrospectively collected from a six consequtive month period. A senior embryologist manually segmentedthe degradated zones of 341 high-quality micrographs of blastocysts. From this ground truth, 10% of the images and their segmentation masks were randomly selected for testing porpuses. All images were preprocessed in four steps, and later passed through 21 different filters (e.g. entropy, Gaussian blur, Laplacian, and Sobel), convolved by 41 texture energy-kernels each, resulting in 861 textures per image. Data augmentation was used on the training set. 50 pixels were randomly selected per zone (background, embryo, and degradated) for each micrograph, and texture-based feature vectors extracted (total database of 140,600 data points), used to train a neural network (three layers with 100 nodes each, Adam optimizer and categorical cross-entropy as the loss function), during 500 epochs with a validation split of 10% of the original datasize, a callback of learning rate reduction (factor of 0.5, patience of 25 epochs, and validation loss as the monitor), and early stopping callback (patience of 60 epochs, validation loss as monitor, and a minimal delta of 0.001). With this texture-based model we computed and concatenated the five masks per image, and trained an autoencoder (AE) consisting of three convolutional and three max-pooling layer for encoding, plus three convolutional and three up-sampling layers for decoding. Model was trained with a mean squared error as the loss function, RMS prop as the optimizer, early stopping and learning rate reduction callbacks (100 epochs), with a 10% validation split. Testing dataset was assessed using Sorensen-Dice coefficient (SDC).

RESULTS: after applying data augmentation techniques, a total of 1228 images became available both for training and validation. After testing, the model obtained a mean SDC of 0.93 on all of the zones; 0.99 when using the background mask alone; 0.72 for the cell mask; and 0.77 for the degraded mask.

CONCLUSIONS: we report an accurate and automated identification of degraded areas within blastocysts, extracted from single static images, and by means of artificial vision. Although a pilot study, successful identification of degenerative patterns within a blastocyst could pave the way to improving already existing embryo classification, and time-lapse algorithms. Further identification of degenerative patterns could help to make better decisions when faced against cryopreserving extremely poor-quality embryos, or discarding "bad looking" embryos with unknown potential. The present tool could also help in the increasing interest around patterns of degradation given different protocols. A larger cohort will be needed for future studies.

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USING AN ARTIFICIAL NEURAL NETWORK (ANN) FOR PREDICTING NUMBER OF MATURE OOCYTES AT RETRIEVAL.

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OBJECTIVE: To develop a prediction model for number of mature oocytes at retrieval using an artificial neural network (ANN).

DESIGN: This was a model-prediction study based on a retrospective cohort of patients who underwent first fresh autologous in vitro fertilization cycles resulting in oocyte retrieval between the years 2016-2019 at a single academic center. Patients were included if anti-Müllerian hormone (AMH) and follicle stimulating hormone (FSH) were recorded within one year of stimulation and were excluded if an aromatase inhibitor was used during the cycle.

MATERIALS AND METHODS: Our dataset consisted of 1011 cycles and was organized into 5 training (n=808) and test (n=203) sets using K-fold cross validation. An ANN was built with the Keras API for TensorFlow and trained on this data. The neural network approximates a function which maps patient- and cycle-specific data (i.e., number of follicles, AMH values, etc.) to the main outcome measure/target variable, number of MII oocytes, using linear regression. Standard regression prediction modeling was also performed and model accuracies were compared by root mean square error (RMSE).

RESULTS: A model for predicting the number of MIIs at oocyte retrieval using parameters available on the day of trigger was designed, implemented, and is currently being beta tested online. Examples of the predicted number of MIIs according to patient- and cycle- specific parameters is shown in the Table. ANN-prediction modeling outperformed standard regression prediction modeling (RMSE: 4.3, and 4.5, respectively). When cycles were limited to those with 12 or fewer MII oocytes retrieved, the RMSE improved to 2.4.

CONCLUSIONS: We have developed a counseling tool to predict the number of mature oocytes at retrieval based on patient-and cycle-specific characteristics available on the day of trigger shot using an ANN, which outperforms standard regression prediction models, and allows for continuous prospective testing and refinement. This tool will be made available to the public following beta testing and we hope that it enhances personalized patient counseling.

	Age (y)	AMH (ng/ml)	FSH dose	Follicles >14mm	Peak E2 (pg/mL)	No. predicted MIIs
Patient 1	35	1.0	5000 IU	10	1700	7
Patient 2	35	3.0	2000 IU	10	3500	12
Patient 3	35	8.0	1500 IU	10	3700	14

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ARTIFICIAL NEURAL NETWORKS APPLIED FOR PREDICTION OF THE IMPLANTATION POTENTIAL BY USING EMBRYO MORPHOLOGY DYNAMICS.

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OBJECTIVE: To describe novel embryo morphology dynamics features capable of predicting implantation potential as input data for an artificial neural network (ANN) model.

DESIGN: A retrospective cohort study was performed including 637 patients, from the oocyte donation program of IVI Valencia, who underwent single blastocyst transfer during two consecutive years. All the embryos were cultured in a time-lapse incubator (Embryoscope Plus®). The study was divided into two phases. Phase1: analysis of the impact of novel embryo parameters on implantation. Phase 2: development of an ANN algorithm for implantation prediction

MATERIALS AND METHODS: All the embryos were evaluated with the Embryoviewer®. Novel morphodynamic parameters were measured with the drawing tools, including: distance and speed of pronuclear migration, blastocyst expanded diameter, inner cell mass area and trophectoderm cell cycle length. Conventional morphokinetic parameters (tpb2, tPNa, tPNf, t2, t3, t4, t5, t6, t7, t8, tSC, tM, tSB, tB, tEB, tHiB) and novel proposed morphodynamic parameters were used as input data for the ANN, in the following

manner: ANN1, conventional morphokinetic parameters; ANN2, novel embryo parameters; ANN3, conventional and novel embryo parameters; and ANN4, those parameters which had significant differences between implanted and non-implanted embryos. The architecture of the ANN was a multilayer perceptron (MLP) with two hidden layers and 15 neurons in each one. Dataset was divided into 85% for learning process by using 5-fold-cross-validation approach and 15% for testing the algorithm. The predictive power was measured by using the area under the curve (AUC) of the receiver operating characteristic (ROC) curve.

RESULTS: Out of the total parameters (novel and conventional morphokinetics), t4, t6, t7, t8, t9, tSC, tM, tSB, tB, tEB, blastocyst expanded diameter and trophectoderm cell cycle length had statistically different values in implanted and non-implanted embryos ($p<0.05$). The results in terms of sensitivity, specificity, accuracy, F-Score and area under the curve for the four ANN models in the testing dataset are represented in the Table I. The higher predictive power was achieved by ANN3 with an AUC of 0.77.

TABLE I.

Artificial Neural Network	Sensitivity	Specificity	Accuracy	F-Score	AUC
ANN1	0.88	0.46	0.71	0.78	0.64
ANN2	0.86	0.58	0.75	0.80	0.73
ANN3	0.82	0.67	0.76	0.80	0.77
ANN4	0.85	0.57	0.74	0.79	0.68

CONCLUSIONS: The novel proposed embryo features have influence on the implantation potential and their combination with conventional morphokinetic parameters is effective as input data for a predictive model based on artificial intelligence.

SUPPORT: The authors' research is supported by The Ministry of Science, innovation and Universities CDTI (IDI-20191102), Industrial PhD grant (DIN2018-009911) and Agencia Valenciana de Innovació (INNCAD00-18-009) awarded to M.M. and E.P.

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IMPACT OF A COMMERICALLY AVAILABLE SPERM SEPERATION DEVICE (ZYMŌT MULTI) ON SPERM DNA QUALITY COMPARED TO DENSITY GRADIENT SEPERATION WITH SWIM UP.

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OBJECTIVE: Isolation of high quality sperm is a pre-requisite for IVF/ICSI to ensure proper fertilization, embryo development and to obtain successful clinical outcomes. The quality of sperm not only entails sufficient motility and morphology, but also involves isolating sperm with high DNA integrity. Various sperm isolation methods exist and some may be superior to others with regard to obtaining sperm with intact DNA. This study compared DNA integrity of sperm isolation using a novel sperm separation device that uses sperm motility and a separation membrane (ZYMŌT Multi) or the traditional density gradient separation (DGS) followed by swim-up approach.

DESIGN: Prospective trial

MATERIALS AND METHODS: Semen samples were obtained from 30 men. All samples were split and processed using both the ZYMŌT MULTI device as well as DGS + swim-up. Briefly, the ZYMŌT preparation entailed adding raw semen to the device inlet port and obtaining isolated sperm from the outlet. DGS + swim-up entailed layer raw semen over the top of a 40%/80% gradient (Puresperm) and spinning the sample at 300xg for 20 minutes followed by two 8 minute washes (Quinn's sperm wash) at 300xg. The pellet was then overlaid by GIVF medium and motile sperm isolated from the top fraction ~1hr later. DNA fragmentation (DFI) was assessed on all isolated samples and also to the raw semen using the TUNEL assay**.** Data were analyzed using ANOVA and Tukey analysis, $p<0.05$.

RESULTS: The DFI of the raw semen was assessed. Use of both sperm separation techniques examined in this study resulted in isolation of sperm with significantly improved sperm DNA integrity compared to sperm from raw semen. There was no statistically difference in in resulting sperm DFI levels between use of ZYMŌT MULTI and DGS + swim up.

	Raw Semen	DGS +Swim-up	ZYMŌT MULTI
Avg Sperm DFI	19.2 ±2.4[a]	7.2±0.9[b]	6.7±0.9[b]

different superscripts represent statistically significant differences between treatments, $p<0.05$

CONCLUSIONS: Different sperm separation techniques can improve sperm DNA integrity compared to sperm found in raw semen. Use the commercial sperm separation device provided no increase in improvement in resulting sperm DNA fragmentation compared to careful sampling of sperm prepared via proper DGS followed by swim-up. Future studies will examine impact of the novel sperm separation device on resulting fertilization, embryo development/aneuploidy and clinical outcomes.

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MACS TECHNOLOGY APPLIED FOR SPERM SELECTION IMPROVES BLASTOCYST QUALITY; A CONTINIOUS EMBRYO MONITORING STUDY.

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OBJECTIVE: To compare the effect of Anexin-V (Magnetic Activated cell sorting) MACS sperm selection method in morphokinetic markers of embryo development, blastulation rate, blastocysts quality, implantation and fertilization rates by using time-lapse monitoring system incubators.

DESIGN: Secondary analysis from a prospective trial.

MATERIALS AND METHODS: A total of 478 patients were distributed in two groups: MACS (MG) n=243 (Swim-up+MACS) vs.Control group (CG) (swim-up)n=235 before ICSI treatment from our oocyte donation program. With the use of Time-lapse technology (Geri, Genea; Australia), we did a complete embryo follow-up with further morphokinetic analysis.

RESULTS: A total of 5232 oocytes were microinyected that were giving rise to 2437 Blastocyst in Day 5 (67.2%) in the MG and (67.9%) (P=0.664). No notable differences between morphokinetic parameters when compared both groups (MG and CG) particularly at early cleavage stages embryos t2(28.36 (95% CI28.05-28.67)-(28.36 (95%CI28.04-28.68)), t3(38.35 (95% CI38.03-38.67)- 38.40 (95%CI38.04-38.76)) and t4(40.84 (95%CI40.40-41.18)-41.37(95%CI40.97-41.77)) were demostrated. These differences were found in t5(51.15 (95%CI50.70-51.60)-53.09(95%CI52.52-53.67)), t8(62.25(95%CI61.62-62.88)-65.31(95%CI64.57-66.05)), and time for Blastulation in both groups. To reach blastocyst complete development, the morphokinetic parameters analysed, tEB (Expanded Blastocyst) (113.65(95% CI112.85-114.45)-113.57(95%CI(111.55-115.59)) and tHB (hatched blastocyst) (118.92 (95%CI (116.67-120.30)-73.80 (95%CI1.76-145.83)) showed comparable results in both groups.

A slight trend towards higher embryo quality was observed in optimal blastocyst rate (A and B) based on inner cell mas quality when compared MG 86.1% (95% CI83.83-88.37) and 51.2% (95%CI35.55-56.85) and CG 83.8 (95% CI81.21-86.39) and 60.0 (95%CI54.99-65.0), respectively. Regarding optimal blastocyst rate based on trophoectoderm quality TE, the data showed a significance increase of blastocyst with higher quality in MG 80.2 (95%CI77.61-82.79) compared with CG 71.0 (95%CI67.87-74.13) in day 5. Considering outcome results a total of 422 blastocyst were transferred, with a mean number of 1.56 (95% CI 1.49-1.63) embryos transferred per cycle in MG and 1.73 (95% CI 1.67-1.80) in CG. A total of 406 blastocyst were cryopreserved, 205 in MG and 201 in CG, a mean number of 2.55 (95% CI 2.28-2.82) embryos were vitrified in the MG and 3.66 (95% CI 3.36-3.96) in the CG per cycle. In both cases showed a significant decrease in MG. Regarding fertilization rate 70.0% (95% CI63.85-76.15) and 75.1(95%CI63.23-86.97) and implantation rate 55.19 (95% CI 49.08-61.30) and 53.20 (95% CI 47.36-58.67) in MG and CG respectively were achieved with comparable results.

CONCLUSIONS: Despite the higher quality of embryos related to the MACS technology application this effect was not detected when morphokinetics were analyzed. Additionally reproductive outcome were comparable. Our results are supported by a consistent sample size.

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EXTERNAL VALIDATION OF AN AI SYSTEM FOR BLASTOCYST IMPLANTATION PREDICTION. Chloe Hardy, MSc,[1] Spilios Theodoratos, MSc,[2] Georgia Panitsa, PhD,[2] Jeanette Walker, BA,[2] Stephen Harbottle, BSc,[1] Ioannis A. Sfontouris, PhD[3] [1]Cambridge IVF, Cambridge, United Kingdom; [2]Business Insight Corporation, Cambridge, United Kingdom; [3]University of Nottingham, Nottingham, United Kingdom.

OBJECTIVE: To assess the performance in a clinical setting of IVFvision.ai, an artificial intelligence (AI) system for blastocyst selection

DESIGN: Retrospective analysis of single blastocyst transfer (SBT) images

MATERIALS AND METHODS: Convolutional Neural Networks were used to develop IVFvision.ai, an algorithm that differentiates between Day-5 blastocysts with a positive or negative implantation outcome. Implantation was confirmed by the presence of an embryonic sac with heartbeat.

External validation of IVFvision.ai was performed at a University IVF Clinic using 113 anonymised Embryoscope images of SBT. Assessed images were taken at 116±h hours post-insemination at the equatorial focal plane.

The predictive ability and reliability of IVFvision.ai to correctly classify blastocysts according to implantation outcome were compared to the KIDScoreD5 v2 prediction algorithm, as well as three expert Clinical Embryologists.

AUC for each predictor was estimated using ROC curve analysis. Sensitivity, specificity, PPV, NPV and accuracy were calculated using crosstabs. Reliability of IVFvision.ai and embryologist assessments was calculated by the Interclass correlation coefficient (ICC). Stepwise logistic regression was used to model predictors significantly associated with implantation controlling for maternal age and fertilisation method.

RESULTS: IVFvision.ai had higher AUC and overall accuracy in predicting implantation compared to KIDScoreD5 and all embryologists (Table 1). The reliability of IVFvision.ai was perfect (ICC = 1.00, 95% CI 1.00 to 1.00), consistently returning the same classification after a triple reading process. The reliability between 3 embryologists was moderate (ICC = 0.744, 95% CI 0.606 to 0.838), significantly lower than that of IVFvision.ai.

Stepwise logistic regression showed that only IVFvision.ai prediction (p=0.008) and fertilisation method (p=0.051) were significantly associated with implantation. The combined model IVFvision.ai+Fert had an AUC 0.740.

CONCLUSIONS: IVFvision.ai is a comprehensive AI system that identifies implantation outcome with high ability, outperforming all human experts and the KIDScore prediction algorithm. The system paves the way for clinical trials to improve the accuracy and efficiency of embryo selection in IVF.

SUPPORT: None

TABLE 1. Predictive characteristics

	AUC	95% CI	Sensitivity %	Specificity %	PPV %	NPV %	Accuracy %
IVFVision.ai	0.675	0.530-0.821	61.9	73.2	54.2	78.9	69.4
KIDScoreD5	0.672	0.538-0.807	66.7	65.9	50	79.4	66.1
Embryologist 1	0.570	0.414-0.725	28.6	85.4	50	70	66.1
Embryologist 2	0.663	0.517-0.809	61.9	70.7	52	78.4	67.7
Embryologist 3	0.628	0.477-0.778	52.4	73.2	50	75	66.1

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FIRST APPLICATION OF ARTIFICIAL NEURONAL NETWORKS FOR HUMAN LIVE BIRTH PREDICTION ON GERI TIME-LAPSE MONITORING SYSTEM BLASTOCYST IMAGES. Lucia Alegre, PhD,[1] Lorena Bori, MSc,[1] María de los Ángeles Valera, PhD Student,[2] Marcelo Fábio Gouveia Nogueira, PhD,[3] André Satoshi Ferreira, Undergraduate,[3] José Celso Rocha, PhD,[3] Marcos Meseguer, PhD[4] [1]IVIRMA Global, Valencia, Spain; [2]IVIRMA Global; IVI Foundation, Valencia, Spain; [3]Universidade Estadual Paulista (UNESP), Faculdade de Ciências e Letras (Câmpus de Assis), Assis - SP, Brazil; [4]IVIRMA Global, Valencia, Spain, Valencia, Spain.

OBJECTIVE: To introduce the analysis of blastocysts images from alternative time-lapse monitoring systems (TLM) by using Artificial Intelligence in the prediction of live birth (LB).

DESIGN: Retrospective cohort Study.

MATERIALS AND METHODS: We used image analysis technology as a tool to evaluate TLM images of 244 blastocyst stage embryos at 111.5 ± 1.5h post ICSI. The embryos were cultured in Geri-TLM incubator (Genea, Australia) until day 5 of development. Of the 244 blastocysts analyzed, from a single embryo transfer program, 200 were used for training (82%) and 44 for a blind test (18%) for prediction of LB by using AI. It was built a model of artificial neuronal network (ANN) to produce a predictable outcome of LB. Several independent numerical variables extracted from standardized TLM images as an input data were used. The efficacy of prediction of live birth was quantified and assessed using confusion matrices (True Positive-TP, True Negative-TN, False Positive-FP, False Negative-FN; Positive Prediction Value-PPV and Negative Prediction Value-NPV), ROC curves and AUC.

RESULTS: The accuracy (ACC) of prediction of live birth by AI using an ANN model was 85.2% (208/244; TP= 68, TN= 140, FP= 19, FN= 17). In the training dataset the ACC was 90.5% (181/200; TP= 58, TN= 123, FP= 14, FN= 5, AUC= 0.868), and in the blind test dataset, ACC was 61.4% (27/44; TP= 10, TN= 17, FP= 15, FN= 12, AUC= 0.634). The PPV, precision with which the ANN model was able to classify correctly a positive LB was 78.2%. In training dataset, the precision was 80.6% for LB+, and in blind test dataset 66.6%. Likewise, the overall NPV, capacity to classify correctly a negative LB, was 89.2%. In training dataset, the NPV was 96.0%, and in blind test dataset 58.6% for LB-. The AUC in the Blind test for positive and negative LB were very similar, 0.634 and 0.618 respectively.

CONCLUSIONS: This is the first ANN model using images from Geri TLM incubator as a target in image analysis technology. The model shows a competitive accuracy, predictive power and precision to improve the efficacy of embryo selection performed by the standard morphology and increasing the odds of LB per embryo transfer.

SUPPORT: The authors' research is supported by grants # 2017/19323-5 from São Paulo Research Foundation (FAPESP).

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NOVEL ARTIFICIAL INTELLIGENCE ALGORITHM FOR IMPROVING EMBRYO SELECTION COMBINING MORPHOKINETICS AND NON-INVASIVE MEASUREMENT OF OXIDATIVE STRESS. María de los Ángeles Valera, PhD Student,[1] José Celso Rocha, PhD,[2] Lorena Bori, M.Sc,[3] Lucia Alegre, PhD,[3] Marcelo Fábio Gouveia Nogueira, PhD,[2] Dóris Spinosa Chéles, Masters Student,[2] Marcos Meseguer, PhD[4] [1]IVIRMA Global; IVI Foundation, Valencia, Spain; [2]Universidade Estadual Paulista (UNESP), Faculdade de Ciências e Letras (Câmpus de Assis), Assis - SP, Brazil; [3]IVIRMA Global, Valencia, Spain; [4]IVIRMA Global, Valencia, Spain, Valencia, Spain.

OBJECTIVE: The aim of this study is to develop an artificial intelligence (AI) model able to predict the life-birth probability of *in-vitro* cultured embryos, combining morphology and morphokinetic (MK) information of their development with their oxidative stress level.

DESIGN: This retrospective study includes 131 transferred embryos (fresh and frozen-thawed) cultured individually in an Embryoscope

(ESD) incubator (Vitrolife, Denmark) until day 5/6. They belong to 100 ICSI cycles performed between May 2017 and December 2018, using autologous or donated eggs. After transfer, the oxidative status of the culture media was assessed by the Thermochemioluminiscence (TCL) Analyzer™ (Carmel diagnostics, Israel) as an indirect measurement of their metabolic activity. A machine learning algorithm was trained using MK data obtained using the *time-lapse* monitoring system, the TCL values and the clinical outcome of each embryo, generating a predictive model of life-birth probability.

MATERIALS AND METHODS: Fertilization was performed following the standard protocol of the clinic. Scoring and selection for transfer/freezing were performed according to the ASEBIR criteria, combining morphological and MK assessment. The oxidative status of 15 μL aliquots of media was measured by the TCL Analyzer, which counts the photons emitted per second (cps) as result of the heat-induced oxidation and modification of the sample. TCL parameters used were H1, H2 and H3 (TCL amplitude at 55, 155 and 255 seconds after heating, respectively), as well as their "sm" variants, resulting from applying a smoothing algorithm to normalize the data. The AI analysis was performed using machine learning algorithms, combining different sets of variables. Data from 105 embryos was used for the training of the machine, and 26 for the simulation.

RESULTS: Properly timed development and higher TCL parameters directly related to higher chances of achieving life-birth, as previously published. Five datasets were formed using different combinations of MK and TCL parameters with the stronger statistic correlation with life-birth result: MK+H1+H2+H3, MK+H1sm+H2sm+H3sm, MK+H1sm, MK+H2sm and MK+H3sm. They were compared to a reference model using only MK. The combination with the highest predictive capacity was MK + H2sm. In the training, the model achieved a 93.6% accuracy for predicting positive life-birth (LB+) and 86.2% for negative (LB-), compared to the 97.9% LB+ and 94.8% LB- using solely MK. The blind test of MK + H2sm model had a stronger predictive power (83.3% LB+, 85.7% LB-) than only MK (66.7% LB+, 85.7% LB-). Other combinations of oxidation variables did not show an improved predictive capacity when compared to the MK algorithm.

CONCLUSIONS: The presented AI algorithm combining MK and TCL parameter H2sm scores a higher predictive power for life-birth than using only MK data. This supports the relevance of the oxidative status of the culture media as an indirect measurement of metabolic activity, higher in embryos that achieve birth. This AI algorithm provides an upgraded score system to assist embryo selection, potentially improving clinical results.

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THE USE OF DEEP CONVOLUTIONAL NEURAL NETWORKS (CNN) TO OBJECTIVELY ASSESS THE ROLE OF ABSTINENCE ON IVF DEVELOPMENTAL OUTCOMES.

Stylianos Vagios, MD,[1] Irene Souter, MD,[1] Caitlin Sacha, MD,[1] Manoj Kumar Kanakasabapathy, MS,[2] Prudhvi Thirumalaraju, BS,[2] Charles L. Bormann, PhD,[1] Hadi Shafiee, PhD[2] [1]Massachusetts General Hospital, Harvard Medical School, Boston, MA; [2]Brigham and Women's Hospital, Harvard Medical School, Boston, MA.

OBJECTIVE: Scientific literature suggests that prolonged abstinence of men negatively impacts sperm parameters, potentially leading, among other, to motility and increased DNA fragmentation. For this reason, the World Health Organization recommends a 2-7-day abstinence period prior to collection for standard semen evaluation. However, it is unclear whether the length of abstinence affects IVF developmental outcomes when utilizing intracytoplasmic sperm injection (ICSI) for fertilization. The aim of this study is to use CNN to objectively assess whether a man's period of abstinence prior to ICSI affects ART developmental outcomes.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS:

Setting: Academic fertility center.

Data from 165 couples undergoing 193 IVF/ICSI/PGT-A cycles from 08/2014 to 12/2019 were analyzed. Freshly ejaculated samples were used for ICSI. Cycles were stratified in three groups based on male partner's abstinence period: 1-2.9 days (Group1, N=110), 3-4.9 days (Group2, N=69), $\geq$5 days (Group3, N=14).

Outcome measures: % of blastocysts and high-quality blastocysts developed on day 5 (D5) (assessed by CNN), predicted % of blastocyst and high-quality blastocyst development (assessed by CNN on D3), % euploid blastocysts, predicted implantation potential (assessed by CNN on D5). Previously validated, highly accurate deep CNN algorithms were used to evaluate the above CNN related outcome measures[1,2].

Statistics: Parametric and non-parametric tests were used as appropriate. P-values $<$0.05 were deemed significant.

RESULTS: The three groups did not differ significantly in male and female partner's ages, incidence of male factor infertility diagnosis, any specific semen analysis parameters, or response to stimulation, the latter assessed by the number of retrieved oocytes. The % of embryos that were classified as blastocysts on D5 did not differ significantly between groups [mean (95%CI): 59.8% (56.2-63.4), 55.3% (50.2-60.3), and 64.4% (51.1-77.8), p: 0.200, groups 1-3, respectively] neither did the predicted % of embryos developing to blastocysts [mean (95%CI): 64.2% (60.4-67.9), 60.2% (54.6-65.8), and 72.8% (62.9-82.7), p:0.174; groups 1-3, respectively]. Similarly, neither the % of embryos that developed to high-quality blastocysts on D5 nor the predicted % of embryos developing to high-quality blastocysts differed significantly between groups. When controlling for maternal age, euploidy rates [Group1: 42.1% (35.8-48.4), Group 2: 44.7% (36.2-53.3), and Group 3 38.9% (18.3-59.5), p:0.836] were, also, not associated with male's abstinence period. Finally, the CNN-predicted implantation potential for each embryo did not differ significantly among our groups [mean (95% CI): 42.8% (41.1-44.6), 40.4% (38.3-42.5), and 43.8% (38.1-49.5), p:0.149; groups 1-3, respectively].

CONCLUSIONS: Our findings do not support a negative impact of prolonged male abstinence on euploidy rates and other ART outcomes, as assessed by a highly accurate and previously validated deep-learning CNN in the setting of ICSI. Such findings could prove of significant value for the counseling clinician.

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2. Thirumalaraju P, Hsu JY, Bormann CL, Kanakasabapathy M, Souter I, Dimitriadis I, Dickinson KA, Pooniwala R, Gupta R, Yogesh V *et al.* Deep learning-enabled blastocyst prediction system for cleavage stage embryo selection. *Fertil Steril* 2019;111: e29.

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THE USE OF DEEP-LEARNING CONVOLUTIONAL NEURAL NETWORKS (CNN) TO OBJECTIVELY COMPARE TWO DIFFERENT EMBRYO CULTURE MEDIA.

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OBJECTIVE: One of the most critical aspects of assisted reproductive technology are the laboratory embryo culture conditions. Little is known about developmental outcome effects of culture media used in IVF. Recently, a rather controversial study comparing in vivo and in vitro derived embryos demonstrated that in vitro embryos had lower morphology than those developed in utero, however there were no differences in aneuploidy rates[1]. Apparently, there is still room for improving IVF culture environments. Many commercially available culture systems claim superiority. Meaningful differences could be identified by eliminating embryologist-grading biases and using CNN-platforms and preimplantation genetic testing for aneuploidy (PGT-A) to compare developmental and genetic outcomes from these systems. The purpose of this study is to assess two different culture media,

Continuous Single Culture (CSC)-Complete and CSC-NX-Complete (Fuji-Film,Irvine,Ca), on embryo developmental outcomes using a validated deep convolutional neural network (CNN) and PGT-A.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: Setting: Academic fertility center.

The study population consists of 1767 embryos derived from 204 ART ICSI cycles between 04/2019 and 12/2019 and cultured in the following media: CSC-Complete (349 embryos, 19.8%) and in CSC-NX-Complete (1418 embryos, 80.2%). PGT-A was performed on 755 embryos (175 cultured in CSC-Complete and 610 cultured in CSC-NX-Complete).

Embryos were cultured in 30 μl drops of medium, overlaid with mineral oil (Ovoil, Vitrolife) and cultured at 37ºC, 5% O_2, 6.5% CO_2 and balanced N_2.

All embryos were cultured and imaged in the Embryoscope™.

Outcome measures: fertilization rate, % of blastocysts and high-quality blastocysts developed on day-5 (D5) (classified using a $CNN^{2,3}$), % of D3-embryos predicted to develop to blastocysts and high-quality blastocysts (measured using a $CNN^{2,3}$), % euploid blastocysts, D5-predicted implantation potential (measured using a $CNN^{2,3}$).

RESULTS: The % of D5 embryos that developed to the blastocyst stage (62.5% and 59.0%, respectively in CSC-Complete vs. CSC-NX-Complete groups, p:0.240) or high-quality blastocyst stage (33.5% vs. 32.6%, respectively in CSC-Complete vs. CSC-NX-Complete groups, p:0.737) did not differ significantly between the two different culture media neither did the predicted % of embryos developing to either blastocysts (66.5% vs. 63.3%, respectively in CSC-Complete vs. CSC-NX-Complete groups, p:0.262). The CNN-predicted implantation potential of embryos did not differ between the CSC-Complete and the CSC-NX-Complete culture systems (42.8% ± 9.7% and 42.6% ± 8.9%, respectively, p:0.933). For biopsied embryos, similar euploidy rates (40.5% ± 33.3% vs. 40.5% ± 33.4%, respectively, p:0.858) were achieved in the CSC-Complete and CSC-NX-Complete media.

CONCLUSIONS: A highly accurate deep CNN found no significant differences between CSC-Complete and CSC-NX-Complete culture media. Therefore, one could argue that both single-step culture media are equally effective for culturing ICSI-derived embryos.

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A PROSPECTIVE MULTI-CENTER, RANDOMIZED STUDY TO COMPARE THE IMPLANTATION RATE (IR) OF EMBRYOS CULTURED AND ASSESSED USING TIME-LAPSE TECHNOLOGY (TLT) VS A CONVENTIONAL INCUBATOR (CI) SYSTEM.

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OBJECTIVE: To investigate if embryo culture and assessment by TLT leads to better clinical outcomes compared with CI with static morphological assessment.

DESIGN: A prospective, randomized, controlled, multicenter study enrolled 1224 women from 7 sites in China (July 2016 to August 2019).

MATERIALS AND METHODS: Women aged ≤35 years with normal ovarian response and uterine cavity, undergoing their first in vitro fertilization/intracytoplasmic sperm injection cycle (standard long protocol), with ≥8 follicles >14 mm per ultrasound on triggering day were eligible. Participants were randomized (1:1) to the Genea Embryo Review Instrument® (GERI®) TLT or CI groups (n=612 each). Embryos were cultured and assessed either in CI with standard morphological grading or GERI® TLT with GERI Assess® 1.2 software, an embryo assessment tool that annotates classification with atypical phenotypes. The two highest quality embryos were transferred on Day 3 and outcome information were collected until 10–12 weeks to verify ongoing pregnancy. The primary endpoint was IR as determined by ultrasound at 5–8 weeks of gestation. Secondary endpoints included number and quality of embryos cultured on Day 3, and clinical pregnancy outcomes. A power analysis indicated that a sample size of 612 subjects per group would provide ≥80% power with two-sided α=0.05 to detect a 27% relative difference in IR between groups. The IR for each treatment group and its asymptotic 95% confidence interval was calculated. Continuous variables were compared by t-test and categorical variables were compared by chi-square test, with a two-sided significance level of 0.05.

RESULTS: In total, 801 participants completed the study (TLT, n=398; CI, n=403). In the TLT group, 358 embryos were transferred, resulting in 246 ongoing pregnancies; in the CI group, 361 embryo transfers resulted in 228 ongoing pregnancies. The calculated IR (95% asymptotic confidence intervals) was 52.1% (48.4–55.8) in the TLT group and 45.7% (42.1–49.4) in the CI group. The between-group difference of 6.4% (1.2–11.6) was statistically significant (P=0.016). Across secondary efficacy indicators, higher clinical pregnancy (n=266/507 vs n=252/506) and multiple pregnancy rates (n=105/246 vs n=81/228) were observed in the TLT group vs the CI group, although the difference was not significant. No statistically significant differences were observed in embryological outcomes, biochemical pregnancy rate, ongoing pregnancy rate, ectopic pregnancy rate, and spontaneous abortion rate. No conclusions can be drawn regarding TLT effect on the live birth rate as patients were only monitored for ongoing pregnancy for 10–12 weeks after transfer.

CONCLUSIONS: The overall IR in the TLT group was statistically significantly higher than that in the control CI group. This may be attributable to the lack of disturbance in the culturing system and greater amount of embryo development information by time-lapse classification with atypical phenotypes vs CI. To our knowledge, this is the first reported assessment of GERI® TLT in China. Chinese Clinical Trial Registry: ChiCTR-IIR-16008758.

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A COMPUTER-VISION BASED TOOL FOR THE AUTOMATIC IDENTIFICATION OF BLASTOCYSTS' REGIONS. A STEP CLOSER TO DECODING TIME-LAPSE?.

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OBJECTIVE: to assess the capabilities of a computer-vision method to automatically identify blastocysts´ regions, from static blastocysts' micrographs

DESIGN: Prospective analysis of retrospectively obtained blastocysts' micrographs from two IVF centers

MATERIALS AND METHODS: a carefully curated dataset of 370 blastocyst images was created from the first 500 images generated at two IVF clinics over six consecutive months. All images were manually segmented identifying regions of interest. From this ground truth, 10% of the images were selected testing. All images were preprocessed, and then passed through 21 different filters (e.g. entropy, Gaussian blur, Laplacian, and Sobel) and convolved by 41 texture energy-kernels each, to identify a total of 861 textures. Data-augmentation was performed on the training set. 50 pixels were randomly select per blastocyst's region of interest , and its texture-based feature-vectors extracted (database of 300,400 data-points), used to training a neural-network (three 400 nodes layers, Adam optimizer, and categorical cross-entropy as the loss-function), during 500 epochs (validation split of 10%), a callback learning-rate reduction (factor of 0.5, patience of 25 epochs,

and validation loss as monitor) and an early stopping callback (patience of 60 epochs, validation loss as monitor, and a minimal delta of 0.001). With this texture-based model we computed five masks for each image within the training-set, and then trained an autoencoder (AE) using the ground-truth masks. This AE consist of three convolutional and three max-pooling layer for the encoding, three convolutional, and three up-sampling layers for the decoding. This model was trained with mean squared error as the loss-function, RMS prop as optimizer, early stopping, and learning rate-reduction callbacks (100 epochs), with a validation-split of 10%. The testing dataset was assessed using the Sorensen-Dice coefficient (SDC).

RESULTS: Following data-augmentation, a total 1,332 images became available for training the system. Overall, the model yield a mean SDC of 0.8744. The blastocoele, background, inner cell mass, trophectoderm, and zona pellucida respectively achieved 0.8399, 0.9690, 0.5684, 0.6586, and 0.7424 respectively.

CONCLUSIONS: Fully automation of the decision making process when using time-lapse has been challenging, partly due to the difficulties that automated blastocyst segmentation present. In this study, we present with an innovative approach to the challenge of blastocyst segmentation with encouraging. The accurate identification of blastocyst regions presented in our results, suggest that blastocyst micrograph segmentation is feasible with a combination of artificial-vision techniques, and an autoencoder to improve its initial result. This approach could pave the way for building further computational tools that might automatically track the regions of interest through time of any given blastocyst.

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IMPROVEMENT OF AN AUTOMATIC PRONUCLEAR DETECTION SYSTEM BY DEEP LEARNING TECHNOLOGY USING MULTI-SLICE IMAGES. Yuta Kida, M.S.,[1] Noritaka Fukunaga, Ph.D.,[1] Sho Sanami, Ph.D.,[2] Hiroyuki Watanabe, M.S.,[1] Yuji Tsuzuki, M.S.,[2] Hiroya Kitasaka, Ph.D.,[1] Seiji Takeda, M.S.,[2] Fumiya Kondo, M.S.,[1] Sho Takeda, B.S.,[1] Yoshimasa Asada, M.D., Ph.D.[1] [1]Asada Ladies Clinic, Nagoya, Japan; [2]Dai Nippon Printing Co., Ltd., Tokyo, Japan.

OBJECTIVE: We are developing an automatic PN detection system utilizing DL with the aim of establishing a more objective embryo evaluation. We have suggested that the embryo evaluation accuracy in PN number by DL using single-slices on the Z-axis of TL images was able to approach that of an embryologist and also reported the detection accuracy of PN can be improved through updating the algorithm(ASRM 2019). In this study, we have constructed a new algorithm by DL using 11 slices on the Z-axis images which were obtained using a new TL device, CCM-iBIS NEXT (NEXT;astec, Japan) and evaluated the detection accuracy.

DESIGN: We constructed the two algorithms of an automatic PN detection system.

Algorithm 1 was constructed by deep learning a total of 588 sequences of TL images (0PN:23, 1PN:27, 2PN:501, 3PN:37) using single slices on the Z-axis of TL images.

Algorithm 2 was constructed by deep learning a total of 920 sequences of TL images (0PN:43, 1PN:40, 2PN:782, 3PN:55) using 11 multi-slices on the Z-axis of TL images.

MATERIALS AND METHODS: We compared the evaluation accuracy of the two algorithms using 982 sequences of TL images (0PN:52 1PN:34 2PN:857 3PN:39) which were not used for learning. The PN number of all the above was assessed by an experienced embryologist who provided the evaluation and used as the correct answer.The chi-square test or Fisher's exact test were used for determining statistical significance.

RESULTS: The accuracy rate of Algorithm 1 was 2PN:70% (601/857), 0PN:92% (48/51), 1PN: 38% (13/34), and 3PN: 46% (18/39), respectively.The accuracy rate of Algorithm 2 was 2PN:90% (765/805), 0PN: 100% (51/51), 1PN: 29% (7/24), and 3PN: 0% (0/36), respectively.Comparing the accuracy rates using a single slice or multi-slice, there was no significant difference between 0PN and 1PN.However, for 2PN, the detection rate was significantly improved in the multi-slice($P<0.05$), in 3PN, the detection rate was significantly lower in the multi-slice($P<0.05$).

CONCLUSIONS: In this study, we have validated an improved detection rate of 90% for 2PN using an automatic pronuclear detection system employing multi- slices of TL images. The 1PN and 3PN embryo appearance rate is low at 3-5%. So, the detection rate is probably low because the small number of these images that can be used for learning. Through the addition of more images for learning, it is hoped that this can be addressed in future research. Further improvement of the accuracy can be expected by continuing to employ deep learning to the acquired TL images, adjusting the learning method and improving the algorithm.

SUPPORT: None.

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NEXT-GENERATION SEQUENCING DEMONSTRATES THAT IDENTIFICATION OF PRESUMED ROUND SPERMATIDS BASED SOLELY ON MICROSCOPIC APPEARANCE IS FREQUENTLY INACCURATE. Brent M. Hanson, MD,[1] Xin Tao, Ph.D,[2] Tianhua Zhao, MD,[3] Andrew F. Carmody, BA,[3] Brian K. Ackerman, MBS,[3] Julia G. Kim, MD, MPH,[1] Kathleen Hong, MD,[1] Philip J. Cheng, MD,[1] James Hotaling, MD,[4] Richard Thomas Scott, Jr., MD[5] [1]IVI-RMA New Jersey, Basking Ridge, NJ; [2]Foundation for Embryonic Competence, Basking Ridge, NJ; [3]IVIRMA, Basking Ridge, NJ; [4]University of Utah School of Medicine Andrology and IVF Laboratories, Salt Lake City, UT; [5]IVI RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: A subset of men with azoospermia lack mature spermatozoa at the time of surgical sperm extraction. Unfortunately, options for these patients are limited. It has been reported that round spermatids, which are haploid precursors to mature spermatozoa, can be successfully injected into human oocytes resulting in healthy offspring (1). However, the success of round spermatid injection (ROSI) relies on the accurate identification of spermatids. Identification is generally guided by cellular appearance during microscopy. This study seeks to evaluate whether next-generation sequencing (NGS) confirms the expected haploid status of cells which are presumed to be round spermatids based on visual characteristics.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: This study was performed at a university-affiliated fertility practice between October 2019 and April 2020. Frozen-thawed testicular tissue samples obtained from men with non-obstructive azoospermia via microsurgical testicular sperm extraction were evaluated for the presence of round spermatids. A cell was presumed to be a round spermatid if it met visual criteria previously described by Tanaka et al., including a diameter of 6-8 μm, an indistinct nuclear membrane, and a lack of distinct nucleoli or pseudopodia (2). Presumed round spermatids were isolated and placed in a hypotonic solution. Samples then underwent targeted NGS to a sequencing depth of 200-300, allowing for single nucleotide polymorphism (SNP) analysis. Ploidy status of the samples was assessed.

RESULTS: A total of 103 presumed round spermatids were analyzed. Overall, 19 samples (18.4%) had unamplified results with targeted NGS and 36 samples (35.0%) yielded nonconcurrent results. Of the 48 samples (46.6%) with interpretable results, 18 (37.5%) were found to be diploid, indicating that visual classification as a round spermatid was incorrect. The remaining 30 out of 48 samples (62.5%) were classified as haploid, consistent with the expected ploidy status for a round spermatid.

CONCLUSIONS: For the population of azoospermic men who only possess immature precursors to spermatozoa, ROSI serves as an opportunity to father biological offspring. However, this study demonstrates that in its current form, ROSI is limited by an inability to accurately distinguish round spermatids from diploid cells with a similar microscopic appearance. In order to improve fertilization rates and provide patients with the highest potential for reproductive success, investigation should focus on the development of new techniques for round spermatid identification.

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SUPPORT: None

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FUTURE OF AUTOMATION: USE OF DEEP CONVOLUTIONAL NEURAL NETWORKS (CNN) TO IDENTIFY PRECISE LOCATION TO PERFORM LASER ASSISTED HATCHING ON HUMAN CLEAVAGE STAGE EMBRYOS. Nicholas Kelly, BA,[1] Charles L. Bormann, PhD,[1] Jessica Dickinson, BA,[1] Andrew D. Meyer, BA,[1] Manoj Kumar Kanakasabapathy, MS,[2] Prudhvi Thirumalaraju, BS,[3] Hadi Shafiee, PhD[3] [1]Massachusetts General Hospital, Harvard Medical School, Boston, MA; [2]Division of Engineering in Medicine, Department of Medicine, Brigham and Women's Hospital, Cambridge, MA; [3]Brigham and Women's Hospital, Harvard Medical School, Boston, MA.

OBJECTIVE: To determine whether a Deep-Learning Artificial Intelligence algorithm can be used to accurately identify the precise location to perform laser assisted hatching on cleavage stage embryos.

DESIGN: Laser assisted hatching (AH) is a procedure designed to enable embryo escape from the zona pellucida (ZP). Studies show that AH may increase the chance of pregnancy in older women with repeat IVF failure and in frozen embryo transfer cycles. This procedure is also widely used on cleavage stage embryos to facilitate herniation and biopsy of trophectoderm cells for Preimplantation Genetic Testing. AH utilizes a 1.48-μm diode laser that can damage embryos if applied too close to blastomeres. Therefore, it's critical for embryologists to only apply AH on a region of the ZP that is furthest away from healthy cells.

MATERIALS AND METHODS: Using a retrospective dataset of human embryos, a deep CNN model was trained and tested to classify between 12 classes at the cleavage stage (70 hours post insemination). Twelve classifications resembled the pattern of digits on a clock, spaced 30 degrees apart to provide an accurate location for laser AH to be applied.

We developed a deep convolutional neural network that was trained with 13908 annotated images of cleavage stage embryos. We classified the location of AH based on the greatest distance between the ZP and healthy blastomeres. The validation test containing 1908 images served to ensure the program training was complete. The developed network was evaluated using another independent set of 3888 cleavage stage embryos images with known AH location classifications

RESULTS: The deep learning CNN was able to correctly identify the appropriate region to apply laser AH on the zona pellucida with 99.41% accuracy with a 95% confidence interval (CI) ranging between 99.11% to 99.62% (n=3888). Furthermore, a receiver operator characteristic (ROC) revealed micro and macro area under the curves (AUC) of 1, which confirmed that the AI can accurately pinpoint the correct location to perform AH.

CONCLUSIONS: The AI trained network can be used to accurately identify the correct location on the ZP to perform laser AH. This study demonstrates the extraordinary power and potential for utilizing CNNs in an ART laboratory to perform complex tasks such as laser AH. Findings from this study may allow for the automation of micromanipulation procedures.

SUPPORT: This work was partially supported by the Brigham Precision Medicine Developmental Award (Brigham Precision Medicine Program, Brigham and Women's Hospital), Partners Innovation Discovery Grant (Partners Healthcare), R01AI118502, and R01AI138800.

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EVIDENCE FOR SUPERIOR BLASTOCYST COHORT RANKING USING ARTIFICIAL INTELLIGENCE BASED ON RETROSPECTIVE CLINICAL PREGNANCY RESULTS. Matthew David VerMilyea, PhD,[1] Milad A. Dakka, PhD,[2] Jonathan MM. Hall, PhD,[3] Sonya M. Diakiw, PhD,[2] Tuc Van Nguyen, PhD,[2] Don Perugini, PhD,[2] Kaylen Silverberg, MD,[4] Michelle Perugini, PhD[2] [1]Ovation Fertility, San Antonio, TX; [2]Presagen and Life Whisperer, Adelaide, SA, Australia; [3]Australian Research Council Centre of Excellence for Nanoscale Biophotonics, Adelaide, SA, Australia; [4]Texas Fertility Center, Austin, TX.

OBJECTIVE: To establish evidence for superior ranking of blastocysts using artificial intelligence (AI) that assesses viability based on Day 5 embryo images. A simulated cohort study was performed to establish a measure of Time-to-Pregnancy (TTP), using AI to rank embryos within cohorts then calculating how many transfers are needed before a successful clinical pregnancy occurs.

DESIGN: Retrospective analysis in private reproductive technology programs.

MATERIALS AND METHODS: An AI model (Life Whisperer) for classifying Day 5 embryo images in terms of viability was developed by training and testing on datasets totaling 3,900 images with a known pregnancy outcome, sourced from 16 clinics across 5 countries.

A simulated cohort study was designed whereby retrospective embryo images from a blind test dataset with known pregnancy outcomes were randomized into 116 groups. Each group represented a simulated patients' cohort of embryos, using cohort sizes based on a known clinical distribution. The AI was used to rank embryos in each cohort from most to least likely to be viable.

We defined a new measure, TTP, as the position of the first embryo in the ranked cohort to give a positive pregnancy outcome. If the first embryo in the cohort resulted in a positive pregnancy, the TTP for that cohort was 1; if the first embryo was negative but the second embryo was positive, the TTP was 2, etc. A lower TTP was interpreted as a superior ranking outcome. Mean TTP value of the AI ranking was compared to the result expected from random chance, since all embryos in the dataset were already chosen by an embryologist and transferred.

RESULTS: The 3,900 embryo images were randomized into 116 simulated cohorts 1,000 times, and the entire set of cohorts were used to provide a bootstrapped statistical analysis. A mean TTP value of 1.506 and standard error of 0.003 was observed for the AI model, compared to a mean TTP of 1.750 and standard error of 0.004 for ranking based on random chance. The differences in mean TTP distribution were modeled as an asymmetric Laplace distribution. Overall, these results translated to a 13.6% improvement in TTP using AI compared to that of random chance, with statistical significance.

CONCLUSIONS: An AI model trained on clinical pregnancy data showed superior ranking ability and a shorter TTP compared with random chance, for simulated cohorts of transferred embryos. Out-of-pocket expenses for IVF are estimated at $19,000 for the first cycle and $7,000 for each additional cycle (Wu, et al. 2014). Given this, the reduction in TTP means a potential cost saving of $1,200 per patient and clinic revenue increase of $4,600 per treatment through the ability to service more higher value first cycle patients. In the USA with 300,000 annual IVF cycles, AI could achieve total patient savings of $360M, and $1.38B increase in revenue for IVF clinics. Globally with over 2.5M cycles, AI could achieve global patient savings of $3B and $13.8B increase in revenue for IVF clinics.

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P-93 4:30 PM Saturday, October 17, 2020

EFFECT OF THE GERI INCUBATOR ON CLINICAL OUTCOMES IN FRESH TRANSFER ART CYCLES. Conor Harrity, MRCOG, MRCPI,[1] Hans Arce, Medical doctor,[2] Rafie Ebrahimi Ghaei, MB BCh BAO LRCPI LRCSI,[1] Declan Keane, MSc, MBA,[3] Claire Moran, PhD[3] [1]ReproMedIreland, Dublin, Ireland; [2]34 Larkfield Way, Dublin, Ireland; [3]ReproMed Ireland, Dublin, Ireland.

OBJECTIVE: The GERI (Genea) incubator combines a closed culture system to provide stable conditions for the embryo, along with timelapse monitoring to aid selection. Although there are strong theoretical arguments that these interventions can improve outcomes, as with other "add ons" there is limited data to demonstrate if they can actually benefit patients.

Assessment of embryo morphology has traditionally required repeated removal from conventional incubators, exposing embryos to fluctuations in environment. Time-lapse Systems (TLS) such as GERI offer two potential advantages:

- Assessment without the need for physical disturbance (closed culture)
- Additional information regarding embryo development, acquired through continuous monitoring

Although there are strong theoretical arguments that these interventions can improve clinical outcomes, there is limited data to demonstrate true benefit to patients, with a Cochrane review (2019) concluding insufficient good quality evidence of any difference between TLS and conventional incubation.

Study question: Does embryo culture in the GERI system have any influcence on blastulation, implantation and pregnancy rates in fresh IVF/ICSI cycles

DESIGN: A retrospective cohort study of all fresh IVF/ICSI blastocyst transfer cycles from Jan 2016 to Dec 2019 was performed. Cleavage stage transfer, elective freeze-all, cycles with no embryos, and female age 42+ were excluded.

MATERIALS AND METHODS: All treatments were in a tertiary level university affiliated reprodictive medicine centre, and 578 cycles met the inclusion criteria. Treatments were divided into those where embryo culture was in standard incubators, and those using GERI. Clinical outcomes were calculated and compared using Chi square analysis for proportions and t-test for means.

RESULTS: Clinical Pregnancy rates were similar between groups (45.0% vs 38.1%, p=0.09), however significantly more embryos were transferred in the traditional incubator cases (1.44 vs 1.17, p<0.0001). There was a significantly higher implantation rate with the GERI cultured blastocysts (38.2% vs 26.1%, p =0.0004). More embryos were available for cryopreservation in the GERI cohort (p=0.0081)

Although age, AMH, number of oocytes retrieved were the same between groups, the fact this this was a retrospective analysis means that bias and the impact of confounding factors cannot be excluded.

CONCLUSIONS: The GERI system has the potential to help outcomes by the use of a closed culture system which could benefit embryo development, along with timelapse monitoring and use of morphokinetics to aid embryo selection and shorten the time to pregnancy.

Although no improvement in pregnancy rate was seen, a significant improvement in implantation rate was found, and less embryos were transferred, possibly indicating improvements in embryo selection in patients who used the GERI incubator system

SUPPORT: NA

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A SYNTHETIC DATA SET OF 3D OOCYTE IMAGES AND MACHINE LEARNING ALGORITHM AS A MODEL TO ASSESS THE REPRODUCTIVE POTENTIAL OF OOCYTES.

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OBJECTIVE: to design a deep convolutional neural network model using synthetic data sets of human oocytes to predict the reproductive potential of real-time oocyte images

DESIGN: development and description of new software for 3 D image analysis of oocytes.

MATERIALS AND METHODS: Real time data sets derived from a library of 2,500 oocyte images with known outcomes were used as models. Simulated images of human oocytes were then generated incorporating a spectrum of attributes associated with outcomes ranging from no fertilization to blastocyst formation. Metadata for the 3 D model was generated using the open source rendering engine, Lux Core Renderer, in an Amazon Web Services-based compute environment. Image variability was controlled through custom software produced by Rendered.AI. Image analysis was performed using a convolutional neural net UNet for biological segmentation image analysis.

RESULTS: We generated a reliable and robust 3 D simulation environment and a superimposable library of procedural generative mesh effects (or synthetic oocyte images) that incorporate real time oocyte features associated across a spectrum of reproductive outcomes noted above. Using this library and a scalable compute environment, we developed fully synthetic 3 D baseline reference datasets of 1,000 3 D oocytes containing representative samples of oocyte imagery and attributes associated with various clinical outcomes. The proposed algorithm is based on a convolutional neural network (CNN) and task specific software to extract attributes from the 2 D image. The algorithm can rapidly expand the image library and add or subtract endless oocyte features into the 3 D model. Run time to generate novel and unique oocyte images is 20 seconds. The software is capable of generating up to 5,000 oocyte images per day depending on feature adjustments.

CONCLUSIONS: Synthetic data sets offer a novel way to develop a limitless library of multi-faceted oocyte images for comparison to real time data images acquired in the embryology lab. We describe a synthetic data set and reference library of 3-D computer-generated oocyte images and an algorithm for feature extraction to predict fertilization of real time 2 D oocyte images. Our software model opens the possibility of using inexpensive synthetic data for training neural networks to identify oocytes with the highest reproductive potential while avoiding the need to collect large amounts of hand-annotated real-time oocyte images and data typically required for training and development. This capability lays groundwork for quantifying and exploring any observable oocyte properties in diverse datasets and eliminates the need and expense for large, annotated libraries to develop image analysis tools to assess oocytes. By using CNN-based machine vision techniques and the software we designed for this purpose, we suggest that these tools may be basically a simpler tool than the current labor intensive and expensive practice of collecting and annotating real time datasets for purpose of image analysis.

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SUPPORT: None

P-95 4:30 PM Saturday, October 17, 2020

AUTOMATIC IMAGE SEGMENTATION AND QUANTITATIVE COMPONENT MEASUREMENTS ON HUMAN BLASTOCYST IMAGES USING ARTIFICIAL INTELLIGENCE (AI) IN ASSESSING MORPHOLOGY GRADING AND PREDICTING IMPLANTATION AND LIVE BIRTH OUTCOMES.

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OBJECTIVE: The present study aimed to identify the correlations between morphology and quantitative parameters of blastocyst components segmented on a still blastocyst image using the Blast-Net AI model and to determine which quantitative parameters would be the most predictive of implantation and live birth.

DESIGN: This is a retrospective cohort study analyzing blastocyst images acquired at 116 ± 2 hours post-insemination between 2012 and 2017, a six-year period. 415 blastocysts from 315 single or double embryo transfers from patients at mean age of 33.3 ± 3.3 years (range: 23 – 38) with a receptive uterine environment were included. All blastocysts were assessed with the Gardner[1] blastocyst scoring system at image acquisition and they were later confirmed by two experienced embryologists. All images analyzed have known implantation and live birth outcomes associated.

MATERIALS AND METHODS: All 415 images were analyzed with the Blast-Net automatic segmentation model as previously described.[2] Each image was segmented into the background, Zona Pellucida (ZP), Inner Cell Mass (ICM), Blastocoel, and Trophectoderm (TE). Each component was then quantitively measured using mathematical algorithms and converted into μm or μm^2 for data analysis. The Blast-Net model provides a confidence score on the segmentation of each component. 22 images (5.3%) failed to meet the 90% confidence inclusion cutoff for ICM and 2 images (0.5%) for ZP. 391 images were included for the determination of average blastocyst radius (BR), average ZP thickness, ZP area, TE area, ICM area and ratio of ZP thickness relative to BR (ZP/BR). The correlations of these parameters and morphology grading were assessed and logistical regression analysis was used to determine the Odds Ratio for each parameter in predicting implantation and live birth.

RESULTS: Among ZP area, average ZP thickness, average BR, and ZP/BR, ZP/BR has the best goodness of fit to the blastocyst expansion. The mean ZP/BR for size 2 expansion is 0.197, 95%CI [0.191, 0.203], size 3 is 0.153, 95%CI [0.149, 0.158], and size 4 is 0.080, 95%CI [0.075, 0.084], and they are significantly different ($p<0.0001$). ICM area and TE area are both significantly different between grade A and B ($p<0.0001$ and $p<0.005$, respectively), but not against grade C, due to the small number of grade C ICM or TE transferred. Mean ICM area for grade A ICM is 3170.4 μm^2, 95%CI [3080.6, 3260.2] and grade B is 2560.9 μm^2, 95%CI [2403.4, 2718.3]. Mean TE area for grade A TE is 4265.8 μm^2, 95%CI [4171.6, 4360.0] and grade B is 4052.6 μm^2, 95%CI [3940.5, 4164.7]. Among ZP/BR, ICM area, and TE area, only ZP/BR is indicative of implantation (OR = 2.59, 95%CI [1.10, 6.10]) and live birth (OR = 2.39, 95%CI [1.02, 5.61]). Blastocysts with a ZP/BR below 0.144 have significantly higher implantation rate (59% vs 48%, $p<0.04$) and live birth rate (53% vs 43%, $p<0.05$) than ones above this threshold.

CONCLUSIONS: Automatic segmentation and quantification of various components of a blastocyst image using the Blast-Net model can potentially offer automation in morphology assessment as well as embryo selection with improved implantation and live birth outcomes.

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EMBRYOLOGIC OUTCOMES IN INTRACYTOPLASMIC SPERM INJECTION (ICSI) CYCLES UTILIZING SPERM SELECTED VIA A MICROFLUIDICS DEVICE COMPARED TO STANDARD

SELECTION. Prachi N. Godiwala, MD, Jane L. Kwieraga, BSc TS, Reeva B. Makhijani, MD, Chantal Bartels, MD, Alison Bartolucci, PhD, Daniel R. Grow, MD, John Nulsen, MD, Claudio A. Benadiva, MD, Lawrence Engmann, MD Center for Advanced Reproductive Services, University of Connecticut School of Medicine, Farmington, CT.

OBJECTIVE: Microfluidics sperm sorting allows for improved selection of normal sperm compared with conventional sperm preparation, but blastulation rate after its use has not been studied. We aim to compare the high-quality blastulation rate in cycles in which sperm was chosen via a microfluidics device versus standard sperm selection.

DESIGN: Single academic IVF center retrospective cohort study.

MATERIALS AND METHODS: The IVF/ICSI cycles of 45 patients aged 18-46 years between 2014-20 utilizing a microfluidics chamber (ZyMot^{TM}) with ICSI for sperm selection were compared to the same patients' previous ICSI cycles in which standard sperm selection was used. Use of microfluidics was based on physician discretion and/or the IVF lab recommendation based on previous low fertilization rate or blastulation rate. For standard selection, after centrifugation and washing by swim-up method sperm was chosen manually based on motility and morphology. In study cycles, motile sperm were manually selected after traversing through a microfluidics chamber. Primary outcome was high-quality blastulation rate ($\geq$3BB by Gardner scoring). Secondary outcomes included fertilization rate, number of high-quality blastocysts frozen, and euploidy rate among IVF cycles using preimplantation genetic testing for aneuploidy (PGT-A). For paired data, McNemar's test was used for categorical and paired T-test for continuous data. A two-sided p-value of <0.05 was considered statistically significant.

RESULTS: Mean patient age, partner age, BMI, and AMH level at the time of standard selection cycle were 37.3 years, 37.7 years, 25.5 kg/m^2, and 2.5 ng/mL, respectively. The majority of patients' primary infertility diagnosis was male factor (42.2%), followed by unexplained (22.2%). 35.6% of patients used the same stimulation protocol for both cycles. The use of PGT-A, mean numbers of oocytes retrieved, and pre- and post-processing sperm parameters were similar. Although the high quality blastulation rate was higher in microfluidics cycles, the difference was not significant. The fertilization rate, euploidy rate and mean number of embryos frozen did not differ significantly (Table 1).

CONCLUSIONS: Microfluidics sperm selection did appear to improve blastulation rate although this was not statistically significant due to the sample size. Further large prospective randomized studies are needed.

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SUPPORT: None

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SEQUENTIAL VERSUS SINGLE STEP CULTURE MEDIA IN RELATION TO EUPLOIDY RATES IN PGTAI PROGRAM: PRELIMINARY DATA.

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OBJECTIVE: To evaluate PGTai results for embryos cultured in sequential versus single step media.

TABLE 1. Embryologic Outcomes

	Standard Selection Cycles	Microfluidics Cycles	p-value
No. of oocytes retrieved (n ± SEM)	10.1 ± 8.8	11.7 ± 8.6	0.08
Fertilization rate (% ± SEM)	54.1 ± 4.6	57.8 ± 3.5	0.49
High-quality blastulation rate (% ± SEM)	25.2 ± 7.3	38.1 ± 4.7	0.15
Number of high-quality blastocysts frozen (n ± SEM)	1.9 ± 0.3	2.8 ± 0.6	0.11
Euploidy rate (% ± SEM)	16.7 ± 8.9	20.1 ± 6.4	0.78

DESIGN: A prospective cohort study including 122 couples that underwent ICSI at a private fertility center in Egypt from December 2019 till April 2020, patient recruitment is still ongoing. Female age $\leq$37 years with $\geq$ 8 mature oocytes. Male partner had normal semen parameters according to WHO 2010. PGT-A was done at the blastocyst stage.

MATERIALS AND METHODS: Injected oocytes from 72 patients were cultured in Continuous Single Culture-NX media (CSC-NX) with 10% SSS (Irvine, USA) while those from 50 patients were cultured in sequential cleavage and blastocyst media with 10% SPS (SAGE, Denmark). All blastocytes with 4BB quality and better according to Gardner's criteria 1999 were eligible for PGT-A using next generation sequencing (NGS) (Miseq illumina, USA). Results were confirmed with PGTai platform (Cooper Surgical, USA). Data were collected, analyzed using SPSS (version 23) and considered significant if p value $\leq$ 0.05.

RESULTS: There were no significant differences in female age, number of mature oocytes nor semen parameters between the two groups.

	Single step media %	Sequential media %	p values
Fertilization rate	75.34	73.59	0.57
Cleavage rate	90.20	90.40	0.64
High quality day 3 embryos	72.94	75.85	0.45
Blastulation rate	64.27	67.07	0.89
High quality day 5/6 embryos	69.53	68.63	0.82
Euploidy rate on day 5	48.62	55.06	0.31
Euploidy rate on day 6	47.12	66.99	0.08
Total euploidy rate	51.76	62.29	0.06
Aneuploidy rate on day 5	31.87	34.32	0.73
Aneuploidy rate on day 6	34.70	26.06	0.31
Total aneuploidy rate	30.53	27.86	0.60
High mosaicism rate on day 5	11.13	2.06	0.01*
High mosaicism rate on day 6	10.63	2.50	0.12
Total high mosaicism rate	10.17	4.09	0.04*
Low mosaicism rate on day 5	5.55	3.84	0.57
Low mosaicism rate on day 6	0.87	4.43	0.21
Total low mosaicism rate	3.09	4.91	0.39

* is a significant value

CONCLUSIONS: Embryos have the same preimplantation developmental competence in both single step or sequential media. However, a significantly high mosaic rate in single step media as well as a non-significant tendency toward higher euploidy rate in sequential media. Hence, our results showed that blastocysts from young patients cultured in sequential media have had a lower high mosaic rate in favor of euploid rate, which may increase the euploid embryos available for transfer.

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SUPPORT: NA

P-98 4:30 PM Saturday, October 17, 2020

LASER ASSISTED HATCHING OF HUMAN EMBRYOS AT FERTILIZATION CHECK, ON DAY 1 OF CULTURE, ALLOWS FOR CONTINUOUS UNINTERRUPTED TIME-LAPSE INCUBATION OF 5+ DAYS, WHILE PRODUCING HATCHING BLASTOCYSTS AS EXPECTED.

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OBJECTIVE: Human embryos must fully hatch from the Zona Pellucida (ZP) for implantation. Furthermore, studies show that implantation rates increase when the embryo has low energy expenditure. Extended culture of embryos to the blastocyst stage does not allow the natural process of hatching to occur, thus necessitating assisted hatching (AH) to breach the ZP for optimal embryo development. This AH is generally performed on day 3 of culture, however this necessitates interrupting any continuous culture of embryos during incubation from day 1 to 7, especially during Time-Lapse. We set out to determine if human blastocysts possess the ability to reach the hatching stage during 5+ days of continuous culture after laser AH is performed two days earlier than standard; at the Day 1 fertilization check.

DESIGN: A retrospective data analysis at a single large private fertility center to analyze blastocyst laser hatching performed on Day 1 when embryos undergo 5+ days of continuous culture in a Time-Lapse incubator.

MATERIALS AND METHODS: Oocytes were retrieved and inseminated using standard clinical practice protocols. 16 -18 hours post insemination, the day 1 fertilization check was performed. Embryos with abnormal fertilization (3PN and MPN) were donated for research and underwent AH using a Hamilton Thorne Lykos Laser at a Pulse setting of 290μs. The laser hatched embryos were placed into a Time-Lapse Embryoscope in order to monitor their ability to form blastocysts and to undergo hatching.

RESULTS: A total of 41 abnormally fertilized embryos were cultured for 5+ days, with only 12 embryos undergoing blastulation, which is an expected rate for abnormal embryo development. All 12 embryos that formed blastocysts, hatched successfully (100%). Initial hatching was observed as early as 95 hours post insemination (3.96 days of culture) and the latest observed at 140 hours (5.83 days) with a mean time to start hatching of 112.31 hours (4.68 days).

CONCLUSIONS: This study demonstrates that laser AH performed on day 1 at the fertilization check can produce hatching blastocysts at the expected rate. This allows practices to place embryos into Time-Lapse incubation with completely uninterrupted continuous culture for 5+ days, until the desired hatching blastocyst stage has been achieved.

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EMBRYO AUTOMATIC DIAGNOSTIC TEST; BLASTULATION, ANEUPLOIDY AND IMPLANTATION RATE PREDICTION.

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OBJECTIVE: To analyze the relationship of the automatic classification test provided on Day 3 by the EevaXtend algorithm (Early embryo viability assessment) system with blastocyst and implantation rate, blastocysts available for biopsy and aneuploidy rates.

DESIGN: Observational, retrospective cohort study.

MATERIALS AND METHODS: The study included 400 patients from our egg donation (193 cycles) and PGT program (207 cycles) from which 5135 embryos generated by ICSI were incubated in a GERI Time-Lapse Incubator (Genea, Australia) with an automatic cell-tracking software (Eeva, Xtend) that classifies embryos from 1 to 5 using: P2 (t3-t2), P3 (t4-t3), egg age, number of cells on day 3 and a texture image analysis (correlated with fragmentation). Blastocyst were classified by morphology using ASEBIR criteria (Asociación para el Estudio de la Biologa de la Reproducción). We analyzed for implantation those cases in which the number of gestational sacs matched with the number of embryos transfer (KID).

RESULTS: The distribution of the embryos classified according to the automatic algorithm was: 1: 25.4%, 2: 20.4%, 3: 15.8%, 4: 17.5%, 5: 20.9%. The percentage of viable embryos (transferred or vitrified) or non viable in each category was: 1: 66% vs 34%, 2: 56.9% vs 43.1%, 3: 49.4% vs 50.6%, 4: 34.6% vs 65.4%, 5: 12.5% vs 87.5% ($p<0.0001$). Of the 5135 embryos categorized, 3551 reached blastocyst stage. Blastocyst rate in each category was: 1: 88.9%, 2: 84%, 3: 76%, 4: 61.9%, 5: 35.4% ($p<0.0001$). We also explored the relationship with blastocysts morphology (ASEBIR) in each Xtend category. 1: A: 11.3%, B: 52.5%, C: 28.2%, D: 8.1; 2: A: 6.6%, B: 50.9%, C: 31.8%, D: 10.7%; 3: A: 5.5%, B: 44.5%, C: 38.1%, D: 11.8%; 4: A: 2.8%, B: 41.2%, C: 34.9%, D: 21.1%; 5: A: 3.6%, B: 25.1%, C: 40.7%, D: 30.5%. ($p<0.0001$). The distribution of the KID embryos (n=777) was: 1: 39.7%, 2: 28.4%, 3: 16.4%, 4: 10%, 5: 5.5%. Implantation rate was: 1: 54.9%, 2: 55.5%, 3: 46.9%, 4: 43.6%, 5: 27.9% ($p<0.005$). The percentage of blastocysts available for biopsy (n=927): 1: 74.3%, 2: 67.8%, 3: 62.4%, 4: 40.1%, 5: 17.6% ($p<0.0001$). We didnt́ find significant differences between the percentage of euploid blastocysts in each category. We also performed a logistic regression model for implantation, in which BMI, type of cycle and standard morphology were included. The model

revealed an OR 2,402 (CI95% 1,161-4,970) (p=0.003) comparing Xtend 1 vs 5.

CONCLUSIONS: There is a direct correlation between Xtend categories, percentage of viable embryos, blastocyst rate and blastocysts available for biopsy. Moreover, the best Xtend categories corresponded to the embryos with better morphology. Regarding the implantation rate, we observed significant differences between categories. Retrospective nature of this study may be a reason for caution; nevertheless, it is the largest sample size reported with this test, based in blastocyst transfer with>90% of single-embryo-transfer. Additionally a multivariable-analysis confirmed the magnitude of the results. It confirms that morphology and automatic time-lapse classifications can be used together to increase success rate in the laboratory.

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P-100 4:30 PM Saturday, October 17, 2020

IDENTIFYING INHERENT POOR QUALITY EMBRYO DATA USING ARTIFICIAL INTELLIGENCE TO IMPROVE AI PERFORMANCE AND CLINICAL REPORTING.

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OBJECTIVE: Analysis of clinical data suggests inherent errors in the classification of Day 5 blastocyst images, where viable embryos are wrongly classified non-viable based on a negative pregnancy outcome. A novel AI technique (UDC) was used to identify and remove mis-classified data to obtain a cleaned dataset which improves AI performance and reduces misleading reporting of AI accuracy.

DESIGN: Retrospective analysis in private reproductive technology programs.

MATERIALS AND METHODS: We assessed ~5,500 static 2D images of Day 5 blastocysts with known clinical pregnancy outcomes. Clinical analysis considered patients under 35 years because they are likely to contain more mis-classified non-viable embryos with patient factors preventing a pregnancy. A novel AI technique (UDC) which identifies incorrectly classified (labeled) data, was used to identify viable embryos incorrectly classified as non-viable. We compared the performance of AI trained using the original embryo dataset and a new cleaned dataset, by assessing accuracy on both an uncleaned and cleaned blind test dataset.

RESULTS: Patients <35 that did not achieve a pregnancy had a higher rate (63.6%) of patient factors (e.g. endometriosis) compared with patients ≥35 (49.1%). For patients <35, 49.2% of embryos transferred did not lead to a pregnancy, despite only 17% of these being deemed non-viable by traditional morphological grading. This indicates that there are many examples of embryos deemed non-viable that are likely viable, but did not result in a pregnancy. These mis-classified cases are deemed poor quality data.

Applying the UDC to the images identified a significant proportion of embryos suspected to be viable but labeled as non-viable. We removed mis-classified nonviable data to create a clean AI training dataset, and a clean test dataset which is used to report the performance of the AI.

Cleaning the training data improved overall AI performance from 59.7% to 61.1%, as measured on an unclean test dataset. There was a large accuracy increase in the (correct) viable class from 76.8% to 80.6%, and a drop in the (misclassified) non-viable class from 37.3% to 35.4%.

When measuring the AI performance of the same model on the cleaned test dataset with mis-classified data removed, we found that the original AI accuracy was under-reported, and the true performance overall was 77.1%. For the non-viable class of embryos the under-reported accuracy was even more pronounced, consistent with a larger amount of poor quality data in this class, and the true performance was actually 58.8%.

CONCLUSIONS: These data suggest that in the class of embryos deemed non-viable due to a negative pregnancy outcome, there are many embryos that are viable and just wrongly classified. The UDC is a unique technique that is effective at identifying these mis-classified cases, which when removed from the AI training datasets results in improved AI performance and enables the true reporting of AI performance. This also calls into question whether it is even possible to achieve the high accuracy (above 90%) reported by others in the literature when embryo viability data is inherently poor quality.

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P-101 4:30 PM Saturday, October 17, 2020

A STRATEGY TO VALIDATE THE INTRODUCTION OF TIME-LAPSE INCUBATOR IN THE LABORATORY.

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OBJECTIVE: To present a strategy to validate the introduction of time-lapse technology in the laboratory for clinical use.

DESIGN: Retrospective case-control study performed at an assisted reproduction clinic in southern Brazil.

MATERIALS AND METHODS: The data refers to a period from January to February 2020 and was collected from electronic records. Inclusion criteria: patients undergoing in vitro fertilization (IVF), with at least two fertilized oocytes. A total of 39 patients were included in the analysis. Embryos from the same patient were then divided into two groups: Group 1, embryos cultured in the Time-lapse technology, and Group 2: embryos cultured in a conventional incubator. A total of 417 inseminated oocytes (G1=210; G2: 207) and 188 blastocysts (G1=111; G2=77) were included. Fertilization rate, embryo development and blastocyst rate were analyzed between groups. Mann–Whitney U-test test was applied. Variables was expressed in median [25th-75th], and statistical significance was defined as p<0.05.

RESULTS: The mean maternal age was 34.6 ± 4.4. When compared Group 1 with Group 2 the following results were observed: inseminated oocytes (5 [4-6] *vs.* 5 [4-7], p=0.800); fertilized oocytes (5 [3-6] *vs.* 4 [3-5], p=0.334); fertilized oocytes rate (fertilized/inseminated) (83.3% [71.4-100.0] *vs* 83.3 % [66.7-100], p=0.657); D3 embryos with more than 6 cells (4 [2-5] *vs.* 2 [1-5] (p=0.028); number of blastocysts (D5 plus D6) (3 [1-4] *vs.* 1.5 [1-3], p=0.039) and blastocysts rate (60.0% [33.3-75.0] *vs* 45% [18,6-61.7], p=0.038).

CONCLUSIONS: In this study, data from 39 patients and 188 blastocysts was sufficient for demonstrating statistical difference regarding to embryo development in different incubators. Hence, the applied methodology in this study may be a strategy to validate the introduction of time-lapse technology in the laboratory for clinical use.

POSTER SESSION: ART PROCEDURES AND TECHNIQUES

P-102 4:30 PM Saturday, October 17, 2020

GERMLINE TRANSMISSION OF DONOR MTDNA IN TRANS-MITOCHONDRIAL MONKEYS.

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OBJECTIVE: To examine efficacy and long-term safety of mitochondrial replacement therapy (MRT) in rhesus macaques.

DESIGN: Five MRT rhesus macaques were produced in 2009-2012 via MRT. This is a form of germline gene therapy developed to prevent transmission of mtDNA mutations from mother to child. We produced MRT monkeys by reciprocal replacement of cytoplasm and mtDNA complement in oocytes from the two different rhesus macaque subpopulations. Their health, development, reproductive fitness and mitochondrial DNA (mtDNA) inheritance was studied for over a decade.

MATERIALS AND METHODS: The study followed approved IACUC protocols at the Oregon National Primate Research Center. The TMB (time-mated breading) and ART (Assisted Reproductive Technologies) cores assisted in sperm and oocyte collections and breeding.

RESULTS: Sperm morphology, count, and motility in MRT adult male monkeys were within normal range and matched to controls. Moreover, when naturally mated with females they produced healthy offspring. The only female MRT monkey was also bred and produced a healthy infant demonstrating a germline transmission of original donor mtDNA to the second generation. During the MRT procedure a small amount of residual maternal mtDNA inevitably persists in oocytes resulting in 1-3% heteroplasmy in MRT monkeys. Dynamics of maternal mtDNA heteroplasmy levels in skin, blood, and urine remained stable in all MRT monkeys. Maternal mtDNA heteroplasmy was also measured in most major internal organs and tissues of post-necropsied animals. Two MRT animals showed a noticeable increase of maternal mtDNA in internal organs reaching 10% in kidney, 12% in stomach and liver and 17% in small intestine.

CONCLUSIONS: These results provide critical long-term safety and efficacy data for clinical applications of MRT. While heteroplasmy levels in peripheral tissues were maintained into adulthood, other internal organs showed an increase. While it is re-assuring that complete reversion was not observed, patients would need to be informed of the risk of potential reversion.

SUPPORT: Burroughs Wellcome Fund, NIH, OHSU institutional funds

P-103 4:30 PM Saturday, October 17, 2020

AUTOMATED OOCYTE AND ZYGOTE DENUDATION USING A NOVEL MICROFLUIDIC DEVICE.

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OBJECTIVE: The aim of the study was to develop an automated denudation device, supervised by a computer vision algorithm, that could reduce shear stress while efficiently removing cumulus cells to allow vitrification and ICSI and for subsequent NI-PGT or metabolomics analysis.

DESIGN: Experimental comparative study using bovine and human cumulus-oocyte complexes in a novel microfluidic device.

MATERIALS AND METHODS: We developed a microfluidic biochip that exerts a particular fluid motion while avoiding egg entrapment within microfluidic channels. Firstly, cow cumulus oocyte complex (COCs) were used due to their size similarity with human COCs. Later human COCs were used. These were either denuded 16-20 hours post insemination for 15 min or were denuded in a second denudation run on day 3 for NI-PGT or metabolomics analysis. Alternatively, COCs were denuded for 15 min pre-insemination. COCs were classified as partially denuded if fertilization assessment, ICSI or vitrification was possible, and completely denuded if no cumulus cells remained (necessary for NI-PGT and metabolomics). Cow COCs controls were manually denuded (Stripper® pipette 145μm ID) to compare shear stress between procedures. Experiments were repeated with the use of human COCs. A Computer Vision model was developed using human COCs in order to optically assess denudation efficiency. In order to obtain meaningful performance metrics, half of the entire dataset was defined as a test set of images, with a balanced ratio of denuded and non-denuded images. The model used was a Pytorch implementation of Resnet18 with ImageNet pretrained weights.

RESULTS: 50 bovine COCs were microfluidically handled post insemination achieving complete (12/50) or partial (38/50) removal of the cumulus cells on day 1, while for day 3 double denudation group, 46 (92%) were completely denuded while the rest remained partially denuded. In comparison, 50/50 (100%) of manually denuded cow COC, achieved complete denudation (post insemination group). In addition, 60% (N=10) cow COCs treated pre-insemination were partially denuded after 15 min of treatment while 100% were partially denuded after one hour of treatment.

Of 20 donated human COCs, 12 were denuded manually and 8 automatically. Those in the automatic group, were all partially denuded enough to see PNs and PBs.

The shear stress of our design was calculated to be smaller than 4.4 Pa, about ten times lower than the one applied by the manual process (~44Pa).

The deep learning algorithm was tested on 20 unseen human oocytes on day 1, with 10 true positives 9 true negatives, and 1 false negative (95% accuracy).

CONCLUSIONS: Complete denudation is key to avoid DNA contamination for non-invasive PGT or metabolomics analysis, while avoiding damage to the oocyte by excessive shear force. Our automated system efficiently denude cow and human COCs with x10 less shear force without human intervention. Using a computer vision algorithm, the device could recognize degrees of denudation to subsequently treat each oocyte individually.

References: He et al., "Deep Residual Learning for Image Recognition", 2015, EEE conference on computer vision and pattern recognition (pp. 770-778)

SUPPORT: Intramural

P-104 4:30 PM Saturday, October 17, 2020

DOES A LOW SERUM ESTRADIOL CONCENTRATION PRIOR TO START OF PROGESTERONE HAVE AN ADVERSE EFFECT ON LIVE BIRTH IN FROZEN EMBRYO TRANSFER CYCLES, EVEN WHEN ENDOMETRIAL THICKNESS IS ADEQUATE?

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OBJECTIVE: To investigate whether a low serum estradiol concentration (E2) during frozen embryo transfer (FET) has an adverse effect on pregnancy outcomes in the setting of an adequate endometrial thickness.

DESIGN: A retrospective cohort study utilizing 2018 data at a private REI practice.

MATERIALS AND METHODS: We evaluated 4 thresholds for serum estradiol (150, 200, 250 and 300 pg/ml) collected at the endometrial measurement prior to starting progesterone. The primary outcome was live birth (LB); secondary outcomes were clinical pregnancy (CP) and spontaneous abortion (SAB). All FET cycles utilized only oral estradiol and when the

Outcome	Threshold Comparisons											
E2 concentration (pg/mL)	<150	>150	p	<200	>200	p	<250	>250	p	<300	>300	p
N (transfers)	235	1981	-	579	1637	-	991	1225	-	1347	869	-
LB	106 (45.1)	957 (48.3)	0.354	274 (47.3)	789 (48.2)	0.718	493 (49.7)	570 (46.5)	0.132	665 (49.4)	398 (45.8)	0.100
CP	132 (56.2)	1200 (60.6)	0.192	337 (58.2)	995 (60.8)	0.275	602 (60.7)	730 (59.6)	0.584	825 (61.2)	507 (58.3)	0.173
SAB	26 (11.1)	233 (11.8)	0.752	61 (10.5)	198 (12.1)	0.315	106 (10.7)	153 (12.5)	0.191	156 (11.6)	103 (11.9)	0.920

endometrium achieved at least 7 mm, double thickness, progesterone in oil was initiated with or without vaginal progesterone. Vitrified-warmed single blastocyst transfer occurred on the 6th day of progesterone. Generalized estimating equations (GEEs) were used to account for repeated cycles and adjusted for age.

RESULTS: 2,216 frozen embryo transfer (FET) cycles from 1920 patients in 2018 were included. The mean endometrial thickness of included cycles on day of progesterone start was 10.1mm. The average E2 concentration on the day that progesterone was initiated was 416 pg/mL. No differences in any outcomes were observed (table 1). Furthermore, estradiol as a linear variable was not associated with live birth (OR 0.99, 95%CI 0.99-1.00)

CONCLUSIONS: In programed FET cycles with an endometrial thickness of 7mm or greater, there was no association between serum estradiol concentration and live birth, clinical pregnancy, or miscarriage. These data suggest that measuring serum estradiol may not be necessary in programmed FET. Further, prolonging estradiol preparation and/or changing estrogen formulation in order to achieve a minimum serum estradiol concentration is likely unnecessary, if endometrial lining is adequate.

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WITHDRAWN

P-106 4:30 PM Saturday, October 17, 2020

AN APPLICATION OF THE ASRM EMBRYO TRANSFER SIMULATOR: CORRELATION OF EJECTION VELOCITY WITH CLINICAL OUTCOMES.

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OBJECTIVE: Embryo transfer (ET) is a crucial last step of IVF. Studies of fluid dynamics during embryo transfer have shown that pressure changes due to ejection speed can lead to increased sheer stress and velocity differences on an embryo during ET (1). However, these parameters are difficult to measure in vivo. The ASRM Embryo Transfer Simulator has the unique ability to record many parameters of a simulated ET. The goal of this study was to examine the ejection velocity during ET using the simulator and determine if there is any correlation with clinical outcomes.

DESIGN: A retrospective cohort study at a large university-affiliated IVF clinic.

MATERIALS AND METHODS: The ASRM simulator was used for training purposes during January 2018. At this institution, the ejection of the embryo during ET is typically performed by the embryologist. Twenty-four embryologists participated in the training and their ET parameters were recorded and de-identified. Each participant performed the simulated ET multiple times and ejection velocities were recorded, as well as their experience in performing live ETs in years. Clinical outcomes from live ETs from January – December 2018 were obtained for each participant, including pregnancy (defined as positive pregnancy test, PR), live birth (LBR), and ectopic rates (EPR). Those who did fewer than 20 live ETs in 2018 were excluded from the analysis. Data were assessed using linear regression.

RESULTS: Twenty embryologists were included in the analysis. They performed the simulated ET a mean of 5 times each (range 2-10). The mean ejection velocity across all participants was 0.21 ml/s (range 0.036-0.63 ml/s). While the measured velocities varied widely between participants, the variability within each participant's repetitions was relatively low. The mean experience for performing ETs was 10 years (range 0-29 years).

The mean PR and LBR per transfer for all ETs during 2018 were 61.8% and 41.1%, respectively. The mean PR among the study participants was 61.9% (range 51.1 to 67.9), and LBR was 40.4% (range 31.9 to 47.3). For both PR and LBR, all except one participant were within 2 standard deviations (SD) of the institution mean. The mean EPR among participants was 0.8% per transfer, compared to 0.7% clinic wide.

The ejection velocity was not associated with PR, LBR, or EPR (p=0.79, 0.31, 0.47). Similarly, participant's years of experience with live ET was not associated with clinical outcomes (p=0.14, 0.82, 0.12).

CONCLUSIONS: Data on whether ejection velocity affects the success of ET is limited by the ability to measure this parameter in vivo. Using the ASRM Embryo Transfer Simulator as a proxy for live ETs, this study found no correlation between embryo ejection velocity and clinical outcomes. Even though no correlation was found, this important step of the ET has not been well studied and may benefit from the use of simulation for standardization.

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SUPPORT: None

P-107 4:30 PM Saturday, October 17, 2020

ASSOCIATIONS BETWEEN EMBRYO BIOPSY AND OBSTETRICAL AND NEONATAL OUTCOMES FOLLOWING FROZEN-THAWED SINGLE EMBRYO TRANSFER.

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OBJECTIVE: Trophectoderm biopsy involves removing several syncytiotrophoblast cells that would become the placenta. Our objective was to determine if removal of trophoblast cells is associated with obstetrical and neonatal outcomes following frozen-thawed embryo transfer.

DESIGN: We linked ART surveillance data (SART-CORS) to birth certificates and maternal and neonatal hospitalization discharge diagnoses in Massachusetts from 2014-2017, considering only singleton births following autologous frozen-thawed single embryo transfers.

MATERIALS AND METHODS: We compared outcomes of those having embryo biopsy (n=585) to those having no biopsy (n=2192), using Chi-square test for categorical and binary variables. We ran logistic regression to calculate adjusted odds ratios (AORs) and 95% confidence intervals (CI) for embryo biopsy vs. no biopsy (reference), adjusting for mother's age, race, education, parity, and BMI.

RESULTS: There were no differences between groups with respect to: pre-eclampsia (AOR=0.72, p=0.20) or eclampsia (AOR=0.74, p=0.22), placental disorders (AOR=0.87, p=0.56), method of delivery (AOR = 0.93, p=0.46), preterm birth (AOR=1.06, p=0.74), low birthweight (AOR=1.01, p=0.98), gestational diabetes (AOR=1.00, p= 0.99), or non-gestational diabetes mellitus (AOR=0.9, p=0.87). However, women having embryo biopsy had a prolonged length of hospital stay compared to those who did not (>3 days for vaginal delivery, >5 days for cesarean section), (AOR= 1.47, p=0.02). Significant diagnoses associated with prolonged maternal hospital stay included hemorrhage (intrapartum and postpartum, 44.8% biopsy vs. 26.1% no biopsy, p=0.005). There was no prolonged stay for neonates following cycles with embryo biopsy (AOR=1.44, p=0.08).

CONCLUSIONS: Considering cryopreserved thawed single embryo transfers, embryo biopsy does not increase the odds for diagnoses of conditions related to placentation (preeclampsia, eclampsia, placental disorders, preterm delivery, or low birthweight). Embryo biopsy is related to increased lengths of maternal hospitalization following delivery due to maternal hemorrhage.

SUPPORT: None.

P-108 4:30 PM Saturday, October 17, 2020

PERINATAL OUTCOME FROM THE TRANSFER OF FROZEN, EUPLOID, BLASTOCYSTS BIOPSIED ON DAY 7.

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OBJECTIVE: The current study aimed to evaluate perinatal outcomes from transfers of euploid embryos that required trophectoderm (TE) biopsy on day 7 due to delayed cavitation.

DESIGN: Retrospective study

MATERIALS AND METHODS: This study included euploid embryos that underwent IVF and preimplantation genetic testing for aneuploidy (PGT-A) from 2011 to 2019. Embryos with morphology ≥4CC (modified Gardner scoring system) were biopsied on day 5. Embryos not ready for biopsy were re-evaluated on days 6 and 7. Euploid blastocysts were grouped by day of TE biopsy. Donor oocyte cycles were excluded. Patient age at IVF and embryo transfer (ET), BMI, AMH, basal antral follicle count (BAFC), endometrial thickness at ET, and morphology grade were covariates. Outcomes included neonatal birth weight, gestational age (GA) at delivery, low birth weight rate (<2500 g), fetal macrosomia rate (>4500g) and preterm delivery rate. ANOVA, chi-squared tests and multivariate linear regression were used for the analysis.

RESULTS: 1,795 blastocysts biopsied on day 5, 950 on day 6, and 32 on day 7 were identified. Blastocysts biopsied on day 7 were more likely to come

	Day 5 (n=1795)	Day 6 (n=960)	Day 7 (n=32)	p value
Age at IVF	35.4 ± 4	35.9 ± 4.1	36.9 ± 3.9	0.001
Age at ET	35.8 ± 4	36.7 ± 4	37.3 ± 4	<0.01
BMI	23.5 ± 4.1	24 ± 4.4	23.6 ± 4.3	0.14
AMH	4.1 ± 4.7	3.1 ± 3.6	3.2 ± 3.6	<0.01
BAFC	11.7 ± 8.1	10.6 ± 7.9	7.4 ± 6	<0.01
Endometrial thickness at ET	9.7 ± 2.2	9.7 ± 2.1	9.5 ± 2	0.83
Expansion grade (%)				<0.01
4	929 (51.8)	260 (27.1)	10 (31.3)	
5	509 (28.4)	311 (32.4)	8 (25)	
6	356 (19.8)	389 (40.5)	14 (43.8)	
ICM grade (%)				<0.01
A	1394 (78.5)	633 (67.4)	14 (48.3)	
B	348 (19.6)	242 (25.8)	9 (31)	
C	33 (1.9)	64 (6.8)	6 (20.7)	
TE grade (%)				<0.01
A	717 (40.4)	336 (35.8)	4 (13.3)	
B	796 (44.8)	374 (39.9)	9 (30)	
C	262 (14.8)	228 (24.3)	17 (56.7)	
Neonatal birth weight	3340 ± 573	3337 ± 545	3286 ± 571	0.89
Low birth weight (%)	105 (6.7)	54 (6.3)	3 (12.5)	0.37
Fetal macrosomia (%)	15 (1)	7 (.8)	0 (0)	0.86
GA at delivery	39.1 ± 2	39.1 ± 1.7	39 ± 1.7	0.85
Preterm delivery (%)	159 (8.9)	88 (9.2)	4 (12.5)	0.69

from women of advanced age at IVF, lower BAFC, and AMH. Day 7 biopsied embryos were more likely to be hatched, have a grade C ICM and grade C TE. Extended culture was not associated with neonatal birth weight, low birth weight rate, rate of fetal macrosomia, GA at delivery, or preterm delivery rate. In the multivariate model, slow-growing embryos were not associated with birth weight (ß= .015, p= .66) or GA at delivery (ß=-.018, p= .65).

CONCLUSIONS: Patients who underwent transfer with embryos biopsied on day 7 had comparable perinatal outcomes to transfers with embryos biopsied on days 5 or 6. These results support the continued utilization of extended embryo culture with PGT-A, as pregnancies from transfers with embryos biopsied on day 7 did not show evidence of impaired placentation.

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SUPPORT: None

P-109 4:30 PM Saturday, October 17, 2020

VITAMIN D3 (25 OH D) LEVELS IN FOLLICULAR FLUID STRONGLY CORRELATE WITH DEVELOPMENTAL POTENTIAL AND GRADES OF EMBRYO IN IVF CYCLES.

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OBJECTIVE: To evaluate if follicular-fluid (FF) levels of Vitamin D3 correlate with the oocyte and embryo developmental competence.

DESIGN: Prospective study of reproductive age women (n=300, 22-42 years) undergoing IVF without any previous history of vitamin D3 supplementation. On day of oocyte pickup (OPU), fluid from first aspirate of each follicle was pooled for each patient and centrifuged to obtain clear follicular fluid. Vitamin D3 levels were measured in FF using RIA diagnostic kits. Sequential culture to blastocyst stage was done and blastocysts were graded as top, good and poor quality as per standard evaluation criteria. All blastocysts were vitrified for transfer in next natural cycle.

MATERIALS AND METHODS: All women underwent controlled ovarian hyper-stimulation (COH) with recombinant FSH. Women with endometriosis, tuberculosis, hydrosalpynx, poor ovarian response ($\leq$ 3 retrieved oocytes) to COH and male partners with severe or moderate male factor were excluded from the study. Cycles were classified into Low (< 41 ng/ml; n=152) and High (> 41 ng/ml; n=148) FF Vitamin D3 groups on the basis of their median values. Rates of fertilization, cleavage, blastocyst formation and grades of blastocysts formed were recorded in both the study groups.

RESULTS: There was no significant difference in age, number of eggs retrieved and mean MII oocytes (p>0.05) between the two study groups. However, rates of fertilization (93.3 $\pm$ 22.6 vs. 86.1 $\pm$ 29.5% P: 0.0205) and cleavage (87.0$\pm$18.5 vs. 79.3$\pm$24.6% p:0.02) were significantly higher in low group than in high FF Vitamin D3 group. Interestingly, although overall Blastocyst formation rate remained comparable (50.3 $\pm$37.9 vs. 54.1 $\pm$ 35.4% : P value 0.3740); the percentage of top (34.4 $\pm$0.4 vs 24.2 $\pm$0.8%, P= 0.0183) and good 37.8 $\pm$ 0.69 vs 21.4 $\pm$ 0.72%, p= 0.0002) grade blastocysts were significantly higher in low FF Vitamin D3 group than in high FF Vitamin D3 group. Importantly, poor quality blastocysts were significantly high in high FF Vitamin. D3 compared to Low FF Vit. D3 group (45.0 $\pm$ 38.5 vs 26.3 $\pm$ 33.0 %, P value: < 0.0001). FF Vit. D3 correlated with top grade blastocysts (Pearson r= 0.56). There have been contradictory results of correlation between serum levels of Vitamin D3 and embryo quality. However, since follicular-fluid is the microenvironment which reflects the fate of follicle and oocyte development, study of this correlationship in FF, as done in our study, seems more logical. Also, with changes in weather conditions and carbon emission affecting the ozone layer all over the world, the natural synthesis of Vitamin D3 seems to be disturbed. Therefore, it is extremely prudent to evaluate this hormone to improve embryo development and pregnancy rates in IVF cycles.

CONCLUSIONS: FF level of Vitamin D3 is potentially predictive of embryo quality and facilitates non-invasive selection of best blastocyst for transfer.

References: None

SUPPORT: None

P-110 4:30 PM Saturday, October 17, 2020

A PROMISING LIGAND AND MICROFLUIDICS SPERM SEX SELECTION METHOD.

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OBJECTIVE: To test the reliability of selecting sex-specific spermatozoa through ATP content modulation in a microfluidics (MF) system.

DESIGN: In 5 years, we processed ejaculates from 98 consenting couples undergoing treatment at our center with a lengthy, custom multilayer density gradient (MDG) system. The proportion of X- and Y-bearing spermatozoa before and after selection was assessed by a targeted karyotype using fluorescent in situ hybridization (FISH). Cycle pregnancy outcomes and offspring sex were recorded. To expedite our selection process while maintaining sperm sex enrichment, we tested a new method utilizing TLR7/8 ligand activation together with an MF system.

MATERIALS AND METHODS: A total of 98 couples were treated at our center (IRB 1306014043) in 120 ICSI cycles. A proprietary MDG method was used to select spermatozoa according to sex. We assessed $\geq$1,000 cells/specimen by FISH to confirm successful selection. Pregnancy outcomes and offspring sex were assessed and compared between the sex-enriched groups. We tested a new selection technique by initially selecting spermatozoa with MF, followed by a 45-minute incubation in HTF medium containing 0.3μM of the TLR7/8 ligand, and then a second round of MF.

RESULTS: Of the couples (maternal age 36.8$\pm$4yrs; paternal age 39.6$\pm$5yrs) included, 53.1% wanted a female child, while 46.9% desired a male child. The initial sperm concentration was 65.4$\pm$26x10^6/ml, with 47.7$\pm$5% motility, normal morphology, and average sperm aneuploidy of 3.3$\pm$4%. After MDG selection, sperm concentration decreased to 24.3$\pm$14x10^6/ml, while motility rose to 94.5$\pm$3% (P<0.0001).

Of the 52 couples who wanted a female child, FISH assessment confirmed a sex-specific enrichment at 80%, which translated to >80% of couples obtaining a female embryo confirmed by PGT-A. The clinical pregnancy rate for these couples was 25.7% (18/70), with a delivery rate of 78.6% (11/14) of the desired sex; the remaining 4 pregnancies are ongoing.

For 46 couples who desired male offspring, FISH analysis confirmed an 80% enrichment for Y-bearing spermatozoa that translated to an equivalent proportion of male embryos confirmed by PGT-A. The clinical pregnancy rate for these couples was 28.0% (14/50), and the delivery rate was 88.9% (8/9) of the desired sex, with 5 ongoing pregnancies.

In a separate non-clinical investigation, we tested our new method on five additional sperm specimens. The proposed ligand activation/MF method yielded >80% spermatozoa enrichment for each sex, confirmed by a karyotype. Moreover, this process was able to maintain spermatozoa sex enrichment within a significantly expedited processing time of 105 minutes, compared to the 180 minutes required for MDG (P<0.0001).

CONCLUSIONS: While we were able to consistently achieve an enrichment of X- and Y-bearing spermatozoa that resulted in an equivalent proportion of embryos and delivery of children of the desired sex, this process is lengthy and tedious. Although this new proposed ligand/MF mechanism requires clinical testing, it demonstrated comparable results in much less time and could therefore be applied to more couples within the same day.

P-111 4:30 PM Saturday, October 17, 2020

MANIPULATION OF PH AT DAY 0 MAY IMPACT BLASTOCYST MORPHOLOGY.

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pH	# ICSIed	# Fert	# PPN	# Blast.	# BXed	Eup /Bxed	Eup /Fert	Eup /Blast	# Cryoed
Experiment (pH 7.40)	808	526 (65%)	5 (0.6%)	316 (60%)	254 (80.3%)	111 (43.7%)	111 (21.1%)	111 (35.1%)	270 (85.4%)
Control (pH 7.27)	817	548 (67%)	8 (1%)	316 (57.7%)	231 (73.1%)	126 (54.5%)	126 (22.9%)	126 (39.8%)	264 (83.5%)
Statistical analysis	n.a.	n.s.	n.s.	n.s.	P<0.01	P <0.05	n.s.	n.s.	n.s.

PPN: poly pronuclei; Blast.: Blastocysts; BXed: Biopsied, the quality of blastocyst should be =>3BB ; Eup: Euploid; Cryoed: Cryopreserved, both biopsied and non-biopsied blastocysts. Blastocyst quality below 2CC not preserved.

OBJECTIVE: In a *in vivo* situation, the pH within the female reproductive tract is not constant. From literature, the pH is high in the fallopian tube at 7.5-7.9 (Ng et al, 2018), while the intra-oocyte pH is about 7.4 (Dale et al, 1998) and gradually decreases to 7.2 in the uterus. In the *in vitro* system, the majority of IVF labs will usually set the percentage of CO_2 in the incubator constant at one point, i.e. 5-7%, with the pH between 7.2 -7.4 (Swain, 2012). The question is why use a higher pH in the initial phase of fertilization since these physiologic pH levels are different. Does it have an affect on fertilization or embryo development?

DESIGN: Prospective study

MATERIALS AND METHODS: During 11/15/2019 – 3/20/2020, all ICSI cycles are included in the study. The age range is 27- 42 with a mean age of 35.8. The study is a paired- t design. For each cycle, half of the number of mature oocytes are assigned to the control group and the other half of mature oocytes are assigned to the experimental group. The control group follows a routine protocol, i.e. culture mature oocytes, fertilization, and embryo development at the same pH at 7.27. The experimental group follows the same protocol except the initial pH is at 7.40 following ICSI. For the experimental group, the culture pH is switched back to the regular pH of 7.27 after verification of presence of pronuclei (about 18 hours after ICSI). Chi-square tests were used for

RESULTS:

CONCLUSIONS: Increasing the pH on day 0 does not result in a significant difference upon fertilization or abnormal fertilization rates. While there is no significant difference upon blastocyst formation rate, the quality of formed blastocyst showed a significant difference for trophectoderm biopsy. It is also interesting to observe that the experimental group showed better quality blastocyst for trophectoderm biopsy while also showing a significantly lower euploid rate by biopsy. There is no significant difference of euploid rate by # Fert or # blast. The results indicate increasing pH at day 0 may enhance developmental morphology but has no effect on total euploid rate of tested blastocysts.

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P-112 4:30 PM Saturday, October 17, 2020

FEMALE EMBRYOS ARE MORE SUSCEPTIBLE TO PERTURBATIONS IN DNA METHYLATION IN FROZEN-THAW EMBRYO TRANSFER CYCLES.

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OBJECTIVE: To examine the effect of embryo vitrification and fetal sex on placental DNA methylation following assisted reproductive technologies.

DESIGN: Prospective cohort study

MATERIALS AND METHODS: Placentas were obtained from singleton pregnancies after: 82 fresh IVF cycles, 64 programmed frozen embryo transfer cycles without PGT (FETs), and 26 full-term unassisted conceptions. Bisulfite treated DNA was analyzed using the 850K MethylationEPIC BeadChip array. CpGs with an adjusted *p*-value less than 0.05 in a two–tailed unpaired t test, and a mean difference in methylation of greater than 0.05 were considered differentially methylated between fresh and frozen samples. ANOVA was used to identify differences in methylation patterns amongst multiple groups with Tukeys adjustments for multiple comparisons.

RESULTS: We found 4847 CpG sites differentially methylated between placentas from fresh and frozen embryo transfers, with 4578 CpGs hypomethylated and 269 hypermethylated in fresh cycles compared to FETs. We found 428 genes with at least 2 CpG sites differentially methylated between groups, including the imprinted genes *DLGAP2*, *SNRPN*, *KCNQ1* and *ATP10A*. For example, we found 9 CpG sites differentially methylated between fresh and frozen embryo transfer cycles in the imprinted gene *DLGAP2* (adjusted p <0.05 for all sites). At these sites, DNA methylation in placentas from FET cycles closely resembled methylation from control, non-IVF unassisted pregnancies, with both FETs and controls differing significantly from fresh embryo transfer cycles. Sex specific analysis uncovered that this overall finding held true only for male fetuses (i.e. cg22763586 p=0.002 fresh vs. frozen). Placentas of female fetuses from FET cycles had similar perturbations in DNA methylation as the placentas of females from fresh embryo transfer cycles. (cg22763586 p=0.13 fresh vs. frozen).

CONCLUSIONS: Embryo transfer following a fresh IVF cycle leads to more perturbations in placental DNA methylation compared to frozen embryo transfer. Nevertheless, female fetuses appear to be more susceptible to perturbations in placental DNA methylation following vitrification and transfer in programmed frozen embryo transfer cycles. Animal studies are necessary to assess whether the changes noted are secondary to the vitrification process and/or the maternal hormonal environment.

SUPPORT: P50 HD068157-07

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DNA METHYLATION DIFFERENCES IN LIVER OF MICE CONCEIVED BY IN VITRO FERTILIZATION.

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OBJECTIVE: IVF generated offspring are believed to be healthy, but display a host of short term (low birth weight, preterm birth) and possibly long-term health problems, including predisposition to hypertension and glucose intolerance. Epigenetic changes are believed to underlie such changes. This study aimed at describing global DNA methylation changes in the liver of adult mice generated by natural mating (control group; flushed blastocysts, FB) or by IVF.

DESIGN: Experimental animal study.

MATERIALS AND METHODS: Mice were generated by IVF (and cultured with KSOM medium with amino acids in 5% oxygen) or by natural mating. Resulting blastocysts were transferred to recipient and offspring growth and phenotype was assessed to 30 weeks of age, at which points animals were sacrificed. Liver was removed and global DNA methylation was assessed in 3 IVF and 3 FB male mice, using whole-genome bisulfite sequencing (WGBS). GREAT was used to associate genes to differentially methylated regions (DMRs; mouse genome build, mm9). G:Profiler (p-adjusted value < 0.05) was used for functional enrichment analysis. Overrepresented gene ontology terms were summarized with REVIGO while canonical pathways were identified with Ingenuity Pathway Analysis (IPA).

RESULTS: Overall, 2,692 DMRs (4.91%) were different between the groups. The majority of DMRs (n=2,286, 84.92%) were hypomethylated in the IVF group and more frequently located 50-500 kb distal to the transcription start sites, particularly in intronic and intergenic regions. Surprisingly, only 0.16% of CpG islands were differentially methylated between IVF and FB liver samples, and only a few DMR were located on known gene promoters (n=283) or enhancers (n=190). The key canonical pathways modified by IVF were the hepatic fibrosis and insulin receptor signaling pathways, while non-redundant biological processes included the developmental and cellular

metabolic processes and transcription from RNA polymerase type II promoter. The main molecular functions enriched were the protein, enhancer, chromatin, and transcription factor binding. In particular, the transcription factors ZF5, E2F, and Kaiso showed the highest statistical significance.

CONCLUSIONS: IVF modifies the DNA methylation signature in the adult liver, resulting in the hypomethylation of genes involved in metabolism and regulation of gene transcription. These findings may shed light into the mechanisms underlying the developmental origin of health and disease.

SUPPORT: R01HD092267 to PFR and UC MEXUS-CONACYT to SLA.

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PREDICTING NUMBER OF MATURE OOCYTES AT RETRIEVAL: A MACHINE-LEARNING MODEL FOR PATIENT COUNSELING.

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OBJECTIVE: To develop a prediction algorithm utilizing both clinical baseline characteristics and cycle-specific parameters to accurately predict (on the day of trigger shot administration) the number of mature oocytes (MII) that will be obtained at oocyte retrieval.

DESIGN: This was a model-prediction study based on a retrospective cohort of patients who underwent their first fresh autologous in vitro fertilization (IVF) cycle between the years 2016-2019. Only cycles that resulted in oocyte retrieval were included.

MATERIALS AND METHODS: A dataset consisting of 1009 first IVF cycles was randomly partitioned into a training group (60% of cycles, N= 606) and a testing group (N= 403). Patient- and cycle-specific characteristics (ex: patient age, anti-Mullerian hormone level, FSH dosage, etc.) were evaluated as model inputs. Three different prediction models were used for cross-validation training with a K-fold of 10, repeated 20 times. The best-performing model (random forest) was validated on the test dataset. Root mean square error (RMSE) was calculated to ascertain model accuracy. RStudio® was used for all statistical analyses.

RESULTS: Baseline and cycle characteristics of the study population are shown in the table. The final model used patient age, day 3 FSH, AMH, FSH dosage, number of follicles >14mm on the day of trigger, and peak serum estradiol level. RMSE of the model was 5.0 oocytes, indicating that the model is able to predict the number of mature oocytes at retrieval ± 2.5 oocytes. The model was most accurate for patients with <14 follicles 14mm or more in diameter on day of trigger (RMSE of 3.8; prediction accuracy: ± 1.9 oocytes). These models are more accurate than our current method of estimation, which uses *only* the number of follicles >14mm on the day of trigger to predict number of MIIs (RMSE 6.0 for the entire cohort and 4.3 for patients with fewer than 14 follicles).

CONCLUSIONS: We have developed a machine-learning model to predict the number of MIIs at oocyte retrieval on the day of trigger shot. The model has an accuracy of ± 1.9 oocytes when used for patients with fewer than 14 visible follicles >14mm on transvaginal ultrasound. Validation will be carried out on a prospective cohort of patients undergoing IVF.

N	1009
Age (y)	36.1 (4.3)
Age Group	
< 35	373 (37%)
35-37	222 (22%)
38-40	244 (24%)
41-42	113 (11%)
> 42	57 (6%)
BMI (kg/m^2)*	26.1 (5.8)
FSH (mIU/mLU)*	7.6 (2.9)
AMH (ng/ml)*	3.1 (3.1)
Infertility Diagnosis (%)	
Not infertile	396 (39)
DOR	213 (21)
Unexplained	151 (15)
PCOS	103 (10)
Tubal Factor	84 (8)
Other/Uterine	43 (4)
Endometriosis	19 (2)
Days of stimulation*	10 (2)
FSH Dosage (IU)*	4000 (1700)
Number of follicles >14mm on day of trigger*	10 (4)
Peak Estradiol (pg/mL)*	2489 (1176)
No. oocytes retrieved*	13 (8)
No. MII oocytes retrieved*	10 (6)

*mean (SD)

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BETTER LATE THAN NEVER?: IMMATURE OOCYTES THAT MATURE IN-VITRO LATER ON THE DAY OF RETRIEVAL AND UNDERGO INTRACYTOPLASMIC SPERM INJECTION ARE A VALUABLE SOURCE OF USABLE EMBRYOS.

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OBJECTIVE: Important questions exist regarding the utility of immature oocytes that subsequently mature in-vitro for assisted reproduction. This study sought to examine outcomes of immature oocytes and the impact of female age, oocyte stage of meiosis at retrieval and timing of progression to metaphase II (MII), and percentage of mature oocytes in the cycle on fertilization, cleavage, and blastulation rates.

DESIGN: Retrospective analysis at a single institution of all consecutive oocyte retrievals for ICSI that included immature oocytes from 2015 to 2019

MATERIALS AND METHODS: Initial maturity stage was assessed at oocyte denudation. Immature oocytes were reassessed later on day 0 and again on day 1 for progression to MII. Intracytoplasmic sperm injection (ICSI) was performed on all MII oocytes on either day 0 or day 1. Fertilization, cleavage, and blastulation rates were compared between 4 groups: 1) initially mature MII oocytes, 2) immature oocytes that reached MII and underwent ICSI later on day 0, 3) metaphase I (MI) to MII on day 1, and 4) germinal vesicle (GV) to MII on day 1.

RESULTS: 10,817 oocytes from 879 women were included. 3,137 (29.0%) were immature; 418 (13.3%) matured later on day 0, and 1,911 (60.9%) matured on day 1. Embryos derived from immature oocytes had lower cleavage and blastulation rates (Table 1). However, late day 0 MII oocytes had significantly improved outcomes compared to those that reached MII on day 1 (cleavage: 74.5% vs. 54.9% OR 2.40 [1.77-3.27]; blastulation: 40.9% vs. 11.3% OR 5.43 [3.65-8.08], P<0.001 both). Ultimately, 12.9% of all transferred or frozen embryos were derived from immature oocytes. Cleavage and blastulation rates, as well as the percent of immature oocytes that contributed to usable embryos, were higher in cycles with lower percentages of mature oocytes at time of retrieval and in women >40 years of age (P<0.001, both).

CONCLUSIONS: Immature oocytes can be a valuable source of usable embryos, however those that mature later on day 0 are five times more likely to undergo blastulation than those that mature on day 1. Routine reassessment of immature oocytes prior to ICSI on day 0 may be worthwhile, and additional assessment on day 1 may also be of use in older patients or those with low percentages of mature oocytes given higher clinical yield in these subgroups.

	Fertilization (%)	Cleavage (%)	Blastulation (%)
		OR (95% CI), P-value	
Mature MII n = 7,680	72.7% (ref)	79.8% (ref)	50.2% (ref)
Late Day 0 MII n = 418	61.0% 0.57 (0.48-0.72) P<0.001	74.5% 0.74 (0.55-0.99) P=0.039	40.9% 0.69 (0.50-0.95) P=0.021
Day 1 MI > MII n = 928	65.5% 0.71 (0.62-0.82) P<0.001	54.3% 0.30 (0.25-0.36) P<0.001	10.1% 0.11 (0.08-0.16) P<0.001
Day 1 GV > MII n = 565	65.3% 0.71 (0.59-0.85) P<0.001	55.8% 0.32 (0.26-0.40) P<0.001	13.1% 0.15 (0.10-0.21) P<0.001

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TRIGGER DAY FSH SUPPLEMENTATION AND EUPLOIDY. Isaac J. Chamani, M.D.,[1] David H. McCulloh, Ph.D.,[2] Frederick L. Licciardi, M.D.[2] [1]NYU School of Medicine, New York, NY; [2]NYU Langone Fertility Center, New York, NY.

OBJECTIVE: Administering additional FSH on trigger-day may improve IVF outcomes by enhancing folliculogenesis and oocyte maturation. Recent reports have demonstrated an increase in oocyte maturation, but not in clinical pregnancy rates, with FSH supplementation. We therefore examined patients undergoing IVF with recombinant human chorionic gonadotropin (rHCG) ovulation triggers, in order to assess the effect of supplementation on ploidy, a valuable predictor of pregnancy, and the cost associated with providing FSH supplementation.

DESIGN: Retrospective cohort

MATERIALS AND METHODS: Patients undergoing GnRH-antagonist IVF cycles, with rHCG ovulation triggers, from 1/2015 through 12/2018, were separated into two groups for comparison: those receiving only trigger injections on trigger day (No Sup), and those also receiving FSH supplementation (Sup). Demographics, days of gonadotropin, #oocytes retrieved, #mature, #blastocysts, and #euploid embryos, were compared (Student's t-test or X^2).

RESULTS: Initial comparisons between the groups revealed a selection bias. No Sup patients had more robust responses, with higher trigger-day estradiol levels ($E2_{trig}$) and more eggs. In order to examine the effect of supplementation in each age group, we created No Sup comparison groups with $E2_{trig}$values indistinguishable from the Sup's. This was done by randomly selecting No Sup patients from the same SART age group and $E2_{trig}$stratum as the Sup patients.

962 patients were included in this matched comparison. 481 received supplementation, and 481 did not. Sup patients had significantly more IUs of gonadotropin administration over more days than No Sup patients. Sup patients also had more oocytes retrieved, oocytes matured, and euploid embryos formed, than No Sup patients (see table). There was, however, no difference in the number of patients who experienced a drop in their estrogen levels on the day after trigger (14.3% and 11.6% respectively, X^2= 1.5539, p > .05).

The overall cost associated with FSH supplementation was $446. However, the cost associated per unit increase of different outcomes varied, and amounted to $1,487 for each euploid embryo.

CONCLUSIONS: Among cycles matched for similar estradiol levels, trigger day FSH supplementation is associated with modest improvements in #oocytes, #mature oocytes, #blastocysts, and #euploid embryos. The increase in cost is significant but small in comparison to total cycle costs.

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CLINICALLY IRRELEVANT EFFECT OF NON-APOPTOTIC SPERM SELECTION BY MAGNETIC ACTIVATED CELL SORTING BEFORE INTRACYTOPLASMIC SPERM INJECTION IN DONATED OOCYTES, AS MEASURED BY CUMULATIVE LIVE BIRTH RATES. Maria Gil Julia, MSc, MRes,[1] Fernando Quintana, Sr., PhD,[2] David Amoros, PhD,[3] Alberto Pacheco, PhD,[4] Cristina Gonzalez-Ravina, PhD,[5] Rocio Rivera-Egea, PhD,[6] Irene Hervas, MSc,[1] Nicolas Garrido, PhD[1] [1]IVI Foundation - IIS La Fe Biomedical Research Institute, Valencia, Spain; [2]IVIRMA Bilbao, Bilbao, Spain; [3]IVIRMA Barcelona, Barcelona, Spain; [4]IVIRMA Madrid, Madrid, Spain; [5]IVIRMA Sevilla, Sevilla, Spain; [6]IVIRMA Valencia, Valencia, Spain.

OBJECTIVE: There is no consensus on the true clinical contribution of annexin V negative, non-apoptotic sperm selection via magnetic activated cell sorting (MACS) in the reproductive outcomes of assisted reproduction techniques due to limited sample size in the literature and expression of success as pregnancy rates per embryo transfer, biasing to the negative, since only the best embryo in the cohort is selected for transfer, neglecting the contribution of the remaining embryos and the sperm selection technique. Measuring cumulative live birth rates (CLBR) per embryos transferred and oocytes used until the achievement of a live birth suppress these biases, offering a more realistic approach. This study aims to assess the effect of MACS on classical reproductive parameters and cumulative rates per embryo replaced and oocyte consumed until achieving the first live birth in patients that underwent intracytoplasmic sperm injection (ICSI) cycles using donated oocytes.

DESIGN: Multi-center retrospective observational cohort study.

MATERIALS AND METHODS: Data from ICSI cycles with donated oocytes (Jan 2008-Feb 2020) in which semen samples underwent standard preparation (control group), or included an added MACS step. T-test and Fisher's exact test were used to compare descriptives and the gestational outcomes per embryo transfer (ET) and, in the case of the live birth rate (LBR), also per completed cycle (CC). Kaplan-Meier curves were plotted to show the CLBR per ET, per number of transferred embryos and per metaphase II oocytes (MII) used. Mantel-Cox tests were performed to compare the obtained curves for each group. The threshold for statistical significance was set at p-value<0.05.

	IU Gndtpn	Days of Gndtpn	#Oocytes	#Mature Oocytes	Fertilization Rate	#Blastocysts	#Euploid
Sup	5078.7+/-1562.9*	11.3+/-2.0*	8.8+/-6.5*	7.0+/-5.5*	73.0%	2.7+/-3.0	1.2+/-1.7*
NoSup	4609.1+/-1530.5*	9.9+/-2.0*	7.9+/-5.0*	7.4+/-4.3*	75.6%	2.4+/-2.2	0.9+/-1.2*

*indicates p < 0.05

RESULTS: Overall characteristics of both groups were similar.

When analysed per ET, controls (n=68151) had a 59.6% biochemical pregnancy rate, whereas MACS (n=1996) showed 60.3%, none were statistical differences, neither were clinical pregnancy, for which the MACS showed a 0.4% (0.92, 1.10) increase or the ongoing gestation rates, for which the MACS had a 3.6% lower rate.

Groups had comparable 41.3% LBR per ET, and a 67.6% per CC (n=967), MACS, vs control showing 42.2% LBR per ET and 66.8% per CC (n=36302).

CLBR in the controls was 58.7% (58.2, 59.2) for two embryos replaced, 65.1% (64.5, 65.6) for three and 78.5% (78.0, 79.1) for four. MACS showed 63.7% (60.3, 66.8), 71.4% (68.0, 74.4) and 81.6% (78.2, 84.4). Kaplan-Meier curves showed a statistically significant difference between both groups in the CLBR per embryo transferred.

Computed per MII used, the control group showed a CLBR 43.2% (42.7, 43.7) for 10 MII and 78.3% (77.7, 78.8) for 15 MII, MACS 35.8% (32.6, 38.8) and 75.6% (71.8, 78.7) respectively, being statistically different.

CONCLUSIONS: In the largest sample size ever reported, our findings suggest that the use of annexin V negative, non-apoptotic sperm by MACS prior to ICSI in oocyte donation, result in less embryos needed to reach the first live birth but no less oocytes, although clinical relevance of this intervention seems very low.

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OOCYTE STIMULATION/TRIGGER PROTOCOL CORRELATES WITH THE PROPORTION OF IMMATURE OOCYTES RETRIEVED IN ASSISTED REPRODUCTIVE TECHNOLOGY CYCLES. Damla C. Gonullu, MD,[1] David H. McCulloh, PhD,[2] Cheongeun Oh, PhD,[2] LeRoy G. Robinson, Jr., PhD,[2] Sana Salih, MD,[1] David L. Keefe, MD[2] [1]Wayne State University School of Medicine, Detroit, MI; [2]NYU Grossman School of Medicine, New York, NY.

OBJECTIVE: The goal of oocyte retrieval in cycles of oocyte cyropreservation and intracytoplasmic sperm injection (ICSI) is to obtain meiosis II (MII) mature oocytes that can be immediately fertilized or frozen without the need for in vitro maturation. The fraction of oocytes that are immature following controlled ovarian hyperstimulation (COH), in other words, arrested in germinal vesicle (GV) or meiosis I (MI) phases of the cell cycle, varies from patient to patient. In this study, we identify parameters that are associated with the proportion of immaturity (P_{im} = number of immature oocytes [GV and MI] / total number of oocytes retrieved [GV, MI, and MII]).

DESIGN: A retrospective chart review of de-identified patient information to investigate the association between COH parameters and the fraction of immature oocytes retrieved per patient undergoing oocyte cryopreservation or ICSI.

MATERIALS AND METHODS: Records for a total of 2771 NYU Langone Fertility Center patients undergoing either ICSI or egg freeze cycles were included. Parameters examined included age, basal cycle day 2/3 follicle-stimulating hormone (FSH) and estradiol (E2) levels, total dose of gonadotropins administered (including FSH and human menopausal gonadotropin [hMG]), fraction of hMG administered, number of days of treatment with gonadotropins, as well as the dose of gonadotropin administered per day, and the trigger method used (human chorionic gonadotropin (hCG) vs. Leuprolide vs. combination of the two). Stepwise multivariable logistic regression was used to identify predictors of immaturity.

RESULTS: The strongest predictor of P_{im} was the trigger method. After adjusting for other parameters, hCG trigger showed 24% immaturity, followed by hCG + Leuprolide trigger showing 22%, followed by Leuprolide trigger alone obtaining only 20% ($p<0.025$). Additionally, more P_{im} was associated with fewer days of gonadotropin administration (4% more immaturity for 3.75 less days of stimulation), and with a higher gonadotropin dose per day (4% more P_{im} for 247 IU/day more gonadotropin). P_{im} was not associated with patient age, total number of oocytes retrieved per patient, total gonadotropin dose administered, fraction of gonadotropin provided by hMG, baseline FSH or E2 levels, or the number of retrievals performed on the same day.

CONCLUSIONS: Leuprolide trigger when combined with a smaller amount of gonadotropins administered per day and a higher number of days of gonadotropin administration yielded the highest proportion of mature oocytes retrieved in this data set. This was independent of the patient's age, baseline FSH and E2 levels, total amount and type of gonadotropins used, number of retrievals performed per day, and the total number of oocytes retrieved per patient.

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ULTRASONOGRAPHIC CHARACTERISTICS OF DEEP INFILTRATING ENDOMETRIOSIS FOLLOWING REPEATED OVARIAN HYPERSTIMULATION: AN OBSERVATIONAL PILOT STUDY. Fabio Barra, MD,[1] Matteo Tantari, MD,[1] Gloria D'Alessandro, MD,[1] Carolina Scala, MD,[2] Simone Ferrero, MD PhD[1] [1]IRCCS Ospedale Policlinico San Martino, Genova, Italy; [2]Istituto G. Gaslini, Genova, Italy.

OBJECTIVE: Ovarian hyperstimulation for in-vitro fertilization (IVF) causes a significant rise in serum estrogens, which may have detrimental effects on endometriosis. The aim of this study is to investigate the impact of repeated ovarian hyperstimulation on the characteristics of deep endometriotic (DIE) nodules at ultrasound.

DESIGN: This was a prospective observational pilot study.

MATERIALS AND METHODS: Women with endometriosis who underwent at least three ovarian stimulation for IVF within 12 months were enrolled. The diagnosis of DIE and ovarian endometriomas (OMA) was performed by transvaginal ultrasound. The following locations of DIE were evaluated: uterosacral ligament, bladder, recto-vaginal, recto-vaginal infiltrating the rectum. The size of DIE nodules and OMA and the intensity of pain symptoms were systematically evaluated one month before each ovarian stimulation within 2 months after ovarian hyperstimulation or the failed transfer. Changes in the volume of DE nodules were ultrasonographically evaluated by the virtual organ computer-aided analysis (VOCAL).

RESULTS: A total of 69 DIE lesions and 19 OMA were diagnosed in 42 women included in the study; the mean (±SD) age of the study population was 38.3 (±2.3). The total number of ovarian hyperstimulations was 182 with a median (range) of 3 (3-5) stimulation for each patient. After the last hyperstimulation, the mean volume of DE nodules significantly increased (4.01 ± 3.07 mm^3 vs. 4.68 ± 3.55 mm^3; $p=0.041$). The volume of DE lesions increased in 59.4% (n=40/69), was stable in 34.7% (n=24/69) and decreased in 8.7% (n=6/69) of cases. A new DIE lesion was diagnosed in 9.5% (n=4/42) of patients. Similarly, the mean volume of OMA significantly increased (3.42 ± 2.45 mm^3 vs. 4.28 ± 3.04 mm^3; $p=0.032$). The mean intensity of dysmenorrhea ($p=0.025$), chronic pelvic pain ($p=0.039$), dyspareunia ($p=0.046$), chronic pelvic pain ($p=0.034$) and dyschezia ($p=0.036$) worsen. One case of bowel sub occlusion in a patient with rectal endometriosis occurred.

CONCLUSIONS: Women with DIE undergoing repeated ovarian hyperstimulation within a short period have a higher risk of lesion size growth and worsening of pain.

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NIPT RESULTS IN PREGNANCIES RESULTING FROM EUPLOID EMBRYO TRANSFERS. Rahana Harjee, MD,[1] Gary S. Nakhuda, MD,[2] Chen Jing, MSc[3] [1]University of, BC, Canada; [2]Olive Fertility Centre, Vancouver, BC, Canada; [3]Biostatistic, Olive Fertility Centre, Vancouver, BC, Canada.

OBJECTIVE: Preimplantation Genetic Testing for Aneuploidy (PGT-A) helps to optimize IVF outcomes by identifying euploid embryos for transfer. The typical approach involves trophoectoderm biopsy at the blastocyst stage, and chromosome copy number analysis with next generation sequencing (NGS). Depending on the technique, error rates of PGT-A are estimated to be 1-4 %; therefore, patients are typically counselled to also undergo routine prenatal screening. Non-invasive prenatal testing (NIPT), which uses maternal and placental circulating cell-free DNA (ccfDNA) to identify chromosomally abnormal pregnancies, can be performed as early as 9 weeks gestation and has shown to have greater diagnostic accuracy than precedent non-invasive prenatal screening. While the benefit of NIPT seems evident as first line aneuploidy screening, it is unknown if NIPT provides additional or discrepant diagnostic information for patients with PGT-A screen embryos.

Our aim was to examine NIPT results for patients who conceived following euploid embryo transfer after PGT-A to determine the frequency of discrepant findings.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: A chart review was completed at an independent fertility centre between April 2015 - January 2020 for patients who underwent single, euploid, frozen embryo transfer as determined by NGS- PGT-A, then chose to have NIPT.

RESULTS: A total of 1723 euploid transfers were performed during these dates. 369 patients elected to have NIPT through the clinic following assisted

reproduction (in vitro fertilization (IVF), in vitro fertilization – intracytoplasmic sperm injection (IVF-ICSI), and frozen embryo transfer), 52 of whom had undergone PGT-A prior to transfer. Patients' ages ranged from 25 to 44 (mean 36.8 years). NIPT results were normal for 48 patients (92.3%), 1 patient (1.9%) had inconclusive results for the sex chromosomes (euploid for numerical chromosomes). 6 patients required an additional test (11.5%) and 3 patients (5.8%) had non-diagnostic results following 2 failed attempts secondary to low fetal ccfDNA fraction. In patients who had NIPT (without PGT-A), 15 patients required a second NIPT test (4.7%), all of which received results following a second sample.

Of the 48 patients with normal NIPT findings, 37 delivered healthy neonates, 1 had a spontaneous loss at 24 weeks secondary to severe preeclampsia, and 10 currently have ongoing pregnancies. One patient elected to terminate after fetal anomalies were detected on anatomic ultrasound, although fetal karyotype was found to be normal.

CONCLUSIONS: Almost all patients who underwent PGT-A with transfer of a euploid embryo, and subsequently obtained diagnostic NIPT results had normal findings (98.0%). The remaining inconclusive or non-diagnostic results may represent limitations of current NIPT technology. While sample size is limited, these results suggest that subsequent to euploid embryo transfer following PGT-A, NIPT may be of questionable additional value. However, given the possibility of malformations without a chromosomal etiology, anatomical ultrasound screening is still indicated.

SUPPORT: None

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THE SAFETY AND EFFECTIVENESS OF MILD GONADOTROPIN STIMULATION/INTRAUTERINE INSEMINATION IN IDIOPATHIC INFERTILITY. DO SHOTS WORK BETTER THAN PILLS? Karissa C. Hammer, MD, Stylianos Vagios, MD, Caitlin Sacha, MD, Irene Dimitriadis, MD, Charles L. Bormann, PhD, Kaitlyn E. James, PhD, Irene Souter, MD Massachusetts General Hospital, Harvard Medical School, Boston, MA.

OBJECTIVE: Ovulation induction (OI) with gonadotropins (Gn) has been associated with higher overall success than oral medication (oral med), albeit higher rate of multiples. Our objective was to compare the success and safety of a mild Gn stimulation/IUI regimen to oral med [clomiphene citrate (CC) or letrozole]/IUI regimen among patients with idiopathic infertility (IdI).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS:

Setting: Academic fertility center.

Patients: Women with IdI undergoing OI/IUI from 12/2003 - 09/2019.

Interventions: Retrospectively reviewed data from 3,155 OI/IUI cycles (1,193 patients). Gn/IUI cycles (n=2,113) were compared to oral med/IUI ones (n =1,042).

Outcomes:

Primary: Clinical pregnancy rate (CPR)/cycle.

Secondary: Spontaneous abortion, non-viable pregnancy (ectopic, biochemical, unknown location), and multiple pregnancy rates (SABR, NVPR, and MPR, respectively), and cycle characteristics: length of stimulation (days), pre-ovulatory follicle number ($\geq$ 13 mm), endometrial thickness (ET), and cycle cancellation due to over-response.

Statistics: Wilcoxon rank sum, x^2-tests, and logistic regression were used. Odds ratios (OR) were calculated utilizing generalized linear mixed effects models, adjusted for age and multiple cycles per patient.

RESULTS: Gn/IUI patients compared to oral med/IUI patients were older, had higher FSH and lower AMH levels [mean (SD): 35.2 (3.6) vs. 33.5 (3.3) years, p<0.001; 7.1 (2.1) vs. 6.9 (1.8) IU/mL, p: 0.005; 3.0 (2.1) vs. 3.5 (2.4) ng/mL, p<0.001; respectively]. Mean (SD) daily FSH dose was 58.9 (45) IU producing a mean (SD): 2.2 (1.4) follicles in the Gn/IUI group.

When comparing Gn/IUI to oral med/IUI cycles, CPR was significantly higher in the former group (CPR: 14.5% vs 11.7%, p: 0.03, respectively), which had higher odds of clinical pregnancy [OR (95%CI): 1.28 (1.0, 1.6), p: 0.03; aOR (95%CI): 1.32 (1.0, 1.7), p: 0.036]. Results did not change when restricting the comparison of Gn/IUI to CC/IUI cycles only [14.5% vs 11.6%, p: 0.026; aOR (95%CI): 1.29 (1.0, 1.6), p: 0.03, respectively].

Gn/IUI compared to oral med/IUI cycles, had significantly shorter stimulation duration, lower cancellation risk, and thicker endometrium [mean (SD): 10.6 (2.2) vs 12.0 (1.8) days, p<0.001; 3.6% vs 6.0%, p: 0.003; 8.6 (2.1) vs 7.2 (2.1) mm, p<0.001; respectively). Mean number of follicles differed between groups but not in a clinically meaningful way [mean (SD): 2.2 (1.4) vs. 2.0 (1.5), p: 0.001, Gn/IUI vs oral med/IUI).

Age-adjusted MPR and SAB rate did not differ between groups [MPR: 12.5% vs 11.5%, p: 0.82, aOR (95%CI): 0.8 (0.4, 1.9, p: 0.63; SAB: 20.8% vs 10.7%, p: 0.013, aOR (95%CI): 1.7 (0.9, 3.4), p: 0.11, Gn/IUI vs oral med/IUI]. NVPR was lower for Gn/IUI cycles [8.8% vs 15.1%, p: 0.042, aOR (95%CI): 0.47 (0.3, 0.9), p: 0.02, respectively].

CONCLUSIONS: Our data suggests that among IdI patients, mild stimulation with Gn is associated with a significantly higher CPR and a lower NVPR, without an increased risk of a multiple pregnancy. Mild stimulation with gonadotropins coupled with IUI is a safe and effective treatment of IdI.

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APPLICATION OF DROTAVERINE IN FROZEN-THAWED CYCLE: A SINGLE COHORT STUDY USING PROPENSITY SCORE ANALYSIS. Tingting Li, Doctor,[1] Panyu Chen, Master,[2] Cong Fang, PHD, MD[2] [1]Reproductive Medicine Research Center, Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; [2]The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: To investigate the clinical value of drotaverine in vitro fertilization-embryo transfer (IVF-ET) in frozen-thawed cycle.

DESIGN: A retrospective study

MATERIALS AND METHODS: A retrospective study was conducted with clinic-based data in the Reproductive Medicine Research Centre of the Sixth Affiliated Hospital of Sun Yat-sen University from Jan 2014 to May 2019. Patients aged below 40 years old underwent their first or second IVF-ET cycle and transferred 1-2 good embryos, Intervention measures were

	Group A (n=422)	Group B (n=422)	*F/X2*	*P*
Age(y)	31.930±3.749	32.76±3.765	0.023	0.881
BMI	21.840±3.075	21.912±2.851	0.796	0.372
Basal FSH(U/L)	7.526±3.423	7.565±3.429	0.002	0.963
Basal LH(U/L)	5.707±5.547	5.791±4.999	0.120	0.729
Basal E2(pg/ml)	45.495±36.017	43.711±23.957	0.812	0.214
Basal PRL	18.868±12.669	18.572±11.992	0.184	0.668
Basal T	0.366±1.560	0.309±1.219	0.571	0.450
AMH (ng/ml)	3.340±3.205	3.350±3.258	0.086	0.969
AFC	11.980±8.244	11.770±8.368	0.064	0.800
Endometrial thickness	10.231±2.143	10.523±2.211	0.078	0.971
Chemical pregnancy rate	48.815% (206/422)	28.436% (120/422)	36.965	0.000
Clinical pregnancy rate	44.313% (187/422)	24.408% (103/422)	37.068	0.000
Implantation rate	29.193% (235/805)	15.273% (126/825)	45.786	0.000
Miscarriage rate	17.112% (32/187)	16.505% (17/103)	0.018	0.895
Multiple pregnancy rate	26.203% (49/187)	22.330 (23/103)	0.534	0.465
Ectopic pregnancy rate	2.674% (5/187)	1.942 (2/103)	0.151	0.647
Live birth rate	35.545% (150/422)	19.905% (84/422)	25.756	0.000

Chemical pregnancy rate=number of biochemical pregnant cycle/number of embryo transfer cycle; Clinical pregnancy rate=number of clinical pregnant cycle/number of embryo transfer cycle; Embryo implantation rate=number of gestational sac/number of embryo transferred;

oral administration of 80mg of drotaverine twice a day for 5 consecutive days from 1 day before embryo transfer. According to the plan of embryo transfer and whether or not to use drotaverine, the patients were divided into 2 groups. The day before D3 embryo transfer, drotaverine was used (group A: 422 cases); The propensity score analysis of SPSS statistical software was used to match the selection of control group (group B: 422 cases).

RESULTS: There were no significantly differences with regard to age, BMI, AMH, and number of antral follicle between 2 groups. The positive rate of HCG (48.815% vs 28.436%), clinical pregnancy rate (44.313% vs 24.408%) and embryo implantation rate (29.193% vs 15.273%) were statistically significant ($p < 0.05$) between 2 groups.

CONCLUSIONS: Drotaverine can significantly improve embryo implantation and pregnancy rate for D3 embryo transfer in frozen-thawed cycle.

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FOLLICULAR ACTIVATION BY INTRAOVARIAN INJECTION OF AUTOLOGOUS PLATELET RICH PLASMA (PRP) IN WOMEN WITH PRIMARY OVARIAN INSUFFICIENCY (POI): IMPACT ON OVARIAN RESERVE AND IVF OUTCOME.

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OBJECTIVE: Primary ovarian insufficiency (POI) affects 1% of reproductive age women, and is characterized by a severe decrease in ovarian reserve prior to 40 years of age. Currently, oocyte donation is the only established treatment modality for women with POI. In this study, we aimed to determine whether intraovarian injection of autologous platelet rich plasma (PRP) improves follicle development, response to ovarian stimulation and in vitro fertilization (IVF) outcome in women with primary ovarian insufficiency (POI).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Women (N=311; age range 24-40) diagnosed with POI based on European Society of Human Reproduction and Embryology (ESHRE) criteria ((i) oligo/amenorrhea for at least 4 months, (ii) an elevated serum FSH >25 IU/l on two occasions 4 weeks apart (iii) onset before the age of 40 years) were included in the study. PRP was prepared from patient's own peripheral blood by centrifugation and injected transvaginally under ultrasound guidance into at least one ovary using a 35 cm 17 G single lumen needle. On the 2-4th days of the second menstrual cycle after the PRP procedure, AFC and serum AMH and FSH levels were re-assessed, and followed up to 6 consecutive months. Women who were found to have at least one antral follicle were started on ovarian stimulation for IVF-ICSI.

RESULTS: PRP treatment resulted in increased AFC (1.7 ± 1.4 vs 0.5 ± 0.5; $p<0.01$) and serum AMH (0.18 ± 0.18 vs 0.13 ± 0.16; $p<0.01$), while serum FSH did not change significantly (41.6 ± 24.7 vs 41.9 ± 24.7; $p=0.87$). After the PRP injection, 23 women (7.4%) conceived spontaneously, 201 (64.8%) developed antral follicle(s) and attempted IVF, and 87 (27.8%) had no antral follicles and therefore did not receive additional treatment. Among the 201 women who attempted IVF, 71 (22.8% of total) could not undergo oocyte retrieval due to stimulation failure or premature ovulation, and 48 (15.4% of total) did not develop embryos due to lack of oocytes at retrieval or failed fertilization. Of the 82 women (26.4% of total) who developed embryos with IVF, 25 preferred to cryopreserve embryos for transfer at a later stage, while 57 underwent embryo transfer resulting in 13 pregnancies (22.8% per transfer, 4% of total). In total, of the 311 women treated with PRP, 25 (8.0%) achieved livebirth/sustained implantation (either spontaneously or after IVF), while another 25 (8.0%) stored cryopreserved embryos.

CONCLUSIONS: Our findings suggest intraovarian injection of autologous PRP might be considered as an experimental treatment option for follicular activation in women with POI. Additional studies with randomized prospective study design are necessary to determine whether this intervention truly results in improved clinical outcomes, through spontaneous conception and/or assisted reproduction.

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PREDICTORS AND CLINICAL SIGNIFICANCE OF RETAINED SINGLE EUPLOID EMBRYOS.

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OBJECTIVE: In approximately 1-4% of embryo transfers, upon flushing the catheter to verify expulsion, a retained embryo is noted.[1-3] Limited data exist regarding the characteristics of euploid embryos that increase the likelihood of retention in the catheter, and on the impact of repeat transfer of retained embryos on pregnancy outcomes.[1-3] The objective of this study is to determine the characteristics of euploid single blastocyst transfer that are associated with retention in the catheter, and to determine the prognosis of repeat ET of retained euploid blastocysts.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: Patients who underwent a euploid FET from 2016-2018 were included in the study. Preimplantation genetic testing for aneuploidy (PGT-A) was performed using Next Generation Sequencing. Euploid FET cycles were separated into groups: Group 1 consisted of cases in which embryo retention was noted upon catheter inspection, and Group 2 consisted of controls in which the embryo was successfully expelled in a single attempt. Baseline demographics, cycle characteristics, and pregnancy outcomes were assessed using comparative statistics and adjusted logistic regression.

RESULTS: A total of 6,703 single euploid FET were identified and included in the analysis, including 76 cycles in Group 1 (1.1%) and 6,627 in Group 2. The groups were similar in terms of age, oocyte age, AMH, BMI, and endometrial thickness. Embryo expansion, inner cell mass grade, trophectoderm grade, and day of trophectoderm biopsy were not associated with the probability of retention within the catheter. Embryo retention was significantly associated with presence of mucus ($p=0.044$) or a mucus plug ($p=0.002$) noted upon inspection of the catheter following embryo transfer. Mucus aspiration, type of catheter used, difficult transfer, cervical dilation, and the quality of the fluid squirt were not associated with embryo retention. Implantation and ongoing pregnancy rates were significantly decreased in Group 1 compared to Group 2 (44.02% vs. 61.3%, OR 0.49, 95% CI 0.31-0.78, $p=0.002$; 37.3% vs. 51.6%, OR 0.56, 95% CI 0.35-0.90, $p=0.014$). A decrease in odds of live birth was seen but this was not statistically significant (37.0% vs. 49.7%, OR 0.59, 95% CI 0.34-1.04, $p=0.06$). Embryo retention was not associated with pregnancy loss or with monozygotic splitting. When controlling for age, oocyte age, AMH, BMI, endometrial thickness, presence of mucus in the catheter and mucus plug, embryo retention was still significantly associated with a decline in implantation rate (OR=0.54, 95% CI=0.32-0.91, $p=0.02$) and ongoing pregnancy rate (OR=0.56, 95% CI=0.33-0.96, $p=0.035$). Live birth rate did not differ significantly between the groups (OR=0.61, 95% CI=0.32-1.14, $p=0.12$).

CONCLUSIONS: Retention was associated with mechanisms indicating difficulty of the transfer rather than embryo characteristics such as expansion or grade. Our data indicates that while a retained euploid frozen-thawed embryo may have a decreased ability to implant, once ongoing pregnancy is established, live birth outcomes are similar.

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SUPPORT: None

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IS MOCK EMBRYO TRANSFER AN ADD-ON? A REVIEW OF CURRENT CLINICAL PRACTICE AND A SYSTEMATIC REVIEW OF PUBLISHED EVIDENCE.

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OBJECTIVE: A systematic review and meta-analysis to assess the assess the effectiveness of mock embryo transfer. We also identified the number of fertility clinics offering mock embryo transfer, the stated justification for offering the procedure, and the associated additional cost.

DESIGN: Systematic examination of fertility clinic websites and systematic review of published randomized trials evaluating the effectiveness of mock embryo transfer.

MATERIALS AND METHODS: We identified fertility clinic websites using google.com. Information was extracted from individual clinic websites related to the provision of embryo transfer and associated costs. The systematic review of published randomized trials was prepared by following Cochrane Collaboration guidelines. Selection of studies, assessment of trial quality, and extraction of relevant data were performed independently by two researchers. Summary estimates and 95% confidence intervals were calculated using random-effects methods.

RESULTS: Worldwide 1,200 clinics and fertility networks, have been identified to offer mock embryo transfer at an average cost of $350 (range $240 to $500). 40 % of identified clinic websites stated that mock embryo transfer was associated with improved success rates.

The systematic search of published literature identified two randomized trials, reporting data from 499 women. Live birth was not reported. Mock embryo transfer increased pregnancy confirmed by ultrasound (OR 1.80, 95% CI 1.07-3.05) when compared to routine care. Mock embryo transfer did not increase biochemical pregnancy (OR 0.91, 95% CI 0.28-2.99) when compared to routine care. There was poor reporting of other secondary outcomes, including ectopic pregnancy, miscarriage, and other adverse events.

CONCLUSIONS: There is insufficient evidence to support the routine use of mock embryo transfer. The uncertainty regarding the procedure's effectiveness should be presented alongside online information pertaining to mock embryo transfer, discussed openly during consultations, and summarised within accessible patient information leaflets and websites. Regulators, including the Human Embryology and Fertility Authority, should consider treating mock embryo transfer as an add on. Using their established system, it would currently be classified as amber: do not offer routinely. Mock embryo transfer may have a role in selected cases.

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SUPPORT: No financial support to disclose.

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DOES THE INTERVAL TIME BETWEEN OVULATION TRIGGERING AND OOCYTE PICK UP AFFECT BIOLOGICAL RESULTS IN LOW, NORMAL AND HIGH OVARIAN STIMULATION RESPONDERS ?

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OBJECTIVE: To assess the effect of time interval between ovulation triggering (OT) and oocyte pick up (OP) on biological results in low, normal and high responders

DESIGN: A prospective observational study performed in the department of Reproductive Medicine in Aziza Othmana Hospital between January and December 2019.

MATERIALS AND METHODS: Inclusion criteria : age between 18 and 42 years old. Controlled ovarian stimulation with antagonist protocol for ICSI.

Exclusion criteria: Mild ovarian stimulation / ovulation triggering by GnRH agonist (OHSS prevention)

We divided patient into poor, normal and high ovarian responders (based on AMH and AFC)

The ovarian stimulation was performed with an antagonist protocol for all patient with recombinant FSH (Gonal F, Merck) and cetrorelix acetate (Cetrotide, Merck). The ovulation triggering was performed when 2 or more follicles reached 17 mm with recombinant HCG (Ovitrelle 250, Merck). The interval time between OT and OP was divided into 4 groups: 35 h (group 1), 36 h (group 2) , 37 h (group 3) and $\geq$ 38 h (group 4).

$\chi 2$ test was used to compare qualitative variables. Student's t-test was used to compare quantitative variables. P-value < 0.05 was considered as statistically significant.

RESULTS: Five hundred and eighty four patients were included: 204 poor responders, 310 normal responders and 70 high responders group. For poor ovarian responders, we did not find a statistical difference for the number of oocyte retrieved (5.8 ; 3.3 ; 3.7 ; 3.6 ; p=0,2) the number of MII (3.8 ; 2.1; 2.4 ; 2.6 ; p=0,2) and the ratio MII/CCO: (0.65 ; 0.63 ; 0.66 ; 0.7é ; p=0,06) in the group 1, 2, 3 and 4 respectively.

For normal ovarian responders, we did not find a statistical difference for the number of oocyte retrieved: (7.7 ; 8.8 ; 8.1 ; 8.5 ; p=0,8) ; the number of MII: (5.2 ; 5.9 ; 5.6 ; 5.5 ; p=0,9) and the ratio MII/CCO (0.67 ; 0,67 ; 0.69 ; 0.64 ;p=0,3) in the group 1, 2, 3 and 4 respectively.

For high ovarian responders, we did not find a statistical difference for the number of oocyte retrieved (22 ; 18 ; 17 ; 23 ; p=0,3); the number of MII (16 ; 11,9 ; 12,1 ; 14 ; p=0,8) and the ratio MII/CCO (0.72 ; 0.66 ; 0,71 ; 0.6 ; p= 0,1) in the group 1, 2, 3 and 4 respectively.

CONCLUSIONS: It is not certain that adjustment of the interval time between OT and OP is necessary according to different ovarian responders in order to improve the IVF output. Moreover; studies are needed to determine if these results are applicable when using a GnRH agonist ovarian stimulation protocol.

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INTRAUTERINE INJECTION OF HUMAN CHORIONIC GONADOTROPIN BEFORE EMBRYO TRANSFER: A RANDOMIZED CONTROLLED TRIAL.

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OBJECTIVE: Human chorionic gonadotropin (hCG) is produced by the syncytiotrophoblast and plays a key role in implantation. However, quality evidence on intrauterine administration of hCG prior to embryo transfer (ET) is lacking. Our study aimed at evaluating whether intrauterine administration of hCG before ET improves in vitro fertilization (IVF) outcomes.

DESIGN: A double-blinded randomized controlled trial (RCT) (NCT03238807) in an University-affiliated IVF center in Assiut, Egypt. The study protocol was approved by the University's Institutional Review Board (IRB) (approval number: 17200094).

MATERIALS AND METHODS: We included infertile women scheduled for intra-cytoplasmic sperm injection (ICSI). After informed consent, women were randomized using a simple computer-generated random allocation in a 1:1 ratio to receive either 500 IU hCG intrauterine (hCG group), or culture media intrauterine (control group) prior to ET. Women in the hCG group received 500 IU of hCG in 0.1 mL of tissue culture media via intrauterine injection 4 minutes before ET, while women in the control group received 0.1 mL of tissue culture media. In both groups, an intra-uterine insemination (IUI) catheter was used for intrauterine administration. The patients and the clinician who conducted the procedure were blinded to the allocated intervention.

Our primary outcome was live birth, while ongoing pregnancy and clinical pregnancy were secondary outcomes. According to the intention-to-treat principle, analyses of outcomes were done and were represented as risk ratios (RRs) with 95% confidence intervals (CIs). We needed a sample size of 204 to show an increase of live birth from 28% to 48% at 80% power with an alpha error of 0.05. Accounting for 8% of drop-outs, we planned to recruit 220 participants.

Due to the COVID-19 pandemic, all IVF procedures have been suspended in our center since March 2020. As a consequence, recruitment was halted on 27 February 2020 at 181 participants. At the time of abstract submission, data on ongoing pregnancy are available. At the congress, we will be able to present data on live birth.

RESULTS: From July 2018 to February 2020, 181 women were randomized into the hCG group (n=90) and the control group (n=91). Baseline and cycle characteristics were comparable between the two groups. In the control group, one woman was lost to follow-up after confirmation of clinical pregnancy. Ongoing pregnancy was 23% (21/90) in the hCG group versus 19% (17/90) in the control group (RR 1.24, 95% CI 0.70 – 2.19), while clinical

pregnancy was 34% (31/90) in the hCG group versus 26% (24/91) in the control group (RR 1.31, 95% CI 0.84 – 2.04).

CONCLUSIONS: From the available data in this RCT, we did not find evidence that intrauterine hCG administration before ET improves ongoing pregnancy rates.

SUPPORT: None

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PROLONGED FOLLICULAR PHASE LENGTH COMPARED TO BASELINE CYCLE NEGATIVELY AFFECTS OUTCOMES IN NATURAL FROZEN EMBRYO TRANSFER CYCLES.

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OBJECTIVE: To determine whether a prolonged follicular phase in a natural frozen embryo transfer cycle as compared to the baseline follicular phase length affects pregnancy outcomes.

DESIGN: Retrospective cohort study performed in an academic hospital setting.

MATERIALS AND METHODS: Patients who utilized natural cycles for their first frozen embryo transfer using autologous day 5 PGT euploid embryos in our IVF clinic between 01/01/2013 and 12/31/2018 were included. Patients were stratified by variance of LH surge day in their natural frozen embryo transfer cycles as compared to their LH surge day in their baseline menstrual cycles (0-6 days longer than baseline and >6 days longer than baseline). Patients with an LH surge earlier than their baseline day of LH surge were excluded. The primary outcomes were pregnancy and live birth rates. Logistic regression adjusted *a priori* for patient age and number of embryos transferred was used to estimate the odds ratio with a 95% confidence interval (CI) for pregnancy outcomes.

RESULTS: A total of 524 natural frozen embryo transfer cycles met inclusion criteria, including 451 cycles in the 0-6 day group and 73 cycles in the >6 day group. The mean age was 37.2 ± 3.9 days in the 0-6 day group and 36.6 ± 4.0 days in the >6 day group. The mean number of embryos transferred was 1.1 in both groups. The pregnancy rate was significantly higher for women with an LH surge day within 6 days of their LH surge at baseline (75.4%) compared to women with an LH surge day >6 days from their baseline (60.3%; OR 0.50; 95% CI 0.30-0.84). Among patients who achieved pregnancy, however, there were no significant differences between the 0-6 day group and the >6 day group for biochemical pregnancies (8.2% versus 6.8%, OR 0.80; 95% CI 0.23-2.79), miscarriage rate (6.2% versus 6.8%, OR 1.12; 95% CI 0.32-3.95), or live birth rate (82.9% versus 86.4%, OR 1.30; 95% CI 0.52-3.22).

CONCLUSIONS: Many frozen embryo transfer cycles using PGT normal embryos take place quickly after fresh stimulated cycles. We have observed that patients often ovulate later than their usual ovulation cycle day at baseline. In cycles with an LH surge >6 days from baseline, the pregnancy rate was significantly reduced compared to those with an LH surge within 6 days from baseline. These observations indicate that a prolonged follicular phase compared to a patient's baseline cycle may alter endometrial proliferation and development, leading to a negative impact on endometrial receptivity. Interestingly, once pregnancy was achieved, pregnancy outcomes were similar between the two groups. However, due to the significantly lower chances of achieving a pregnancy in the first place, we conclude that women undergoing a natural frozen embryo transfer cycle who ovulate beyond 6 days from their baseline LH surge day should consider postponing their frozen embryo transfer to another cycle.

SUPPORT: None

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THE RELATIONSHIP BETWEEN NUMBER OF FOLLICLES 14MM OR GREATER AT TIME OF TRIGGER OF PREGNANCY RATES IN IUI CYCLES IN WOMEN 38 YEARS AND OLDER.

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OBJECTIVE: To determine the pregnancy rate at IUI in women 38-42 years of age based on number of mature follicles stimulated.

DESIGN: A Retrospective Cohort Study

MATERIALS AND METHODS: A database was created of all women aged 38-42 years old who underwent IUI with stimulation at the McGill University Reproductive Centre between 2009-2018. The database contains 1597 IUIs from 944 women, 1574 has data of follicle size at hCG-trigger. All subjects were stimulated with either clomiphene (n=240), letrozole (n=176) or FSH (n=1158). ANOVA, chi square tests, and stepwise multivariate logistic regression were performed. The primary outcome was clinical pregnancy rate per cycle (intrauterine fetal pole and heartbeat), and 2nd outcomes were rate of pregnancy & amp; multiple pregnancy. Data presented are X±SD or %. Power analysis requires 785 cycles for an effect size of 0.1, alpha 0.05 and β=0.80.

RESULTS: Clinical pregnancy rates per stimulation agent were similar (p=0.87). Based on serum (chemical) pregnancy rates (p=0.93), clinical pregnancy rates (p=0.21) and multiple pregnancy rates per clinical pregnancy were similar (p=0.33) (see table). Baseline demographics were compared in the follicle groups. Female age (p=0.03), previous deliveries (p=0.04), maximum endometrial thickness (p=0.02), and serum basal FSH level (p=0.03) differed. However male age (p=0.64,) and basal serum estradiol levels (0.20), FSH (p=0.27) levels, AFC (p=0.17), and Total Motility Sperm (TMS) count (0.06) did not differ.

When stepwise multivariate logistic regression with 1 mature follicle stimulated is taken as the bench mark and controlling for age, total motility sperm count (TMS), number of previous deliveries, antral follicular count, and endometrial thickness, in no cases did having more mature follicles improve clinical pregnancy rates (table).

CONCLUSIONS: Surprisingly, number of stimulated value mature follicles did not relate to outcomes at IUI in women 38-42 years of age. Interestingly in subjects requiring triggering prior to development of any mature follicles, pregnancy rates remained robust (9%). Overall pregnancy rates in this older group were acceptable at 7% per IUI cycle.

SUPPORT: I accept complete responsibility for the data at the time of submission. I verify that I am in compliance with HIPPA standards to protect the privacy of the patients discussed in my presentation. I either have received written authorization from the patients, have removed any identifiable images or patients records from my presentation, or my presentation does not pertain to any patient treatment.

# of mature follicles at hCG	Chemical Pregnancy	Clinical Pregnancy	Multiple Pregnancy	95% CI for clinical pregnancy rate compared to 1 follicle as benchmark (MV regression)	P value MV logistic Regression for predictor of clinical pregnancy
0	8/86	8/86	0/8	0.33-37.6	0.30
1	87/983	67/983	1/67	N/A	N/A
2	35/385	28/385	2/28	0.53-6.5	0.34
3	12/94	6/94	2/6	0.43-13.9	0.31
4	2/22	2/22	0/2	0.16-3.2	0.67
5	0/4	0/4	0/4	N/A	0.996

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AFFORDABLE IVF: DETERMINANTS OF LIVE BIRTH OR ONGOING PREGNANCY AFTER FIRST CYCLE OF LETROZOLE (LTZ) – GONADOTROPIN (GN) MILD STIMULATION, IMMEDIATE ICSI, AND INTRAVAGINAL EMBRYO CULTURE. Nicholas A. Cataldo, MD, MPH,[1] Karen R. Hammond, DNP, CRNP,[1] Lisa J. Ray, MS, HCLD,[2] Cecil A. Long, MD[1] [1]America Institute for Reproductive Medicine, Birmingham, AL; [2]ART Labs Unlimited, Streamwood, IL.

OBJECTIVE: To determine what patient and cycle factors are associated with a favorable outcome when mild ovarian stimulation and immediate ICSI are combined with intravaginal embryo culture.

DESIGN: Observational cohort of all 252 women with their first cycle start on this protocol in our practice from 6/2018 to 12/2019 who planned fresh transfer, comprising nearly all our first ART cycles. Later patient cycles were censored for lack of 24-week follow-up. Ongoing pregnancy (24+ weeks' gestation) or live birth (OP/LB) was modeled by logistic regression.

MATERIALS AND METHODS: Women were non-tobacco users with BMI <40 kg/m^2. LTZ x5 days was started 4 d after oral contraceptives were stopped, then overlapped on its 5th day with customized dose gonadotropins. No GnRH analogs were used. Cycle monitoring was repeated if necessary before hCG trigger; retrieval was 35 hr later under mild sedation in a hospital office. Metaphase (M) oocytes were immediately treated by ICSI and placed with media into an INVOcell (INVO Biosciences, Sarasota, FL), which was secured in the upper vagina by a diaphragm. Typically after 5 days, if available 1-2 blastocysts (blasts) were transferred. We modeled OP/LB according to patient and stimulation factors and oocyte and embryo outcomes using JMP Pro 12.0.1 (SAS Institute, NC).

RESULTS: Mean female age was 34.2 ($\pm$4.6) yr; 25% had AMH <1.0 ng/mL, 67% were nulliparous, and 42% had prior pregnancy loss(es). Stimulations used 5–10 mg/day LTZ (5 mg in 69%) plus 1000 ± 500 units FSH over a median of 4 days (range 1-9). Only one follicle scan was done in 79%. Cancellation rate was 15%. Retrievals successfully obtained M-stage oocytes in 93% (M-2 in 78%), with a mean of 1.9 M-2's and 1.3 M-1's. Transfer [of blast(s)] followed 82% [60%] of 202 successful retrievals, with 93% of transfers on Day 5. There were 47 pregnancies ongoing or resulting in live birth.

By univariable regression, factors associated ($p<0.05$) with OP/LB included age (odds ratio [OR] 0.92/yr; 95% confidence interval [CI] 0.85–0.98); total number of metaphase (M) oocytes (OR 1.24; 95% CI 1.08–1.42) and M-2 oocytes (OR 1.50; 95% CI 1.24–1.84) retrieved; and number of blasts obtained (OR 2.47; 95% CI 1.67–3.81). LTZ at 10 mg/d and higher daily GN dose were each negatively associated with OP/LB.

No association of OP/LB was found with serum AMH, (nulli)parity, prior pregnancy loss, M-1 oocytes retrieved, or transfer of 2 *vs.* 1 blast. A non-significant negative trend was found for association of OP/LB with cycle-day-3 E_2 ($p=0.08$) and total GN dose ($p=0.09$), and a positive trend with number of embryos transferred ($p=0.07$).

After adjustment for M-2 oocyte number, LTZ dose ($p<0.01$) and total GN dose ($p<0.015$) were each negatively associated with OP/LB; age retained borderline significance ($p=0.07$).

CONCLUSIONS: Our lower-cost ART protocol, with LTZ-based mild stimulation, few monitoring visits, and intravaginal embryo culture, is more successful in younger women. M-2 oocyte yield and blast formation are predictive for successful pregnancy, but transfer of a second blast did not improve outcome. Higher LTZ and GN doses as employed were not associated with greater success.

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CLINICAL VALIDATION SUPPORTS THE CONCEPT OF UNIVERSAL WARMING PROTOCOLS FOR VITRIFIED HUMAN OOCYTES. Cristina Labrado, B.Sc., José Manuel Navarro, M.D. Instituto para el Estudio de la Biología de la Reproducción Humana, Sevilla, Spain.

OBJECTIVE: Human oocytes are commonly cryopreserved using a combination of vitrification and warming solutions under specific instruction for use. However, the respective warming solutions might not always be available. Vitrified oocytes may be stored for long periods or shipped to other centres. Such circumstances could result in the use of warming kits of alternative brands with different formulations and protocols, i.e. not related to the kits used for vitrification. Although many warming kits show certain similarities, they have not been comprehensively cross validated and could potentially impact survival and development rates. It is therefore of general interest to know the compatibility of a new warming protocol with already cryopreserved oocytes. It has previously been reported that vitrification and warming solutions of different brands can be successfully combined. The aim of this study was to validate if oocytes previously vitrified with a DMSO-based (dimethyl sulfoxide) kit at room temperature can be successfully warmed in a kit from another manufacturer with a different composition and used at a different temperature (37^{o}C).

DESIGN: Single centre, prospective data collection during a transition period (August 2017 to December 2019) from one oocyte vitrification and warming procedure/protocol to another.

MATERIALS AND METHODS: Oocytes from both IVF patients and donors were collected 36 hrs post HCG administration, denuded after 2.5 hrs and vitrified after a further 0.5 hrs. Vitrification was performed with a DMSO-containing kit at room temperature using an open device (VT801/Cryotop, Kitazato, Japan). Oocytes were warmed at 37°C (RapidWarm Omni, Vitrolife, Sweden). All procedures were performed according to manufacturer's recommendations. Oocytes were fertilised and cultured until day 3 or day 5/6, followed by embryo transfer or re-vitrification for later use. Survival, fertilisation and implantation rates were measured.

RESULTS: Totally, 592 oocytes from 52 patients and donors were vitrified and warmed. The survival rate was 92.3% (108/117) for patient oocytes and 92.2% (438/475) for donated oocytes. Fertilisation rate was 74.1% (80/108) and 76.5% (335/438) for patient and donor oocytes, respectively. A mean number of 2.2 and 1.8 embryos were transferred per recipient for patients and acceptors, respectively. Implantation rates were 52.9% (9/17) for patients and 50.0% (28/56) for acceptors.

CONCLUSIONS: The results show that oocytes vitrified with VT801 can be warmed with RapidWarm Omni. Here we used solutions designed for warming of oocytes at physiological temperature, which has the advantage of minimising temperature changes which can potentially result in improved performance of vitrification outcome. This information is important in view of potential stock-out situations and reassuring to provide continuity in laboratory activities and patient treatment. It will also help clinics to avoid the concomitant use of two different products and methods during the transition from one manufacturer to another.

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DEVELOPING A MINIMUM DATA SET, KNOWN AS A CORE OUTCOME SET, FOR IVF RESEARCH. James M. N. Duffy, DPhil MRes PG HCL MBChB BSc (Hons),[1] Yusuf Beebeejaun, MRCOG MBBS,[2] Cindy Farquhar, FRANZCOG FRCOG MD MPH[3] COMMIT: Core Outcomes Outcome Measures for Infertility Trials [1]Institute for Women's Health, University College London, Greater London, United Kingdom; [2]King's College London, London, United Kingdom; [3]University of Auckland, Auckland, New Zealand.

OBJECTIVE: To develop a minimum data set, known as a core outcome set, for IVF research.

DESIGN: Consensus development study. Core outcomes were identified using an eDelphi survey (372 participants from 41 countries) and consensus development meeting (27 participants from 11 countries).

MATERIALS AND METHODS: Potential core outcomes were identified by extracting outcomes previously reported in infertility trials. These outcomes were entered into a three-round eDelphi survey. Professionals, researchers, and people with fertility problems were asked to score the importance of each outcome. Based on their feedback, potential core outcomes were prioritised, and subsequently discussed in a consensus development meeting. Using the modified Nominal Group Technique, a minimum data set for future IVF research was agreed.

RESULTS: A longlist of 101 potential core outcomes was developed. When considering the Delphi survey, 261 healthcare professionals, 57 researchers, 54 people with fertility problems, from 41 countries, participated. Twenty-eight consensus outcomes were identified and discussed during the consensus development meeting. 14 healthcare professionals, seven researchers, and six people with fertility problems, from 11 countries, participated in the consensus development meeting. A minimum data set for IVF research was agreed (Table 1).

TABLE 1. A minimum data set for IVF research.

1 Number of embryos available for transfer or freezing
2 Biochemical pregnancy
3 Viable intrauterine pregnancy confirmed by ultrasound accounting for singleton pregnancy, twin pregnancy and higher multiple pregnancy
4 Pregnancy loss accounting for ectopic pregnancy, miscarriage, stillbirth and termination of pregnancy
5 Live birth
6 Number of embryo transfer procedures leading to a live birth
7 When applicable → time to pregnancy leading to live birth
8 Gestational age at delivery
9 Birth weight
10 Neonatal mortality
11 Major congenital anomaly
12 Serious adverse events including:
12.1 Ovarian hyperstimulation syndrome
12.2 Pelvic infection
12.3 Life threatening bleeding
12.4 Emergency surgery
12.5 Admission to level two or three care
12.6 Serious medication reaction
12.7 Death

CONCLUSIONS: Embedding the core outcome set within IVF research should ensure the comprehensive selection, collection, and reporting of core outcomes, including live birth, pregnancy confirmed by ultrasound, and pregnancy losses. Research funding bodies, the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) statement, and over 80 speciality journals, including *Fertility and Sterility*, have committed to implementing this core outcome set.

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AUTOMATED VITRIFICATION AND WARMING OF OOCYTES MEDIATED BY A NOVEL MICROFLUIDICS DEVICE.

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OBJECTIVE: The purpose of this study is to develop a microfluidic device to automate the critical process of vitrification and thawing procedures, providing standardization, minimizing inter and intra-center variability, and reducing hands on time.

DESIGN: Experimental comparative study of both vitrification and warming of bovine and human oocytes using an automated microfluidics device (Davitri, Overture Life).

MATERIALS AND METHODS: a microfluidics system has been developed that infuses the solutions required in a central well, where the oocytes are placed, and withdraws the spent solutions. The system and the protocols were first tried in bovine oocytes, which are of similar size as human, and later on human donated oocytes. After 24 hours of maturation the cumulus oocyte complex (COCs) were denuded manually and vitrified using the palm-size Davitri device. The scripts controlling the process are based on the Kitazato protocol. Once the procedure was validated with bovine, frozen human oocytes from donors were warmed and vitrified automatically and fresh human oocytes were vitrified and warmed automatically.

RESULTS: 100 fresh bovine oocytes were vitrified automatically and warmed manually, 5 of them were lost during the procedure and 84 oocytes survive after culture (88%), compared to 80% for a control group. Also 50 fresh bovine oocytes were vitrified manually and warmed with the microfluidics device, and 48 of them survived (96%).

Donated frozen human oocytes (N=19) were warmed automatically, and 12 survived (63.15%) compared to 80% expected (1,2). Those 12 were re-vitrified automatically and 71% survived thawing compared to 70% expected after re-vitrification (3).

After these promising results 4 fresh human mature oocytes from an egg donor were automatically vitrified and manually warmed of which 100% survived. Also, 13 fresh immature oocytes were automatically vitrified and manually warmed of which 11/13 (86.6%) survived.

CONCLUSIONS: The automation of vitrification and thawing of eggs is an improvement in assisted reproduction by allowing constant high survival rates with reduced hands-on time. Here we provide proof of concept that the Davitri microfluidics device is able to vitrify and warm both bovine and human oocytes with high survival rates.

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SUPPORT: Private funding (Overture Life).

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TRANSFER OF CHROMOSOMAL-ABNORMAL EMBRYOS, PREVIOUSLY REFUSED SUCH TRANSFERS.

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OBJECTIVE: To determine IVF cycle outcomes after transfer of embryos previously by preimplantation genetic testing for aneuploidy (PGT-A) diagnosed as chromosomal abnormal and previously refused such transfers.

DESIGN: Cohort study.

MATERIALS AND METHODS: Since April of 2016, 50 patients moved 249 embryos to our center that by PGT-a were characterized as chromosomal-abnormal (mosaic-aneuploid or aneuploid) and their original IVF centres were not willing to transfer. Two additional patients convinced their local centers to transfer the embryos after consulting with our center, while 2 of our own patients insisted on PGT-A against our advice. Their embryos were, therefore, included. This study, thus, reports on 54 patients, 40 (74.1%) of which have since undergone at least one selective embryo transfer (total cycles, n=45), involving 112 embryos and excluding survivable trisomies and sex chromosome abnormalities.

RESULTS: Patient age was 42.4 ± 3.7 years; 63% were Caucasian, 20% Asian and 17% of African descent; 30 (75.0%) had at least one prior pregnancy but only 11 (27.5%) achieved live birth; 25/40 (62.5%) had at least one miscarriage. Further evidence for poor IVF prognosis was that over half of embryos were day-6/7 blastocysts, with poorer pregnancy chances than day-5 blasts; 50/112 (44.6%) transferred embryos had 1 chromosomal abnormality (10 mosaic, 40 aneuploid), 54 (48.2%) had 2 or more (complex) and 8 (7.1%) were undiagnosed (degraded DNA). Pregnancy-, likely miscarriage- and likely live birth rates were per patient and per cycle, respectively, 15/40 (37.5%), 8/15 (53.3%) and 7/40 (17.5%) and 15/45 (33.3%), 8/15 (53.3%) and 7/45 (15.6%). Among pregnancy losses, 7/8 occurred before fetal heart and one was consequence of a septic amniocentesis at 18 weeks. All deliveries and ongoing pregnancies were sex-concordant with a transferred mosaic embryo; 6/8 (75%) transfers with a single mosaic abnormality resulted in live birth or ongoing pregnancy; 4/7 (57%) miscarriages were

chromosomal-concordant between PGT-A and products of conception (POCs) and, therefore, likely caused by chromosomal-abnormal embryos; 2 patients declined testing of POCs; 1 chromosomal-normal 46, XX miscarriage (with maternal contamination ruled out), was discordant, likely, miscarried because of an autoimmune disease.

CONCLUSIONS: Even in very poor prognosis patients of advanced age, transferring selected embryos, by PGT-A labelled as chromosomal-abnormal, therefore, creates significant pregnancy and live birth chances and, therefore, in conjunction with genetic counselling, should not be refused by their IVF centers.

SUPPORT: Intramural funds from The Center for Human Reproduction and Foundation for Reproductive Medicine.

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ALTERNATIVE BLASTOCYST VITRIFICATION WARMING-DILUTION APPROACHES: DO VIRTUES OF THE KISS PRINCIPLE APPLY?

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OBJECTIVE: The global shipment of embryos has become commonplace, yet universal warming protocols for various vitrification systems (devices and solutions) are not widely used. The aim of our study is to validate effective protocols that can ease concerns regarding the warming of vitrified blastocysts sent to outside laboratories, including international shipments, when alternatives to their typical commercial products are needed.

DESIGN: Prospective, randomized study. An apriori arrangement of 4 sugar solution treatments was applied post-warming: A) fresh I.C.E. solutions; B) frozen-thawed I.C.E. solutions (i.e., stored in LN_2); C) sucrose; and D) honey (commercial grade, multi-floral).

MATERIALS AND METHODS: Research consented, discard blastocysts (>2BB quality) vitrified by the microSecure method in I.C.E. non-DMSO solutions (>7.9M glycerol/EG) were rapidly warmed in 1 of 4 solution treatment groups. The initial pilot study included 20 blastocysts per group accounting evenly for quality and batch effects before randomly assigning the treatment. Solutions A and B were a commercial I.C.E. product (T1-T4), whereas C and D were lab-made, filtered stock H-HTF+additive solutions (1M sucrose w/v and 10% honey v/v, respectively). The latter solutions both required heating and agitation over a 30 min period to completely mix into suspension before 0.22μm filtration. All treatments involved a 4-step dilution (3 min/step, 50% reduction/step, 21°C) prior to isotonic equilibration (LG-H+additives; 5 min at 37°C), followed by 18-24 hr in vitro group culture/microdroplet (5 embryos/drop). Survival, based on osmotic responsiveness and cellular integrity/fullness was visually assessed at 0 and +2 hr, followed by overnight blastocyst expansion and continued development. Potential differences were assessed using Chi-squared statistics.

RESULTS: There was no differences ($p>0.05$) in blastocyst survival (95-100%) or in-vitro development (85-95%) was observed between treatments.

CONCLUSIONS: This study proves that a variety of non-permeating sugar-based dilution solutions can be effectively used to elute concentrated cryoprotective agents from blastomeres independent of source. We, and others, have previously advocated for the use of 1M sucrose as a universal diluent. Furthermore, we have now proven that a natural product, honey, composed predominantly of fructose and glucose, is also an efficient low-cost, readily available option for any lab around the world to safely extract potentially toxic cryoprotectants from cells. Finally, we have validated that thaw solutions stored in cryovials can be frozen in LN_2 and maintain functionality, thus facilitating the potential transcontinental shipment of vitrified material with procedurally compliant thaw solutions transported in the same LN_2 dry-shipper. Additional validation replicates are planned with an open device/DMSO-EG system, but we do not anticipate a dilution treatment effect.

SUPPORT: None

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SUPRISING RATE OF REBOUND IN FOLLICLE GROWTH AFTER CESSATION OF OVAIAN STIMULATION IN INITIAL NON-RESPONDERS.

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OBJECTIVE: To follow-up on the prior anecdotal observation that non-responders to ovarian stimulation, at times, spontaneously demonstrate follicle growth after sudden withdrawal of gonadotropin stimulation ("rebound"), and to prospectively quantitate such rebound rates.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: We investigated 49 consecutive patients, absolutely unresponsive to maximal exogenous gonadotropin stimulation, for a so-called rebound response to ovarian stimulation. Such a response was defined as rebound in follicle growth after complete failure to respond to maximal gonadotropin stimulation (600IU daily) over up to 5-7 days. A patient was considered to have a successful rebound if, following complete withdrawal of exogenous gonadotropin stimulation for 3-5 days, at least 1 growing follicle became visible on vaginal ultrasound and peripheral estradiol levels increased. At that point gonadotropin stimulation was reinstated in form human menopausal gonadotropin (hMG) at 225IU/day until ovulation was induced with human chorionic gonadotropin (hCG, 10,000IU). Oocyte retrieval was performed in routine fashion.

RESULTS: Median age of study patients was 40.5 ± 5.1 years (range 23-52). Women with and without rebound did not differ significantly in age (40.0± 6.0 vs. 41.0 ± 7.0 years, P=0.405). FSH levels trended lower in women with positive rebound (20.9 ±20.8 vs. 40.0 ± 58.7 mIU/mL; P=0.071); AMH levels, through extremely low in both groups, were even significantly lower in women with no rebound (0.0 ±0.1 vs. 0.1 ±0.2 ng/mL, P=0.003). Initial baseline estradiol (E2) levels did not differ (P=0.769) but last E2 levels before hCG did (45.2 ±19.4 vs. 162.0 ±70.1 (P<0.01). Among 49 patients, 24 (49.0%) demonstrated a rebound and 25 (51.0%) did not. Among the former, 21 (87.5%) reached retrieval of 1-3 oocytes and 15 (30.6%) reached embryo transfer.

CONCLUSIONS: A successful rebound in almost half of prior completely non-responsive patients was an unsuspected response rate, as was retrieval of 1-3 oocytes in over half of rebounding patients. Attempting rebounds may, thus, represent another incremental step in very poor prognosis patients before giving up on utilization of autologous oocytes. Here presented findings, furthermore, create a rational for investigating the underlying physiology leading to such an unexpectedly high rebound rate.

SUPPORT: Intramural funds from The Center for Human Reproduction and Foundation for Reproductive Medicine.

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THE NEW STANDARD FOR OVULATION TRIGGERING SHOULD BE GNRH AGONIST OVER HCG DURING CONTROLLED OVARIAN STIMULATION FOR IVF/ICSI: A SYSTEMATIC REVIEW AND META-ANALYSIS.

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OBJECTIVE: Gonadotropin-releasing hormone agonists (GnRHa) represent an alternative way for ovulation triggering after controlled ovarian stimulation compared to the use ofhuman chorionic gonadotropin (hCG)before *in vitro* fertilisation (IVF) or intracytoplasmic sperm injection (ICSI) treatment. GnRH triggering isconsidered more physiologicaldue to the endogenous LH and FSH surges. However, the benefit of GnRHa over hCG triggering on oocyte maturation remains controversial. The objectives of this study were to evaluate whether GnRHa triggering improves oocyte maturation, clinical outcomes and safety compared to hCG triggering during controlled ovarian stimulation for IVF/ICSI.

DESIGN: Systematic review and meta-analysis of randomized controlled clinical trials.

MATERIALS AND METHODS: Searches were conducted on MEDLINE, EMBASE, the Cochrane Library, ClinicalTrials.gov and

EudraCTfrom January 1990 to June 2019, using the following keywords:'GnRH agonist', 'hCG', 'triggering'. Two independent reviewers carried out study selection, bias assessment using RoB2 tool and data extraction according to Cochrane methods. Random-effect meta-analysis was performed followed by pre-specified sensitivity and subgroup analyses.The primary outcomes were the total number of retrieved oocytes and the number of mature oocytes.

RESULTS: A total of 32studies were included in the meta-analysis. Mean-numbers of retrieved oocytes [difference in means (95% CI) 0.96 (0.25, 1.67); p< .01; n=28] and mature oocytes [0.69 (0.04, 1.33); p< .05; n=12] were statistically significantly higherafterGnRHa than after hCG triggering. After dual triggering (hCG and GnRHa), the differences in means were 1.21 (0.34, 2.08) [p< .01; N=9] for number of retrieved oocytes and 0.53 (0.02, 1.04) [p<0.05; N=8] for number of mature oocytes. No difference in clinical pregnancy [Risk ratio 1.02 (0.90, 1.15); p= .79; n=24], ongoing pregnancy [0.98 (0.84, 1.15); p= .84; n=15] and live birth [1.01 (0.71, 1.42); p=0.97; n=5] were shown. GnRHa was associated with lower global incidence of OHSS [Odds ratio 0.25 (0.08, 0.74); p= .01; n=20] and of severe OHSS [0.21 (0.05, 0.96); p< .05; n=20].

CONCLUSIONS: Evidence suggests that final triggering should be performed using GnRHa, which allows to achieve a potential higher number of retrieved and mature oocytes with comparable clinical outcomes and lower OHSS risk.

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PROSPECTIVE RANDOMIZED COMPARATIVE TRIAL BETWEEN ESTRADIOL HEMIHYDRATE AND ESTRADIOL VALERATE FOR ENDOMETRIAL PREPARATION IN FROZEN-THAWED EMBRYO TRANSFER CYCLES. Kundan Vasant Ingale, Sr., MBBS, DGO, DNB, FICOG, Kalyani Kundan Ingale, MBBS, DGO, DNB, Anjum Asif Shaikh, BAMS Nirmiti Clinic. Center for Assisted Reproduction, Pune, India.

OBJECTIVE:

• To compare Implantation rate, Clinical Pregnancy rate, Ongoing pregnancy rate after FET cycles between two study groups

• To compare endometrial thickness and Pulsatility index in arterioles in sub endometrial region achieved during FET cycles between two study groups

DESIGN: Prospective Randomized Comparative trial

MATERIALS AND METHODS: Total 103 patients undergoing frozen embryo transfer cycles were randomly selected who underwent in vitro fertilization with ovarian stimulation by rFSH with GnRh Antagonist protocol followed by intracytoplasmic sperm injection (ICSI) to produce at least minimum 1-2 blastocyst. During FET Cycles, endometrial preparation was done by exogenously administered estrogen for 30 days in Downregulated cycles by GnRHa Depot preparation. Group A included those patients who received Estradiol Hemihydrate for endometrial preparation during FET cycles (n=53) and Group B included those patients who received Estradiol Valerate (n-50) for endometrial preparation during FET cycles

RESULTS: Out of 103 patients, 75 patients got pregnant (72.81%). There was no statistically significant difference in endometrial growth in both groups (10.9 ± 2.5mm vs 10.9mm±2.2mm; P=1.0000). There was no significant difference in Pulsatility index (PI) in arterioles in sub endometrial region between both groups (1.26±0.14 vs 1.23±0.17, P = 0.3297).

There was significant difference in implantation rate (87.7% vs 71.1%; P = 0.0444) and ongoing pregnancy rate (75.5% vs 53.33%, P =0.0244) between Estradiol Hemihydrate and Estradiol Valerate group respectively. Though the clinical pregnancy rate was higher in Estradiol Hemihydrate group (75.5% vs 60%), it was not statistically significant (P=0.1074). There was no significant difference between biochemical pregnancy & miscarriage rate (10.2% vs 11.11%; P=0.8886, 12.24% vs 14.2%; P=0.7641) in both groups.

CONCLUSIONS: Our study demonstrated that Estradiol Hemihydrate is better estrogen compound than Estradiol Valerate not only for optimum endometrial growth but also to improve reproductive outcome in FET cycles.

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SIMPLE NATURAL ALTERNATIVE PROCEDURE (SNAP) METHOD FOR BLASTOCYST BIOPSY. Anthony R. Anderson, D.HSc, Darleen Taylor, B.Sc., Elizabeth Williams, B.Sc., Donna Covington, B.Sc., Ursula Balthazar, M.D. Aspire Fertility San Antonio, San Antonio, TX.

OBJECTIVE: To evaluate different lasers to the SNAP method for blastocyst biopsy

DESIGN: Retrospective cohort study evaluating PGT-A success with an alternative biopsy method.

MATERIALS AND METHODS: A total of 857 day 5 and 6 embryos were biopsied for PGT-A using Octax laser, Hamilton Thorne Zilos laser and mechanical SNAP procedure for embryo sampling. Embryos were evaluated on day 3 and assisted hatched for via laser ablation. Embryos on day 5 and day 6 with a distinct inner cell mass and multiple cells herniating form the zona pellucida were biopsied for PGT aneuploidy testing. Embryo biopsy consisted of laser removal of 5 to 7 cells from the trophectoderm juxtaposed to the inner cell mass. The biopsied cells were treated according to the reference laboratory protocol for off site aneuploidy screening. Embryos available for testing were vitrified and stored under liquid nitrogen until results were obtained from the reference laboratory.

RESULTS: There was no significant difference between any of the biopsy methods evaluated. A total of 232 (60%) from 384 embryos were euploid and 2% no amplification using the Octax Laser. The Hamilton Thorne Zilos laser resulted in 151 (59%) euploid from 256 embryos biopsied and 2.3% no amplification. The SNAP method resulted in 122 (56%) euploid of 217 embryos biopsied and 0.9% no amplification.

Additionally, there was not significant difference in ongoing pregnancy and implantation with the various biopsy methods. The Octax, HT Zilos, and SNAP methods resulted in an implantation of 74% (53/72), 76% (48/63) and 80% (34/42) respectively. Ongoing pregnancy outcome for the three groups were 53/71 (74%) for the Octax laser, 45/62 (73%) for the HT Zilos, and 33/41 (80%) for the SNAP method (not significant)

CONCLUSIONS: This study evaluates the efficacy of differing lasers and biopsy methods. Although there was no significant difference with the various methods, the SNAP method did trend toward a higher implantation per embryo transferred and lower no amplification per embryo biopsied. This study also shows that if the even of a laser failure the SNAP method is a very good alternative for evaluating aneuploidy in embryos.

SUPPORT: None

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LIVE BIRTH RATES AND OVARIAN HYPERSTIMULATION SYNDROME (OHSS) RISK WITH RECOMBINANT FOLLITROPIN ALFA BIOSIMILAR PREPARATIONS VERSUS ORIGINATOR PREPARATIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS. Su Jen Chua, Bachelor of Medicine,[1] Salvatore Longobardi, MD,[2] Ben W. Mol, MD, PhD Prof,[3] Rui Wang, MD PhD,[4] Christos Venetis, MD, MSc, PhD,[5] Ashleigh Storr, PhD,[6] Thomas M D'Hooghe, MD, PhD[7] [1]Barwon Health, Victoria, Australia; [2]Merck Healthcare KGaA, Darmstadt, KS, Germany; [3]Monash University, School of Medicine, Melbourne, VIC, Australia; [4]Monash University, Melbourne, VIC, Australia; [5]University of New South Wales, Sydney, NSW, Australia; [6]Flinders Fertility, Adelaide, SA, Australia; [7]Merck Healthcare KGaA, Darmstadt, Germany.

OBJECTIVE: Follitropin alfa is used for ovulation induction or stimulation of multifollicular development in women undergoing assisted reproductive technologies (ART). Published randomized controlled trials (RCTs) comparing originator follitropin alfa and biosimilar preparations were not powered to assess clinically relevant outcomes. We performed a systematic review and meta-analysis to compare clinically relevant outcomes between the originator and biosimilar preparations across head-to-head RCTs.

DESIGN: Systematic review and meta-analysis

MATERIALS AND METHODS: Medline, Embase, Cochrane, Web of Science and clinical trial registries were searched for RCTs comparing biosimilars with originator follitropin alfa. Search results were screened for eligibility by two reviewers. The main endpoint was live birth. Secondary endpoints included clinical and ongoing pregnancy, ectopic pregnancy and ovarian hyperstimulation syndrome OHSS (moderate or severe), as well as cumulative live birth, ongoing pregnancy and clinical pregnancy. A fixed-effect model for meta-analysis was used to analyze the data and relative risks (RRs) with 95% confidence intervals (CIs) were calculated for each outcome. The I^2 statistic was used to evaluate heterogeneity.

RESULTS: From the 273 records identified, four RCTs were eligible for analysis. Live birth rate was significantly lower with biosimilar (Bemfola®/Afolia®, Ovaleap® and Primapur®) versus (vs) originator (GONAL-f®/GONAL-f RFF®) preparations (RR 0.83, 95% CI 0.71–0.97; n=1881). Clinical and ongoing pregnancy rates were also lower with biosimilar vs originator

preparations and there were no differences observed in risk of OHSS or ectopic pregnancy (Table). Evidence level was moderate to low.

TABLE. Relative risks for outcomes with biosimilar versus originator preparations of follitropin alfa

Outcomes	RR (95%CI)
Live birth (4 RCTs, n=1881, I^2=0%)	0.83 (0.71–0.97)
Clinical pregnancy (3 RCTs, n=1771, I^2=0%)	0.82 (0.70–0.95)
Ongoing pregnancy (3 RCTs, n=781, I^2=0%)	0.81 (0.67–0.99)
OHSS (4 RCTs, n=1881, I^2=5%)	1.33 (0.75–2.36)
Ectopic pregnancy (3 RCTs, n=1509, I^2=0%)	1.16 (0.39–3.43)
Cumulative live birth (4 RCTs*, n=1881, I^2=0%)	0.85 (0.73–0.97)
Cumulative clinical pregnancy (3 RCTs, n=1771, I^2=0%)	0.84 (0.73–0.96)
Cumulative ongoing pregnancy (3 RCTs, n=781, I^2=0%)	0.91 (0.77 – 1.07)

*Only data from the 1st cycle of Ovaleap® study are included, only Ovaleap® used in subsequent cycles. CI, confidence interval; OHSS, ovarian hyperstimulation syndrome; RCT, randomized controlled trial; RR, relative risk.

CONCLUSIONS: This meta-analysis suggests that there is a risk for inferior live birth and clinical and ongoing pregnancy rates with biosimilars vs originator preparations.

SUPPORT: FUNDING: Merck KGaA, Darmstadt, Germany

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HUMAN UTERINE LAVAGE: EMBRYO SAFETY AND FIRST LIVE BIRTHS FROM IN VIVO CONCEIVED GENETICALLY SCREENED BLASTOCYSTS.

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OBJECTIVE: To determine the impact of the uterine lavage procedure on human embryos. To determine the implantation and live birth rate of in vivo conceived blastocysts obtained by uterine lavage.

DESIGN: Two separate protocols. Protocol #1, Human Blastocyst Safety Study: Uterine lavage of a known number of human in vitro fertilization (IVF) blastocysts from silicon uterus model then cultured for 24 hours in an embryology laboratory. Protocol #2, Lavage Feasibility Study: Observational case series of 9 embryo transfer procedures performed at an outpatient fertility center. Human Blastocyst Safety Study performed before Lavage Feasibility Study.

MATERIALS AND METHODS: Human Blastocyst Safety Study:

Five uterine lavage procedures performed after 4-6 human IVF blastocysts per uterine lavage were placed into a silicon uterus model. Human IVF blastocysts had been previously donated for research purposes. Three uterine lavages performed with standard intrauterine suction and two performed with increased intrauterine suction. Recovered embryos were cultured for 24 hours.

Lavage Feasibility Study:

In vivo conceived embryos recovered by uterine lavage five days after intrauterine insemination were available for embryo donation. In vivo embryos were the result of prior controlled ovarian stimulation cycles in oocyte donors and intrauterine insemination with donor sperm. Nine embryo transfer procedures performed with in vivo conceived embryos recovered by uterine lavage. One to two embryos were transferred to eight infertile women.

RESULTS: Human Blastocyst Safety Study:

92% (23/25) of IVF blastocysts placed into uterine model were recovered after uterine lavage. 95% (20/21) of IVF blastocysts recovered with standard intrauterine suction were viable after 24 hours of culture. 75% (6/8) of IVF blastocysts recovered with increased intrauterine suction were viable after 24 hours of culture.

Lavage Feasibility Study:

Nine ETs were performed with 14 blastocysts in eight women resulting in a blastocyst implantation rate of 36% (5/14), clinical pregnancy rate of 44% (4/9) and live birth rate of 44% (4/9). There has been the birth of five infants from the four delivered pregnancies with one set of twins.

CONCLUSIONS: This is the first report of live births and ongoing pregnancies from genetically screened human euploid blastocysts obtained by uterine lavage. The nonsurgical uterine lavage office procedure represents the only current approach to obtain in vivo conceived embryos and provides a benchmark for comparison to standard in vitro cultured blastocysts. Live births of in vivo conceived blastocysts represents the validation that the nonsurgical uterine lavage procedure allows simplified access to naturally conceived embryos. Due to its simplicity, uterine lavage may be useful in screening embryos for preimplantation genetic testing for aneuploidy and/or for known genetic diseases in fertile and infertile couples.

SUPPORT: Financial support from Previvo Genetics Inc.

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EQUIVALENT BIOCHEMICAL PREGNANCY RATE BETWEEN FRESH AND FROZEN EMBRYO TRANSFERS.

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OBJECTIVE: To determine if there is a difference in biochemical pregnancy rates as a marker of early pregnancy loss between fresh and frozen embryo transfer cycles with fair or high quality embryos.

DESIGN: Single center retrospective cohort.

MATERIALS AND METHODS: All cycles completed between the years 2015-2019 at a single academic institution were reviewed. Fresh embryo transfers included in analysis were limited to autologous, day 5 embryo transfer of fair or good quality embryos only (3BC/3CB or higher according to Gardner's grading scale). Cycles with transfer of poor-quality embryos were excluded (any embryo with a lower grade of 3CB/3BC). Frozen embryo transfers included all autologous blastocyst transfers of fair or good quality embryos. A total of 1,890 cycles were evaluated which included 1,419 frozen embryo transfers and 471 fresh embryo transfers. Chi-square tests and multivariable logistic regression were used to assess associations and account for potential confounding.

RESULTS: Overall pregnancy rates did not differ between frozen and fresh embryo transfers (69.1% vs 71.1%, p=0.40). Live birth rates were also consistent between groups at 41.23% for frozen embryo transfer and 44.37% for fresh transfer (p=0.23). Biochemical pregnancy rates as a percentage of total transfers were 9.6%. There was no difference in biochemical pregnancy rate for frozen or fresh embryo transfer (9.6% vs 10.6%, p=0.52) When adjusted for BMI and age at cycle start, the OR of biochemical pregnancy for fresh embryo transfer is 1.13 [95% CI 0.80-1.59].

CONCLUSIONS: There is no significant difference in biochemical rates between fresh and frozen embryo transfers. This suggests the early pregnancy loss rate may not be affected by the changes involved in fresh embryo transfer cycles including the supraphysiologic hormonal milieu.

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AUTOLOGOUS PLATELET-RICH PLASMA INJECTION INTO THE ENDOMETRIUM IN PATIENTS WITH UTERINE FACTOR INFERTILITY. Zulfiia Nurudinovna Efendieva, Dr,[1] Inna Anatolyevna Apolikhina, Professor,[2] Elena Anatolyevna Kalinina, Professor,[2] Tatiyana Anatolyevna Fyodorova, Professor,[2] Dmitriy Mikhailovich Belousov, Dr,[2] Timur Khaisamudinovich Fathudinov, Professor[2] [1]I.M. Sechenov First Moscow State Medical University, Ministry of Healthcare of Russian Federation, Moscow, Russian Federation; [2]National Medical Research Center for Obstetrics, Gynecology and Perinatology named after Academician V.I.Kulakov of Ministry of Healthcare of Russian Federation, Moscow, Russian Federation.

OBJECTIVE: The study aims to evaluate the effectiveness of autologous platelet-rich plasma (PRP) injection during histeroscopy in infertile patients with thin endometrium which is refractory to conventional treatment.

DESIGN: Prospective interventional study.

MATERIALS AND METHODS: All patients signed informed consent for medical intervention and participation in the study. The study included 42 patients aged 18-38 years (34.9 (3.6) years) with an endometrial thickness (EMT) of $\leq$7 mm during the mid-luteal phase of menstrual cycle, who had a history of implantation failures or canceled embryo transfer (ET) cycles due to a thin endometrium. During the mid-luteal phase transvaginal ultrasound was performed to all patients to assess the EMT, as well as Doppler examination, and endometrial aspiration biopsy to further assess its receptivity. PRP was prepared from 400 (50) ml of autologous blood by two-stage centrifugation and reinfusion of the patient's autoerythrocytes. All patients were injected 40 (5) ml of autologous PRP into the most altered areas of endometrium with an endoscopic needle with a diameter of 0.6/1.16 mm through the operating channel of the hysteroscope to a depth of 0.2-0.3 mm on the 6th - 8th day of the proliferative phase of the menstrual cycle preceding the ET. The duration of the intervention was on average 15 minutes. In the new menstrual cycle, patients took orally administered estradiol valerate, starting from the 3rd-4th day with initial dose of 4 mg per day with subsequent correction according to the endometrial response. The daily maximum dose was 10 mg. In the mid-luteal phase patients underwent a control ultrasound examination by the same specialist to assess the EMT. Patients who reached the optimal EMT were transferred one good quality embryo. Posttransfer support was performed by 600 mg of micronized progesterone intravaginally per day until the results of serum β-chorionic gonadotropin were obtained. Numerical parameters were presented as M (SD) and Me (Q1; Q3). Statistical significance was determined at $p<0.05$.

RESULTS: In study population 71.4% of patients (30/42) had a history of cancellation of ET cycles due to inadequate endometrial growth. The mean EMT on the previous-cycle mid-luteal phase was 5.4 (4; 6) mm. After PRP treatment, EMT was 7.5 (7; 9), which was significantly thicker than initial values ($P<0.001$). The clinical pregnancy rate was 33.3% (14/42) after ET. Three patients had a livebirth after ET, 3 patients had a miscarriage at 7-8 weeks, and 8 pregnancies develope normally in accordance with the gestation period. There were no cases of transmission/allergic reactions or infectious complications in any patient. The study is ongoing, and Doppler parameters and endometrial receptivity are being evaluated.

CONCLUSIONS: The study has demonstrated for the first time a new approach to the treatment of women with infertility caused by thin endometrium which is refractory to conventional hormonal and "vascular" treatment methods. Further research is needed to provide the opportunity for the women with refractory thin endometrium to conceive without surrogacy.

SUPPORT: None

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TOP TEN RESEARCH PRIORITIES FOR MEDICALLY ASSISTED REPRODUCTION. James M. N. Duffy, DPhil MRes PG HCL MBChB BSc (Hons),[1] Cindy Farquhar, FRANZCOG FRCOG MD MPH,[2] Priority Setting Partnership for Infertility[1]Institute for Women's Health, University College London, Greater London, United Kingdom; [2]University of Auckland, Auckland, New Zealand.

OBJECTIVE: To develop the top 10 research priorities for medically assisted reproduction.

DESIGN: International consensus development study including healthcare professionals, researchers and people with fertility problems.

MATERIALS AND METHODS: Potential research questions were collated from an initial international survey, a systematic review of national and international fertility guidelines, and Cochrane systematic reviews. A rationalized list of confirmed research uncertainties were prioritized in an international survey. Prioritized research uncertainties were discussed during a consensus development meeting.

RESULTS: The initial survey was completed by 388 participants, from 40 countries, and 111 potential research questions were submitted. By reviewing 14 clinical practice guidelines and 162 Cochrane systematic reviews, a further 50 potential research questions were identified. A rationalized list of 101 confirmed research uncertainties were entered into an interim prioritization survey completed by 317 respondents from 43 countries. The top 10 research priorities for female and unexplained infertility were identified during a consensus development meeting involving 41 participants from 11 countries (Table 1).

CONCLUSIONS: We anticipate these research priorities will help research funding organizations and researchers to develop their future research agenda. Healthcare professionals, professional organisations, and patient advocacy groups should champion the research priorities to highlight the many unanswered questions which need to be addressed in order to improve the outcomes of people with fertility problems.

FIGURE 1. Top ten research priorities for medically assisted reproduction.

1	What are the causes of implantation failure?
2	What is the optimal treatment for women who are poor responders undergoing IVF to increase live birth rates?
3	What is the optimal method of sperm selection in IVF cycles?
4	In couples with unexplained infertility does intrauterine insemination increase live birth rates when compared with other assisted reproductive techniques, including IVF?
5	In couples with unexplained infertility what is the optimal number of intrauterine insemination cycles before moving to IVF?
6	What is the optimal method of embryo selection in IVF cycles?
7	What are the factors which affect cycle to cycle variability in the number and quality of oocytes produced in an IVF cycle?
8	What is the optimal time interval between ovulation and intrauterine insemination?
9	What is the emotional and psychological impact on children born using donor gametes?
10	What is the emotional and psychological impact of repeated fertility treatment failure?

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SIGNIFICANT IMPROVEMENT IN SPERM MOTILITY IN SEMEN SAMPLES FROM ASTHENOZOOSPERMIC MEN BY USING CONTROLLED INCUBATION PROTOCOLS WITH SINGLE CONTINUOUS CULTURE MEDIUM (CSCM®). Juliana Risso Pariz, PhD, Caroline Ranéa, BSc, Jorge Hallak, PhD Universidade de Sao Paulo, Sao Paulo, Brazil.

OBJECTIVE: To test different incubation periods and to assess an appropriate commercially available medium to improve the performance of semen samples from asthenozoospermic men.

DESIGN: Prospective study

MATERIALS AND METHODS: Semen samples (progressive motility <32%) from 54 asthenozoospermic patients (men aged 21-45 years) were used in the study after signed the informed consent form. Fresh semen samples separated by a discontinuous density gradient or by simple washing, were incubated in different culture media and then analyzed. Four different culture media were studied: a) Single Continuous Culture Medium (CSCM®) containing 10% Human Serum Albumin (HSA®); b) Sperm Rinse medium (SR®) supplemented with fructose and carnitine; c) *In Vitro* Fertilization Medium (G-IVF®) with fructose and 15% Synthetic Serum Substitute (SSS®) and; d) a control group in which Human Tubal Fluid (HTF®) supplemented with 15% SSS® was used. The last one represents the most commonly used medium by labs worldwide. Samples were then

incubated at 37°C in a 5% CO_2 atmosphere for 2-hour (defined as the optimal incubation time in previous study). Sperm parameters were then analyzed both in fresh samples and after incubation in different media: manual sperm analysis; motility via Sperm Computer Analysis (SCA®); sperm chromatin integrity via Sperm Chromatin Structural Assay (SCSA®); Reactive Oxygen Species level (ROS) by chemiluminescent detection and mitochondrial activity by staining with 3.3′-diaminobenzidine (DAB). Data were analyzed using the IBM SPSS software. Analysis of variance (ANOVA) and independent student *t*-tests were used to evaluating statistical significance ($P<0.05$).

RESULTS: CSCM® medium demonstrated a significant increase in post-incubation motility (progressive motility = 24.55±13.97%; total motility = 41.17±19.06%) compared to pre-incubation parameters (progressive motility = 8.33±6.82; total motility = 26.61±18.10%; $P<0.025$). For all other culture media, no significant differences were observed in seminal parameters.

CONCLUSIONS: Asthenozoospermic men may have significant improvement in their semen samples in the andrology lab after a 2-hours incubation in CSCM®+HSA® medium. This technique has proven to be very attractive because of its efficiency, low cost and ease of reproduction.

SUPPORT: Miss Ranéa was a recipient of a Master scholarship from the São Paulo Research Foundation (FAPESP, process number 2017/03599-1). Dr. Pariz received research grant from the FAPESP (process number 2019/24800-2). Prof. Dr. Hallak received research grant from the FAPESP (process number 2018/26171-0).

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CLINICAL PREGNANCY IN FROZEN EMBRYO TRANSFER WITH FRESH VERSUS VITRIFIED METAPHASE II OOCYTES IN AN EGG DONATION PROGRAM: A RETROSPECTIVE STUDY.

Carlos Manuel Duarte, Sr., Bachelor,[1] Victor Hernán Nuñez, Bachelor,[2] Mayra Alessandra Guzman, Bachelor,[1] Paola Stephanie Olavegoya, Bachelor in biology,[1] Carlos Alberto Vivar, Bachelor,[1] Elder Omar Benites, Bachelor,[3] Urso Victor Rodriguez, MSC,[3] Carlos Alfredo Vergara, Bachelor[3] [1]Biologist, Lima, Peru; [2]Clinical Embryologist, Lima, Peru; [3]Medical director, Lima, Peru.

OBJECTIVE: Determine the impact of vitrification process on the embryo development and clinical pregnancy rate in assisted reproduction treatments with frozen embryo transfer (FET) in an egg donation program.

STUDY DESIGN: Retrospective study was performed at Niu Vida in Lima, Peru during 2018-2019. A total of 77 cycles were included. We used oocytes from donors which fertility was proved and blastocyst transfer was performed in a delayed artificial cycle.

Cases with at least one optimum quality blastocyst were included. An exclusion criteria was Oligoasthenozoospermia. We assigned two groups, Group A: FET cycles with fresh oocytes and Group B: FET cycles with frozen-thawed oocytes.This study was declared exempt by the clinic's ethics committee.

MATERIALS AND METHODS: Oocytes were obtained applying FSH / LH, antagonists (one follicle of 14 mm) and triptorelin®.

We injected oocytes with seminal samples at a minimal concentration of 10 x 106 spz / ml separated by density gradients. Only metaphase II oocytes maturation stages were considered. Cryotech® protocol was used for vitrification and the thawing process. For endometrial preparation progesterone and progynova were used. Embryo transfers were performed minutes after thawed, post evaluation of embryo survival.

Variables analyzed: receptor age, fertilization rate, blastocyst rate per fertilized oocyte, ongoing clinical pregnancy rate, number of oocytes assigned per receptor, fertilized and blastocysts.

Stata 12.1 software was used for statistical analyses. We use T Student's test for continuous variables normally distributed and chi-square test for categorical variables. Statistical significance was set at $p < 0.05$.

RESULTS: Receptor's ages were not significantly different among groups evaluated (Group A: 42.71 ± 4.13 and Group B: 42.7 ± 4.90, p 0.49). Nevertheless, the number of oocytes assigned per receptor was higher in patients who received FET coming from fresh oocytes cycles (Group A: 13.33 ± 3.87, Group B: 10.75 ± 3.58, $p <0.004$).

The fertilization rate (Group A: 11.93 ± 3.79, Group B: 8.78 ± 3.33, $p <0.001$) and the number of blastocysts developed (Group A: 6.95 ± 3.44 and Group B: 5.15 ± 2.56, $p <0.014$) were higher for Group A compared to Group B.

Our results suggest that there is no significant difference ($p <0.05$) neither in the blastocyst formation rate (Group A: 58.29% and Group B: 58.72%, $p <0.90$) or the clinical pregnancy rate (Group A: 60% and Group B: 62%, $p <0.61$).

CONCLUSIONS: We conclude that in our egg donation program there is no impact of the vitrification process neither in the blastocyst formation rate nor on the clinical pregnancy rate.

In addition, patients undergoing assisted reproduction procedures with FET and donated oocytes have the same possibility to become pregnant regardless of whether fresh or frozen-thawed oocytes were used for their procedures.

SUPPORT: None

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NORMAL FERTILIZATION AND BLASTOCYST DEVELOPMENT RATES OF IN-VITRO FERTILIZATION INSEMINATION VS INTRA CYTOPLASMIC SPERM INJECTION.

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OBJECTIVE: In-vitro fertilization has been highly successful using both conventional insemination (IVF) and intracytoplasmic sperm injection (ICSI) methods for fertilization. Despite many studies comparing IVF versus ICSI outcomes, there is insufficient evidence that supports one method is superior to the other. We set out to determine if results differ for fertilization and blastocyst development when comparing IVF vs ICSI.

DESIGN: Retrospective data analysis of laboratory outcomes of IVF vs ICSI cycles at a large, private fertility center.

MATERIALS AND METHODS: All 2018 IVF and ICSI cycles underwent ovulation induction per standard clinical protocols. Oocyte retrievals were performed, and oocytes for ICSI were denuded one-hour post retrieval; and incubated for one additional hour until ICSI was performed. By comparison, IVF of oocytes was performed two hours post retrieval. Spermatozoa used in both procedures were isolated following a single gradient centrifugation processing. A total of 11,861 oocytes were exposed to sperm; with 1,115 by IVF and 10,489 by ICSI. Normal and abnormal fertilizations and blastocyst developmental rates were analyzed for both procedures. Data was analyzed using Chi-square analysis with $p<0.05$ set for significance.

RESULTS: Normal fertilization, the presence of 2 pronuclei (2PN), was significantly lower in the IVF group (59.5% vs 67.0%; $p<0.0001$). Abnormal fertilization, the presence of $\geq$ 3 pronuclei, was significantly higher in the IVF group (4.6% vs 1.2%; $p <0.0001$). However, overall blastocyst formation rates were not statistically different between the two groups (52.1% in the IVF group and 49.5% in the ICSI group).

CONCLUSIONS: According to our findings, ICSI results in a significantly higher normal fertilization rate, as well as a significantly lower abnormal fertilization rate compared to conventional IVF. These differences alone account for an approximately 10% decrease in the overall number of developing embryos when using IVF. This data demonstrates that ICSI produces more useable embryos, which may be substantially beneficial for patient's long-term outcomes using ART technologies.

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INTRAOVARIAN INJECTION OF AUTOLOGOUS PLATELET RICH PLASMA (PRP) ENHANCES OVARIAN FOLLICULOGENESIS.

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OBJECTIVE: To determine the efficacy of PRP on ovarian folliculogenesis in women with severe diminished ovarian reserve (DOR).

DESIGN: Retrospective data analysis at a fertility center with university-based affiliation.

MATERIALS AND METHODS: 140 patients (mean age 43.9 ± 0.5) with severe DOR at a single fertility clinic had their antral follicle count (AFC) measured by transvaginal ultrasound before (baseline, week 0) and after (once weekly for a total of 6 weeks) bilateral intraovarian PRP injection. The PRP was prepared from the patient's own peripheral blood

TABLE. AFC at baseline before PRP and after PRP on weeks 1 through 6 following the procedure.

Week	AFC before PRP	AFC after PRP	p-value (comparison against baseline week 0)
0 (baseline)	Both ovaries 1.24 ± 0.16 Right ovary 1.04 ± 0.20 Left ovary 1.44 ± 0.25	—	
1	—	Both ovaries 1.78 ± 0.22 Right ovary 1.55 ± 0.28 Left ovary 2.10 ± 0.34	0.0007
2	—	Both ovaries 1.53 ± 0.17 Right ovary 1.42 ± 0.23 Left ovary 1.64 ± 0.24	0.0014
3	—	Both ovaries 1.57 ± 0.16 Right ovary 1.48 ± 0.22 Left ovary 1.67 ± 0.28	0.0012
4	—	Both ovaries 1.5 ± 0.18 Right ovary 1.41 ± 0.22 Left ovary 1.59 ± 0.29	0.0016
5	—	Both ovaries 1.58 ± 0.26 Right ovary 1.58 ± 0.26 Left ovary 2.14 ± 0.33	0.0012
6	—	Both ovaries 1.77 ± 0.33 Right ovary 1.77 ± 0.33 Left ovary 1.91 ± 0.30	0.0008

and injected in the cortex of each ovary under transvaginal ultrasound guidance under intravenous sedation. Data are expressed as mean ± SEM. Repeated measures ANOVA was performed to compare the AFC changes over the period of the study in both ovaries as well as in the right and the left ovary separately.

RESULTS: Compared to baseline (week 0), the total AFC in both ovaries, the AFC in the right ovary (p-value <0.05 for all), and the AFC in the left ovary (p-value <0.05 for all) were significantly increased following PRP on weeks 1, 2, 3, 4, 5 and 6 (Table).

CONCLUSIONS: These preliminary data show that PRP can stimulate follicular development for at least 6 weeks following the intraovarian injection. Whether these findings reflect better hormonal milieu or better pregnancy rates in infertile women with severe DOR will be determined in our future continuing studies.

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ON THE UTILITY OF THE ENDOMETRIAL RECEPTIVITY ASSAY (ERA) TO CORRECT RECURRENT IMPLANTATION FAILURE (RIF): NOT AS SIMPLE AS IT SEEMS. Bruce I. Rose, MD, PhD,[1] Lauren Cover, RN,[1] S. E. Brown, MD[2] [1]Brown Fertility LLC, Jacksonville, FL; [2]Mayo Clinic College of Medicine and Science, Jacksonville, FL.

OBJECTIVE: To use information from ERA testing to improve ongoing/delivered pregnancy rates of patients with RIF

DESIGN: A prospective non-experimental series

MATERIALS AND METHODS: The ERA test (Igenomix, Miami, FL) measures mRNA from endometrial tissue produced from 228 genes during a mock frozen embryo transfer (FET) cycle. Using a determination of up and down regulation of transcripts, an optimal time for embryo transfer is recommended. The test is standardized to evaluate endometrial tissue obtained after approximately 120 hours of progesterone exposure to an estrogen treated endometrium.

Brown Fertility routinely performs embryo transfers of vitrified/warmed embryos after approximately 144 ± 3 hours of progesterone exposure to estrogen treated endometrium. This protocol results in an overall pregnancy rate of 59.1% (164 transfers).

Patients with two or more failed transfers of at least 3 high quality (or 2 known euploid) embryos (with at least 1 FET) were offered the opportunity to have ERA testing done during a mock FET cycle. Patients were informed of the cost of this test, that it was unlikely to be covered by their insurance, and that we had no experience as to whether or not it would be helpful for them.

RESULTS: Twenty-four patients elected to have this testing done from 2016-2019. The average age of these patients was 36.6 ± 5.7 years. They had had a total of 174 embryos transferred during 94 transfers resulting in 5 clinical pregnancies and one live birth. Of these 174 embryos, 75 were created using donor oocytes from young women.

Biopsies were adequate to obtain ERA results on 21 patients (87.5%). Of the 21 patients with results, 81% (17) had results suggesting the need to modify the transfer time interval of their next FET cycle from our normal protocol (144 ± 3 hours).

The results of the subsequent FET cycles using the modification suggested by the ERA results were as follows:

Clinical pregnancy rate per transfer- 76.5% (13/17)

Implantation rate- 50% (16/32)

Ongoing or delivered pregnancy rate per transfer- 58.8% (11/17)

CONCLUSIONS: Results from ERA testing were highly effective in enabling 58.8% of our patients with severe RIF to achieve ongoing pregnancies.

The interpretation of the significance of this series is less straightforward. Most of this practice's patients were able to achieve a live birth after FET at 144 ± 3 hours of progesterone exposure. However, those that repetitively fail to do so can be identified by ERA testing and a modification of their transfer timing can effectively result in a viable pregnancy.

These observations suggest that the ERA is unlikely to define the "universal/true" implantation window for all patients. The implantation window likely occurs at a range (120-144 hours) of times. However, there is a subset of women (those with RIF at 144 hours) for whom the ERA test is effective in identifying their narrow window of implantation at approximately 120 hours.

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DIFFERENCES IN MORPHOKINETICS PARAMETERS BETWEEN EUPLOID MALE AND FEMALE BLASTOCYSTS AND ITS POTENTIAL IMPLICATION ON CLINICAL PREGNANCY RATES. Aline R. Lorenzon, PhD,[1] Catherine Jacobs, BSc,[2] Mariana Nicolielo, BSc,[2] Fabiana Mendez, BSc,[2] Mauricio B. Chehin, MD, PhD,[3] Eduardo LA. Motta, MD, PhD,[2] Jose Roberto Alegretti, MSc[4] [1]Scientific Coordinator, Huntington Medicina Reprodutiva, Sao Paulo, Brazil; [2]Huntington Medicina Reprodutiva, Sao Paulo, Brazil; [3]Huntington Medicina Reprodutiva, São Paulo, Brazil; [4]Huntington Medicina Reprodutiva, Embryology Department, Sao Paulo, Brazil.

OBJECTIVE: Differences on male and female metabolism and kinetics have been reported in early embryo development. However, there is still no consensus regarding the influence of sex on embryo's morphokinetics parameters, although recent studies pointed differences in morphokinetics markers for reproductive outcomes. We aimed to investigate if the embryo sex affects morphokinetics and implantation rates in euploid transfers and if those parameters are related to clinical pregnancy rates.

DESIGN: Retrospective cohort study (December 2017 to December 2019), analyzing morphokinetic parameters collected from a time-lapse

system from 482 euploid embryos. Embryo transfers and clinical pregnancies were followed up.

MATERIALS AND METHODS: Patients with clinical indication to IVF treatment and blastocyst biopsy (NGS platform) were included (n=257). All oocytes retrieved were fertilized by ICSI and cultured in a time-lapse system (Embryoscope Plus, Vitrolife). Euploid embryos were morphologically graded according to Gardner's system and also followed morphokinetic parameters on time of pronucleous fading (tPNf), time to 2-cell(t2), time to 3-cell (t3), time to 4-cell (t4), time to 5-cell (t5), time to 8-cell (t8) and time to blastulation (tB). Chi-square or t-test were used for statistical analysis.

RESULTS: From 482 reported euploid blastocysts, 240 were male (49,8%) and 242 females (50,2%). Maternal age was similar between male and female groups (38,13±3,62 versus 38,40±3,78, p=0.3009). Analysis of morphokinetics parameters revealed that at t8, male embryos were faster than females (58,61±9,93 versus 59,85±8,89, p=0.0349). Other morphokinetic parameters analyzed were similar between genders. Two-hundred twenty-seven embryos were transferred and had known implantation outcomes. Clinical pregnancy rates were similar between male and female (48,8% versus 56,8%, p=0.2329). Maternal age in positive and negative clinical pregnancy were similar between genders (male: 38,30±2,90 versus 38,47±2,95, p=0.8705 and female: 38,55±3,38 versus 38,19±4,72, p=0.7078, respectively). Morphokinetics parameters in positive and negative clinical pregnancy in male embryos were not statistically different. However, in female blastocysts, clinical pregnancy was correlated with faster t5 and t8 (t5: 48,84±6,30 versus 50,95±6,95, p=0.0416 and t8: 57,01±7,20 versus 62,22±10,15, p=0.0029, respectively). Morphology grades between male and female embryos were not different between good quality embryos (grades A and B – 80% versus 76%) and poor quality embryos (at least one grade C – 20% versus 24%, p=0.2736).

CONCLUSIONS: Our results showed that euploid male blastocysts are faster at t8, however the clinical pregnancy rate is correlated to t5 and t8 only for female euploid embryos. The morphokinetic parameters, as a tool for embryo selection, is an increasing demand in IVF routine mainly after the time-lapse technology's implementation. The differences in morphokinetics between male and female blastocysts must be taken into consideration at the time of selection of the embryo with best potential of clinical pregnancy.

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STUDY OF LET 7 MIRNAS IN CUMULUS CELLS OF WOMEN UNDERGOING IVF. Sofoklis Stavros, MD, PhD,[1] Despoina Mavrogianni Dr, PhD,[2] Elmina Papatheodorou, Biologist,[1] Maria Poulimenea, Biologist,[1] Rami Raouasnte, MSc,[2] Dimitris Loutradis, Professor,[1] Peter Drakakis, Professor[2] [1]Molecular Biology of Reproduction Unit and Recurrent Abortions Unit, Assisted Reproduction Division, Athens, Greece; [2]Molecular Biology of Reproduction Unit and Recurrent Abortions Unit, Assisted Reproduction Division, Athens, Greece, Greece.

OBJECTIVE: To investigate the expression of let7b and let 7c genes in women undergoing IVF

DESIGN: This is a single-centre study carried out in the molecular biology laboratory of the IVF unit of a gynecological and obstetrics department spanning the period September 2018 to September 2019. We studied the expression of let 7b and c genes in cumulus cells of 25 women undergoing IVF treatment

MATERIALS AND METHODS: RNA was extracted from cumulus cells of 25 women using Monarch total RNA kit. Subsequently cDNA was synthesized by using Takara primescipt cDNA synthesis kit and Real time PCR (LightCycler480II) using SYBR Green and specific primers for let 7b and c genes was applied.

RESULTS: The expression of let 7b was higher (mean value of Cp 28.7) than the expression of let7c (mean value of Cp 36.2), indicating that the let 7b gene may be a biomarker, associated with the maturation and function of cumulus cells. High expression levels of various let-7 family members have been reported in cumulus cells. Additionally, let-7 miRNAs are negatively associated with pluripotency although they are highly expressed in oocytes indicating a high degree of tissue specificity of miRNA expression. Our findings are in accordance with previous results and underline the likelihood that they are involved in regulating different processes at specific time points.

CONCLUSIONS: Our findings show that the let7b gene has a higher expression than the let7c gene in cumulus cells indicating a possible mechanism involving miRNAs in female infertility. The limitations of our study include our small group size. Larger sample would be valuable and potentially helpful in critically evaluating our findings. Detecting candidate genes associated with overexpressed or downregulated miRNAs such as let 7b appears essential, for the better understanding of the mechanism underlying the oocyte-cumulus cells complex

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OUTCOMES AND CHARACTERISTICS OF PATIENTS WHO UNDERGO INTRAUTERINE INSEMINATION IMMEDIATELY FOLLOWING FAILED OOCYTE RETRIEVAL. Pietro Bortoletto, MD, Stephanie Willson, MD, Phillip A. Romanski, MD, Owen Davis, M.D., Zev Rosenwaks, M.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To describe the patient and cycle characteristics of women who undergo intrauterine insemination (IUI) immediately following an oocyte retrieval in which no oocytes are retrieved.

DESIGN: Retrospective cohort study conducted at a university-affiliated center.

MATERIALS AND METHODS: We identified women at our center who underwent controlled ovarian stimulation or natural cycles that culminated in an oocyte retrieval procedure. Of these women, we then identified those who had no oocytes retrieved and were advised to undergo an IUI on the same morning. All women undergoing IUI had at least one patent fallopian tube and access to sperm with adequate semen parameters. We report the mean (standard deviation) for each patient and cycle level variable.

RESULTS: Between 2009 and 2020, a total of 157 unique cycles were identified in which women had no oocytes retrieved. Of these, 49 women (27.7%) then underwent IUI on the same day. The mean (SD) age for this group was 40.3 (3.8), parity was 0.5 (0.6), BMI (kg/m^2) was 25.1 (6.9), and AMH (ng/ml) was 0.3 (0.3). Ninety percent had been diagnosed with diminished ovarian reserve, with a mean of 3.6 (3.1) previous IVF attempts. Thirteen (26.5%) were on natural cycle protocols, 31 (63.3%) were on GnRH antagonist protocols, and 5 (10.2%) were on GnRH agonist protocols. One in three women (31.3%) had a leading follicle (>10mm) on cycle day 2/3 with a mean size (mm) of 13.3 (3.7). The mean follicular size (mm) on the day of trigger was 19.9 (2.8), with a mean of 1.9 (1.4) total follicles greater than 14mm in size. Over ninety percent underwent a pure 10,000 IU HCG trigger, while 8.2% (n=4) received a combined trigger. The mean LH (IU/L) was 8.2 (6.0) on the day of trigger and 40.0 (47.7) post-trigger. Twenty-two percent experienced a post-trigger fall in their estradiol levels (pg/mL), with a mean drop of 17.9% (13.8). None of the 49 women became pregnant as a result of the IUI. Fourteen percent (n=7) went on to deliver a live-born child with subsequent ART treatment at our center.

CONCLUSIONS: The practice of offering IUI for patients who have no oocytes retrieved is not supported by our data. However, patients can be counseled that even though they failed to have oocytes retrieved in one cycle, we have shown that 1 in 7 such patients go on to deliver a live-born baby.

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TOWARDS AUTOMATED SELECTION OF EMBRYOS FOR IVF BY THE INVESTIGATION OF CHANGES IN RELATIVE ENTROPY OVER TIME. Shunping Wang, PhD,[1] Dhananjay Bhaskar, MSc,[2] Shiyun Zou, MS,[2] Denny Sakkas, PhD[3] [1]Women & Infants' Fertility Center, Providence, RI; [2]Brown University, Providence, RI; [3]Boston IVF, Waltham, MA.

OBJECTIVE: We propose a novel image recognition framework, based on machine learning, to assess embryo quality and viability for in-vitro fertilization (IVF) treatment using time-lapse images obtained from a morphokinetic system (EmbryoScope).

DESIGN: We quantified morphometric changes in time-lapse images obtained from the EmbryoScope using relative entropy, which measures changes in the distribution of pixel intensities over time. We processed the time-series data using dynamic time warping (DTW) to automatically assess the pace of development of embryos relative to each other. Lastly, we employed machine learning to predict embryo quality and interpreted results by computing the marginal effect of input features on the predicted outcome.

MATERIALS AND METHODS: Our data consisted of time-lapse images for 395 embryos obtained from frozen donor eggs at a university affiliated IVF clinic. Images were taken at an interval of 20 mins at 7 different focal planes over 1-6 days by the EmbryoScope. In addition, each embryo was associated with an outcome (cryo-preserved, transferred or discarded) and ground-truth assessment of embryo quality by embryologists at different time points. We preprocessed the images (segmentation and registration) prior to relative

entropy calculation. For each patient, the RE data was normalized to a reference embryo, using the DTW algorithm to identify lag/lead during development. Embryo quality prediction was performed using a multi-layer perceptron and results were interpreted using partial dependence plots and the Local Interpretable Model-Agnostic Explanations (LIME) algorithm.

RESULTS: Our investigation revealed that early milestones in embryo development (disappearance of pronuclei, stages of cleavage, compaction, etc.) correspond to spikes in relative entropy that can be easily detected. Embryos that stall in development exhibit persistently low entropy which indicates lack of cell division and rearrangement. The pace of development of an embryo, relative to a reference embryo was quantified using DTW and interesting cases where an embryo that lags in development early but is able to catch up later could be readily identified. Our preliminary findings from supervised classification suggest that the time taken to reach developmental milestones can be used to identify promising candidates for implantation as soon as day 3. We achieved classification accuracy of approx. 70% (excl. embryos that failed to develop) with limited observation up to advanced cleavage stage (9+ cells). Accuracy increased by 10-15% upon including time taken to form morula and blastocyst.

CONCLUSIONS: We have successfully developed a novel methodology to assess embryo development in a clinical setting. Compared to traditional assessment by embryologists, our approach provides unbiased, quantifiable determination of changes in embryo morphology. Combined with our novel framework of DTW and machine learning, this approach provides an excellent tool for automated selection of quality embryos, which is transparent and easily interpretable.

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TO CURETTE OR NOT TO CURETTE; EFFICIENCY OF OOCYTE RETRIEVAL TECHNIQUE. Seifeldin Sadek, MD,[1] Hadi Ramadan, M.D.,[2] Tamar Matitashvili, MD,[1] Laurel Stadtmauer, MD, PhD[1] [1]Jones Institute, Norfolk, VA; [2]Eastern Virginia Medical School, Norfolk, VA.

OBJECTIVE: To assess the effect of follicular curetting on oocyte yield during retrieval

DESIGN: This is a retrospective review on all patients that underwent oocyte retrieval from January 1st, 2016 until August 31st, 2019 35 hours after trigger with 10,000 units hCG.

MATERIALS AND METHODS: The main outcomes measured were oocytes retrieved and clinical pregnancies. Oocyte yield was defined as the total number of oocytes retrieved / the number of follicles >12 mm in diameter (measured in 2 dimensions) on the day of the hCG trigger

RESULTS: A total of 818 patients were included in this study, 671 underwent curetting while 147 did not. There were no differences in patient demographics, Anti-Mullerian hormone, average follicular size, peak estradiol levels and quantity of follicles on day of trigger. Retrievals that were performed using a curetting technique had a significantly increased number of oocytes retrieved 12.4 ± 8.1 versus 10.7 ±7.5 (p=0.011), mature (M2) oocytes retrieved 8.1 ± 6.4 versus 6.9 ± 6.0 (p=0.03), number of 2PNs 6.75 ± 5.3 versus 5.6 ± 4.9 (p=0.013), number of embryo's frozen 3.1 ±3.4 versus 2.5 ± 3.2 (p=0.036), and a significantly shorter duration of retrieval 25.4 minutes ±8.2 versus 27.5 minutes ± 10.6 (p=0.02). Curetting was also associated with an increased clinical pregnancy rate of 45% versus 36% (p=0.035) and an increased rate of OHSS 8% versus 3% (p=0.041). However, curreting resulted in a non-significant increase in oocyte yield 98.0% ± 4.8 versus 92.7% ± 4.9 (p=0.2) and M2 yield 61.6% ± 4.0 versus 60.7 ± 4.2 (p=0.8)

CONCLUSIONS: The technique of oocyte retrieval with curetting significantly increased the number oocyte and M2 oocyte retrieved, but it did not result in a significant increase of yield in either one. This was still associated with improved cycle outcomes, such as the number of embryo's frozen and clinical pregnancies. However, curetting seemed to be associated with an increased rate of OHSS, which could be due to the increased release of estradiol with associated with granulosa cell mechanical damage.

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DOSE ADJUSTMENT OF FOLLICLE-STIMULATING HORMONE (FSH) DURING OVARIAN STIMULATION AS PART OF MEDICALLY-ASSISTED REPRODUCTION IN CLINICAL STUDIES: A SYSTEMATIC REVIEW COVERING 10 YEARS (2007–2017). Human M. Fatemi, MD, PhD,[1] Wilma Bilger, PhD,[2] Deborah Denis, PhD,[3] Georg Griesinger, MD, PhD,[4] Antonio La Marca, MD, PhD,[5] Salvatore Longobardi, MD,[6] Mary C. Mahony, PhD, HCLD,[3] Xiaoyan Yin, PhD,[3] Thomas M D'Hooghe, MD, PhD[6] [1]IVIRMA Middle East Fertility Clinic, Abu Dhabi, United Arab Emirates; [2]Merck Serono GmbH, Darmstadt, Germany; [3]EMD Serono, Inc., Rockland, MA; [4]University Hospital Schleswig-Holstein, Lübeck, Germany; [5]University of Modena and Reggio Emilia and Clinica Eugin Modena, Modena, Italy; [6]Merck Healthcare KGaA, Darmstadt, Germany.

OBJECTIVE: Individualization of FSH starting dose is standard clinical practice during ovarian stimulation. Furthermore, gonadotropin dose is regularly adjusted during ovarian stimulation to avoid hyper- or hypo-ovarian response and possibly to improve endometrium and oocyte quality. This study evaluated the frequency and direction (increase/decrease) of recombinant-human FSH (r-hFSH) dose adjustments in clinical trials.

DESIGN: Systematic review

MATERIALS AND METHODS: PubMed was searched for articles (published 6 Sept 2007 to 6 Sept 2017) that allowed dose adjustment within the study protocol and reported ≥1 dose adjustment of r-hFSH in women receiving ART treatment. Data on study design, dose adjustment and patient characteristics were extracted. Point-incidence estimates were calculated per study and overall. The Clopper–Pearson method was used to calculate 95% confidence intervals for incidence where adjustments occurred in <10% of patients; otherwise a normal approximation method was used.

RESULTS: 1409 publications were identified; 18 (6630 cycles) reported r-hFSH dose adjustment. Five studies (1359 cycles) reported data for an unspecified dose increase or decrease, 10 (3952 cycles) reported dose increases and 11 (5123 cycles) reported dose decreases. The studies were performed in women with poor, normal and high responses, with one study reporting in oocyte donors and one in obese women. The median day for dose adjustment was Day 6. The dose adjustments for individual studies are shown in the Table.

CONCLUSIONS: This review highlights that dose adjustment during treatment does occur during clinical trials of patients undergoing ART treatment if allowed by the study design and protocol, with dose increases occurring more commonly than dose decreases. The allowance and the use of dose adjustments in clinical trials suggest that healthcare providers consider adjusting the dose during treatment a worthwhile approach for improving treatment outcomes and/or reducing risks. The incidence of this dose adjustment in routine clinical practice and its impact on clinical outcomes requires further evaluation.

SUPPORT: Â Funding: Merck KGaA, Darmstadt, Germany

TABLE. Reported dose adjustments

	Unspecified dose increase or decrease	Dose increase	Dose decrease
Overall, point estimate, % (95% CI)	45.3 (42.7, 48.0)	19.2 (18.0, 20.5)	9.5 (8.7, 10.3)
Point estimate in individual studies, range, % (95% CI)	26.8 (13.3, 40.4) to 72.7 (64.0, 81.5)	3.0 (0.8, 5.3) to 58.5 (45.2, 71.8)	1.9 (−1.8, 5.5) to 53.4 (47.0, 59.8)

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DEVELOPMENT OF AN ARTIFICIAL INTELLIGENCE-BASED ASSESSMENT MODEL FOR PREDICTION OF PREGNANCY SUCCESS USING STATIC IMAGES CAPTURED BY OPTICAL LIGHT MICROSCOPY DURING IVF. Jared Geller, NA (Undergraduate Student),[1] Ineabelle Collazo, BS,[2] Raghav Pai, BS,[1] Nicholas Hendon, BS,[2] Soum D. Lokeshwar, BS, MD, MBA,[1] Himanshu Arora, PhD,[1] Sabrina A. Gerkowicz, MD,[2] Katherine L. Palmerola, BS, MD,[2] Ranjith Ramasamy, M.D[1] [1]University of Miami Miller School of Medicine, Miami, FL; [2]IVFMD, South Florida Institute for Reproductive Medicine, Miami, FL.

OBJECTIVE: Conventional embryo evaluation for in-vitro-fertilization (IVF) involves manually grading human embryos using various microscopic observations in different planes. However, this process has been shown to be subjective, time consuming, and costly. Our primary objective was to create and assess a model using artificial intelligence, namely convolutional neural networks and transfer learning, to aid in the selection of high-quality embryos for transfer following IVF.

DESIGN: A recent study has utilized deep learning models and public datasets, mainly the Inception V1 network and ImageNet weights, to predict chance of pregnancy given a day 5 embryo image. We hypothesized that we can improve this existing model by using deep convolutional neural networks and transfer learning on a moderately sized novel dataset.

MATERIALS AND METHODS: A total of 361 static images from four IVF laboratories across South Florida were initially netted. This allowed for the development of a Softmax layer with three target classes as the final layer of the network. Given an embryo image, the model would predict: pregnancy, no pregnancy, or live birth. Next, new data augmentation techniques were used to reduce variance in our model and increase our training set 10-fold.

RESULTS: The algorithm achieved 59% accuracy for the 2-class model (pregnancy vs. non-pregnancy); however, there was not any casual signal linked to the three-class model. This limited dataset achieved slightly lower accuracy than conventional embryo selection, and continuous improvements in accuracy are ongoing with the addition of more images. This is currently the first and only algorithm incorporating static images, rather than the less generalizable previous time-lapse imaging.

CONCLUSIONS: For individuals undergoing IVF, embryo transfer is the culmination of an extensive emotional, physical, and financial journey. The goal of every fertility center is to optimize chance of pregnancy in order to best help the patient. Traditional embryo quality assessment leads to discrepancies among embryologists, thus, the use of our artificial intelligence algorithm in embryo selection has the potential to reduce subjectivity, shorten time to pregnancy, and improve patient outcomes by identifying embryos with the highest potential for successful pregnancy.

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THE BENEFICIAL EFFECT FOR LBR OF SERUM LH (5-10IU/L) ON TRIGGER DAY WITH GNRH ANTAGONIST PROTOCOL. Yanru Hou, MD., Li Tian, MD Peking University People's Hospital, Beijing, China.

OBJECTIVE: To investigate the effect of various serum LH on trigger day with GnRH antagonist protocol in patients receiving in-vitro fertilization (IVF) /Intracytoplasmic sperm injection (ICSI) for pregnancy outcomes.

DESIGN: A retrospective, single-center cohort study.

MATERIALS AND METHODS: **Setting:** We retrospectively reviewed the medical documents of patients receiving IVF/ICSI with fresh embryo transfers in the Reproductive Medicine Center of Peking University People's Hospital between January 2016 and December 2018.

Patients: 894 patients were included and divided into three groups by various serum LH on trigger day.

Interventions: Group A ,Group B and Group C were defined as LH concentration <1.0 IU/l, ≥ 1.0 IU/l and ≤ 5.0 IU/l, >5.0 IU/l and ≤ 10.0 IU/l on trigger day during the cycle, respectively.

Main Outcome Measures: implantation rate, clinical pregnancy rate, early pregnancy loss rate and live-birth rate (LBR).

RESULTS: Pregnancy results were compared among these three groups. There was significant difference in implantation rates between Group A and Group C (20.57%versus 35.90%, respectively). The clinical pregnancy rates (35.42% versus 48.65%) and LBR (29.17% versus 41.89%) appeared higher in Group C, though the differences were not significant. According to Multivariate logistic regression analysis, compared with Group A, the LBR of Group B(OR=4.160, $P = 0.039$) and Group C(OR=5.037, $P = 0.034$) increase and the differences were significant.

CONCLUSIONS: Our study has proposed Chinese patients in 5-10 IU/l of the serum LH on trigger day with GnRH antagonist protocol may have better clinical outcomes than 1-5IU/l of LH. So the serum LH on trigger day with GnRH antagonist protocol should not be very low. The level of LH should be beneficial for outcomes in our suggested LH range. Whereas, we still need more adequate sample size and multi-center research to make RCTs and in-depth study on the mechanism.

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INTRAUTERINE ADMINISTRATION OF A PHENOL-POLOXAMER GEL DISRUPTS EPITHELIAL INTEGRITY SUPPORTING DEVELOPMENT AS A PERMANENT CONTRACEPTIVE. Tanner J. Grenz, B.S.,[1] Lauren Drew Martin, DVM,[2] Shan Yao, MD,[1] Jeffrey T. Jensen, MD, MPH,[3] Ov D. Slayden, PhD,[4] Carol B. Hanna, Ph.D.[5] [1]Senior Research Assistant, Beaverton, OR; [2]Assistant Chief/Associate Surgical Veterinarian, Beaverton, OR; [3]Oregon Health & Science University, Portland, OR; [4]Professor, Beaverton, OR; [5]Oregon National Primate Research Center, Beaverton, OR.

OBJECTIVE: Transcervical administration of 30% phenol in a mucilage or paste will induce fallopian tube occlusion and provide permanent contraception for women but administration of these materials is difficult and inconsistent. We evaluated delivery of phenol in a thermally responsive poloxamer-based gel that is liquid at room temperature and a gel at 37°C. We hypothesized this gel would be easy to administer and provide controlled delivery and release of the phenol sufficient to induce permanent epithelial damage to the fallopian tubes and uterine horn.

DESIGN: In vivo guinea pig study.

MATERIALS AND METHODS: Phenol release rates from gels containing 16.5% P407 poloxamer, 0.46% sodium alginate, and 0% (control gel), 5%, 7.5% or 10% phenol were determined by LC-MS/MS following incubation in saline at 37°C up to 24 hours. Based on these results, we evaluated 10% phenol gel in guinea pigs (*cavia porcellus*). Estrous cycles were synchronized with 0.22 mg Altrenogest for fifteen days followed by 5 days of withdrawal. Up to 4 mL of gel supplemented with 16% contrast reagent and either 10% or 0% (control) phenol was administered transcervically in n=18 animals and bilateral uterine horn fill was visualized by fluoroscopy with minimal syringe pressure reported during delivery. Reproductive tracts were collected at 1, 7 and 30 days post treatment, segmented, and embedded in paraffin. Epithelial integrity of the uterine horns and fallopian tubes were evaluated by hematoxylin/eosin staining. Masson's Trichrome was used to quantify changes in collagen deposition and data was analyzed by One-way ANOVA ($P < 0.05$).

RESULTS: Phenol release from the 5% and 7.5% gels declined to baseline by 4 and 24 hours, respectively. In contrast, the 10% gel displayed sustained release, >80% for 24 h. Tracts exposed to control gel (n=9) showed no change in histology relative to naive animals across all time points. In contrast, the 10% gel disrupted the uterine mucosa at day 1 in all animals and 1/3 displayed fragmented epithelium and cellular debris in the fallopian tubes. On day 7, the uterine horns appeared to be inflamed with 2/3 showing evidence of re-epithelialization and 1/3 animals had complete tubal epithelial damage. By day 30 the endometrium in all animals had mostly recovered but focal tubal occlusion with collagen deposition was present in 1/3 animals. There was no difference in the proportion of collagen present in the tracts across all treatments, however animals that received the 10% gel tended to have increased collagen content in the uterine horn and fallopian tubes compared to controls at 7 and 30 day time points.

CONCLUSIONS: Poloxamer-based gels are tissue inert and provides controlled delivery of phenol to target regions of the reproductive tract. The guinea pig reproductive tract anatomy differs from primates in that rodents lack a muscular intramural fallopian tube, the site most susceptible to sclerosant-based occlusion. However, our observation that phenol containing gel initiated tissue occlusion events supports our broad goals to develop tubal sclerosants for permanent contraception.

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HORMONAL CONTRACEPTIVE USE IS ASSOCIATED WITH SIGNIFICANTLY LOWER AMH LEVELS IN WOMEN OF REPRODUCTIVE AGE. Sharon Briggs, PhD,[1] Eduardo Hariton, MD, MBA,[2] Talia Shirazi, MA,[1] Avner Hershlag, MD.[1] [1]Modern Fertility, San Francisco, CA; [2]University of California, San Francisco School of Medicine, San Francisco, CA.

OBJECTIVE: To evaluate the effects of contraceptive methods on anti-Mullerian hormone (AMH) levels in women of reproductive age.

DESIGN: Prospective cross-sectional analysis of serum AMH levels and survey data.

MATERIALS AND METHODS: 9,014 participants between ages 21 and 46 who used at-home fertility hormone testing between June 2018 and April 2020 and had consented to research were included in the study. Participants with prior diagnoses of polycystic ovary syndrome (PCOS) or primary ovarian insufficiency (POI) were excluded. Mean (SD) age, BMI, and AMH were 31.4 years (4.3), 25.9 kg/m2 (6.2), and 3.46 ng/ml (2.87), respectively. Five contraceptive methods had a large enough sample size (n > 100) to be included in the final analysis: combined oral contraceptives (COC) (n=1,301), levonorgestrel IUD (LNG-IUD) (n=1,012), implant (n=141), ring (n=209), and copper IUD (n=317).

Linear regression models were used to estimate relevant covariates that predicted AMH levels. Of the potential covariates investigated (contraceptive type, age, BMI category, number of cigarettes smoked per month, age of menarche, race/ethnicity, household income, and years of education), only current age, contraceptive type, and age at menarche significantly predicted AMH levels. A linear regression model was fitted to estimate the variance in AMH that can be predicted by contraceptive use after adjustment for current age and age of menarche, the significant covariates we identified.

RESULTS: Mean AMH levels were significantly lower in women using each hormonal contraceptive, but not the copper IUD, compared to women not on contraception after controlling for age and age of menarche. COCs (-26.36%) and the ring (-28.72%) were associated with the largest percent declines in mean AMH levels. Progestin-only methods, the implant (-17.29%) and LNG-IUD (-6.55%), were associated with smaller, but still significant, percent declines. Mean AMH levels were not significantly different in women using the copper IUD (-1.26%) compared to those not on contraception.

CONCLUSIONS: AMH levels may be lower due to contraceptives, but AMH is still a useful predictor of ovarian reserve. The use of combined contraception is associated with larger differences in AMH levels while progestin-only methods are associated with smaller differences that, while statistically significant, may not be of clinical significance.

Having more precise estimates of the impact of contraceptive methods on AMH makes it easier to interpret these values in women on contraceptives. In many cases, whether a woman is on or off contraceptives, the followup would be similar: a normal AMH indicates normal ovarian reserve, while low AMH, unlikely to represent more than a 28% decline in contraceptive users, requires followup. Among users with an intermediate AMH level (roughly between 0.8 and 1.3 ng/ml), followup is more nuanced.

These data should eliminate the common practice of stopping COCs before measuring AMH, which could result, at times, in unwanted pregnancies. Clinicians should incorporate these findings when counseling women who tested AMH while on hormonal contraceptives.

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CHARACTERIZATION OF WOMEN ACCORDING TO THEIR SEXUAL SATISFACTION AFTER TREATMENT WITH THE NOVEL VAGINAL PH REGULATOR (VPR™) DURING THE AMPOWER STUDY. Michael A. Thomas, MD,[1] Kelly R. Culwell, MD, MPH,[2] Clint Dart, MS,[3] Brandon Howard, PhD.[2] [1]University of Cincinnati, Cincinnati, OH; [2]Evofem Biosciences, Inc., San Diego, CA; [3]Health Decisions, Inc., Durham, NC.

OBJECTIVE: The novel vaginal pH regulator (VPR™) is a non-hormonal, woman-controlled contraceptive vaginal gel. This analysis describes the characteristics of women in the phase 3 AMPOWER trial who reported better sex satisfaction after 1 cycle of VPR use vs those who did not.

DESIGN: AMPOWER was a single-arm, open-label, multi-center trial based in the United States (NCT03243305).

MATERIALS AND METHODS: Women aged 18-35 years administered one prefilled applicator of VPR intravaginally ≤1 hour before intercourse. The primary study objective was contraceptive efficacy over 7 cycles. Sexual satisfaction was an exploratory endpoint, assessed via questionnaires administered at baseline and after 1, 5, and 7 cycles of VPR use. Women reported a score assessing how VPR use impacted their sex lives: "lot better than before"=1, "little better"=2, "no different"=3, "little worse"=4, "lot worse"=5. Sensitivity analyses for sexual satisfaction were conducted with respect to women's demographic, obstetric, and contraceptive histories.

RESULTS: Sexual satisfaction data were available for 1118 women enrolled in AMPOWER. After 1 cycle of VPR use, 497 (44.5%) women reported sex life as a lot better or a little better than before ("satisfied"), 570 (51.0%) reported no difference, and 51 (4.6%) reported that their sex lives were a little or a lot worse (together, "no difference/worse"). A mean sexual satisfaction score improvement of 0.5 was observed ($p<0.0001$). Mean (±SD) age (27.5±4.6 satisfied; 28.0±4.3 no difference/worse), mean BMI

(28.3±7.6 satisfied; 29.1±8.0 no difference/worse), and race (70.2% white satisfied; 71.8% white no difference/worse) were similar between groups. The most common recently used (last 6 months) contraceptive methods were male condom, oral contraceptive, and withdrawal. Among women reporting satisfaction, 19.1% had recently used male condoms, 7.0% used oral contraceptives, and 3.0% used withdrawal method. Among women reporting no difference/worse satisfaction, 16.1% had recently used male condoms, 9.3% used oral contraceptives, and 3.5% used withdrawal method. Among women recently using male condoms, 48.7% reported satisfaction, 51.3% reported no difference/worse. Among women recently using oral contraceptives, 37.6% were satisfied, 51.3% were no difference/worse; and among women recently using withdrawal method, 40.1% experienced improvement, 59.6% reported no difference/worse. Mean (±SD) number of past pregnancies was similar between groups (1.4±1.9 satisfied; 1.5±1.5 no difference/worse). 40.4% of women reporting sexual satisfaction had no past pregnancies, 54.12% had 1-4, and 5.4% had ≥5. Among women reporting no difference/worse satisfaction, 38.3% had no past pregnancies, 54.3% had 1-4, and 7.4% had ≥5. Mean (±SD) number of full-term deliveries was also similar between groups (0.9±1.3 satisfied; 0.9±1.2 no difference/worse).

CONCLUSIONS: Demographic characteristics, recent contraceptive methods, and obstetric history were comparable between women who reported better sex satisfaction with VPR and those who did not.

SUPPORT: Evofem Biosciences, Inc.

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USE OF CONTRACEPTION AMONG ULTRA-ORTHODOX JEWS: A MATCHED CASE-CONTROL STUDY.

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OBJECTIVE: The fertility of the ultra-Orthodox Jewish population is known to be exceptionally high. Our aim was to study the little-known family planning practices of this religious conservative population.

DESIGN: In a prospective case-control study, we assessed the frequency and type of contraceptive use among ultra-Orthodox compared to secular Jewish women. We also studied the awareness to various forms of birth-control and the sources of information regarding contraceptives in this unique population.

MATERIALS AND METHODS: The study was based on comprehensive interviews with ultra-Orthodox women (N=160), compared with a control group of secular Jewish women (N=80). The size of the group of non-ultra-Orthodox participants was determined based on statistical analysis of a pilot study.

RESULTS: The mean±SD age was 29.1±6.4 and 31.3±8.2 years for ultra-Orthodox and secular women. Of the ultra-Orthodox women, 57.5% reported ever using birth control compared to 86.0% of the secular women ($p<0.001$). The majority, 83.1%, of ultra-Orthodox women reported requesting religious guidance before using contraception. Among ultra-Orthodox women, reporting previous contraceptive use, the most common birth control methods were oral contraceptive pills by 81.5%, IUDs by 27.1% and spermicides by 36.9% versus 78.2%, 15.9% and 2.8%, respectively, among matched secular women.

CONCLUSIONS: Contraceptive use among ultra-Orthodox Jewish women is indeed less prevalent than in the secular population. However, it is more widespread and common than stereotypes might portray. IUDs and spermicides were more frequently used by ultra-Orthodox women. A significant majority of ultra-Orthodox women interviewed consult a Halachic or religious authority prior to using contraception.

SUPPORT: Non restricted grant from the Israeli Society of Contraception and Sexual Health

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THE EFFECTS OF ORAL CONTRACEPTIVES IN HUMAN ENDOMETRIAL STEM CELLS DERIVED FROM MENSTRUAL BLOOD.

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OBJECTIVE: This study aimed to evaluate whether the use of oral hormonal contraceptives alters the characterization of endometrial mesenchymal stem cells of women in reproductive age.

DESIGN: controlled prospective study.

MATERIALS AND METHODS: Study groups were established according to the use or not of oral hormonal contraceptives (OHC group and control group), 20 women were recruited to participate in this study, being 10 users of the oral contraceptives and 10 non-users. Isolation of endometrial mesenchymal stem cells from menstrual blood from each individual woman were analyzed in duplicates. The menstrual blood was collected from healthy volunteers aged between 20 and 35 years. Collection was performed with a menstrual collector in saline solution supplemented with antibiotic/antimycotic and subsequent isolation of endometrial mesenchymal stem cells. Cells were kept in a humidified environment at 37°C and 6% CO_2 and cultivate in culture medium with 10% FBS and 1% antibiotic/antimycotic for cellular expansion until confluence. Alterations in the endometrial mesenchymal stem cells characterization were determined by Flow Cytometry with mesenchymal markers CD105 and CD90 and hematopoietic markers CD45 and CD31. Statistical analysis of the data was performed using the software SPSS 18.0. The data were tested for normality and if it didn't have a normal distribution, it was standardized by z-score. Student's t-test was applied and an alpha error of 5% was adopted.

RESULTS: Isolation in cell culture proposed proved to be effective. The standardization tests for menstrual blood collection showed visual variation in endometrial mesenchymal stem cells amount obtained by isolation in cell culture, regardless of the group studied. There was no statistical differences between groups regarding by Flow Cytometry characterization: in OHC group, cells showed 91,4% and 98% of labeling for CD105 and CD90 mesenchymal cell markers, respectively and 0,42% and 13,5% for CD45 and CD31 hematopoietic markers, respectively. In control group, cells showed 98,9% and 99,2% of labeling for CD105 and CD90 mesenchymal cell markers, respectively and 0,24% and 5,52% for CD45 and CD31 hematopoietic markers, respectively. The experiments were validated by reading 10,000 cells per tag.

CONCLUSIONS: With this preliminary data, we concluded that the use of oral contraceptives does not affect the characterization and consequent development of human endometrial mesenchymal stem cells derived from menstrual blood.

SUPPORT: The present work was performed with support from CNPq, Conselho Nacional de Desenvolvimento CientíficoÂ e Tecnológico - Brasil.

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CONTRACEPTIVE CHOICES BY WEIGHT STATUS AMONG WOMEN IN THE UNITED STATES: AN ANALYSIS OF THE 2015-2017 NATIONAL SURVEY OF FAMILY GROWTH.

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OBJECTIVE: Over 40% of adult women in the United States have obesity. Exploring the differences in contraceptive use among women with normal weight, overweight, and obesity will improve understanding of fertility and unintended pregnancies in reproductive-aged women. Our objective was to examine contraceptive choices by weight among women in the United States.

DESIGN: This was a retrospective, cross-sectional study utilizing data from the 2015-2017 National Survey of Family Growth (NSFG).

MATERIALS AND METHODS: The 2015-2017 NSFG is a population-based survey conducted by the National Center for Health Statistics division of the Centers for Disease Control and Prevention that is nationally representative of the United States household population between ages 15-49 years. The NSFG includes information on participants' general and reproductive health, pregnancy, infertility, and use of contraception. Analyses of data were from 5,554 women, aged 15-49 years. Body mass index (BMI) was calculated based on self-reported height and weight and was divided into four categories. Those with a BMI <18.5 kg/m2, 18.5–24.9 kg/m2, 25.0–29.9 kg/m2, and ≥30.0 kg/m2 were classified as being underweight, normal, overweight and having obesity respectively. We excluded from analyses women < 20 years and those > 44 years old, those that were pregnant or recently delivered and those trying to get pregnant but included those with a history of previous tubal ligation. We used Chi-squared test to determine the relationship between the different contraceptive choices and weight

variables. We performed multinomial logistic regression analysis to determine the relationship between each contraceptive choice and each weight category. Statistical analyses were performed using R version 3.6.1.

RESULTS: Compared to women of normal weight, those that are overweight were more likely [1.56 (1.09-2.21), p=0.01] to use female sterilization and less likely [0.69 (0.49-0.98), p=0.04] to use oral contraceptive pills. Similarly, women with obesity were [2.09 (1.50-2.91), p <0.001] more likely to use female sterilization and were [1.9 (1.15-3.16), p=0.01] more likely to use Depo Provera than women of normal weight. In addition, women with obesity were less likely [0.68 (0.49-0.95), p=0.02] to use the pill and less likely [0.59 (0.36-0.94), p=0.03] to use male sterilization compared to women of normal weight.

CONCLUSIONS: Female sterilization use was the method of choice for contraception in women who are overweight and women with obesity compared to their normal weight counterparts. Women with obesity are also less likely to use contraceptive pills and instead more likely to use Depo Provera for contraception.

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EXPLORING TECHNOLOGY-BASED INTERVENTIONS TO IMPROVE ORAL CONTRACEPTIVE PILL ADHERENCE: A CROSS-SECTIONAL SURVEY. Anne Nichols Flynn, MD,[1] Rachel Galvao, BA,[2] Arden McAllister, MPH,[1] Sarita Sonalkar, MD, MPH[1] [1]University of Pennsylvania, Philadelphia, PA; [2]University of Pennsylvania Perelman School of Medicine, Philadelphia, PA.

OBJECTIVE: 1) To describe the resources that oral contraceptive pill (OCP) users access for information about missed pills, and 2) to assess OCP users' desire for technology-based (text messaging, application, web-based) resources to manage missed pills.

DESIGN: A cross-sectional online and telephone survey of OCP users.

MATERIALS AND METHODS: We enrolled women aged 18-44 receiving a prescription for OCPs between October-December 2017 at 3 clinical locations at the University of Pennsylvania, and excluded those receiving OCPs for non-contraceptive indications. Our electronic survey primarily assessed how participants obtain information at the time of a missed pill, what information they would prefer to access, and whether they would use additional information if it was available. We collected demographics, duration of OCP use, number of missed pills in the past month, reasons for missed pills, use of reminder systems, patient's recall of provider counseling, discussion of missed pills by a provider, and knowledge of what to do after a missed pill. We distributed the surveys by email with a telephone contact for non-responses. We performed all analyses in Stata 15.1. The University of Pennsylvania Institutional Review Board approved this study.

RESULTS: We sent surveys to 666 patients with responses from 211 (32%). Of these, 21% (n=45) were ineligible due to discontinuation of OCPs, leaving a remaining sample of 166. Nearly half of participants (47%, n=76, 95% CI 39.0-54.4%) did not seek any additional information about how to manage their subsequent pills after missing a pill. When missing a pill, patients slightly preferred non-technology-based information (57%, n=93, 95% CI 49.3-64.5%) over technology-based information (43%, n=70, 95% CI 35.5-50.7%). Most reported they would use information at the time of missed pills if they had access to it (76%, n=124, 95% CI 68.9-82.0%). The majority of respondents were white (57%, n=94) and had a median age of 29 (IQR 26-33). Approximately half (47%, n=78) reported OCP use of 5 or more years in duration. About half (52%, n=86) missed one or more pill in their last pill pack, with an overall median of one pill missed (IQR 0-1), usually due to forgetting (61%, n=97) or being away from home (23%, n=37). Of participants who used a reminder system (n=112), the majority of users either set an alarm (46%, n=61) and/or put the pill in the same place every day (42%, n=55). The majority of participants reported receiving counseling on what to do after missing a pill (68%, n=112), as well as side effects (70%, n=116) and risks (54%, n=89) of taking OCPs. Most were not asked about missed pills at their follow up visit (49%, n=81), or had no follow up visit (28%, n=46). The vast majority (89%, n=147) knew what to do after missing a single pill.

CONCLUSIONS: This study indicates that OCP users desire more accessible information at the time of missed pills. User-friendly technology and non-technology-based solutions may facilitate OCP adherence and improved management of missed pills.

SUPPORT: N/A

P-165 4:30 PM Saturday, October 17, 2020

REPRODUCTIVE AUTONOMY AND CHOICE OF CONTRACEPTIVE METHOD. Deena Elwan, MD, Shandhini Raidoo, MD, MPH. University of Hawaii, Honolulu, HI.

OBJECTIVE: Reproductive autonomy, defined as having control over whether and when to use contraception, become pregnant, or continue a pregnancy, is important for young adults since parents and partners may have significant influence in their contraceptive decision-making. The primary outcome of this study was to assess if reproductive autonomy correlates with young women's choice of contraceptive method.

DESIGN: Cross-sectional survey.

MATERIALS AND METHODS: We electronically distributed a nationwide survey to sexually active women ages 18-25 years via the Mechanical Turk (MTurk) crowdsourcing marketplace. The survey included questions from the *Reproductive Autonomy Scale,* a previously validated questionnaire by Advancing New Standards in Reproductive Health (ANSIRH), demographic questions, and questions about birth control use. Descriptive statistics were performed and logistic regression models were constructed to determine if the reproductive autonomy subscales were associated with birth control use overall and long acting reversible contraception (LARC) use specifically.

RESULTS: Of the 250 respondents that completed our survey, 48 were excluded from analysis because they were currently pregnant, attempting to conceive, or not sexually active within the past six months. The average age was 23.7 years old and 78% of participants were White. Ninety-one percent of participants reported completing at least some college or greater. Eighty-three percent of women reported using birth control. Among birth control users, oral contraceptive pills (49.7%) were the most commonly used contraceptive method followed by intrauterine devices (16%) and male condoms (13%). Twenty-six percent of participants reported using either an intrauterine device or contraceptive implant as their contraceptive method. Most participants scored high on the reproductive autonomy scales, with mean scores for decision-making, freedom from coercion and communication of 2.59 (range 0-3), 3.74 (range 0-4) and 3.61 (range 0-4) respectively. Current birth control users (n=167) scored significantly higher on the decision-making subscale than those not currently using birth control (n=35, 2.63 vs 2.44, p= .01). Among women who reported current contraceptive use, those using a LARC (n=44) scored significantly higher on the freedom from coercion (3.91 vs 3.71, p= .01), and communication (3.75 vs 3.57, p = .02) scales than those using less effective methods (n=123). A logistic regression model to predict birth control use revealed that, when controlling for age, race, marital status and education, women who scored higher on the freedom from coercion subscale were significantly more likely to use birth control (AOR 2.89, 95% CI 1.03-8.09, p= .04). A similar model predicting LARC use demonstrated that women who scored higher on the decision-making subscale were more likely to use a LARC method (AOR 4.35, 95% CI 1.10-17.30, p= .04).

CONCLUSIONS: Reproductive autonomy correlates with a young woman's choice to use birth control, and those with higher autonomy were more likely to choose the most effective methods.

SUPPORT: The Lakshmi Devi and Devraj Sharma Endowment Fund

P-166 4:30 PM Saturday, October 17, 2020

REPRODUCTIVE HEALTH AMONG FEMALE RESIDENT PHYSICIANS. Cristina Adelia Zottola, MD,[1] Adi Katz, MD, FACOG, FACS,[1] Tung Ming Leung, PhD,[2] Moti Gulersen, MD, MSc[3] [1]Northwell Health-Lenox Hill Hospital, New York, NY; [2]Feinstein Institute for Medical Research, Great Neck, NY; [3]Northwell Health-North Shore University Hospital/Long Island Jewish Medical Center, Manhasset, NY.

OBJECTIVE: This study aimed to explore reproductive health practices among current female resident physicians in ACGME accredited programs in the United States.

DESIGN: This was an exploratory cross-sectional study utilizing a survey distributed through RedCap. A recruitment email was sent to ACGME accredited residency programs in the United States for distribution to female trainees across all years of training. The survey included 17 questions addressing demographics and various reproductive health practices such as contraception, pregnancy, and egg freezing.

MATERIALS AND METHODS: Respondents were classified according to medical specialty and average number of hours worked per week. Descriptive statistics, including frequency distribution, were used for categorical variables, while mean, median, standard deviation, interquartile range, minimum, and maximum values were used for continuous variables. Chi square or Fisher's Exact test was performed to determine differences in the distribution of reproductive health practices among specialty and work hour groups.

RESULTS: A total of 229 respondents were included in the study (26% Obstetrics and Gynecology (OBGYN), 22% Internal Medicine, 10% Pediatrics, 10% Emergency Medicine, 8% General Surgery, 24% Other). The distribution by age and marital status was similar across the specialty groups. Most respondents had an OBGYN visit within the past year (44.3%), while 22.6% had an OBGYN visit more than 3 years prior. Most respondents (88%) experienced a barrier in visiting an OBGYN provider during residency, and lack of time was the most common reason reported. Ninety-two percent of respondents were using contraception (39% long acting reversible contraception and 32% ring or oral contraceptive pills). Most respondents (87%) were not pregnant at the time of the survey or trying to conceive during residency, and this was not significantly different across the specialty groups (p=0.2663). Forty-five percent of respondents felt that if they got pregnant during residency, it would negatively affect the way their peers viewed them as physicians. Over half (54%) of the respondents felt that their medical profession negatively impacted their plans for fertility, and this was not significantly different across specialty groups (p=0.3716).

CONCLUSIONS: Our data demonstrate that most female residents experienced a barrier in seeing an OBGYN provider and nearly half of the respondents felt that pregnancy during their training would negatively affect their image as a physician. Additionally, our data shows that over half of the respondents felt that their medical profession negatively impacted their plans for fertility. Based on our analysis, we recommend placing additional emphasis on reproductive health needs when addressing the wellness of medical residents. Identifying opportunities for improvement in this area could help diminish the escalating problem of physician stress and ultimately improve residents' reproductive health needs.

POSTER SESSION: COVID-19

P-167 4:30 PM Saturday, October 17, 2020

TO TREAT OR NOT TO TREAT: PERCEPTIONS OF THE INITIAL AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE COVID-19 RECOMMENDATIONS AMONG WOMEN'S HEALTH PROVIDERS.

Ashley M. Wiltshire, MD,[1] Tia Jackson-Bey, MD MPH,[2] Zachary Walker, MD,[1] Jasmine L. Chiang, MD,[1] Deidre Gunn, MD,[1] William W. Hurd, MD, MPH[1] [1]University of Alabama at Birmingham, Birmingham, AL; [2]University of Illinois at Chicago, College of Medicine, Chicago, IL.

OBJECTIVE: On March 17, 2020 ASRM published "Patient Management and Clinical Recommendations During the Coronavirus (COVID-19) Pandemic" a statement for clinical management of infertility care based on the anticipated burden of COVID-19 at that time. Receptivity of these initial recommendations has varied across the media, patients, and women's health providers. Our objective is to evaluate the perception of the initial ASRM COVID-19 associated recommendations held by women's health providers.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: After IRB exemption was obtained, an electronic survey was sent to all women's health providers, including physicians, mid-level providers and nurses, in all subspecialties of obstetrics and gynecology at a single large academic center. All data is being collected anonymously and stored in a REDCap database. Preliminary analysis was done with REDCap to be followed by further statistical analysis once data collection is complete.

RESULTS:Of the 278 eligible providers, the survey response rate is 40% (n=112), representing 8 OB/GYN sub-specialties and all categories of providers. The majority of respondents are female (81%) and $\leq$40 years of age (67%). Most providers view infertility treatment as elective, specifically defined as not a medical necessity (44%). Of the 29% of providers who reported provision of infertility care, 69% reported practice changes between March 16- 31and another 19% initiated practice changes after March 31st. Six percent of the surveyed providers continued all fertility treatment in the same manner as before the pandemic; 15% cancelled all fertility treatment immediately, 33% completed treatment for patients currently in cycle but cancelled new cycle starts and 30% continued some treatment on case-by case basis. Safety concerns for the practice (94%), shared decision making with patients (84%), and ASRM guidance (69%) were amongst the most important factors to impact continuation of fertility treatment.

After reviewing a summary of initial ASRM recommendations provided within the survey, 67% of all participants viewed the recommendations as fair, and 71% as reasonable. Most (43%) agreed that ASRM recommendations should be enforced for all patients despite patient opinion. Sixty-six percent agreed that some degree of infertility treatment should be allowed currently, however the least supported treatment type was in vitro fertilization (32%). Regardless of infertility diagnosis, 70% did not feel that women should refrain from planned conception during the pandemic.

CONCLUSIONS: Considering the immediate and long term impact of the COVID-19 pandemic on fertility care delivery, a better understanding of perceptions regarding infertility management during this time is important. In doing so, we must consider the full spectrum of women's health providers. Our study shows overall support for the initial ASRM recommendations from women's health providers within our institution. We intend to use the methods used for this study to conduct a larger assessment of women's health providers nationwide.

SUPPORT: none

P-168 4:30 PM Saturday, October 17, 2020

PERCEIVED STRESS, INSOMNIA SEVERITY, AND THE IMPACT OF EVENTS AMONG IN VITRO FERTILIZATION (IVF) PATIENTS DURING THE CORONAVIRUS DISEASE 2019 (COVID-19) PANDEMIC.

Ariana Kam, BA,[1] Jennifer Gottfried, BS,[2] Julia E. Mieleszko, BA,[2] You J. Kim, BS,[2] Edward J. Nejat, MD, FACOG,[2] Janelle Luk, MD, FACOG[2] [1]Generation Next Fertility, New York, NY; [2]■■■.

OBJECTIVE: The objective of this study was to evaluate the Perceived Stress Scale, Insomnia Severity Index, and Impact of Events Scale-Revised scores of patients at a fertility clinic in Manhattan during the coronavirus disease 2019 (COVID-19) pandemic.

DESIGN: Surveys were administered to 220 patients at a fertility clinic in Manhattan during the COVID-19 pandemic. The surveys included a 7-item questionnaire on patient demographics, the Perceived Stress Scale (10-item questionnaire), the Insomnia Severity Index (7-item questionnaire), and the Impact of Events Scale-Revised (IES-R, 21-item questionnaire).

MATERIALS AND METHODS: Online surveys were administered to 220 patients at Generation Next Fertility (GNF), located in Manhattan. Percentages of patients who met different thresholds along the Perceived Stress Scale, Insomnia Severity Index, and the IES-R questionnaires were calculated. We excluded one question from the standard 22-item IES-R questionnaire: "During the past seven days with respect to (insert event) have you felt yourself acting or feeling like you were back at that time?" All patients who did not respond to the Perceived Stress Scale, Insomnia Severity Index, and/or IES-R questionnaires were excluded from the respective analyses. Multiple linear regression was run to determine if surpassing a high school education and being unemployed were correlated with higher Perceived Stress Scale scores. A p-value of less than 0.05 was considered as statistically significant.

RESULTS: According to the results of the Perceived Stress Scale, 66.9% of patients at the Manhattan-based fertility clinic self-reported experiencing moderate stress during the COVID-19 pandemic. 21.9% and 11.2% of patients perceived low and high stress, respectively. There was no statistically significant relationship between the demographic variables of not surpassing a high school education and being unemployed and the perceived stress levels of IVF patients during the COVID-19 pandemic. Additionally, the results of the Insomnia Severity Index survey demonstrated that 43.7% of patients self-reported no clinically significant insomnia, 39.5% self-reported subthreshold insomnia, 15.6% self-reported clinical insomnia of moderate severity, and 1.2% self-reported severe clinical insomnia. Furthermore, the results of the IES-R survey showed that 52.1% of patients self-reported scores high enough to indicate that post-traumatic stress disorder (PSTD) is of clinical concern, 27.1% of patients self-reported scores at the cut-off level or higher for a probable diagnosis of PTSD, and 18.8% of patients self-reported scores that are high enough to suppress immune system functioning (for even 10 years after the COVID-19 pandemic).

CONCLUSIONS: According to surveys administered at an IVF clinic in Manhattan, the majority of the patients self-reported moderate stress, no clinically significant levels of insomnia, and PTSD levels of clinical concern during the COVID-19 pandemic. Not surpassing a high school education and

being unemployed did not influence patients' perceived stress levels during the COVID-19 pandemic.

References: Christianson, Steven, and Joan Marren. "The impact of event scale-revised (IES-R)."Â *Medsurg Nurs*Â 21.5 (2012): 321-322.

Cohen, Sheldon, T. Kamarck, and R. Mermelstein. "Perceived stress scale."Â *Measuring stress: A guide for health and social scientists*Â 10 (1994).

Morin, Charles M., et al. "The Insomnia Severity Index: psychometric indicators to detect insomnia cases and evaluate treatment response."Â *Sleep*Â 34.5 (2011): 601-608.

P-169 4:30 PM Saturday, October 17, 2020

MATURE HUMAN OOCYTES AND PRE-IMPLANTATION EMBRYOS ARE SUSCEPTIBLE TO SARS-COV-2 INFECTION BASED ON THE PRESENCE OF ACE2 AND TMPRSS2 PROTEINS.

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OBJECTIVE: SARS-CoV-2 entry in host cells requires the presence of angiotensin-converting enzyme 2 (ACE2) as the extracellular receptor, and the serine protease TMPRSS2 to cleave the viral spike protein for incorporation into the host cell. Basigin (BSG/CD147) may also act as an ACE2 independent receptor mechanism. The cysteine protease cathepsin-L (CTSL) may also cleave the viral spike proteins and facilitate cell entry. The objective of this study was to characterize the mRNA and protein expression of these cellular entry receptors and proteases in female reproductive cells to determine their susceptibility to SARS-CoV-2 infection.

DESIGN: Prospective Research Study.

MATERIALS AND METHODS: Materials and Methods: Oocytes (GV, MII), follicular cells (cumulus, CC; granulosa, GC) and embryos (1 cell, 1C; blastocyst, BL) were collected from a minimum of three different patients per sample type, with consent. Samples were analyzed for mRNA expression of *ACE2, CD147, TMPRSS2,* and *CTSL* genes relative to GAPDH using RT-qPCR. Primers were validated using human mixed tissue cDNA. Protein quantification was performed by immunoblotting using the Jess system (ProteinSimple) optimized to detect over 10 proteins/5-10 oocytes or embryos. Antibodies for ACE2, CD147, TMPRSS2, and CTSL proteins were validated and then used to determine protein abundance relative to total protein. Data were obtained from three independent biological replicates and analyzed using one-way ANOVA.

RESULTS: Results from q-PCR analysis revealed high ($p<0.05$) abundance of *ACE2* transcripts in GV and MII oocytes compared to CC, GC, and BL. ACE2 protein was present in all the samples, but was relatively higher ($p<0.17$) in M2 oocytes, 1C, BL, and CC compared to GV oocytes and GC. TMPRSS2 protein was abundant in MII oocytes, 1C, and BL, and was present but at low levels in GV oocytes and follicular cells. Protein abundance of CD147 was five-fold higher ($p<0.05$) in GV and ~1.5 fold higher in GC compared to all other samples analyzed. No CTSL protein was observed with the expected molecular weight (38 kD), although a 55 kD band (a possible isoform) was detected in GV oocytes and CC.

CONCLUSIONS: Cumulus and granulosa cells are least susceptible to SARS-CoV-2 infection due to the lack of required receptors and proteases. Co-expression of the protein for ACE2 and TMPRSS2 in MII oocytes, zygotes, and blastocysts suggests that these reproductive cells are susceptible to SARS-CoV-2 infection. In conclusion, using a combined approach of mRNA and protein analysis from the same samples suggests that mature human oocytes and preimplantation embryos have the cellular machinery required for SARS-Cov2 entry, although we do not know if this occurs in vivo. The potential for viral infection in oocytes and embryos has important ramifications for ART. Care must be taken to avoid introduction of the virus to the embryo while in the ART laboratory, as well as potentially introducing the virus from an infected embryo to laboratory workspaces.

P-170 4:30 PM Saturday, October 17, 2020

WE ARE HERE FOR YOU: INFERTILITY CLINIC WEBSITE COMMUNICATION DURING THE ESCALATING STAGES OF THE COVID-19 PANDEMIC.

Holly Mehr, MD MSEd,[1] Tia Jackson-Bey, MD MPH,[2] Michelle Vu, MD,[2] Victoria Lee, BS,[1] Christopher Herndon, MD,[3] Jacqueline Ho, MD MS,[4] Lusine Aghajanova, MD PhD,[5] Molly M. Quinn, MD[1] [1]University of California, Los Angeles, Los Angeles, CA; [2]University of Illinois at Chicago, College of Medicine, Chicago, IL; [3]University of Washington, Seattle, WA; [4]University of Southern California, Los Angeles, CA; [5]Stanford University, Stanford, CA.

OBJECTIVE: On March 17th, ASRM published guidance for REI clinics regarding infertility treatment during the COVID-19 pandemic. The recommendations advised against initiation of new fertility treatment cycles outside of emergent fertility preservation. Our objective was to evaluate what SART-member fertility clinics communicated to the public and their patients via clinic websites during this time period.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: Between 4/20/20 and 4/24/20, SART-member fertility clinic websites were reviewed for REI-specific COVID-19 messages (REI-CM). The REI-CM was evaluated for: type of treatment offered, and to whom; adherence to updated ASRM guidance; and citation of ASRM (or other) guidance. Each website was evaluated by two reviewers and arbitrated by a third in the case of discrepancies. Practice size, type, and location were abstracted from SART. Clinics were classified by whether they were under a shelter in place (SIP) order and the duration of that order. Chi squared analyses were performed to determine associations between clinic demographics and patterns in messaging.

RESULTS: 381 SART-member clinics maintained active websites. Of those, 249 (65.3%) had REI-CM. The presence of REI-CM was more common in private than academic practices (73% vs 38%, $p<0.001$) and with increasing practice volume: 38% of clinics with <200 annual cycles vs 91% of clinics with >1000 cycles ($p<0.001$). There was a trend toward increased REI-CM use in states with a SIP order for ≥30 days (70% of 212, $p=0.064$).

ASRM guidance was cited in 61% (n=152) of REI-CM; however, only 33% (n=82) outlined treatment practices that reflected ASRM guidance published at the time of the data extraction. Adherence to ASRM guidelines was more common in academic than private practices (54% vs 31%, $p=0.02$) but was not correlated with size of practice or geographic region.

Conversely, 18% (n=44) of practices announced treating patients on a "case-by-case basis" with definitions ranging from specific ("women with AMH <0.7") to vague ("as determined by our providers alongside our patients"). Additionally, 9% of REI-CM (n=23) announced continued treatment regardless of a patient's clinical urgency. This messaging was more common in groups doing >1000 cycles a year (18%, $p=0.009$), with a trend toward practices in the northeast (16%, $p=0.113$) and in states with SIP orders lasting <30 days (14%, $p=0.09$). Clinics treating all-comers were less likely to cite ASRM than other clinics (41% vs 62%, $p=0.045$). However, 75% (n=14) cited COVID-19 guidance from WHO, CDC and state and local governments.

CONCLUSIONS: While public messaging may not reflect the actual practices of a clinic, this study reveals heterogeneity in how clinics incorporated ASRM recommendations and responded to the early stages of the COVID-19 pandemic. Academic practices were more likely to indicate their adherence to ASRM recommendations. High volume groups were more likely to communicate with their patients about what treatments they offered and to treat patients outside ASRM guidance. Lessons learned may inform optimal response in future waves of COVID-19.

References: American Society for Reproductive Medicine. Patient Management and Clinical Recommendations During The Coronavirus (COVID-19) Pandemic. Available at https://www.asrm.org/globalassets/asrm/asrm-content/news-and-publications/covid-19/covidtaskforceupdate2.pdf.Â Accessed on May 26, 2020

P-171 4:30 PM Saturday, October 17, 2020

THE IMPACT OF CORONAVIRUS DISEASE 2019 (COVID-19) ON THE RELATIONSHIP BETWEEN THE STRESS LEVELS OF IN VITRO FERTILIZATION (IVF) PATIENTS AND THE AMOUNT OF TIME SPENT TRYING TO GET PREGNANT.

Ariana Kam, BA,[1] Jennifer Gottfried, BS,[2] Julia E. Mieleszko, BA,[2] You J. Kim, BS,[2] Mehriniso Khaydarova, BS,[2] Edward J. Nejat, MD, FACOG,[2] Janelle Luk, MD, FACOG[2] [1]Generation Next Fertility, New York, NY; [2]■ ■ ■.

OBJECTIVE: The objective of this study was to determine the impact of coronavirus disease 2019 (COVID-19) on in vitro fertilization (IVF) patients' stress levels, insomnia, and risk of post-traumatic stress disorder (PSTD) relative to the amount of time each patient spent trying to get pregnant.

DESIGN: Surveys were administered to 220 patients at a fertility clinic in Manhattan during the COVID-19 pandemic. The surveys included a 13-item questionnaire regarding fertility plans in relation to the COVID-19 pandemic, a 10-item Perceived Stress Scale questionnaire, a 7-item Insomnia Severity Index questionnaire, and a 21-item Impact of Events Scale-Revised (IES-R) questionnaire.

MATERIALS AND METHODS: Surveys were administered online to 220 patients at Generation Next Fertility in Manhattan. IVF patients were categorized according to the amount of time they spent trying to get pregnant (less than 6 months, between 6 months-1 year, between 1-2 years, between 2-3 years, between 3-4 years, and greater than 4 years). Multiple linear regression was run to determine if the amount of time patients spent trying to get pregnant was related to their Perceived Stress Scale scores, Insomnia Severity Index scores, and IES-R total scores. We excluded individuals who did not answer the Perceived Stress Scale, Insomnia Severity Index, and IES-R questionnaires. A p-value of less than 0.05 was considered as statistically significant.

RESULTS: There was a statistically significant relationship between Perceived Stress Scale scores during the COVID-19 pandemic and attempting to get pregnant for less than 6 months (p=0.00837), between 1 year and 2 years (p=1.96e-08), between 2 and 3 years (p=7.93e-07), between 3 and 4 years (p=1.24e-06), and greater than 4 years (p=1.93e-05). The relationships between Insomnia Severity Index scores during the COVID-19 pandemic and attempting to get pregnant for between 6 months and 1 year (p=0.0462), between 1 year and 2 years (p=1.26e-05), between 2 and 3 years (p=0.00465), between 3 and 4 years (p=0.000685), and greater than 4 years (p=0.0114) were statistically significant. There was a statistically significant relationship between IES-R scores during the COVID-19 pandemic and attempting to get pregnant for less than 6 months (p=0.003322), between 1 year and 2 years (p=9.22e-06), between 2 and 3 years (p=0.000671), between 3 and 4 years (p=0.000175), and greater than 4 years (p=0.008695). Spending between 3 and 4 years trying to get pregnant had the largest impact on the Perceived Stress Scale, Insomnia Severity Index, and IES-R scores.

CONCLUSIONS: Spending between 3 and 4 years attempting to get pregnant had the largest impact upon IVF patients' perceived stress, insomnia severity, and risk of PTSD during the COVID-19 pandemic.

References: Christianson, Steven, and Joan Marren. "The impact of event scale-revised (IES-R)."Â *Medsurg Nurs*Â 21.5 (2012): 321-322.

Cohen, Sheldon, T. Kamarck, and R. Mermelstein. "Perceived stress scale."Â *Measuring stress: A guide for health and social scientists*Â 10 (1994).

Morin, Charles M., et al. "The Insomnia Severity Index: psychometric indicators to detect insomnia cases and evaluate treatment response."Â *Sleep*Â 34.5 (2011): 601-608.

P-172 4:30 PM Saturday, October 17, 2020

TELEMEDICINE AND AT-HOME IVF KIT: NOVEL APPLICATION DURING THE COVID-19 PANDEMIC. Zaher Merhi, MD, HCLD, John Zhang, MD, PhD. SUNY Downstate University and New Hope Fertility Center, New York, NY.

OBJECTIVE: During the COVID-19 pandemic, access to fertility has been difficult due to fear of contracting the virus. Many patients, especially those with diminished ovarian reserve (DOR), strongly desire to pursue their fertility treatments that include oocyte and/or embryo freezing for fertility preservation because it is a time-sensitive matter fearing the loss of all their ovarian reserve. Given this challenging situation and in order to minimize the repeated office visits for monitoring during an IVF cycle, we aimed to test the efficacy of a new modality for IVF treatment using telemedicine and a patented kit called At-HOME IVF kit.

DESIGN: Large fertility clinic with university affiliation.

MATERIALS AND METHODS: A retrospective study assessed the outcome of using telemedicine with At-HOME IVF kit in patients who have DOR (n=22) based on previous history of poor ovarian response, previously documented low serum anti-Mullerian hormone (<1 ng/mL), elevated day 3 follicle-stimulating hormone (>10 mIU/mL), or low antral follicle count (<8). Patients desired either embryo (n=17) or oocyte (n=5) freezing. Telemedicine was used for consultation in order to reduce the total waiting time for seeking fertility treatment and to minimize office visits. The kit was mailed to the patient's home, contained no injectable medications and contained all the necessary medications needed for ovarian stimulation, ovulation suppression, and oocyte maturation trigger. The oral pills were clomid 100 mg taken from cycle day 3 until cycle day 11 and letrozole 5 mg taken from cycle day 3 until cycle day 7, the vaginal pill was the GnRH antagonist (Elagolix) 50 mg taken on cycle days 9 and 11, and nasal spray (lupron 30 IU) taken on cycle days 12 and 13. Oocyte retrieval was then performed on cycle day 14. Each patient took the medications included in the kit without office visits for monitoring and presented only on the day of the oocyte retrieval. The main outcome included the number of oocytes and embryos (cleavage-stage or blastocyst-stage) cryopreserved. Because of the COVID-19 pandemic, embryo transfer was not currently recommended or performed. Data are presented as mean ± sem.

RESULTS: The mean age of the participants was 39.9 ± 0.9 years. Upon presentation on the day of oocyte retrieval, blood hormonal testing and transvaginal ultrasound showed that none of the patients had ovulated and that all patients had appropriate ovarian stimulation response with the number of mature follicles (>18mm) up to 8 (3.3 ± 0.4). All patients underwent oocyte retrieval with 21 out of 22 patients having up to 8 mature oocytes collected (2.4 ± 0.4). Ten out of 17 patients who underwent IVF had up to 4 embryos cryopreserved at either the cleavage-stage or blastocyst stage.

CONCLUSIONS: During the global health emergency and current/future pandemics due to a highly transmissible infectious organism, oocyte and embryo cryopreservation can be performed without frequent monitoring and without the injectable medications using At-HOME IVF kit. This will allow patients with DOR the possibility of proceeding with fertility treatments with minimum exposure to office visits.

SUPPORT: None

P-173 4:30 PM Saturday, October 17, 2020

RELATIONSHIPS BETWEEN SPECIFIC INFERTILITY DIAGNOSES AND FERTILITY QUALITY OF LIFE (FERTIQOL), INSOMNIA, AND PERCEIVED STRESS DURING COVID-19 PANDEMIC. Jennifer Gottfried, BS, Ariana Kam, BA, You J. Kim, BS, Julia E. Mieleszko, BA, Edward J. Nejat, MD, FACOG, Janelle Luk, MD, FACOG. Generation Next Fertility, New York, NY.

OBJECTIVE: The objective of this study was to determine if different infertility diagnoses impacted patients' scores on the FertiQol questionnaire, Insomnia Severity Index (ISI), and Perceived Stress Scale (PSS) during the COVID-19 pandemic. The study also investigated if patients who were forced to discontinue their fertility treatment during the COVID-19 pandemic had different FertiQol scores than patients who were able to continue.

DESIGN: Surveys were administered to 220 patients at a fertility clinic in Manhattan during the COVID-19 pandemic. The surveys included a 36-item FertiQol questionnaire assessing Fertility Quality of Life in men and women experiencing fertility problems. The surveys also asked patients to specify their infertility diagnoses (polycystic ovary syndrome, diminished ovarian reserve, uterine factor, endometriosis, or male infertility). Patients were further given a 7-item ISI questionnaire and a 10-item PSS questionnaire. Finally, the surveys asked whether patients were forced to disrupt their fertility treatment plans due to the COVID-19 pandemic.

MATERIALS AND METHODS: Using multiple linear regression, we looked for statistically significant relationships between different infertility diagnoses and FertiQol scores. For this regression, we excluded all individuals who did not know their infertility diagnosis, had unexplained infertility issues, answered that they were fertile, or did not answer the FertiQol questionnaire. We also used multiple linear regression to look for statistically significant relationships between different infertility diagnoses and levels of insomnia and between different infertility diagnoses and perceived stress. Next, using Welch's t-test, we investigated if patients who discontinued their fertility treatments during the COVID-19 pandemic had a different mean FertiQol score from patients who continued treatment. We excluded all individuals who were not currently undergoing treatment and who did not answer the FertiQol questionnaire. A p-value less than 0.05 was considered statistically significant.

RESULTS: The majority of the IVF patients sampled self-reported moderate stress (66.9%). There was no statistically significant relationship between the exact etiology of an IVF patient's infertility diagnosis and the patient's FertiQol score. There was also no statistically significant relationship between the exact etiology of an IVF patient's infertility diagnosis and the patient's ISI nor PSS scores. Patients who discontinued their fertility treatments during COVID-19 did not have different FertiQol scores from patients who were able to continue.

CONCLUSIONS: The majority of the IVF patients sampled self-reported moderate stress during the COVID-19 pandemic. Interestingly, the exact etiology of an IVF patient's infertility diagnosis did not have

a statistically significant impact upon his or her Fertility Quality of Life, ISI, and PSS scores during this time period. Patients who were forced to discontinue their fertility treatments due to COVID-19 did not have different FertiQol scores from patients who were able to continue.

P-174 4:30 PM Saturday, October 17, 2020

IMPACT OF COVID-19 ON QUALITY OF LIFE AND PATIENT SATISFACTION AMONGST PATIENTS SEEKING FERTILITY EVALUATION AND TREATMENT. Hillary Pearson, M.D.,[1] Rachel P. Gerber, MD,[1] Stephanie R. Brownridge, M.D.,[2] Randi H. Goldman, M.D.,[2] Christine Mullin, M.D.[2] [1]Department of OBGYN, North Shore University Hospital/Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY; [2]Northwell Health Fertility, North Shore University Hospital/Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: The purpose of this study was to assess the effect of the pause on fertility treatments, due to the COVID-19 pandemic, on patients' fertility quality of life (FQoL).

DESIGN: Web-based survey.

MATERIALS AND METHODS: Patients seeking fertility care at a single academic fertility center from 1/2020 - 3/2020 with valid email addresses were surveyed. Patient demographics, evaluation or treatment type, history, satisfaction with newly instituted TeleHealth, viewpoint on ASRM guidance, and an adapted version of the validated Fertility Quality of Life Questionnaire (FQoL) were assessed. FQoL score was the primary outcome and was used to quantitatively assess the impact of COVID-19 on patients' FQoL. Student's T-tests were used to compare FQoL scores between patients who experienced a delay in evaluation or treatment vs. those who did not.

RESULTS: Four hundred fifty-six patients received a survey link and 38.8% (177/456) responded. The most common delayed treatments were intrauterine inseminations (36.0%), frozen embryo transfers (35.2%), and oocyte retrievals (26.4%). 37.3% (66/177) of patients had a TeleHealth appointment with a provider. The majority (90.9%) were dissatisfied with their encounter; however, 42.4% would consider utilizing TeleHealth in the future. Of 125 patients who experienced delays, 12.8% agreed with the decision to pause treatments and 41.6% disagreed. The remaining 45.6% patients neither agreed nor disagreed.

Of the 54.2% (96/177) of patients that completed the adapted FQoL survey in its entirety, those with delayed fertility evaluation or treatment (n=77) had significantly lower mean FQoL scores than those who did not experience a delay (76.6 vs 86.5, p=0.01). 52% of patients who completed FQoL questions agreed with the pause of fertility treatments; they had significantly higher FQoL scores than those who disagreed (82.0 vs. 71.8, p<0.005).

	No Delay (n=52)	Delay (n=125)	P value
Average FQoL average*	86.5	76.6	0.01
% Utilized TeleHealth	23.1	43.2	0.01
% Desires future TeleHealth	32.7	50.4	<0.01
% Impartial or agreed with treatment pause	30.8	48.0	<0.01

*Data from 96 patients who completed FQOL questions.

CONCLUSIONS: Patients who experienced delays in fertility care due to COVID-19 reported lower FQoL compared to those who did not. Less than half of patients agreed with guidance suggesting a delay in treatments, despite continued access to care via TeleHealth. Although efforts were made to maintain open lines of communication and patient access to care during the pandemic via TeleHealth, the majority of patients were dissatisfied with their experience, regardless of delays. In spite of their experience, nearly half of participants expressed interest in using TeleHealth for future fertility care.

SUPPORT: None.

P-175 4:30 PM Saturday, October 17, 2020

PATIENTS UNDERGOING ASSISTED REPRODUCTIVE CYCLES ARE MORE LIKELY TO FOLLOW UP AFTER ATTEMPTED OUTREACH COMPARED WITH INTRAUTERINE INSEMINATION CYCLES DURING THE COVID-19 PANDEMIC. Chelsea Boltja, PA-C,[1] John J. Zhang, MD, PhD,[2] Meir Olcha, MD[3] [1]Physician Assistant, New York, NY; [2]New Hope Fertility Center, New York City, NY; [3]New Hope Fertility Center, New York, NY.

OBJECTIVE: As COVID-19 has been spreading rapidly both globally and throughout the US, public fear of contracting and spreading the virus has greatly hindered access to medical care including fertility clinics. Given the time-sensitive nature of fertility treatment, especially in older women, the American Society of Reproductive Medicine published updated guidelines for clinics to safely resume fertility services on April 24, 2020. The purpose of this study was to assess whether contacting established patients who missed or cancelled follow-up appointments via phone calls improved patient retention in the midst of the COVID-19 global pandemic.

DESIGN: Practice management analysis.

MATERIALS AND METHODS: Patients undergoing fertility treatment during the COVID-19 pandemic and who missed scheduled follow-up appointments were contacted by designated clinical staff members. Patients who desired to continue their treatment were offered either physical appointments or telehealth consultations. The contacting staff member documented patient responses and demographics in a master spreadsheet. Approximately 1-4 weeks after the patients were initially contacted, their charts were revisited to determine if the follow-up prompted patients to pursue future treatment. A Chi-square test was used to compare outcomes between Assisted Reproductive Technology (ART) cycles and Intrauterine Insemination (IUI) cycles.

RESULTS: There were 700 patients identified who underwent 215 IUI cycles and 709 ART cycles in the form of Egg Retrieval (ER) or Embryo Transfer (ET) between January 2020 - April 2020. The average age of all patients undergoing IUI and ART was 37.9 and 39.6, respectively (p=0.001). The clinical team contacted 88 IUI and 213 ART patients who missed a follow-up appointment scheduled 2 weeks after undergoing their procedure. Of those contacted, 13 (15%) IUI patients and 72 (34%) ART patients scheduled appointments with their physicians (p=0.001). Fear about COVID-19 was cited as the most common reason for missing their follow-up appointment (p=0.001).

CONCLUSIONS: These data support contacting patients lost to follow-up in order to improve patient retention rates. Patients who had undergone ART treatment were more likely to resume care compared to those who had IUI treatment. One explanation is that IUI patients may be more comfortable delaying active treated while attempting unmonitored timed intercourse cycles at home. There also may be differences in the population of patients undergoing ART vs IUI cycles, such as fertility prognosis or financial implications. Tracking patients during the pandemic also identified those who became pregnant post-procedure and helped ensure early monitoring when appropriate, but this data is not presented here. Lastly, the follow-up initiative provided clinical teams with a unique opportunity to assess patient satisfaction, as well as employee productivity during these difficult times.

References: None

SUPPORT: None

P-176 4:30 PM Saturday, October 17, 2020

COVID-19 PANDEMIC: A SURVEY ASSESSING CLINICAL PRACTICE CHANGES IN REPRODUCTIVE MEDICINE ACROSS THE NATION. Andrea Starostanko, M.D.,[1] Sophia D. Halassy, M.D., M.S.,[2] Abhinav Hasija, BS, MS,[3] Brady Gelvin, M.D.,[4] Michael A. Thomas, MD,[5] Julie Sroga Rios, MD,[6] Suruchi Thakore, MD[7] [1]University of Cincinnati Center for Reproductive Health, West Chester Township, OH; [2]Ascension Providence Hospital, Southfield, MI; [3]The Ohio State University- Fisher College of Business, Columbus, OH; [4]University of Cincinnati College of Medicine, Cincinnati, OH; [5]University of Cincinnati, Cincinnati, OH; [6]University of Cincinnati, West Chester, OH; [7]University of Cincinnati Medical Center, West Chester, OH.

OBJECTIVE: Currently, there is limited data regarding the implications of infection with COVID-19 on reproductive or pregnancy outcomes. Given the lack of knowledge, the American Society for Reproductive Medicine (ASRM) released recommendations on March 17th, 2020 for reproductive

health providers to guide clinical practice during this global pandemic. The primary objective of this study was to determine practice preparedness, clinical changes, compliance with ASRM recommendations, and patient/reproductive health provider reactions in response to the COVID-19 pandemic. The secondary objective was to assess whether these changes will alter the practice patterns of reproductive health providers in the future.

DESIGN: Survey study distributed nationally to American reproductive health providers and practice staff between April 13th to May 19th, 2020.

MATERIALS AND METHODS: The survey was distributed using social media platforms and subspecialty specific list-servs utilized by reproductive health providers. To ensure survey question face validity, expert review and interim analysis of the responses was conducted. Statistical analysis was performed with Chi squared tests using R software.

RESULTS: A total of 134 responses were received of 612 surveys distributed. There was a significant difference in the method by which reproductive health practices received the ASRM recommendations, with e-mail being the most common for private practice, and word-of-mouth for academic practice ($p=0.02$). Once distributed, the academic providers were significantly more likely to follow guidelines compared to those in private practice ($p=0.006$). Most practices implemented guidelines, regardless of specialty and location, within one week of publication (March 16-20th), however academic providers implemented them earlier (March 9-13th) ($p=0.002$). The majority of practices completed their last embryo transfer within one to two weeks (March 16-27th). Continued unmonitored ovulation induction was more commonly offered to the Midwest population compared to the rest of America ($p=0.03$), regardless of practice type ($p=0.07$). Overall, the patients' responses to practice changes were well received. Nonetheless, specialists at academic practices were significantly more likely to offer their patients mental health resources ($p=0.001$). Provision of telehealth, whether before, during, or planning for after the COVID-19 pandemic, did not yield any statistically significant results.

CONCLUSIONS: The guidelines proposed by ASRM have had an obvious impact on reproductive care during the COVID-19 pandemic. Reproductive health practice changes were quickly implemented once received. Although the patient population was undoubtedly affected, patients were understanding regarding the need for delay in care.

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UNIVERSAL SCREENING OF COVID-19 IN ASYMPTOMATIC PATIENTS STARTING FERTILITY TREATMENT IN NEW YORK CITY. Alex Robles, MD,[1] Brittany Noel Robles, MD, MPH,[2] Laura C. Gemmell, MD,[1] Paula C. Brady, MD,[1] Eric J. Forman, M.D.,[3] Zev Williams, M.D., PhD.[3] [1]Columbia University Medical Center, New York, NY; [2]Wyckoff Heights Medical Center, Brooklyn, NY; [3]Columbia University Fertility Center, New York, NY.

OBJECTIVE: To evaluate a protocol of universal symptom and viral screening prior to initiation of controlled ovarian hyperstimulation among patients receiving care in New York City.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Prior to initiation of controlled ovarian hyperstimulation for oocyte cryopreservation or in vitro fertilization cycles, patients were screened by phone for symptoms of fever, cough, sore throat, recent travel or contact with confirmed COVID cases. If negative, patients were scheduled for nasopharyngeal swabs at our center the following day, with visits spaced at 15 minute intervals to avoid crowding. Upon presentation for swab testing, patients were again screened for symptoms and fever. Nasopharyngeal swabs were collected in accordance with the Center for Disease Control (CDC) guidelines, and delivered to the university's clinical microbiology laboratory. The swabs were tested using the Roche Cobas 6800 SARS-CoV-2 test, a qualitative assay, using real-time reverse transcriptase polymerase chain reaction (RT-PCR) test (Roche Diagnostics, USA), with results delivered in the same day. A negative test result was required prior to patients' baseline ultrasound and bloodwork the following morning. This study was conducted from April 21- May 21, 2020,

RESULTS: The study sample included 151 asymptomatic patients who were tested for SARS-CoV-2 via nasopharyngeal swab. Overall, 149 (98.68%) tested negative for COVID-19, 1 (0.66%) tested indeterminate, 2 (1.32%) tested invalid, and 0 (0%) tested positive for COVID-19. Of the 149 patients who have tested negative, 81 have successfully undergone oocyte retrieval without complications. One patient screened positive for symptoms at the time of swab presentation and was instructed to return for testing in 2 weeks.

CONCLUSIONS: The incidence of COVID-19 infection among asymptomatic patients seeking fertility treatment in NYC is low. We have demonstrated that fertility care can safely resume in a way to limit risk to our patients, staff, and our physicians working in the epicenter of infection.

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THE IMPACT OF COVID-19 ON FERTILITY CARE: AN EVALUATION OF SOCIETY FOR ASSISTED REPRODUCTION TECHNOLOGY (SART) MEMBER CLINICS' WEBSITES. Seth J. Barishansky, M.D., M.S.,[1] Miriam A. Andrusier, M.P.H.,[2] Elizabeth A. Dilday, M.D.,[3] Angela K. Lawson, Ph.D.,[4] Luis R. Hoyos, M.D.[5] [1]The George Washington University School of Medicine and Health Sciences, Washington, DC; [2]SUNY Downstate Health Sciences University, Brooklyn, NY; [3]Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, University of California, Los Angeles, Los Angeles, CA; [4]Northwestern University Feinberg School of Medicine, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Chicago, IL; [5]UCLA, Los Angeles, CA.

OBJECTIVE: To evaluate the available COVID-19 content in regard to fertility care on the websites of Society for Assisted Reproductive Technology (SART) member clinics.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: From March 17 to March 30, 2020, following the release of the first American Society for Reproductive Medicine (ASRM) COVID-19 recommendations, SART member clinics' websites were examined. The presence of information on COVID-19 and pregnancy implications, acknowledgement of and compliance with ASRM recommendations, description of Centers for Disease Control and Prevention (CDC) risk mitigation strategies and local health department guidelines, as well as advertisement of telehealth and available mental health resources were queried. Websites were categorized by practice size (small: <500 vs. large: ≥ 500 cycles/year), type (academic vs. private) and degree of statewide COVID-19 burden based on CDC data (low: 0-1000; high: ≥ 1000 diagnosed cases). Group differences were evaluated using χ^2.

RESULTS: Larger clinics, compared to smaller, were more likely to report COVID-19 information, acknowledge and comply with ASRM recommendations, mention CDC risk mitigation strategies and local health department guidelines, discuss pregnancy implications and advertise telehealth [88% (130/148) vs. 64% (146/227); 49% (72/148) vs. 32% (72/227); 52% (77/148) vs. 34% (75/227); 76% (112/148) vs. 53% (120/227); 50% (74/148) vs. 31% (71/227); 36% (53/148) vs. 21% (48/227) and 38% (101/148) vs. 29% (119/227), respectively, $P<0.05$, all values]. Academic clinics, compared to private, were more likely to report COVID-19 information and report CDC risk mitigation strategies [87% (77/89) vs. 70% (199/286); 76% (68/89) vs. 57% (164/286), respectively, $P<0.05$, all values]. Private clinics were more likely to acknowledge and quote $\geq 3/5$ ASRM key recommendations but tended to devise individualized guidelines [44% (126/286) vs. 20% (18/89); 28% (80/286) vs. 12% (11/89) and 34% (97/286) vs. 4% (4/89), respectively, $P<0.05$, all values]. Private clinics were also more likely to advertise telehealth and discuss pregnancy implications [63% (179/286) vs. 46% (41/89) and 37% (106/286) vs. 20% (18/89), respectively, $P<0.05$, all values]. Only 35/375 websites offered mental health resources. Degree of statewide COVID-19 burden did not appear to impact the information available on clinic websites.

CONCLUSIONS: Clinic size and type of practice, rather than COVID-19 burden, influenced websites use for patient education and care during the pandemic. Telehealth advertisement as well as adherence to regulatory agencies' and societal recommendations were more common in larger clinics. Private clinics more frequently devised individualized patient care guidelines, addressed common concerns about the effect of COVID-19 on pregnancy, and made telehealth more readily accessible. The exclusion of such information on clinic websites may be a missed opportunity to support and educate patients about fertility treatment during a uniquely vulnerable time.

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PATIENT PERCEPTIONS AND IMPACT OF FERTILITY TREATMENT CANCELLATION RELATED TO COVID-19. Hanna Kim, MD, Josette C. Dawkins, MD, David M. Owen, MD/Ph.D, Bruce R. Carr, MD, Ellen Wilson, MD. UT Southwestern Medical Center, Dallas, TX.

OBJECTIVE: To assess the knowledge, attitudes, and perception of burdens on patients after fertility treatment cancellations in response to the COVID-19 pandemic.

DESIGN: A web-based survey involving people who experienced cancellations to fertility treatment due to COVID-19 precautions.

MATERIALS AND METHODS: A survey link was disseminated though online infertility forums and groups in the USA. Survey data was collected and stored via REDCap and then analyzed with descriptive statistics and Chi square test.

RESULTS: A preliminary data set of 208 respondents was used. 99% of respondents were female and either married or in a relationship. The median age was 33 years (range 23-44 years) with 1-12 years of infertility (mode 2 years). Respondents included a wide range of infertility diagnoses and all common modes of treatment. In this population, 78.8% reported that they were in the middle of their treatment when cycles were cancelled while 21.1% were cancelled prior to starting. Most reported anxiety and stress (79.6%) but also understanding of the situation (68.9%). The major factors contributing to anxiety and stress were lost treatment time (50.7%), younger age (< 35 years 90.5% vs 78.8% in >35 years, p value 0.024), and desire for increased communication and emotional support. The data showed that only 20.2% of patients perceived the support from their clinics as adequate. These patients who felt supported generally reported personal phone calls from their doctors and continued outlets of communication to ask questions and receive updates. People reporting perceptions of less support were more likely to have reported getting a recorded message or email with some even stating that the lack of communication caused them to seek out other fertility clinics to feel more supported. Additionally, 36% of patients desired more emotional support, and only 3.1% reported being provided additional resources such as mental health counseling. 57.7% of patients had positive perceptions of telemedicine as a resource for the future even though most (75%) had not tried it in the past. Finally, data showed that the type of cycle affected stress levels: ovulation induction reported most stress 89% followed by in vitro fertilization 80% then frozen embryo transfer 62.9%. Patients even suggested a system to help prioritize more urgent patients over others.

CONCLUSIONS: Infertility patients suffered significant stress related to their cycle cancellation from COVID-19. Despite being most worried about lost treatment time, patients advocated for a triage system to prioritize those with poorer prognosis when planning for safe return of fertility treatment. Additionally, consensus showed that personal and ongoing communication is key in patients' perception of support. Virtual support platforms and telemedicine may provide a valuable and supplemental outlet to improve patient communication, emotional support, and access to providers. Moving forward, incorporating this technology into standard practice will likely enhance patient satisfaction and help decrease anxiety and stress particularly when patients need to delay fertility treatment.

SUPPORT: None

P-180 4:30 PM Saturday, October 17, 2020

IVF TREATMENT PRE- AND POST- THE ASRM COVID-19 PAUSE.

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OBJECTIVE: The coronavirus (COVID-19) pandemic has forever reshaped the United States health care system. However, assisted reproductive technology (ART) treatment remains an essential form of medicine. Reproductive practices have since incorporated vigilant practices regarding social distancing, ample use of Personal Protective Equipment (PPE), and consistent decontamination protocols in order to mitigate risk of COVID-19 infection. Altogether, changes to standard operating procedures within ART treatment centers are anticipated to support patient safety without compromising quality of reproductive care. Finally, there is ample evidence of the mental health burden stemming from this pandemic with regard to anxiety and depression in both healthcare workers and patients. Given the current uncertainty, our study evaluates IVF cycle outcome in a New York City patient cohort prior to and subsequent to the ASRM COVID-19 task force's recommended treatment pause.

DESIGN: Retrospective cohort analysis.

MATERIALS AND METHODS: The study includes patients who underwent a single, euploid frozen-thawed embryo transfer (FET) from January 1st, 2020 to May 18th, 2020. Cohorts were separated into two groups based on period of IVF treatment (Group 1: Treatment prior to the COVID-19 pandemic pause; Group 2: Treatment subsequent to the COVID-19 pause). Primary outcome included early pregnancy rates. Chi squared test was used and statistically significance was considered at p= <0.05.

RESULTS: A total of 601 single, euploid FET cycles in which pregnancy outcomes coming prior to the COVID-19 pandemic pause (n=526) were compared to outcomes subsequent to COVID-19 (n=75). No differences were found in early pregnancy rates among cohorts (Table 1).

TABLE 1. IVF Treatment Cycle Outcomes During COVID-19

Groups	Positive Pregnancy Count
Group 1: Prior to Covid-19 Pause (n=526 FET Cycles)	396 (75.2%)
Group 2: Era of Covid-19 (n=75 FET Cycles)	59 (76.2%)

* p-value = 0.75.

CONCLUSIONS: The COVID-19 pandemic has placed an unprecedented burden on patients, physicians, and the entire healthcare system. Urgent treatments, including reproductive care, were postponed, as scarce resources needed to be re-directed. Resumption of treatment required modification in workflow, staffing, decontamination protocols, and utilization of PPE. Although the patient experience has changed, our study is first to demonstrate implantation rates were not compromised in an era of COVID-19. Importantly, our preliminary data suggests that the stress and anxiety that pervade modern COVID-era reproductive care do not alter outcomes. With an abundance of caution, a modern fertility clinic can work to "flatten the curve," abide by guidelines, and deliver safe and effective patient care.

SUPPORT: None

P-181 4:30 PM Saturday, October 17, 2020

FERTILITY PRESERVATION DURING THE COVID-19 PANDEMIC: MODIFIED BUT UNCOMPROMISED.

Kara N. Goldman, M.D., Jennifer Elvikis, MSN, RN, Elnur Babayev, MD, MSc, Kristin Smith, B.S. Northwestern University, Chicago, IL.

OBJECTIVE: During the peak of the COVID-19 pandemic, our clinic remained operational for patients with cancer and other fertility-compromising medical conditions requiring urgent fertility preservation (FP). As patients with cancer are at a higher risk of death or serious illness from COVID-19, our FP approach was modified for patient safety. We sought to characterize FP care during the peak of our city's COVID-19 shelter-in-place order and compare outcomes to historical controls.

DESIGN: Retrospective cohort study with historical controls.

MATERIALS AND METHODS: We analyzed all medically-indicated FP cycles completed from March 17, 2020 (ASRM COVID-19 Task Force initial recommendation to suspend fertility treatments) until May 11, 2020 (ASRM update no. 4). Cycles performed during the same time period in 2019 were compared as historical controls. Data were analyzed using student's T-test, Mann-Whitney-U, or Fisher's Exact test where indicated ($p<0.05$).

RESULTS: Despite suspension of routine fertility care, our center managed 27 urgent FP cycles for 24 patients. 3 cycles were cancelled for acutely decompensating lymphoma, no response to gonadotropins (prior chemotherapy), and symptomatic COVID-19, respectively. 24 cycles from 21 patients were analyzed. Of 11 embryo cryopreservation cycles, 6 underwent FDA screening for future gestational carrier. More cycles were initiated in 2020 vs. 2019 (27 vs. 19), including significantly more embryo cryopreservation cycles (45.8% vs. 5.2%, $p<0.005$). Diagnoses were equally divided between breast cancer (29% vs 37%), leukemia/lymphoma (37.5% vs. 26.3%), and other (33.3% vs. 36.8%) ($p>0.05$). There was no difference in mean age (30 ±7 vs 28 ±7), AMH (2.9±2.0 vs. 4.2±3.1), or days of ovarian stimulation (11±1 vs. 11±2) ($p>0.05$) but patients retrieved in 2020 utilized significantly more gonadotropin (4770±1480 vs. 3846±1438, $p=0.04$). Notably, patients managed during COVID-19 had significantly fewer monitoring visits (5±1 vs. 6±1, $p=0.02$), and 37.5% of cycles utilized a blind trigger injection (without monitoring). Despite modifications, there was no difference in no. of oocytes retrieved (19±14 vs. 22±12) ($p>0.05$). All cycles (majority random-start) were timed to ensure anesthesiology availability for retrieval given COVID coverage responsibilities. Extensive safety precautions were employed including appropriate personal protective

equipment, telemedicine when possible, and office-wide social distancing. One patient who recovered from COVID-19 successfully and safely completed FP.

CONCLUSIONS: At our center FP care remained uninterrupted but appropriately modified during COVID-19. We completed more cycles compared to 2019, absorbing patients from centers facing COVID-related closures. Despite significantly fewer monitoring visits and more than one-third of trigger shots administered blindly, outcomes were optimal and equivalent to historical controls. Our center's experience illustrates that FP care can be adapted without compromising outcomes; long-term modifications should be considered given the continued vulnerability of this population.

SUPPORT: Friends of Prentice

P-182 4:30 PM Saturday, October 17, 2020

PATIENT REACTIONS ON SOCIAL MEDIA TO THE ASRM COVID TREATMENTS SUSPENSIONS.

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OBJECTIVE: On March 17, 2020, the American Society for Reproductive Medicine (ASRM) issued its initial recommendations regarding patient management and infertility treatment during the ongoing COVID-19 outbreak. Included were recommendations to suspend initiation of new treatment cycles, including those of patients of advanced age or diminished ovarian reserve. The purpose of this study was to survey patient opinions and reactions, as expressed on social media, to these recommendations and the three subsequent updates.

DESIGN: Cross sectional study.

MATERIALS AND METHODS: We surveyed "r/Infertility," a group with 17,800 members on the social medial site Reddit, for reactions following each of the initial four ASRM recommendations. Comments were made in individual "COVID/Coronavirus Mega Threads" on the days surrounding the March 17th, March 30th, April 13th, and April 24thannouncements. We categorized posts based on their content, and quantified the number of posts per category. Categories included emotional reaction, resulting concerns, shared empathy, exchanges of advice and information.

RESULTS: 344 posts made by 148 users were categorized. The largest number of posts (n=90, 26.2%) expressed empathy to difficult news that was shared by another user. 82 posts (23.8%) discussed the future uncertainty, and 13 posts (3.8%) expressed an uncertainty in their clinics present policy. The most common emotional reaction was of disappointment (n=38, 11.1%), but others also expressed anger, anxiety, and frustration (5.2%, 6.4%, and 7.3% respectively). A total of 23 posts (6.7%) expressed frustration specifically at treatment being cancelled mid-cycle.

A small number of comments questioned aspects of the guidelines, and expressed frustration with ASRM (7, 2.0%), but more users expressed concerns regarding the risk of becoming pregnant ((17, 4.9%), and none questioned the validity of the guidelines. A significant portion of users questioned whether patients with diminished ovarian reserve should be restricted as well, or whether they should be given priority when treatments resume (21, 6.1%). Several users questioned why the general population was not being cautioned about becoming pregnant (9, 2.6%), and also expressed annoyance regarding comments made in the general population of an upcoming COVID "baby boom" as a result of the self-quarantining taking place (13, 3.8%). 38 posts exchanged advice (11.1%) and 83 posts offered information (24.1%).

CONCLUSIONS: We surveyed a popular social media site for patient responses to the recent ASRM COVID guidelines, and demonstrate that while users overwhelmingly endorsed the treatment suspension, they struggled with the disappointment, frustration and anxiety that came with the delay in their care, the backlog that will result when treatments resume, and the uncertainty surrounding present and future ASRM/clinic policies. In particular, patients with diminished ovarian reserve, and those whose treatment was canceled mid-cycle, were distraught by the lack of differentiation in the COVID guidelines.

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MOTHERHOOD PLAN: HAS IT CHANGED IN FACE OF THE COVID-19 PANDEMICS?

Daniela Paes de Almeida Ferreira Braga, PhD, Amanda Souza Setti, MSc, Assumpto Iaconelli, Jr., MD, Edson Borges, Jr., PhD. Fertility Medical Group / Sapientiae Institute, Sao Paulo, Brazil.

OBJECTIVE: The novel coronavirus (Covid-19) outbreak led to a public health emergency of international concern, putting health organizations on alert. World authorities implemented suppression plans to control community spread, including restrictions to non-urgent medical care. Assisted reproduction centers had to adapt to these restrictions. The infertility diagnosis and reproductive treatments possess an inherent psychological burden. This associated with the uncertainty of the consequences of the passage of time in the prognosis of treatments may impact on patient's psychological health. The goal for the present study was to investigate whether women seeking fertility care have different perception concerning the impact of Covid-19 on the motherhood plan than a target population?

DESIGN: Prospective randomized study.

MATERIALS AND METHODS: From 22/April/2020 to 25/may/2020, a survey through an online-platform was conducted. Participants were randomized by age in one of the two groups: ART-GROUP (n=92), including patients seeking for fertility treatment, but still didn't start their cycles or INTERESTED-GROUP (n=92), including participants interested in the subject, who accessed the website of a university-affiliated IVF-center. Participants in the ART-GROUP were invited via e-mail, with a cover-letter outlining the survey and a link to access it. Participants in the INTERESTED-GROUP accessed the questionnaire via website. Information on demographic data and their perceptions in face of the COVID-19 pandemics and the motherhood plan was collected. Women were asked: (i) How do you see the possibility of becoming pregnant after the beginning of the COVID-19 pandemic? (ii) How long do you think that suppression strategies will last? and (iii) Did you postpone your plans to become pregnant? If yes, why?

RESULTS: Most patients in the ART-GROUP were married or in a common-law relationship (83.6%), while a half of women in the INTERESTED-GROUP were in the same situation (50.0% $p<0.001$). When asked about the possibility of becoming pregnant, after the beginning of the pandemic, 47.8% of the ART-GROUP stated to believe the pandemic could affect their plans, while only 28.2% of the INTERESTED-GROUP stated the same ($p=0.035$). Concerning the duration of the suppression strategies, 64.1% of patients in ART-GROUP stated to believe the suppression strategies will be over by July, while only 18.5% of women in the INTERESTED-GROUP believed the same ($p<0.001$). The plan to become pregnant was postponed by 41.3% of the ART-GROUP and by 57.6.1% of the INTERESTED-GROUP ($p=0.341$). The main reasons that led people to this decision were fear of getting sick (52.6% vs. 73.6%, $p=0.083$, for ART-GROUP and INTERESTED-GROUP, respectively) and economic reasons (47.3% vs. 24.5%, $p=0.085$ FOR ART-GROUP and INTERESTED-GROUP, respectively).

CONCLUSIONS: Besides the fear of becoming sick, the economic burdens are the main reason for the delay in the motherhood plain, especially among women seeking for fertility care. This may be due to the fear of future economic instabilities and the fact that, in Brazil, ART do not qualify for reimbursement.

SUPPORT: None.

P-184 4:30 PM Saturday, October 17, 2020

USING VIDEO VISITS FOR NEW PATIENT EVALUATIONS DURING COVID-19.

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OBJECTIVE: With the rapid expansion of telehealth use during COVID-19, it remains unknown how video visits are being used to evaluate male infertility particularly when patients are not able to undergo a physical exam. We sought to assess what diagnoses were seen and which tests were pursued as part of the new patient evaluation. Herein we summarize a single institution's experience with video visits for male infertility during COVID-19.

DESIGN: Retrospective case series of patients with male infertility managed via video visits.

MATERIALS AND METHODS: We identified video visits completed at our institution between March 23, 2020 and April 29, 2020 for male infertility. We included new patients visits and return visits for men 18 years of age or older completed by two andrology-trained urologists. We collected and categorized scheduled visit type; visit completion rate; patient demographic and referral information; primary diagnoses; and laboratory and imaging tests ordered for new patient evaluations.

RESULTS: There were 51 scheduled video visits with 21 (41.2%) new patient and 30 (58.8%) established patient encounters. Eight (15.7%) video

visits were cancelled—7 re-scheduled and 1 converted to a telephone encounter due to technical issues—and 6 (11.8%) were no-shows. The median age was 32 years (range 22 – 48) and most patients were referred by their primary care provider or their partner's reproductive endocrinologist (53% and 18%, respectively).

For the 38 completed video visits, primary diagnoses included 11 (29%) idiopathic cases, 11 (29%) endocrinologic derangements, and 9 (24%) cases had anatomic contributors to infertility such as varicocele, previous vasectomy or ejaculatory duct obstruction. Additional diagnoses included genetic abnormalities (5%), concurrent partner evaluation (3%), sperm DNA integrity concerns (3%), active infection with pyospermia (3%), and post-operative hematoma (3%).

Of the 17 completed new patient visits, most were diagnosed with idiopathic 6 (35%) or anatomic (24%) conditions. Only 4 new patients (24%) had previously undergone an examination by a urologist. Eleven new patients (65%) required additional hormonal testing, 5 (29%) required another semen analysis, and 5 (29%) had scrotal ultrasound ordered due to inability to perform a physical exam due to limited use of outpatient clinics during COVID-19. Three (18%) required genetic testing, 2 (12%) a pituitary MRI, and 1 (6%) required DNA fragmentation testing.

CONCLUSIONS: Due to COVID-19, use of video visit has expanded to include new patient, male infertility evaluations. The most commonly ordered tests for these men included additional hormonal testing, additional semen analyses, and scrotal ultrasounds. While the physical exam is a crucial aspect of the infertility work-up, this series suggests that video visits could help ensure that a complete evaluation takes place even before a man undergoes a physical exam in clinic.

SUPPORT: Dr. Dupree receives Grant Funding from BCBSM for quality improvement work with Michigan Value Collaborative but this funding was not used to support this abstract

P-185 4:30 PM Saturday, October 17, 2020

COVID 19 PANDEMIC: ANXIETY AMONG PATIENTS WITH INFERTILITY IN IRAN. Elham Neisani Samani, MD,[1] Farzaneh Nemati, MD[2] [1]University of Massachusetts, Amherst, MA; [2]Qazvin University of Medical Sciences, Qazvin, MA, Iran (Islamic Republic of).

OBJECTIVE: A unprecedented spread of novel coronavirus disease (COVID-19) has influenced all over the world. However, the psychological effects of the pandemic on the general population, particularly patient with infertility, is lacking. The present study investigated the anxiety and worries in infertile patients during the COVID-19 outbreak.

DESIGN: Case-Control.

MATERIALS AND METHODS: Study was conducted using an online survey to assess anxiety and worries of patients with infertility who were being treated in a private Artificial Reproductive Technology (ART) center from 1th Jan to 15th March 2020. Two researchers followed up with the respondents, among whom 130 returned their questionnaires.

RESULTS: Among the responders, 92.30% (n=120, case group) obtained scores higher than 5 on the Beck Anxiety Inventory (BAI). Patients with infertility have shown statistically significant effects of COVID 19 on psychology, worries, and mean scores in the Beck Anxiety Inventory (BAI). Statistical analysis was performed using SPSS version 25. Chi-Square and Spearman correlation tests were applied to control confounders and assess the relation of the patient's response concerning age and educational level.

CONCLUSIONS: This study revealed the effects of the Covid-19 pandemic on the anxiety level and worries of the patients with infertility. Our results illustrated effective strategies are needed to provide psychosocial support to these individuals during the crisis.

POSTER SESSION: CRYOPRESERVATION

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DISTURBANCE IN OOCYTE MEMBRANE LIPIDS DURING EQUILIBRATION STEP OF THE VITRIFICATION PROTOCOL. Thalita S. Berteli, MSc,[1] Eduardo D. Borges, MSc,[1] Caroline M. Luz, MSc,[1] Christina R. Ferreira, PhD,[2] Paula A. Navarro, MD, PhD,[1] Alessandra A. Vireque, PhD[3] [1]Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo - Departamento de Ginecologia e Obstetrícia, Ribeirão Preto-SP, Brazil; [2]Purdue University - Metabolite Profiling Facility, Bindley Bioscience Center, IN; [3]Invitra – Assisted Reproductive Technologies LTD, Supera Innovation and Technology Park, Ribeirão Preto-SP, Brazil.

OBJECTIVE: In order to obtain a stable glassy state in the vitrification process, it is necessary to combine high cooling rates, small volumes of highly concentrated cryoprotectant solutions and short exposure times. During equilibration phase of oocyte vitrification, the exposure time varies from 10 to 15 minutes according to manufacturers' recommendations and a dynamic flow of water and solutes occurs through plasma membrane, a step closely related to oocyte quality maintenance after warming. Studies investigating oocyte lipid profile, especially lipids related to membrane lipid bilayer, may be useful to evaluate the impact of the equilibration protocol of vitrification on oocyte cryotolerance. Here we report the feasibility of the targeted lipidomics using multiple reaction monitor profiling (MRM-profiling) to investigate and monitor the impact of the exposure times to equilibration solution (ES) during vitrification on lipid profile of mice oocytes.

DESIGN: Experimental study.

MATERIALS AND METHODS: C57BL/6J mice oocytes (3 replicates; n=20 oocytes/group) were collected after superovulation with eCG and hCG and exposed to ES (Irvine Scientific) for distinct durations. The two groups were vitrified following the manufacturer recommended protocol: 10-minute total duration (oocytes stay for 6 minutes in third drop - ES10) or a shorter, 7-minute total protocol (oocytes stay for 3 minutes in the third drop - ES7). At the final step of equilibration, oocytes were washed 3 times in methanol: H_2O solution (1:3 v/v) and kept at -80^{o}C until lipid extraction. Lipids, equivalent to a pool of 5-7 oocytes per group/replicate were extracted using *One Step Methanol* protocol and flow injected into the triple quadrupole spectrometer equipped with an electrospray ion source (ESI-MS). Lipid classes were analyzed by MRM-profiling. The relative ion intensities values were evaluated using univariate (change fold, t-test, volcano plot), and multivariate analysis (PCA, PLS-DA, cluster analysis). Most informative lipid species in each group were sorted out using the partial least square discriminant analysis (PLS-DA) variables of importance (VIP) scores >1.

RESULTS: A relative ion intensity overrepresentations for saturated free fatty acids C19:0, C20:0 and C22:0 was observed in ES10 (change fold>2; $p< 0.05$) when compared to ES7 group. In the PCA scores, ES7 and ES10-CTR oocytes showed a tendency of discrimination at PC1 (68,8% of variability explained) and 4 membrane phospholipids (phosphatidylcholines and sphingomyelins) classified by PLS-DA were downregulated in ES10, indicating the presence of lipid composition changes in mice oocyte membrane due to amount of equilibration time used for the vitrification protocol.

CONCLUSIONS: Even slight changes in vitrification protocol such as the duration of the equilibration phase impacted the lipid profile of mice oocytes and could be monitored by MRM-profiling. Our results indicate that shorter time exposure in ES compared to long equilibration recommended by the manufacturer (7 min versus 10 min, respectively) is related to less disturbance of the plasma membrane of mice oocytes.

CNPq (process n. 305173/2019-7), Trial registration number: CEUA-FMRP/USP-107/2017.

SUPPORT: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) – process n. Â 88887.371487/2019-00; Fundação de Apoio ao Ensino, Pesquisa e Assistência do Hospital das Clínicas da FMRP – USP (FAEPA); Invitra Assisted Reproductive Technologies LTDA.

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IMPACT OF OOCYTE VITRIFICATION AND SUPPLEMENTATION OF THE VITRIFICATION MEDIA WITH ANTIOXIDANTS AND FATTY ACIDS ON LIPID PROFILE OF MICE BLASTOCYSTS. Thalita S. Berteli, MSc,[1] Eduardo D. Borges, MSc,[1] Caroline M. Luz, MSc,[1] Christina R. Ferreira, PhD,[2] Alessandra A. Vireque, PhD,[3] Paula A. Navarro, MD, PhD[1] [1]Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo - Departamento de Ginecologia e Obstetrícia, Ribeirão Preto-SP, Brazil; [2]Purdue University - Metabolite Profiling Facility, Bindley Bioscience Center, IN; [3]Invitra – Assisted Reproductive Technologies LTD, Supera Innovation and Technology Park, Ribeirão Preto-SP, Brazil.

OBJECTIVE: To investigate the impact of oocyte vitrification on lipid profile of mice blastocysts by comparing blastocysts originated from fresh and from vitrified oocytes subjected to in vitro fertilization. Also, to assess the effects of supplementing the vitrification media with antioxidants and unsaturated fatty acids by comparing blastocysts vitrified with Irvine Scientific, a

commercial standard vitrification media; Tvitri-4, produced in small scale for research by INVITRA®, based on the standard composition with four modifications including carbohydrate trehalose instead sucrose, reduced non-permeant cryoprotectant concentration, and addition of two aminoacids; and Tvitri-4 supplemented with L-carnitine (LC) and oleic and linoleic fatty acids (FA).

DESIGN: Experimental study.

MATERIALS AND METHODS: 23 C57BL/6J females were superovulated with 5UI eCG followed by 5UI hCG and oocytes (n=562; 4 replicates) were randomly divided in 4 groups: fresh control group (FC), vitrified using Irvine (IRV), Tvitri-4 (T4), or supplemented Tvitri-4 (T4-LC/FA) media. Fresh or vitrified-thawed oocytes were inseminated with $1x10^6$ sptz/ml and cultivated for 96 or 120 hours in *KSOM (Cosmo bio co., LTD)* incubated at 37°C with 5% CO_2. Blastocysts of each group were individually fixed in methanol/water. Lipids were extracted using *One Step Methanol* protocol (9 blastocysts/group) and flow injected into the triple quadrupole spectrometer equipped with an electrospray ion source. Lipids were analyzed using the multiple reaction monitoring profiling (*MRM*-profiling) method and values of relative intensities of ions detected in each group were compared using univariate (one-way ANOVA, volcano plot) and multivariate analysis (PLS-DA).

RESULTS: One-way ANOVA (p-value ≤ 0.05) showed that 90 out of the 125 lipids were differently expressed among the four groups, while a comparison between the vitrified groups showed no difference. Two by two comparisons between the control and vitrified groups using volcano plot (p-value ≤ 0.05, fold-change ≥ 1.5) detected 55, 17, and 11 significant features between FC vs. IRV, FC vs. T4, and FC vs. T4-LC/FA, respectively; all of them more abundant in the FC group. Partial least square discriminant analysis (PLS-DA) variables of importance (VIP scores) higher than 1.3 followed the same pattern and identified the phosphatidylinositol containing 36 carbon and one unsaturation in the fatty acyl residues - PI(36:1), and phosphatidylcholines PC(38:4), PCo(36:5), PC(34:1), and PC(30:0) among the top features; the exception being the free stearic acid (C18:0), which was the top feature in the FC x T4-LC/FA comparison, being more abundant in the latter.

CONCLUSIONS: Vitrification changed the lipid profile of mice blastocysts causing an overall reduction on lipid abundances that affected PC lipids the most. This effect was more apparent in IRV, followed by T4, and T4-LC/FA suggesting that supplementation of media with L-carnitine and unsaturated fatty acids may have protective effects on lipid content of blastocysts from vitrified oocytes, whose impacts needs further investigation.

CNPq (process n. 305173/2019-7), Trial registration number: CEUA-FMRP/USP-107/2017.

SUPPORT: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) – process n. Â 88887.371487/2019-00; Fundação de Apoio ao Ensino, Pesquisa e Assistência do Hospital das Clínicas da FMRP – USP (FAEPA); Invitra Assisted Reproductive Technologies LTDA.

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OPTIMAL STORAGE TEMPERATURE FROM THAWING OF CRYOPRESERVED OVARIAN TISSUE TO TRANSPLANTATION: XENOTRANSPLANTATION INTO NUDE MICE.

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[1]Kyono ART Clinic, Human Ovarian-tissue Preservation Enterprise (HOPE), Tokyo, Japan; [2]Niigata University, Brain Research Institute, Niigata, Japan.

OBJECTIVE: Human ovarian tissue cryopreservation, an essential method of fertility preservation, has led to the birth of more than 180 healthy babies around the world. Although there are many reports on cryopreservation and transplantation of ovarian tissues, the optimum storage conditions after thawing are still unclear. In this study, we performed xenotransplantation of ovarian tissue into nude mice to determine what kind of storage conditions are appropriate.

DESIGN: Prospective controlled animal study.

MATERIALS AND METHODS: We used ovaries derived from four SD rats at 10 weeks of age. Each ovary was cut in half, then 16 slices were cryopreserved by the slow freezing method (using 1.5M DMSO as cryoprotectant). Then, the tissues were thawed and stored at 4°C, RT (24°C), or 37°C for 2.5 hours in DPBS buffer. They were grafted under the kidney capsule of an ovariectomized nude mice (8-20 weeks old). Five IU PMSG and 5 IU hCG was injected once into mice at about 4 weeks after transplantation. Engraftment and follicle development in each group was compared with that in the control group (immediately grafted after being thawed).

RESULTS: The engraftment rates of frozen-thawed ovarian tissues were assessed in the control group (100%), 4°C group (87.5%), RT group (84.6%), and 37°C group (50.0%). The engraftment rate was significantly decreased when the tissues were stored at 37°C compared with those of the other groups ($P < 0.05$). The rates of engrafted ovarian tissues with macroscopically confirmed follicles were assessed in the control group (61.5%), 4°C group (71.4%), RT group (45.5%), and 37°C group (33.3%). Those rates in the RT and 37°C groups decreased compared with the control and 4°C groups although there was no significant difference. The follicles were aspirated and oocytes were collected in the control group (9), 4°C group (12), RT group (3), and 37°C group (1).

CONCLUSIONS: Storing the frozen-thawed tissues at 4°C led to a successful engraftment and follicle development. Although the tissues were well engrafted, there was little follicular growth in the RT group compared with the 4°C group. The storage at 37°C resulted in poor engraftment and follicle development. This study showed that the storage temperature of frozen-thawed ovarian tissues affects the engraftment and/or follicle development. Frozen-thawed ovarian tissues should be transplanted immediately after being thawed. In case they need to be kept a while before transplantation, storage at lower temperatures is recommended.

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HIGH SECURITY CLOSED DEVICES ARE EFFICIENT AND SAFE FOR VITRIFICATION TO PROTECT HUMAN OOCYTES FROM THE RISK OF VIRAL CONTAMINATION ESPECIALLY DURING THE COVID-19 PANDEMIC.

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OBJECTIVE: To compare the efficacy of high security versus open devices for human oocytes vitrification.

DESIGN: Prospective study. Between October 2015 and April 2020, 737 patients (775 oocytes cryopreservation cycles) were randomly assigned to two Groups:

Group 1: 368 patients (389 vitrification cycles) by High Security Vitrification™ (HSV)

Group 2: 369 patients (386 vitrification cycles) by Cryotop® open system.

Vitrification was performed in case of Ovarian Hyper Stimulation Syndrome, failure semen production and supernumerary oocytes.

MATERIALS AND METHODS: All patients attending IVF and Infertility Center, University Hospital S.Orsola (Italy), were stimulated with recombinant-follicle stimulating hormone and gonadotropin releasing hormone analogues. Oocyte retrieval by transvaginal needle aspiration was performed 36 hours after ovulation triggering with recombinant Human chorionic gonadotropin injection. Metafase II oocytes were vitrified by Kuwayama's protocol (2005) and microinjected after warming.

RESULTS: Results are shown in Table 1.

CONCLUSIONS: The efficacy of vitrification was assessed in vitro using survival, fertilization and cleavage rates and in vivo after embryo transfer by pregnancy, implantation and miscarriage rates.

Results shows no statistically significant differences using HSV or Cryotop® for oocytes vitrification. Therefore, in order to ensure safety, especially during the current COVID-19 pandemic, the use of the closed device eliminates the potential sample contamination during vitrification and storage without compromising its in vitro and in vivo survival and development.

TABLE 1.

	TOTAL	GROUP 1: HSV	GROUP 2: Cryotop	P
Patients	737	368	369	
Vitrification cycles	775	389	386	
Age (m ± ds)	36.03 ± 3.90	36.18 ± 3.92	35.88 ± 3.88	.285
Age (range)	25-46	25-46	26-44	
Oocytes frozen (m±ds)	4389 (6,67 ± 3,55)	1980 (5,09 ± 3,09)	2409 (6,24 ± 4,0)	
Warming cycles	624	354	270	
Oocytes thawed (m±ds)	2564 (4,12 ± 1,53)	1469 (4,15 ± 1,65)	1095 (4,06 ± 1,41)	
Oocytes survived (%)	1835 (71,6)	1032 (70,3)	803 (73,3)	.096
Oocytes microinjected (m±ds)	1386 (2,23 ± 0,89)	792 (2,25 ± 0,95)	594 (2,20 ± 0,82)	.320
Normal Fertilization (%)	1006 (72,6)	561 (70,8)	445 (74,9)	.104
Cleaved Embryos (%)	910 (90,5)	508 (90,6)	402 (90,3)	.994
N° Transfer	545	297	248	
Transferred Embryos (m±ds)	917 (1,69 ± 0,74)	512 (1,66 ± 0,79)	405 (1,71 ± 0,69)	.127
Pregnancy/Transfer (%)	174/545 (32.0)	79/248 (31.8)	95/297 (32.0)	.953
Implantation rate	180/917 (19.6)	80/405 (19.7)	100/512 (19.5)	1.000
Miscarriage rate	38/174 (21.8)	17/79 (21.5)	21/95 (22.1)	.927

No statistically significant differences was observed between the two groups in biological and clinical outcomes.

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STATUS QUO – OR IS IT TIME TO RECONSIDER THE VITRIFICATION METHOD RELATIVE TO THE RISK OF EMBRYO DISEASE TRANSMISSION IN CRYOSTORAGE?

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OBJECTIVE: The current global pandemic has triggered concerns regarding the potential infectivity of the SARS-CoV-2 virus to blastomeres known to possess ACE-2 receptors. In 2010, Pomeroy and coauthors reviewed the negligible risks associated with the potential cross contamination of human reproductive tissues, gametes and embryos in cryostorage. The purpose of this investigation is to explore changes in ART lab practices over the last decade that could warrant a reassessment of the latter AAB/CRB embryo cryopreservation guidelines relative to disease transmission potential.

DESIGN: Retrospective analysis of clinical practices that may alter the way we look at acceptable risks in embryo vitrification (VTF) and cryostorage methods. Specifically, we will investigate the effectiveness of a validated closed VTF system relative to zona pellucida (ZP)-intact and non-intact blastocyst cryopreservation. Additionally, we will discuss the merits and need for safer cryostorage systems.

MATERIALS AND METHODS: Human blastocysts were vitrified in a closed, aseptic device system and rapidly-warmed and sucrose diluted using standard procedures. From 2009 to 2012, 90% of all vitrified blastocysts had an intact ZP without the need for pre-VTF collapsing due to the use of I.C.E. non-DMSO solutions (>7.9M glycerol/EG). Between 2012-2014 we transitioned into 100% of all embryos experiencing laser ZP ablation and or blastocyst biopsying procedures by 2015. The latter trophectoderm exposed blastocysts were effectively contained in flexipettes which were weld-sealed into CBS straws without risk to possible pathogen exposure in liquid nitrogen cryostorage. Chi-squared analysis was used to assess differences ($p<0.05$) in survival and pregnancy outcome data.

RESULTS: The routine application of ZP-exposed trophectoderm and blastocyst biopsying improved ($p<0.05$) our survival rates from 95% (1066 of 1126 BL) to 99.4% (3352 of 3373 BL) with increased ($p<0.05$) embryo implantation efficiency (46% vs 69% implantation using 1.91 vs 1.07 blastocysts/FET, respectively).

CONCLUSIONS: The protective barrier of an intact ZP to potential pathogen exposures is no longer a clinical reality for cryopreserved blastocysts. Although we agree that the relative risks of embryo disease transmission in cryostorage remain negligible, why take any risks when highly effective closed VTF systems (ICE straw, HSV, μS-VF, VitriSafe) have been established over the last decade? Alternatively, we question whether the use of LN_2-vapor storage tanks for open-VTF systems alleviates potential airborne viral cross-contamination, while they most certainly create a greater risk for potential embryo wastage as discussed by Pomeroy et al. (2010) and overtly realized by recent tank failure experiments and known catastrophic events. Finally, it is worth noting that embryos vitrified in an insulated straw environment are more resistant to detrimental additive temperature fluxes that can occur under sub-optimal cryostorage handling procedures. So, we ask, is it time to reconsider the status quo of embryo good tissue practices when viral pandemics are a reality?

References: Pomeroy KO, Harris S, Conaghan J, Papadakis M, Centola G, Basuray R, Battaglia D. Storage of cryopreserved reproductive tissues: evidence that cross-contamination of infectious agents is a negligible risk. Fertil Steril. 2010;94:1181–1188.

SUPPORT: NONE

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RESEARCH ON THE RELATIONSHIP BETWEEN THE CAPACITY OF EMBRYO STORAGE TANKS AND THE ESTIMATED EMBRYO SALVAGE PERIOD WHEN TANKS ARE DAMAGED.

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OBJECTIVE: Keeping liquid nitrogen (LN_2) tank properly is extremely important for an ART clinic. As the accident in the U.S. in 2018 showed, a tank failure causes serious damage for embryos and patients. However, there's no detailed information as to what to do when tanks are damaged. In our previous study, we indicated that a damaged 10L tank can keep freezing for 7-8 hours if it retains a certain level of LN_2. In this study, we analyzed the influence of tank capacity on the estimated embryo salvage period in a simulated tank failure.

DESIGN: Prospective experimental trial.

MATERIALS AND METHODS: We prepared 3 tanks of different capacity (XT10, HC20, HC35, Taylor-Wharton, USA). All tanks were filled up to full with LN_2. To simulate tank failure, we drilled a 2mm diameter hole in the vacuum valve of each tank. A temperature prove was set in a plastic sleeve of cane in the tanks. We measured the temperature and LN_2 levels every 15 min for the first hour. Then, they were measured every hour to until the rise in temperature began. After the temperature initiated to rise, they were measured every 15 min to until the temperature reached -80 °C, which is the temperature at which embryos start to get damaged. Before tank failure simulation, temperatures and LN_2 level of each tank were measured every 24 hours for 7 days to see the temperature and LN_2 volume shift without tank damage.

RESULTS: Speed of LN_2 level decrease of the 10, 20 and 35L tank was 4.6, 4.5, and 2.8 cm/h, respectively. The temperature at the start of measurement for all tanks was -196 °C. In the 10L tank, the rise in temperature began when the remaining LN_2 level was 1cm. In the 20 and 35L tanks, it began

when the LN_2 was gone. The time at which the rise in temperature began was 6h45min for the 10L tank, 8h00min for the 20L tank, and 11h45min for the 35L tank, respectively. The time it took for the temperature to reach -80 °C for the 10, 20, and 35L tanks were 7h54min, 8h41min, and 14h14min, respectively. The decrease in LN_2 levels of the 10, 20, and 35L tanks for 7days without a drilled hole were 2cm, 4cm, and 4cm, respectively. The temperature remained at -196 °C in all tanks without tank damage.

CONCLUSIONS: In this study, the speed of LN_2 decrease of the 35L tank was slower than that of the 10 and 20L tanks when damaged. The larger the capacity of the tank, the longer it took for the temperature rise to begin and for the temperature to reach -80 °C. There was a difference of 6h20min between the 10L and 35L tanks to reach -80 °C. Therefore, it should be kept in mind that the rescue duration of embryos over the tank failure vary depending on each tank capacity.

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AN UPDATE IN SPERM CRYOPRESERVATION: DETERMINATION OF MELATONIN CONCENTRATION USED AS ANTIOXIDANT AGENT IN PRE-FREEZING SAMPLES. Larissa Namie Chiba, Bsc, Ana Clara Monteiro Barduchi, Bsc, Mayara Rodrigues, Bsc, Heloisa Faquineti, Bsc, Juliana Risso Pariz, PhD, Jorge Hallak, PhD. Androscience, Science and Innovation Center in Andrology and High-Complex Clinical and Andrology Laboratory, Sao Paulo, Brazil.

OBJECTIVE: To determine the melatonin concentration used as antioxidant agent in pre-freezing semen samples.

DESIGN: Prospective study.

MATERIALS AND METHODS: Fifteen semen samples from male volunteers (21-45 years of age) in Androscience – Science and Innovation Center and High-Complexity Clinical and Research Andrology Laboratory, Sao Paulo, Brazil, were included in this study, from August 2019 to April 2020. As inclusion criteria, were adopted fresh samples (FS) with seminal volume $\geq$1.5 ml, sperm concentration $\geq$15 millions/ml and leukocytes $<$1.0 million/ml. After initial seminal and functional analysis, each sample was divided to evaluate different melatonin final concentrations: 0.01mM, 2.0mM and 3.0 mM of melatonin, added in cryoprotectant solution Test Yolk Buffer®. One samplem was cryopreserved with melatonin (control sample). Sperm viability, DNA fragmentation (SCSA®), and reactive oxygen species (ROS, luminol) levels were analyzed before and after cryopreservation.

RESULTS: Significant reduction was identified in sperm concentration, total and progressive motility and increase of ROS in postthaw samples compared to fresh samples ($p<0.05$). Motility parameters and reactive species of oxygen have improved in samples supplemented with 3mM and 0,01mM respectively ($p<0.05$). No differences were observed in DNA fragmentation.

CONCLUSIONS: The present results demonstrated slight positive effect on sperm motility and cryosurvival rate in samples with 3mM of melatonin. In a previous study carried out by our research group, 2 mM melatonin pre-cryopreservation and 2 mM caffeine in postthaw samples with progressive motility> 32% had beneficial effects on seminal quality. Therefore, we can suggest that the positive effect of melatonin depends on the initial quality of the cryopreserved samples.

References: Pariz, et al.Â Melatonin and Caffeine Supplementation Used, Respectively, as Protective and Stimulating Agents in the Cryopreservation of Human Sperm Improves Survival, Viability, and Motility after Thawing compared to Traditional TEST-Yolk Buffer. Oxidative Medicine and Cellular Longevity, 2019.

Sanchez, et al. Vitrified sperm banks: the new aseptic techinique for human spermatozoa allows cryopreservation at -86C. J Androl, 2012.

SUPPORT: Miss Chiba was a recipient of an undergraduate scholarship from the São Paulo Research Foundation (FAPESP, process number 2019/22137-4).

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VITRIFICATION WITH CUMULUS CELLS: IMPACT ON FERTILIZATION AND SUBSEQUENT EMBRYO DEVELOPMENT. Rocío Soledad Iaizzo, BSc, María Lovaglio Diez, BSc, Noelia Jorgelina Hechenleitner, BSc, Ariel Octavio Ahumada, PhD. Procrearte, Buenos Aires, Argentina.

OBJECTIVE: Assess the impact of leaving cumulus cells in fresh and thawed oocytes, and its consequences on fertilization and embryo development. Moreover, investigate whether the corona radiata has a protective effect on the oocyte during vitrification.

DESIGN: 718 oocytes were divided into 4 groups: fresh with cumulus ("group A"; n = 359), fresh denuded ("group B"; n = 123), thawed with cumulus ("group C"; n = 92) and thawed denuded ("group D"; n = 144).

IVF results were measured by fertilization, cleavage and blastulation rates, and top quality blastocysts percentage. These results were compared between groups A and B, and between groups A and C, while survival rate was compared between groups C and D.

MATERIALS AND METHODS: For total denudation, oocytes were exposed to a 30 U hyaluronidase solution during 30 seconds. The remaining cells were removed by using capillaries. Partial denudation was done by exposing oocytes to the same solution but only during 10 seconds, and washed with larger-gauge capillaries. For vitrification, the Kitazato protocol was used. Oocytes were inseminated with approximately 30,000 sperm cells in 20μl drops of Global Total for Fertilization under mineral oil. Embryos were cultured in groups of up to three, at 37°C, 6.5 CO_2 (pH 7.28) and 5% O_2, in 20μl drops of Global Total under mineral oil.

For statistical analysis, contingency tables with chi-square test were done. P-values <0.05 were considered significant.

RESULTS: Statistically significant differences were found in fertilization rate between group A (76,6%) and group B (41,4%), appreciating better results in group A (p=0,0009). Regarding other parameters, no differences were found between these groups. Regarding survival rates, no significant differences were found between groups C and D. Among the groups A and C, there were no differences in IVF results.

CONCLUSIONS: Presence of granulosa cells is vital for normal fertilization rates, in both fresh and thawed oocytes. However, it did not affect survival or blastulation rates.

The survival rate in thawed oocytes did not change according to the presence or absence of cumulus cells. This indicates that the corona radiata does not accomplish a protective function, as described by some authors. However, their presence does not impact negatively either. Therefore, it is not necessary to denude the oocytes before vitrification, which would benefit maturation, and the possibility of performing conventional IVF instead of ICSI.

The ICSI technique is used on thawed oocytes to solve the potential low fertilization rate through conventional IVF in fully denuded oocytes. However, the fact that the cumulus cells maintain the oocyte's fertilizing ability even after vitrification corroborates that it would be possible to perform conventional IVF instead of ICSI in thawed oocytes with their cumulus cells. This would decrease the workload in laboratories, and improve the results, since IVF is a less invasive and more physiological technique.

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RETROSPECTIVE STUDY TO COMPARE BETWEEN HYALURONAN ENRICHED MEDIUM AND BLASTOCYST TRANSFER MEDIUM FOR FROZEN EMBRYO TRANSFER(FET) AND ITS IMPACT ON CLINICAL PREGNANCY RATE (CPR) IN PATIENTS WITH 2 OR MORE IVF-ICSI CYCLE FAILURES. Fiyazur Rahman, M.Sc,[1] , P.hDAnkita Gupta, scholar,[2] Dr. Rashmi Sharma, MD, DNB, FICOG,[3] Rohan Sharma, B.Sc,[4] Dr. Navkiran k Kaur, Ph.D.[5] [1]chief embryologist, New delhi, India; [2]Senior embryologist, Noida, India; [3]head of department, New Delhi, India; [4]Jr. Embryologist, New Delhi, India; [5]Assistant professor, Noida, India.

OBJECTIVE: To study the impact of use of hyaluronan enriched medium on CPR in frozen embryo cycles as compare to blastocyst culture medium in 2 or more IVF-ICSI failure.

DESIGN: This was a retrospective observational study.

MATERIALS AND METHODS: Record of all FET patients were analyzed in past one year and those patient who went FET with prior history of 2 or more IVF failure were included in this study, irrespective of the three stage of embryo transferred (D-3, D-4 and D-5). The transfer cycles where age of women was more than 40 yrs were excluded along with cycle where donor gametes were used. 195 patient fulfill the inclusion criteria out of which in 114 patients hyaluronan enriched medium was used. these patients were categorized as Group A while in 81 patients blastocyst culture media was used and categorized as Group B.

RESULTS: The two groups found to be comparable in baseline characteristics. The CPR was found to be 42.1 % (48/114) in group A verses 35.8%(

29/81)in group B . No statistically significant difference was observed between these two groups (p =0.375).

CONCLUSIONS: Use of Hylarunon enriched medium for frozen embryo transfer in patients with 2 or more IVF failures is not associated with statistically significant improvements in clinical pregnancy rate as compared to blastocyst transfer medium

References: s. Chao (2008)

SUPPORT: no

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THE DEVIL IS IN THE DETAILS: DISTRIBUTION OF CRYOPRESERVED OOCYTE MATURATION STAGE FOR PATIENTS UNDERGOING ONCOLOGY-INDICATED FERTILITY PRESERVATION.

Elnur Babayev, MD, MSc,[1] Danielle E. Strom, MD,[1] Emma C. Trawick, M.D.,[2] Kara N. Goldman, M.D.[3] [1]Northwestern University, Chicago, IL; [2]Northwestern University, Feinberg School of Medicine, Chicago, IL; [3]Northwestern University Feinberg School of Medicine, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Chicago, IL.

OBJECTIVE: For patients with cancer undergoing fertility preservation, a careful balance exists between cryopreserving all oocytes, including immature oocytes, and providing realistic expectations regarding future reproductive potential of cryopreserved gametes. The objective of this study was to characterize oocyte maturity and success with in vitro maturation (IVM) prior to oocyte cryopreservation by age and medical diagnosis.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Oncology-indicated fertility preservation cycles completed between Jun/2011 and Dec/2018 were reviewed. Maturation stage of oocytes retrieved and cryopreserved were recorded. 149 stimulation cycles were available for analysis. Data are presented as mean±SD ($p<0.05$). One-way ANOVA or Kruskal-Wallis test were used for statistical analysis.

RESULTS: The mean age was 29±6, BMI 27±8, AMH 3.0±2.6 ng/ml, with a mean 11±2 days of ovarian stimulation, 3685±1751 units of total gonadotropin used, and peak estradiol level 1959±1237 pg/ml. As expected, the number of retrieved and cryopreserved oocytes per cycle decreased with age. All GV oocytes were cryopreserved on the day of retrieval and comprised 8-15% of all cryopreserved oocytes. Metaphase I (MI) oocytes were either frozen on the day of retrieval (3-6% of all cryopreserved oocytes) or in vitro matured overnight. The proportion of cryopreserved oocytes at metaphase II stage (MII) on the day of retrieval (Day 0, range 71-82% of all oocytes) or following IVM (Day 1, 1-5% of all oocytes), as well as the proportion of MI and GV oocytes were not different across age groups. The proportion of frozen eggs at different maturation stages also did not differ by diagnosis.

CONCLUSIONS: Our data did not demonstrate a difference in maturation stage of cryopreserved oocytes by age or clinical diagnosis. Notably, in a large fertility preservation program approximately 20% of oocytes are cryopreserved at the GV or MI stage or following IVM. Studies suggest that patients undergoing medically indicated fertility preservation may overestimate their likelihood of success with cryopreserved gametes; this may be of particular consequence among patients freezing immature or in vitro matured oocytes with lower pregnancy potential. Patients must be carefully counseled to ensure realistic expectations of success with cryopreserved gametes.

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WITHDRAWN

POSTER SESSION: EARLY PREGNANCY

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IMPACT OF NON-VISUALIZED PREGNANCY LOSS HISTORY ON THE OUTCOME OF COUPLES WITH UNEXPLAINED RECURRENT PREGNANCY LOSS.

Sunaina Sharma, MD, MSc,[1] Sarka Lisonkova, MD, PhD,[1] Boris Kuzeljevic, MA,[2] Paul Yong, MD, PhD,[1]

	<25yo (n=37)	25-34yo (n=74)	35-37yo (n=20)	>38yo (n=18)	p value
Oocytes retrieved	16±9	16±9	13±7	8±6	p=0.002
Oocytes frozen	15±8	14±9	10±5	7±5	p=0.0001
Metaphase II frozen on D0 (%) of total frozen	80±16%	76±23%	82±19%	71±28%	p=0.6
Metaphase II frozen on D1 (%) of total frozen	1±3%	5±11%	5±14%	2±6%	p=0.5
MI % of total frozen	6±9%	6±12%	3±8%	5±9%	p=0.6
GV (%) of total frozen	11±15%	11±16%	8±13%	15±27%	p=0.7

Mohamed Ali Bedaiwy, M.D., Ph.D.[3] [1]The University Of British Columbia, Vancouver, BC, Canada; [2]BC Children's Hospital Research Institute, an agency of the Provincial Health Services Authority, Vancouver, BC, Canada; [3]University of British Columbia, Vancouver, BC, Canada.

OBJECTIVE: Unexplained recurrent pregnancy loss (uRPL) includes non-visualized pregnancy loss (NVPL, i.e. preclinical), visualized pregnancy loss (VPL, i.e. clinical), and Mixed (combination of VPL and NVPL) types of pregnancy losses. Our objective was to evaluate the association between the types of prior pregnancy losses and the outcome of the subsequent pregnancy in a cohort of uRPL women.

DESIGN: A retrospective cohort study approved by ethics board (Approval number: H13-03306).

MATERIALS AND METHODS: Women with uRPL who were referred to the RPL centre at British Columbia Women's Hospital (BCWH), between from January 1, 2011 to August 31, 2017 (n=806) were included. Their clinical evaluations were completed according to the American Society of Reproductive Medicine (ASRM) guidelines. Data were collected using Research Electronic Data Capture (REDCap) data management platform. We compared women who had only non-visualized pregnancy losses (NVPL) with women who had only visualized pregnancy losses (VPL) and those with both types of uRPL with respect to demographic and clinical characteristics. We also compared pregnancy outcomes (successful pregnancy $\geq$10 weeks gestation vs. miscarriage at $<$ 10 weeks gestation) among women with NVPL vs VPL groups. Logistic regression was used to adjust for potential confounders.

RESULTS: There were 142 (18%) women with only NVPL, while 152 (19%) women had only VPL. The remaining 512 (63%) women had a mixture of both. In this cohort of 806 women, 679 had a subsequent pregnancy within 12 months, among these, 397 (58.4%) pregnancy reached $\geq$10 weeks' gestation, and 282 (41.5%) of pregnancies were miscarried ($<$10 week's gestation). Successful pregnancy reaching $\geq$10 weeks occurred in 45.4% (69/152) women with VPL, in 35.2% (50/142) women with NVPL, and in 54.3% (278/512) of women with both types (mixed group).

Compared to women with VPL, women with NVPL were more likely to have prior primary pregnancy losses (AOR = 2.26, 95% CI = 1.32 – 3.86), and prior history of therapeutic abortions (AOR =4.26 and 95% CI = 1.65 – 11.02). Among those who became pregnant, women with VPL were more likely to remain pregnant at or beyond 10 weeks' gestation (AOR = 1.94, 95% CI = 1.03 – 3.66).

CONCLUSIONS: Our study suggests that exclusive NVPLs are prevalent in women with uRPL. Women who had only NVPL were more likely to experience miscarriage at $<$ 10 weeks' gestation compared with women with VPL in their subsequent pregnancy.

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MATERNAL SERUM B-HCG LEVELS IN THE PERI-IMPLANTATION PERIOD ARE PREDICTIVE OF RISK FOR 3RD TRIMESTER HYPERTENSIVE DISORDERS IN IVF PREGNANCIES. Samantha Simpson, MD,[1] Seth Guller, PhD,[2] Lubna Pal, MBBS[1] [1]Yale University, Orange, CT; [2]Yale School of Medicine, Orange, CT.

OBJECTIVE: In patients conceiving with in vitro fertilization and embryo transfer (IVF-ET), β-chorionic gonadotropin (β-hCG) levels are measurable in the maternal serum as early as 10 days after ET. The progressive rise in serum β-hCG levels that occurs in the first few weeks of pregnancy are indicative of the degree to which the invading trophoblast is successfully implanting. Because inadequacy of trophoblastic invasion of maternal decidua is a recognized mechanism underlying development of hypertensive disorders of pregnancy, we aimed to examine the predictive potential of peri-implantation levels of β-hCG for subsequent development of hypertensive disorders of pregnancy.

DESIGN: Prospective longitudinal cohort study at an academic fertility center.

MATERIALS AND METHODS: Infertile patients attaining a positive pregnancy test following blastocyst ET (between 10/ 2017 and 03/ 2019) were eligible. Serial estimates of β-hCG levels were performed at 48-hour intervals, as per standard clinical care, until level of $>$2,500 IU/mL, when intrauterine gestation/s were confirmed by transvaginal ultrasound. For the purpose of this work, singleton pregnancies were followed until delivery. The course of pregnancy and occurrence of pre-eclampsia or gestational hypertension (two systolic blood pressures $\geq$140 or diastolic $\geq$90 more than 6 hours apart prior to delivery) were monitored. Relationship between peri-implantation maternal serum β-hCG levels (log-transformed) with incident hypertensive disorders in the third trimester was examined using student's t-test; multivariable logistic regression analysis was used to examine relationship between β-hCG levels and pregnancy related hypertensive disorder after controlling for body mass index (BMI), age and race.

RESULTS: In singleton pregnancies conceived with IVF-ET, as early as between days 12-15 after blastocyst ET, β-hCG levels were significantly lower in those pregnancies that were eventually complicated by hypertensive disorder in the 3rd trimester (n=9) compared to those with an uneventful course (n=71), (days 12/13, 496.5mIU/mL (range 199-846) vs. 717mIU/mL (194-2920), p=0.03; days 14-15, 1225mIU/mL (339-1960) vs. 1690mIU/mL (400-4110) , p=0.03]. Multivariable logistic regression analysis adjusting for age, BMI and race using a propensity score approach identified serum β-hCG thresholds of less than 530mIU/mL on days 12/13 and less than 1230mIU/mL on days 14/15 following ET as predictive of incident pregnancy related hypertensive disorder in the 3rd trimester (26.6% v 5.9%, OR 6.6, 95% CI 1.01 – 43.4, p=0.049).

CONCLUSIONS: Precisely timed β-hCG serum levels after IVF-ET may be the earliest marker of risk for hypertensive disorders in the current pregnancy.

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RISK FACTORS FOR SUBCHORIONIC HEMATOMA AFFECTED PREGNANCIES IN THE INFERTILE POPULATION. Erin Inman, MD,[1] Daniel Miranian, MD,[2] Micaela J. Stevenson, BS,[3] Molly B. Moravek, MD, MPH,[1] Samantha B. Schon, MD, MTR[4] [1]University of Michigan, Ann Arbor, MI; [2]Obstetrics and Gynecology, University of Michigan, Ann Arbor, MI; [3]University of Michigan Medical School, Ann Arbor, MI; [4]Reproductive Endocrinology and Infertility, University of Michigan, Ann Arbor, MI.

OBJECTIVE: Subchorionic hematoma (SCH) is common, however, is of unknown significance among the infertile population as most studies evaluate women without a history of infertility or with naturally conceived pregnancies. The objective of this study was to identify risk factors for SCH affected pregnancies in the infertile population.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: CPT codes were used to identify all obstetric (OB) scans performed at a single infertility clinic from 1/2015-3/2018. All viable intrauterine pregnancies on initial OB scan were included for analysis (n=1210). Chart review was performed to identify the presence of SCH. Data on patient demographics, fertility treatments, and pregnancy outcomes were collected. Bivariate analysis was performed to compare pregnancies with and without SCH, and multivariable logistic regression was used to identify independent risk factors for SCH.

RESULTS: The prevalence of SCH was 12.5% (n = 151). Prevalence of SCH did not vary significantly by age, race, or fertility treatment groups. Male-factor infertility was more prevalent among patients with SCH compared to those without SCH (34.4% versus 24.6%, p = 0.009). There were no other differences in SCH across other infertility diagnoses. In donor egg, in vitro fertilization, and frozen embryo transfer pregnancies, trophectoderm grade (good, fair, and poor) and stage of transfer (blastocyst or cleavage) did not vary significantly between pregnancies with and without SCH. However, use of 81-162mg aspirin was more common among patients with SCH compared to those without (49.7% versus 38.6%, p = 0.01) as well as the use of IM progesterone supplementation (16.6% versus 9.6%, p = 0.009).

After adjusting for age, factors significantly associated with SCH were the number of prenatal ultrasounds (aOR 1.72 [95% CI: 1.32-2.24], p$<$.0001) and vaginal bleeding (aOR 3.31 [2.20-5.50], p$<$.0001). Gynecologic complications (including fibroids, endometrial polyps, endometriosis, adenomyosis, and polycystic ovarian syndrome) were associated with decreased odds of SCH (aOR 0.61 [0.41-0.89], p=0.01).

CONCLUSIONS: Male-factor infertility and aspirin use are more common among infertile patients with SCH. While vaginal bleeding and number of prenatal ultrasounds were risk factors for SCH, a significant gynecologic history was protective for SCH.

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PREDICTIVE VALUE OF EARLY SERUM HCG LEVELS IN PROGRAMMED FROZEN EMBRYO TRANSFER CYCLES. Brady I. Magaoay, BA,[1] Pietro Bortoletto, MD,[2] Adamantios Athanasiou, MD,[2] Antonia Iliana Athanasiou, MD,[2] Phillip A. Romanski, MD,[2]

Daylon James, PhD,[2] Steven Spandorfer, MD[2] [1]Weill Medical College of Cornell University, New York, NY; [2]The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To determine if early serum hCG assessment (2-8 days post-blastocyst transfer) in patients achieving a pregnancy following a programmed frozen embryo transfer (FET) cycle can predict subsequent miscarriage.

DESIGN: Retrospective cohort study conducted at a university-affiliated center.

MATERIALS AND METHODS: Women with a positive hCG (>0.2 mIU/mL, Roche Cobas e801 assay) ≥ 10 days after a programmed FET cycle were categorized into two groups: early positive versus early negative hCG (between 2-8 days post-ET). Women with a vanishing twin or non-singleton live births were excluded. Only single blastocyst transfers were analyzed. Miscarriage, defined as demise of a clinical intrauterine gestation, was the primary outcome. Live birth rate was the secondary outcome. A multivariable logistic regression was performed to examine the association between both early hCG groups and miscarriage while controlling for the use of donor oocytes and the day of early hCG assessment. Odds ratios (OR) with 95% confidence intervals (CI) were estimated.

RESULTS: In total, 337 pregnant patients met inclusion criteria, of which 123 (36.5%) had a negative early hCG and 214 (63.5%) had a positive early hCG. Maternal age (35.7 vs. 36.4, p=0.20), BMI (24.0 versus 23.9 kg/m^2, p=0.51), and the use of donor oocytes (12.8 vs. 15%, p=0.59) were similar between the two groups. The median number of days post-ET of early hCG assessment was statistically different between the early negative versus early positive hCG groups (3 vs. 5 days post-ET, p<0.001), respectively. The mean (SD) early positive hCG level was 18.7 (25.2) mIU/mL. In the univariate analysis, a positive early hCG was associated with a 55% reduction in the odds of subsequent miscarriage compared to a negative early hCG (10.0 vs. 19.7%, OR: 0.45, CI: 0.24-0.86). After controlling for the use of donor oocytes and days of early hCG assessment, the model estimate did not change (OR: 0.44, CI: 0.19-0.99). There was no difference in live birth rates between the two groups (36.8 vs. 37.7, p=0.860).

CONCLUSIONS: In patients who become pregnant after a programmed FET cycle, an early positive hCG 2-8 days after transfer is associated with a significant reduction in the odds of a subsequent miscarriage. A strategy of early hCG assessment may allow for more individualized counseling and expectations setting regarding cycle success for patients and providers alike.

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LUTEAL PHASE PROGESTERONE SUPPORT DOES NOT IMPROVE ONGOING PREGNANCIES IN TRUE NATURAL CYCLE CRYOPRESERVED BLASTOCYST EMBRYO TRANSFERS. Ian Waldman, MD,[1] Catherine Racowsky, PhD,[1] Emily Disler, BS,[1] Ann M. Thomas, PhD,[2] Andrea Lanes, PhD,[1] Mark D. Hornstein, MD[1] [1]Brigham and Women's Hospital, Boston, MA; [2]Brigham & Women's Hospital, Boston, MA.

OBJECTIVE: To study the addition of progesterone luteal phase support for cryopreserved blastocyst transfers in natural cycles not using an ovulatory trigger (i.e. "true" natural cycles).

DESIGN: Retrospective cohort study in a single academic medical center.

MATERIALS AND METHODS: All patients who underwent day 5 or day 6 true natural cycle cryopreserved transfer between July 30, 2012 and June 30, 2018 were screened for inclusion. Evaluation of outcomes following progesterone supplementation was compared to those who did not receive luteal phase progesterone support. The primary outcome was ongoing pregnancy rate at discharge of care to the patient's obstetrician, typically around 8-12 weeks gestational age. Secondary outcomes were positive serum human chorionic gonadotropin (HCG) level, implantation rate, clinical pregnancy rate, miscarriage/abortion rate, ectopic pregnancy rate, and multifetal gestations.

RESULTS: 229 patients were included in the analysis with 149 receiving luteal phase progesterone supplementation and 80 receiving no luteal phase support. Patient demographic and cycle characteristics and embryo quality were similar between the two groups. No difference was seen in ongoing pregnancy rate (49.5% vs. 47.5%, p=0.8738), clinical pregnancy rate (50.3% vs. 47.5%, p= 0.7483), positive HCG rate (62.4% vs. 57.5%, p=0.5965), miscarriage/abortion rate (5.4% vs. 2.5%, p=0.2622), ectopic pregnancy rate (0% vs. 1.3%, p=0.3493), or multifetal gestations (7.4% vs. 3.8%, p=0.3166).

CONCLUSIONS: The addition of progesterone luteal phase support in true natural cycle cryopreserved blastocyst transfers does not improve cycle outcomes.

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RETAINED PRODUCTS OF CONCEPTION AFTER EARLY PREGNANCY LOSS: A CLOSER LOOK. Vaishnavi Purusothaman, MD, MA,[1] Emma M. Rosen, MSPH,[2] Linnea R. Goodman, MD[1] [1]University of North Carolina, Chapel Hill, NC; [2]UNC Gillings School of Public Health, Chapel Hill, NC.

OBJECTIVE: Missed abortion is an unfortunate, yet common outcome following fertility treatment. The rate of retained products of conception (RPOC) after early pregnancy loss has been reported to be 0.4% - 3.8%. The primary purpose of this study was to assess and compare the incidence of RPOC after manual vacuum aspiration (MVA) or medical management of early pregnancy loss.

DESIGN: Retrospective cohort of patients seen at a university fertility program who underwent treatment for early pregnancy loss between January 2014 and January 2020.

MATERIALS AND METHODS: Patients were categorized into two groups: MVA group, and medical management group (vaginal misoprostol with or without oral mifepristone). Clinical information and laboratory results were collected from chart abstraction. RPOC and intrauterine adhesions were defined as presence of such findings on follow-up Saline Infusion Sonography (SIS) and/or Hysteroscopy. Statistical analysis was performed using SAS. T-tests and Fisher's exact tests were used where appropriate; unadjusted and adjusted risk ratios were calculated. Models were adjusted for history of RPOC and history of miscarriage.

RESULTS: A total of 110 patients with a mean age of 34.8+/- 4.3 years were identified as having a missed abortion requiring intervention with MVA (n = 56) and medical management (n =54). The mean gestational age at diagnosis was 7.6 +/-1.0 weeks, and 89.1% of patients conceived after IVF. There was no difference in age, race, BMI, parity, gestational age at time of diagnosis, or history of previous intrauterine surgery between groups. 80% of patients underwent follow up ultrasound (62.5% in the MVA group vs. 98.2% in the medical management group; p <0.01). In total, 57.2% of patients underwent uterine cavity evaluation, of which 93.7% were uterine cavity evaluation utilizing saline for improved cavity evaluation (SIS) and 6.3% were cavity evaluation with hysteroscopy. The incidence of RPOC after MVA and medical management was 13.0% and 29.4%, respectively. After controlling for prior history of miscarriage and prior history of retained products, the adjusted risk ratio for incidence of RPOC after MVA was 0.40 (95% CI 0.16-1.01). On follow-up imaging, there were noted to be 4 cases of adhesions in the MVA group (10.8%) and 1 in the medical management group (3.7%) (RR 2.92, 95% CI 0.3-19.9).

CONCLUSIONS: The incidence of RPOC in both treatments groups was noted to be much higher than the previous reports. This difference may be secondary to close surveillance and post-treatment uterine cavity evaluation with SIS and/or hysteroscopy in a fertility practice. The incidence of RPOC was also higher after medical management. These findings may better inform patient counseling and underscore the importance of close follow up after early pregnancy loss to ensure prompt diagnosis and treatment of RPOC.

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THE ASSOCIATION BETWEEN ECTOPIC PREGNANCY AND INFLAMMATORY BOWEL DISEASE, IRRITABLE BOWEL SYNDROME, AND CELIAC DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS. Jonah Imee Ramirez Talavera, BSc,[1] Allison Parrill, BSc,[1] Mohamed Ali Bedaiwy, M.D., Ph.D.,[2] Chris Elsayad, MD, FACP,[3] John C. Riggs, MD,[3] Bo Peng, Ph.D.[1] [1]American University of the Caribbean, School of Medicine, Cupecoy, Sint Maarten (Dutch part); [2]University of British Columbia, Vancouver, BC, Canada; [3]Nassau University Medical Center, East Meadow, NY.

OBJECTIVE: Ectopic pregnancy affects about 1% of women of reproductive age. Previous studies that compare risk of ectopic pregnancy (EP) in women with Inflammatory Bowel Disease (IBD), Irritable Bowel Syndrome (IBS) and Celiac Disease (CD) to the general population have yielded inconsistent results. The objective of our study is to provide a systematic

assessment of the risk of EP in women with IBD, IBS as well as CD compared to women without these diseases.

DESIGN: Systematic review and meta-analysis

MATERIALS AND METHODS: Literature search was conducted from MEDLINE and Web of Science using MESH terms: “ectopic pregnancy”, “tubal pregnancy”, “inflammatory bowel disease”, “ulcerative colitis”, “Crohn’s disease”, “irritable bowel syndrome” and “celiac disease”. Peer-reviewed publications and abstracts written in English, published from the database inception date to April 30th, 2020, about the association between EP and IBD, IBS, and CD were included. Included abstracts were cross-checked with publications to avoid duplication. Studies that did not report the outcomes of comparison, were unable to extract data from, or did not contain disease-free controls were excluded. Quality assessment was conducted based on GRADE criteria. Mantel-Haenszel test was used to analyze the association between the binary outcomes (ectopic pregnancy or intrauterine pregnancy) and the binary comparisons (disease or disease-free). Data from cohort studies were presented with Risk Ratio (RR) with 95% Confidence Interval (CI). Heterogeneity between studies was presented with I^2 and P-value.

RESULTS: 471 articles were retrieved from the MEDLINE and Web of Science literature search. A total of five population-based cohort studies that investigated the association between EP and IBD, IBS, and CD were included. Analysis was performed based on a total number of 23,879 patients with IBD (11,221 with ulcerative colitis and 12,658 with Crohn’s disease) and 9,276,714 controls, showing elevated risk of EP in women with IBD (RR=1.25, 95% CI 1.12 to 1.39, P<0.00001; heterogeneity: I^2 =21%, P=0.26) comparing to control women. Interestingly, the risk of EP is significantly increased in women with Crohn’s disease (RR=1.46, 95% CI 1.26 to 1.68, P<0.00001; heterogeneity: I^2 =54%, P=0.14) but not ulcerative colitis (RR=1.03, 95% CI 0.87 to 1.22, P=0.73; heterogeneity: I^2 =0%, P=0.43) compared to controls. In addition, increased risk of EP was observed in a cohort of 26,543 women with IBS (RR=1.45, 95% CI 1.25 to 1.69, P<0.00001) compared to 73,457 women without IBS. However, no significant difference (RR=1.12, 95% CI 0.95 to 1.32, P=0.19; heterogeneity: I^2 =49%, P=0.16) was observed between the risk of EP in 6,319 women with CD and 63,166 women without CD.

CONCLUSIONS: Possible evidence of associations between EP and Crohn’s disease as well as IBS were observed; however, not with ulcerative colitis and CD. These results should be considered with caution, owing to high heterogeneity and relatively small study sizes among included research. Thus, continued research is needed to delineate the pregnancy implications of IBD, IBS and CD.

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PREGNANCY ULTRASOUND MEASUREMENTS AND EARLY PREGNANCY LOSS: VALIDATION OF A PREDICTIVE MODEL. Irene Peregrin-Alvarez, MD,[1] Jennifer C. Gordon, MD,[1] Patricia Goedecke, MS,[1] Laura Detti, MD[2] [1]University of Tennessee Health Science Center, Memphis, TN; [2]Cleveland Clinic, Cleveland, OH.

OBJECTIVE: We aimed to prospectively validate the use of gestational sac (GS), yolk sac (YS) diameter, crown-rump length (CRL), and embryonal heart rate (HR) dimensions to identify patients at risk for early pregnancy loss.

DESIGN: This was a prospective cohort study of first trimester pregnancies where GS, YS diameter, CRL, and HR measurements were serially obtained via weekly transvaginal ultrasound (TVUS) from 6 through 10 weeks’ gestation.

MATERIALS AND METHODS: We studied patients at our Institution who were evaluated and treated for infertility. The mode of conception included spontaneous, ovulation induction with, or without, intrauterine insemination (IUI), and in vitro fertilization (IVF). TVUS was obtained in singleton, and multiple pregnancies followed from 6 through 11 weeks’ gestation with serial measurements of the GS and YS diameter, CRL, and HR. Non-parametric tests and logistic regression models were used for comparisons of distributions and testing of associations.

RESULTS: We examined a total of 82 patients with 89 pregnancies; 82 of which were singleton pregnancies; 6 were twins (12 fetuses); and 1 was triplets (3 fetuses). There were a total of 97 fetuses. Nineteen patients had 24 pregnancy losses. Nomograms were developed showing the changes of the evaluated parameters in ongoing pregnancies, as well as in pregnancy loss. We previously developed a logistic model for prediction of early pregnancy loss (Detti et al 2020) that showed that in failed pregnancies, all the parameters showed significant changes, with different temporal onsets. This model was used to determine the accuracy of detection of failed pregnancies before the event. This accuracy was different by gestational age (average of 72% detection rate) showing the less accuracy in the earliest ultrasounds at 6 weeks (57%) and at 11 weeks (30%). The highest accuracy was shown at the ultrasounds performed at 8, 9 and 10 weeks.

CONCLUSIONS: Our study confirmed our previous results showing that a small GS and a large YS reliably predicted early pregnancy loss from occurrence, with the YS reliably predicting this outcome in advance. The accuracy for our prediction model was different by gestational age, showing the less accuracy in the earliest ultrasounds at 6 weeks and 11 weeks, with the highest accuracy being found at 8, 9 and 10 weeks. These findings have important implications for patient counseling during early pregnancy care.

References: 1.Â Detti L, Francillon L, Christiansen ME, et al. Early pregnancy ultrasound measurements and prediction of first trimester pregnancy loss: A logistic model.Â *Sci Rep*. 2020;10(1):1545. Published 2020 Jan 31. https://doi.org/10.1038/s41598-020-58114-3

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4.Â Ashoush, S., Abuelghar, W., Tamara, T. & Aljobboury D. Relation between types of yolk sac abnormalities and early embryonic morphology in frst-trimester missed pregnancy loss. J Obstet Gynaecol Res., 42(1), 21–8, https://doi.org/10.1111/jog.12837 (2016 Jan).

P-205 4:30 PM Saturday, October 17, 2020

PREGNANCY LOSS RATES BY DEVELOPMENTAL STAGE AFTER SINGLE EUPLOID FROZEN-THAWED EMBRYO TRANSFER. Devora Aharon, MD,[1] Joseph A. Lee, BA,[2] Jeffrey Klein, MD,[2] Matthew A. Lederman, MD,[2] Beth McAvey, MD,[1] Alan B. Copperman, MD[1] [1]Icahn School of Medicine at Mount Sinai, New York, NY; [2]Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Patients who conceive naturally experience a predictable decline in pregnancy loss rates as they progress in gestational age, from a 15-25% global loss rate to 3-5% once cardiac activity is observed.[1,2] The objective of this study is to determine the rate of loss at each stage of early pregnancy following single euploid FET.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients who underwent a single euploid FET from 2016-2018 were included in the study. Patients with confirmed pregnancy, defined as bHCG $\geq$2.5 mIU/mL, were analyzed. Preimplantation genetic testing for aneuploidy (PGT-A) was performed using Next Generation Sequencing. Primary outcome was pregnancy loss rate at the following stages: 1. Initial HCG positive; 2. second HCG rise; 3. presence of gestational sac; 3. presence of yolk sac; 4. presence of fetal pole; 5. presence of cardiac activity; 6. discharge from the practice with ongoing pregnancy. Results were stratified according to history of prior clinical pregnancy loss. Multinomial logistic regression was used to determine the association of covariates with pregnancy loss at each stage, with generalized estimating equations to account for repeated patients.

RESULTS: A total of 7092 single euploid FET cycles were observed, 2685 of which resulted in pregnancy and were included in the study. Of these, 345 FET were performed in patients with one prior loss and 50 in patients with $\geq$2 prior losses. Rates of pregnancy loss following each developmental stage for patients with and without a history of prior pregnancy loss are shown in Table 1. Multinominal logistic regression showed that among patients with no prior loss, patient age, oocyte age, BMI, AMH, BAFC, and endometrial thickness were not associated with pregnancy loss at any stage. Among patients with any history of loss, endometrial thickness was negatively associated with pregnancy loss (p=0.03).

CONCLUSIONS: High loss rates despite transferring screened embryos indicate a significant contribution of non-genomic factors to reproductive failure. While screening for embryonic competency accounted for maternal age, other factors were found to contribute to likelihood of pregnancy loss including endometrial thickness among patients with a prior loss. Personalized management must take into account a multifactorial approach when counseling patients about the likelihood of early pregnancy loss.

TABLE 1. Rate of pregnancy loss following each developmental stage

Pregnancy stage	No prior loss (N=2290)	1 prior loss (N=345)	≥2 prior losses (N=50)
Positive HCG	20.6%	25.7%	36.0%
HCG rise	20.3%	25.7%	34.7%
Gestational sac	17.5%	21.4%	31.9%
Yolk sac	14.9%	15.5%	27.2%
Fetal pole	12.1%	13.5%	25.6%
Cardiac activity	10.1%	12.0%	21.9%
Discharge	5.7%	7.6%	8.5%

References: 1. Fritz, Marc A., and Leon Speroff.Â *Clinical Gynecologic Endocrinology and Infertility*. 9th ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2019.

2. Jacobs PA, Hassold T. Chromosome abnormalities: origin and etiology in abortions and livebirths. In: Vogel F, Sperling K, editors. Human genetics. Berlin: Springer-Verlag; 1987:233–44.

SUPPORT: None

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IS EARLY HCG PREDICTIVE OF PREGNANCY AFTER ESET IN BOTH FRESH AND FET CYCLES? Fady I. Sharara, M.D., Anna Lysenko-Brockman, MS, Haneen Taha, MS. Virginia Center for Reproductive Medicine, Reston, VA.

OBJECTIVE: Most ART programs perform β-hCG measurement 9-12 days after embryo transfer(ET) to detect a pregnancy. A prior study using hyperglycosylated hCG in a small sample size showed that a single measurement 6 days after ET had 100% sensitivity and specificity in identifying biochemical and ongoing pregnancies. We sought to determine whether routine serum β-hCG measurement at 5-6 days after ET is predictive of ART outcome. This is important in patient counseling if we can stop P supplementation early in cases of negative tests, especially if taking painful IM P supplementation.

DESIGN: Prospective single center.

MATERIALS AND METHODS: A total of 241 patients undergoing eSET (elective single embryo transfer) had their "early" serum β-hCG measured 5-6 days after ET, and the "official" serum β-hCG was done 9-10 days after ET. There were 91 fresh ET and 150 FET cycles. A test was positive if the β-hCG measurement was ≥ 3 IU/L. All tests were performed at a commercial laboratory with offices around the US (LabCorp).

RESULTS: In the 91 fresh ET cases observed, 65 had positive and 26 had negative "early"β-hCG tests measured 5-6 days post ET. Of the 65 positive β-hCG tests, 10 (15.4%) were biochemical, 9 (13.8%) were pregnancy losses (SAB), and 46 (70.8%) were live births. Of the 26 negative tests, 24 (92.3%) were negative on days 9-10 and 2 (7.6%) were positive on days 9-10. Both positive results on day 9-10 ended with biochemical losses. In the 150 FETs observed, 81 had positive and 69 had negative "early" β-hCG. Of the 81 positive, 19 (23.5%) were biochemical pregnancies, 7 (8.6%) had SAB, and 55 (67.9%) were ongoing/live births. Of the 69 negative β-hCG tests measured 5-6 days post FET, 4 (5.7%) were then positive on day 9-10, 3 resulting in biochemical pregnancies and one live birth. The mean "early" β-hCG levels in the IVF group was 27.03 IU/L which was significantly higher than in the FET 14.09 IU/L ($P<0.001$). There were significant differences in early β-hCG results between ongoing/delivered and biochemical pregnancies in both fresh and FET groups ($P<0.001$), but not between ongoing/LB and SAB. However, by first β-hCG level on days 9-10 there were no differences in the mean β-hCG between the 2 groups ($P=0.04$). ROC for fresh ET showed a cut off value of 7 IU/L. The test can detect with 90% sensitivity a 96% specificity with 3.8% false positive (AUC=0.972). For FET it showed a cut off value of 3.7 IU/L. The test can detect with 89% sensitivity a specificity of 94% with 5.7% false positive (AUC=0.964) (Figure 1).

CONCLUSIONS: Early serum β-hCG measured 5-6 days after ET in eSET cycles is very predictive of successful pregnancies. A negative test 5-6 days after ET is associated with a negative 9-10 day β-hCG test in both fresh and FET cycles. In the fresh group, an early negative β-hCG was 100% predictive of no live births, but in the FET group an early negative in the FET group led to a single live birth (99.33% predictive of no live births). FET cycles were associated with lower early β-hCG levels than fresh transfers but became similar to fresh cycles on the first day of actual pregnancy test. This information is of potential benefit in counseling women undergoing ART.

References: Strom et al,Â J Assist Reprod Genetics 2012;29:609-14.

SUPPORT: None

P-207 4:30 PM Saturday, October 17, 2020

CHROMOSOMAL ASSOCIATIONS AND GENOMIC INSTABILITY IN IDIOPATHIC RECURRENT PREGNANCY LOSS(RPL), A PILOT SCALE STUDY. Abhik Chakraborty, M.Sc(Masters in Science),[1] Smriti Sanchita, B.S.,[2] Birendranath Banerjee, P.hD[3] [1]INSPIRE Senior research fellow, Bhubaneswar, India; [2]UCLA, Los Angeles, CA, India; [3]Associate Professor, Bhubaneswar, India.

OBJECTIVE: The emotional issues adjoining pregnancy loss become magnified exponentially when miscarriage take place on a repetitive basis. But there are very limited studies correlated with stress in recurrent pregnancy loss (RPL). Telomeres maintain the integrity and stability of our genetic material by protecting our chromosomes. We hypothesized that stress induced background genomic instability and telomere loss plays a pivotal role in unexplained RPL. We aimed to investigate any possible link between background genomic instability, telomere loss and early unexplained recurrent pregnancy loss in a cohort of subjects along with age and sex matched controls.

DESIGN: Participation of a cohort of 50 couples (100 individuals) experiencing with 2 or more earlier pregnancy losses, and struggling for natural conception in a age and sex matched study for elucidating any possible role of chromosomal associations and genomic instability in recurrent pregnancy loss.

MATERIALS AND METHODS: Blood samples were collected from each RPL couple in heparin and EDTA vials along with a consent form for participation in this study. Karyotyping was performed from heparinized blood to screen common/unique chromosomal anomalies associated with unexplained RPL. The lymphocytes were isolated from EDTA blood and subjected for isolation of DNA, RNA and preparation of whole cell protein lysate. The background genomic instability status was examined by using cytokinesis blocked micronucleus (CBMN) assay. We also checked the telomere length of the individuals by quantitative real time PCR (qRT-PCR) and Quantitative-Fluorescent In-Situ Hybridization (Q-FISH). The functional telomeric integrity of telomeric shelterin complex were evaluated through western blot analysis.

RESULTS: Karyotyping analysis demonstrated few novel translocations responsible for RPL, which were not reported previously. In our cohort, we observed that 83 individuals out of 100 were reported karyotypically normal. This prompted us to further examine these karyotpically normal individuals for their background genomic instability. We found that 38.5% (32 out of 83) individuals have high background of genomic instability as compared with the control samples. Next, we investigated the telomere length of the patients with high genomic instability by qRT-PCR and observed that 28.125% (9 out of 32) exhibited loss of telomeres. Q-FISH (PNA-FISH) analysis of these subjects also showed loss in Telomeric signals. Furthermore, western blot analysis of some of the key players of the shelterin components showed reduced level of expression of these proteins in the RPL subjects.

CONCLUSIONS: Apart from numerical or structural chromosomal anomalies background genomic instability leading to loss of telomeres may play a critical role in promoting RPL. This work will further lead to identification of novel biomarkers associated with unexplained recurrent pregnancy loss and it will further help in real time monitoring based on molecular analysis of the couple experiencing recurrent pregnancy failure and aid them with better possibility of conception.

SUPPORT: This study was supported by Department of Science and technology (DST), Government of India, INSPIRE fellowship IF/150135 and in-DNA Life Sciences PVT. LTD.

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LUTEAL PHASE SUPPORT WITH PROGESTERONE DOES NOT IMPROVE PREGNANCY RATES IN PATIENTS UNDERGOING CONTROLLED OVARIAN STIMULATION WITH LETROZOLE. Elizabeth A. Dilday, M.D., Luis R. Hoyos, M.D.,

Molly M. Quinn, MD, Lindsay Kroener, MD. Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, University of California, Los Angeles, Los Angeles, CA.

OBJECTIVE: Luteal phase support with progesterone is associated with improved pregnancy rates in controlled ovarian stimulation (COS) cycles using gonadotropins, but not in cycles using clomiphene citrate (1). In COS cycles using letrozole, there are limited data to support its use. Our objective was to determine whether luteal phase progesterone in letrozole COS cycles improves clinical pregnancy rate (CPR).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All letrozole COS cycles from 1/2018 to 3/2020 at an academic fertility practice were screened for inclusion. Cycles were excluded if canceled, if severe male factor (<5 million total motile sperm), or if any additional stimulation medications were used. Cycles were classified based on presence or absence of luteal progesterone support. When given, vaginal micronized progesterone 200 mg BID or TID was initiated two days after intrauterine insemination (IUI) or timed intercourse (TIC). Use and dose of luteal support were provider-dependent. Primary outcome was CPR. Secondary outcomes included spontaneous abortion (SAB) and biochemical pregnancy. Univariate logistic regressions were done to evaluate possible predictor variables for CPR. Significant covariates including age, anti-Müllerian hormone (AMH) level, intrauterine insemination (IUI) versus timed intercourse (TIC), diagnosis of ovulatory dysfunction, and multi-follicular development (>1 follicle ≥ 14 mm) were included in a multivariate analysis evaluating the relationship between progesterone use and odds of clinical pregnancy. Statistical analysis included exact chi-square, logistic regression or linear regression with adjustments for clustering, and general estimating equations logistic models, where appropriate.

RESULTS: A total of 276 COH cycles in 156 patients were included. Of these cycles, 221 used vaginal progesterone and 55 did not. The groups were comparable with respect to body mass index (BMI), AMH level, nulliparity, and multi-follicular development. Patients who received progesterone luteal support were 1.8 years older (mean 35.2 versus 33.4 years, p<0.001) and were more likely to undergo IUI than TIC (IUI in 75.6% of cycles with progesterone versus 56.4% of cycles without progesterone, p=0.007). The unadjusted CPR was 11.8% with progesterone and 10.9% without progesterone (p=0.847). There were no differences in SAB (9.4% versus 0%, p=0.999) or biochemical pregnancy (3.1% versus 14.3%, p=0.331). After adjusting for significant covariates including age, AMH level, diagnosis of ovulatory dysfunction and multi-follicular development, the odds for clinical pregnancy were not significantly improved in cycles using luteal progesterone (OR 1.36, 95% CI 0.60-3.12, p=0.464).

CONCLUSIONS: Luteal support with vaginal progesterone, which comes with additional cost and discomfort for patients, does not significantly improve CPR in COS cycles using letrozole. Eliminating progesterone in these cycles could improve the patient experience by simplifying treatment without compromising outcomes. Larger randomized studies are needed to validate these results.

References: 1. Green KA et al.Â Progesterone Luteal Support After Ovulation Induction and Intrauterine Insemination: An Updated Systematic Review and Meta-Analysis.Â Fertil Steril.Â 2017 Apr;107(4):924-933.e5. https://doi.org/10.1016/j.fertnstert.2017.01.011.

SUPPORT: The research described was supported by NIH/National Center for Advancing Translational Science (NCATS) UCLA CTSI Grant Number UL1TR001881.

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ASSOCIATION OF EARLY BETA HUMAN CHORIONIC GONADOTROPIN WITH ISCHEMIC PLACENTAL DISEASE AFTER IN-VITRO FERTILIZATION.

Jaimin S. Shah, M.D.,[1] Nina Resetkova, M.D., M.B.A.,[2] Michele R. Hacker, Sc.D., M.S.P.H.,[1] Laura E. Dodge, Sc.D., M.P.H.[1] [1]Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA; [2]Boston IVF, Waltham, MA.

OBJECTIVE: Determine whether initial or 2-day percent increase in serum beta human chorionic gonadotropin (βhCG) is associated with ischemic placental disease (IPD) in singleton pregnancies after autologous or donor IVF.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Women who had a singleton live birth or an intrauterine fetal demise (IUFD) resulting from IVF from 1999 through 2017 and who delivered at our institution were included. Cycles were included if they had at least one serum βhCG. The primary outcome was IPD (IUFD due to placental insufficiency; pre-eclampsia; placental abruption; and small for gestational age [birthweight <10th percentile]). Two-day percent increase was extrapolated for cycles with βhCG measured 1, 3, or 4 days after the initial measurement. We used generalized estimating equations to estimate mean βhCG with 95% confidence intervals, adjusting for maternal age and cycle type.

RESULTS: Of 2,275 IVF cycles linked to singleton deliveries, 259 (11%) were excluded; 69 (3%) had no initial βhCG measurement, and 190 (8%) had βhCG measured at an inappropriate time. Of the remaining 2,016, 93% were autologous and 7% were donor IVF cycles. Median age (interquartile range) was 36 (33-39) and 42 (39-44) years for autologous and donor IVF, respectively. Initial βhCG was not associated with IPD or any component of IPD for singleton IVF pregnancies (Table 1). Among the 888 pregnancies with two βhCG measurements, the mean 2-day increase in βhCG was significantly higher in those without placental abruption than those with abruption (Table 1).

CONCLUSIONS: Among singleton autologous and donor IVF cycles, initial serum βhCG was not associated with IPD or its components, but a lower 2-day increase in βhCG was associated with placental abruption.

TABLE 1. Mean initial βhCG and mean 2-day increase in βhCG for IPD and components of IPD among singleton IVF pregnancies

Outcome	Initial βhCG (mIU/mL) n=2,016	*p* value*	Outcome	2-day increase (%) n=888	*p value**
IPD or IUFD		0.54	**IPD or IUFD**		0.37
Yes (n=346)	248 (186-309)		*Yes (n=154)*	162 (81-244)	
No (n=1670)	253 (193-312)		*No (n=734)*	177 (76-278)	
Preeclampsia		0.42	**Preeclampsia**		0.31
Yes (n=136)	261 (198-324)		*Yes (n=58)*	160 (72-248)	
No (n=1880)	250 (190-310)		*No (n=830)*	178 (78-278)	
Placental abruption		0.17	**Placental abruption**		0.02
Yes (n=57)	230 (163-297)		*Yes (n=26)*	138 (53-223)	
No (n=1959)	253 (193-313)		*No (n=862)*	177 (79-274)	
SGA		0.31	**SGA**		0.63
Yes (n=197)	242 (179-306)		*Yes (n=92)*	166 (86-245)	
No (n=1819)	252 (192-312)		*No (n=796)*	174 (77-271)	

Data are shown as mean (95% confidence intervals).
*Adjusted for maternal age and cycle type (donor, autologous fresh, autologous frozen).
SGA, small for gestational age; IUFD, intrauterine fetal demise.

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DOES THE TIMING OF ENDOMETRIAL BIOPSY IMPACT THE DETECTION OF ENDOMETRIAL PLASMA CELLS? Alisha Tara Tolani, MD, Emily Elizabeth Ryan, MD, Ann Katherine Folkins, MD, Ruth Bunker Lathi, MD. Stanford University, Stanford, CA.

OBJECTIVE: Chronic endometritis (CE) has been associated with recurrent pregnancy loss (RPL) and recurrent implantation failure. Incidence rates vary due to significant heterogeneity in biopsy timing and diagnostic criteria. Our group previously demonstrated that plasma cells are found in 59% of endometrial biopsies (EMBs) in the follicular phase compared to 18% in the luteal phase, which led us to question whether menstruation or hormonal changes in the follicular phase impact the diagnosis of CE. The purpose of this study was to assess the incidence and density of endometrial plasma cells in the early versus late follicular phase.

DESIGN: This is a retrospective cohort study of patients undergoing EMB in the follicular phase at a single academic center.

MATERIALS AND METHODS: EMBs performed between 2018 and 2020 were included. The early follicular phase was defined as the end of menses through day 8 of the menstrual cycle. The late follicular phase was defined as 9-14 days after menses. Patients with a prior CE diagnosis or abnormal uterine pathology were excluded. EMBs were assessed by gynecologic pathologists via H&E stain and CD138 immunohistochemistry. Plasma cell density was reported as rare (1-2 per slide), scattered ($\geq$ 3 per slide), or clusters. Continuous variables were compared using t-tests, and categorical variables were compared with chi-square tests.

RESULTS: Plasma cells were found in 74% of EMBs performed in the early follicular phase compared to 45% in the late follicular phase. Although the study was not powered to detect differences in plasma cell density, plasma cells were most commonly noted to be scattered (39%) in the early follicular and rare (18%) in the late follicular phase. See Table 1 for complete results.

CONCLUSIONS: Our data demonstrate that plasma cells are more likely to be detected at higher densities in EMBs performed during the early compared to the late follicular phase. These findings may represent the influence of estrogen levels or menstruation on the endometrium. Further studies with larger cohorts are needed to establish the optimal timing of EMB and determine the clinical significance of low-density endometrial plasma cells.

TABLE 1. The presence of plasma cells in the early versus late follicular phase

	All Follicular	Early Follicular	Late Follicular	p-value
N	75	31	44	–
Cycle Day (median, range)	9 (4-13)	7 (4-8)	10 (9-13)	–
Age (mean)	35.6	36.6	35.0	0.08
BMI (mean)	25.0	24.9	25.1	0.9
Parity				
Live Births (mean)	0.4	0.6	0.3	0.41
Prior Miscarriages (mean)	2.2	2.6	2.0	0.23
Presence of plasma cells				
Negative for plasma cells (n, %)	32 (43)	8 (26)	24 (55)	0.01
Positive for plasma cells (n, %)	43 (57)	23 (74)	20 (45)	
Rare (n, %)	16 (21)	8 (26)	8 (18)	
Scattered (n, %)	19 (25)	12 (39)	7 (16)	
Clusters (n, %)	7 (9)	2 (6)	5 (11)	

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INTRAUTERINE PATHOLOGY IS ASSOCIATED WITH HIGHER INCIDENCE OF ENDOMETRIAL PLASMA CELL INFILTRATE. Alisha Tara Tolani, MD, Emily Elizabeth Ryan, MD, Ann Katherine Folkins, MD, Ruth Bunker Lathi, MD. Stanford University, Stanford, CA.

OBJECTIVE: Chronic endometritis (CE) is a critical contributor to infertility, recurrent pregnancy loss (RPL), and recurrent implantation failure. The presence of endometrial plasma cells is suggestive of a diagnosis of endometritis; however, the effect of intrauterine pathology such as fibroids, polyps, and retained products of conception on the surrounding endometrial plasma cell infiltrate is unclear. The purpose of this study was to compare plasma cell infiltrate from endometrial biopsies (EMB) in patients with normal and abnormal cavity evaluations.

DESIGN: This is a retrospective cohort study of patients undergoing EMB for evaluation of endometritis at a single academic fertility clinic.

MATERIALS AND METHODS: All patients undergoing EMB between January 2018 and January 2020 were included. Uterine cavity evaluation was performed via hysteroscopy or saline sonogram. Patients with a prior CE diagnosis were excluded. EMBs were evaluated by gynecologic pathologists for plasma cells on H&E stain and via CD138 immunohistochemistry. Plasma cell frequency was reported as rare (1-2 cells per slide), scattered ($\geq$3 cells per slide), or clusters. Continuous variables were compared using t-tests, and categorical variables were compared with chi-square tests.

RESULTS: Of the 201 EMBs that met inclusion criteria, thirty-four (17%) were performed in patients with abnormal uterine cavities - 20 had polyps, 7 had retained POC, and 5 patients had fibroids. Plasma cells were found in 71% of EMBs from abnormal cavities compared to 41% of EMBs from normal cavities (p=0.03). Plasma cell density was significantly higher in the abnormal cavity group compared to the normal cavity group – 54% vs. 26% had scattered or clusters of plasma cells (p= 0.002). See Table 1 for results.

CONCLUSIONS: Intracavitary pathology is associated with a significantly higher frequency and density of endometrial plasma cells. Further studies with larger cohorts are needed to assess the relationship between plasma cells and specific intrauterine pathologies and to determine whether the plasma cell infiltrate is truly infectious in etiology or secondary to the presence of intrauterine pathology.

TABLE 1. Plasma cell infiltrate among infertility patients with normal and abnormal uterine cavities

	Normal uterine cavity	Abnormal uterine cavity	p-value
N	167	34	–
Demographics			
Age (mean)	37.0	37.4	0.51
BMI (mean)	25.2	24.0	0.53
Parity			
Live Births (mean)	0.3	0.5	0.02
Miscarriages (mean)	1.5	1.9	0.30
Diagnosis			
Infertility (n, %)	105 (62)	24 (70)	0.24
RPL (n, %)	75 (45)	13 (37)	0.47
Presence of Plasma Cells			
Negative for plasma cells (n, %)	98 (59)	10 (29)	< 0.01
Positive for plasma cells (n, %)	69 (41)	24 (71)	
Rare (n, %)	32 (19)	7 (21)	
Scattered (n, %)	23 (14)	12 (35)	
Clusters (n, %)	12 (7)	3 (9)	

SUPPORT: None

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IMPACT OF ROUTE OF PROGESTERONE ADMINISTRATION ON OUTCOMES OF PREGNANCIES AFFECTED BY SUBCHORIONIC HEMATOMA FOLLOWING FROZEN IVF CYCLES. Daniel Miranian, MD,[1] Erin Inman, MD,[2] Micaela J. Stevenson, BS,[3] Emily K. Kobernik, MPH, MS,[2] Molly B. Moravek, MD, MPH,[2] Samantha B. Schon, MD, MTR[4] [1]Obstetrics and Gynecology, University of Michigan, Ann Arbor, MI; [2]University of Michigan, Ann Arbor, MI; [3]University of Michigan Medical School, Ann Arbor, MI; [4]Reproductive Endocrinology and Infertility, University of Michigan, Ann Arbor, MI.

OBJECTIVE: Recent data have suggested that intramuscular (IM) progesterone for luteal support during frozen embryo transfer (FET) cycles may lead to higher ongoing pregnancy rates compared to vaginal (PV) progesterone. Since subchorionic hematoma (SCH) has been shown to be associated

with increased risk of early pregnancy loss in a fertile population, it is possible that there is an association between route of progesterone for FET and SCH. The objective of this study was to investigate if route of progesterone during FET impacted the rate of SCH and subsequent pregnancy outcomes. We hypothesized that SCH would be lower in patients on IM progesterone.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: CPT codes were used to identify all obstetric scans performed at a single infertility clinic from 1/2015-3/2018. All viable intrauterine pregnancies visualized on initial obstetric ultrasound following autologous FET (n=324) were included for analysis. Chart review was performed to identify the presence of SCH. Data on patient demographics, comorbidities, baseline laboratory parameters, route of progesterone supplementation, and pregnancy outcomes were collected. Bivariate analysis was used to compare pregnancy outcomes between FET cycles that received IM progesterone versus FET cycles that received PV progesterone supplementation alone.

RESULTS: 88 (27.2%) received IM containing progesterone regimens compared to 236 (72.8%) that received PV progesterone. SCH was significantly more likely to occur in FET cycles that were supplemented with IM progesterone compared to FET cycles supplemented with PV progesterone alone (23.9% vs 13.1%, p=0.02). However, there was no difference in the rate of 1st trimester losses (19.3% vs 20.8%, p=0.77), 2nd trimester losses (1.2% vs 0.4%, p=0.47), or live birth rates (80.2% vs 80.7%, p=0.93) between FET cycles supplemented with IM progesterone versus PV progesterone. Additionally, there was no difference between maternal complications such as hypertensive disorders (18.2% vs 20.9%, p=0.61) or gestational diabetes (9.1% vs 4.7%, p=0.13). The median age of delivery for both groups was 39 weeks (p=0.14) and there were no differences between the rates of preterm premature rupture of membranes, placental abruption, preterm labor, or preterm birth.

CONCLUSIONS: Although SCH was unexpectedly more common in FET cycles with IM progesterone compared to PV, the pregnancy outcomes were not significantly different between these two groups. These results are reassuring that detection of SCH on early ultrasound following FET may be a benign finding with no impact on clinical outcomes. However, further investigation is warranted to determine if these effects are consistent among a larger sample size.

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DIFFERENCES IN EARLY ULTRASOUND AND FETAL GROWTH KINETICS BETWEEN NON-HISPANIC WHITE AND BLACK WOMEN. Victoria S. Jiang, MD,[1] Audrey M. Marsidi, MD,[2] Caroline Violette, MD,[1] Audrey J. Gaskins, ScD,[3] Jessica B. Spencer, MD, MSc,[2] Carolyn Drews-Botsch, Ph.D, MPH[3] [1]Emory University School of Medicine, Department of Gynecology and Obstetrics, Atlanta, GA; [2]Emory University School of Medicine, Division of Reproductive Endocrinology and Infertility, Atlanta, GA; [3]Emory University, Rollins School of Public Health, Atlanta, GA.

OBJECTIVE: Formulas used to estimate fetal size by ultrasound have been historically based on predominantly white cohorts. The purpose of this study was to assess early ultrasound measurements of crown rump length, growth velocity, and pregnancy outcomes among non-hispanic white and black women given the known racial differences in pregnancy outcomes. Previous studies have been unable to examine whether early measures of embryonic size differ by race due to the relative under-representation of black women undergoing fertility treatments.

DESIGN: Retrospective cohort, academic fertility practice, January-December 2018.

MATERIALS AND METHODS: This cohort included 156 women who conceived via intrauterine insemination (IUI), intercourse with ovulation trigger injection, or in-vitro fertilization (IVF). Only women with a singleton pregnancy and documented fetal cardiac activity between 6 weeks and 6 weeks 6 days gestation were included. Multiple gestation, spontaneous conception, and first trimester miscarriages were excluded. A minimum of two serum hCG measurements were obtained, typically 2 or 4 days apart. Transvaginal ultrasound was used to confirm intrauterine pregnancy and measure crown rump length and fetal heart rate. Average ultrasound age (AUA) was calculated using the Hadlock formula. Differences in the mean and standard deviation of embryo growth parameters were evaluated using student t-tests. Multiple linear regression was used to account for important potential confounders including method of conception (IUI, IVF with fresh embryo transfer, IVF with frozen embryo transfer), maternal age, maternal BMI, and sex of the embryo.

RESULTS: 59 black (37.8%) and 97 non-hispanic white (62.1%) women met inclusion criteria. In our cohort, black women were older (p<0.01) and had a higher BMI (p<0.01) than white women. Tubal factor without hydrosalpinx (33.9% vs 10.3%, p<0.01) and uterine factor (16.9% vs 3.1 %, p<0.01) were more prevalent in black women than white women. Black and white women did not differ in the likelihood of livebirth, miscarriage, development of hypertension or intrauterine growth restriction. There was a trend toward higher rates of preterm delivery (31.9% vs 17.4%, p=0.07) in black women. Unadjusted fetal pole measurements of black women were smaller (0.91 cm ± 1.68) than those of white women (0.61 cm ± 1.72), but this difference was not significant and was attenuated by adjusting for mode of conception, obesity, and maternal age. No significant difference was observed in rates of embryo growth or hCG levels between groups

CONCLUSIONS: Among women who conceived following fertility treatment with IUI, intercourse with ovulation trigger injection, or IVF, no significant differences were noted in early measurements of hCG, embryonic size, growth velocity, or pregnancy outcomes between black and white women. Black women had a non-significant trend towards smaller crown rump lengths at the time of early ultrasound and higher likelihood of preterm birth. Our study was limited by sample size and additional studies involving larger cohorts may be important in validating these findings.

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ASSOCIATION OF -308G>A, -238G>A, -376G>A SNPS OF TNF GENE IN WOMEN WITH RECURRENT ABORTIONS IN A GREEK POPULATION. Sofoklis Stavrou, MD, Ph.D.,[1] Despoina Mavrogianni, Dr, PhD,[1] Evagelos Basamakis, MSc,[1] Alexandros Psarris, M.D., M.Sc., Ph.D.,[1] Dimitris Loutradis, Professor,[2] Peter Drakakis, Professor[1] [1]Molecular Biology of Reproduction Unit and Recurrent Abortions Unit, Assisted Reproduction Division, Athens, Greece, Greece; [2]Molecular Biology of Reproduction Unit and Recurrent Abortions Unit, Assisted Reproduction Division, Athens, Greece.

OBJECTIVE: To detect a possible association between -308G>A, -238G>A, -376G>A SNPs of TNFa gene in women with recurrent abortions.

DESIGN: This is a prospective, single-centre study carried out at the molecular biology laboratory of gynecological and obstetrics department spanning the period January 2015 to November 2017. We studied the association between the presence of -308G>A, -238G>A, -376G>A polymorphisms and recurrent abortions in 90 women with RSA and 90 controls.

MATERIALS AND METHODS: Genomic DNA was extracted from peripheral blood samples using PureLink Genomic DNA Kit. PCR was performed using specific primers to amplify the studied polymorphisms. The amplified PCR products were sequenced using the ABI Prism 3130 Genetic Analyzer, Applied Biosystems. Variants were validated using the sequencing Analysis v 5.2 software.

RESULTS: A significant association was detected between the presence of -308 G variant and the absence of RSA (p=0.048). No detection of -376A variant was detected and no association was revealed between -238 polymorphism and abortions. Moreover, a possible association between the combination of genotypes and the presence of RSA did not reveal any statistical association. Although It has been suggested that the above TNFα polymorphisms are associated with an increased risk for recurrent spontaneous abortions, published literature worldwide are controversial so far. Ethnic differences or combinations of different SNPs may contribute to the diversity of the results.

CONCLUSIONS: The present study revealed a statistically significant association between -308G>A and the presence of abortions, no detection of A variant in -376G>A SNP and no association between -238 G>A and recurrent abortions. No association was detected between abortions and combination of genotypes. Further research to ascertain a possible combination of TNF polymorphisms in RSA is required. Differences in the genetic backgrounds of various ethnic populations should also be considered. Identification of TNF polymorphisms associated with RSA may lead to new pathophysiology insights, improved diagnostics, and novel treatment approaches.

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WITHDRAWN

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MINIMALLY INVASIVE FERTILITY SPARING TREATMENT IN NON-TUBAL ECTOPIC PREGNANCIES CAN RESULT IN HIGH SUBSEQUENT LIVE BIRTH RATES. Katherine E. Kostroun, MD,[1] Kathryn M. Goldrick, MD,[1] Jennifer F. Knudtson, MD,[1] Alia M. Yaghi, MD,[1] Cheria C. Brown, RN,[1] Randal D. Robinson, MD[2] [1]University of Texas Health Science Center San Antonio, San Antonio, TX; [2]University of Texas Health Science Center San Antonio, San Antonio, SC.

OBJECTIVE: Ectopic pregnancies represent 2% of all recognized pregnancies, and of these, less than 5% are non-tubal in location (1). Improvements in ultrasound technology and appropriate follow up with serial quantitative HCG levels and the development of specific diagnostic criteria for nontubal ectopic pregnancies have improved earlier diagnostic confirmation and management. Expectant management of non-tubal ectopic pregnancies can result in adverse outcomes including hemorrhage, uterine rupture, and need for hysterectomy (2). Many studies have shown the safety and efficacy of conservative treatment in these pregnancies, but very few have reported outcomes for subsequent pregnancies (3,4). The aim of this study was to evaluate treatment regimens and outcomes of patients with nontubal ectopic pregnancies, and specifically identify outcomes of subsequent pregnancies.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: This study evaluated women ages 18-50 with the ICD code of 'Ectopic Pregnancy' who, on chart review, were noted to have cervical, cesarean scar, or cornual/interstitial ectopic pregnancies in a university hospital system with a large Hispanic population from January 2010 to May 2020. Information regarding patient demographics, clinical, laboratory, and imaging data used for diagnosis, as well as treatment plans and outcomes were collected from electronic medical records and stored in a REDCap database. Descriptive evaluation of the data was performed.

RESULTS: A total of 445 ectopic pregnancies were identified with 40 non-tubal ectopic pregnancies (9%), including 11 cervical ectopics (28%), 13 cesarean scar ectopics (33%), and 16 cornual/interstitial ectopics (40%). Out of these patients, 34 (85%) had successful fertility sparing treatment including systemic methotrexate (n=25, 74%), intrafetal KCl (n=10, 29%), intragestational methotrexate (n=8, 24%), cornual wedge resection (n=8, 24%), dilation and curettage (n=3, 9%), and uterine artery embolization (n=3, 9%). Six (15%) underwent total hysterectomy. Out of the patients who underwent conservative therapy, 10 (29%) had subsequent pregnancies, with 13 confirmed gestations and a total of 7 confirmed live births (54%). Only one patient was noted to have an adverse pregnancy outcome complicated by a second interstitial pregnancy that was successfully treated with surgical resection. It took an average of 6.3 weeks for the quantitative hCG level to reach a negative hCG value after treatment and ranged from 1 to 15 weeks before resolution.

CONCLUSIONS: Our results support that there is an increase in the prevalence of nontubal ectopic pregnancies and comprised 9% of all ectopics in our case series. This study demonstrates the importance, safety, and high efficacy of minimally invasive, fertility sparing treatment in non-tubal ectopic pregnancies, and the possibility for high live birth rates after conservative treatment. Patients should be counseled that it could take up to 15 weeks after minimally invasive treatment to complete resolution via a negative hCG level.

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SUPPORT: K23 HD097307 (JFK)

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DYSREGULATED EMBRYONIC PLACENTATION IS MORE SIGNIFICANTLY ASSOCIATED WITH RISK OF EARLY SPONTANEOUS PREGNANCY LOSS THAN MATERNAL UTERINE SIGNALING. Sydney L. Lane, PhD, Blair R. McCallie, BS, William B. Schoolcraft, MD, Mandy G. Katz-Jaffe, PhD. Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Biochemical pregnancy loss (BPL) rates have remained persistent at 12-15% despite significant developments in *in vitro* fertilization including improved embryo culture, aneuploidy screening, and endometrial receptivity testing. In order to elucidate factors important for early pregnancy maintenance that could lead to BPL, we utilized a mouse model to investigate sites of implantation corresponding to viable embryos or spontaneous embryo resorption (miscarriage).

DESIGN: Uterine and placental gene expression of implantation sites corresponding to either viable or spontaneously resorbing embryos from early murine pregnancy.

MATERIALS AND METHODS: Female wild-type, outbred CF-1 pregnant mice were identified on day 10.5 of embryonic development for collection of uterine implantation sites containing either viable embryos (controls) or embryos that were in the early stage of resorption and not yet hemorrhagic. Total RNA was isolated from embryonic placentas (n=6 per group) and maternal uterine tissue (n=5 per group). Quantitative real-time PCR was performed on the QuantStudio 5 (Applied Biosystems) for key implantation and early pregnancy genes including: *Cd81*, *Glrx*, *Bdnf*, *Cox2*, *Ptgs2*, *Vegfa*, and *Icos*. Gene expression data were analyzed by the REST software (Qiagen) and Student's t-test, with significance at $P<0.05$.

RESULTS: Embryonic placental expression of *Cd81* was significantly increased in embryo resorption sites ($P<0.001$). Elevated *Cd81* inhibits cytotrophoblast invasion, indicating that insufficient placentation may have contributed to early pregnancy loss. Expression of embryonic placental *Glrx* was decreased in resorption sites ($P<0.01$), suggesting that heightened oxidative stress hindered placentation and/or maternal-fetal communication resulting in fetal loss. On the maternal side, expression of the paracrine growth factor *Bdnf* was decreased in uterine tissue from embryo resorption sites ($P<0.01$). Previous studies have reported increased *Bdnf* in the pregnant uterus and reduced *Bdnf* in uterine flushings from repeat implantation failure patients. In contrast, genes involved in tissue remodeling, angiogenesis, and decidualization (*Cox2*, *Ptgs2*, *Vegfa*), immune balance (*Icos*), trophoblast invasion (*Cd81*), or pinopode formation (*Glrx*) were not differentially expressed in maternal uterine tissue between viable and resorbing implantation sites.

CONCLUSIONS: The etiology of BPL is likely diverse and complex. Our preliminary data suggest that dysregulated embryonic placentation is more significantly associated with risk of early pregnancy loss than maternal uterine signaling. As lipid composition and amino acid metabolism are important for implantation, ongoing studies will utilize liquid chromatography mass spectrometry to identify metabolite changes that correlate with these observed significant embryonic placentation changes.

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WITHDRAWN

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LEUKEMIA INHIBITORY FACTOR IN RECURRENT PREGNANCY LOSS: IS THERE ANY ROLE OF LIFESTYLE INTERVENTION?

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OBJECTIVE: Leukemia inhibitory factor (LIF), has been cited to play important role in embryo development and implantation. This pleiotropic cytokine affects a range of events in implantation, such as, endometrial receptivity, embryo-endometrial interaction, stromal decidualization, trophoblast invasion and blastocyst development. Lower levels of LIF have been found in blood and endometrial tissue of women with recurrent pregnancy loss (RPL). The objective of this study was to assess the levels of LIF in plasma of women with RPL and healthy fertile females. Further evaluation was done to assess the effect of yoga based lifestyle (YBL) on the levels of LIF in RPL patients.

DESIGN: Phase I- Case control study, Phase II- Prospective single arm exploratory study.

MATERIALS AND METHODS: This study was conducted on non-pregnant women with history of recurrent pregnancy loss (RPL, N=30) and healthy fertile females with proven fertility. Blood samples were obtained from the patients as well as controls and EDTA plasma was separated for estimation of LIF by ELISA. The patients were further recruited for structured YBL program and after obtaining samples (pre-yoga, day 0) the samples were obtained after enrolment in the program for 30 days (post-yoga, day 30) and LIF levels were estimated.

RESULTS: The plasma levels of LIF in non-pregnant women with history of RPL were estimated to be significantly lower as comapred to healthy fertile females ($p=0.0107$). An increase in the plasma levels of LIF was seen in women wth RPL after the end of active intervention of 30 days from the base-line values measured at day 0 ($p=0.0291$).

CONCLUSIONS: LIF has been shown to play an indispensible role in initiating embry-endometrial interaction, and facilitating implantation along with uterine decidualization, trophoblast invasion and blastocyst development. The current study supports the hypothesis that lower levels of LIF are found in women with RPL and infertility. To the best of our knowledge the present study is one of the first studies to analyze the effect of yoga based lifesyle on the inflammatory markers affecting embryonic implantation the patients with RPL.

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DOES ADDING HYDROXYCHLOROQUINE TO EMPIRIC TREATMENT IMPROVE THE LIVE BIRTH RATE IN REFRACTORY OBSTETRICAL ANTIPHOSPHOLIPID SYNDROME?

Allyssa Hooper, MSc, BSc,[1] Arianne Y. K. Albert, PhD,[2] Mohamed Ali Bedaiwy, M.D., Ph.D.[1] [1]University of British Columbia, Vancouver, BC, Canada; [2]Women's Health Research Institute, Vancouver, BC, Canada.

OBJECTIVE: To investigate the live birth rate (LBR) when using hydroxychloroquine (HCQ) in addition to the standard of care therapy, low-dose aspirin and low molecular weight heparin, in women with refractory obstetrical antiphospholipid syndrome (APS).

DESIGN: A systematic literature search using EMBASE, MEDLINE, PubMed, Cochrane Library, and Web of Science was performed from inception to April 2020. Relevant search terms included: Hydroxychloroquine or Plaquenil, and "Antiphospholipid Syndrome" or Antiphospholipid Syndrome/, and abortion or miscarriage* or obstetric* or pregn* adj4 loss or abortion, habitual/.

MATERIALS AND METHODS: We included studies that evaluated the use of HCQ during pregnancy in women with primary APS. The primary outcomes of interest were LBR and pregnancy loss (PL) and the secondary outcomes of interest included maternal complications, neonatal complications, and gestational term of delivery. For studies to be eligible, outcome data with an explicit mean LBR or PL for both the study and control groups were required. We excluded studies that included patients with systemic lupus erythematosus (SLE) and secondary APS.

RESULTS: The search produced a total of 479 results. Following duplicate removal 249 remained and each title and abstract was reviewed. Subsequently, 59 full texts were selected for full review and an additional 44

were excluded, leaving 15 studies for qualitative analysis. Included in the 15 studies were 4 case reports, 3 RCT protocols, 2 prospective studies, and 6 retrospective studies. Due to the limited number of retrospective studies and the high level of heterogeneity a meta-analysis was not possible.

The LBR was significantly improved in 3 retrospective studies. Mekinian et al in 2017 demonstrated an improved LBR from index to subsequent pregnancy (n=49) of 29% to 86% ($p<0.0001$) with the addition of 400mg daily HCQ. Similarly, Sciascia et al in 2016 demonstrated an increase in LBR between control (n=119) and 400mg daily HCQ treated (n=51) pregnancies from 57.1% to 66.7% ($p<0.05$). Interestingly, Ruffatti et al in 2018 demonstrated a dose dependent effect of HCQ, with 400mg daily resulting in a 94% LBR as compared to 200mg daily at 79.5% ($p=0.036$).

Pregnancy loss percentage was significantly improved in 4 retrospective studies. Mekinian et al in 2015 demonstrated a significant reduction from index to subsequent (n=49) pregnancy from 81% to 19% ($p<0.05$) and in 2017 a reduction from 76% to 14% ($p<0.0001$). Sciascia et al in 2016 demonstrated a reduction in fetal loss beyond the 10th week of gestation from 10.9% to 2% ($p<0.05$) and Ye et al in 2017 demonstrated a reduced PL of 22.7% to 11.1% ($p=0.012$) following 200mg BID HCQ treatment.

CONCLUSIONS: There are no RCTs to evaluate the impact of HCQ on LBR in patients with APS. Retrospective studies demonstrated that HCQ may be an effective treatment in patients with refractory obstetrical APS as it has been demonstrated to improve LBRs in patient's non-responsive to empiric anti-thrombotic therapies. However, RCTs that standardize patient selection criteria and explicitly analyze the use of HCQ as a refractory APS treatment are needed.

POSTER SESSION: EDUCATION

P-221 4:30 PM Saturday, October 17, 2020

THE VOICE OF INFERTILITY: A REVIEW OF FERTILITY PODCASTS. Alexandra Peyser, M.D., Baruch Abittan, M.D., Christine Mullin, M.D., Randi H. Goldman, M.D. Northwell Health Fertility, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: Podcasts are audio recordings distributed across the Internet that users can listen to on a computer or mobile device. There has been rapid growth in the awareness of podcasting with an estimated 70% of the US population now familiar with this term. The objective of this study was to review the availability, content, and authorship of podcasts on the topic of fertility and to compare those hosted by physicians vs. patients.

DESIGN: Content analysis.

MATERIALS AND METHODS: A search for podcasts relating to the search term 'fertility' was performed using 10 podcast hosting platforms, including: Anchor, Apple Podcasts, Spotify, Google Podcasts, Podbean, Overcast, Stitcher, Breaker, Castbox, and RadioPublic. Only English-language series and those in which the overlying theme was fertility-based were included. Information relating to each podcast was recorded, including: title, subject, host type, number of episodes, frequency of episodes, country of origin, number of ratings, and status regarding whether the podcast was active or inactive. The Chi-square test was used for comparison of proportions and the Mann-Whitney U test was used for continuous variables. A p value of <0.5 was considered significant.

RESULTS: One hundred thirty one podcasts met inclusion criteria. The dates of publication ranged from 2009-2020, with a total of 4,760 episodes aired. The most common subject was patient education relating to fertility, which involved the patient experience (62%) followed by fertility awareness (30%), and Third Party Reproduction (13%). Most podcasts were targeted toward patients. Podcasts were hosted by patients (40%), holistic health professionals (28%), physicians (16%), third party agencies (11%), and others, including fertility nurses, social workers, nutritionists, pharmacists, and attorneys (5%). Approximately 11% of podcasts were hosted by private industry, while <2% were organized from academic institutions and <1% from fertility societies. The majority originated from the US (92%) with a smaller percentage from Australia (4%) and the UK (3%). When comparing podcasts hosted by physicians vs. patients, there was no difference in overall content ($p= .07$), frequency of episodes ($p=0.77$), number of episodes ($p=0.63$) and number of ratings ($p=0.47$).

CONCLUSIONS: A large number of fertility podcasts exist with most hosted by patients describing their fertility experiences. Physicians, particularly board certified Reproductive Endocrinologists, should consider having a stronger presence in the podcast industry as a way to best inform patients about evidence-based practices. Further research regarding the profile of the fertility podcast audience, listener motivation, and user experience would be valuable for optimizing usage of this medium.

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RESIDENT PERCEPTIONS OF FERTILITY CARE IN THE LOW RESOURCE SETTING: PRELIMINARY DATA FROM THE FERTILITY PASSPORT PROGRAM. Rachel Ruderman, MD, MPH, Mary Tate, MD, MPH, Emily Lin, MD, Jacqueline Lee, MD, Stephanie Cai, MD, Luce A. Kassi, MD, Bahar D. Yilmaz, MD, Christina E. Boots, MD, MSCI. Northwestern University Chicago, IL.

OBJECTIVE: To assess resident perceptions of their ability to provide infertility care in a low resource setting.

DESIGN: This study includes data from an ongoing Accreditation Council for Graduate Medical Education funded Back to Bedside project, the "Fertility Passport Program," which addresses fragmentation and resident burnout when providing infertility care in low resource settings using an educational intervention (a video) and a tool (a "passport") to streamline the outpatient evaluation. Obstetrics and gynecology residents who practice at a county hospital and a tertiary academic center were surveyed.

MATERIALS AND METHODS: This cross-sectional study utilized a questionnaire of which seven items were on a five-point Likert scale. Residents were queried on confidence in providing infertility care in the low-resource setting, adequacy of clinic time, and confidence in patient knowledge, understanding and ability to complete their workup. For analysis, scores of "1" and "2" were combined to form the category 'disagree' and scores of "4" and "5" were combined to form the category 'agree'.

RESULTS: Of the 47 residents surveyed, 44 responded (93.6%). Over half felt comfortable in their counseling on infertility (54.5%) though most felt that there was insufficient time to address fertility-related issues (70%). Most residents were not confident that patients understood the concept of infertility and reasons for tests that were ordered (70%) or that they would complete their infertility workup (68%).

	Agree % (n)	Neutral % (n)	Disagree % (n)
I feel comfortable addressing infertility-related issues in this patient population.	36% (16)	34% (14)	34% (14)
I feel confident in my ability to counsel patients on infertility and reproduction.	54.5% (24)	29.5% (13)	16% (7)
I feel there is enough time in clinic to address infertility-related issues.	7% (32)	23% (10)	70% (31)
I know how to complete a work-up for infertility.	72% (32)	20% (9)	7% (3)
I feel confident my patient understands the concept of infertility and reasons for the tests we have ordered.	9% (4)	20% (9)	70% (31)
I feel confident my patient knows how to complete the next steps in her infertility work-up.	2% (1)	23% (10)	75% (33)
I feel confident my patient will complete her infertility work-up.	7% (3)	25% (11)	68% (30)

CONCLUSIONS: Our results suggest a discrepancy between resident knowledge base and the perception of patients' understanding of infertility, as well as their ability to complete the evaluation. This finding suggests a need for better patient education and care coordination in the low-resource environment. More data is needed as this program continues to discern whether the Fertility Passport Program is successful in helping to improve the delivery of fertility care in this setting.

SUPPORT: Accreditation Council for Graduate Medical EducationÂ (ACGME)

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A CONTENT AND QUALITY EVALUATION OF ACGME-ACCREDITED REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY FELLOWSHIP PROGRAM WEBPAGES. Alexandra Peyser, M.D., Baruch Abittan, M.D., Christine Mullin, M.D., Randi H. Goldman, M.D. Northwell Health Fertility, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: Prospective Reproductive Endocrinology and Infertility (REI) fellows often rely on the Internet to obtain valuable information regarding the unique qualities of different fellowship programs. The aim of this study was to analyze the content of websites of ACGME-accredited REI Fellowship programs in the United States and to determine whether there were differences in content across geographic regions.

DESIGN: Content analysis.

MATERIALS AND METHODS: All ACGME-accredited REI Fellowship websites as of March 2020 were evaluated and reviewed using 20 criteria in the following nine domains: program overview, contact information, application information, curriculum, current fellows, research, alumni, faculty, and fellowship benefits. Website content was compared across geographic regions (Northeast, Midwest, South and West) of the United States. A Chi-square univariate analysis was used with $p < 0.05$ considered statistically significant.

RESULTS: Out of the 48 accredited REI fellowship programs, 45 (94%) had a dedicated website. The most commonly available information included a program description (90%), clinical sites (85%), application requirements (79%) and application deadline (70%). Approximately two-thirds shared information regarding research requirements and didactics (66% for each). More than half (52%) of programs did not disclose their interview dates on their websites. Current fellows were featured in 56% of websites with their pictures in 41%, and ongoing research in 21%. Salary and alumni information were included in only 15% and 13% of sites, respectively. When comparing content by geographic region, programs in the South had less information regarding application requirements ($p<0.001$), interview dates ($p=0.026$), and clinical sites ($p=.04$) compared to all other regions. There was no difference among other criteria.

CONCLUSIONS: REI fellowship websites have significant variability in content available to applicants, and many are lacking information about core fellowship requirements. An informative and well-constructed website has the potential to improve perception of a graduate program. Further studies are needed to ascertain the specific interests of REI applicants, and their satisfaction with the content of currently available webpages.

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FERTILITY KNOWLEDGE AND VIEWS ON EGG FREEZING AND FAMILY PLANNING AMONG SURGICAL SPECIALTY TRAINEES. Karine Matevossian, DO,[1] Anne Rivelli, MA, MPH,[1] Meike L. Uhler, M.D.[2] [1]Advocate Lutheran General Hospital, Park Ridge, IL; [2]Fertility Centers of Illinois, Chicago, IL.

OBJECTIVE: Describe fertility knowledge and viewpoints on family planning among United States (U.S.) residents and fellows.

DESIGN: Cross sectional survey.

MATERIALS AND METHODS: The Advocate Aurora Health Institutional Review Board approved this study. A 32-question Qualtrics survey was emailed to trainees across U.S. training programs, including residencies/fellowships in the following fields: obstetrics/gynecology (OB-GYN); ophthalmology; otolaryngology; and neuro, plastic, general, and orthopedic surgery. Pearson Chi-square tests were used to address accuracy of fertility knowledge by training specialty groups (OBGYN vs. others), gender (female vs. male), and program type (community vs. academic). Family plans and viewpoints are also described. All analyses were performed using SAS, version 9.4.

RESULTS: A total of 447 surveys were collected from October 2019 to January 2020. Participants included 309 residents, 94 fellows, and 44 with unknown status. Participants mostly identified as female (73%), ages 26-30 (48%), Caucasian (69%), married (59%) and heterosexual (95%) with no children (72%). Three questions were used to evaluate fertility knowledge: 1) age at initial decrease in women's fertility, 2) age at significant decrease in women's fertility, and 3) average success rate of one IVF cycle. Most notably, regarding knowledge of age at initial decrease in women's fertility, non-OBGYN trainees had 2.49 times greater odds of answering correctly relative to OBGYN trainees ($p=0.0011$) and females had 0.77 times lesser odds of answering correctly relative to males ($p=0.3791$).n general, trainees in academic programs had a higher percentage of correct responses than those in community programs, but the differences were not statistically significant (Q1-17% vs 13%, Q2-68% vs 58%, Q3-49% vs. 44%). Descriptively, more females were single (19% vs. 13% of males) and less were married (55% vs. 74% of males). Relative to males, females had 2.89 times increased odds of having zero children ($p<0.0001$) and 1.33 times increased odds of reporting postponed plans for children ($p=0.2438$). Among female respondents, 48% would consider freezing oocytes, but less than 4% of respondents have frozen oocytes. Respondents cited a variety of reasons for postponing children including career plans, concerns about a lack of time to care for a child and availability of childcare, and concerns for their co-residents/fellows.

CONCLUSIONS: This study indicates differences in knowledge regarding fertility; more specifically, despite gender or focused training in reproductive endocrinology and infertility, females and OBGYN trainees are not necessarily more well-versed in basic female fertility knowledge relative to their counterparts. Also, female trainees are less likely to have children or be married, and more likely to report plans to postpone children, highlighting differences in family planning by gender. Fertility-focused educational interventions for OBGYN trainees are necessary. More research into barriers for family plans, particularly by gender, are also merited.

SUPPORT: none

P-225 4:30 PM Saturday, October 17, 2020

SUITABILITY OF MULTI-DOSE VERSUS SINGLE DOSE GONADOTROPIN INJECTION PENS FOR ART USE: A USABILITY PEN STUDY. Helen Saunders, BSc (HONS),[1] Linda Bjaergestad Lamp, BSN,[2] Hasan Donat, MSc,[3] Monja Messner, MSc,[4] Maren Reder, BSc,[5] Helen Kendrew, RGN[6] [1]Medical Affairs Director, Geneva, Switzerland; [2]STOCKHOLM IVF AB, Stockholm, Sweden; [3]Junior Clinical Project Manager, Geneva, Switzerland; [4]Associate Director Research, Berlin, Germany; [5]Research Executive, Berlin, Germany; [6]Clinic Director, United Kingdom.

OBJECTIVE: The success of ovarian stimulation during ART can be impacted by the correct administration of the gonadotropins. The objective of this usability study was to evaluate the suitability of single dose versus multi-dose pens for fertility treatment by investigation of the Instructions for Use (IFU), the dosing steps and the risk of critical errors which could potentially lead to dose administration or safety issues.

DESIGN: The study was performed in 4 European countries (Germany, United Kingdom, France and Spain) to assess 3 pens (Bemfola (single use), Gonal F and Ovaleap (multi-use)) used by nurses and fertility patients. Based on each IFU the individual steps required to administer medication were identified. Critical steps, defined as those which could potentially lead to administration errors if not adhered to correctly were identified for each pen. Participants also assessed their confidence in selecting/administration of correct doses.

MATERIALS AND METHODS: Each nurse performed a mock injection of 150IU, with each of the 3 pens. To eliminate any bias, the order of assessment of pens followed a rotation plan. Patients were then trained with each pen according to the IFUs by an external moderator using a 150IU injection. The patients then carried out independently a further 150IU followed by a 225IU injection with each pen. During each injection, the total number of handling errors, defined as any steps missed or carried out incorrectly, versus total number of steps was recorded.

RESULTS: Overall, 24 patients and 19 nurses participated in the study. The critical error rates reported among nurses was 9%, 24% and 49% for Bemfola, Ovaleap and Gonal-f respectively, whilst among patients the corresponding rates were 4%, 16% and 38% respectively. The main critical error reported with Bemfola was the attachment of the needle where both groups tried to screw on the needle rather than push/click as per the IFU instructions. With Ovaleap, the main errors reported were the incorrect/lack of priming, to ensure correct functioning of the pen, prior to injection and the incorrect use of the dose adjustment button rather than the administration button to carry out the injection. With Gonal-f, the main errors reported were the complete omission of the priming step, when required, and failure to ensure complete dose was administered, especially when the dose was not available in the pen, resulting in delivery of an incomplete dose. Overall, 63%, 37% and 0% of nurses chose Bemfola, Gonal-f and Ovaleap respectively regarding the pen which they would have most confidence that the patient would inject the

correct dose at home. This compared to 67%, 29% and 4% respectively for the patients.

CONCLUSIONS: This study shows that overall single use pens have less steps and in turn a lower chance of critical handling errors leading to potential dosing errors or safety issues. Following the IFU's, especially when experienced nurses are training both patients and less experienced nurses is essential to a successful treatment cycle. Incorrect instruction, particularly with the multi-dose pens, can lead to patient error and in turn a less favourable outcome.

P-226 4:30 PM Saturday, October 17, 2020

SURVEY ON PERCEPTION OF GERMLINE GENE THERAPY AMONG JAPANESE MEDICAL STUDENT. Tomonari Hayama, M.D., Ph.D.,[1] Akifumi Ijuin, M.D.,[1] Ai Miyakoshi, M.D.,[1] Haru Hamada, M.D.,[1] Mitsuru Komeya, M.D., Ph.D.,[1] Teppei Takeshima, M.D., Ph.D.,[1] Shinnosuke Kuroda, M.D.,[1] Yasushi Yumura, M.D., Ph.D.,[1] Mariko Murase, M.D., Ph.D.,[1] Etsuko Miyagi, M.D., Ph.D.,[2] Hideya Sakakibara, M.D., Ph.D.[1] [1]Yokohama City University Medical Center, Yokohama, Japan; [2]Yokohama City University School of Medicine, Yokohama, Japan.

OBJECTIVE: Germline gene therapy (GGT) has potential to be radical treatment approach for monogenic genetic disorder. Because recent CRISPR technology enables us to edit human genome with high efficacy and lowest off-targeting, technical issues for GGT have been almost solved. Mitochondrial replacement therapy (MRT) is also only radical germline gene therapy for heritable mitochondrial disease. Japanese government has issued a statement prohibiting GGT, including MRT, and emphasizing the need for discussions in a wide range of perspectives. A few surveys of Japanese general adults had already shown they generally accepted the use of GGT for monogenic genetic disorder. However, because they know little about GGT, surveys still had limitation to clarify actual Japanese people attitude.

DESIGN: Medical student attitude survey results are thought to be similar to results of young patient final attitude. Here, we conducted a survey of Japanese medical students who might perfectly understand that GGT would have not only potential to be radical treatment for monogenic genetic disorder but also detailed risk for ethics.

MATERIALS AND METHODS: Under the ethical review of Yokohama City University, we recruited 80 medical students (18-24 y.o.) who learn only clinical medicine lecture (not yet bed-side) and evenly explained GGT as fore- and anti- side in bio ethics lecture. Surveys were performed by description style for Q & A, trying to catch opinions from wide rang of perspectives.

RESULTS: A 74% (59/80) of medical students agreed to clinical trial for monogenic disorder GGT by CRISPR. An 82% (65/80) agreed to clinical trial for MRT. Furthermore, 35% (28/80) and 59% (47/80) agreed to clinical treatment for GGT and MRT.

CONCLUSIONS: Our results indicate that the Japanese people will accept the use of GGT and MRT on the future, if they can completely understand the benefit and risk for ethics. To achieve complete understanding about GGT and MRT, it is still important that scientists and science communicators create more opportunities for the public talk. It is also important to continuously track changes in the acceptance for GGT and MRT by various people groups.

POSTER SESSION: LGBTQ

P-227 4:30 PM Saturday, October 17, 2020

REVERSIBILITY OF HORMONAL AND CYCLIC DISRUPTIONS IN A TRANSGENDER MOUSE MODEL AFTER CESSATION OF TESTOSTERONE THERAPY. Prianka H. Hashim, BS, BA, Hadrian M. Kinnear, BA, Gillian E. Rubenstein, -, Faith L. Chang, -, Likitha Nimmagadda, -, Margaret A. Brunette, MS, Vasantha Padmanabhan, MS, PhD, Ariella Shikanov, PhD, Molly B. Moravek, MD, MPH. University of Michigan Ann Arbor, MI.

OBJECTIVE: Suppression of luteinizing hormone (LH) levels and acyclicity has been widely observed in transgender men with gender-affirming testosterone (T) therapy, but it is unknown if LH levels return to baseline and regular cycles resume after stopping T. Estrous cycles can be an indicator for the regular functioning of the hypothalamic-pituitary-gonadal axis, including LH secretion as a measure of GnRH secretion in the hypothalamus. The aim of this study was to determine the impact of T therapy on the reproductive axis (LH secretion and estrous cyclicity), and investigate reversibility following cessation of T, using a previously established transgender mouse model.

DESIGN: Translational Animal Study.

MATERIALS AND METHODS: Ten 9–10-week-old C57BL/6NHsd female mice were injected with 0.90 mg of T enanthate injections once weekly for 6 weeks and then injections were stopped. Ten age-matched control mice received weekly injections with a sesame oil vehicle. Daily vaginal cytology from all mice and weekly blood collection for analysis of T levels from half the mice were undertaken. From the other half, serial blood samples were collected to profile pulsatile diestrus LH levels before and during T administration, after T cessation and at time of sacrifice (~4 estrous cycles following resumption of cyclicity). Serial sampling for LH analysis began 5 hours after vivarium lights were turned on and involved collection of 6 μl of blood every 10 minutes from the lateral tail vein over a fixed 3-hour period. Blood samples were vortexed immediately in buffer to prevent clotting. Data were analyzed in GraphPad Prism to generate descriptive statistics and used Welch's t-test or Mann-Whitney as appropriate.

RESULTS: After 1–2 weeks of T treatment, all T-treated mice stopped cycling and were in persistent diestrus. T-treated mice resumed cycling 3.5–10 weeks following cessation of T treatment. Control mice cycled regularly throughout. Weekly serum samples showed that, during T treatment, serum T levels rose to concentrations similar to those observed in male mice (8.0 $\pm$ 1.1 ng/mL vs. control mice 0.27 $\pm$ 0.07 ng/mL; mean $\pm$ SD, $P = .008$). Serum T levels dropped back down to female levels after cessation of T treatment and subsequent washout period (0.5 $\pm$ 0.1 ng/mL vs. control mice 0.51 $\pm$ 0.07 ng/mL; mean $\pm$ SD, $P = .71$). After 3 weeks of T treatment, serial diestrus blood collection showed suppression of mean LH levels during T administration (0.61$\pm$ 0.07 ng/mL vs. 0.84 $\pm$ 0.09 ng/mL in age-matched control mice, $P < .001$). This LH suppression occurred during the period of acyclicity in T-treated mice. Preliminary single timepoint data of terminal LH levels during diestrus are indicative of no significant difference between T-treated and control mice following T cessation.

CONCLUSIONS: Cessation of T treatment reverses acyclicity, and preliminary results indicate T-induced suppression of LH can be reversed following T cessation. These data denote that changes of the hypothalamic-pituitary-gonadal axis due to T therapy may be reversible, and therefore may not impact long-term reproductive function.

SUPPORT: NIH (R01-HD098233 (MBM), F30-HD100163 (HMK), T32-HD079342 (HMK)), ASRM / SREI (MBM), UMOR (AS), P50-HD28934 (UVA Ligand Core).

P-228 4:30 PM Saturday, October 17, 2020

FERTILITY PRESERVATION IN A TRANSGENDER MAN WITHOUT PROLONGED DISCONTINUATION OF TESTOSTERONE: A CASE REPORT AND LITERATURE REVIEW. Kristy Cho, MD, FRCSC,[1] Rahana Harjee, MD,[2] Jeffrey Roberts, MD, FRCSC,[1] Caitlin Dunne, MD, FRCSC[3] [1]Division of Reproductive Endocrinology and Infertility, University of British Columbia, Vancouver, BC, Canada; [2]Department of Obstetrics and Gynaecology, University of British Columbia, Vancouver, BC, Canada; [3]Division of Reproductive Endocrinology and Infertility, University of British Columbia, Burnaby, BC, Canada.

OBJECTIVE: When proceeding with hormone therapy or gender affirming surgery, transgender patients should have the option of undergoing fertility preservation [1]. Prior to assisted reproductive technology, transgender men have traditionally had to discontinue exogenous testosterone for up to 6 months or until resumption of menses [2]. The process and experience associated with stopping testosterone has proven to be distressing for patients [3]. This report explores the feasibility of proceeding with fertility preservation in a transgender man without an extended period of androgen cessation and without the resumption of menstruation.

DESIGN: Case report and literature review. Consent was obtained from the patient for publication.

MATERIALS AND METHODS: We present a seminal case report of oocyte cryopreservation in a transgender man without stopping testosterone therapy beforehand. We also performed a literature review, which identified 5 publications reporting on the outcomes of oocyte cryopreservation in transgender men on testosterone therapy.

RESULTS: A 28-year-old transgender man had been taking testosterone for 3 years. He presented to a university-affiliated fertility clinic requesting oocyte cryopreservation before hysterectomy and bilateral salpingo-oophorectomy. He expressed a desire to proceed without stopping testosterone. Pre-treatment AMH was 1.89 ng/mL. A standard antagonist protocol was used with the addition of letrozole to minimize estrogenic side effects. Testosterone therapy was stopped for only three doses (immediately prior to and during COS). Thirteen oocytes were retrieved, 11 were mature and vitrified. In total, the time off of testosterone was 24 days. In all prior publications, testosterone was stopped for 3-6 months prior to starting ART [2-6].

CONCLUSIONS: This is a seminal case report demonstrating the feasibility of ovarian stimulation without a prolonged period of testosterone cessation in a transgender man. Future studies with a larger sample size should be carried out to confirm these findings. The short duration of time off testosterone may improve the patient's experience, increase treatment acceptability, and decrease gender dysphoria for transgender men considering fertility preservation.

The manuscript has subsequently been accepted for publication by F&S Reports.

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6. Rodriguez-Wallberg, KA., et al., Preserving eggs for men's fertility- a pilot experience with fertility preservation for female-to-male transsexuals in sweden. Fertil Steril, 2014. 102:e160–e161.

SUPPORT: This abstract has been accepted at PCRS, however it was not presented as the conference was cancelled due to the COVID 19 pandemic.Â

POSTER SESSION: REPRODUCTIVE IMMUNOLOGY

P-229 4:30 PM Saturday, October 17, 2020

TIGIT PROMOTE IMMUNE TOLERANCE AT THE FETO-MATERNAL INTERFACE.

Wenyan Fu, M.D.,[1] Zetong Ma, M.D.,[2] Shi Hu, Ph.D.[2] [1]Shanghai Ninth People's Hospital, Shanghai, China; [2]Second Military Medical University, Shanghai, China.

OBJECTIVE: The perfect synchronization of maternal immune-endocrine mechanisms and those of the fetus is necessary for a successful pregnancy. We sought to determine the function role of T cell immune receptor with Ig and ITIM domains (TIGIT), a co-inhibitory receptor, at the maternal-fetal interface and further expand the translational relevance of TIGIT in reproductive medicine.

DESIGN: Recombinant TIGIT-Fc fusion proteins by linking the extracellular domain of TIGIT and silent Fc fragments were generated and characterized. Human samples were collected and decidual immune cells were isolated for in vitro analysis. A mouse model of stress-induced pregnancy failure were employed to investigate the therapeutic role of TIGIT.

MATERIALS AND METHODS: We utilized cell-based models to study the function of TIGIT and TIGIT-Fc protein in decidual immune cells. Cell assays, flow cytometry, qPCR, cytokine analysis, multiplex bead array and mouse models were employed to investigate the mechanisms of action and pharmacodynamic readouts.

RESULTS: We found the TIGIT-Fc fusion protein with a silent Fc fragment did not trigger cytotoxic effect and has good pharmacokinetic parameters. The treatment with TIGIT-Fc of human decidual antigen presenting cells (APCs), the decidual dendritic cells (dDCs) and decidual macrophages (dMϕs) increased the production of interleukin 10 and induced the decidua APCs to powerfully polarize the decidual $CD4^+$ T cells towards a classic T_H2 phenotype. We further proposed that progesterone and Notch signalling shows a synergistic effect on the transcriptional regulation of TIGIT in decidual immune cell subsets. Moreover, The administration of TIGIT-Fc to CBA/J pregnant mice at preimplantation induced $CD4^+$ forkhead box $P3^+$ ($Foxp3^+$) regulatory T cells and tolerogenic dendritic cells and increased pregnancy rates in a mouse model of abortive stress.

CONCLUSIONS: We obtained new experimental evidence to support an immune-tolerance role of TIGIT at the maternal-fetal interface and demonstrated the therapeutic potential of TIGIT-Fc to restore immune tolerance in failing pregnancies.

P-230 4:30 PM Saturday, October 17, 2020

CO-EXPRESSION OF ACTIVATING AND INHIBITORY RECEPTORS ON PERITONEAL FLUID NK CELLS IN WOMEN WITH ENDOMETRIOSIS.

Shinichiro Saeki, MD,[1] Atsushi Fukui, MD, PhD,[2] Hiroaki Shibahara, MD, PhD,[2] Toru Kato, MD, PhD,[2] Yu Wakimoto, MD,[2] Mai Chuxian, Ph.D. Student,[2] Mayu Yamamoto, Master's Student,[2] Ryu Takeyama, MD[2] [1]Hyogo College of Medicine, Nishinomiya, Japan; [2]Hyogo College of Medicine, Nishinomiya, Hyogo, IL, Japan.

OBJECTIVE: Abnormal function of peritoneal immune cells may cause to the onset and progress of pelvic endometriosis. We have previously reported that the expression of natural cytotoxicity receptor (NCR) including NKp46 on peritoneal fluid NK (pfNK) cells is decreased in women with pelvic endometriosis. NK cell expresses not only NKp46, but also various kinds of activating or inhibitory receptors on its surface. The aim of this study is to investigate participation of NK cells in women with endometriosis by analyzing the co-expression of activating or inhibitory receptors on NK cells and to investigate the immunological relationship between endometriosis and peritoneal fluid immune cells abnormalities.

DESIGN: Case control study.

MATERIALS AND METHODS: We collected peritoneal fluid NK (pfNK) cells and peripheral blood NK (pNK) cells from women who underwent laparoscopic operation for pelvic endometriosis (Endometriosis group, n=6) and control women who underwent laparoscopic operation for benign gynecological diseases such as uterine myoma or ovarian cyst (Controls: 3 cases of uterine fibroids, 4 cases of ovarian cysts, n=8). The co-expression of activating receptors(CD16, NKp46, NKG2C, NKG2D) and inhibitory receptors(CD158a, NKG2A) on pfNK cells (CD56) was analyzed using 6 color flow cytometry. All patients had given informed consent prior to entering the study, and the study was approved by the institutional review board.

RESULTS: The percentage of $CD16^+/CD56^{dim}$ pfNK cells was significantly lower in endometriosis group compared with controls ($p<0.01$). The percentage of $NKp46^+/CD56^+$ pfNK cells was not different between the two groups.

For the expression of activating NK cell receptor NKG2C, the percentage of $NKp46^{bright}/NKG2C^{bright}$ pfNK cells showed a significant increase in endometriosis group compared with controls ($p<0.01$), while that of $NKp46^{brigh}/NKG2C^{dim}$ pfNK cells showed a significant decrease ($p<0.01$). For the expression of NK cell inhibitory receptors NKG2A, the percentage $NKp46^{bright}/NKG2A^{bright}$ pfNK cells showed a significant increase in endometriosis group compared with controls ($p<0.01$), while that of $NKp46^{bright}/NKG2A^{dim}$ pfNK cells showed a significant decrease ($p<0.05$).

CONCLUSIONS: It is suggested that pfNK cells can be classified according to the difference for the intensity of fluorescence of NKG2C, NKG2A and NKp46. Furthermore, the cytotoxicity of pfNK cells may be different depending on the intensity of those receptor expression. We previously reported that $NKG2C^{bright}$ or $NKG2A^{bright}$ NK cells are cytokines producing cells and $NKG2C^{dim}$ or $NKG2A^{dim}$ NK cells are cytotoxic cells. Therefore, it may be speculated that the increase of cytokine-producing pfNK cells and the decrease of cytotoxic pfNK cells in endometriosis group may allow the attachment of endometrial cells and progress of endometriotic lesion.

P-231

WITHDRAWN

RESULTS: ***Identifying potential core outcomes:*** A long list of 55 potential core outcomes was developed by extracting outcomes reported in 54 endometriosis trials.

Determining core outcomes: When considering the Delphi survey, 354 participants, from 29 countries, responded. Eighteen consensus outcomes were identified and discussed during the consensus development meeting. Twenty-four participants, from 7 countries, engaged in the consensus development meeting. A minimum data set for endometriosis research was agreed (Table 1).

TABLE 1. Core outcome set for endometriosis.

1 Viable intrauterine pregnancy confirmed by ultrasound accounting for singleton, twin and higher multiple pregnancy
2 Pregnancy loss accounting for ectopic pregnancy, miscarriage, stillbirth and termination of pregnancy
3 Live birth
4 Gestational age at birth
5 Birth weight
6 Neonatal mortality
7 Major congenital anomaly
8 Adverse events
9 Patient satisfaction with treatment
If applicable: time to pregnancy leading to live birth

Determining how core outcomes should be defined: Forty-four potential definitions were identified. Twenty-seven participants, from 11 countries, took part in the consensus development meeting and agreed consensus definitions for individual core outcomes.

CONCLUSIONS: Embedding the core outcome set within future endometriosis research should ensure the comprehensive collection and reporting of core outcomes. Research funders, the SPIRIT statement, and over 80 speciality journals, including *Fertility and Sterility,* have committed to implementing this core outcome set.

References: Hirsch M, **Duffy JMN**, Barker C, Hummelshoj L, Johnson N, Mol B, Khan K, Farquhar C. A protocol for developing, disseminating, and implementing a core outcome set for endometriosis. *BMJ Open* 2016; 6(12): e013998.

SUPPORT: This research was funded by the Catalyst Fund, Royal Society of New Zealand, Auckland Medical Research Fund, and Maurice and Phyllis Paykel Trust.

POSTER SESSION: ENDOMETRIOSIS

P-232 4:30 PM Sunday, October 18, 2020

DEVELOPING A MINIMUM DATA SET FOR RESEARCH EVALUATING TREATMENTS FOR INFERTILITY ASSOCIATED WITH ENDOMETRIOSIS.

James M. N. Duffy, DPhil MRes PG HCL MBChB BSc (Hons),[1] Martin Hirsch, MRCOG MD(Res) MBBS,[2] Cindy Farquhar, FRANZCOG FRCOG MD MPH[3] ENDO:outcomes: An international collaboration harmonising outcomes outcomes measures for endometriosis research. [1]Institute for Women's Health, University College London, Greater London, United Kingdom; [2]University College London Hospitals NHS Foundation Trust, Greater London, United Kingdom; [3]University of Auckland, Auckland, New Zealand.

OBJECTIVE: To develop a minimum data set for research evaluating fertility treatments for endometriosis.

DESIGN: Consensus development study engaging professionals, researchers and women with endometriosis.

MATERIALS AND METHODS: ***Identifying potential core outcomes:*** Potential core outcomes were identified by extracting outcomes previously reported in endometriosis trials.

Determining core outcomes: Potential core outcomes were entered into a three-round eDelphi survey. Respondents were asked to score the importance of each outcome. Based on their feedback, potential core outcomes were prioritized, and subsequently discussed during a consensus development meeting. Using the modified Nominal Group Technique, a minimum data set was agreed.

Determining how core outcomes should be defined: A long list of potential definitions was developed by identifying definitions which had been reported by formal definition development initiatives, clinical practice guidelines and Cochrane reviews. Potential definitions were discussed in a consensus development meeting. Using a formal consensus development method, consensus definitions were developed.

P-233 4:30 PM Sunday, October 18, 2020

MURINE AVATARS FOR PRECISION MEDICINE IN ENDOMETRIOSIS.

Valerie A. Flores, MD,[1] Cagdas Sahin, MD,[1] Hugh S. Taylor, M.D.[2] [1]Yale School of Medicine, New Haven, CT; [2]Yale University School of Medicine, New Haven, CT.

OBJECTIVE: Endometriosis is a chronic, gynecologic disease afflicting 1-in-10 reproductive-aged women. Response to medical therapy is highly variable as endometriotic lesions do not consistently respond to first-line, progestin-based therapy. We have previously demonstrated in a retrospective study that progesterone receptor (PR) status in lesions can predict response to progestins. Low PR status was associated with a $<10\%$ chance of response, suggesting that some women may benefit from alternative hormonal therapy as first-line. Here, we utilize murine avatars to test human endometriotic lesion response to two different hormonal regimens. We hypothesize this approach will allow clinicians to individualize effective, timely treatment for this debilitating disease.

DESIGN: Patient-Derived Xenograft Murine Model.

MATERIALS AND METHODS: Eight-week old NOD/SCID mice underwent transplantation of endometrioma lesions (5mm) collected from women undergoing surgery for endometriosis. Immunohistochemistry was performed to determine PR expression in lesions prior to implantation. The Histo- Score was used to quantify PR status as *High* or *Low*. Two weeks following transplantation, mice underwent daily subcutaneous injections with vehicle (DMSO), Medroxyprogesterone acetate (MPA, 50ug), or GnRH antagonist, Cetrotide (100ug); n=6-9 lesions per group. After 1 month of treatment mice were sacrificed, lesions collected, and measured. Student's t-test was used for statistical analysis.

RESULTS: Lesions with high PR demonstrated near-complete response to MPA compared to lesions with low PR ($p<0.05$). Average post-treatment

size in high PR lesions was 1.25mm^3 compared to 24.7mm^3 in low PR lesions. As expected, high PR lesions responded completely to GnRH antagonist (i.e., 0 mm) ($p< 0.05$). While lesions with low PR responded poorly to MPA, they responded well to antagonist with a similar degree of response as seen in high PR lesions responding to MPA (>3-fold decrease in lesion size). Untreated lesions with high PR demonstrated slower growth compared to lesions with low PR.

CONCLUSIONS: Use of murine avatars to test clinical response is a novel approach to endometriosis, which currently remains difficult to treat. Hormonal suppression is a cornerstone of therapy, however response can be unpredictable. We have previously shown that women with low PR lesions respond poorly to progestin-based therapy. Here we validate our prior work in a mouse xenograft model by demonstrating that lesions with low PR expression do not respond to progestin-based therapy. We demonstrate that lesions with low PR respond to antagonist therapy in a manner similar to response of high PR lesions to MPA; we anticipate this response will be clinically meaningful in patients. The use of murine avatars can allow clinicians to predict an individual's response to therapy, avoid trialing futile treatments, and allowing a precision medicine approach to endometriosis.

SUPPORT: SRI/Bayer Discovery Grant

P-234 4:30 PM Sunday, October 18, 2020

M^{6}A METHYLATION REGULATORS CONTRIBUTE TO THE EUTOPIC ENDOMETRIUM AND MYOMETRIUM DYSFUNCTION IN ADENOMYOSIS.

Junyu Zhai, M.D. Ph.D.,[1] Shang Li, M.D.,[2] Sushmita Sen, B.S.,[1] Yanzhi Du, M.D. Ph.D.,[2] Linda C. Giudice, MD, PhD[1] [1]University of California, San Francisco, San Francisco, CA; [2]Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China.

OBJECTIVE: The goal of this *in silico* and lab-based experimental study was to explore a possible role for N6-methyladenosine (m^{6}A) in adenomyosis.

DESIGN: Through bioinformatic analysis of the data from Gene Expression Omnibus (GEO) database, we investigated the role of m^{6}A methylation regulators in the pathogenesis of adenomyosis. Then human samples were used to validate the results of *in silico* analysis.

MATERIALS AND METHODS: Gene expression profiles of both the endometrium and myometrium of women with and without adenomyosis were obtained from the publicly available GEO database separately. The expression, co-expression and possible target genes of the 16 m^{6}A methylation regulators were investigated using bioinformatic analysis such as Wilcox test, Spearman correlation and WGCNA. Finally, the total m^{6}A content, expression of m^{6}A methylation regulators and possible target genes of m^{6}A regulators were validated using qRT-PCR in both the endometrium and myometrium of adenomyosis women and controls. The clinical samples were collected from the Endometrial Tissue and DNA Bank at UCSF (IRB # 10-02786).

RESULTS: In the endometrium, STRING database analysis revealed that *METTL3* functions as a "hub" gene of m^{6}A methylation regulators, and the genes involved in m^{6}A regulation, including *METTL3*, *FTO*, *ZC3H13* and *YTHDC1* expression, were significantly decreased in cases versus controls. Functional, co-expression and correlational analyses of endometrium from cases versus controls revealed decreased total m^{6}A levels, induced by *METTL3*, and the downstream elevated *insulin-like growth factor-1(IGF1)* and *D-Dopachrome Tautomerase* (*DDT),* with the latter two having known functions in epithelial proliferation and cell migration, which are important processes in the pathogenesis of adenomyosis in endometrium.

M^{6}A methylation regulators, including *RBM15/15B*, *ALKBH5*, *FTO*, *YTHDF1/2*, *KIAA1429*, *HNRNPC*, *METTL3*, *ZC3H13* and *YTHDC2,* were also differentially expressed in the myometrium from cases versus controls. We validated decreased total m^{6}A levels and differential expression of m^{6}A methylation regulators using qRT-PCR and tissues available from our biorepository. Possible target genes, including *cadherin 3(CDH)*, *sodium channel β-subunit 4* (*SCN4B)* and *placenta-specific protein 8 (PLAC8),* which are involved in cell adhesion, muscle contraction and immune response in the myometrium of adenomyosis patients were also validate.

CONCLUSIONS: Thus, through extensive public database mining and validation of select genes with qRT-PCR, this study, for the first time, implicates m^{6}A and its methylation regulators in the pathogenesis of adenomyosis. Decreased *METTL3* and total m^{6}A levels in endometrium of adenomyosis patients may contribute to cell proliferation and invasion through *IGF1* and *DDT.* Furthermore, in the myometrium, m^{6}A methylation regulators work as a cluster and play roles in cell adhesion, muscle contraction and immune response. In conclusion, m^{6}A methylation regulators may be involved the pathogenesis of adenomyosis through aberrant expression and actions in both the uterine endometrium and myometrium.

SUPPORT: This research was supported by The NIH Eunice Kennedy Shriver National Institute for Child Health and Human Development P50 HD055764-12,Â National Centers for Translational Research in Reproduction and Infertility Program (LCG), the Kerfuffle Foundation (LCG).

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VARIATION IN THE PERCENTAGE OF ENDOMETRIAL P16-POSITIVE SENESCENT CELLS IN CONSECUTIVE MENSTRUAL CYCLES.

Dimitar Parvanov, PhD, Rumiana Ganeva, MSc, Nina Vidolova, MSc, Georgi Stamenov, MD/PhD. Nadezhda Women's Health Hospital, Sofia, Bulgaria.

OBJECTIVE: Recently, it was found that p16^{ink4a}-positive senescent cells are involved in endometrial receptivity and participate in the acute cellular remodelling at the time of embryo implantation. Our previous research showed that the percentage of glandular p16-positive cells and luminal epithelial p16-positive cells is strongly associated with successful implantation and live births. The aim of the present study was to compare the percentage of p16-positive cells in the glandular and luminal epithelial compartments of the human endometrium during the mid-luteal phase in two consecutive menstrual cycles.

DESIGN: We measured the percentage of p16^{ink4a}-positive cells by immunohistochemistry in endometrial biopsy samples of 94 women in two consecutive menstrual cycles.

MATERIALS AND METHODS: This is a prospective observational study of 94 fertile women who had two endometrial biopsies during the mid-lutheal phase (7 days after LH surge) in two consecutive natural cycles. Patients older than 40 years, with BMI$<$18 kg/m^2 or BMI$\geq$30 kg/m^2, endometriosis, polycystic ovary syndrome (PCOS), endometrial polyps, abnormal uterine development and hydrosalpinx were excluded from the study.

Endometrial biopsies were obtained by pipelle suction and they were immediately fixed in 10% formalin. The endometrial tissue was submitted to paraffin embedding for histological determination and subsequent analysis. Immunohistochemistry (IHC) was performed on the paraffin-embedded sections by Novolink Polymer Detection System (Leica Biosystems, Wetzlar, Hesse, Germany). We used monoclonal antibody against p16^{ink4a} (Master Diagnostica, Granada, Spain) to identify senescent endometrial epithelial cells. The percentage of p16+ cells in each tissue compartment was calculated after enumeration by two independent investigators in multiple endometrial sections. Values were expressed as mean $\pm$ SD. Paired t-test was used to compare the percentage of p16-positive cells between the two time points. $P<0.05$ was considered statistically significant.

RESULTS: The percentage of p16-positive cells in the endometrial glands during the mid-luteal phase of the cycle ranged between 0.12% and 53.22%, while it varied between 1.39% and 85.29% in the luminal epithelium. The temporal change in the percentage of p16-positive cells varied at both time points between 0.55% and 15.56% in the endometrial glands, and between 1.58% and 30.74% in the endometrial luminal epithelium. In addition, for both endometrial glands and luminal epithelium, the proportion of p16+ senescent cells was not significantly different between the two time measurements ($p=0.56$ and $p=0.93$, respectively). In 80% of the patients the difference in the percentage of p16-positive cells at both time points was lower than 20% in the endometrial luminal epithelium and lower than 9% in the luminal epithelium.

CONCLUSIONS: The percentage of endometrial epithelial p16-positive senescent cells is relatively constant in human endometrium during the mid-luteal phase in consecutive menstrual cycles.

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SIRT1 AND PROGESTERONE (P4) RESISTANCE AND ENDOMETRIOSIS: IMPLICATIONS FOR INFERTILITY MANAGEMENT.

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OBJECTIVE: Progesterone (P4) resistance is now considered a central element in endometriosis pathology, but the mechanism and role of P4 resistance in normal uterine function is not understood. SIRT1, an epigenetic regulator that targets key P4-regulated genes, is up-regulated in inflammatory pathologic conditions such as endometriosis, and over-expressed at all stages of the menstrual cycle. We hypothesize that SIRT1 is a central regulator of P4-resistance may also have a role in both normal uterine physiology.

DESIGN: Basic research using the mouse model and immunohistochemistry of human endometrial samples.

MATERIALS AND METHODS: 1) SIRT1 was histologically examined in normal implantation sites in mice during early pregnancy. To investigate the role of SIRT1 in endometrial function and endometriosis, we generated uterine specific *Sirt1* knock-out ($Pgr^{cre/+}Sirt1^{f/f}$) and overexpression ($Pgr^{cre/+}ROSA26^{LSL\text{-}Sirt1}$) mice. 2) The effect of SIRT1 on female fertility was examined in $Pgr^{cre/+}Sirt1^{f/f}$ mice. 3) To assess the effect of SIRT1 over-expression on endometriosis, we surgically induced endometriosis in mice using endometrium from $Pgr^{cre/+}ROSA26^{LSL\text{-}Sirt1}$ and control mice. 4) Treatment with SIRT1 inhibitor EX-527 was used in $Pgr^{cre/+}ROSA26^{LSL\text{-}Sirt1}$ mice. 5) Human endometrium throughout the cycle including menses was immunostained for SIRT1 in control and endometriosis cases.

RESULTS: 1) SIRT1 was expressed in the decidua of pregnant mice only on the day of implantation, day 5.5 of pregnancy. 2) Uterine specific *Sirt1* knock-out mice were infertile and exhibited implantation failure. 3) In the endometriosis mouse model, SIRT1 over-expressing mice have a significantly increased incidence of endometriotic lesions compared to control mice. 4) Infertile SIRT1 over-expressing mice exhibited normal implantation after treatment with EX-527, a SIRT1 inhibitor. In normal human controls ($n = 30$), SIRT1 immunostaining was undetectable during the proliferative and secretory phase endometrium but dramatically elevated only at menses ($p < 0.001$). In endometriosis cases ($n = 39$), SIRT1 was uniformly elevated in both proliferative and secretory phases.

CONCLUSIONS: Together, these results demonstrate that P4-resistance appears to be a natural phenomenon, mediated by SIRT1, and likely required for normal menstruation in women and successful implantation in the mouse. Over-expression of SIRT1 leads to worsening endometriosis and implantation failure in the mouse model which can be rescued by treatment with EX-527. In normal human controls, SIRT1 appears only at menses and may play a role in expediting the transition from secretory to proliferative state at menses. In endometriosis, SIRT1 is pathologically over-expressed in the endometrium and likely contributes to infertility and the pathogenesis of this disease. Timing of SIRT1 expression appears vital for normal physiologic P4-resistance, with functions at menses and implantation, but aberrant expression leads to implantation failure in both mice and humans.

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CONCOMITANT ENDOMETRIOSIS IN PATIENTS UNDERGOING HYSTERECTOMY WITH SUSPECTED ADENOMYOSIS.

Adela G. Cope, MD, Zaraq Khan, MD, Wendaline M. VanBuren, MD, Isabel C. Green, MD, Tatnai L. Burnett, MD. Mayo Clinic, Rochester, MN.

OBJECTIVE: The current study aims to evaluate the prevalence of concomitant endometriosis in patients undergoing laparoscopic hysterectomy (LH) with suspected adenomyosis. Prior studies have estimated this rate to be 11-37.5%[1-3] but have been limited by lack of laparoscopic pelvic assessment or clinical diagnosis of endometriosis without histologic confirmation.

DESIGN: Retrospective case series at an academic medical center.

MATERIALS AND METHODS: Premenopausal women who underwent LH and had suspected adenomyosis by imaging or confirmed by pathology between 10/1/2015-8/31/19 were included. Close peritoneal inspection was performed, and any visible lesions were excised to capture all cases of endometriosis. Descriptive statistics were performed.

RESULTS: A total of 105 patients met inclusion criteria with a mean age of 42.8±5.8 years old. The most common indications for surgical intervention were dysmenorrhea or pelvic pain (n=89, 84.8%) and/or abnormal uterine bleeding (n=87, 82.9%). Of the 68 women with suspected adenomyosis on imaging, 39 were confirmed on pathology (57.3%). Peritoneal lesions were excised in 81 patients (77.1%), with positive pathology for endometriosis in 64 of 81 (79.0%). Concomitant endometriosis was identified in 69% of women with suspected adenomyosis based on preoperative imaging (47 of 68) and 56% of women with confirmed adenomyosis on pathology (42 of 75). In patients with dysmenorrhea or pelvic pain, the rate of concomitant endometriosis was 77.0% (47 of 61) in those with suspected adenomyosis on imaging.

CONCLUSIONS: Endometriosis was found in 77.0% of women with suspected adenomyosis and dysmenorrhea or pelvic pain, suggesting a role for careful examination of the pelvis at hysterectomy in this population. Further confirmation with a larger sample size and pain outcome data would assist with clinical decision making and counseling.

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HEAT SHOCK PROTEIN 90 INHIBITOR 17-AAG SUPPRESSES THE GROWTH OF ENDOMETRIOSIS IN VITRO AND IN VIVO BY INHIBITING ESTROGEN RECEPTOR TRANSCRIPTIONAL ACTIVITY.

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OBJECTIVE: To investigate the effect of HSP90 inhibitor 17–AAG on the growth of endometriosis in vitro and in vivo.

DESIGN: Pharmacologic interventions in human endometriotic stromal cells and in an experimental mouse model of endometriosis.

MATERIALS AND METHODS: Patient recruitment was carried out at the Sixth affiliated Hospital of Sun Yat-sen University from January 2018 to May 2020. Ectopic endometrium (endometriotic tissue, n=15) was collected from patients with ovarian endometriosis undergoing laparoscopy.- Primary cultured human endometriotic stromal cells were prepared. Cells were incubated with 10nM, 100nM, 1μM and 10μM 17-AAG for 24 h. The 3-(4,5-dimethylthiaziazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay, colorimetric 5'-bromo-2'-deoxy-uridine (BrdU) incorporation assay and Caspase-Glo luminescent-based assays were used to test the cell viability, proliferation ability and apoptosis. Transcriptional activity of estrogen receptor (ER) was measured by luciferase activity after transient transfection of an ERE-tk-Luc reporter construct that contained the consensus estrogen-responsive elements (EREs) sequences. Furthermore, we modeled endometriosis in 30 female C57BL6 mice by intraperitoneal injection of allogeneic endometrial fragments. We divided the mice to 10ug/g and 30ug/g 17-AAG group, control group and vehicle group.

RESULTS: 17-AAG inhibited the viability and proliferation of human primary endometriotic stromal cells in a dose-dependent manner from the concentration of 10nM and 100nM 17-AAG respectively. The caspase-3 activities were enhanced significantly in endometriotic stromal cells from 100nM to 10μM 17-AAG treatments. Transcriptional activity of ER were also inhibited significantly by 17-AAG in a dose-dependent way. In mouse model, no obvious weight loss was observed in all groups, and there was no significantly difference in daily weight between those four groups after 30 days of administration. Compared with the model control and vehicle group, the size of ectopic lesions in the treatment group was significantly reduced. The serum TNF-α level was significantly decreased in the treatment group, but there was no statistical difference in the level of serum AMH/E2/P of mice in each group.

CONCLUSIONS: HSP90 inhibitor 17-AAG controls the growth of endometriosis by inhibiting transcriptional activity of ER. HSP90 inhibitor could provide a hopeful way for better understanding of estrogen signaling on the pathogenesis of endometriosis, as well as for potential clinical application on endometriosis pharmacotherapy.

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TOFACITINIB LEADS TO LESION REGRESSION AND ALTERED STAT3 SIGNALING IN ENDOMETRIOSIS. Alexander Kotlyar, MD,[1] Ramanaiah Mamillapalli, PhD,[2] Valerie A. Flores, MD,[3] Hugh S. Taylor, M.D.[2] [1]Yale School of Medicine, Oange, CT; [2]Yale University School of Medicine, New Haven, CT; [3]Yale School of Medicine, New Haven, CT.

OBJECTIVE: We sought to determine if a Janus kinase-inhibitor, Tofacitinib, could affect JAK/STAT signaling in endometriosis and affect lesion size in-vivo.

DESIGN: In-vitro culture and mouse model.

MATERIALS AND METHODS: Gene expression levels in primary cells were assessed by qPCR using primers for HIF1a, and VEGF. Protein expression from in-vitro experiments was performed via western blotting and densitometry. Endometriosis was induced in C57BL/6 mice using heterologous uterine horn transplantation. Lesions were allowed to form over four weeks and Tofacitinib and vehicle were administered via oral gavage at a concentration of 10mg/kg over four weeks.

RESULTS: We first assessed the in-vitro effect of Tofacitinib. This agent reduced HIF1a and VEGF mRNA levels at 12 and 24hrs of treatment. Following 24 hrs of exposure, Tofacitinib effectively reduced STAT3 phosphorylation in Ishikawa cells ($p<0.05$), and patient-derived stromal ($p<0.01$) and epithelial cells ($p<0.01$) from eutopic endometrium. Expression of HIF1a was significantly reduced with Tofacitinib treatment of endometrial stromal and epithelial cells from control patients, but not in patients with endometriosis. Using a mouse model of surgically-induced endometriosis ($n=20$), daily Tofacitinib treatment led to lesion regression ($p<0.01$) and reduced adhesion burden ($p<0.001$).

CONCLUSIONS: This study suggests that inhibition of JAK/STAT signaling using Tofacitinib may be a viable method for the treatment of endometriosis. By reducing STAT3 phosphorylation, lesion size and adhesive disease are both reduced.

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SYMPATHOMIMETIC AMINE TREATMENT VERY EFFECTIVE FOR RELIEVING PELVIC PAIN IN WOMEN EVEN WHEN HORMONAL THERAPY AND SURGERY WERE NOT SUFFICIENT. Paul A. Carpentier, MD, CFCMC,[1] Barbara Meier, BSN,[1] Jerome H. Check, M.D., Ph.D.,[2] Donna Summers, M.S.[3] [1]The Long Island Gianna Center for Women's Health and Fertility, Babylon, NY; [2]Cooper Medical School of Rowan University, Camden, NJ; [3]Cooper Institute for Reproductive Hormonal Disorders, P.C., Mt. Laurel, NJ.

OBJECTIVE: There had been several published case reports finding that treatment with dextroamphetamine sulfate (DS) resulted in considerable improvement of various types of pelvic pain from endometriosis or adenomyosis including dysmenorrhea, dyspareunia, mittelschmerz, vulvodynia, vulvovaginitis, chronic pelvic pain, backaches, and chronic pelvic pain of bladder origin. These reports all seem to come from one treatment center. A search of the literature did not find any published series. The purpose of this study was to corroborate or refute claims that DS can effectively relieve pelvic pain even when conventional medical and/or surgical therapy was not effective. Case reports may establish that a given therapy can be effective but do not provide information as to whether only a minority of women will respond. Thus, the goal of this study was to determine, in a short time period, the likelihood of success.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: Patients complaining of significant pelvic pain were recruited. It was ascertained if they had failed previous medical therapy including NSAIDs, progestin therapy (oral contraceptives, norethindrone, etc.), estrogen suppression with gonadotropin releasing hormone agonists, e.g., leuprolide acetate, or had failed surgical therapy. All had moderate to severe pain. They were prescribed 10 - 30mg extended release dexamphetamine salts qAM providing 12.5 – 37.6mg of dextroamphetamine sulfate. They were re-evaluated in 3 months and questioned as to whether they had 1) marked relief of pain, 2) moderate relief of pain, or 3) little or no relief.

RESULTS: Thirty-one were recruited for the study. Six dropped out for various reasons. 27 of the 31 had been previously unsuccessfully treated with oral contraceptives, progestins, or progesterone, or leuprolide acetate. All 31 had previously used NSAIDs, and 18 had prior surgical therapy. After 3 months of treatment 17 of 25 (68%) reported that the pain was markedly improved. An additional 2 found moderate relief, so that 76% after 3 months on a relatively small dosage of DS had moderate to marked relief of pain.

CONCLUSIONS: In a totally independent treatment center from the one initially reporting this novel therapy for pelvic pain, we were able to corroborate their findings. Moreover, by evaluating a series of patients we ascertained that this treatment works very quickly in the majority of patients despite their failure to improve previously with conventional medical and/or surgical therapy. Increasing the dosage of DS may further improve the pain. The advantage of DS is that it allows a woman to conceive while being treated, in contrast to standard medical therapy. Surgery may diminish ovarian reserve. Future studies should determine if relieving pain, and therefore inflammation, may translate into correcting infertility problems. DS may work by releasing dopamine from sympathetic nerve fibers which in turn, diminishes cellular permeability, thus inhibiting permeation of irritants causing excessive inflammation.

SUPPORT: None

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CHARACTERIZATION OF VAGINAL SECRETION MICROBIOTA IN INFERTILE WOMEN WITH CHRONIC ENDOMETRITIS. Kotaro Kitaya, M.D.,[1] Yoko Nagai, Ph.D.,[2] Suguru E. Tanaka, Ph.D.,[2] Yoshiyuki Sakuraba, Ph.D.,[2] Tomomoto Ishikawa, M.D.[1] [1]Reproduction Clinic Osaka, Osaka, Japan; [2]Varinos Inc., Tokyo, Japan.

OBJECTIVE: Some interventive procedures including hysteroscopy, endometrial biopsy, and endometrial fluid (EF)/tissue aspiration for local microbiota are required for diagnosis of chronic endometritis (CE). In addition, the results of EF/endometrial tissue microbiota do not always reflect the accurate information in the uterine cavity due to inevitable contamination of vaginal microorganisms in the process of trans-vagino-cervical sample collection. The aim of this study is to investigate the feasibility of the vaginal secretion (VS) microbiota as a screening tool for CE.

DESIGN: We diagnosed CE in infertile patients by three methods (i) hysteroscopy, (ii) endometrial biopsy and histopathology/immunohistochemistry, and (iii) VS/EF microbiota analysis using next generation sequencing. The results were compared to characterize the VS microbiota in CE and non-CE patients.

MATERIALS AND METHODS: A total of 123 infertile women were enrolled in the study under written informed consent. Hysteroscopy was performed in the proliferative phase of the menstrual cycle followed by endometrial biopsy. The paired VS/EF samples were obtained in the secretory phase of the same cycle. VS was collected using a sterile swab followed by thorough cleansing/disinfection of vaginal cavity and EF aspiration using a pipette. Hysteroscopic CE was diagnosed according to the criteria proposed by International Working Group for Standardization of CE Diagnosis. Histopathologic CE was diagnosed with immunohistochemistry for a endometrial stromal plasmacyte marker CD138. The VS/EF microbiota was analyzed by pyrosequencing of variable region 4 of bacterial 16S rRNA. The diversity indices were calculated. Fisher's exact, Wilcoxon rank-sum, adjusted Welch's *t* test were used for statistics.

RESULTS: CE was diagnosed in 16.2% of patients (20/123, hysteroscopic CE in eight patients and histopathologic CE in 20 patients).There were no differences in α-diversity (Shannon index, Chao1 richness, and phylogenetic diversity whole tree) and β-diversity (PERMANOVA test) indices between the CE and non-CE group ($p > 0.21$). The detection rate ($p = 0.030$, OR 8.91, 95% CI 1.39- 57.3) and bacterial abundance ($p = 0.0062$) of *Rhodanobacter* in the EF microbiota of the CE group (15.0%, 3/20) was higher than in that of the non-CE group (1.9%, 2/103). Meanwhile, the detection rate ($p = 0.0033$, OR 0.08, 95% CI 0.004-0.52) and bacterial abundance ($p = 0.0073$) of *Streptococcus* in the VS microbiota was significantly lower in the CE group (5.0%, 1/20) than in the non-CE group (38.8%, 40/103). The detection rate ($p = 0.042$) and bacterial abundance ($p = 0.045$) of *Enterococcus* in the VS microbiota was significantly lower in the CE group (0%, 0/20) than in the non-CE group (17.5%, 18/103). By contrast, the detection rate and bacterial abundance of *Lactobacillus* in the EF/VS microbiota was similar between the two groups ($p > 0.19$).

CONCLUSIONS: Our findings suggest that VS microbiota in infertile CE patients is characterized by reduction in the detection rate and bacterial abundance of two lactic acid-producing bacteria *Streptococcus* and *Enterococcus*, but not of *Lactobacillus*.

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BOWEL OCCULT MICROSCOPIC ENDOMETRIOSIS IN RESECTION MARGINS IN DEEP COLORECTAL ENDOMETRIOSIS SPECIMENS HAS NO IMPACT ON THE LONG-TERM RISK OF RECURRENCE. Simone Ferrero, MD, PhD,[1] Umberto Leone Roberti Maggiore, MD, PhD,[2] Ennio Biscaldi, MD,[3] Michele Altieri, MD,[4] Valerio Gaetano Vellone, MD, PhD,[5] Cesare Stabilini, MD, Phd,[6] Fabio Barra, MD[4] [1]DINOGMI, University of Genova, Genova, Italy; [2]Department of Gynecologic Oncology, IRCCS National Cancer Institute, Milan, Italy; [3]Department of Radiology, Galliera Hospital, Genova, Italy; [4]IRCCS Ospedale Policlinico San Martino, Genova, Italy; [5]Anatomic Pathology, Genova, Italy; [6]DISC, University of Genova, Genova, Italy.

OBJECTIVE: The variables influencing the risk of recurrence after segmental resection for rectosigmoid endometriosis are mostly unknown. This study aimed to assess if the risk of recurrence is influenced by the presence of bowel occult microscopic endometriosis (BOME) implants in colorectal resection specimen margins.

DESIGN: Prospective study.

MATERIALS AND METHODS: This study included patients who underwent segmental resection for rectosigmoid endometriosis and had a follow-up of at least 5 years. Every year the patients underwent an assessment of pain (measured on a 10 cm VAS scale), intestinal symptoms (measured on a 10-point Likert scale), gastrointestinal function (measured using the Gastrointestinal Quality of Life Index, GIQLI), and quality of life (assessed using the Endometriosis Health Profile-30, EHP-30). Also, the patients underwent transvaginal ultrasonography to evaluate the presence of deep endometriosis recurrence. Magnetic resonance enema was performed in symptomatic patients with ultrasonographic suspicion of deep endometriosis recurrence. Outcomes were compared between patients with and without BOME implants in colorectal resection specimen margins.

RESULTS: 72 patients were included in the study. 13 patients had BOME implants in colorectal resection specimen margins. Therefore, BOME was found in 18.1% of patients (in one margin in 8 patients and in both margins in 5 patients). Patients with and without BOME implants were similar in demographic and surgical characteristics (length of the rectosigmoid specimen removed, size of the largest intestinal endometriotic nodule, depth of infiltration of endometriosis in the intestinal wall, distance between the lower margin of the lesion and the anal verge, associated deep endometriotic lesions). The median length of follow-up was 9 years (range, 5-14 years); there was no significant difference in the length of follow-up between patients with and without BOME (p=0.282). 67 patients (93.1%) of the patients used some type of hormonal therapies during follow-up. 34 patients (47.2%) conceived during follow-up. No significant difference was observed in pain symptoms, intestinal symptoms, gastrointestinal function, and quality of life between patients with and without BOME. At five-year follow-up, imaging diagnosis of rectosigmoid endometriosis recurrence was observed in 5 patients without BOME implants (8.5%; 95% CI, 2.8%-18.7%) and 2 patients with BOME implants (15.4%; 95% CI, 1.9-45.4%; p=0.580). In 6 out of 7 patients, the diagnosis of rectosigmoid endometriosis recurrence was confirmed by surgery and histology.

CONCLUSIONS: This study suggests that BOME implants do not affect the long-term risk of rectosigmoid endometriosis recurrence. Also, BOME implants do not influence postoperative symptoms. The major limitation of the study is the small sample size. The primary strength of the study is the long-term follow-up.

SUPPORT: None.

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CHRONIC ENDOMETRITIS IN WOMEN WITH SUSPECTED RETAINED PRODUCTS OF CONCEPTION AND THEIR REPRODUCTIVE OUTCOMES. Simone C. Elder, MD, Pietro Bortoletto, MD, Phillip A. Romanski, MD, Steven Spandorfer, MD. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To determine if women who underwent operative hysteroscopy for suspected retained products of conception (rPOC) have histopathologic evidence of chronic endometritis (CE).

DESIGN: Retrospective cohort conducted at a university-affiliated center.

MATERIALS AND METHODS: We identified women who underwent operative hysteroscopy for suspected rPOC. Histopathologic evidence of CE on final surgical pathology was the primary outcome. Secondary outcomes included subsequent pregnancy outcomes following diagnosis, stratified by treatment status.

RESULTS: A total of 111 women were analyzed, of which 26 (23.4%) were diagnosed with CE. Compared to those without CE, women diagnosed with CE had a lower median gravidity (1 vs. 2, p=0.021) and were twice as likely to have undergone a prior operative hysteroscopy (42.3 vs. 18.8 %, p=0.015), with polypectomy (54.6%) being the most common indication. Of those diagnosed with CE, 84.6% were also diagnosed with retained products of conception compared to 75.3% without CE (p=0.32). Of the 111 patients, subsequent pregnancy data was available for 63 of them. There was no difference in pregnancy rate (61.5 vs 54%, p=0.626) between those with and without CE. Once pregnant, miscarriage (37.5 vs 25.9%, p=0.524) and live birth rates (50 vs. 55.6%, p=0.782) were similar between groups. Women with CE received antibiotic treatment 57.7% of the time, the most common being doxycycline (42.3%). Five women underwent repeat endometrial sampling after antibiotic treatment, only 1 of which had persistent CE. Of the women with CE who were treated with antibiotics (n=10), 8 became pregnant and 4 had a live birth. There were patients with CE who were not treated with antibiotics, none of which became pregnant.

CONCLUSIONS: Nearly 1 in 4 women undergoing hysteroscopy for rPOC were incidentally diagnosed with CE. The role of CE as a causative agent for retained products versus a response to the pregnancy loss is not clear. In this cohort, a diagnosis of CE did not negatively impact subsequent reproductive outcomes.

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WITHDRAWN

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ALTERED EXPRESSION OF ATP-MEDIATED PURINERGIC SIGNALING PATHWAYS IN MACAQUES WITH ENDOMETRIOSIS. Fangzhou Luo, BS,[1] Ov D. Slayden, PhD[2] [1]Oregon National Primate Research Center, Beaverton, OR; [2]Professor, Beaverton, OR.

OBJECTIVE: To assess the expression of nucleotide-converting and purine-converting enzymes Adenylate Kinase 1 (ADK1), Adenylate Kinase 2 (ADK2), and ectonucleotidase CD73 in the endometrium and endometriotic lesions of rhesus macaques.

DESIGN: Real-time PCR and immunohistochemical analysis of macaques with endometriosis.

MATERIALS AND METHODS: We compared endometrium from endometriosis-free rhesus macaques (*Macaca mulatta*) with "eutopic" endometrium and "ectopic" endometriotic lesions from monkeys with endometriosis. Samples were examined from the proliferative and secretory phases of the menstrual cycle (n=5/group). Transcript expression of ADK1, ADK2, and CD73 was assayed by q-RT-PCR carried out on an ABI7900HT FAST Real-Time PCR System normalized to S10 RNA. Samples were fixed, embedded in paraffin and 5μm sections were subjected to IHC with antibodies targeting ADK1 (Invitrogen 15485), ADK2 (Invitrogen 29365), and CD73 (Abcam 175396).

RESULTS: IHC showed strong cytoplasmic ADK1 staining in the epithelium and the stroma in diseased endometrium, and very strong cytoplasmic staining in both cell types in the lesion. ADK1 transcript was found unregulated in the proliferative phase in both endometrium and endometriosis. ADK2 localized to both the epithelium and the stroma in healthy tissue in both proliferative and secretory phase. In endometriosis, secretory eutopic endometrium showed weak staining. In the lesion, strong ADK2 staining was seen in the epithelial cells in both menstrual stages. A significantly higher level of ADK2 transcript was shown at eutopic site at proliferative stage when compared with the secretory counterpart. A significant decrease was noted in the diseased secretory endometrium compared with healthy secretory endometrium. CD73 localized to epithelial, stromal and endothelial cells in healthy endometrium. Weaker staining was seen in the secretory eutopic and ectopic tissues. In the diseased endometrium, CD73 staining was negligible to none in the epithelium. In the lesion, epithelial staining of CD73 was completely lost. A significant decrease in CD73 transcript was seen in the eutopic secretory endometrium.

CONCLUSIONS: The glycolytic phenotype and insulin resistance (previously found in our studies), combined with altered expression of AK1, ADK2 and CD73 may contribute to inflammation associated with endometriosis.

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A PROSPECTIVE STUDY TO EVALUATE THE USE OF BOWEL PREPARATION BEFORE THREE-DIMENSIONAL RECTAL WATER CONTRAST TRANSVAGINAL ULTRASONOGRAPHY FOR DIAGNOSING RECTOSIGMOID ENDOMETRIOSIS. Fabio Barra, MD,[1] Matteo Tantari, MD,[1] Giulio Evangelisti, MD,[1] Carolina Scala, MD,[2] Simone Ferrero, MD PhD[1] [1]IRCCS Ospedale Policlinico San Martino, Genova, Italy; [2]Istituto G. Gaslini, Genova, Italy.

OBJECTIVE: To evaluate the impact of bowel preparation on the diagnostic parameters of three-dimensional rectal water-contrast transvaginal ultrasonography (3D-RWC-TVS) in women with suspicion of rectosigmoid endometriosis.

DESIGN: This was a single-center prospective comparative pilot study.

MATERIALS AND METHODS: Women referred to our institution for the suspicion of rectosigmoid endometriosis between January 2018 to December 2019 were included. Patients underwent 3D-RWC-TVS with and without bowel preparation within an interval of 1-8 weeks. Bowel preparation consisted in a low-residue diet given in the two days before the ultrasonographic exam and a rectal enema administered a few hours before it. During the two RWC-TVS, acquisitions of images by 3D rendering were made in the sagittal and coronal planes. After storing data file, the two exams were separately analyzed offline by two experienced sonographers, blinded to the results of bidimensional RWC-TVS. The findings of 3D-RWC-TVS with and without bowel preparation were compared with surgical and histological results.

RESULTS: Overall, 31 out of 51 patients (60.8%) had rectosigmoid endometriosis at surgery; 13 women underwent segmental bowel resection, 6 discoid resection, and 12 rectal shaving. 3D-RWC-TVS without previous bowel preparation had a significantly lower performance for diagnosing the presence of rectosigmoid endometriosis than 3D-RWC-TVS with bowel preparation (p=0.046). The sensitivity (SE), specificity (SP), positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+) and negative likelihood ratio (LR-) of 3D-RWC-TVS with bowel preparation were 87.1% (95% CI, 70.2-96.4%), 90.0% (68.3-98.8%), 93.1% (78.3-98.1%), 81.8% (64.1-91.9%), 8.7 (2.3-32.6) and 0.1 (0.1-0.4). The SE, SP, PPV, NPV, LR+ and LR- of 3D-RWC-TVS without bowel preparation were 71.0% (52.0-85.8%), 70.0% (45.7-88.1%), 78.8% (64.4-88.1%), 60.1% (45.5-74.3%), 2.4 (1.2-4.8) and 0.4 (0.2-0.8); 3D-RWC-TVS with bowel preparation described more accurately largest diameter and volume of rectosigmoid nodules (p<0.001 and p<0.001). There was no significant difference in diagnosing the presence of multifocal disease between the two exams (p=0.69).

CONCLUSIONS: Before performing 3D-RWC-TVS, bowel preparation may be necessary in order to avoid presence of feces, which may negatively impact the visualization of endometriotic rectosigmoid nodules.

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A NOVEL LOW-DOSE COMBINATION DRUG THERAPY FOR ENDOMETRIOSIS THAT INCREASES PROGESTERONE RECEPTOR TO ENHANCE PROGESTIN EFFICACY. Elliott G. Richards, MD, Emily L. Esakov, PhD, Ofer Reizes, PhD. Cleveland Clinic Foundation, Cleveland, OH.

	No Endometriosis			Endometriosis					
				Endometrium			Lesion		
	Prol.	Sec.	*P*	Prol.	Sec.	*P*<	Prol.	Sec.	*P*<
ADK1	1.1±0.1 **[++]**	0.6±0.1 **[++]**	ns	1.2±0.2 **[+++]**	0.4±0.1 **[++]**	0.01	2.2±0.2 **[++++]**	0.9±0.29 **[++]**	0.01
ADK2	1.0±0.1 **[++]**	1.1±0.1 **[+++]**	ns	1.2±0.1 **[+++]**	0.6±0.15 **[++]**	0.01	1.4±0.3 **[+++]**	1.2±0.3 **[+++]**	ns
CD73	0.2±0.8 **[++]**	3.0±1.4 **[+++]**	ns	0.12±0.06 **[++]**	0.4±0.1 **[+]**	ns	1.56±1.46 **[++]**	0.98±0.8 **[+]**	ns

OBJECTIVE: Endometriosis is an estrogen-dependent disease that is a leading cause of pelvic pain and infertility worldwide. While ectopic endometrial tissue should theoretically regress with progesterone treatment, resistance to progesterone is common, limiting the effectiveness of hormonal therapies to treat established disease and to prevent post-surgical disease recurrence. We sought to apply a quality-by-design (QbD) approach to develop a novel sensitizing therapy for endometriosis by targeting progesterone receptor (PR) expression.

DESIGN: Our group has previously successfully utilized a QbD approach to develop a novel combination of clinical compounds to induce estrogen receptor alpha (ESR1) in hormone-positive breast cancer cells to sensitize them to tamoxifen therapy; similar to endometriosis, many types of breast cancer are resistant to hormonal therapies. This QbD approach leverages advanced automation technology and predictive mathematical modeling to investigate the additive and synergistic effects of combinatorial drug treatment on gene expression in immortalized cell lines.

MATERIALS AND METHODS: We selected 12 different compounds that are either known to be involved in sex hormone signaling, used in the treatment of endometrioid ovarian cancer (arising from endometriosis), and/or currently used or under investigation for the treatment of endometriosis. Using our custom-design QbD platform, we measured the relative effects of these compounds, each at concentrations well below their efficacious dose, on a variety of genes in 12Z cells (an immortalized endometriotic cell line).

RESULTS: We identified five drugs (belinostat, celecoxib, everolimus, bentamapimod, and paclitaxel) that in combination have a synergistic effect on PR expression. *In vitro* studies confirmed elevated PR expression in both RNA and protein. After three days of drug treatment on 12Z cells compared to controls, combinatorial drug treatment resulted in a 8.8 fold increase in PR expression levels with no change in ESR1 levels.

CONCLUSIONS: This work offers a novel combinatorial drug therapy and proof-of-concept for endometriosis treatment. It also provides new insight into the mechanisms by which known endometriosis drugs reduce disease burden. Efforts are underway to utilize a mouse model of endometriosis to determine whether this drug cocktail can enhance PR expression and thereby efficacy of progestin therapy. Future work will involve determining the precise molecular pathways by which these drugs act to enhance PR expression.

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INVESTIGATING THE ROLE OF INFERTILITY IN ENDOMETRIOSIS RISK.

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OBJECTIVE: The goal of this study was to provide evidence that the risk of endometriosis is elevated in the presence of other symptoms even when infertility is absent or unknown.

DESIGN: We used electronic health record data from the University of Utah Healthcare enterprise data warehouse (EDW) in a retrospective study. A Bayesian network was developed to calculate the risk of having endometriosis, given the presence of specific comorbidities.

MATERIALS AND METHODS: From the EDW data, International Classification of Diseases, (ICD-10) codes, were used to identify patient conditions. Due to the long diagnostic delay of endometriosis, we included all conditions regardless of temporality. ICD codes most associated with endometriosis in the data and supported by the literature were selected as nodes in the Bayesian network.

The structure and probabilities of the network were learned from the data. Each node of the network represented a condition that could be present, absent, or unknown. Based on the learned conditional probabilities in the network, we calculated an absolute risk (AR) and relative risk ratio (RR) for endometriosis. While the AR indicates the probability of a person having endometriosis, the RR reflects how many times more at risk the patient is compared to the population average.

RESULTS: Data from over 1.6 million patients was included in the analysis with 7785 patients diagnosed with endometriosis. The selected conditions were infertility, dysmenorrhea, pelvic pain, dyspareunia, uterine fibroids, endometrial polyps, pelvic inflammatory disease (PID), irregular menstruation, cervical cancer, abdominal pain, and anxiety disorders. Dysmenorrhea resulted in the highest risk when infertility was absent or unknown.

TABLE. Selected results for relative risk ratio of endometriosis.

Condition Present	Infertility Present	Fertility Unknown	Infertility Absent
Dysmenorrhea	59.6 ± 4.34	50.5 ± 4.64	49.6 ± 3.82
Irregular menstruation	35.9 ± 7.92	49.1 ± 4.92	47.7 ± 3.36
Pelvic pain	75.7 ± 2.34	47.2 ± 3.93	44.8 ± 3.16
PID	76.8 ± 7.99	42.0 ± 3.30	37.8 ± 4.65
Uterine fibroids	51.0 ± 10.3	38.1 ± 9.85	36.8 ± 9.95
Dyspareunia	57.9 ± 4.69	32.1 ± 2.64	29.6 ± 2.07

CONCLUSIONS: Previous studies have supported an association between endometriosis and infertility. Indeed, it is a driving factor in the diagnosis of endometriosis. There is a significant diagnostic delay for endometriosis patients; however, those with infertility have less diagnostic delay. We found the risk for having endometriosis is significantly elevated when other comorbidities are present even when infertility is absent. This study provides evidence that symptomatic patients should be evaluated for endometriosis even when the patient is fertile or the fertility status of the patient is unknown.

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IMPACT OF ENDOMETRIOSIS ON SEXUAL LIFE OF WOMEN AND PARTNERS: RESULTS FROM THE ENDOVIE SURVEY.

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OBJECTIVE: Endometriosis affects mostly young, sexually active women during different phases of their sexual life. Symptoms include painful periods, pelvic pain, chronic fatigue and dyspareunia that can lead to negative impact on their sexuality. The objective of this study was to evaluate the

impact of endometriosis on couple's sexual life among women with the condition and their partners.

DESIGN: A prospective cross-sectional web-based survey.

MATERIALS AND METHODS: An online survey was conducted in women suffering from endometriosis from January 15th to February 3rd, 2020. The sample population of women with endometriosis was targeted and investigated through the Ipsos Access Panel that gathers data from 235,171 French subjects (n=803) and EndoFrance, a French non-profit organization for endometriosis (=754). Another online survey was conducted among 100 partners of women with endometriosis throughout the Ipsos AccessPanel. The 2 questionnaires were constructed with the directing committee of the study and aimed to assess experience and perceptions with endometriosis, including the impact of the condition on affective and sexual life as evaluated on a scale of 0 to 10 (0 for very low impact to 10 for very high impact).

RESULTS: The main survey included 1,557 women (33% deep endometriosis, 22% endometrioma, 13% superficial endometriosis). Their average age was 42.2±12.8 years and 70% were in a relationship. The disease had started at an average age of 23.8±10.2 years old. Among first symptoms, 78% experienced painful periods, 66% pelvic pain, 54% chronic fatigue and 50% dyspareunia. Sexual life was the main impacted area of women's lives with an impact rated 5.5±3.5 out of 10; in 48% of the cases the impact was severe ($\geq$ 7). Furthermore, 71% were often/very often confronted with decrease in libido and 58% refrained often/very often from having sexual intercourse for several weeks or even months. The average rating of women for the impact of endometriosis on couple's life was 4.9±3.4 out of 10 and 38% rated scores $\geq$ 7. 568 women (37%) faced often/very often reproaches from their partner concerning their complaints related to their endometriosis and 28% of women report that their partners blame them for not being able to have children. Moreover, 25% of the women felt often/very often the desire to separate from their spouse. Among the 100 partners (92 men and 8 women) surveyed, the impact of endometriosis on sexual life was rated 4.2±3.2 out of 10. Being afraid of hurting their partner during sexual intercourse, having refrained from having sexual intercourse, and being faced with decreased libido were situations often/very often reported by 49%, 24% and 18% of partners, respectively. The impact of endometriosis on their couple's life was rated 3.6±2.8 out of 10.

CONCLUSIONS: The study provided evidence that endometriosis has a main impact on sexual and couple's life in women with the condition but also, although lower, among the partners. Health professionals should consider this important aspect of couples' lives to improve the quality of life of women suffering from endometriosis and that of their partners.

SUPPORT: Financial support of the ENDOVIE survey was provided by Gedeon Richter France.

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FREQUENCY OF AND SWITCHING BETWEEN HORMONAL CONTRACEPTIVES IN WOMEN WITH ENDOMETRIOSIS UP TO 8 YEARS BEFORE DIAGNOSIS.

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OBJECTIVE: Combined estrogen-progestin oral contraceptives (COC) is one of the first-line treatment options for endometriosis, despite limited evidence of efficacy in all types of endometriosis-associated pain. In a small online survey of women with diagnosed endometriosis (N=441; mean age 28), 40% of women had been prescribed 3 or more COCs for relief of endometriosis-associated pain. This may be due to clinician's lack of understanding of effectiveness of COCs in the different types of endometriosis-associated pain, inappropriate application of the "OC failure" concept and the lack of implementation of goal oriented, time bound treatment plans. We aimed to characterize the frequency of and switching between types of COCs and other hormonal contraceptives (HC) within a real-world population of women with endometriosis. Given the well documented multi-year delay between symptom onset and surgical diagnosis, we focused on the 8 years prior to endometriosis diagnosis.

DESIGN: Longitudinal descriptive analysis within an electronic medical records (EMR) database (Optum, 2007-2019).

MATERIALS AND METHODS: We identified 20,179 women with incident endometriosis, defined by ICD code in the medical record, and 8+ years of activity in the EMR system prior to diagnosis. We included 44 individual HC types (mono-, bi-, tri-, quadphasic and extended cycle COCs, progestin only pills, IUDs, implants, injections, rings and patches) captured through written prescriptions, which capture the clinician's "intention to treat". Analyses were stratified by the presence of most common endometriosis-associated pain symptoms, defined by ICD diagnosis code for dysmenorrhea, dyspareunia and pelvic pain.

RESULTS: Mean age at diagnosis was 47 years (5% <25, 17% 25-34, 78% 35+ years) and 71% had presence of pain. Overall, 6180 (31%) women were prescribed at least 1 HC during the 8 years before diagnosis, with a mean of 1.8 (SD: 1.1) types. The frequency of any HC use was higher in women with pain (37.2%) than in women without (14.5%) and in women diagnosed at younger ages (71% in women <25, 58% in women 25-34 and 22% in women 35+ years). The most commonly prescribed HC were monophasic COCs [10 mcg ethinyl estradiol & 1 mg norethindrone (20%); 20 mcg ethinyl estradiol & 0.1 mg levonorgestrel (12%); 35 mcg ethinyl estradiol & 1 mg norethindrone (13%); 35 mcg ethinyl estradiol & 0.25 mg norgestimate (26%)], progestin-IUDs (Mirena; 17%), progestin-only pills (15%) and injections (depoprovera; 18%). Among HC users, 19% of women used $\geq$3 types of HCs (21% of women with pain, 11% of women without) and 7% of women used $\geq$4 types (8% of women with pain, 2% of women without).

CONCLUSIONS: Over 8 years prior to diagnosis, 31% of women with endometriosis used at least 1 HC within the 8 years prior to diagnosis, and this was more common in women with pain symptoms and in women diagnosed at younger ages. Switching between HC types was less frequent than in previous studies, which may be explained by the older age at diagnosis in this real-world data source. Better understanding and implementation of the OC failure concept and goal-oriented time bound approaches are needed.

SUPPORT: The study was funded by AbbVie

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DOES GNRH DOWN REGULATION AMONGST WOMEN WITH ABNORMAL BCL6 AND/OR BETA 3 INTEGRIN EXPRESSION IMPROVE IMPLANTATION RATES? AN INTERIM ANALYSIS.

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OBJECTIVE: Does GnRH agonist treatment in patients with abnormal expression of BCL6 and/or beta 3 integrin restore implantation rates to a comparative level with those patients without known endometrial receptivity abnormalities?

DESIGN: A single-institutional, retrospective convenience cohort analysis of 44 patients with recurrent implantation failure was performed comparing patients with abnormal expression of BCL6 and/or beta 3 integrin treated to GnRH agonist therapy versus 39 patients with tubal factor infertility in 2019.

MATERIALS AND METHODS: Patients were identified using CPT diagnostic/billing codes. A manual review of electronic medical records was used to screen for patients that met the inclusion criteria. PC SAS version 9.4 was used for analyses. The statistical level of significance was set to 0.05. The nonparametric Mann-Whitney test was used to compare GnRH agonist versus tubal factor for continuous variables. Fisher's exact tests were used to make comparisons on categorical variables.

RESULTS: After accounting for age, BMI, gravity, parity (p-values of 0.72, 0.59, 0.94, and 0.74 respectively) the only significant descriptive characteristic identified was prior ART (0.003) skewed towards prior treatment in those patients with recurrent implantation failure. Of the 44 patients identified to have recurrent implantation failure, 25 underwent GnRH agonist therapy and subsequent embryo transfer. Of these patients, 21 had successful implantation defined as a positive beta-HCG. Thirty-nine patients were identified to have tubal factor infertility. Within this cohort, 15 underwent embryo transfer resulting in 12 successful implantations.

TABLE 1.

Outcome	Recurrent implantation failure N=25	Tubal factor N=15	P-value
Positive beta-hCG	21 (84%)	12 (80%)	0.9569
Live birth	5 (20%)	7 (47%)	
Currently pregnant (>10wk GA)	8 (32%)	2 (13%)	
SAB	1 (4%)	1 (7%)	
Biochemical pregnancy	4 (16%)	2 (13%)	
Negative beta-hCG	4 (16%)	3 (20%)	

CONCLUSIONS: Endometriosis affects 20-40% of women with infertility and is known to decrease fecundity by approximately 50%. There is a high correlation between elevations of BCL6 and inadequate secretion of beta 3 integrin and a concurrent diagnosis of endometriosis. Further, research has shown that patients with abnormal BCL6 and beta 3 integrin expression have approximately an 18% pregnancy rate in their next transfer attempt versus 70% pregnancy rate in those patients with normal expression.

Our preliminary data suggests that GnRH agonist treatment in patients with abnormal expression of BCL6 and/or beta 3 integrin restores implantation rates to a comparative level with those patients without known endometrial receptivity abnormalities.

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SUPPORT: None

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PERSISTENCE OF RECTAL ENDOMETRIOSIS FOLLOWING LAPAROSCOPIC SHAVING OF RECTOVAGINAL NODULES INFILTRATING THE RECTUM.

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OBJECTIVE: While recurrence of deep endometriosis after shaving of rectovaginal endometriosis has been extensively studied, no data exists on the postoperative persistence of rectal endometriosis. The objective of this study was to assess the risk of rectal endometriosis persistence following laparoscopic shaving of rectovaginal nodules.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: This study included patients who underwent shaving for rectovaginal nodules infiltrating the rectum. During surgery, the pararectal spaces were longitudinally opened to avoid injury of the hypogastric and splanchnic nerves. The diseased rectum was mobilized. The endometriotic nodule was excised by shaving using cold scissors, electrosurgery or the Harmonic scalpel device (Ethicon Endo-Surgery). At 3- and 6-month from surgery, the presence of persistent endometriosis was assessed by rectal-water contrast transvaginal ultrasonography (RWC-TVS). At each follow-up, the patients were asked to rate the satisfaction with treatment that was assessed according to a five-category scale (very satisfied, satisfied, neither satisfied nor dissatisfied, dissatisfied, very dissatisfied). Variations in pain symptoms were assessed using a 10 cm visual analogue scale. Changes in intestinal symptoms were measured using a 0-10-point numeric rating scale.

RESULTS: 96 patients were included in the study. At 3-month follow-up, persistence of rectal endometriosis was observed in 4 patients (4.2%; 95% CI, 1.1%-10.3). The nodules were observed in the area where the rectal shaving was performed; hyperechogenicity of the intestinal wall was observed and, in two patients, it was possible to observe the suture performed after shaving. The mean (± SD) diameter of the persistent rectal endometriotic nodule detected at ultrasonography was 8.7 ± 2.1 mm; its mean (± SD) volume assessed by virtual organ computer-aided analysis was 184.8 (± 117.6) mm^3. Pain and intestinal symptoms were significantly improved by surgery. 29 patients (30.2%) were very satisfied, 52 were satisfied (54.2%), 14 were neither satisfied nor dissatisfied (14.6%), and 1 patient was dissatisfied (1.0%). Among the patients with persistence of endometriosis, three were satisfied and one patient was neither satisfied nor dissatisfied. The 6-month follow-up confirmed the persistence of rectal endometriosis in the 4 patients. The mean diameter of the persistent endometriotic nodule detected at ultrasonography was 8.3 ± 1.5 mm. Concerning the satisfaction with the treatment, 34 patients (35.4%) were very satisfied, 56 were satisfied (58.3%), 5 were neither satisfied nor dissatisfied (5.2%), and 1 patient was dissatisfied (1.0%).

CONCLUSIONS: Persistence of small ultrasonographically detectable rectal endometriotic lesions occurs in approximately 4% of patients undergoing laparoscopic shaving of rectovaginal nodules infiltrating the rectum. Although these patients have significant improvement in pain and intestinal symptoms, their long-term follow-up is required to establish the clinical relevance of persisting rectal endometriosis.

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EVALUATION OF ENDOMETRIOMA PATHOPHYSIOLOGY AND RELATED OVARIAN DAMAGE BY PTEN / AKT APOPTOSIS SIGNALING PATHWAY.

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OBJECTIVE: To investigate the role and significance of PTEN/AKT apoptosis signaling pathway in the occurrence and changes in ovarian reserve for patients with endometriosis in the manner of ovarian reserve markers.

DESIGN: Prospective Cohort Study.

MATERIALS AND METHODS: This prospective study was conducted at a tertiary University Hospital between May 2019 and April 2020. Patients between 18-38 years old, who underwent cystectomy for benign ovarian pathologies were included in the study. Patients were divided into two groups according to their ovarian pathologies, respectively; endometrioma and the other benign cysts (control). Tissue samples were collected from the cyst wall right after the surgery, and gene expression of PTEN/AKT for the tissue samples were interpreted with real-time PCR analyses. Gene expressions of two groups were compared. Additionally, PTEN/AKT expressions were evaluated between patients with diminished and normal ovarian reserve markers (evaluated with serum Anti-mullerian hormone (AMH) levels and antral follicle counts) for all samples.

RESULTS: A total of 40 age matched patients with endometrioma (n=20), and with the other benign ovarian cysts (dermoid, serous, mucinous, hemorrhagic cyst). (n=20) were included for tissue sample evaluation. The mean (SD) age was 31.1 (±5,8) and 31.2 (±6,0) years in endometrioma and other cyst groups respectively (p:0,937). The mean antral follicle count of the endometrioma group was significantly lower than the control group. (p:0,028). In the Endometrioma group, PTEN expression ratio was higher 1,69-fold than the other group with no statistical significance. For AKT gene expression there was a significant 5,99-fold increase in the endometrioma group ($p<0.01$). When patients totally were divided by diminished versus normal ovarian reserve, the PTEN expression ratio of patients with diminished ovarian reserve was 4,92-fold lower than the normal ovarian reserve group ($p<0.01$) PTEN expression showed a positive correlation with serum AMH levels overall. ($r:0.48$, $p<0.01$).

CONCLUSIONS: The alteration of PTEN expression may be a vital part of the pathological and physiological mechanisms in endometriosis and related diminished ovarian reserve. However, the potential mechanisms underlying abnormal expression the pathway and its role have not been thoroughly elucidated. In this study, AKT expression was found higher in the endometrioma group. Meanwhile, PTEN expression was lower for DOR patients overall. Our results suggest that these expression alterations for the PTEN/AKT apoptosis signaling pathway should be considered for further investigation for the prevention of endometriomas and related ovarian damage.

SUPPORT: None.

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PAIN AND HEALTH RELATED QUALITY OF LIFE IN WOMEN WITH ENDOMETRIOSIS SCHEDULED FOR IN-VITRO-FERTILIZATION (IVF).

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OBJECTIVE: This study aimed to compare health related quality of life (HRQOL) and pain scores between women with endometriosis and disease-free women undergoing IVF.

DESIGN: Prospective observational cohort study.

MATERIALS AND METHODS: Infertile women scheduled for IVF who attended a tertiary assisted conception unit from January 2017 to June 2019 were counseled to complete RAND SF-36 (HRQOL) questionnaire and Visual analogue scale (VAS) for painful symptoms related to dysmenorrhea, dyspareunia and non-cyclic chronic pelvic pain. Participants were counseled to complete the questionnaires in their baseline visit, prior to enrollment in IVF work up. HRQOL questionnaire is an instrument that comprised 8 sub-scales and 2 major component scores; physical (PCS) and mental (MCS) component scores. Consented women were categorized into 2 groups based on endometriosis disease status. Group 1 comprised women with endometriosis, while group 2 included women without evidence of endometriosis (reference group). The HRQOL and VAS scores were compared between the 2 groups at baseline. Comparisons between groups were evaluated utilizing the t-test, Wilcoxon rank sum test, chi-square test and regression analysis as appropriate.

RESULTS: Among 640 women indicated for IVF and screened, only 224 subjects consented to complete the questionnaires. Out of the consented IVF women, 65 subjects (29%) have evidence of endometriosis and were allocated to group 1. Groups 1 and 2 were comparable in age, BMI, duration of infertility, and prior IVF trials. Moreover, group 1 women were more likely to have a surgery/laparoscopy than group 2 (97% vs 66.6%, $p<0.003$). There was a significant trend for lower scores among the 8 subscales of HRQOL in group 1 compared to group 2 ($p<0.001$).
Endometriosis women had significant lower MCS and PCS compared to women without endometriosis (median (IQR);53(18.9)vs.61.3(19.2), $p<0.001$; 50.6(24.4)vs.67.5(23.8),$p<0.001$, respectively). The median of VAS scores for painful symptoms was higher in the endometriosis group ($p<0.001$). The highest scores were reported for dysmenorrhea in endometriosis women compared to the reference group (median (IQR) 8(3) vs.5(3),$p<0.001$). In addition, subgroup analysis according to endometriosis stage demonstrated comparable baseline pain and HRQOL scores between women (n=41, 63.1%) with minimal and mild endometriosis, and women (n=24,36.9%) with moderate and severe disease. Utilizing stepwise multivariable regression analysis, dysmenorrhea was the only painful symptom that was associated with low MCS and PCS (aOR = 1.3,95%CI=1.1 -1.5,$P<0.009$; aOR = 1.3,95%CI=1.1 -1.6,$P<0.005$).

CONCLUSIONS: IVF women with endometriosis have higher baseline pain scores and lower quality of life compared to their disease-free counterparts.

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IMPACT OF ENDOMETRIOSIS ON PARTNER'S DAILY LIFE : RESULTS FROM THE ENDOVIE SURVEY.

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OBJECTIVE: Endometriosis is a chronic condition which has been shown to negatively impact women's quality of life and may strain couple intimacy. There is scarce evidence about the impact of endometriosis on partners. The objective of this study was to collect perceptions and experiences concerning endometriosis in partners of women suffering from endometriosis.

DESIGN: A prospective cross-sectional web-based survey.

MATERIALS AND METHODS: An online survey was conducted in partners of women suffering from endometriosis from January 21st to 28th, 2020. The investigated sample group (n=100) was taken from a targeted population among the Ipsos Access panel that gathers data from 235,171 French subjects. The 21-point questionnaire was constructed by the directing committee of the study and aimed to assess the impact of endometriosis on partner well-being and daily life, evaluated on a scale of 0 to 10 (0 for very low impact to 10 for very high impact).

RESULTS: The survey included 92 men and 8 women, all partners of a woman suffering from endometriosis. Most of them (78%) were at least 45 years old and had been in the relationship for over 13 years (63%). For 75%, the diagnosis of the partner's endometriosis was made after the start of the relationship. Upon diagnosis of endometriosis, the dominant feelings in partners were concern, understanding and compassion but 17% also reported negative feelings such as embarrassment or disgust. Half of them considered that, for their partner, they were the only person that they could count on but 40% reported also having had negative feelings towards their partner.

The average rating for impact of endometriosis on sexual and couple's life were 4.2±3.2 and 3.6±2.8 out of 10, respectively. Furthermore, 49% declared being often/very often afraid of hurting their partner during sexual intercourse, 44% were confronted with a decrease in their partner's libido and 18% with their own decrease in libido. 24% reported having often/very often refrained from having sexual intercourse, and 15% abstained from planning to have a child. The psychological impact, the impact on leisure and on relationships with friends and family were less significant with an average rating of 3.3±2.2, 2.7±2.8 and 2.0±2.5 out of 10 respectively. Endometriosis also had an impact on partner's emotions with 26% reporting that they often/very often did not understand the expectations of their partners during pain associated with endometriosis and 19% feeling guilty about blaming their partner. Within the couple, 21% considered that endometriosis was taboo, the subject was raised less than once a month by 43% of couples, or even never for 8%.

CONCLUSIONS: This study provides new insights concerning impact of endometriosis on partners of women who suffer from this disease and demonstrate that endometriosis has a significant effect on their sexual and couple's life. This study highlights the need of greater awareness on partner impact of endometriosis and the importance of counseling both partners in the management of endometriosis.

SUPPORT: Financial support of the ENDOVIE survey was provided by Gedeon Richter France.

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ENDOMETRIAL STAINING FOR CD138 AS A MARKER OF CHRONIC ENDOMETRITIS DOES NOT PREDICT FAILED IMPLANTATION.

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OBJECTIVE: Chronic endometritis, diagnosed by endometrial biopsy and analysis for plasma cells, has been implicated as a cause of implantation failure. Staining for CD138, an antigen specific to plasma cells, is the current standard for diagnosis. Previous studies examining chronic endometritis and pregnancy outcomes included patients treated with antibiotics prior to transfer and those who transferred embryos of unknown ploidy status. The aim of this study was to examine the prevalence of plasma cells in patients who underwent endometrial biopsy with no subsequent intervention prior to euploid single embryo transfer (SET) to determine if the presence of plasma cells predicts failed implantation.

DESIGN: Case-control study.

MATERIALS AND METHODS: Endometrial biopsies were obtained from patients undergoing IVF at the time of retrieval. Paraffin embedded endometrial sections were stained using mouse mono-clonal antibody for CD138 (B-A38, Sigma), with tonsil tissue known to contain plasma cells serving as a positive control. Two independent reviewers examined five randomly selected HPFs in each sample, and the results were averaged. Patients underwent euploid SET in a subsequent cycle. Sustained implantation (SI) was defined as fetal heartbeat at discharge. Logistic regression was used to determine if there were significant differences in implantation rates based on presence or absence of CD138.

RESULTS: Fifty-six patients were included, n=28 with SI and n=28 with failed implantation (Table 1). Patient age, baseline AMH and FSH, BMI, day of blastulation and embryo morphology were not significantly different between groups. There was no difference in mean number of plasma cells/HPF between those who sustained implantation and those who did not. Only a minority of samples demonstrated $\geq$ 1 plasma cell per HPF.

CONCLUSIONS: The majority of patients who underwent CD138 staining for plasma cells exhibited at least one plasma cell in five randomly selected HPFs, indicating that some plasma cells are present in women with normal endometrial receptivity. Further analysis is needed to determine what, if any, threshold of plasma cells is associated with decreased implantation.

TABLE 1. Comparison of age, ovarian reserve, embryo quality, and prevalence of plasma cells between patients with and without SI.

	No implantation (n= 28)	Sustained implantation (n=28)	p value
AGE (mean, SD)	34.1 ± 3.8	33.9 ± 4.2	NS
Day 3 FSH (mean, SD)	7.2 ± 1.6	6.7 ± 1.8	
AMH (mean, SD)	3.7 ± 2.1	4.7 ± 3.5	
BMI (mean, SD)	26.0 ± 4.6	26.5 ± 4.4	
Day 5, 6, 7 Blasts	36%, 53%, 11%	36%, 61%, 3%	
Mean # of plasma cells/HPF	0.5 ± 0.4	0.4 ± 0.3	
No plasma cells	2/28 (7%)	5/28 (18%)	
0.1-0.9 plasma cells/HPF	22/28 (79%)	21/28 (75%)	
≥1 plasma cell/ HPF	4/28 (14%)	2/28 (7%)	

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CHRONIC ENDOMETRITIS (CE) BY CD138 IN AN INFERTILE POPULATION: A NON-SELECTION STUDY DISCOVERING BASELINE PREVALENCE AND EFFECT ON EARLY EUPLOID EMBRYO IMPLANTATION.

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OBJECTIVE: The diagnosis and management of CE is debated[1-4]. Since many patients undergoing assisted reproductive technology (ART) are only tested after treatment failure, definitive management remains imprecise. The objectives of this study were to 1) determine the prevalence of CE in infertility patients and 2) the impact of CE on euploid embryo implantation.

DESIGN: Prospective, blinded, non-selection study of patients undergoing IVF/PGT-A.

MATERIALS AND METHODS: All IVF/PGT-A patients cycling between 6/2019 - 3/2020 were eligible. Exclusion criteria were: 1) age 42+, 2) embryo banking/not planning ET, 3) planning untested/fresh/mosaic ET. Consented subjects underwent a standardized endometrial biopsy (EMB) at retrieval. EMB results by a single laboratory were blinded until after single euploid ET resulted in 1) +heartbeat, 2) confirmed SAB or 3) negative hCG. Primary outcome was 1) presence/absence of CE, defined as 1+ plasma cell by CD138/section and 2) ongoing pregnancy rate. Secondary outcomes included number of plasma cells/section and stratified pregnancy outcomes. Power analysis for a prevalence of 20%[5] with a 95% confidence = 246 subjects. Statistical analyses included Student's t-test, Fischer's Exact, logistic regression with $p<0.05$ considered significant.

RESULTS: 104 subjects consented and underwent EMB. Seven withdrew after EMB with 97 eligible for FET. In all biopsied patients, the mean age was 36.1±3.2 years (range 28-41), 66.4% identified as Caucasian, and the most frequent infertility diagnosis was primary/unexplained infertility (42.3%). On 3/17/20, in compliance with ASRM's COVID recommendations, all IVF/FET cycles and recruitment stopped, at which time 54/97 had undergone FET/unblinding. There were no differences in age (p=0.83), distribution of race/ethnicity (p=0.57) or infertility diagnoses (p=0.77) between transferred and untransferred patients. Due to COVID cycle stop, unblinded biopsies were reviewed for result only (not unblinded), showing 25/104 biopsies (24.0%) positive for CE with plasma cells ranging 1-34. Demographics of transferred patients showed 46 (85.2%) had a programmed ET, 50 (92.6%) with a grade 3-5Bb or higher, and a median time to ET of 56 days. Overall, 39 (72.2%) had an ongoing pregnancy. 20.4% (11/54) had CE with plasma cells ranging 1-14. Subjects with CE had an ongoing pregnancy rate of 63.6% (7/11) that was not significantly different than 74.4% (32/43) in those subjects that were CE negative (p=0.48). Logistic regression showed no difference in ongoing pregnancy when stratified by cycle type, time to ET, lining thickness, embryo day or grade, and plasma cell count. To date, the SAB rate after implantation was similar (2/7 CE positive vs. 1/32 in CE negative, p=0.07). Notably, plasma cell count had an AOR 0.822 (0.668-1.01) and the only 2 SABs seen in patients with CE had plasma cell counts >10.

CONCLUSIONS: We found a baseline prevalence of roughly 24.0% in ART patients that, to date, did not affect the ongoing pregnancy rate. Further analysis with a larger cohort to examine 1) the SAB rate, 2) alternative definitions of CE, and 3) the impact of COVID are necessary.

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THE ASSOCIATION OF ADENOMYOSIS WITH UTEROPLACENTAL INSUFFICIENCY AND PREECLAMPSIA IN WOMEN UNDERGOING ICSI CYCLE. Can Benlioglu, M.D., Erkan Kalafat, M.D., Yavuz Emre Sukur, M.D., Batuhan Ozmen, Professor, Murat Sonmezer, M.D., professor, Cem Somer Atabekoglu, Professor. Ankara University, Turkey.

OBJECTIVE: To explore the association of adenomyosis with maternal and perinatal outcomes in women undergoing ICSI.

DESIGN: Prospective cohort study over a 2-year period between 2018 and 2020.

MATERIALS AND METHODS: Women with ongoing pregnancy (>20 weeks) after ICSI were included. Exclusion criteria were oocyte donation cycles, high-order pregnancies and women with uterine fibroids, hydrosalpinx, or stage 3-4 endometriosis according to revised AFS criteria. Adenomyosis was diagnosed according to MUSA group consensus statement. The analysis groups were divided into women with and without adenomyosis. The primary outcomes were prevalence of preeclampsia and composite adverse perinatal outcomes (small-for-gestational age at birth, neonatal care unit admission, asphyxia, preeclampsia, preterm delivery). Secondary outcome was the difference of uterine artery Doppler pulsatility index between two groups. Group comparison of primary and secondary outcomes were performed using Bayesian inference methods (Metropolis Hastings MCMC) with vague priors due to limited sample size. The results were reported as mean difference between the groups, 95% credible intervals (CrI) and the probability of significant difference. Additional results were reported via frequentist statistical methods.

RESULTS: There were 486 ongoing ICSI cycles during the study period and 101 (20.8%) ongoing pregnancies were eligible for inclusion. The adenomyosis prevalence was 18.8% (19/101). The prevalence of preeclampsia (21.1 vs. 13.4%) and composite adverse perinatal outcomes (63.1 vs. 42.7%) were higher in women with adenomyosis. Bayesian analysis showed the probability of preeclampsia (probability 84.1%, mean difference: 7.7%, 95% CrI: -11.7%-27.2%) and composite adverse perinatal outcomes (probability 99.5%, mean difference: 29.6% 95% CrI: 7.3%-51.8%) could be higher in women with adenomyosis compared to those without. First trimester mean uterine artery pulsatility index was higher in women with adenomyosis compared to those without (probability: 99.5%, mean difference: 0.32, 95% CrI: 0.07 to 0.57). Results of additional adverse pregnancy and neonatal outcomes are available in Table 1.

CONCLUSIONS: Women with adenomyosis show signs of uteroplacental malperfusion during the first trimester and possibly have an increased risk of preeclampsia and composite adverse perinatal outcomes.

Adverse Outcome	Adenomyosis (number, percentage)	Control (number, percentage)
Preeclampsia	4 (21.1)	4 (13.4)
SGA at birth	7 (36.8)	9 (10.9)
Preterm Delivery	8 (42.3)	15 (18.3)
NICU admission	7 (36.8)	7 (8.5)
Asphyxia	2 (10.5)	2 (2.4)

SUPPORT: None.

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IMPACT OF ENDOMETRIOSIS ON ANXIETY, DEPRESSION AND QUALITY OF LIFE AND ITS ASSOCIATION WITH PREGNANCY OUTCOMES IN INFERTILE PATIENTS AT A TERTIARY LEVEL INFERTILITY CENTRE IN INDIA. Kanad Dev Nayar, M.D., DGO., FICOG, Poonam Nayar, Ph.D, Shweta Gupta, MD, MRCOG, Minal Singh, DGO, DNB, Ratnaboli Bhattacharya, MD, DNB, FNB, MRCOG, Gaurav Kant, M.Sc, Rahul Gahlot, M.D., Dip. Clinical Embryology, Kapil Dev Nayar, MBBS. Akanksha IVF Centre, Delhi, India.

OBJECTIVE: Endometriosis is one of the most common gynecological diseases and affects around 30-50 % of women with infertility. Symptoms of endometriosis as well as infertility often affect psychological and social functioning of patients. The current study was undertaken to assess the level of psychological distress in infertile patients with and without endometriosis. Screening and management should be considered during routine assessment since neglect of mental health might have negative impact on couple‘s infertility treatment and outcomes. The aim of the current study was to evaluate if infertile patients with endometriosis have increased levels of anxiety,

depression and poor quality of life parameters when compared to endometriosis free infertile controls and if it affects pregnancy outcomes.

DESIGN: A single centre cross sectional study was carried out at a tertiary care infertility centre in India from 1st January 2019 through 31st December 2019.

MATERIALS AND METHODS: Three hundred patients consented to participate in the study. One hundred and fifty infertile patients with endometriosis (Group A) were matched with 150 endometriosis free infertile controls. (Group B).For assessing levels of anxiety and depression Hamilton's Rating Scales (HAM-A, and HAM-D) were used. Core Fertility and Quality of Life Questionnaire (FertiQoL) was used to index the quality of life. Primary outcomes were the prevalence of anxiety& depression in infertile patients with and without endometriosis and secondary outcome was the quality of life and its association with pregnancy outcomes (clinical pregnancy rates and live birth rates) in the two groups.

RESULTS: The baseline prevalence of anxiety in (Group A) was 42% and in (Group B) was 29.33% ($p>0.05$);baseline prevalence of depression in infertile patients with endometriosis(Group A) was 40% and in endometriosis free infertile controls(Group B) was 28%($p>0.05$), both were statistically significant. The HAM-A scores and HAM-D scores in infertile patients with endometriosis (Group A) and endometriosis free infertile controls (Group B)(14.48±6.34vs. 12.78±7.65 [t=2.095 ; p= <0.05,] 13.84±6.12 vs. 12.34±6.67 [t=;2.029 p <0.05]) the difference was statistically significant.

There was a statistically significant difference in Ferti QoL scores between the two groups (46.06±11.03,72.15±14.65 t = 17.42 $p<0.05$). QoL scores were significantly and positively associated with pregnancy outcomes (i.e., clinical pregnancy rate($p<0.05$), live birth rate ($p<0.05$).

CONCLUSIONS: Endometriosis with Infertility is a complex disorder with psychological distress which is much greater than in Endometriosis free infertile controls. Clinicians should routinely evaluate infertile patients with endometriosis from a mental health perspective. Psychotherapy and pharmacotherapy would help improve quality of life thus helping patients cope up with financial and emotional burden of their treatment and will also help to improve overall pregnancy outcome of the ART treatment.

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SUPPORT: NIL

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PELVIC INFLAMMATORY DISEASE IS AN AGGRAVATING FACTOR ON ENDOMETRIOSIS WOMEN DEVELOPING OVARIAN CANCER: A STUDY OF 2-MILLION-SAMPLE LONGITUDINAL HEALTH AND WELFARE DATABASE IN TAIWAN.

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OBJECTIVE: Previous studies have mentioned the links between endometriosis or pelvic inflammatory disease and ovarian cancer. Recently evidences have also showed endometriosis associated with ovarian cancer might depend on chronic inflammation and impaired immune surveillance. Besides, few studies have mentioned that inflammation might cause relationship between microbiota and ovarian cancer. However, the role of microbiota is still unclear on ovarian cancer. Due to above reasons, we have analyzed the interaction between endometriosis and pelvic inflammatory disease for identifying the risk of ovarian cancer.

DESIGN: A retrospective study with a 2-million-sample longitudinal health and welfare database, cancer register and death registry in Taiwan.

MATERIALS AND METHODS: Selecting patients who are diagnosed as endometriosis or pelvic inflammatory disease between January 2000 to December 2015 from a 2-million-sample longitudinal health and welfare database. The exclusion criteria are patients with previous cancer history before endometriosis or pelvic inflammatory disease diagnosis.

Five groups are divided on women with endometriosis, pelvic inflammatory disease, endometriosis first then pelvic inflammatory disease, pelvic inflammatory disease first then endometriosis later, and health women. We used to two steps for preventing potential confounding factors and bias. One step was using propensity score matching (PSM) and another step was applying with inverse probability of treatment weighting (IPTW). The logistic regression model was applied for occurrence event of ovarian cancer.

RESULTS: Women with endometriosis or pelvic inflammatory disease in Taiwan have increased risk for development of ovarian cancer compared with health women. The ovarian cancer risk is higher on women with endometriosis and pelvic inflammatory disease compared with other groups (endometriosis, pelvic inflammatory or health women, $P<0.001$). The developing malignancy rate is also higher compared with endometriosis groups.

CONCLUSIONS: Our data show women with endometriosis and pelvic inflammatory disease have increased risk for development of ovarian cancer. This finding might match not only the concept of pre-cancer but also the inflammation on microbiota on pelvic cavity.

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SUPPORT: No

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IDENTIFICATION OF TRANSCRIPTOMIC CHANGES TO EUTOPIC ENDOMETRIUM BY PRESENCE OF ENDOMETRIOTIC CYSTS – HARNESSING THE POWER OF EXISTING NONHUMAN PRIMATE DATASETS.

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OBJECTIVE: To identify significant changes to eutopic endometrium by presence of endometriotic cysts, removing confounding effects of hyperandrogenemia (T) and/or western style diet (WSD). Increased susceptibility to endometriosis was previously reported in a cohort of rhesus monkeys following treatment with mild hyperandrogenemia in the presence/absence of WSD [1].

DESIGN: Retrospective analysis of an existing non-human primate RNA-seq dataset.

MATERIALS AND METHODS: Details of treatment of rhesus macaques within this cohort are published [2]. Following 4.5 years of treatment Tru-cut biopsies were obtained in the secretory phase to collect endometrial tissue. RNA was extracted, and paired-end sequencing was performed followed by analyses of contrasts Control (C) vs T, WSD vs T+WSD and T vs T+WSD groups (n=4-6/group [3]), and between endometriosis Stages 0-II (n=16), and females with mild (Stage III) to moderate (Stage IV) endometriosis diagnosed at/within 6 months of biopsy (n=6) to detect significantly altered RNAs (Differentially Expressed RNAs (DEs)). Venn Diagram analyses were used to identify lists of gene products unique to contrast of Stages 0-II vs III&IV, and overlap between these three lists, followed by PANTHER gene ontology enrichment analyses.

RESULTS: 2,171 DE RNAs were altered in the eutopic endometrium of females with advanced stages of endometriosis. A previous analysis found the greatest number of gene products identified by contrasts of T vs T+WSD, WSD vs T+WSD, and C vs T [3]. Venn diagram analyses identified 164 DEs associated with advanced endometriosis found in C vs T contrast DEs, 386 of T vs T+WSD DEs, and 57 of WSD vs T+WSD. Removing these potentially confounding gene products resulted in 2007, 1785, and 2114 RNAs remaining in contrasts of Stages 0-II vs III&IV (Advanced endometriosis DEs), with 77% overlap. Enrichment of gene products in WNT-signaling (21-fold, p=0.02) and CCKR signaling (13-fold, p=0.03) pathways, monoamine transmembrane transporter activity (7-fold, p=0.02), and inosine monophosphate metabolic process (5-fold, p=0.037) were identified. Underrepresented processes included innate immune responses (p=7.8E-4) and cytokine activity (p=0.03).

CONCLUSIONS: This analyses show conversely, if confounding gene processes associated with T and/or WSD are removed from the dataset, a suppression of normal immune function within the eutopic endometrium of

females with more advanced stages of endometriosis. This could aid in disease progression. Funded by P50-HD071835 (ODS), and P51-OD011092 (ONPRC).

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SUPPORT: P50-HD071835 (ODS), and P51-OD011092 (ONPRC)

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ADENOMYOSIS AND PERITONEAL ENDOMETRIOSIS EXHIBIT A CLONAL RELATIONSHIP WITH EUTOPIC ENDOMETRIUM. Maria Facadio Antero, MD,[1] Lihong Li, MD,[2] Tiffany Chu, BS,[2] Leslie Cope, PhD,[2] Tian-Li Wang, MD,[2] Ayse Ayhan, MD, PhD,[2] Tamer A. Seckin, MD,[3] James H. Segars, MD,[4] Ie-Ming Shih, MD, PhD[2] [1]John Hopkins University School of Medicine, Baltimore, MD; [2]Johns Hopkins School of Medicine, Baltimore, MD; [3]Lenox Hill Hospital/Northwell Health System, New York, NY; [4]Johns Hopkins University School of Medicine, Baltimore, MD.

OBJECTIVE: To determine if their is a clonal relationship between ectopic and eutopic endometrium in patients with adenomyosis and endometriosis.

DESIGN: Whole exome sequencing analysis.

MATERIALS AND METHODS: This was a retrospective study where formalin-fixed parrafin-embedded tissue blocks were obtained from patients undergoing gynecological surgery for endometriosis and adenomyosis from 2014-2018 at Johns Hopkins Hospital. The diagnoses were validated by an independent pathologist upon reviewing H&E slides. Using laser capture microdissection, the stromal and epithelial components for both ectopic and eutopic endometrium were separated. Whole exome sequencing was performed to analyze the somatic mutations in glandular epithelium and stroma separately in paired adenomyosis, peritoneal endometriosis and matched endometrium to infer their clonal relationship. To determine somatic sequence mutations, matched normal-appearing smooth muscle, fallopian tube or colonic epithelium were also analyzed and acted as controls.

RESULTS: We found somatic mutations in epithelium and stroma of all tissue types. Cancer-driving mutations were only found in the epithelium. Based on somatic mutations, we demonstrated clonal development not only in epithelial but stromal components in adenomyosis and peritoneal endometriosis, with a distribution of mutant allele frequency suggestive of mono-clonality. Alongside private mutations, both lesions in either epithelial or stromal parts shared the same selection-neutral mutations as matched endometrium in most of informative cases, indicating a derivation from the same founder progenitor cells in the endometrium.

CONCLUSIONS: Our data demonstrate that adenomyosis, peritoneal endometriosis and ectopic endometrium are progenies from an ancestral endometrial progenitor cell following distinct evolutionary trajectories.

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A PROSPECTIVE PILOT ULTRASONOGRAPHIC STUDY TO EVALUATE IMPACT OF PREGNANCY ON CHARACTERISTICS OF DEEP INFILTRATING ENDOMETRIOSIS AND ENDOMETRIOMAS. Fabio Barra, MD,[1] Carolina Scala, MD,[2] Gloria D'Alessandro, MD,[1] Simone Ferrero, MD PhD[1] [1]IRCCS Ospedale Policlinico San Martino, Genova, Italy; [2]Istituto G. Gaslini, Genova, Italy.

OBJECTIVE: Hormonal environment may impact the appearance of endometriotic lesions during pregnancy. The objective of this study is to evaluate the change of ultrasonographic features of deep infiltrating endometriosis (DIE) and endometriomas after delivery in pregnant women.

DESIGN: This was a prospective single-center study.

MATERIALS AND METHODS: Spontaneous pregnant women with a previous ultrasonographic diagnosis of endometriosis were included in this prospective study. Women did not have received hormonal drugs for endometriosis for at least three months before the last ultrasound evaluation of endometriosis. The ultrasonographic characteristics of endometriotic nodules were compared between the evaluation performed before conception and that performed at 40-60 days after delivery by a single experienced operator. The following locations of DIE were evaluated: uterosacral ligament, vagina, bladder, rectovaginal septum, and rectosigmoid. Changes in the volume were assessed by using the virtual organ computer-aided analysis (VOCAL).

RESULTS: A total of 34 patients (61 DIE lesions; 22 endometriomas) were included; the mean (±SD) age of the study population was 33.4 (±2.8). The mean overall volume of DIE nodules was not significantly different before pregnancy compared to after pregnancy regardless of their localization (2.67 ± 3.42 cm^3 vs. 2.39 ± 2.63 cm^3; p=0.22). The mean volume of the largest nodule of each woman was not significantly different (3.13 ± 3.62 mm^3 vs. 3.09 ± 4.43 mm^3; p=0.29). The volume of DIE lesions decreased in 21.3% (n=13/61), was stable in 75.4% (n=46/61), and increased in 3.4% (n=2/61) of cases. The volume of endometriomas was significantly higher before pregnancy (3.22 ± 2.83 mm^3 vs. 2.56 ± 2.71 mm^3; p<0.001). The ultrasonographic appearance of DIE and endometriomas did not significantly change. During the pregnancies, patients did not experience complications related to endometriosis.

CONCLUSIONS: Women affected by endometriosis do not have a substantial change in dimension and characteristics of DIE lesions during pregnancy. Differently, they have a significant decrease in size of endometriomas.

P-267 4:30 PM Sunday, October 18, 2020

INSTAGRAM USERS' CONTENT ON ENDOMETRIOSIS- DOES ENDOMETRIOSIS AWARENESS MONTH MAKE A DIFFERENCE? Andrea M. Gochi, MS, Noelle Coen, BS, Shaokui Ge, PhD, Mallory A. Stuparich, MD, Samar Nahas, MD, Sadikah Behbehani, MD. UC Riverside School of Medicine, Riverside, CA.

OBJECTIVE: To quantitatively compare Instagram user content before and during Endometriosis Awareness Month.

DESIGN: cross sectional study.

MATERIALS AND METHODS: The first 7 public Instagram posts using the hashtag #endometriosissurgery that fit inclusion criteria were evaluated daily in March- Endometriosis Awareness Month (EAM) (n=217) and the month prior- February (n= 202). Posts were reviewed for the following content: "endo" in the Instagram account name, emotional content, educational content, outcomes of surgery, complications of surgery, posted questions, medical history, symptoms pre-operation, posted pictures, fertility, medications, comfort in pets, alternative therapies, and number of Instagram followers. The association of each categorical variable and time period (before or during EAM) was evaluated by Chi-square test, and the number of followers of each Instagram account that posted was tested by Poisson Univariate regression.

RESULTS: When compared to the month prior to EAM, there were more posts that had both educational (66 [30.41%] vs 25 [12.38%], OR= 3.09, p <0.0001) and emotional content (114 [52.53%] vs 59 [29.21%], OR= 2.68, p< 0.0001) made during EAM, respectively. In contrast, posts during EAM were less likely to comment on surgical outcomes (20 [9.22%] vs 82 [40.58%], OR= 0.15, p<0.0001) and personal medical history (12 [5.53%] vs 59 [29.21], p<0.0001, respectively) when compared to the month prior. In addition, posts during EAM were made by Instagram accounts with more followers (averaged 1796 with SD of 4621) than posts made during the previous months (averaged 1413 with SD of 2540, p<0.0001). Compared to the number of followers in posts made by Instagram accounts in February, the number in EAM increased 1.27 times (p<0.0001), on average. There were no differences noted in the other variables.

CONCLUSIONS: Instagram content posted during EAM includes more emotional (OR= 2.68) and educational (OR= 3.09) content when compared to the month prior to EAM. Furthermore, Instagram accounts with more followers appear to be more active during EAM, as opposed to the month before. These results illuminate the discrepancy between the content posted before and during EAM and highlights the need for consistent visibility and awareness of endometriosis throughout all months, which may improve the education of and emotional support to women undergoing surgery for endometriosis.

P-268 4:30 PM Sunday, October 18, 2020

IMPACT ON WOMEN WITH ENDOMETRIOSIS AND PELVIC INFLAMMATORY DISEASE ON ENDOMETRIAL CANCER DEVELOPMENT: A RETROSPECTIVE COHORT STUDY IN TAIWAN. Cheng-Yang Hsu, MD,[1] Hui-Wen Lo, MD,[2] Eing-Mei Tsai, MD, PhD[1] [1]Kaohsiung medical university hospital, Kaohsiung, Taiwan; [2]Kohsiung Medical University, Kaohsiung, Taiwan.

OBJECTIVE: Endometrial cancer is thought association with endometriosis or pelvic inflammatory disease by previous studies. The possible explanations on endometriosis and endometrial cancer are genetic mutation and imbalanced hormone receptor expression. Recently, the role of vaginal microbiota modulation on endometrial hyperplasia or cancer is focused on the oestrogen changes. For evaluating the impact of vaginal microbiota modulation on endometriosis women, we design this retrospective study.

DESIGN: A population-based study using a 2-million-sample longitudinal health and welfare database, cancer register and death registry in Taiwan.

MATERIALS AND METHODS: From 2-million-sample longitudinal health and welfare database, the inclusion criteria is patients who match the diagnosis as endometriosis and/or pelvic inflammatory disease between January 2000 to December 2015. The exclusion criteria is patients who have cancer history before endometriosis or pelvic inflammatory disease before. They would divided into 4 groups: endometriosis, pelvic inflammatory disease, endometriosis and pelvic inflammatory disease, and healthy women. For decreasing potential confounding factors and bias, we used propensity score matching (PSM) and inverse probability of treatment weighting (IPTW). The logistic regression model was applied for occurrence event of endometrial cancer.

RESULTS: Increasing risk of endometrial cancer is found on women with endometriosis and pelvic inflammatory disease in Taiwan. The risk is significantly higher compared to endometriosis, pelvic inflammatory disease, or healthy women groups (p<0.001).

CONCLUSIONS: Women with endometriosis and pelvic inflammatory disease have increased risk of developing endometrial cancer. This finding might match the concept of hormone changes and vaginal microbiota modulation on women with endometriosis and pelvic inflammatory disease.

References:

1.Łaniewski, P., Ilhan, Z.E. & Herbst-Kralovetz, M.M. The microbiome and gynaecological cancer development, prevention and therapy.Â *Nat Rev Urol*Â 17,Â 232–250 (2020).

SUPPORT: No

P-269 4:30 PM Sunday, October 18, 2020

PREDICTED LEVELS OF PREOPERATIVE ANTI-MULLERIAN HORMONE IN WOMEN WITH ENDOMETRIOSIS-ASSOCIATED INFERTILITY. William Butler, MD, Sarah E. Byrd, MD, Kelly JANE. Tipton, MD, Kristina C. Hawkins, MD, Abdelmoneim Younis, DVM, PhD HCLD, Mercer University School of Medicine, MACON, GA.

OBJECTIVE: The aim of the study is to examine correlation of preoperative AMH level with the diagnosis of endometriosis and reproductive outcome achieved in women undergoing laparoscopy for pelvic pain or infertility.

DESIGN: IRB approved retrospective study using univariate analysis to compare age corrected AMH values with stages of endometriosis and pregnancy outcomes of women who presented with a complaint of infertility and were found to have endometriosis at the time of laparoscopic evaluation.

MATERIALS AND METHODS: A chart review was performed in patients who chose to undergo laparoscopic evaluation for tubal/peritoneal factors as a potential cause of their infertility and who attempted to achieve pregnancy after surgery. 338 subjects, who had AMH levels measured with normal or induced ovulation, normal male factor and patent Fallopian tubes were identified. Clinical pregnancy rates were determined after spontaneous and COH/IUI cycles within one year. Stages of endometriosis and age corrected AMH levels were compared using analysis of covariance. Race, gravidity/parity, and presence or absence of polycystic ovarian syndrome (PCOS) were additional variables included in the analysis model. All statistical evaluation was performed using SPSS.

RESULTS: Mean AMH values with SD, pregnancy rates and endometriosis status for selected ages of patients with or without PCOS is shown in Table 1. Regardless of the presence of PCOS or not, AMH levels were significantly (P<0.05) lower in patients with endometriosis than aged matched no endometriosis. Clinical pregnancy rates were significantly better in patients without endometriosis (<0.005). Presence of PCOS had a statistically significant effect on AMH values within age groups.

CONCLUSIONS: Women with endometriosis with or without PCOS have lower aged matched AMH levels, suggesting decreased ovarian response, as indicated by the significantly reduced cumulative pregnancy rates. The study

TABLE 1. Predicted AMH values & Clinical Pregnancy rate for selected ages based upon presence or absence of endometriosis & PCOS

Age	No Endometriosis & No PCOS (N=104)	Endometriosis (N=175)	Endometriosis & PCOS (N=36)	No Endo with PCOS (N=23)
< 25 yrs	3.48 ± 2.2 (6)	2.26 ± 1.5 (9)	5.26 ± 4.22 (6)	8.01 ± 6.84 (7)
25-34 yrs	2.48 ± 1.31 (46)	2.07 ± 1.26 (55)	8.36 ± 7.35 (9)	5.17 ± 4.47 (14)
35-40 yrs	1.50 ±0.25 (42)	0.87 ± 0.28 (16)	6.44 ± 1.11 (3)	3.77 ± 0.88 (2)
>41 yrs	0.67 ± 0.50 (10)	0.42 ± 0.63 (1)	0	0
Clinical Pregnancy (%)	61.5% (64/104)	42.9% (75/175)	50.0% (18/36)	82.6% (19/23)

clearly indicate that endometriosis is linked with decline AMH levels and clinical pregnancy suggesting adverse effects of the disease process in reproductive function and ovarian reserve.

SUPPORT: None

P-270 4:30 PM Sunday, October 18, 2020

THE IMPACT OF ENDOMETRIOSIS ON EMBRYO MORPHOKINETICS. Natalia C. Llarena, MD,[1] Tommaso Falcone, M.D.,[2] Nina Desai, Ph.D., HCLD[3] [1]Cleveland Clinic Foundation, Cleveland, OH; [2]cleveland Clinic, cleveland, OH; [3]Cleveland Clinic, Beachwood, OH.

OBJECTIVE: Data suggest that women with endometriosis have impaired oocyte and embryo quality, and higher rates of abnormal embryo development. Time-lapse microscopy (TLM) provides a uniquely detailed perspective on embryonic development and allows for quantitative evaluation of cell cycle parameters. The objective of this study is to compare kinetic parameters between embryos derived from women with and without endometriosis.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Sixty-three oocyte retrievals were performed for 45 patients aged 18-39 undergoing in vitro fertilization (IVF). Patients with endometriosis had the diagnosis confirmed either by laparoscopy or the presence of endometrioma on imaging. Control patients without endometriosis underwent IVF for the indications of (1) prior salpingectomy/tubal ligation, (2) male factor infertility not requiring surgical sperm retrieval, (3) IVF with donor egg, or (4) uterine factor infertility. Patients with polycystic ovarian syndrome, recurrent pregnancy loss, or unexplained infertility were excluded. Observations were made on 491 fertilized oocytes (336 from controls, and 124 from women with endometriosis) cultured in the EmbryoScope using TLM. Timing of cell divisions t2,43,t5,t8, morula formation tM),start of blastulation (tSB) blastocyst formation (tB) and expanded blastocyst (tEB) were determined. Incidence of multinucleation and specific cleavage dysmorphisms were also monitored. Kinetic data and cycle outcomes were analyzed retrospectively. Optimal kinetic ranges for specific endpoints were based on published literature.

RESULTS: The mean patient age in the endometriosis and control groups was similar (34 $\pm$ 4). A total of 76 embryos were transferred. Mean ET number was 1.1 $\pm$ 0.26 and 1.5 $\pm$ 0.47 for endometriosis and control group, respectively. Fertilization rates were significantly lower in women with endometriosis compared to controls (56% vs 76%, $p < 0.001$); however, there were no significant differences in implantation (64% vs 53%, p=NS), clinical pregnancy (69% vs 55%, p=NS), or live birth rates (69% vs 50%, p=NS). There were no significant differences in multinucleation rates, or the incidence of direct uneven cleavage. Overall, embryos derived from women with endometriosis were less likely than controls to fall within optimal kinetic ranges for the start of blastulation (time $<$ 96.2 hours; 22 vs 35%, $p = 0.02$) and expanded blastocyst (time $\leq$ 116 hours; 42 vs 59%, $p < 0.001$). The cohort of embryos transferred showed more favorable kinetic parameters than the overall cohort. Among the embryos transferred, there were no differences in the proportion of embryos falling within optimal kinetic ranges between the endometriosis and control groups.

CONCLUSIONS: Specific timings for the start of blastulation and expanded blastocyst formation have been associated with both implantation potential and aneuploidy rates. A lower proportion of embryos from endometriosis patients exhibited optimal timings for these late developmental end points. However, high clinical pregnancy and live birth rates were still achieved.

POSTER SESSION: ENVIRONMENT AND REPRODUCTION

P-271 4:30 PM Sunday, October 18, 2020

LAND USE AND SEMEN QUALITY: A SINGLE FERTILITY CENTER COHORT STUDY. Eun-Hye Jo, M.D.,[1] Tae Ki Yoon, M.D, Ph.D.,[1] You Shin Kim, M.D, Ph.D.,[1] Inn Soo Kang, MD, PhD,[1] Mi Kyoung Koong, MD, PhD,[1] Hyeok Kim, MD, PhD,[1] Young Sang Kim, M.D,[2] Myung Joo Kim, M.D.,[1] Seung-Ah Choe, M.D.,[1] Ran Kim, M.D.,[1] Eun Jeong Yu, MD,[1] Yun Jung Hur, M.D.,[1] Ji Hye Kim, M.D.,[1] Hannah Kim, MD[1] [1]CHA Fertility Center Seoul Station, CHA University, Seoul, Korea, Republic of (South); [2]CHA Seoul Fertility Center, OB&GY, Seoul, Korea, Republic of (South).

OBJECTIVE: There are growing interests regarding the potential impact of physical environment of residential area on reproductive potential of human. This study was to explore the association between built environment and semen parameters in men who visited for fertility evaluation.

DESIGN: This study is a retrospective cohort study using the data of 7,762 men who have undertaken semen analysis at a single fertility center between January 2016 and September 2019.

MATERIALS AND METHODS: Excluding those diagnosed with varicocele, azoospermia, cryptorchidism, and known chromosomal abnormality, we obtained initial semen analysis results of a total of 7,762 men. Environmental exposures were distance to fresh water (river, lake, creek), distance to major roadway, and neighborhoodgreenness measured by Normalized Difference Vegetation Index (NDVI)within 500m. Outcome indicators were sperm concentration, % of progressive motility and normal morphology by strict criteria.Linear and logistic regression models including clustered effect by district were used for standardized value of sperm concentration, % of progressive motility and normal morphology.

RESULTS: Median age was 39 years and majority were manager, professional or white-collar workers (96.9%). Mean distance to fresh water and major roadway was 443.7 and 3250.0m, respectively. NDVI within 500m was -0.13 on average. In multivariable analyses using quartile scales of environmental exposures, higher distance to fresh water was associated with generally low sperm count which did not reach statistical significance. Men with 2nd quartile of distance to major roadway was showed lower progressive motility (ß = 0.121, P= 0.024). Highest quartile of neighborhood greenness was associated with lower % of normal morphology compared to lowest quartile exposure (ß = -0.176, P = 0.005).

CONCLUSIONS: We observed an association betweenbuilt environment and semen quality of men with infertility history. To confirm this finding, we suggest further studies exploring potential impact of built environment on male infertility in different settings.

P-272

WITHDRAWN

P-273 4:30 PM Sunday, October 18, 2020

AMBIENT AIR POLLUTION AND OVARIAN RESERVE: A SINGLE CENTER COHORT STUDY. Hannah Kim, MD, Seung-Ah Choe, M.D., You Shin Kim, M.D, Ph.D., Tae Ki Yoon, M.D, Ph.D. CHA Fertility Center Seoul Station, CHA University, Seoul, Korea, Republic of (South).

OBJECTIVE: Mounting evidence show possible association between air pollution and reproductive potential of human. Our study assessed the association between air pollution and markers of ovarian reserve in women who visited a fertility center.

DESIGN: 2,276 women who visited a single fertility center were included for study and their ovarian reserve were assessed. Average concentration of pollutant where enrolled women lived were measured to see the correlation between air pollution and ovarian reserve.

MATERIALS AND METHODS: This study included 2,276 women aged between 20 and 50 who visited a single fertility center from Jan. 2016 to Sep. 2018. Ovarian reserve was assessed by measuring serum FSH and AMH on menstrual day 3. Hourly concentrations of fine particulate matter (PM_{10}), NO_2, CO, SO_2, and O_3 measured at 269 air quality monitoring sites across country was used. Based on daily mean concentrations of each air pollutant, average concentration was computed for within 1, 3, 6 and 12 months. Ovarian reserve indicators were observed to expected AMH ratio, FSH $>$ 20IU/mL and AMH $<$ 0.5ng/mL. We assessed the association between concentration of six air pollutants and ovarian reserve indicators adjusting for individual socio-demographic, lifestyle, and spatiotemporal factors.

RESULTS: Mean age of women was 36.6 $\pm$ 4.2. Majority (n=1431, 62.9%) was working at the time of ovarian reserve test and 51 (2.2%) had past smoking history. Mean FSH and AMH were 9.2 $\pm$ 6.4 IU/mL and 3.3 $\pm$ 3.1 ng/mL, respectively. Prevalence of high FSH was 3.4% (n=69) and decreased AMH was 10.3% (n=235). AMH ratio was 0.8 $\pm$ 0.7 on average. In linear regression models, an IQR-increase of 1 month-average of PM_{10} concentration (adjusted ß coefficient=-0.06, 95%confidenceinterval:-0.11, 0.00) and NO_2 concentration (-0.07, 95%CI:-0.12 -0.01) was associated with lower AMH ratio. Except O_3, there were generally negative association between air pollutants concentration and AMH ratio which did not reach statistical significance. In the models for binary outcomes, OR of high FSH was 2.00 (95% CI: 1.08 3.72) per IQR-increase of 12 month-average concentration of SO_2. On the other hand, OR of high FSH was 0.33 (95% CI: 0.13 0.82) with IQR-increase of O_3 concentration within 1 month.

CONCLUSIONS: Higher exposure to PM_{10} and SO_2 was associated with low ovarian reserve in infertile patients, highlighting the importance of the air pollution to infertility.

P-274 4:30 PM Sunday, October 18, 2020

ENVIRONMENTAL CONTAMINANTS INFLUENCE GAMETE DEVELOPMENT BUT NOT HORMONE PROFILES OF PATIENTS UNDERGOING IVF. Lindsay L. Penrose, PhD,[1] Shiva Khalili, M.D.,[1] Dixie Leung, M.D.,[1] Khaliq Ahmad, PhD,[1] Samuel D. Prien, PhD[2] [1]Texas Tech University Health Sciences Center, Lubbock, TX; [2]Texas Tech University Health Sciences Center AND Texas Tech University, Lubbock, TX.

OBJECTIVE: The influences of environmental contaminants on human health, including fertility, are well documented. Previous research from this laboratory has demonstrated the potential effects of agricultural and other industrial pollutants on ART outcomes. In these earlier studies, differences were demonstrated in the available sperm, the number of oocytes recovered, the number of healthy oocytes, and the number of atretic oocytes in patients living in rural and urban environments ($P < 0.05$). However, fertilization rates and pregnancy outcomes did not appear to be influenced by the maternal home environment. These data would suggest that environmental factors can influence the oocyte quality. As organic pollutants can affect hormone cascades, the objective of the present study was to determine if hormone profiles were different in patients from urban and rural environments undergoing ART procedures.

DESIGN: A chart review evaluating the relationship between patient environments and hormone profiles during assisted reproductive technologies outcomes.

MATERIALS AND METHODS: Hormone profiles were reviewed for ART procedure reports from 2014-2017 (N= 163) and were categorized into urban, mainly urban, mainly rural, and rural populations based on zip-code information. Data included precycle profiles, down-regulation, maximum estrogen levels, and pregnancy outcomes. Data were then recategorized between different types of environmental regions (heavy versus limited agrochemical use). Finally, the data were then grouped to correspond to periods of heavy agrochemical use, such as during the growing season for regional crops, and analyzed for each hormone. Data were compared by ANOVA, independent Student's t-test, or Chi-square.

RESULTS: No differences were found between the hormonal profiles of patients for any of the hormones reviewed regardless of the environment of their home residence ($P = 0.118$). Further, there appeared to be no difference between the hormonal profile of patients from different agricultural regions where agrochemical used varied from intense to minimal ($P = 0.077$). Finally, there were no differences seen in the hormonal profiles of patients undergoing treatment cycles during periods of intense versus minimal agrochemical use ($p = 0.127$).

CONCLUSIONS: Previous research has demonstrated differences in egg quality in patients from rural versus urban areas in an agricultural region heavily dependent or organic agrochemicals in the American Southwest. However, current data suggest the changes in oocyte quality are independent of hormonal profile and may be influenced during the hormone-independent stage of follicular development as follicles progress from the primordial to the primary stage of development. Further research will be needed to determine how these compounds influence oocyte development.

SUPPORT: None

P-275 4:30 PM Sunday, October 18, 2020

DISRUPTION OF MALE FETAL REPRODUCTIVE DEVELOPMENT BY EXPOSURE TO BISPHENOLS. Emily G. Hurley, MD,[1] Tony De Falco, Ph.D.[2] [1]University of Cincinnati, West Chester, OH; [2]Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

OBJECTIVE: To evaluate the effects of bisphenol A (BPA) and its analogues, bisphenol S and F (BPS, BPF), on fetal mouse testis development.

DESIGN: Experimental investigation at an academic-affiliated research laboratory utilizing CD-1 (IGS) mice.

MATERIALS AND METHODS: Fetal mouse testes at 12.5 days post coitum were cultured for 48 hours with 1 μM of BPA, BPS or BPF treatment and analyzed with immunofluorescence, quantitative polymerase chain reaction (qPCR) and RNA sequencing. Immunofluorescence was used to evaluate changes in vasculature and number/appearance of germ cells, Leydig cells and Sertoli cells. For qPCR, fold changes in mRNA levels relative to control were analyzed using a $\Delta\Delta$Ct method with results calculated as a mean $\pm$ SD. A two-tailed Student t-test was performed to calculate p values, in which $p<0.05$ was considered statistically significant. For RNA sequencing, RNA was extracted and libraries were created using the Illumina protocol, Nextera XT DNA Sample Preparation Kit and sequenced with the Illumina NextSeq 500 instrument. Differentially expressed genes (DEGs) were determined using the R package DESeq2 v.1.26.0 with a log2 fold change $\geq$0.4 and false discovery rate $\leq$ 0.05 when evaluating the combined bisphenol versus control groups and a log2 fold change $\geq$1 when comparing each bisphenol versus control separately. RNA sequencing was also evaluated using Gene Set Enrichment Analysis.

RESULTS: The morphologic appearance of fetal testes and key gene targets (*Amh*, *Sox9*, *Cyp17a1*, *Kdr*, *Ddx4*) were not found to be significantly affected by bisphenol exposure. However, RNA sequencing provided evidence that bisphenol exposure resulted in significant differential gene expression in the exposed gonad. There were a total 387 DEGs identified when analyzing bisphenol (all 3 compounds collectively) versus control groups. Bisphenol exposure resulted in upregulation of gene sets involved in organ morphogenesis/development and immunity and significant downregulation of gene sets involved in gamete generation and sexual reproduction. Gene sets involved in RNA binding/posttranscriptional regulation of gene expression were also downregulated. When analyzing the data for each bisphenol separately versus each control, a total of 1417, 1193 and 1320 DEGs were identified for BPA, BPS and BPF respectively. BPA, BPS and BPF resulted in upregulation of 8 shared genes and downregulation of 77 shared genes, with multiple of these genes having a role in reproduction. BPA and BPF caused more similar effects compared to BPS. All three bisphenols resulted in downregulation of gene sets involving gamete generation; however, the normalized enrichment scores were much lower for BPS compared to BPA and BPF.

CONCLUSIONS: Bisphenol exposure results in altered gene expression in fetal mouse testes, which may ultimately lead to reproductive dysfunction and possibly transgenerational inheritance through effects on germ cells. BPS and BPF share some similar effects on differential gene expression and overall are likely not safe alternatives to BPA.

SUPPORT: Prelude Scientific Advisory Board Grant

P-276 4:30 PM Sunday, October 18, 2020

STRESS-FORCES EMBRYONIC STEM CELLS TO INCREASE EXPRESSION OF HEPATITIS A AND HERPES SIMPLEX 1 VIRUS RECEPTORS AND TWO GENES NECESSARY FOR COVID-19 UPTAKE.

Elizabeth E. Puscheck, MD, MS, MBA,[1] Sudipta Dutta, Ph.D.,[2] Mohammed Abdulkareem Abdulhasan, Ph.D.,[3] Katherine Gurdziel, Ph.D.,[2] Steven J. Korzeniewski, Ph.D.,[4] Douglas Ruden, Ph.D.,[2] Daniel Rappolee, Ph.D.[2] [1]InVia Fertility, Hoffman Estates, IL; [2]Wayne State University, Detroit, MI; [3]Reproductive Stress 3M, Inc., Grosse Pointe Farms, MI; [4]Wayne State University School of Medicine, Detroit, MI.

OBJECTIVE: Determine whether various stresses change the expression in embryonic stem cells (ESC) and their differentiated lineages, of a large set of viral receptors and susceptibility genes.

DESIGN: Experimental.

MATERIALS AND METHODS: ESC were tested by bulk or single cell (sc) RNAseq after 72 hr exposures to 0-300 mM hyperosmotic sorbitol (with stemness-maintaining Leukemia Inhibitory Factor, LIF) to quantify stress-forced differentiation. Controls for normal stemness were LIF+ and normal differentiation were LIF-. RNA was isolated by RNAeasy lysis or 10XGenomics Dropseq, RNA quality was checked by Agilent TapeStation, cDNA was synthesized using Lexogen's QuantSeq library kit, and barcoded, multiplexed and sequenced by Illumina NovaSeq 6000. Data were demultiplexed by CASAVA software and FC expression was compared between conditions. In triplicate experiments, significant fold change (FC) genes ($FC \geq 2$; $FDR \leq 0.05$, $P < 0.05$) identified affected pathways. Proliferation or death were assayed by Hoechst staining or Trypan blue staining, respectively. Validating studies including qPCR.

RESULTS: Using bulk RNAseq it was shown that VIM and TMPRSS2, two genes necessary for Covid-19 cell uptake are up-regulated significantly as measured by P-value and FDR. VIM is up-regulated 5.6 fold higher at 300 mM sorbitol compared with normal differentiation and TMPRSS2 is also up-regulated 3.1 fold higher by high sorbitol despite LIF presence. Havcr1 the hepatitis A virus receptor was up-regulated 55 fold over normal ESC differentiation with significance by p-Value and FDR. Pvrl1 the Herpes simplex 1 (HSV1) virus receptor was up-regulated 4.5 fold compared with ESC undergoing normal differentiation by LIF removal.

CONCLUSIONS: These are proof-of-principle studies that suggest that some viruses have high susceptibility when ESC and their progeny differentiated lineages undergo hyperosmotic stress. HSV1 is known to cross the placenta, and recent data suggest that Covid-19 may cross the placenta and induce IgM detected in cord blood. We intend to extend these tests using Phthalates and cortisol and to test human embryonic stem cells for similar stress-enhanced susceptibility.

SUPPORT: Funding: NIH 1R41ES028991-01 and NIEHS P30 CURES Pilot grant

POSTER SESSION: FEMALE INFERTILITY DIAGNOSIS AND TREATMENT

P-277

REASSIGNED

P-278 4:30 PM Sunday, October 18, 2020

IDENTIFYING GENETIC BIOMARKERS OF OVARIAN RESERVE.

Alison Gruber, MD,[1] Deanna Brasile, DO,[2] Will Dampier, PHD,[1] Joshua Chang Mell, PHD,[1] Karen Berkowitz, MD[1] [1]Drexel University College of Medicine, Philadelphia, PA; [2]Main Line Fertility, West Chester, PA.

OBJECTIVE: Diminished Ovarian Reserve (DOR) is a major cause of infertility in women. However, current tests used to assess ovarian reserve in infertile women are limited and do not predict the probability of pregnancy or live birth. Previously, we demonstrated that CHTF18, a conserved DNA replication protein, plays critical roles in mammalian fertility and meiosis. *Chtf18*-null female mice exhibit age-dependent subfertility and a phenotype that closely resembles women with DOR. Our objective is to evaluate *CHTF18*, the human ortholog, and other functionally related genes as possible novel biomarkers of ovarian reserve.

DESIGN: Prospective Clinical Research Study.

MATERIALS AND METHODS: We enrolled 212 Caucasian or Asian women aged 30-45 and placed them into three groups by serum AMH (ng/mL): 1) Infertile women with serum AMH $\geq$ 1.0; 2) Infertile women with serum AMH $<$ 1.0; and 3) Fertile women with serum AMH $\geq$ 1.0. Utilizing a knowledge-based informatics approach and the Human Meiosis Reactome Database, we identified 33 genes functionally related to *CHTF18*. Genomic DNA was isolated from peripheral blood leukocytes and candidate genes were enriched with Illumina TruSeq amplification. Next Generation Sequencing was conducted and bioinformatics analyses were performed with the Broad Institute's standard genome variant pipeline to identify both known and novel

genomic variants. Potential covariates such as age, BMI, smoking, and surgical history were statistically controlled with Ridge regression.

RESULTS: We used a custom sequencing plate to enrich coverage of the candidate genes by an average of 3750-fold. After converting AMH values to age-adjusted percentile scores, we found that women with serum AMH < 1.0 had the lowest AMH percentile scores, as expected, with most falling below 20^{th} percentile for their age. Infertile controls with serum AMH ≥ 1.0 had a range of percentile scores that clustered mainly above 20^{th} percentile. Fertile controls had the highest values, ranging from 30^{th} percentile to 100^{th} percentile. We projected the adjusted AMH values across the variants to evaluate which ones might be altering AMH values, and found 11 variants within the *IGF2* locus that appear to be significantly associated with DOR (OR= 4; $p<0.05$, t-test). We also analyzed the effect of the variants on AMH and found that variants associated with low AMH were present in *IGF2* and *IGF2R*. We analyzed the variants with both linear and non-linear regression models to assess how much they impacted the AMH values and found that they accounted for at least 20-26% of the observed age-adjusted AMH values. Preliminary analyses also suggest a possible association of *CHTF18*, *PRDM9*, *SMC5*, *DMC1, ESR1* with DOR, and additional algorithms are being used to identify and verify significant variants in these genes.

CONCLUSIONS: Our results thus far suggest that genetic variants in *IGF2*, *CHTF18*, and other related genes may be associated with low AMH and DOR. Since the age at which DOR impacts fertility cannot be precisely predicted, we propose that genetic biomarkers could be used to identify women at risk, allowing them to make earlier reproductive choices.

P-279 4:30 PM Sunday, October 18, 2020

ASSOCIATIONS BETWEEN INFERTILITY AND SEXUAL HEALTH IN U.S. FEMALE AND MALE VETERANS. Ginny L. Ryan, MD, MA,[1] Marie E. Thoma, PhD, MHS,[2] Andrea Holcombe, MS, PhD,[3] Anne Sadler, PhD, MS,[3] Bradley J. Van Voorhis, MD,[4] Alicia Y. Christy, MD,[5] Michelle A. Mengeling, MS, PhD[3] [1]Center for Access and Delivery Research and Evaluation, Iowa City, IA; [2]University of Maryland, College Park, MD; [3]Iowa City VA Health Care System, Iowa City, IA; [4]University of Iowa, Iowa City, IA; [5]Veterans Administration, Kensington, MD.

OBJECTIVE: To identify associations between lifetime infertility measures and sexual health in Veterans.

DESIGN: Cross-sectional survey study of 1407 female and 1601 male U.S. Veterans aged 20-45.

MATERIALS AND METHODS: Data were collected using computer-assisted telephone interviews. Lifetime infertility was defined as: 1) twelve or more consecutive months of unprotected intercourse without pregnancy (UI), 2) twelve or more months of trying before any pregnancy (time to pregnancy (TTP)), and 3) ever diagnosis of infertility in participant and/or partner (DX). All Veterans were asked about any past history of sexually transmitted infection (STI) and satisfaction with sexual function. If dissatisfied, they were asked about 5 specific problems based on the Female Sexual Function Index (FSFI): interest, sensation, lubrication, orgasm and pain. Additionally, female Veterans were asked to self-report pelvic inflammatory disease or chronic pelvic pain. Male Veterans were asked to self-report ejaculatory or erectile dysfunction. Infertility prevalence and sexual health characteristics were analyzed by sex.

RESULTS: 84.9% of participants reported having unprotected intercourse and among those 49.6% reported having twelve or more consecutive months of intercourse without pregnancy. Among those ever pregnant (65.3%; n=919), 45.3% (n=416) reported twelve or months of TTP. Overall, 11.7% (n=165) reported ever being diagnosed with infertility. Depending on the infertility measure used, past sexually transmitted infection was associated with infertility in both female and male Veterans (UI measure: 35.1% with infertility vs. 28.6% without infertility in females, p=0.016; TTP measure: 20.1% with infertility vs. 15.2% without infertility in males, p=0.05). Both female and male Veterans with infertility were also more likely to report dissatisfaction with sexual function (UI: 22% with infertility vs. 15.2% without infertility in females, p=0.003; UI: 18.7% with infertility vs. 14.8% without infertility for males, p=0.049).

Female Veterans dissatisfied with sexual function were more likely to report pain with sex if infertile than sexually dissatisfied female Veterans without infertility (DX measure: 78.4% with infertility vs. 51.2% without infertility, p=0.002). Consistent with this finding, chronic pelvic pain (only queried in females) was associated with infertility (DX measure: 11.4% with infertility vs. 4.9% without infertility, p=0.0003). Erectile dysfunction (only queried in males) was also associated with infertility (DX measure: 12.9% with infertility vs. 7.5% without infertility, p=0.15).

CONCLUSIONS: Besides the expected association between STIs and infertility, our study suggests there may also be a relationship between sexual dysfunction and infertility in female and male Veterans. Further research is needed to better elucidate these associations, including the finding of higher rates of pain and erectile dysfunction in the sub-populations of Veterans who had ever been diagnosed with infertility by a healthcare provider.

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CHARACTERIZATION OF TELOMERE STATUS DURING OVARIAN AGING IN THE SAMP8 (SENESCENCE ACCELERATED MOUSE PRONE 8) MODEL. Alba M. Polonio, MSc,[1] María T. González-García, MSc,[1] Isabel Córdova-Oriz, MSc,[1] Marta Medrano, Lab Technician,[2] Lucía Chico-Sordo, MSc,[1] Juan A. Garcia-Velasco, MD, PhD,[2] Elisa Varela, PhD[3] [1]IVI Foundation, IIS La Fe, Valencia, Spain; [2]IVI-RMA Madrid, Rey Juan Carlos University, Madrid, Spain; [3]IVI-RMA Madrid, Madrid, Spain.

OBJECTIVE: SAMP8 mouse model recapitulates the signs of reproductive aging observed in women. The SAMP8 females at six months of age, present shorter estrous cycles, ovulate less oocytes, with chromosome misalignments and spindle aberrations, and show a declining of their fertility. This study aims to assess whether alterations in the telomere pathway underlie the accelerated reproductive senescence of the SAMP8 model and to elucidate whether telomere maintenance is altered in the offspring of aged mothers.

DESIGN: Prospective study.

MATERIALS AND METHODS: We used SAMP8 adults (seven months-old; reproductive senescence) and young females (three months-old; fertile). As a control, we used SAMR1 model, which does not show signs of premature reproductive senescence. Three and seven months-old SAMP8 females were mated with young fertile males. The weight, size, survival and number of pups per litter were analysed. Follicle count from three and seven months-old SAMP8 and SAMR1 females was measured. SAMP8 and SAMR1 ovaries were used for quantitative FISH with a telomeric probe to check for telomere length at different ages. Telomere length and aberrations were evaluated in mouse embryonic fibroblasts (MEF) that came from SAMP8 and SAMR1. The survival curve of both models was evaluated.

RESULTS: In litters from the SAMP8 females at 3 and 6-7 months old, there were differences in several parameteres such as the number of pups (6.67 vs 5.17), the size (47.81 *vs* 44.73 at day 15, p=0.0003) and weight (8.4 *vs* 6.47 at day 15, $p<0.0001$). The percentage of litters in which we found dead pups during the first weeks of life was higher in 7 months-old mothers than in 3 months-old mothers (25% vs 33%, repectively) . We found a sharper decay in the number of antral follicles with age in the SAMP8 (12.67 *vs* 2, p=0.0235), compared with SAMR1 model (7.83 *vs* 5.11, p=0,1328). However, there were not statistically significant differences in the number of antral follicles in SAMP8 and SAMR1 old females (2 *vs* 5.11, respectively), suggesting that the process of fertilization or embryo development may be altered. The telomere length of MEF from older mothers is statistically significantly shorter than the telomere length of MEF from younger mothers (31.75 vs 37.89, p=0.0002). The survival curve of both SAMP8 and SAMR1 confirms the aging phenotype published for the model.

CONCLUSIONS: Telomeres of embryos from older mothers are statistically significantly shorter than those from younger mothers. Size and weight of pups from older mothers are altered, as well as size and survival of the litters from older mothers. Our preliminary results suggest that the telomere pathway is altered in the SAMP8 mouse model. Therefore, it is possible that the reproductive senescence phenotype observed in SAMP8 can be due to alterations in the telomere pathway, which may have consequences in the offspring of older mothers.

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THERAPEUTIC STRATEGY TO IMPROVE THE QUALITY OF AGED OOCYTES. Mandy G. Katz-Jaffe, PhD, Jason C. Parks, BS, Blair R. McCallie, BS, Sydney L. Lane, PhD, Rachel Makloski, RN, William B. Schoolcraft, MD. Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: A significant amount of the age-related reduction in reproductive efficiency is overcome with a euploid embryo transfer. Nevertheless, for women in their forties there are other factors contributing to reproductive senescence and lower IVF success rates. Aging is associated with an imbalanced redox state in the ovaries, with increased reactive oxygen species (ROS) relative to naturally occurring antioxidant signaling. The aim of our study was to determine whether restoration of redox balance using a polyphenol rich antioxidant would counter aging-related oxidative stress in the ovary, serving as a therapeutic strategy to improve aged oocyte quality.

DESIGN: Prospective intervention cohort study.

MATERIALS AND METHODS: Female infertility patients (n=121; 38.1 ± 3.5 years; median 39) consented to 1800 mg/day of encapsulated, freeze-dried naturally occurring açaí pulp, *Euterpe oleracea* (total polyphenol content 6,618 mg GAE/100 g, oxygen radical absorbance capacity 208, 628 μmol TE/100 g) for 8-16 weeks preceding an IVF cycle (mean 9.9 ± 2.2; variability due to menstrual cycle dates). Patient outcomes were analyzed using two-tailed, paired Student's t-test, with significance at $P < 0.05$. For mechanistic studies, female outbred CF-1 mice were naturally aged (9-12 months old) before administration of 4mg/day of the same antioxidant. Control females (9-12 months old) received the same balanced nutritional feed but without the açaí. Murine ovarian RNA was isolated and transcriptome analysis performed with CodeLink™ Mouse Whole Genome (Applied Microarrays), qPCR validation (REST 2009 software; Qiagen) and Ingenuity Pathway Analysis (Qiagen), significance at $P < 0.05$.

RESULTS: In a paired comparison patient analysis with and without antioxidant administration, cycles with intervention resulted in increased oocytes collected following ovarian stimulation (17.4±0.9 vs 15.5±0.8, P=0.0085) and a greater number of blastocysts developed (5.1±0.3 vs 2.9±0.3, P<0.0001). Additionally, in a subset of patients with pre-implantation genetic testing for aneuploidy, more euploid blastocysts were identified (2.9±0.3 vs 1.0±0.2, P<0.0001). To date, 100 frozen embryo transfers have resulted in 75 healthy live births or ongoing pregnancies with no pre- or post-natal complications. In aged mice, antioxidant intervention lead to an improved ovarian transcriptome including upregulated β-adrenergic signaling, cell growth and antioxidant pathways, and downregulated apoptosis and pro-inflammatory signaling (P<0.05). Additionally, in aged mice, antioxidants increased the expression of several antioxidant genes (*GPX1*, *SOD2*, and *GSR; P*<0.05*)* in the oocyte.

CONCLUSIONS: This study provides preliminary evidence that antioxidant intervention with a potent scavenger of oxygen free radicals and ROS, has therapeutic benefit prior to ovarian stimulation to improve aged oocyte quality. Candidates for the underlying molecular mechanisms include transcriptional changes in β-adrenergic signaling, anti-inflammatory processes as well as improvements in ovarian and oocyte antioxidant signaling.

SUPPORT: None

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WITHDRAWN

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CURRENT STATE OF CLINICAL TRIALS IN INFERTILITY: A COMPREHENSIVE ANALYSIS OF THE CLINICALTRIALS.GOV DATABASE.

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OBJECTIVE: To characterize the landscape of interventional clinical trials for infertility, and to identify factors associated with trial non-completion. We hypothesized that sponsor type and trial location would be associated with trial non-completion.

DESIGN: Retrospective analysis of domestic and international clinical trials registered with ClinicalTrials.gov from 2010-2020.

MATERIALS AND METHODS: ClinicalTrials.gov was queried for completed, suspended, terminated, and withdrawn interventional clinical trials using the search term "infertility." Logistic regression was used to examine whether sponsor type and trial location were associated with trial non-completion with and without adjusting for intervention type, trial

TABLE 1: Trial non-completion and logistic regression results

		Unadjusted		Adjusted	
	Non-completion rates	OR (95% CI)	P value	OR (95% CI)	P value
Industry vs. non-industry	11% vs. 19%	0.53 (0.23, 1.20)	0.13	0.66 (0.22, 1.96)	0.45
Domestic vs. international	32% vs. 16%	2.49 (1.48, 4.18)	<0.01	0.93 (0.42, 2.06)	0.86

OR = odds ratio; CI = confidence Interval.

primary outcome, gender, number of sites, randomization, enrollment size, and trial phase.

RESULTS: Five-hundred and six trials were included in the analysis. Most trials (82%) were conducted outside the United States. A minority (12%) of trials were sponsored by industry with the remainder sponsored by academic, public, or private organizations. Most trials involved drug (48%) or procedural (22%) interventions. A majority (85%) of trials included only female participants. Few trials (4%) provided information on demographics of study participants, such as race or ethnicity. Overall, 18% of trials were not completed. Rates of non-completion by sponsor type and trial location, as well as the results of the logistic regression models, are reported in Table 1. Domestic trial location was associated with higher non-completion rate; however, this association was no longer significant after adjustment. Industry-sponsored trials had a lower non-completion rate compared to non-industry trials, but this relationship was not statistically significant before or after adjustment.

CONCLUSIONS: Far more interventional clinical trials for infertility are conducted internationally than in the United States. Men are underrepresented in clinical trials for infertility, and trial participant demographics are severely under-reported. US trials had higher rates of non-completion, but this was not statistically significant after adjustment. Sponsor type was not associated with trial non-completion. Future efforts should be directed at greater transparency into the demographics of study participants and the creation of more trials addressing male-factor infertility.

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MISDIAGNOSED SEPTATE UTERUS IN WOMEN SCHEDULED FOR IN-VITRO-FERTILIZATION (IVF): A 5-YEAR COHORT STUDY. Ahmed M. Abdelmagied, MD,[1] Ahmed M. Abbas, MD,[1] Dina M. Habib, MD,[1] Mohammed Khairy Ali, MD,[1] Osama S. Abdalmageed, MD,[1] Karim S. Abdallah, MSc,[2] Fawzia Ahmed Habib, MD[3] [1]Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; [2]Department of Obstetrics and Gynecology,School of Medicine, Monash University, Melbourne, VIC, Australia; [3]Department of Obstetrics and Gynecology, Faculty of Medicine, Taibah University, Madinah, Saudi Arabia.

OBJECTIVE: This study aimed to evaluate the diagnostic accuracy of three-dimensional ultrasound (3D-US) and hysterosalpingography (HSG) in the differentiation between arcuate and septate uterus in women scheduled for IVF compared to hysteroscopy and/or laparoscopy examination (HL) , the gold standard.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Infertile women indicated for IVF who attended a tertiary assisted conception center from 2015 till the end of 2019 were screened. Subjects with suspected diagnosis of arcuate and septate uterus based on HSG were considered. Only reports that included analysis of the outer and inner uterine fundal contours as well as the length of the fundal internal indentation during 3D-US and HL evaluations were studied. Two standard classifications, ASRM-2016 and CUME-2018, were utilized for imaging and endoscopic analysis of the uterine morphology to appropriately define each anomaly. The final diagnosis of the anomalies was based on HL, the gold standard. All cases of septate uterus underwent combined hysteroscopy and laparoscopy examination to confirm the final diagnosis, and to guide the hysteroscopic septal incision. The analysis was according to the STARD guidelines for reporting diagnostic accuracy studies. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy and the level of agreement by kappa statistics were calculated for the diagnostic modalities.

RESULTS: Among 1840 women planned for IVF, a cohort of 196 women (10.7%) included in the final analysis. Utilizing ASRM-2016 criteria, 3 categories of uterine anomalies were diagnosed by HL: arcuate uterus (n=83, 42.3%), septate uterus (n=80, 40.8%), and bicornuate uterus (n=11, 5.6%). Others had 1-1.5 cm internal fundal indentations with angles <90 degrees, so were left unclassified (n=22, 11.2%). Sensitivity, specificity, PPV, NPV, and accuracy of HSG were 70%, 90%, 83%,81%, and 82%, respectively. 3D-US yielded perfect diagnostic accuracy (100%) and perfect agreement with HL in identifying all anomalies. On the other hand, the agreement between HSG and HL was only in 161 cases (82.1%), (κ=0.65,CI: 0.55-0.75). For septate uterus, 24 cases (24/80;30%) were misdiagnosed by HSG as arcuate uterus, while for bicornuate uterus, HSG misdiagnosed all of them as septate uteri. When utilizing CUME-2018 criteria for uterine septum diagnosis, the unclassifiable uteri by ASRM-2016 classification would increase the proportion of septate uteri misdiagnosed as arcuate uteri by HSG (46/102,45.1%) (Relative risk:1.5, CI:1.01 - 2.2, P <0.04).

CONCLUSIONS: Women for IVF with suspected fundal depression on HSG should be examined by 3D-US in order to identify subtle septae that can substantially affect implantation. The rate of identifying these septae is affected by the definition system utilized by clinicians.

References: 1- ASRM. Uterine septum: a guideline. Fertil Steril 2016; 106: 530-540 2- Congenital Uterine Malformation by Experts (CUME): better criteria for distinguishing between normal/arcuate and septate uterus? Ultrasound Obstet Gynecol 2018; 51: 101-109.

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INTRA- AND INTER-CYCLE VARIABILITY OF ANTI-MÜLLERIAN HORMONE (AMH) LEVELS IN HEALTHY WOMEN MEASURED WITH ELECSYS AMH PLUS IMMUNOASSAY: THE BICYCLE STUDY. Marieke Biniasch, M Med,[1] Ruediger Paul Laubender, PhD,[2] Martin Hund, PhD,[3] Katharina Buck, PhD,[2] Christian De Geyter, MD[1] [1]Reproductive Medicine and Gynecological Endocrinology, Universitätsspital Basel, University of Basel, Basel, Switzerland; [2]Roche Diagnostics GmbH, Penzberg, Germany; [3]Roche Diagnostics International Ltd., Rotkreuz, Switzerland.

OBJECTIVE: To determine variability of anti-Müllerian hormone (AMH) serum levels during the natural menstrual cycle between different women (inter-subject), between separate menstrual cycles within a woman (inter-cycle), and within a menstrual cycle (intra-cycle). Understanding variation in AMH levels may aid with assessment of ovarian reserve and provide a reliable prediction of response to ovarian stimulation in women undergoing assisted reproduction.

DESIGN: A prospective, single-center study using the Elecsys® AMH Plus immunoassay to quantify AMH levels in healthy women.

MATERIALS AND METHODS: Eligible women were aged 18–40, had regular, natural menstrual cycles (i.e. not using any hormonal drugs) between 28–32 days, and a BMI of 19–26 kg/m^2. Serum samples were collected every two days during two separate menstrual cycles with a menstrual cycle in between. Serum AMH levels were measured using the Elecsys AMH Plus assay on the cobas e 411 analyzer (Roche Diagnostics Ltd). Menstrual cycle lengths were standardized to 28 days. Mixed-effects periodic regression models based on Fourier series were performed to evaluate the inter-subject, inter-cycle, and intra-cycle variability. The mesor (mean value based on distribution of values across the cycle[s]) allowed for evaluation of inter-subject and inter-cycle variability; peak-to-peak (PtP) amplitude allowed for evaluation of inter-cycle and intra-cycle variability. Separation of the biological and analytical variabilities was determined by analysis of two remeasured AMH levels, with the original AMH levels, to provide triplicate results. The relationship between AMH levels and progesterone levels was investigated.

RESULTS: A total of 42 women were assessed over two non-subsequent cycles, with a further five women included for one cycle only. Compared with inter-cycle variability, time series plots of AMH levels indicated substantial variability between women (inter-subject variability). Statistical modelling showed large inter-subject variation in both the mesor and PtP amplitude. In addition, for each participant, intra-cycle variability was higher than inter-cycle variability. The inter-cycle mesors showed a strong correlation between cycles (r=0.95), while the PtP amplitude was weakly correlated (r=0.23). Moderate correlation between the mesor and PtP amplitude was seen across both cycles (cycle 1: r=0.63; cycle 2: r=0.65). Coefficient of variation (CV) of unexplained biological variability and analytical variability was 10.8%. Triplicate results provided a CV of unexplained biological variability of 9.6% and reproducibility (analytical variability) of 3.5%. The analyses also demonstrated that the time interval in which serum AMH decreased within a cycle (within Days 14 and 20) was related to the time interval with the largest increase in progesterone levels (within Days 16 and 22).

CONCLUSIONS: Inter-subject and intra-cycle variability of AMH levels were larger than inter-cycle variability. This study also showed that unexplained biological variability was higher than analytical variability of the Elecsys AMH Plus assay.

SUPPORT: This study was funded by Roche Diagnostics International Ltd. Third-party medical writing assistance was provided by Ashlie Butler (Gardiner-Caldwell Communications, Macclesfield, UK) and was funded by Roche Diagnostics International Ltd.

DOES DELAY IN THE DIAGNOSIS OF RUDIMENTARY HORN PREGNANCY IN PATIENTS WITH UNICORNUATE UTERI IMPACT TREATMENT OUTCOME?

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OBJECTIVE: Rudimentary horn pregnancy (RHP) is a very rare form of ectopic pregnancy (EP) that tends to rupture in the second trimester. Similar to other EPs, the treatment of RHPs is excision, hence delay in diagnosis (DID) can be detrimental. Our objective is to determine whether DID of RHP in patients with unicornuate uteri (UCU) impacts the treatment outcome.

DESIGN: Retrospective cohort study of published case reports in PubMed database.

MATERIALS AND METHODS: A computerized PubMed search of case reports of RHP from 2007 to 2020 was performed using the key words; unicornuate uterus, rudimentary horn, pregnancy, case. Data was analyzed with SPSS version 26.

RESULTS: Of the 97 published cases, due to limited information available, 95 cases were included, 40 (42.1%) in which the diagnosis of RHP was made at first encounter and 55 (57.9%) in which the diagnosis was delayed. Out of these cases, it was possible to calculate the median [range] length of delay (35 [1-1825] days) in only 32 cases. Of 95 cases, 27 (28.4%), 5 (5.3%), 61 (64.2%), 1 (1.1%), underwent laparoscopy, laparoscopy converted to laparotomy, laparotomy, and methotrexate injection respectively. Diagnosis was made at autopsy in one case.

CONCLUSIONS: Diagnosis of RHP was significantly more likely to be made at first encounter when patients were known to have a uterine anomaly. DID was associated with a significantly higher GA at the time of treatment but there was no significant difference in the proportion of fetuses that were alive upon entrance to the abdomen, rate of ruptured RH and hemoperitoneum. Out of all of the cases, only one maternal death was reported. Therefore, delaying surgery to confirm a diagnosis of RHP does not adversely impact the maternal fetal outcome.

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	Diagnosis Made at First Encounter	Diagnosis Delayed	P-value
Age (years)*	n=38, 27.2±6.9	n=55, 26.2±4.7	0.42
Gravidity**	n=34, 2 [0-4]	n=51, 2 [1-8]	0.21
Parity >20weeks**	n=33, 0 [0-3]	n=52, 1 [0-5]	0.53
Gestational age (GA) at diagnosis (weeks)**	n=40, 12 [5-39]	n=54, 18 [5-42]	**0.001**
Patient with known history of a uterine anomaly	3/40 (7.5%)	18/54 (33.3%)	**0.003**
Patient with known history of RH	3/40 (7.5%)	3/54 (5.6%)	0.70
History of prior EP	3/32 (9.4%)	4/47 (8.5%)	1.0
Pain symptom on admission	23/38 (60.5%)	27/51 (52.9%)	0.52
Hemoperitoneum on admission	13/38 (34.2%)	19/49 (38.8%)	0.82
Estimated amount of hemoperitoneum (L)**	n=34, 0 [0-5.0]	n=45, 0 [0-4.0]	0.46
Emergent surgery done	31/39 (79.5%)	41/54 (75.9%)	0.80
Ruptured RH found at surgery	14/39 (35.9%)	22/55 (40.0%)	0.80
Pregnancy in peritoneal cavity at operation	9/36 (25.0%)	14/53 (26.4%)	1.00
Fetus alive prior to/at surgery	14/32 (43.8%)	26/53 (49.1%)	0.66
RH excised at surgery	35/38 (92.1%)	51/54 (94.4%)	0.69

*(n=numbers, mean±SD).
**[n=numbers, median(range)].

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TOP TEN RESEARCH PRIORITIES FOR FEMALE AND UNEXPLAINED INFERTILITY.

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OBJECTIVE: To develop the top 10 research priorities for female and unexplained infertility.

DESIGN: International consensus development study.

MATERIALS AND METHODS: Potential research questions were collated from an initial international survey, a systematic review of national and international fertility guidelines, and Cochrane systematic reviews. A rationalized list of confirmed research uncertainties were prioritized in an international survey. Prioritized research uncertainties were discussed during a consensus development meeting.

RESULTS: The initial survey was completed by 388 participants, from 40 countries, and 131 potential research questions were submitted. By reviewing nine clinical practice guidelines and 162 Cochrane systematic reviews, a further 136 potential research questions were identified. A rationalized list of 48 confirmed research uncertainties were entered into an interim prioritization survey completed by 317 respondents from 43 countries. The top 10 research priorities for female and unexplained infertility were identified during a consensus development meeting involving 41 participants from 11 countries (Table 1).

TABLE 1: Top 10 research priorities for female and unexplained infertility.

1	Can age-related infertility be prevented?
2	Can a predictive model be developed, tested, and validated to compare the outcomes of different management strategies for couples with unexplained infertility?
3	In couples with unexplained infertility, what is the optimal assisted reproductive technique?
4	Can a predictive model for fertility based upon ovarian reserve tests be developed, tested, and validated?
5	In women at risk of age-related infertility does standardized fertility assessment before attempting expectant management improve live birth rates?
6	What causes unexplained infertility?
7	In women with uterine fibroids what is the optimal management strategy to preserve fertility?
8	In women with otherwise unexplained infertility does hysteroscopic removal of an endometrial polyp increase live birth rates?
9	In women with mild intrauterine adhesions and otherwise unexplained infertility, does removal increase live birth rates?
10	In women with a uterine septum and otherwise unexplained infertility does hysteroscopic resection increase live birth rates?

CONCLUSIONS: We anticipate these research priorities will help research funding organizations and researchers to develop their future research agenda. Healthcare professionals, professional organisations, and patient advocacy groups should champion the research priorities to highlight the many unanswered questions which need to be addressed in order to improve the outcomes of people with fertility problems.

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THE USE OF VIRTUAL REALITY TECHNOLOGY IN INFERTILE WOMEN UNDERGOING IN VITRO FERTILIZATION-EMBRYO TRANSFER: A RANDOMIZED CONTROLLED TRIAL.

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OBJECTIVE: Embryo transfer (ET) is a crucial event in determining in vitro fertilization (IVF) outcome, perceived by many patients as the culmination of treatment. Therefore, it is often a stressful procedure for patients. We hypothesized that the stress accompanying this procedure may be inversely correlated with cycle outcome. The use of complementary therapies to reduce anxiety and improve IVF outcome is increasing. Various interventions

have been studied, but their efficacy remains uncertain. Virtual reality (VR) technology, has been gaining attention over the past two decades, owing to evidence of it's therapeutic potential for anxiety management and stress reduction. This study aimed to examine the possible effect of VR exposure on anxiety level and clinical pregnancy rate (CPR) in women undergoing IVF-ET.

DESIGN: A prospective randomized controlled trial (Clinical Trials.gov Protocol Registration: NCT04394962).

MATERIALS AND METHODS: The study was conducted at the CReATe Fertility Centre (Toronto, Canada) after obtaining REB approval. Recruitment period was May 2019-March 2020 (suspended due to Covid-19). Infertile women aged 21-45-year-old using own ovum or older using donor eggs, starting a frozen ET cycle, were recruited. All participants provided a written informed consent before study entry. Exclusion Criteria were contraindications to use VR technology, anxiety disorder and major uterine anomalies. Participants were withdrawn if ET was cancelled. Patients were randomized (1:1) into 2 groups: A. Study group: 15-30 minutes of passive VR exposure (calming environment of choice) before ET; B. Control group: routine care only. Anxiety was assessed at 3 time points: T1=recruitment; T2=pre ET; T3=Post ET, using the validated "State-Trait Anxiety Inventory" questionnaire, heart rate (HR) and blood pressure (BP) measurements. The primary outcome was the CPR and the secondary outcomes were patients' anxiety parameters. T-test or chi square were used as appropriate. $P<0.05$ was considered statistically significant.

RESULTS: Seventy six patients were included in the analysis, 38 in each study arm. Patient and cycle characteristics were comparable between the groups. The mean VR exposure time was 23.2 $\pm$14.1 minutes, the majority chose a beach environment (78.9%) and stated they would recommend VR (75.3%). No serious adverse events were reported. HR was higher in T2 vs T1 and T3 ($p=0.002$), but the mean BP and HR did not differ between the groups. T1 and T2 'trait' anxiety scores were comparable between the groups. No significant differences were found between the VR group to control in the 'state' anxiety scores during T2 (40.3 vs 39.3) and T3 (38 vs 38), respectively ($P>0.05$). CPR was comparable between the VR and the control group (50% vs 34.2%, respectively; $p=0.42$).

CONCLUSIONS: This is the first study to assess VR use in assisted reproduction. The preliminary findings suggest that VR exposure prior to ET does not reduce patients' anxiety levels. Although non-significant, a higher CPR trend in the VR group suggests that this intervention may have a beneficial effect, but a larger sample size is needed to confirm this.

SUPPORT: CReATe Fertility Centre

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REGULATION OF OVIDUCT HOMEOSTASIS AND FERTILITY BY PAX2 AND PAX8 GENES. Abdul Soofi, PhD University of Michigan, Ann Arbor, MI.

OBJECTIVE: In mouse and humans, the development regulatory genes Pax2 and Pax8 are expressed in ovarian duct surface epithelia, yet the function of these genes and proteins in adult females remains unclear. By Generating double & single KO mouse modules of Pax2 and Pax8 we investigate their roles in maintaining the integrity of the oviductal cells. Our studies directly address aspects of oviduct epithelial homeostasis and the effects on fertility.

DESIGN: To create Pax2, Pax8, and Pax2/8 double mutants specifically in oviduct epithelia and characterize changes in gene expression, epithelial cell integrity, and fertility.

MATERIALS AND METHODS: We will implement detailed analyses of oviducts isolated at various times post tamoxifen administration from mice with conditional Pax2, Pax8, or both alleles, using the Ovigp1-CreER driver. Mice will also carry reporter allele ($Gt(ROSA)26Sor^{tm4(ACTB-tdTomato,-EGFP)Luo}$) to mark all active Cre expressing cells with cell surface EGFP. In addition to defining novel functions for Pax proteins in the oviduct, we will utilize state-of-the-art methods for single cell analyses, transcriptomics, and chromatin remodeling.

RESULTS: Mutation of Pax2 and Pax8 in adult female oviducts results in significant changes in gene expression and morphology. Loss of both Pax2 and Pax8 resulted in infertility (Table 1). To date, most of the preliminary data was obtained from Pax2/8 double mutants since we were concerned with redundancy and expected the most significant phenotypes in the double mutants. Analyses of histology, immunohistochemistry and changes in gene expression of total RNA from whole oviducts isolated after tamoxifen administration. For a rapid first pass screen, we compared controls ($Pax2^{f/f};Pax8^{f/f}$) to single Pax mutants and Pax2/8 double mutants ($Pax2^{f/f};Pax8^{f/f}$; *Ovigp1-CreER*) by Affymetrix microarrays. These data show hundreds of changes in gene expression levels upon Pax2 or Pax8 deletion, with significant overlap between the Pax2 and Pax8 mutants but also expression changes unique to each single mutant.

TABLE 1. Fertility of Oviduct Specific Pax Mutants

Genotype	# females	# plugs	Litters	Litter size
$Pax2^{f/f}$, $Pax8^{f/f}$, Ovi-Cre	5	15	0	0
$Pax2^{f/f}$, $Pax8^{f/f}$,	4	12	12	6-9
$Pax8^{f/f}$, Ovi-Cre	3	6	2	6-7

CONCLUSIONS: Little is known regarding the mechanisms underlying epithelial homoeostasis, the proteins that determine cell fates, and epithelial integrity in the adult oviduct. Pax8 expressing secretory cells are thought to give rise to ciliated cells, which help move the oocyte down the duct and Pax2 is associated with cilia motility and physiology. Using a conditional KO model of Pax2 & Pax8 will allow us to understand those mechanisms and identify future novel therapeutic targets for diagnostics and treatments

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IUI AFTER LH SURGE: HOW SOON IS TOO SOON? Samantha Simpson, MD, Lubna Pal, MBBS Yale University, Orange, CT.

OBJECTIVE: Intrauterine insemination (IUI) following ovulation induction (OI) or in a natural cycle is a first line treatment for many etiologies of infertility. The timing of IUI in relation to ovulation trigger or spontaneous luteinizing hormone (LH) surge, as well as the number of IUI attempts that should be made remains a subject of debate. Many patients prefer a single IUI, whether due to expense of treatment or feasibility of making it to an office appointment on short notice. Sperm can theoretically survive in the female reproductive tract for up to 72 hours. The timing of oocyte(s) release is approximately 35-36 hours after the LH surge; following ovulation, the window of fertilization is restricted to approximately 24 hours. Therefore, it is logical to conclude that as long as the IUI is undertaken within two days of the LH surge, the actual timing of the procedure should not influence the probability of conception. Existing evidence on whether IUI cycle outcomes, such as ongoing pregnancy or live birth, differ following a single IUI timed at either 12 or 36 hours after LH surge is sparse.

DESIGN: Retrospective cohort study at a single academic fertility center.

MATERIALS AND METHODS: All patients presenting for a planned single IUI between January 2018 and December 2019 were eligible. Evidence of bilateral tubal patency, and yield of $\geq$ 15 million /mL sperm in the IUI sample were inclusion criteria. The IUI timing was specified based on timing of hCG induced ovulation (n=260) or by evidence of a positive urinary LH surge reading occurring 12 hours or less after a previous negative reading (n=16). OI treatments included clomiphene (n= 152), letrozole (n=76), or injectable gonadotropins (n=35). Relationships between timing of IUI with ongoing pregnancy greater than 16 weeks (OP) and live birth (LB) were calculated.

RESULTS: 197 women undergoing 276 cycles with single IUI were included in the analyses. In 75 cycles, IUI was performed 12-16 hours following hCG trigger or LH-surge; IUI was performed 36-40 hours after trigger or LH-surge in 201 cycles. 32 cycles successfully lead to live birth or ongoing pregnancy >16 weeks gestation (11.6% of cycles). OP/LB following IUI differed based on timing of IUI. After adjusting for age, BMI, OI regimen, and endometrial thickness, the likelihood for OP/LB was threefold higher than the IUI was timed at 36-40 hours following trigger or LH surge, compared to 12-16 hours (14% v 5%, OR 3.0, 95% CI 1.00-9.81, $p=0.047$).

CONCLUSIONS: In women undergoing IUI for infertility management, the timing of IUI is an independent predictor of IUI cycle outcome.

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HIGH EXPRESSION OF PGAM FAMILY MEMBER 5 (PGAM5) IS ASSOCIATED WITH DIMINISHED OVARIAN RESPONDER IN CUMULUS CELLS. Li-Te Lin, PhD,[1] Chia-Jung Li, Ph.D,[2] Kuan-Hao Tsui, M.D; Ph.D[2] [1]Kaohsiung Veterans General Hospital, Kaohsiung City, Taiwan; [2]Department of Obstetrics and Gynecology, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan.

OBJECTIVE: Is high PGAM5 expression associated with diminished ovarian responder (DOR) in cumulus cells as well as assisted reproductive technology (ART) outcome, and what is the underlying mechanism of action of PGAM5?

DESIGN: Experimental laboratory study.

MATERIALS AND METHODS: In a prospective study, fresh granulosa cells were obtained from 48 women aged 20–40 years who underwent IVF with embryo transfer and who were divided into two groups: the diminished ovarian reserve (DOR) group (n = 20) and the control group (n = 28). Patient characteristics including age, infertility duration, body mass index, FSH, anti-Müllerian hormone (AMH) and cumulus cell PGAM5 expression levels, autophagy, mitochondrial mass were analysed.

RESULTS: The Drp1 in the DOR group was activated and the PGAM5 translocated to the outer membrane of the mitochondria, the formation of lysosomes increased, thereby increasing the fission of mitochondria. We further observed a significant reduction in the mass of the mitochondria in the DOR group and a severe imbalance, and the formation of LC3, which in turn caused mitophagy.

CONCLUSIONS: High PGAM5 expression levels in cumulus cells were related to DOR, which may be involved in the clinical outcome of ART by promoting mitophagy and affecting mitochondrial function.

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DETECTION OF CLOCK rs11932595 POLYMORPHISM IN WOMEN WITH RECURRENT PREGNANCY LOSS (RPL). Despoina Mavrogianni, Dr, PhD,[1] Helen Pandi, Biologist,[1] Sofoklis Stavrou, MD, Ph.D.,[1] Dimitris Loutradis, Professor,[2] Peter Drakakis, Professor[1] [1]Molecular Biology of Reproduction Unit and Recurrent Abortions Unit, Assisted Reproduction Division, Athens, Greece, Greece; [2]Molecular Biology of Reproduction Unit and Recurrent Abortions Unit, Assisted Reproduction Division, Athens, Greece.

OBJECTIVE: To evaluate whether the Clock gene Polymorphism rs11932595 is associated with recurrent pregnancy loss in women within the Greek population.

DESIGN: This is a case-control study consisting of 57 women with a history of two or more recurrent miscarriages before the 24th week of gestation and 61 women with no history of pathological pregnancies and at least one live birth.We studied the expression of Clock gene Polymorphism rs11932595.

MATERIALS AND METHODS: DNA was extracted from blood and in all samples the genomic region of CLOCK containing the rs11932595 polymorphism was amplified by applying the Polymerase Chain Reaction (PCR). Subsequently, the PCR product was sequenced, in order to detect the specific polymorphism.

RESULTS: Results have indicated that 50 out of 57 women of the RPL group (87.7%) and 41 out of 61 women in control group (67.2) carry the polymorphic allele. Evaluation of the results showed that there is a statistically significant positive correlation between the presence of the polymorphism and the medical history of RPL.

CONCLUSIONS: This particular study, carried out for the first time in the Greek population, verifies the results of recent studies which have indicated that the CLOCK gene rs11932595 SNP is related with the presence of recurrent abortions. A possible correlation of polymorphisms present in CLOCK gene and miscarriages may lead to a better understanding of the recurrent pregnancy loss mechanism.

POSTER SESSION: FERTILITY PRESERVATION

P-293

REASSIGNED

P-294

REASSIGNED

P-295 4:30 PM Sunday, October 18, 2020

COMPARISON OF HUMAN ANTRAL FOLLICLES OF XENOGRAFT VERSUS OVARIAN ORIGIN REVEALS DISPARATE MOLECULAR SIGNATURES. Limor Man, M.D, M.Med.Sc, Nicole Lustgarten, PhD, Eleni Kallinos, B.S, Kolbe Hancock, MD, Nikica Zaninovic, Ph.D., Glenn Schattman, MD, Zev Rosenwaks, M.D., Daylon James, PhD Weill Cornell Medicine, New York, NY.

OBJECTIVE: The activation, growth and maturation of oocytes to an ovulatory phase, termed folliculogenesis, is governed by the orchestrated activity of multiple specialized cells types within the ovary, yet mechanisms governing diversification and behavior of discrete cellular sub-populations within follicles are poorly understood. We set out to identify and characterize unique subsets among the granulosa (GC), theca (TC) and stromal cell fractions, and to compare the molecular profiles of these sub-populations when isolated from native ovarian versus xenograft-derived antral follicles.

DESIGN: Small antral follicles (< 5mm) were isolated from ovaries of organ donors or patients undergoing whole ovarian resection for fertility preservation. These were compared to antral follicles that developed in long term (> 14 weeks) xenografts of cryopreserved/thawed human ovarian cortex. Immunostaining, flow cytometry, bulk and single-cell RNA sequencing were used to segregate and interrogate discrete follicle-derived cell fractions.

MATERIALS AND METHODS: The GC fraction was first purified from 3 small (2-3 mm) ovary-derived antral follicles and subjected to bulk RNA sequencing to identify candidate surface molecules that may specifically identify follicle cell sub-types. Candidate factors were screened using immune-staining and flow cytometry of xenograft and ovary-derived follicles. 22 unique single-cell library preparations (∼100,000 cells) representing fractions from 13 individual follicles (8 ovary origin, 5 xenograft origin) and 6 women were prepared, sequenced and analyzed.

RESULTS: Analysis of GC, TC and stromal subpopulations deconstructed phenotypic diversification during early antral follicle development, identifying secreted factors that are differentially enriched between mural and oophorus GCs, and segregating stromal/support and steroidogenic activity between theca externa and interna, respectively. Numerous factors were differentially expressed in follicles of xenograft versus ovarian origin, highlighting the potential contribution of humoral factors to follicular development that have not been considered, to date.

CONCLUSIONS: These data shed light on previously undescribed subpopulations of both GC and TC compartments and provide a systems level portrait of cellular diversification in early antral human follicles.

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THE USE OF DYDROGESTERONE TO PREVENT LH PEAK IN RANDOM-START OVARIAN STIMULATION FOR FERTILITY PRESERVATION. Marouen Braham, Associate Professor,[1] Khadija Kacem, Associate Professor,[1] Zeineb Zemni, Medical Doctor,[1] Sarah Amari, Medical Doctor,[1] Wissal Jaafar, Medical Doctor,[1] Sana Chtourou, Assistant Professor,[2] Manel Hamdoun, Associate Professor,[1] Linda Debbabi, Medical Doctor,[1] Nozha Chakroun, Professor,[1] Olfa Bahri, Professor,[1] Fethi Zhioua, Professor,[3] Anis Fadhlaoui, Associate Professor[3] [1]Aziza Othmana University hospital, Tunis, Tunisia; [2]Reproductive Medecine Laboratory. Aziza Othmana University Hospital., Tunis, Tunisia; [3]Aziza Othmana Hospital , department of gynecology and obstetrics, tunis, Tunisia.

OBJECTIVE: Compare the efficacy of oral dydrogesterone to prevent LH peak during ovarian stimulation versus usual antagonist protocol in fertility preservation cases with oocyte vitrification.

DESIGN: Randomized prospective study from August 2019 to March 2020 at the Gynecology, Obstetric and Reproductive Medicine department of the Aziza Othmana University Hospital.

MATERIALS AND METHODS: Inclusion criteria: All patients underwent controlled ovarian stimulation for fertility preservation via oocyte vitrification.

Exclusion criteria: Patients with hormone-dependent diseases (breast cancer, systemic lupus).

Random-start ovarian stimulation was conducted with 300 IU of recombinant FSH for all patients.

Patients were randomized into 2 groups on the day of the onset of ovarian stimulation: Group 1: prevention of LH peak using Dydrogesterone orally: 10 mg three times a day; beginning the first day of ovarian stimulation. Group 2: Prevention of LH peak by subcutaneous injection of Cetrotelix 0.25 mg per day from the first day of ovarian stimulation.

Ovulation was triggered with 0.2 mg triptoreline. Oocyte pickup took place 37 hours later, either vaginally or per urethral transvesical route (for virgin patients).

$\chi 2$ test was used to compare qualitative variables. Student's t-test was used to compare quantitative variables. P-value < 0.05 was considered as statistically significant.

RESULTS: Forty-seven patients were included in our study: 22 in Group 1 and 25 in Group 2. There was no significant difference regarding the clinical characteristics of the 2 groups (Group 1 vs Group 2) in terms of age (23.14 ± 5.07 vs 23.8 ± 5.7 , p: 0.7), BMI (21.63 ± 3.6 vs 22.48 ± 4.03 , p: 0.5), AMH levels (2.04 ± 1.24 vs 3.3 ± 1.93, p: 0.06), the duration of ovarian stimulation (9.14 ± 1.55 vs 9.33 ± 1.79 , p: 0.5), the number of follicles with a diameter > 15 mm on the day of triggering (7.62 ± 4.1 vs 7.5 ± 3.3, p: 0.6) and plasma oestrogen levels on the day of triggering ovulation (2587 ± 1601 vs 2083 ± 1163, p: 0.1) Moreover, pickup results were similar (goupe 1 vs group 2) for the number of CCOS(12.71 ± 7.7 vs 12.29 ± 7.6 , p: 0.3) and the number of mature oocytes (9.85 ± 5.9 vs 9 ± 6.7 , p: 0.9). It should be noted that LH monitoring was performed in all patients and the difference was not significant either.

CONCLUSIONS: Prevention of premature LH peak during COS is possible using dydrogesterone in Random-start protocols for fertility preservation, excluding cases of hormone-dependant diseases.

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MODIFIED RNA ENCODING FOR ANTI-MULLERIAN HORMONE CONFERS OVARIAN PROTECTION FROM CYCLOPHOSPHAMIDE IN BOTH MOUSE AND HUMAN XENOGRAFT MODELS. Limor Man, M.D, M.Med.Sc,[1] Eleni Kallinos, B.S,[1] Lior Zangi, PhD,[2] Zev Rosenwaks, M.D.,[1] Daylon James, PhD[1] [1]The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY; [2]Icahn school of Medicine at Mount Sinai, NYC, NY.

OBJECTIVE: Women and young girls are at risk of ovarian failure secondary to chemotherapy treatment. The risk varies according to type, amount of chemotherapy, and patient's age at treatment (1). Several groups are studying different compounds that may protect the ovary using diverse models (2). In mice, AMH was found to protect primordial follicle (PF) pool loss due to cyclophosphamide (Cp) treatment (3,4). We investigated the potential of modified RNA encoding for Anti-Mullerian hormone (ModRNA-AMH) to protect ovarian pool when administered before Cp in both wild-type (WT) mice and on xenografted human ovarian tissue.

DESIGN: Murine model: intraovarian injection (IO) (saline/murine ModRNA-AMH) followed by intraperitoneal (IP) injection 24 hours later (saline/Cp). A total of 4 arms, 6 ovaries in each. Ovaries were harvested 2 weeks after the first chemotherapy injection.

Xenotransplantation model: human ovarian tissue transplanted into immunocompromised mice for two weeks, followed by: intra-graft (IG) injection (buffer) followed by an IP injection 24 hours later (saline/Cp), or IG injection of human ModRNA-AMH followed by IP Cp. A total of 3 arms, 4 grafts in each group in the short term (2 weeks after first Cp injection), and 8 grafts in each arm in the long term (12 weeks after the first Cp injection).

MATERIALS AND METHODS: In the murine model, we used 6-week old C57/B6 females.

In the xenograft model, we co-transplanted human ovarian cortical tissue from 12- and 29-years old organ donors, with endothelial cells, into NOD scid gamma (NSG) mice.

Cp was administered at the dose of 60mg/Kg and the protocol was repeated a week later.

After harvest of the ovaries/xenografts, histologic sections using H&E staining and light microscopy were used for counting of follicles.

RESULTS: In WT mice, we found retention of PF similar to the controls, Saline - IO /saline -IP; 49±12.10, ModRNA-AMH/saline 53.33±7.81 compared to ModRNA-AMH/Cp 47.17±13.61. A 50% decreased was noted with saline/Cp 26.5±9.01. In xenografts, in the short term, retention of PF was markedly improved with ModRNA-AMH pre-treatment. Buffer-IG/Cp-IP 9.41±10.91% PF, vs 56.24±39.44% with IG-ModRNA-AMH/Cp. Notably, the percentage of PF was similar to grafts treated with buffer/saline 51.67± 4.04%. Interestingly, long-term grafts treated with ModRNA-AMH/Cp yielded 3 antral follicles (AF), similar to 2 AF that were found in the buffer/saline, while only 1 AF was present in the buffer/Cp group. Moreover, the density of follicles in the ModRNA-AMH/Cp condition was normalized, while it was reduced in the buffer/Cp treated group.

CONCLUSIONS: In this study we evaluated the potential for ModRNA-AMH to confer a benefit to ovaries/ovarian tissue in the presence of CP and demonstrated retention of the PF pool in the short term and improved output in the long term. Administration of ModRNA-AMH provides an optimal mode of delivery due to its high efficiency and transient protein expression without eliciting a substantial innate immune response. Intra-ovarian administration before chemotherapy may confer a fertoprotective benefit with minimal expense and intervention.

Patent filing- "Using AMH modRNA to protect ovarian follicles against toxic effects from chemotherapy". Docket number 9222

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SUPPORT: Internal funding, CRMI

P-298

WITHDRAWN

P-299 4:30 PM Sunday, October 18, 2020

OUTCOMES OF FERTILITY PRESERVATION IN WOMEN WITH ENDOMETRIOMA BEFORE AND/OR AFTER OVARIAN CYSTECTOMY. Hyun Kyoung Lee, M.D., Yeon Hee Hong, MD., Jung Ryeol Lee, MD, PhD Seoul National University Bundang Hospital, Seongnam, Korea, Republic of (South).

OBJECTIVE: Endometrioma is a major risk factor of infertility, reducing ovarian reserve and the quality of oocytes. Moreover, when it is surgically removed, ovarian reserve is further reduced. Therefore, women with endometrioma in reproductive age can be suitable candidates for fertility preservation (FP) before surgery. The purpose of this study is to analyze the outcomes of oocyte or embryo cryopreservation in women with endometrioma. We compared the controlled ovarian stimulation (COS) outcomes with infertile women without endometrioma and with other benign cysts. Subgroup analyses were done according to the laterality of endometrioma and COS repeat orders.

DESIGN: A retrospective study

MATERIALS AND METHODS: A total of 52 women with endometrioma were enrolled. Patients took baseline AMH and trans-vaginal ultrasonography before surgery. Patients were counseled about oocyte or embryo cryopreservation if she was expected to have a lower ovarian reserve. Inclusion criteria were typical sonographic features of endometrioma, planned ovarian cystectomy, and oocyte or embryo cryopreservation before surgery. Gonadotropin-releasing hormone antagonist protocols were conducted for COS. Primary outcomes were number of retrieved mature (MII) oocytes and cryopreserved oocytes. We used 1:1 propensity score matching analysis to compare COS outcomes of patients with endometrioma and infertile patients without endometrioma.

RESULTS: A total of 52 COS cycles from 52 patients were included. Patients with endometrioma showed lower AMH (1.20 [0.83, 2.17] vs. 2.96 [2.20, 3.90] ng/ml, $p \leq 0.001$), number of retrived MII oocytes (5.0 [3.0, 8.0] vs. 6.0 [5.0, 11.0], p=0.041),and number of cryopreserved oocytes (3.0 [2.0, 6.0] vs. 6.5 [4.0, 8.3], p=0.014) than matched control infertile patients. Total gonadotropin dose was significantly higher in endometrioma patients (2400 [2100, 2400] vs. 2025 [1743.75, 2400] IU, p=0.003). 21 women underwent repeated COS for 2 to 4 times. The number of cryopreserved oocyte at first to fourth cycles were 3.50 [2.00, 6.00], 5.00 [2.50, 7.50], 3.00 [2.75, 4.75], 3.00 [2.50, 3.50], respectively. Cumulative number of cryopreserved oocytes was 8, 11.5, 14.50 for 2, 3, and 4 times, having a cumulative effect.

CONCLUSIONS: Controlled ovarian stimulation of women with endometrioma for fertility preservation is feasible and effective. Patients with endometrioma who has plan for ovarian cystectomy should be counseled about oocyte or embryo cryopreservation. Furthermore, repeated COS cycles can increase cumulative number of cryopreserved oocytes.

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SUPPORT: None

P-300 4:30 PM Sunday, October 18, 2020

INHIBITING NECROPTOSIS OF SPERMATOGONIAL STEM CELL AS A NOVEL STRATEGY FOR MALE FERTILITY PRESERVATION. Guihua Liu, Ph.D.,[1] Xing Yang, Ph.D.,[1] Tingting Li, Doctor[2] [1]The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; [2]Reproductive Medicine Research Center, Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: Fertility preservation is a common concern for male cancer survivors of reproductive age. However, except for testicular tissue cryopreservation which is not very effective, there is no feasible and precise therapy capable of protecting spermatogenesis for prepubertal boys prior to or during gonadotoxic treatment. This study aims to investigate the effects of inhibiting necroptosis of spermatogonial stem cell (SSC) in fertility preservation.

DESIGN: Animal study was designed.

MATERIALS AND METHODS: Male mice aged 12 weeks were used to establish gonadotoxicity with two intraperitoneal injections of busulfan at a total dose of 40 mg kg^{-1}. The mouse model and the primary cultured mouse SSCs were used to characterize the relationship between necroptosis of SSC and gonadotoxicity. Meanwhile, the effects of an inhibitor of necroptosis pathway, RIPA-56, were observed at day 36 in the mouse model of busulfan induced gonadotoxicity.

RESULTS: The number of SSCs was decreased but the level of necroptosis was up-regulated at day 18 after busulfan treatment in testes from gonadotoxic mice. Further experiments in primary cultured cells showed that the necroptosis caused the cell death in busulfan induced SSCs.

After suppressing RIPK1 throughout the seminiferous epithelium cycle (36 days), when compared to the model group, those in the RIPA-56 group had a decreased loss of spermatogenic cells as shown by histology and an increased Johnsen's score ($P<0.001$), the testis/body weight ratio ($P<0.05$) and the protein expression of SSCs ($P<0.001$) .Moreover, the quantities of SSCs and epididymal spermatozoa were restored after intervention with RIPA-56, indicating a series of beneficial effects by targeting the necroptosis of SSCs in mice undergoing busulfan treatment.

CONCLUSIONS: Our findings reveal that the necroptosis of SSCs plays a critical role in busulfan induced gonadotoxicity and may be a potential target for male fertility preservation.

SUPPORT: No

P-301 4:30 PM Sunday, October 18, 2020

DUAL-TRIGGERING WITH HUMAN CHORIONIC GONADOTROPIN AND GONADOTROPIN RELEASING HORMONE AGONIST IS BENEFICIAL FOR ACQUISITION OF MATURE OOCYTES IN LETROZOLE-COMBINED OVARIAN STIMULATION CYCLES. Yeon Hee Hong, MD.,[1] Jung Ryeol Lee, MD. PhD.,[2] Chang Suk Suh, MD. PhD.,[3] Seok Hyun Kim, MD. PhD.[2] [1]Seoul National University Bundang Hospital, Seongnam, Korea, Republic of (South); [2]Seoul National University College of Medicine, Seoul, Korea, Republic of (South); [3]Sheikh Khalifa Specialty Hospital Ras Al Khaimah, RAK City, United Arab Emirates.

OBJECTIVE: It is critical to set up an efficient maturation method to increase the yield of mature oocytes, especially for cancer patients with fewer chances of fertility preservation (FP) before gonadotoxic therapy. The purpose of this study is to investigate whether dual triggering with human chorionic gonadotropin (hCG) and gonadotropin-releasing hormone agonist (GnRHa) for final oocyte maturation improve the controlled ovarian stimulation (COS) outcomes for women undergoing FP.

DESIGN: Retrospective study

MATERIALS AND METHODS: A total of 317 patients undergoing COS using GnRH antagonist protocol for FP were enrolled. Patients' basal characteristics and COS outcomes were analyzed according to triggering methods. The control group (n=208) used 250 μg of recombinant hCG (rhCG), and the study group (n=109) used 250 μg of rhCG and 0.2mg of triptorelin for triggering. All information was collected via medical records. Subgroup analyses were done for patients with decreased ovarian reserve (DOR) defined as AMH<1.1ng/mL (n=74), with endometrioma (n=88), or with breast cancer and endometrial cancer using 5mg of letrozole during the COS cycles (n=73). The main outcomes are the number of mature oocytes and the maturation rate. Continuous variables were compared using either the Student t-test or Mann-Whitney test. The chi-square test was used for categorical variables. P-value < 0.05 was considered statistically significant. SPSS version 25.0 was used for statistical analyses.

RESULTS: The mean age, BMI, and AMH in all patients are 31.4±6.3 years, 21.3±3.0 kg/m^2, and 2.6±2.6 ng/mL, respectively. There was no significant difference in basal characteristics and the number of total and mature oocytes between the two groups. Subgroup analyses for women with endometrioma or DOR showed similar results. However, the dual-trigger group had significantly higher number of mature oocytes than the hCG trigger group in breast and endometrial cancer patients using letrozole during COS cycles (7.0±6.4 vs. 4.3±3.6, p=0.041). The maturation rate was higher in the dual-triggering group, though it was not statistically significant

(60.5±28.3 vs. 48.2±28.0, p=0.072). The rate of ovarian hyperstimulation syndrome is comparable between the two groups (6.3% vs. 0%, p=0.189).

CONCLUSIONS: The dual triggering method significantly increases the yield of mature oocytes and could be a useful method for final oocyte maturation in breast and endometrial cancer patients using letrozole-combined COS regimen.

P-302 4:30 PM Sunday, October 18, 2020

EGG FREEZING CRACKS UP TO BE A VIABLE FERTILITY PRESERVATION (FP) METHOD: FIFTEEN YEARS OF AUTOLOGOUS OOCYTE (AO) THAW OUTCOMES AT A LARGE UNIVERSITY-BASED FERTILITY CENTER. Sarah Druckenmiller Cascante, MD, Shannon Devore, MD, Jennifer K. Blakemore, MD, Tsai-Ling Lee, MS, Caroline McCaffrey, PhD, James A. Grifo, MD, PhD NYU Langone School of Medicine, New York, NY.

OBJECTIVE: AO cryopreservation (cryo) is widely used for FP, but published thaw data is scarce. Our aim was to review our AO thaws.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Patients (pts) who thawed AOs at our university-based fertility center from 2004-2019 were reviewed. Pts were excluded if cryo was performed for a medical indication, as research, due to lack of sperm, due to a natural disaster or in combination with embryos. Pts were also excluded if they had cancer or planned to use a gestational carrier. Outcomes included implantation (IR), spontaneous abortion (SABR) and ongoing pregnancy + live birth (LBR) rates. Statistics included Mann-Whitney U and Fisher's exact tests, with $p<0.05$ as significant.

RESULTS: We reviewed 468 pts (median age at first cryo 38y, range 27-46y), who underwent 677 cryos (89% at our center, 8% elsewhere, 2% at both), 523 thaws and 360 embryo transfers (ET). Cryo involved vitrification for 69%, slow freezing for 4% and both for 27% of pts. Median time between first cryo and first thaw was 4y. Overall AO cryo survival was 79%, M2 cryo survival was 80% and 2PN fertilization (fert) was 66%. 441 thaws (84%) led to $\geq$1 embryo for fresh ET, trophectoderm biopsy (TEBX) or cryo while 82 thaws (16%) led to no embryos for ET, TEBX or cryo. Of thaws with TEBX, 65% had $\geq$1 euploid embryo. 142 ETs (39%) were fresh, with 2% using rush biopsied embryos. 218 ETs (61%) were frozen, with 97% using biopsied embryos. In euploid ETs (n = 205), IR was 64%, SABR was 10% and LBR was 55%. In non-biopsied ETs (n = 146), IR was 28%, SABR was 14% and LBR was 32%. There were 8 mosaic and 1 aneuploid ET. See table for outcomes by age. In total, our pts have 155 babies (11 twin, 1 triplet) and 19 ongoing pregnancies (2 twin) from AO cryo. 51 pts (11%) have remaining frozen AOs and 117 (25%) have euploid or untested embryos.

CONCLUSIONS: AO cryo is a viable FP method and led to live birth in 32% of pts, comparable to our center's 34% LBR per intended retrieval[1] and the national 26% LBR per intended retrieval in pts of similar age (38-40y)[2].

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SUPPORT: None.

P-303 4:30 PM Sunday, October 18, 2020

MEDICALLY-INDICATED OOCYTE (OC) AND EMBRYO CRYOPRESERVATION (EC) IN PATIENTS WITH NON-ONCOLOGIC CONDITIONS: 5 YEARS OF EXPERIENCE AT AN URBAN UNIVERSITY-BASED FERTILITY CENTER. Amani Sampson, B.A.,[1] Emily Michelle Weidenbaum, MD,[1] Jennifer K. Blakemore, MD,[2] Gwendolyn P. Quinn, Ph.D.,[1] James A. Grifo, MD, PhD[2] [1]NYU Langone School of Medicine, New York, NY; [2]NYU Langone Prelude Fertility Center, New York, NY.

OBJECTIVE: The use of OC and EC, a standard option of fertility preservation (FP) for patients with cancer, has expanded to include non-oncologic medical conditions that may affect future fertility, such as cardiomyopathy. Our objective was to examine the distribution of non-oncologic medically-indicated FP by indication and FP type at our center.

DESIGN: Retrospective Cohort of all medically-indicated non-oncologic (MINO) FP from 1/2013-12/2018.

MATERIALS AND METHODS: All medically-indicated OC and EC cycles in the study time period were reviewed. All cycles of patients with cancer or planned oocyte/embryo cryopreservation were excluded. Cycles were reviewed for demographics, FP type, indication, cycle number and outcome, return rate, and live births. Descriptive results are reported as median (range). Statistical analyses included Mann-Whitney and Fisher's exact, with $p<0.05$ considered significant.

RESULTS: 421 cycles from 302 patients were reviewed: 284 OC and 137 EC. A total of 115 cycles from 81 patients with a non-oncologic condition were included representing 26% of all medically-indicated OC and 35% of medically-indicated EC respectively. Median cycle number was 1 for both OC and EC, with a range of 1-5 cycles. Median age at time of cycle start was 34 (range 13-44) for the cohort. OC patients were significantly younger than EC patients (33 vs 35, $p<0.003$). Median number of oocytes retrieved was 14 (range 0-76) and there was not a difference between OC and EC patients (13 vs 15, p=0.34). The median number of euploid embryos for EC patients was 1 (range 0-7). Patients were grouped by medical indication and compared, as shown in Table 1. To date, 9 EC patients have pursued pregnancy with gestational carriers and 3 more underwent a total of 6 frozen embryo transfers resulting in 4 livebirths. No OC patients have returned yet for oocyte warming.

TABLE 1: Distribution of MINO FP by Indication and Cycle Type

Indication	OC	EC	p-value
Chronic Medical Condition planning gonadotoxic therapy (eg. Ulcerative colitis)	13%	4%	.43
Sex Chromosome Disorder	21%	0%	.014
Transmen prior to gender affirmation	9%	0%	.32
Hereditary Cancer Susceptibility Syndromes	29%	12%	.16
Hereditary Condition (Non-Cancer)	0%	8%	.09
Benign/Congenital GYN Condition (eg. Endometriosis)	29%	44%	.21
Contraindication to Pregnancy (eg. Cardiomyopathy)	0%	32%	.0001

Age at first cryo (no. pts)	Median M2s thawed per pt / Median AOs thawed per pt	Embryos for fresh ET + TEBX + cryo / 2PN fert (%)	Euploid embryos / TEBX embryos (%)	Pts with $\geq$ 1 ET (%)	Euploid ETs / All ETs	IR (%)	SABR (%)	LBR (%)	Pts with $\geq$ 1 baby or ongoing pregnancy from AO cryo (%)
All ages (468)	12 / 14	1588 / 3781 (42)	383 / 1260 (30)	280 (60)	205 / 360 (57)	208 / 478 (44)	20 / 185 (11)	162 / 360 (45)	150 (32)
<38y (191)	14 / 15	742 / 1697 (44)	228 / 636 (36)	122 (64)	112 / 164 (68)	99 / 191 (52)	9 / 90 (10)	80 / 164 (49)	75 (39)
38 – 40y (216)	10.5* / 12*	701/ 1699 (41)	147 / 531 (28)*	129 (60)	85 / 162 (52)*	87 / 222 (39)*	8 / 77 (10)	67 / 162 (41)	61 (28)*
>41y (61)	9* / 12*	145 / 385 (38)*	8 / 93 (9)**	29 (48)*	8 / 34 (24)**	22 / 65 (34)*	3 / 18 (17)	15 / 34 (44)	14 (23)*

* = lower than the <38y age group
** = lower than the <38y and 38 – 40y age groups

CONCLUSIONS: Non-oncologic indications represent 30% of medically-indicated FP cycles at our center. Many women pursue MINO FP for GYN conditions affecting fertility. Notably, more women with sex chromosome disorders pursued OC compared to pregnancy contraindications in the EC group. These results advocate for further research on the support, counseling, and referral needs of women with MINO conditions.

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PLANNED OOCYTE CRYOPRESERVATION (PL-OC) IN WOMEN AGE 40-45. Bat-Sheva L. Maslow, MD, MSCTR, Leslie B. Ramirez, PhD, Michael M. Guarnaccia, MD, MPH, Joshua U. Klein, MD Extend Fertility, New York, NY.

OBJECTIVE: Women 40-45, particularly if unpartnered, consider Pl-OC to preserve opportunity for a genetic child in the future. According to SART, IVF live birth rates for women >40 are <12% and cycle cancellation rates are as high as 20%. Limited data exist on Pl-OC process and outcomes in this age group, particularly for women 43+.

This study aimed to identify rates of Pl-OC in women age 40-45 following appropriate evidence-based counseling. We hypothesized that women 43+ and those with lower AMH would be less likely to proceed with Pl-OC.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All women age 40-45 presenting for a complimentary Pl-OC assessment (consisting of AMH/AFC) and physician consultation at Extend Fertility Medical Practice, a large single-center oocyte cryopreservation program from 1/1/18-5/25/20 were included. Counseling included specific evidence-based algorithms for oocyte yield based on age and AMH, as well as estimated live birth outcomes based on published aneuploidy data, and where relevant, discussion of the lack of live birth data for women 43+.

Median AMH levels were calculated overall and by age, for the entire cohort and those who chose Pl-OC. Mean number of MII oocytes cryopreserved per cycle and mean number of cycles per patient were also calculated. Comparisons were made using Kruskal-Wallis, *t*-test, and X^2 where appropriate.

RESULTS: 474 women age 40-45 presented for complementary consultation and were included in the study. Following their consultation, 117/474 (24.6%) proceeded with Pl-OC.

CONCLUSIONS: With effective counseling, even in this low efficacy group, women with the highest chances of success can have the opportunity to attempt Pl-OC with a low cycle cancellation rate.

Age at Retrieval (*n*)	Eggs Retrieved	MII Eggs
14 (3)	14.0	10.0
15 (3)	18.7	12.3
16 (2)	29.0	18.5
17 (3)	25.0	21.7
19 (3)	21.0	14.3
20 (5)	15.8	12.0
21 (4)	16.0	13.5
22 (8)	24.9	20.3
23 (18)	28.6	21.3
24 (24)	23.8	16.9
25 (25)	25.2	15.2
Gynecologic Age at Retrieval (*n*)	**Eggs Retrieved**	**MII Eggs**
0 (1)	22.0	16.0
2 (2)	17.0	11.5
3 (1)	5.0	5.0
4 (4)	23.8	15.0
6 (2)	15.0	13.0
7 (2)	16.0	14.0
8 (6)	22.5	19.8
9 (16)	24.3	18.2
10 (14)	26.4	14.1
11 (12)	27.4	19.8
12 (17)	28.4	21.5
13 (8)	22.6	14.1
14 (4)	19.5	15.5

TABLE 1: Demonstrates data for the entire cohort and those who chose Pl-OC (cycling cohort)

	Total Cohort		*Cycling Cohort*			
Age	N	AMH Median±IQR	N(%)	AMH Median±IQR	Frozen MII/Cycle Mean±SD	# of Cycles/Patient Mean±SD
40	156	1.22±1.78	47 (30.2)	1.80±2.21	7.14±5.28	1.77±1.21
41	122	0.75±1.66	27 (22.1)	1.37±2.13	6.61±5.98	2.08±1.90
42	87	0.58±1.18	27 (31.0)	1.01±1.70	7.57±5.64	1.33±0.61
43	47	0.58±1.04	6 (12.8)	1.81±2.45	5.50±4.64	1.79±0.98
44	37	0.50±0.90	6 (16.2)	0.85±1.20	5.07±5.09	1.80±0.94
45	25	0.35±0.55	4 (16.0)	0.81±0.65	3.33±1.63	2.33±1.21
Total	474	0.77±1.35	117 (24.6)	1.34±1.89	6.68±5.45	1.83±1.38

Women who chose not to cycle had lower Median AMH (0.62±1.20 vs 1.34±1.89, p<0.001) and were more likely to be 43+ (OR 0.45 CI 0.25-0.80; 16/109 vs. 101/365 p=0.005) compared to those who cycled. Of those who cycled, only 8/117 (6.8%) had a cycle cancelled for poor response or 0 oocytes cryopreserved.

P-305 4:30 PM Sunday, October 18, 2020

DOES AGE OR GYNECOLOGIC AGE AFFECT OUTCOMES OF OOCYTE CRYOPRESERVATION IN PERI-PUBERTAL AND ADOLESCENT FEMALES? Nicole D. Yoder, MD,[1] Emily E. Auran, MD,[1] David H. McCulloh, Ph.D.,[2] Mary Elizabeth Fino, MD[3] [1]NYU School of Medicine, New York, NY; [2]NYU Langone Fertility Center, New York, NY; [3]NYU Langone Prelude Fertility Center, New York, NY.

OBJECTIVE: Current data on fertility preservation outcomes in peri-pubertal and adolescent females is limited, with most data originating from oncofertility studies. Few studies explore outcomes in those undergoing fertility preservation for gender dysphoria or other non-oncologic indications. Our objective was to review fertility preservation outcome in patients with gender dysphoria and non-oncologic indications under age 25 at a single academic institution. Specifically, we sought to investigate egg retrieval outcomes as they relate to patient age, gynecologic age (age from menarche to egg retrieval), and AMH.

DESIGN: Retrospective case series

MATERIALS AND METHODS: Patients undergoing oocyte retrieval at an academic institution between age 14 and 25 from 1/2000 to 1/2020 were identified. Included patients were those undergoing egg retrieval for non-medical indication, transgender patients, and egg donors. Patients with ovarian pathology and Sex chromosome disorders including Turners syndrome were excluded. Patients with a cancer diagnosis were excluded given non-traditional stimulation, as well as the potential for cancer to impact ovarian response. Age of menarche and AMH level prior to cycle were identified by chart review. Cycles were evaluated by number of eggs retrieved and number of metaphase II (MII) oocytes. Comparisons were made between cycle outcome and patient age, gynecologic age, and AMH at cycle start.

RESULTS: 73 patients were included. There were 10 patients with gender dysphoria, 44 egg donors, and 19 patients undergoing elective egg retrieval. Neither age nor gynecologic age were correlated with number of eggs retrieved (n=88, r=0.16; n=86, r=0.16 respectively) or number of MII

eggs (n=88, r=0.05; n=86, r=0.10). AMH value was positively correlated to number of eggs retrieved (n=83, r=0.29) and number of MII eggs (n=83, r=0.26).

CONCLUSIONS: Overall, in young female patients undergoing egg retrieval for non-oncologic indication, neither age nor gynecologic age were predictive of egg retrieval outcome. As seen in other populations, AMH value may positively correlate with egg retrieval outcome in young females. Further research with a larger study population may elucidate ideal timing for egg retrieval or donation in these peri-pubertal and adolescent females.

P-306 4:30 PM Sunday, October 18, 2020

FACTORS THAT INCREASE LIKELIHOOD OF USE OF CRYOPRESERVED SPERM IN AYA MALES UNDERGOING FERTILITY PRESERVATION. Kathryn M. Goldrick, MD, Molly Bergen, BS, Randal D. Robinson, MD, T. Arthur Chang, PhD, HCLD, ELD, Mario Octavio de la Pena, Jr., BS, Jennifer F. Knudtson, MD University of Texas Health Science Center, San Antonio, TX.

OBJECTIVE: An estimated 12,400 AYA patients are diagnosed with cancer each year, but due to advances in treatment, almost 80% of those diagnosed will achieve long term survival (1). These treatment advances include multimodal chemotherapeutic regimens, radiation, and surgery which can have reproductive consequences. The most effective and established means of fertility preservation for men prior to chemotherapy is sperm cryopreservation, which is used by 99% of male AYA patients who undergo fertility preservation (2). However, a systematic review of 11,798 male patients who underwent fertility preservation for cancer showed that the usage rate of cryopreserved sperm was only 8% (3). The objective of this study is to determine factors associated with an increased likelihood of usage of cryopreserved sperm for AYA males who undergo fertility preservation.

DESIGN: Retrospective chart review at an academic fertility center.

MATERIALS AND METHODS: A retrospective chart review of AYA males ages 15-39 who underwent fertility preservation by sperm cryopreservation for cancer and/or future gonadotoxic treatment at an academic fertility center between 2009 and 2019 were identified, and demographic, clinical, and laboratory data were collected in REDCap database. Patient attributes were assessed to see what factors, if any, are associated with an increased likelihood of fertility preservation and future use of cryopreserved sperm. Statistical analysis was performed via Chi-square.

RESULTS: In this population of 118 AYA males that cryopreserved sperm, they were primarily Hispanic (30%, n=36) had testicular cancer (36%, n=43) and an average age of 24. The most common planned treatment was chemotherapy (78%, n=92). Four of the 118 patients, a total of 3%, have returned to use their cryopreserved sperm. Three of these four patients had testicular cancer and were 2-3 years from their cancer treatment. There were 14 patients who discarded cryopreserved sperm and 5 who transferred sperm to another institution. Assuming the 5 patient who transferred their sperm did use it, there would be 8% of the samples used. The total motile count of the cryopreservation analysis was lower for patients who used their cryopreserved sample compared to those who discarded, but this was not statistically significant (32.8M vs 105.6M, p=0.2).

CONCLUSIONS: At our center, only a small percentage of cryopreserved sperm banked from the AYA males with cancer and/or planned gonadotoxic treatment is being used. Type of cancer, time from cancer treatment, and TMC on cryopreservation analysis may be predictive of future use of sperm and could be useful in counseling patients undergoing sperm cryopreservation.

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SUPPORT: K23 HD097307 (JFK)

P-307 4:30 PM Sunday, October 18, 2020

CARE GAPS IN FERTILITY PRESERVATION SERVICES FOR RESIDENT PHYSICIANS: *A SURVEY OF FERTILITY PRESERVATION AWARENESS AND INSURANCE COVERAGE*. Ashley S. Kim, M.D., Amy S. Dhesi, M.D., Sami I. Jabara, M.D., Marsha B. Baker, M.D., M.P.H Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA.

OBJECTIVE: To assess awareness and attitudes towards fertility preservation services for resident physicians, as well as availability of covered benefits.

DESIGN: Cross-sectional survey

MATERIALS AND METHODS: Surveys were emailed to program directors of Accreditation Council for Graduate Medical Education (ACGME) residency programs across five medical specialties: Obstetrics and Gynecology, Pediatrics, Internal Medicine, Family Medicine and General Surgery. From March through May 2020, 102 voluntary responses were collected. Fertility preservation was defined as oocyte or sperm cryopreservation for elective purposes, transgender care or cancer. Respondents were queried about demographics, formalized education on fertility preservation for trainees, availability of insurance coverage and attitudes about coverage. Descriptive statistics were used to analyze responses. Qualitative data in the form of open-ended comments were also collected.

RESULTS: Of the 102 total responses, 29 (28%) were obtained from Obstetrics and Gynecology (OBGYN), 25 (25%) from Family Medicine, 19 (19%) from Pediatrics, 18 (18%) from General Surgery, and 11 (10%) from Internal Medicine. While almost half (45%) of program directors revealed that their residents have expressed concern regarding delayed childbearing or future fertility, formal discussion of fertility preservation options appears limited. Only 10% of program directors report formal didactics with residents about elective oocyte cryopreservation, with the majority of those programs being from OBGYN. Less than 5% of programs report having formal didactics about fertility preservation for transgender care or cancer. Most program directors across all specialties personally support fertility preservation as a covered benefit for their residents (78%), but resident access to fertility preservation services is limited with 6% of respondent programs offering coverage for elective oocyte cryopreservation, and 12 % offering coverage for elective oocyte cryopreservation for residents with new cancer diagnoses. Programs reporting fertility preservation coverage for residents are predominantly in the Northeast, consistent with the mandated fertility coverage for many states in that region.

CONCLUSIONS: This study suggests that barriers to fertility preservation services for resident physicians include the lack of formal didactics across specialties and limitations of state mandated coverage. This study provides novel data supporting the need for enhanced discussion and awareness to bridge the gap in access to care for fertility preservation services among resident physicians.

P-308 4:30 PM Sunday, October 18, 2020

RELUGOLIX COMBINATION THERAPY IMPROVES UTERINE FIBROID-ASSOCIATED PAIN DURING MENSTRUAL AND NON-MENSTRUAL DAYS: RESULTS FROM THE LIBERTY PHASE 3 PROGRAM. Ayman Al-Hendy, MD, PhD,[1] Andrea S. Lukes, MD, MHSc,[2] Roberta Venturella, MD, PhD,[3] Yulan Li, PhD,[4] Rachel B. Wagman, MD,[5] Elke Hunsche, PhD,[6] Elizabeth A. Stewart, MD.[7] [1]Department of Surgery, University of Illinois at Chicago, Chicago, IL; [2]Carolina Women's Research and Wellness Center, Durham, NC; [3]Magna Graecia University of Catanzaro, Catanzaro, Italy; [4]Myovant Sciences, Inc., Brisbane, CA; [5]Myovant Sciences Inc., Brisbane, CA; [6]Myovant Sciences GmbH, Basel, Switzerland; [7]Mayo Clinic Department of OB/GYN, Reproductive Endocrinology and Infertility, Rochester, MN.

OBJECTIVE: To evaluate the effect of Relugolix combination therapy (Rel-CT) on pain symptoms associated with uterine fibroids (UF) in the Phase 3 LIBERTY studies.

DESIGN: LIBERTY 1 and LIBERTY 2 were multinational, randomized, double-blind, placebo-controlled studies that evaluated the effect of Rel-CT (once-daily relugolix 40 mg, estradiol 1 mg, norethindrone acetate 0.5 mg) on heavy menstrual bleeding (HMB) in women with UF. UF-associated pain was a secondary endpoint of each study.

MATERIALS AND METHODS: The pain-evaluable population was defined as women with moderate to severe UF-associated pain at baseline (maximum pain $\geq$ 4 on the 0–10 numerical rating scale during the 35 days before randomization and >80% compliance to the e-diary completion). Analyses included the prespecified endpoint of the proportion of women with no/minimal UF-associated pain at Week 24 (maximal pain score $\leq$ 1 during the last 35 days of treatment) in the pain-evaluable population, as well as additional analyses of subgroups of patients with moderate/severe pain during menstrual and non-menstrual days at baseline. Treatment comparisons were performed on the pooled data from the LIBERTY 1 and 2 studies using the Cochran–Mantel–Haenszel test stratified by baseline menstrual blood loss volume (<225 mL vs $\geq$225 mL).

RESULTS: In total, 277 patients in the pooled dataset were pain-evaluable: 126 patients randomized to Rel-CT and 151 randomized to placebo (54% of the combined LIBERTY 1 and 2 cohort). Most of the pain-evaluable patients (117 in the Rel-CT group and 145 in the placebo group) reported moderate/severe pain during menstruation, while 65 patients in the Rel-CT group and 74 in the placebo group had moderate/severe pain on non-menstrual days. After 24 weeks of treatment, a significantly greater proportion of patients in the Rel-CT group (45.2%) had no/minimal UF-associated pain during the last 35 days of treatment, compared with the placebo group (13.9%, $p<0.0001$). The percentages of women reporting no/minimal UF pain during menstrual days (65.0% vs 19.3%; $p<0.001$) and during non-menstrual days (44.6% vs 21.6%; $p=0.004$) were significantly higher in patients on Rel-CT vs placebo, respectively, at Week 24. The mean percentage of menstrual days with pain medication use decreased with Rel-CT from 35.9% at baseline to 7.2% at Week 24; the placebo group had a small reduction from 34.7% at baseline to 25.5% at Week 24. Adjusting for increased analgesic use at Week 24 vs baseline did not impact the results.

CONCLUSIONS: Once-daily Rel-CT treatment for 24 weeks led to a significant reduction of UF-associated pain in patients with moderate to severe pain at baseline. Both pain during menstrual and non-menstrual days improved with Rel-CT. The significant reduction in measures of pain is clinically meaningful and relevant to patients, and is supported by quality-of-life improvements that have been observed in the LIBERTY program.

P-309 4:30 PM Sunday, October 18, 2020

UTERINE FIBROID-CAUSING MUTAGENESIS INDUCED BY DEVELOPMENTAL EXPOSURE TO ENDOCRINE DISRUPTING CHEMICALS IS MEDIATED VIA ABROGATION OF NUCLEOTIDE EXCISION REPAIR PATHWAY IN MYOMETRIAL STEM CELLS THROUGH UPREGULATION OF TGF-β1. Maria Victoria Bariani, Ph.D., Hoda Elkafas, B. Pharm, MSc, Mohamed Ali, BPharm, MSc, Qiwei Yang, PhD, Ayman Al-Hendy, MD, PhD. Department of Surgery, University of Illinois at Chicago, Chicago, IL.

OBJECTIVE: The cause of uterine fibroid (UFs) is largely unknown, but it is well established that one of the major risk factors for the development of these tumors is early environmental exposure to endocrine-disrupting chemicals (EDCs). It has been shown that UFs originate from abnormal stem cells (SCs) in the myometrium (MM) that acquire a driver mutation in pivotal genes such as Tsc-2 (Eker rat) or Med12 (human), and there is evidence that DNA repair capacity could be involved in the emergence of such mutations. Furthermore, the pleiotropic cytokine TGF-β1 has been related to UF development. Recent studies have suggested a link between TGF-β1 and the DNA damage response with implications for tumor initiation and growth. In this context, this work aimed to evaluate the possible role of TGF-β1 and the nucleotide excision repair (NER) on the tumorigenesis process on EDC-exposed MMSCs.

DESIGN: Laboratory research studies using an Eker rat fibroid model MMSCs.

MATERIALS AND METHODS: Female Eker rats were received subcutaneous injections of 10 μg of Diethylstilbestrol (DES, endocrine-disrupting chemical) per rat per day or 50 μl of sesame seed oil (vehicle, VEH) on days 10, 11, and 12 after birth. MMSCs were isolated from 5 months adult MM tissue (N=5 for each group) using Stro-1 and CD44 surface markers. Whole-genome RNA-sequencing was performed in VEH- and DES-MMSCs to determine global gene expression profiles. Latent-TGFβ-binding protein 1 (Ltbp-1), Tgf-β1, Xpc, Ddb1, and Ddb2 (three proteins involved in DNA damage recognition on NER pathway) mRNA levels in VEH- and DES-MMSCs were measured using qRT-PCR. Thrombospondin 1 (TSP-1), LTBP1, TGF-β1, XPC, and DDB1 protein expressions were evaluated by Western Blot (WB). Two-tailed unpaired Student t-test was used to assess any statistically significant differences (P-value<0.05).

RESULTS: The RNA-seq data analysis demonstrated that the expression of 19 genes belonging to TGF-β1 signaling were altered in DES-MMSCs compared to VEH-MMSCs. Moreover, 6 genes involved in the NER pathway showed changes in RNA expression between DES-MMSCs. The mRNA levels of Ltbp-1 and Tgf-β1 in MMSCs showed an increase when animals were exposed neonatally to DES. Regarding NER related genes, Xpc, and Ddb2 were higher in DES-MMSCs than VEH-MMSC, while Dbb1 mRNA levels showed the opposite results ($p<0.05$). The protein levels of TSP-1, LTBP1, and TGF-β1 were increased in DES-MMSCs compared to VEH-MMSCs ($p<0.05$). We did not find differences in XPC protein levels ($p>0.05$). However, DDB1 protein levels were upregulated in DES-MMSCs in comparison to VEH-MMSCs.

CONCLUSIONS: Our results showed that early-life exposure to DES provokes changes in TGF-β1 and NER pathways on MMSCs, therefore it could increase the predisposition to develop UFs later in life. Further studies are needed to determine the relation between TGF-β1 and NER pathways on DES-exposed MMSCs and parallel studies in the human uterus.

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U54 MD007602
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P-310 4:30 PM Sunday, October 18, 2020

THE YAP INHIBITOR VERTEPORFIN REGULATES ACTIVIN-A/SMAD SIGNALING AND MECHANOTRANSDUCTION IN UTERINE FIBROID CELLS. Md Soriful Islam, PhD, Sadia Afrin, PhD, Joshua T. Brennan, MPH, Subbroto Kumar Saha, PhD, Mostafa A. Borahay, MD, PhD, James H. Segars, MD. Johns Hopkins University School of Medicine, Baltimore, MD.

OBJECTIVE: Uterine fibroids are mechanically stiff fibrotic tumors of the uterus. Activin A, a member of the TGF-β superfamily, is overexpressed in fibroids and is known to increase expression of extracellular matrix (ECM) proteins. The increased stiffness of ECM in fibroids leads to activation of mechanotransduction signaling. Hippo is a key pathway that regulates cell growth and fibrosis in response to stiffness of ECM. YAP (yes-associated protein), a transcriptional effector of Hippo signaling, is also overexpressed in fibroids. Here, we investigated whether YAP contributes to mechanical signaling in fibroid cells via activin-A/SMAD.

DESIGN: Translational research study using human myometrial (P51M) and uterine fibroid (P51F) cells.

MATERIALS AND METHODS: To explore the role of YAP in regulating activin-A/SMAD signaling and mechanotransduction, we used the YAP inhibitor, verteporfin. Protein and/or mRNA levels of the key components of activin-A/SMAD and mechanotransduction pathways were measured using real time qPCR and western blot, respectively, following treatment with verteporfin at 1μM for 24 hrs. We included proteins involved in mechanical signaling, such as FAK, and mRNA for integrins. Statistical significance was defined as a $p<0.05$.

RESULTS: We observed increased mRNA levels of activin-A (*INHBA*) (4.1-fold) in fibroid compared to myometrial cells. Treatment of verteporfin reduced mRNA levels of activin-A ($p<0.001$) and its receptors *ACVR2A* ($p<0.001$) and *ACVR1B* ($p<0.05$), but not *ACVR2B* ($p=0.14$) in fibroid cells. Verteporfin also inhibited *SMAD2* mRNA and phosphorylated SMAD2 protein in fibroid cells ($p<0.05$). PAI-1 represents downstream target of activin A and is known to mediate fibrosis, which highly expressed at mRNA (2.5-fold) and protein (2.1-fold) levels in fibroid compared to myometrial cells. Verteporfin treatment significantly reduced both mRNA and protein levels in both cell types ($p<0.05$). The initiators of mechanotransduction signaling, integrin receptors *ITGB1* (1.3-fold), but not *ITGA6* (0.8-fold), were highly expressed in fibroid compared to myometrial cells. Treatment of verteporfin significantly decreased both *ITGB1* and *ITGA6* transcript levels in both cell types ($p<0.001$). The cytoplasmic kinase *FAK* mRNA was also elevated in fibroid (1.3-fold) compared to myometrial cells; and levels were reduced by verteporfin treatment ($p<0.05$). Notably, levels of phosphorylated FAK were also reduced by verteporfin treatment ($p<0.01$). AKAP13, a target of FAK, was increased (mRNA) in fibroid cells (1.4-fold) and was also suppressed by verteporfin treatment ($p<0.01$). Furthermore, we found that the increased levels of phosphorylated ERK1/2 (1.6-fold) in fibroid compared to myometrial cells were also reduced after verteporfin treatment ($p<0.05$).

CONCLUSIONS: Verteporfin reduced key components of activin-A/SMAD signaling and its downstream target PAI-1, as well as key mechanotransduction signaling factors. These results suggest crosstalk between Hippo/YAP signaling and activin-A/SMAD and ERK 1/2 pathways in regulation of critical genes involved in cell growth and fibrosis.

SUPPORT: Ines Mandl Research Foundation (to MSI) and Howard W. and Georgeanna Segar Jones Endowment (to JHS).

P-311 4:30 PM Sunday, October 18, 2020

SINGLE CELL TRANSCRIPTOMES FROM UTERINE FIBROIDS AND FIBROID-FREE MYOMETRIUM ELUCIDATE MYOMETRIAL TUMORIGENESIS.

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OBJECTIVE: Uterine fibroids represent the most common benign tumors in women in reproductive age. It has been reported that they arise from a single dysregulated myometrial smooth muscle cell. However, the underlying tumorigenic mechanism remains unclear and because of that, surgery has been the gold standard for their treatment. Our primary motivation stems from the need to better understand the cellular hierarchy of uterine fibroids and myometrium, leveraging the high resolution of single cell RNAseq. We aim to identify cell types and states that are unique to the fibroids, based on their molecular signatures. This may point towards more targeted and less invasive treatment strategies for the disease, and better elucidate the mechanism of myometrial tumorigenesis.

DESIGN: scRNAseq analysis were performed from uterine fibroids (F), fibroid-free matched myometrium (M) and healthy myometrium (hM) from 7 patients, presenting a high- resolution transcriptomic map decoupled in cell type and state.

MATERIALS AND METHODS: After tissue dissociation, full length cDNA libraries of 5332 individual cells were prepared using an adapted SmartSeq2 protocol. Nextera XT DNA Sample Preparation kit was used for library preparation. Each cell was sequenced on a NovaSeq to ~1e06 reads/cell. Additional quality control and bioinformatic analyses were performed using custom R scripts.

RESULTS: Dimensional reduction revealed that F, M and hM consist of 14 cell types and states. Canonical markers and highly differentially expressed genes identified major lineages of smooth muscle cells (SMC), fibroblasts (FB), vascular smooth muscle cells, lymphatic endothelia (LEC), vascular endothelia, macrophages / dendritic cells and mast cells. We discovered that the tumor (F) and the non-tumor (M/hM) tissues differ most drastically in FB, SMC, LEC. LEC is more abundant in the tumor. For both SMC and FB, we identified states that are enriched in tumor and non-tumor, respectively, and report signatures that differentiate the two states.

CONCLUSIONS: Single-cell transcriptomic analyses revealed cellular hierarchies that are common or different among F, M, and hM. Cell types and states that are unique to F and their expression signatures might provide molecular targets for less invasive treatment of these benign tumors.

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STAT3 AND AP-1 SIGNALING IN HUMAN UTERINE LEIOMYOMA CELLS IS REGULATED BY GONADAL HORMONES.

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OBJECTIVE: Uterine leiomyomas are benign tumors regulated by gonadal hormones and are composed of an abundance of disorganized extracellular matrix. We have demonstrated that the expression of ECM proteins including collagen and fibronectin are modulated by activated STAT3 and TGFβ3 in leiomyoma cells, indicating an interaction between the two pathways. Our objective in this study was to characterize the changes in STAT3 protein in response to estrogen, progesterone and combination of both. We further examined the interaction between JAK/STAT pathway and downstream regulators of signaling pathways.

DESIGN: Laboratory study.

MATERIALS AND METHODS: Leiomyoma cell lines were exposed to estradiol, progesterone and combination of both. Leiomyoma cells were exposed to AP-1 inhibitor, SR11302 for various time points. STAT3 pathway proteins were analyzed using western blot analysis. Data is presented as fold difference +/- SEM; with fold difference in density units between untreated and treated samples and normalized for internal control. Student t-test and Wilcoxon-Signed Rank test were used for nonparametric statistical evaluation. Values below $p<0.05$ were considered significant.

RESULTS: In leiomyoma cells, both estradiol (E2) and progesterone (P4) increased the expression of pSTAT3 by 1.34+/-0.062-fold and 1.39+/-0.052-fold, respectively. Combination of the two hormones (E2+P4) resulted in a higher fold increase in pSTAT3 (1.74+/-0.006-fold) protein. Increased expression of pSTAT3 by the hormones was confirmed using anti-estrogens and anti-progestin. AP-1 (activating protein-1) transcription factor proteins that include c-jun and c-fos are known to interact with JAK/STAT pathway. In leiomyoma cells, inhibiting the AP-1 pathway resulted in a significant decreased expression (0.72+/-0.09) in activated STAT3 protein after 24hr exposure.

CONCLUSIONS: Human uterine leiomyoma cells demonstrate a crosstalk between gonadal hormones and STAT3 signaling with increased activation of STAT3. Increase in pSTAT3 leads to increased production of fibrosis-related proteins such as collagen. The common pathway for multiple signaling pathways in leiomyomas appears to involve AP-1.

SUPPORT: Military Womens Health Award, Uniformed Services University of the Health Sciences

P-313 4:30 PM Sunday, October 18, 2020

THYROID DYSFUNCTION AND FIBROIDS IN LATINA/LATINX (LLX) FEMALES: INSIGHTS FROM THE ENVIRONMENT, LEIOMYOMAS, LATINAS, AND ADIPOSITY STUDY (ELLAS).

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OBJECTIVE: A retrospective analysis published in 2014 showed an association between hypothyroidism and uterine fibroids (UFs) in European populations, however, there are a paucity of studies on the relationship between thyroid pathophysiology and UF prevalence. Here we use the ELLAS cohort to explore the relationship between a prior diagnosis of thyroid dysfunction, and/or TSH levels, and UF prevalence in LLX reproductive aged females.

DESIGN: Cross-sectional analysis of data from a prospective longitudinal cohort study.

MATERIALS AND METHODS: All study members were participants in ELLAS, an NIH funded community engaged longitudinal study, and were between the ages of 21-50 years at the time of enrollment. Participants had completed the first visit of the study which included detailed questionnaires on demographics and medical history including questions regarding prior diagnosis of thyroid disease. Additionally, blood samples were collected to assess TSH levels and vaginal probe pelvic ultrasounds were performed to determine the presence of UFs in each participant. All ultrasounds were performed by a single ultrasonographer and all images were reviewed by a single blinded expert reviewer. The study was IRB approved by University of

Michigan and statistical associations were determined using Chi-squared and Wilcoxon rank-sum tests.

RESULTS: To date, 633 participants have enrolled and 537 participants have completed the baseline visit, including pelvic ultrasound and blood sample. The mean age of participants was 37.4 ± 6.9 years and mean BMI was 29.9 ± 6.5 kg/m2. 7.1% of all participants had been told by a health professional that they had a thyroid condition and 9.7% of all participants had fibroids on ultrasound. 6.8% of participants without UFs on ultrasound had a prior diagnosis of a thyroid condition vs. 9.6% of participants with UFs on ultrasound (p = 0.47). Mean TSH of all participants was 2.35 ± 1.51 mIU/L. Mean TSH of participants with ultrasound-confirmed UFs was 2.33 ± 1.36 mIU/L vs 2.35 ± 1.52 mIU/L in participants without UFs on ultrasound (p= 0.85).

CONCLUSIONS: This cross-sectional analysis did not find a significant association between UF prevalence, TSH levels, and/or self-reported prior diagnosis of a thyroid condition in LLX reproductive-aged females. More research is needed to further characterize the potential association between fibroids and thyroid disease in different racial and ethnic groups and to understand the mechanisms behind the association.

SUPPORT: This work was supported by the NIMHD grant R01MD011570.

P-314 4:30 PM Sunday, October 18, 2020

N^6-METHYLADENOSINE REGULATORS IN PREVALENCE AND BURDEN OF BLACK WOMEN IN UTERINE FIBROIDS.

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OBJECTIVE: Uterine fibroids (UFs) are monoclonal tumors arising in the myometrium, and are the most common tumors of reproductive age women. Although UFs impact the quality of life of women of all ethnicities, this disease is more prevalent and more severe among African American (AA) women compared with Caucasian (CC) women. To date, little is known about the mechanism of this ethnic disparity. An increasing body of evidence demonstrates that abnormal genetic and epigenetic alterations contribute to development of UFs. Recently, another layer of gene regulation at the RNA level, i.e., RNA epitranscriptomics has gained increased attention and interest in the research community. To date, over 150 post-transcriptional modifications of RNA have been identified. Among them, N6-methyladenosine (m^{6}A) is the most abundant, dynamic and reversible modification involved in many biological events and diseases. However, the knowledge of epitranscriptomics in UFs is completely lacking.

DESIGN: Laboratory research studies using human myometrium and UFs tissues

MATERIALS AND METHODS: Human UFs (n=14) and adjacent myometrium tissues (MyoF, n=14) were collected at time of hysterectomy. Western blot (WB) was performed to determine the protein levels of m^{6}A writers (METTL3, WTAP, VIRMA, and RBM15) and Readers (YTHDC1, and YTHDF2). Student's t-test was used to determine the significant difference.

RESULTS: Our studies demonstrated that 62.5% (5 of 8) of AA patients exhibited an upregulation of METTL3 in UFs compared to MyoF while only 16.7% (1 of 6) of CC patients showed upregulation of METTL3. On the other hand, 37.5% AA women and 83.3% CC women showed downregulation of METTL3 in UFs compared to MyoF respectively. These data suggest that this key m^{6}A writer may contribute to the ethnic disparities of UFs. In addition, we measured the adaptors of m^{6}A writers (WTAP, VIRMA, RBM15), no trend of differential expression between UFs and MyoF in both AA and CC population was observed. Next, we determined the protein levels of key m^{6}A readers YTHDC1 and YTHDF2, and demonstrated that a significant upregulation of YTHDC1 and YTHDF2 in UFs over MyoF was found ($p<0.05$) in AA women, but not in CC women. Moreover, 87.5% (7/8) of AA exhibited upregulation of YTHDC1 and YTHDF2 respectively, while only 33.3% (2/6) and 50% (3/6) of CC showed upregulation of YTHDC1 and YTHDF2 respectively.

CONCLUSIONS: These results suggest that abnormal epitranscriptomic alteration, e.g. the METTL3-m^{6}A-YTHDC1/YTHDF2 signaling axis could be involved not only in the pathogenesis of UFs, but also contributing to increased UF prevalence and burden in AA women. Further studies are needed to determine the expression patterns of m^{6}A regulators in a large sample size, and characterize the role of m^{6}A regulators in pathogenesis of UFs.

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COMPARATIVE ANALYSIS OF FK506-BINDING PROTEINS 51 (FKBP51) AND 52 (FKBP52) IN UTERINE FIBROIDS COMPARED TO NORMAL MYOMETRIUM.

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OBJECTIVE: FK506-binding protein 51 (FKBP51) and 52 (FKBP52) are immunophilins and common co-regulators of transcription meditated by the glucocorticoid receptor (GR), progesterone receptor (PR) and androgen receptor (AR). While FKBP51-PR or -GR binding inhibits transcriptional activity, FKBP51-AR binding induces AR-mediated transcription. FKBP52 has the opposite effect on PR and GR transcriptional activity, enhancing transcription. Although all three steroid receptors are expressed in both uterine myometrial and fibroid cells, the steroid-induced proliferative response of fibroid cells differ from that in adjacent myometrial cells, indicating aberrant steroid signaling in fibroids. GR signaling represses, whereas AR signaling induces proliferation in fibroids. Our previous research revealed increased FKBP51 expression in uterine fibroids. Since competition for binding to steroid receptors by both immunophilins induce opposite functions, we hypothesize that an increased ratio of FKBP51 to FKBP52 in fibroid vs. myometrial tissues will dysregulate steroid receptor signaling thereby contributing to fibroid proliferation. Thus, this study sought to investigate the relationship between FKBP51 and FKBP52 levels in uterine fibroids compared to normal myometrium.

DESIGN: Basic science laboratory research

MATERIALS AND METHODS: Paired myometrial vs. fibroid tissue from proliferative (n=11) and secretory (n=10) phases were processed for protein extraction for immunoblot analysis. Immunoblotting was performed using a goat polyclonal FKBP51 antibody and a rabbit FKBP52 antibody. Data were compared by a paired t-test. $P< 0.05$ was considered statistically significant.

RESULTS: Immunoblot results in uterine fibroid tissue revealed significantly lower FKBP52 levels compared to FKBP51 (Mean: 1.04 vs. 1.46; P=0.018). However, no difference was detected in myometrial samples, between FKBP52 and FKBP51 levels (Mean: 0.721 vs. 0.681, P=0.685). Comparison of the FKBP51 to FKBP52 ratio in matched myometrial samples to fibroid samples revealed no statistically significant difference. Cycle dependent analysis of uterine fibroid tissue also revealed significantly lower FKBP52 versus FKBP51 levels in the proliferative phase (Mean± SEM: 0.92±0.15 vs. 1.32±0.084; P=0.035), but not in secretory uterine fibroid tissue.

CONCLUSIONS: These results demonstrate that there is reduced expression of FKBP52 compared to FKBP51 in uterine fibroid tissue. The increased FKBP51 level compared to FKBP52 is likely implicated in dysregulation of steroid signaling by blocking GR and/or PR action as well as stimulating AR action to promote proliferation of fibroid cells. Inhibition of FKBP51 in fibroid cultures or increasing expression of FKBP52 may help clarify the exact role of these two immunophilins in uterine fibroid pathogenesis.

SUPPORT: None. Of note, this abstract was originally submitted to the Pacific Coast Reproductive Society 2020 Annual Meeting which was cancelled. After cancellation, PCRS allowed for abstracts to be published or withdrawn. This abstract was withdrawn and was not published so as to allow for this updated abstract to be submitted to ASRM.

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ACTIVATION OF SIRTUIN 3 BY NATURAL COMPOUND HONOKIOL INHIBITS HUMAN UTERINE FIBROID PHENOTYPE.

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OBJECTIVE: Uterine Fibroids (UFs) are the most common benign tumors in women of reproductive age with subsequent significant quality of life and

economic negative impact. Current treatment options are primarily surgical and no US Food and Drug Administration approved medical treatment is available so far. Natural compounds may be beneficial for UFs patients as safe non-hormonal therapeutic option. Honokiol (HKL) is a natural compound that showed promising anti-fibrotic effects in several diseases via activation of Sirtuin3 (SIRT3), yet to be explored in UF.

DESIGN: Cell culture study of immortalized human leiomyoma and patient-matched myometrium cells treated with honokiol and hexafluoro honokiol.

MATERIALS AND METHODS: Human uterine leiomyoma (HuLM) and normal uterine smooth muscle (UTSM) cells were treated with (5μM-100μM) of HKL or its synthetic agonist hexafluoro honokiol (HEX), and cell proliferation was assessed by MTT assay after 24, 48 and 72 hr. Protein expression of several UF phenotype related markers were measured in both HKL or HEX treated HuLM (24 hr) and compared or untreated cells using western blot (WB) analysis, including fibrosis related markers {collagen type1 (COLL1A) and fibronectin (FN)}, proliferation markers {Cyclin D1 (CCND1) and (PCNA)}, tumor related marker (P21). Protein expression of Sirt3 was measured in matched UF and myometrium patients' tissues (n=6) from African American (AA) and Caucasian (CC) patients. Student-t test was used for statistical analysis and $p<0.05$ was considered significant.

RESULTS: HKL and HEX showed a potent anti-proliferative effect on HuLM cells in a concentration and time dependent manner ($p<0.05$), HKL inhibit HuLM cell growth significantly starting at 5 μM, while HEX showed inhibitory effect at higher dose (50 μM). Interestingly, normal UTSM cells showed resistant effects to both treatment as compared to HuLM at all used doses suggesting selective growth-inhibitory effect on HuLM not UTSM. HKL treatment at 20-50 μM for 24 hr. significantly decreased protein levels of COLL1A, CCND1 and PCNA while increased protein levels of FN1 in HuLM cells compared to untreated control in dose dependent manner ($p<0.05$). p21, Bax, and cleaved caspase-3 protein expression did not change in response to HKL treatment. Moreover, WB analysis showed that normal myometrial tissues from both AA and CC patients expressed higher Sirt3 protein expression as compared to its matched UF tissue ($p<0.05$), suggesting that Sirt3 activation using HKL might exert anti-UF effects.

CONCLUSIONS: Our studies provide a novel link between Sirt3 and UF phenotype. HKL exhibited a promising anti-fibrotic effect via activation of this link. HKL might offer a promising therapeutic option as safer non-hormonal long term and cost-effective treatment against UFs with potential clinical utility, yet pending further research.

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SURGICAL AND OBSTETRICAL OUTCOMES OF SINGLE PORT LAPAROSCOPIC MYOMECTOMY: RESULTS OF 502 CASES. Jung Ryeol Lee, MD., PhD., Yeon Hee Hong, MD., Eunjin Song, MD. Seoul National University Bundang Hospital, Seongnam, Korea, Republic of (South).

OBJECTIVE: Single-port laparoscopic myomectomy (SPLM) has been introduced as an effort to minimize the invasiveness of the surgical method. Previous studies reported comparable surgical and better cosmetic outcomes of SPLM than conventional multi-port laparoscopic myomectomy. However, there have been few studies reported obstetric outcomes of SPLM. This study aims to analyze the surgical and obstetric outcomes of 502 SPLM cases performed for 10 years.

DESIGN: A retrospective single-center study.

MATERIALS AND METHODS: A total of 502 patients undergoing SPLM for symptom relief or due to myomas that continue to grow from October 2009 to December 2019 were enrolled. The patients who had combined surgery with other surgical departments were excluded. Patients' demographics, operative variables, and obstetrical outcomes were analyzed. All information was collected according to the electronic medical record and/or patients' answers. Continuous parameters were compared using either Student t-test or Mann-Whitney's test as appropriate. The proportions were compared using the chi-square test. P-value <0.05 was considered statistically significant.

RESULTS: The mean age and BMI of the patients were 40.5±6.7 years and 22.9±3.4 kg/m^2. The mean diameter of the largest myoma and the total number of myomas removed were 6.7±2.5 cm and 2.2±2.1, respectively. The intramural type was the most common (57.4%), and subserosal (28.1%) and submucosal (6.0%) types follow. The mean operation time and hemoglobin drops were 112.1±45.0 min and 1.6±1.1 g/dL. The rate of postoperative complications was 8.4% (42/502), and the major complications were transfusion (3.0%, 15/502) and wound problem (3.0%, 15/502). Of the women of childbearing age (n=397), 55 women who tried to become pregnant. The pregnancy, miscarriage, and live birth rates were 72.7% (40/55), 3.6% (2/55), and 63.6% (35/55), respectively. Of the remaining 3 women, 2 patients are currently pregnant state. Pregnancy was confirmed in the remaining 1 woman, but we could not obtain the obstetrical outcomes because she could not be contacted afterward. Among confirmed 35 live birth cases, 85.7% (30/35) of them delivered at full term, and 91.4% (32/35) had cesarean section delivery. No intrapartum or postpartum complication was reported. The three most common obstetrical complications were preterm labor (5.7%, 2/35), gestational diabetes (5.7%, 2/35), and placenta previa (2.9%, 1/35).

CONCLUSIONS: Our results show that operative and subsequent obstetric outcomes of SPLM are feasible and satisfactory. SPLM is a safe and effective treatment option for women with myomas who require surgery and wish to get pregnant after surgery.

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IN VITRO COLLAGEN CLEARANCE OF OVARIAN FIBROSIS TISSUE WITH PURIFIED COLLAGENASE I. Rumiana Ganeva, MSc, Dimitar Parvanov, PhD, Nina Vidolova, MSc, Ivaylo Stoykov, MSc, Georgi Stamenov, MD/PhD. Nadezhda Women's Health Hospital, Sofia, Bulgaria.

OBJECTIVE: Ovarian dysfunction is often caused by ovarian fibrosis. This condition is associated with excessive proliferation of ovarian fibroblasts and deposition of extracellular matrix. The fibroid tissue contains substantial amounts of altered and disordered collagens. Available treatment options are limited and not sufficiently efficient. One approach is the direct targeting these collagens with collagenase.

The aim of this study was to evaluate the efficacy of *Clostridium histolyticum* collagenase type I on in vitro collagen clearance in ovarian fibrous tissue.

DESIGN: Research study. Comparison of collagen distribution in ovarian fibroid tissue samples after in vitro treatment with *Clostridium histolyticum* collagenase type I at different concentrations and time exposure.

MATERIALS AND METHODS: Ovarian tissue was obtained from 10 patients undergoing scheduled ovariectomy. Twelve tissue cubes (0.5cm^3) from each biopsy were injected with 1 ml collagenase I (EC 3.4.24.3, Genaxxon) (0.1, 1, or 5 mg/ml) diluted in PBS or with 1 ml PBS (control). Samples were then incubated in DMEM F12 at 37°C for 30 min, 60 min and 12 h. Tissue samples from each collagenase concentration and time point were paraffin embedded and sectioned for Masson's trichrome staining.

Mean outcomes: percentage of fibrosis and the structural preservation of the tissue.

Statistics: ANOVA, using SPSS v21.

RESULTS: Mean fibrosis in the untreated ovarian samples was 75±7% and remained the same in the PBS injected tissues through all time points. Treatment of the ovarian fibroid tissues with collagenase I have led to time and dose dependant decrease of collagen-stained area at all concentrations tested.

After 30 minutes of incubation the collagen staining remained high in all samples: 69±6% (0.1 mg/ml), 50±4% (1 mg/ml) and 46±5% (5 mg/ml) and the tissue structure were preserved.

One hour treatment with collagenase I have led to significant decrease in the fibrosis in all concentrations tested when compared to the untreated tissues ($p<0.05$). Also the collagen reduction differed between the three concentrations significantly: 52±5% (0.1 mg/ml), 10±8% (1 mg/ml) and 5±3% (5 mg/ml) ($p<0.05$). The 5 mg/ml collagenase treated samples showed tissue structural deformation.

Treatment with collagenase I for 12 hours reduced significantly the fibrosis up to 5±2% (0.1 mg/ml), 3±1% (1 mg/ml) and 2±1% (5 mg/ml) when compared to the control ($p<0.05$). Longer incubation times ($\geq$60 minutes) with collagenase (>1 mg/ml) reduced stiffness and treated tissue lost their initial shape and structure. Only 0.1 mg/ml treated tissue cube preserved its initial structure.

CONCLUSIONS: *Clostridium histolyticum* collagenase I was shown to be efficient for in vitro collagen clearance of ovarian fibrosis tissue while preserving the tissue structure. The most appropriate concentration of the collagenase for treatment of 0.5 cm^3 ovarian tissue cubes was 0.1 mg/ml

for 12 hours. Additional clinical trials are needed for the evaluation of the efficacy and safety of this treatment approach in humans.

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A SYSTEMATIC REVIEW OF UTERINE-SPARING MINIMALLY INVASIVE TREATMENTS FOR FIBROID BLEEDING. Jiahui Zhang, BA,[1] Bhuchitra Singh, MD, MPH, MS,[2] Virginia-Arlene Acosta Go, MD,[3] James Segars, MD.[2] [1]Renaissance School of Medicine at Stony Brook University, Stony Brook, NY; [2]Johns Hopkins University School of Medicine, Baltimore, MD; [3]Saint Joseph Hospital, Denver, CO.

OBJECTIVE: To evaluate and compare the efficacy of available uterine-sparing, minimally invasive, surgical treatment modalities for the management of bleeding symptoms associated with uterine fibroids.

DESIGN: A systematic literature review using PRISMA methods and standards.

MATERIALS AND METHODS: We conducted a systematic review on April 20, 2020 of full-text English-language studies published on PubMed from inception. Observational studies and randomized controlled trials were included. Only studies including pre-menopausal women with a confirmed diagnosis of uterine fibroids were included. Participants must have reported heavy menstrual or abnormal uterine bleeding at baseline and undergone a uterine-sparing, minimally invasive fibroid treatment. The severity of bleeding was assessed through validated questionnaires such as The Uterine Fibroid Symptom and Quality of Life (UFS-QOL) questionnaire before and after treatment. Patients were excluded if another etiology for their bleeding was more likely.

RESULTS: The initial search yielded 2,327 articles. After review of titles, abstracts, and full text, 49 studies met eligibility criteria and comprised the dataset. For all treatment modalities, patients reported lower quality of life score and worse bleeding symptoms at baseline than after treatment. Six studies assessing laparoscopic and hysteroscopic myomectomy reported short-term resolution of abnormal uterine bleeding in up to 85% of patients and maintenance of symptom resolution at up to 8 years postoperative. Comparison between different routes of myomectomy demonstrated no difference on long-term follow up ($p>0.05$). Results of seven studies demonstrated significant shortening and decrease in the amount of bleeding in at least 80% of patients following uterine artery embolization. Three studies suggested that the combination of laparoscopic uterine artery occlusion with myomectomy resulted in preferential improvement in bleeding symptoms over myomectomy alone. Two studies suggested that laparoscopic uterine artery occlusion may be inferior to uterine artery embolization in the reduction of heavy menstrual bleeding. Promising results were reported for newer techniques including cryomyolysis, radiofrequency ablation, and magnetic resonance-guided focused ultrasound surgery, though available literature did not demonstrate superiority of one technique over another for long-term reduction of uterine bleeding.

CONCLUSIONS: Evidence indicates a high clinical efficacy for all minimally invasive treatment modalities in the reduction of bleeding symptoms associated with fibroids. These techniques allow for uterus preservation and increase treatment options for patients seeking relief from symptomatic uterine fibroids.

SUPPORT: Supported, in part, by the Howard and Georgeanna Jones Research Endowment.

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THE ROLE OF UTERINE FIBROIDS IN HUMAN ENDOMETRIAL ANGIOGENESIS. Antonia Navarro, PhD,[1] Ayman Al-Hendy, MD, PhD.[2] [1]University of Illinois at Chicago, Chicago, IL; [2]■■■.

OBJECTIVE: Uterine fibroids (UF) are benign tumors in women of reproductive age, they cause heavy menstrual bleeding (HMB), leading to severe anemia and subsequent major negative effects on quality of life. The aim of this study is to investigate the effects of human uterine leiomyoma smooth muscle cells (HuLM) and HuLM-derived exosomes on growth and angiogenesis of the human endometrium-related endothelial cells.

DESIGN: We designed an in vitro study using HuLM secretome and HuLM-derived exosome and human endometrial microvascular endothelial cells (HEMEC) to understand the molecular mechanisms by which uterine fibroids mediates their proliferative and angiogenic properties that ultimately cause heavy menstrual bleeding.

MATERIALS AND METHODS: Human endometrial microvascular endothelial cells were treated with HuLM secretome and HuLM-derived exosome at several time points and different concentrations. Then, we measured cell proliferation via BrdU incorporation assay, and will also examine by RT-PCR, FACS and immunoblotting for the expression of proliferation and angiogenesis markets such as PCNA, Cyclin D1, VEGF, VEGFR2 and endoglin.

RESULTS: We observed that both HuLM secretome and HuLM-derived exosomes cocultured with HEMEC increased cell proliferation, and this increase is more significant 60% ($P<0.01$) in HEMEC cocultured with HuLM secretome for 48 hours. We propose that this effect is associated with the up-regulation of specific markers for proliferation (PCNA and cyclin D1), and work is in progress in our lab. HuLM secretome and HuLM-derived exosomes treatments also increased considerably the expression of several angiogenesis markers such as VEGF, VEGFR2 and endoglin compared to untreated cells.

CONCLUSIONS: Our study suggests that both human leiomyoma cells (HuLM) secretome and HuLM-derived exosomes have strong paracrine effect on human endometrial microvascular endothelial cells, likely containing bioactive factors that enhance endometrial angiogenesis, which eventually cause heavy menstrual bleeding. Further characterization of these factors can lead to novel druggable therapeutic targets to improve health care for women with uterine fibroids associated heavy menstrual bleeding.

POSTER SESSION: GENETIC COUNSELING

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LIKELIHOOD FOR REACHING EMBRYO TRANSFER FOLLOWING EXCLUSION-BASED NON-DISCLOSURE PREIMPLANTATION GENETIC TESTING FOR MONOGENIC CONDITIONS (PGT-M). Katrina Merrion, MS, Nina Wemmer, MS. Natera, Inc., San Carlos, CA.

OBJECTIVE: Non-disclosure (ND) preimplantation genetic testing (PGT) for monogenic disorders (PGT-M) via in vitro fertilization (IVF) is an option for individuals at risk for having a late-onset dominant condition. One method involves testing the patient for a familial mutation without disclosing the results, and blinding them to whether their embryos are tested via PGT-M with concurrent PGT for aneuploidy (PGT-A) if they have the mutation, or via PGT-A only if they do not. Exclusion-based testing is an alternate method which does not require the patient's mutation status to be known. Rather, by determining which of the patient's chromosome homologs with the gene of interest was inherited from their affected parent, embryos that inherit that copy of the chromosome are excluded from transfer due to the potential risk for inheriting the mutation. Exclusion-based testing eliminates the risk for accidental disclosure of the patient's mutation status but may exclude unaffected embryos from transfer if the patient does not have the familial mutation. Patients may consider cryopreservation of potentially at-risk embryos in case they pursue testing for themselves at a later time. In this study, we review the likelihood of unaffected and euploid embryo results using exclusion-based ND testing.

DESIGN: Retrospective analysis of trophectoderm (TE) biopsy results from IVF patients referred for exclusion-based ND PGT-M with concurrent PGT-A.

MATERIALS AND METHODS: For each case, a mutation/clinical diagnosis report for the affected relative and samples from the couple and the at-risk patient's parent(s) were required. TE biopsies were shipped to a lab for genotyping using Illumina Cyto12 SNP-based microarrays with informatics.

RESULTS: Twenty-five patients underwent exclusion-based ND PGT-M for 7 disorders (Huntington's Disease (HD), n=19; Spinocerebellar ataxia (SCA) type 3, n=1; SCA type 6, n=1; Polycystic kidney disease, n=1; Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL), n=1; Familial TTR amyloidosis, n=1; Creutzfeldt-Jakob disease, n=1). A total of 273 TE samples from 46 IVF cycles were tested (average of 5.9 embryos/cycle, range 1-21). Average maternal age was 33.1 years (range 26.2–41.9 years). 73.9% (34/46) of cycles had at least one euploid and unaffected embryo. Analysis by maternal age groups indicated that the chance of having at least one euploid and unaffected embryo was 83.3% (5/6) for <30 years, 76.7% (23/30) for 30-34 years, and 60% (6/10) for women ≥35 years.

CONCLUSIONS: Exclusion-based ND testing avoids the risk of accidental disclosure of a patient's mutation status, while allowing a relatively

high rate of having an embryo for transfer after a single IVF cycle. This information may be useful for counseling patients considering ND exclusion-based PGT-M and discussing the potential need for additional IVF cycles in order to reach transfer, especially for women of advanced maternal age. Although ND exclusion-based testing is most commonly performed for HD, here we demonstrate that this method can be utilized for other dominant late-onset conditions.

SUPPORT: Natera, Inc.

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INCREASING SCALE AND THROUGHPUT OF TELEHEALTH GENETIC COUNSELING ACROSS THE SPECTRUM OF REPRODUCTIVE CARE, WHILE MAINTAINING HIGH PATIENT SATISFACTION. Kiley Johnson, MS, Jill Davies, MS, Colleen Caleshu, MS. GeneMatters, Minneapolis, MN.

OBJECTIVE: Multiple professional societies recommend genetic counseling alongside reproductive genetic testing, including the American Society for Reproductive Medicine and the American College of Obstetrics and Gynecology. However, access to genetic counselors (GCs) continues to be an issue. Efforts are being made to remedy this with increased GC throughput and novel approaches to service delivery. We sought to describe one such approach by examining the volume, scope, and capacity of a high throughput telehealth genetic counseling service that provides care to reproductive patients across the country.

DESIGN: Retrospective review of consult data from a telehealth genetic counseling service.

MATERIALS AND METHODS: We examined data for reproductive genetic counseling consults that occurred between 1/1/2018 and 12/31/2019. Extracted data included indication, time required to complete consult, and patient satisfaction. To assess throughput, the number of reproductive consults a GC could complete per week was estimated.

RESULTS: In 2018, 541 reproductive genetic counseling consults were performed, and 1922 were performed in 2019. Care was provided to patients from reproductive endocrinology clinics, genetic testing laboratories, and maternal fetal medicine clinics. Indications included carrier screening, preimplantation genetic testing (PGT), egg donor screening, abnormal aneuploidy screen, advanced maternal age, ultrasound findings, and family history of a genetic condition. The mean time to complete all aspects of a consult (preparation, counseling, and writing genetic counseling summary report) was 40.6 minutes (standard deviation 6.7 minutes). At 40.6 minutes per consult, a full-time GC working in this efficient and high-throughput model can perform 53 consults per week, assuming the same mix of routine and complex cases. This is more than double the weekly caseloads for reproductive GCs reported by the National Society of Genetic Counselors (15.6-20.5 consults per week), which primarily represents traditional lower throughput models. Despite the high throughput nature of the service, patient satisfaction remained high during the study period (95.6%). Consistent with their complexity, PGT consults took longer than other consults in preparation and counseling (preparation: 13.0 minutes vs. 4.0 minutes, $p<0.001$; counseling: 29.2 minutes vs. 16.0 minutes, $p<0.001$; documentation: 10.4 minutes vs. 9.0 minutes, $p=0.18$). In contrast, carrier screening consults took less time than other consults (preparation: 5.5 minutes vs. 9.6 minutes, $p<0.001$; counseling: 18.3 minutes vs. 21.2 minutes, $p<0.001$; documentation: 7.5 minutes vs. 11.4 minutes, $p<0.001$).

CONCLUSIONS: Genetic counseling provided by a national telehealth organization covers the full range of reproductive indications, from routine to complex. The approach is scalable, with a 3.5 fold increase in consult volumes from 2018 to 2019. Given the high patient satisfaction, increased throughput, and nation-wide nature of this approach, it is a promising option for increasing access to reproductive genetic counseling.

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PATHOGENIC VARIANTS WITHIN ACMG SECONDARY FINDINGS GENES IN 24,591 HEALTHY INDIVIDUALS USING CLINICAL EXOME SEQUENCING FOR CARRIER SCREENING. Pere Mir Pardo, PhD,[1] Joaquin Panadero, MSc,[1] Gema Escribano, MSc,[1] Jorge Jimenez-Almazán, PhD,[1] Roberto Alonso, MSc,[1] Claudia Abellan, MSc,[2] Carlos Simon, MD, PhD,[3] Julio Martin, MSc.[1] [1]Igenomix, Valencia, Spain; [2]INCLIVA/University of Valencia, Valencia, Spain; [3]Professor University of Valencia, INCLIVA, Founder and Head of the Scientific Advisory Board, Igenomix, Paterna (Valencia), Spain.

OBJECTIVE: Expanded carrier screening (ECS) aims to reduce the burden of recessive single-gene disorders by identifying the genetic risk for the offspring of individuals in reproductive age. ECS using exome sequencing could also reveal information that may influence on individual's health. A significant group of clinically actionable genes are the secondary findings (SF) list defined by the ACMG. Our objective was to assess the frequency of SF pathogenic variants in individuals undergoing ECS.

DESIGN: Retrospective analysis of clinical exome data from an ECS program to assess the frequency of pathogenic variants for the 59 SF gene list defined by the ACMG.

MATERIALS AND METHODS: A database was built using anonymized sequencing data of 24,591 clinical exomes (TruSight One sequencing panel; Illumina) intended for ECS before Assisted Reproductive Techniques, from September 2015 to June 2019. Females represented the 50.9% (12,525) of tested individuals and males the remainder 49.1% (12,066). Distribution between patients and gamete donors was 59.3% (14,588) *vs* 40.7% (10,003), respectively. All patients self-reported European ancestry except a subset of 475 Emirati individuals. Sequencing data were processed using a proprietary bioinformatic pipeline for the 59 genes included in the ACMG recommendations for reporting of secondary findings (ACMG SFv2.0) (Kalia et al., 2016). Variant pathogenicity was performed in compliance with ACMG-AMP guidelines (Richards et al., 2015) using an in-house algorithm, private and public databases, and updated literature, only (likely) pathogenic variants were considered as a SF.

RESULTS: The overall frequency of individuals with pathogenic variants was 2.6% (n=636). No differences in the frequency of SF was found between genders neither between patients and donors. At least one (likely) pathogenic variant was identified in 39 of 59 ACMG genes. In total, 344 unique variants were detected in 652 alleles. The most frequent pathogenic variant was the X-linked NM_000169.2:c.427G>A in *GLA* gene (n=19). *BRCA1* and *BRCA2* were the most frequently positive called genes, with 95 unique pathogenic variants detected in 131 individuals (20.6%).

When dividing by ancestry, same frequency of SF was found in Emiratis (2.5%) and European (2.6%). In contrast, differences were found for the most frequently positive genes. Top-three positive genes among Emiratis were *SCN5A*, *KCNQ1* and *RYR1*; while for Europeans were *BRCA2*, *MYBPC3* and *LDLR*. Remarkably, the variant most frequently detected in European-ancestry individuals (NM_000169.2:c.427G>A in GLA) was not detected in Arabs. Conversely, 6 out of 10 unique variants found in Arabs were not detected in the large European database.

CONCLUSIONS: The analysis of the ACMG SF genes provided evidence of pathogenicity in 2.6% of the tested individuals. Same frequency was found among genders and patient-donor status, as well as for European and Emirati populations. However, genetic heterogeneity was found among the two populations both at the gene and at the variant level.

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WHAT TO ADVISE TO PATIENTS WITH ONE GOOD QUALITY BLASTOCYST? PGT-A OR NOT? OUTCOMES OF 1737 CYCLES. Murat Cetinkaya, M.D., PhD, Cigdem Cinar Yapan, MsC, Mehmet Ali Tufekci, PhD, Hakan Kadir Yelke, MsC, Yesim Kumtepe Colakoglu, MsC, Semra Kahraman, MD. Prof. Istanbul Memorial Hospital, Istanbul, Turkey.

OBJECTIVE: Preimplantation Genetic Testing for Aneuploidy (PGT-A) has been extensively studied and shown to improve pregnancy rates per transfer particularly in advanced maternal age patients ($\geq$35 years old), decrease risk of miscarriage, as well as shorten time to have a healthy birth. These benefits are more apparent if PGT-A is performed on multiple blastocysts. However, application of PGT-A for couples who have only one blastocyst to be biopsied is still in debate. The aim of this study is to compare different age groups with a single good quality blastocyst and evaluate the clinical outcomes of transferring with or without a PGT-A cycle.

DESIGN: This retrospective study was based on 1737 cycles initiated between 2017 and 2020 in Istanbul Memorial Hospital and resulted with a single good quality blastocyst. Preimplantation genetic testing for aneuploidy (PGT-A) represent 886 cycles and a total of 851 cycles were transferred without PGT-A.

MATERIALS AND METHODS: The single blastocyst was tested as euploid in only 108 out of 886 PGT-A cycles (19.5%). The overall ongoing pregnancy rate was 53.7% in PGT-A cycles and 28.2% in untested cycles. For the PGT-A group, 90 patients were <35, 93 between 35-37, 185 between 38-

39, 326 between 40-42 and 192 were ≥43. For the untested group, 434 patients were <35, 182 between 35-37, 79 between 38-39, 92 between 40-42 and 64 were ≥43. Chi-square test was applied for categorical group comparisons. PGT-A was done by NGS ReproSeq on Ion Torrent S5 (ThermoFisher) following trophectoderm biopsy.

RESULTS: In the <35 age group, ongoing pregnancy rates (OPRs) per transfer were 58.8% and 36.8% in the tested and untested group, respectively (p= 0.0672). In the 35-37 age group, OPRs were 64% and 32.9% (p= 0.0026); in the 38-39 age group 36.3% and 13.9% (p= 0.0076); in the 40-42 age group 57.1% and 6.5% (p<0.0001), in the ≥43 age group 80% and 5% (p <0.0001), with and without PGT-A, respectively.

In the group without PGT-A, under 35 years of age, OPRs per initiated cycle were found to be higher than the group with PGT-A (20.6% vs. 11%; p<0.0001), showing that the underlying cause for infertility may not be directly related with aneuploidy but other clinical factors may be in play. For the 35-37 age group, OPRs per initiated cycle were 15.6% and 17.2% (p=0.0058), for the 38-39 age group 4.3% and 6.5% (p=0.0502), for the 40-42 age group 1.6% and 5% (p=0.5409) and for the ≥43 age group 1.1% and 2% (p=0.2695), in the untested and tested groups, respectively.

CONCLUSIONS: Above 35 years of age, OPRs per embryo transfer and per initiated cycle are higher in the PGT-A group when compared to the untested group. Therefore, PGT-A is a good option for women who are above 35 years of age and have low number of blastocysts.

SUPPORT: No financial support needed for the study.

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PGT-A INCIDENTAL FINDING: RECURRENT MOSAIC SEGMENTAL ANEUPLOIDY INDICATIVE OF BENIGN FAMILIAL VARIANT.

Rachel A. Donnell, MMSc, CGC,[1] Lauren Thomas Garrett, MS, CGC.[2] [1]Seattle Reproductive Medicine, Seattle, WA; [2]Pacific Northwest Fertility, Seattle, WA.

OBJECTIVE: To describe the first known cases of recurring mosaic segmental aneuploidy (RMSA) identified through PGT-A and present the results of subsequent genetic testing.

DESIGN: Case report.

MATERIALS AND METHODS: At a single clinic, results of 396 PGT-A cases were reviewed from February 2019 to December 2019 for RMSA. RMSA was defined as 3 or more embryos with the same mosaic deletion or duplication with the same breakpoints.

RESULTS: Two cases were identified.

Case 1: A G0, 37-year-old female with a history of primary infertility and male factor (oligospermia) underwent IVF with PGT-A. PGT-A results identified 3 out of 14 embryos with a mosaic dup(22)(pter-q12.1).

Case 2: A G0, 34-year-old female with a history of primary infertility and male factor (oligospermia). The family history was suggestive of a chromosomal translocation and parental karyotype results were consistent with 45,XX,der(13;14)(q10;q10) and 46,XY. IVF with PGT-SR was recommended. PGT-A results from the first cycle were abnormal and identified 2 out of 4 embryos with a mosaic dup(12)(q24.32-qter). PGT-A results from the second cycle identified 2 out of 2 embryos with the same mosaic duplication.

These results can suggest an underlying parental translocation, so all parents underwent karyotype analysis. Results of all karyotypes were normal except for the patient previously identified with a robertsonian translocation.

In our second case, parental fluorescence in situ hybridization (FISH) for the distal 12q arm and SNP microarray were performed. Results of both tests were normal. However, the lab commented that the female patient had a 1.7Mb interstitial triplication of 12q24.32 in all cells. The triplication did not contain any genes of clinical significance.

CONCLUSIONS: To our knowledge, these are the first descriptions of RMSA identified through PGT-A. By definition, mosaic abnormalities occur at random, yet we identified two cases of recurring mosaic duplications that were suggestive of dominant inheritance.

In our first case we did not identify an inheritable cause. In the second, a parent was found to carry a benign 12q24.32 triplication in all cells that explained the recurring finding in her embryos. A 1.7Mb interstitial triplication is below the resolution of NGS which may explain why the embryos were classified as mosaic and highlights the limitations of NGS.

RMSA may be indicative of a uniform copy number variation (CNV) in a parent and follow up testing should be considered to determine the clinical significance and true breakpoints. Embryos reported with benign CNV can be suitable for transfer and may help couples undergoing IVF pursue less treatment.

Although we did not identify an inheritable cause in our first case, it is unlikely that the recurrent mosaic duplication occurred by chance alone. One hypothesis is that these findings may be suggestive of an inherited benign autosomal fragile site. 22q12.2 is a known common fragile site (FRA22B).

As clinics continue to consider mosaic embryo transfer, it will be important to investigate the clinical significance of RMSA and this may warrant additional parental follow up testing.

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GENOMICS ANALYSIS OF MATERNAL EXOMES REVEALS NEW CANDIDATE GENES AND PATHWAYS FOR THE DIAGNOSIS AND PREDICTION OF RECURRENT PREIMPLANTATION EMBRYO ARREST IN IVF CYCLES.

Semra Kahraman, MD, Prof.,[1] Fulya Gokdagli Sagir, MD,[1] Beril Yuksel, MD, Assoc. Prof.,[1] Murat Cetinkaya, M.D., PhD,[1] Meral Gavaz, MSc,[1] Burcu Kara, BSc,[1] Mesut Yesil, MSc,[1] Gunkut Akar, MSc,[1] Silvia Buonaiuto, BSc,[2] Gianluca Damaggio, MS,[2] Marco Fabiani, PhD,[3] Adriano De Marino, PhD,[3] Vincenza Colonna, PhD,[2] Carlos Simon Prof, MD,[4] Antonio Capalbo, PhD.[3] [1]Istanbul Memorial Sisli Hospital, Istanbul, Turkey; [2]Institute of Genetics and Biophysics, National Research Council (CNR), Naples, Italy; [3]Igenomix, Marostica, Italy; [4]Igenomix Foundation, Valencia, Spain.

OBJECTIVE: The aim of our study was to discover whether genomic analysis of maternal exomes is capable of identifying new target genes to improve infertility diagnosis in cases with recurrent preimplantation developmental embryo arrest.

DESIGN: Genetic analysis.

MATERIALS AND METHODS: The study was conducted at Istanbul Memorial Hospital ART and Reproductive Genetics Unit between December 2018-November 2019 in cooperation with Igenomix, Italy. Ten women, five with consanguinity history, four being the offspring of first-cousin marriage with a history of recurrent embryo developmental failure in multiple IVF cycles were recruited. WES was performed *(Agilent SureSelect whole-exome capture and Illumina sequencing technology).* Variant calling against the reference genome GRCh38 was done using Freebayes and identified on average 436k high quality variants per samples. According to Ensembl classification 2.8% are expected to have high (0.25%) or moderate (2.56%) disruptive impact in the gene product. Variants were filtered on a per-individual base using a number of criteria (frequency <0.05% in the 1000 Genomes and gnomeAD; severity as estimated by Ensembl; the functional effect using the CADD score above the 90 percentile and variants location in genes highly intolerant to loss of function, pLI>0.9. Finally variants retained had to be in genes relevant to the early embryonic development (3600 gene list). To control for false positives, we run the same filtering on 100 replicates of 10 random samples from the publicly available Human Genome Diversity Project data set, and we filtered out variants falling in genes showing up in 50% of the hundred replicates, controlling for random occurrence of hits.

RESULTS: Overall, 1700 unique variants in 1281 unique genes were retained after filtering, most involved in lethal embryonic pathways. Thirty-one unique retained variants have high impact and among them sixteen are splice variants and nine are stop-gains. Each sample carries on average 185.9 (10.0 s.d.) potentially detrimental variants. Of particular relevance two individuals had pathogenic variants in SPAG5, an essential component of the mitotic spindle required for normal chromosome segregation and progression into anaphase. Furthermore, two individual showed pathogenetic variants in the zinc finger protein 91 (ZFP91). The knockdown of ZFP91 reduces FOXA1 polyubiquitination and cellular progression in embryonic and cancer cells. Finally, three samples share the G allele of the rs1217009744 variants in homozygosis in the *SHANK3* gene.

CONCLUSIONS: Exome analysis of women with recurrent embryo arrest successfully identifies genomic variants lethal at the embryonic stage, thus providing a diagnostic tool. However, functional genomics studies and validation in an independent cohort of patients with preimplantation embryo arrest phenotype and of different ethnicity is required to corroborate these findings. The generation of polygenic models will also further contribute to increasing discovery rate and to the development of more general and powerful predictive models for this phenotype.

SUPPORT: None

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NOT ALL PREIMPLANTATION GENETIC TESTING IS CREATED EQUAL: EVALUATING PATIENT OPINIONS BASED ON TEST TYPE. Jennifer L. Garbarini, MS, CGC, Dina Nusblat, MS, CGC, Marie Discenza, MS, CGC. CooperSurgical, Trumbull, CT.

OBJECTIVE: Evaluate patient motivations for pursuing preimplantation genetic testing (PGT), insurance coverage implications and utility of PGT to their In-vitro fertilization (IVF) cycle.

DESIGN: IVF can be combined with PGT. Patients seeking to reduce hereditary disease risk for monogenic disorders can pursue PGT-M. Those with a chromosome rearrangement can have embryos tested for unbalanced outcomes (PGT-SR). Additionally, patients can screen embryos for aneuploidy (PGT-A). Increased availability of testing requires providers to understand patient motivations, potential barriers and how to integrate PGT into an IVF cycle.

MATERIALS AND METHODS: All patients undergoing pre-test genetic counseling through CooperGenomics were eligible to take a survey.

RESULTS: Between April 2019- May 2020, there were 169 respondents; 100 PGT-A, 16 PGT-SR, and 53 PGT-M (with and without PGT-A).

Patients were asked whether PGT contributed to their deciding to pursue IVF. 38/51 (75%) PGT-M patients and 10/16 (63%) PGT-SR patients stated that PGT was a "very important" factor in deciding to pursue IVF. PGT-A patients were less likely to pursue IVF for the purpose of PGT; 16% cited PGT as a reason for pursuing IVF.

PGT-M and PGT-SR patients were similarly motivated to pursue IVF, even if insurance coverage was not available. More than two-thirds of PGT-M and PGT-SR patients would continue IVF in the absence of insurance coverage. PGT-A patients were mixed, with 44/96 (46%) stating that they would continue IVF in the absence of insurance coverage; 39/96 (41%) patients were uncertain

9% (32/165) of all respondents previously had genetic counseling for PGT. Specifically, 9/98 (9%) PGT-A patients, 6/16 (38%) PGT-SR patients and 17/51 (33%) PGT-M patients previously had genetic counseling for PGT. CooperGenomics genetic counseling was rated "useful" or "very useful" by 93% (90/97) of PGT-A patients, 88% (14/16) of PGT-SR patients and 88% (45/51) of PGT-M patients.

For PGT-A patients, the most common reasons for pursuing PGT were "infertility" and "doctor recommended". For PGT-M patients, "carriers of the same genetic disease" and "personal/family history of a genetic disease" and PGT-SR patients reported "previous miscarriage(s)" and "personal/family history of a chromosomal condition".

CONCLUSIONS: Overall, patients pursuing PGT-M and PGT-SR had similar goals for PGT. They report that PGT is a very important factor in deciding to pursue IVF and are more likely to pursue IVF without insurance coverage as compared to PGT-A patients. Importantly, insurance coverage is a main reason why patients without an underlying genetic condition or aberration may pursue PGT. Patients pursuing PGT-M or PGT-SR rate PGT as very important to their IVF cycle as it may be the only reason for pursuing IVF. Although PGT is an important reason for these patients to pursue IVF, the majority have not spoken with a genetic counselor regarding PGT yet found genetic counseling for PGT useful. It is important to understand the motivations of patients seeking IVF and utility of PGT for each patient.

SUPPORT: CooperSurgical

POSTER SESSION: HEALTH DISPARITIES

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INFLUENCE OF MALE PARTNER RACE ON USE AND OUTCOMES OF ASSISTED REPRODUCTIVE TECHNOLOGIES. Adriana Nicholson Vest, PhD,[1] Lauren M. Kipling, MPH,[2] Heather S. Hipp, MD,[1] Jennifer F. Kawwass, MD,[3] Akanksha Mehta, M.D., M.S.[4] [1]Emory University School of Medicine, Atlanta, GA; [2]Emory University Rollins School of Public Health, Atlanta, GA; [3]Emory University School of Medicine, Division of Reproductive Endocrinology and Infertility, Atlanta, GA; [4]1365 Clifton Road NE, Building B, Atlanta, GA.

OBJECTIVE: There are persistent racial disparities in outcomes from assisted reproductive technologies (ART), though the majority of studies have focused on the female partner. This work aims to investigate the association of race with reproductive choices and outcomes, especially in regards to paternal race and male factor infertility.

DESIGN: A retrospective cohort study using an existing institutional dataset, representing a racially and ethnically diverse patient population.

MATERIALS AND METHODS: We included all non-sperm donor in-vitro fertilization (IVF) cycles performed at our institution from 2014-2019. Cycle-level data that is collected and submitted to the Society for Assisted Reproductive Technology Clinical Outcomes Reporting System (SART CORS) was included. We compared demographic and clinical characteristics of age, BMI, infertility diagnoses, number of previous IVF cycles, use of preimplantation genetic testing (PGT), use of donor oocytes, freeze-all cycles, and the outcomes of pregnancy, miscarriage, and live birth, stratified by male and female partner race.

T-test and Fisher's exact test were used to compare continuous and categorical data, respectively. Significance was set as $p<0.05$.

RESULTS: A total of 2,030 IVF cycles involving 1,084 couples were examined. Fifty percent of male partners were White, 28% Black, 13% Asian, 2% Hispanic, 2% Other, and 4% non-reported. The majority of couples (88%) shared a common race category.

Non-White men were significantly older in age (39.3 vs 37.4 yr), had a higher BMI (29.1 vs 28.0 kg/m^2), and were more likely to have an older female partner (36.7 vs 35.5 yr) compared to White men. Black men were more likely to have a diagnosis of male factor infertility (39%) than non-Black men (White – 34%, Asian – 28%). Black men and their partners were less likely to proceed with PGT (14%) than White (19%) or Asian men (19%). Use of freeze-all cycles and donor oocytes did not vary significantly among the races. Asian males had the highest average number of prior cycles at 1.24, followed by Hispanics (0.96), Whites (0.93), and Blacks (0.88). Black males had the highest average number of prior pregnancies at 1.38, followed by Asians (1.22), Whites (1.1), and Hispanics (1.08).

White men were more likely to have higher clinical pregnancy rate (44% vs 38%) and live birth rate (37% vs 30%) than non-White men. Miscarriage rates were not significantly different among the races.

CONCLUSIONS: In this uncontrolled analysis of a diverse patient population, paternal race was found to be associated with IVF cycle characteristics and reproductive outcomes. These findings highlight the importance of including paternal demographic data in the assessment of reproductive care and outcomes. Future analysis controlling for confounding variables such as female partner age and etiology of female infertility will help to determine whether male factors contribute independently to outcomes.

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AFRICAN AMERICAN WOMEN HAVE LOWER ODDS OF LIVE BIRTH FROM DONOR EGG IVF. Jasmine Aly, MD,[1] Kate Devine, MD,[2] Samad Jahandideh, PhD,[2] Alicia Y. Christy, MD,[3] Alan H. DeCherney, MD,[1] Micah J. Hill, DO.[1] [1]Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD; [2]Shady Grove Fertility Center, Rockville, MD; [3]Veterans Administration, Kensington, MD.

OBJECTIVE: African American women have poorer ART outcomes compared to Caucasian women and the etiology is unknown. Studies have found African American women to have fewer mature oocytes, fertilized oocytes, and lower blastocyst development rates compared to Caucasian women, suggesting that competence of the oocyte may play a role. Our objective is to assess ART clinical outcomes in African American women, while controlling for oocyte quality by using the oocyte donor–recipient model.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A total of 1,101 African American and 5,373 Caucasian recipients of fresh and frozen donor oocytes were included. Donor characteristics included age 21-32, BMI between 18 to 29.9, non-smoking status, high school graduate status, AMH $>$ 2 and AFC$>$ 15. All recipients underwent single embryo transfer. Statistical analyses of clinical outcomes was performed using chi-square analysis, t-test, or Mann-Whitney U. $P<$ 0.05 was considered statistically significant.

RESULTS: African American recipients were older (42.8 years old vs 41.5 years old; $p<0.001$), and more likely to have tubal disease (6.9 % vs 1.8 %; $p<0.001$). Mean BMI was higher in the African American recipient group (28.1 kg/m^2 vs 25.4 kg/m^2; $p<0.001$). Presence of ovulation disorders, DOR, endometriosis, and uterine factor infertility were the same in both groups. African Americans had a lower odds of pregnancy in fresh and frozen cycles (fresh- 59.8% vs 70%; $p<0.001$, frozen- 41.5% vs 50%; $p<0.001$).

Pregnancy Outcome (%): Fresh Donor Oocyte Cycle	African American (n=492)	White (n=2641)	*p*-value	**p*-value (adjusted)
Positive ß-Hcg	59.8	70.0	<0.001	<0.001
Clinical Intrauterine Gestation	53.0	62.1	<0.001	0.004
Spontaneous Abortion	10.2	10.6	0.800	0.243
Livebirth	40.2	49.9	<0.001	0.005
Pregnancy Outcome (%): Frozen Donor Oocyte Cycle	**African American (n=609)**	**White (n=2732)**	***p*-value**	***p*-value (adjusted)**
Positive ß-Hcg	41.5	50.0	<0.001	<0.001
Clinical Intrauterine Gestation	33.5	48	<0.001	<0.001
Spontaneous Abortion	8.4	11.9	0.020	<0.001
Livebirth	22.3	33.7	<0.001	<0.001

*Adjusted for age, BMI, diagnosis (tubal disease, uterine factor, endometriosis, DOR).

Live birth was decreased in African Americans in fresh and frozen cycles (fresh- 40.2% vs 49.9%; $p=<0.001$, frozen-22.3% vs 33.7%; $p<0.001$). Differences remained statistically significant after adjustment for age, BMI, and diagnosis) (Table 1).

CONCLUSIONS: When using a donor oocyte model, ART outcomes including odds of pregnancy, clinical intrauterine gestation, and live birth rate remain lower in African American women, even after controlling for BMI, uterine factor and tubal factor. These data suggest that poorer ART outcomes in African American patients may be due to factors other than oocyte quality.

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THERE IS A DISPARITY IN ART OUTCOMES BETWEEN ASIAN AND CAUCASION WOMEN IN OOCYTE DONATION CYCLES. Jasmine Aly, MD,[1] Micah J. Hill, DO,[1] Samad Jahandideh, PhD,[2] Alicia Y. Christy, MD,[3] Alan H. DeCherney, MD,[1] Kate Devine, MD,[2] Frank E. Chang, MD.[2] [1]Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD; [2]Shady Grove Fertility Center, Rockville, MD; [3]Veterans Administration, Kensington, MD.

OBJECTIVE: To assess ART clinical outcomes in Asian patients while controlling for oocyte quality by using the oocyte donor–recipient model, given that several studies have shown that Asian women have poorer ART outcomes compared to Caucasian women and the etiology of this disparity is unknown.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A total of 459 Asian recipients and 2,641 Caucasian recipients of fresh donor oocytes were included. Donor characteristics included age 21-32, BMI between 18 to 29.9, non-smoking status, high school graduate status, AMH > 2 and AFC> 15. All recipients underwent single embryo transfer. Statistical analyses of clinical outcomes between groups were performed using chi-square analysis and t-test or Mann-Whitney U. $P< 0.05$ was considered statistically significant. GEE models were used to adjust for age, BMI, and primary diagnosis.

RESULTS: Recipient baseline characteristics including age, number of previous FET, and primary infertility diagnosis were largely similar amongst Asian and Caucasian recipients. Asian recipients were more likely to have ovulation disorders and PCOS (3.5% vs 1.6%; $p<0.009$). Mean BMI was lower in the Asian recipient group (23.5kg/m^2 vs 25.4 kg/m^2; $p<0.001$). There was no difference in clinical pregnancy, or spontaneous abortion between the groups. Live birth was decreased in Asians compared to Caucasian recipients (43.6% vs 49.9%; $p=0.014$). This difference remained statistically significant after adjustment for age, BMI, and diagnosis (Table 1).

Pregnancy Outcome (%)	Asian (n= 459)	Caucasian (n=2641)	*p*-value	**p*-value (adjusted)
Clinical Intrauterine Gestation	58.2	62.1	0.12	0.08
Spontaneous Abortion	12.2	10.6	0.35	0.11
Livebirth	43.6	49.9	0.01	0.003

* Adjusted for age, BMI, diagnosis (tubal disease, uterine factor, endometriosis, DOR).

CONCLUSIONS: The decrease in ART live birth in Asian patients persisted even in a fresh donor oocyte model. While this decrease was small, it highlights the need for continued research into the etiologies of ethnic disparities seen in ART.

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RACIAL DISPARITIES IN FROZEN EMBRYO TRANSFER SUCCESS. Quetrell D. Heyward, MD, MBA,[1] Jessica R. Walter, MD,[1] Snigdha Alur-Gupta, MD MSCE,[1] Arnav Lal,[2] Dara S. Berger, PhD,[1] Samantha Butts, MD, MSCE,[1] Clarisa Gracia, MD, MSCE.[1] [1]University of Pennsylvania, Division of Reproductive Endocrinology and Infertility, Philadelphia, PA; [2]University of Pennsylvania, Philadelphia, PA.

OBJECTIVE: Racial and ethnic disparities in pregnancy outcomes have been reported after fresh in vitro fertilization (IVF) cycles, but there are limited data on disparities after frozen embryo transfers (FETs). The objective of this study was to compare pregnancy and live birth rates after FETs among women of different self-reported race/ethnicity groups and explore the effect of patient, protocol, and cycle characteristics on success.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: Women undergoing an autologous FET between January 2013 and March 2020 were included. Co-maternity, surrogacy, donor oocyte/embryo cycles, or those not surviving the thaw were excluded. Demographics and clinical characteristics including self-reported race and ethnicity were abstracted from the medical record. Continuous variables were compared using the Student's t-test or Mann–Whitney U test while the $\chi 2$ or Fisher's exact tests were used to compare categorical variables. Multivariable logistic regression was used to examine the relationships between pregnancy, live birth, and race while adjusting for potential confounders.

RESULTS: White, Black, and Asian women underwent a total of 1664 (73.7%), 257 (11.4%), and 336 (14.9%) frozen embryo cycles, respectively. Only 3.4% of the population self-identified as Hispanic/Latino. Programmed FETs were performed in 83.4% of all cycles (n=1975). Black women were significantly older at the time of egg retrieval, had a higher prevalence of fibroids, higher BMIs, were less likely to transfer PGT-tested blastocysts, and less likely to undergo a single embryo transfer when compared to non-Black women ($p < 0.05$).

Overall, Black women were significantly less likely to achieve pregnancy after FET when adjusting for age, BMI, parity, and number of embryos transferred compared to non-Black women (AOR 0.68, 95% CI 0.51-0.92, p=0.01). Though there was no significant overall difference in live birth rates, endometrial preparation protocol modified the effect of race on live birth. Black women were significantly less likely to achieve a live birth after a natural cycle FET compared to non-Black women (37.1% vs 13.0%, p=0.02), a difference not observed with programmed FETs (42.2% vs 40.0%, p=0.5). A sub-analysis investigating lower implantation rates showed no racial differences in mean estradiol or progesterone within 24 hours of transfer or endometrial morphology in programmed FETs (n=1680). Results were unchanged when restricting the analysis to women without fibroids and non-PGT cycles.

CONCLUSIONS: In this study using a diverse cohort of more than 2000 women, Black race was associated with a significantly lower rate of embryo implantation following FET independent of the effects of endometrial preparation protocol, PGT, and established predictors of treatment success. Our finding that racial differences in live birth after FET may depend on the endometrial preparation protocol is novel and requires further study. Disparities in success are not only important for patient counseling, but also warrant further investigation to develop strategies to improve success rates in Black women.

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COMPARISON OF PREGNANCY AND LIVE BIRTH OUTCOMES FOLLOWING FRESH EMBRYO TRANSFER BETWEEN BLACK AND WHITE PATIENTS WITH CONCORDANT BMI CLASSIFICATION. Phillip A. Romanski, MD, Pietro Bortoletto, MD, Steven Spandorfer, MD. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To compare the pregnancy and live birth outcomes between black and white women with concordant body mass index (BMI, kg/m^2) classifications following controlled ovarian hyperstimulation with a planned fresh embryo transfer.

DESIGN: Retrospective cohort study was performed in an academic hospital setting. Each patient's first oocyte retrieval with planned autologous fresh embryo transfer in our IVF clinic between 01/01/2012 and 12/31/2018 was included. Patients with uterine factor infertility were excluded (black: n=29, white: n=147). Patients were stratified by race (black vs. white) and BMI classification: normal weight (18.5-24.9; black: n=69, white: n=2,113) and overweight (25.0-29.9; black: n=60, white: n=569).

MATERIALS AND METHODS: The primary outcomes were pregnancy and live birth rates. Logistic regression adjusted *a priori* for patient age and the number of embryos transferred was used to estimate the OR with a 95% CI among the BMI study groups for pregnancy outcomes. A secondary analysis of singleton pregnancies was performed to assess delivery outcomes.

RESULTS: A total of 2,811 oocyte retrievals resulting in 2,601 embryo transfers met inclusion criteria. In the normal-weight cohort, the rate of no transfer was significantly lower in the white patients (7.2%) compared to the black patients (14.2%; OR 2.19 (1.10-4.38)). The difference in no-transfer rate was due to a higher rate of unplanned cryopreservation in the black patients (60.0%) compared to the white patients (36.4%). In overweight patients, the no-transfer rate was similar between the white (8.1%) and black (5.0%) patients. After embryo transfer in normal-weight patients, there were no statistically significant differences between the white compared to black patients for pregnancy (60.0 vs 49.1%; OR 0.71 (0.42-1.21)), miscarriage (7.4 vs 10.2%; OR 1.33 (0.56-3.16)) or live birth rates (42.3 vs 32.2%; OR 0.74 (0.41-1.31)). Similarly in overweight patients, there were no statistically significant differences between the white compared to black patients for pregnancy (57.6 vs 61.4%; OR 1.22 (0.69-2.15)), miscarriage (8.2 vs 14.0%; OR 1.80 (0.80-4.06)) or live birth rates (38.1 vs 36.8%; OR 1.00 (0.56-1.78)). Among singleton deliveries, the preterm delivery (<37 weeks gestation) and C-section rates were similar between the white and black patients in both BMI classifications: Normal-weight preterm birth (7.7% vs 6.7%; OR 0.86 (0.11-6.64)) and overweight preterm birth (8.4 vs 21.1%; OR 2.78 (0.79-9.80)).

CONCLUSIONS: Previous studies have reported worse IVF outcomes in black compared to white patients. This has been theorized to be due to increased obesity and uterine factor infertility in black patients. In this study, we compared pregnancy outcomes after removing these potential confounders and we indeed observed similar pregnancy and live birth rates after embryo transfer between black and white patients. Normal-weight black patients had a higher no-transfer rate in our cohort; however, this was explained by a higher proportion of unplanned cryopreservation and not due to an increased rate of no embryos available for transfer.

SUPPORT: None

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COMPARISON OF LIVE BIRTH OUTCOMES IN FRESH EMBRYO TRANSFER IVF CYCLES BETWEEN ASIAN AND WHITE WOMEN WITH CONCORDANT BMI CLASSIFICATION. Phillip A. Romanski, MD, Pietro Bortoletto, MD, Steven Spandorfer, MD. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To compare the pregnancy and live birth outcomes between Asian and white women with concordant body mass index (BMI, kg/m^2) classifications following controlled ovarian hyperstimulation with a planned fresh embryo transfer.

DESIGN: We conducted a retrospective cohort study in an academic hospital setting of patients who underwent their first oocyte retrieval with planned autologous fresh embryo transfer in our IVF clinic between 01/01/2012 and 12/31/2018. Patients were stratified by race (Asian vs. white) and BMI classification: underweight (<18.5; Asian: n=70, white: n=127) and normal weight (18.5-24.9; Asian: n=797, white: n=2,221).

MATERIALS AND METHODS: The primary outcomes were pregnancy and live birth rates. Logistic regression adjusted *a priori* for patient age and the number of embryos transferred was used to estimate the odds ratio with a 95% confidence interval (CI) among the BMI study groups for pregnancy outcomes. A secondary analysis of singleton pregnancies was performed to assess delivery outcomes.

RESULTS: A total of 3,215 oocyte retrievals resulting in 2,985 embryo transfers met inclusion criteria. After embryo transfer in the underweight cohort, the pregnancy rate was significantly higher in the white patients (66.7%) compared to the Asian patients (43.5%; OR 0.44; 0.23-0.82). A similar association was observed in the normal-weight cohort (59.8% vs. 49.9%, respectively; OR 0.70; 0.59-0.83). In the underweight cohort, the live birth rate trended higher in the white patients (48.3%) compared to the Asian patients (33.3%; OR 0.62; 0.22-1.17), but was not statistically significant. In the normal-weight cohort, the live birth rate was significantly higher in the white patients (42.2%) compared to the Asian patients (32.8%; OR 0.72; 0.60-0.86). Among singleton deliveries, the preterm delivery rate (<37 weeks gestation) was similar among underweight (white: 13.0% versus Asian: 5.6%; OR 0.68 (0.07-6.92)) and normal-weight patients (white: 7.7% versus Asian: 8.4%; OR 1.12 (0.63-1.99)). Further, c-section rates were similar among underweight (white: 32.6% versus Asian: 22.2%; OR 0.49 (0.13-1.89)) and normal-weight patients (white: 34.2% versus Asian: 37.1%; OR 1.06 (0.76-1.48)).

CONCLUSIONS: Worse IVF outcomes in Asian compared to white patients have been reported previously and attributed to an increased proportion of underweight patients in the Asian population. However, even when stratifying by BMI, we observed that Asian women have worse pregnancy outcomes compared to white women. Further, live birth rates were worse among normal-weight patients. In the underweight cohort, despite a non-significant difference in live birth rates, the 15% absolute decrease in live births in Asian patients is clinically significant. Since worse IVF outcomes in Asian compared to white patients are not entirely due to weight, further studies should focus on alternative explanations to develop improved treatment strategies for these patients.

SUPPORT: None

P-334 4:30 PM Sunday, October 18, 2020

DO SOCIOECONOMIC DEMOGRAPHIC PROFILES BY ETHNICITY AND REGION MAKE A DIFFERENCE IN THE OBJECTIVE ASSESSMENT OF THE ONCOFERTILITY EDUCATIONAL INFORMATION ON NCI-DESIGNATED CANCER CENTER WEBSITES IN THE US - A FIVE YEAR COMPARISON. Janelle M. Jackman, MBBS,[1] Christopher de Haydu, MD,[2] Melody A. Rasouli, MD, MBA,[3] Angela H. Liu, MD,[3] Kajal Verma, MD,[3] Sriram Eleswarapu, MD, PhD,[4] Cindy M. Duke, MD, PhD.[5] [1]The Camran Nezhat Institute, Palo Alto, CA; [2]University of Miami, Miami, FL; [3]University of Nevada, Las Vegas, Las Vegas, NV; [4]University of California, Los Angeles, Los Angeles, CA; [5]University of Nevada, Las Vegas and Nevada Fertility Institute, Las Vegas, Las Vegas, NV.

OBJECTIVE: Fertility preservation (FP) is an important aspect to consider in patients diagnosed with cancer. Though guidelines recommend discussing FP with patients in the reproductive age group prior to cancer treatment, this is not always followed. Hospital websites should also serve as a source for information related to FP but were previously shown to be devoid of this information, especially in areas with a prevalent minority ethnic background. This study aims to assess if there are any improvements in socio-demographic health disparities & the availability and quality of information on FP on major cancer center websites based on the ethnicities in the location.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: National Cancer Institute Designated Cancer Centers (NCICC) & Cleveland Clinic Foundation (CCF) were evaluated. Centers were analyzed based on the US Census Bureau data for their

location and the FP information given on the center's website. A previously developed validation rubric for FP/oncofertility content quality standards using a scoring system, developed by this group, for commonly accepted definitions & terminology was utilized. Specific queries included: 1) Discuss the risk of cancer treatment on fertility? 2) Discuss the FP options 3) Is there a designated page for FP? 4) Is there a link to other resources for FP counseling? 5) Counseling on cancer survivorship or parenting after cancer? 6) Female fertility discussion? 7) Male fertility discussion? 8) Affiliation with an Academic institution. Chi-square tests were performed to assess for differences between FP website scores (individually & within Regional groups); analysis was also performed to assess for any correlation between socioeconomic/racial differences within States/Regions where NCICC are located. Multivariate logistic regression analyses are ongoing.

RESULTS: 65 oncology clinics identified. 37% of websites had information on FP under all 8 questions asked, a distinct increase over the past 5 years from 3%. Previously 50% lacked information in 4 or more questions, whereas now only 15%. Remarkably, the information on the websites were generally consistent regardless of the prevalent ethnic background of the people living in the area of the center. Thus, there were no differences observed in the quality of information regardless of ethnic predominance. Two statistically significant disparities were found. In centers where the city contained the highest ratios of Caucasians, there was a higher level of counseling on cancer survivorship on the websites ($p=0.041$). Also, in counties with higher prevalence of Asian ethnicity, the websites had more information on male FP ($p<0.019$).

CONCLUSIONS: NCICC websites are now more consistent in the quality of onco-fertility preservation information that they provide; an improvement over the past 5 years. Ethnic makeup of the state, county or city is no longer significantly associated with the quality of patient centered oncofertility web-based resources. These findings show a big improvement and demonstrate a bridging of the health disparity gap in one major aspect of health care.

P-335 4:30 PM Sunday, October 18, 2020

SINGLE MOTHERS BY CHOICE: DEFINING AND UNDERSTANDING SINGLE WOMEN UNDERGOING IN VITRO FERTILIZATION. Samantha L. Estevez, M.D., Baruch Abittan, M.D., Mary Rausch, MD. Northwell Health Fertility, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: Single women undergoing in vitro fertilization (IVF) with the goal of achieving a pregnancy during the cycle are a unique and little-studied patient population. The objectives of our study were to define and compare this population to the general IVF population and to assess trends within this group over time.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: From 2008-2019, our institution completed a total of 14,171 cycles, of which 352 cycles involved a single woman. A single woman (SW) was defined as a patient who did not have either a male or female partner and was not undergoing fertility preservation. Between 2008 and 2019, 6060 unique IVF patients and 148 unique SW were identified. We compared patient age, hormone levels, use of preimplantation genetic testing (PGT), and per-transfer pregnancy outcomes (pregnancy, spontaneous abortion, and livebirth rate) between the IVF patients and SW. We then assessed trends in the patient demographics, IVF indications, and outcomes within the SW cohort over the study period. Statistical analysis was performed using chi-square, Fisher-exact test, and t test.

RESULTS: In SW cycles, patients had an average age of 40.4 years, FSH value of 11.34 IU/L, and AMH value of 2.75ng/mL. In evaluating reasons for infertility, we found the most common in the SW cohort included advanced maternal age/diminished ovarian reserve (50.7%), unexplained (26.3%), tubal factor (6.8%), and PCOS (4.7%). Comparing cycles involving SW to the general IVF population, SW were significantly older (40.4 years vs. 36.3 years, $p<0.01$). All other baseline characteristics, as well as pregnancy outcomes examined, were not significantly different. Evaluating trends within the SW cohort, we subdivided the time frame into 3 time periods: 2008-2001 (T1), 2012-2015 (T2), and 2016-2019 (T3). There was a significant increase in IVF utilization by SW during the study period, from 0.8% (13/1645) of the IVF population in T1, to 2.5% (50/1991) in T2, and 4.6% (111/2424) in T3 ($p<0.01$). Use of PGT within the SW cohort increased with time (0% in T1 to 37.7% in T3, $p=0.002$). However, overall PGT utilization is significantly higher among all patients as compared to the SW cohort in T3 (56% vs 38%, $p=0.003$).

CONCLUSIONS: No study has been previously performed to assess whether there has been a corollary rise in rates of IVF for single women as "non-traditional" parents and "single mothers by choice" have gained visibility. Excluding fertility preservation, we found a significant increase in SW undergoing IVF over the past twelve years. The majority of SW were undergoing IVF for advanced maternal age and diminished ovarian reserve. Many SW approach fertility treatment without an infertility diagnosis and usually attempt IUIs first. Interestingly, SW were significantly older than the general IVF population, and age may be playing a larger role in why IUI fails and IVF is necessary within this group. A closer look at this group is warranted to determine which women may benefit from altered protocols, such as earlier IVF treatment, to achieve pregnancy.

SUPPORT: No financial support to disclose.

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INVESTIGATION OF THE RACIAL DISPARITIES AMONGST SEMEN ANALYSES IN WHITE, BLACK, HISPANIC, AND ASIAN MEN. Zachary Walker, MD, Lindsay Rucker, MD, John Owen, MD, MSPH, Ashley Wiltshire, MD, Lacey M. Kendall, BS, Johnathan W. Edmonds, PhD, HCLD/ELD/TS, Deidre Gunn, MD. University of Alabama at Birmingham, Birmingham, AL.

OBJECTIVE: To assess the relationship between different racial-ethnic groups and rates of abnormal semen analysis (SA).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All men who underwent a SA between January 1, 2017 and December 31, 2019 at a single tertiary care center were considered for the study sample. Those with an unknown race-ethnicity, varicocele, history of testicular surgery (e.g., varicocelectomy, vasectomy, or vasectomy reversal), genetic anomalies, congenital absence of bilateral vas deferens, prior testosterone use, or prior exposure to chemotherapy/radiation were excluded. Samples obtained via testicular sperm extraction, postejaculatory urine, or analyzed $\geq$1 hour from being received were also excluded. The World Health Organization (WHO) 2010 criteria was used to determine normal semen parameters. If a second SA was interpreted as normal following an initial abnormal result, the result was considered normal for the analysis. Racial-ethnic groups comprised White, Black, Hispanic, and Asian. Chi-square and Fisher's exact test were used to compare categorical variables. ANOVA was used to compare continuous variables among groups

Table 1. Differences in Semen Analysis based on Race-Ethnicities using ANOVA

	White (reference) N = 508	Black N = 188	Hispanic N = 24	Asian N = 30	P value
Semen volume (mL)	3.0	2.6*	2.8	2.7	0.008^{+}
Semen pH	8.3	8.2	8.2	8.2	0.99^{+}
Sperm concentration (million/mL)	75	47*	108	98	<.0001^{+}
Total sperm count (million)	226	122*	279	239	<.0001^{+}
Percentage of motile spermatozoa (%)	55	48	60	56	0.01^{+}
Percentage of morphologically normal spermatozoa (%)	4.1	3.2	4.6	3.9	0.04^{+}
Total motile sperm count (millions)	149	82*	196	150	<.0001^{+}

*Multiple range t-test ($p<0.05$). $^{+}$Controlled for age.

and logistic regression modeled the relationship between SA result and selected predictors.

RESULTS: In total, 872 SAs were initially performed. Only 750 met inclusion criteria, yielding 456 Normal and 294 Abnormal results. Only Race-ethnicity ($p<0.0001$) and Age ($p=0.003$) were statistically significant in the baseline demographics. 54% of Black men had an abnormal semen analysis. Black men were more likely to have hypospermia, oligozoospermia, and lower total motile sperm counts (Table 1). In a logistic regression model, controlling for age and using White as the referent group, only Blacks had lower odds for a normal SA (OR=0.49, 95% CI 0.35, 0.70).

CONCLUSIONS: Black men are more likely to have an abnormal SA based on the WHO 2010 criteria. Black men seeking infertility treatment should be educated on the incidence of abnormal SA and actively seek male infertility evaluation. Future studies should be conducted to discover if there are potential ethnic based normative values for interpretation of SA.

P-337 4:30 PM Sunday, October 18, 2020

INFERTILITY AMONG VETERANS: VARIATION IN DEFINITIONS AND SOCIODEMOGRAPHIC CHARACTERISTICS. Marie E. Thoma, PhD, MHS,[1] Michelle A. Mengeling, MS, PhD,[2] Anne Sadler, PhD, MS,[2] Amy M. J. O'Shea, PhD,[2] James C. Torner, PhD, MS,[3] Judy E. Stern, PhD,[4] Bradley J. Van Voorhis, MD,[3] Alicia Y. Christy, MD,[5] Ginny L. Ryan, MD, MA.[6] [1]University of Maryland, College Park, MD; [2]Iowa City VA Health Care System, Iowa City, IA; [3]University of Iowa, Iowa City, IA; [4]Dartmouth-Hitchcock, Lebanon, NH; [5]Veterans Administration, Kensington, MD; [6]University of Iowa Hospitals and Clinics, Iowa City, IA.

OBJECTIVE: Veterans face unique exposures that may influence fertility, yet our current understanding is limited by inconsistencies in how infertility measures are defined and operationalized. The objective of this study was to compare measures of lifetime infertility and infertility care among military Veterans.

DESIGN: A national sample of U.S. military Veterans aged 20-45 years, consisting of 1406 women and 1599 men with functional reproductive anatomy at birth.

MATERIALS AND METHODS: Consistent with the standard definition of infertility, lifetime infertility was defined as a time-to-pregnancy (TTP) $>$ 12 months. However, TTP was ascertained in two ways: 1) all consecutive months of unprotected intercourse (TTP_UI) or 2) only months reported trying to conceive (TTP_TC). Receipt of infertility care was ascertained as ever diagnosed or treated for infertility. Data were collected using computer-assisted telephone interviews. Infertility prevalence, odds ratios (OR), and corresponding 95% confidence intervals (CI) associated with key sociodemographic characteristics (parity, age, marital status, education, race/ethnicity, income per $10,000) were assessed by sex. Associations were estimated by multivariable logistic regression.

RESULTS: Using all periods of unprotected intercourse (TTP_UI) resulted in a higher prevalence of lifetime infertility in women (45.5%) and men (42.1%) compared with definitions that included only reported months of trying (TTP_TC: 22.4% and 16.9%, respectively). Not having had a prior child and older age (40+) were associated with increased odds of infertility for both women (OR=2.19, 95% CI: 1.48-3.23; OR=1.90, 95% CI: 1.24-2.93, respectively) and men (OR=2.99, 95% CI: 1.92-4.65; OR=1.57, 95% CI: 1.04-2.38, respectively) for TTP_TC, but not TTP_UI. Compared to lifetime infertility study measures, women and men reported lower prevalence of infertility diagnosis (13.7% and 10.7%) and treatment (8.4% and 5.6%), respectively. Sociodemographic characteristics associated with infertility care included higher income (Diagnosis: OR=1.03, 95% CI: 1.01-1.06; Treatment: OR=1.05, 95% CI: 1.02-1.08) among women and higher education (bachelor's degree or higher) (Diagnosis: OR=2.56, 95% CI: 1.32-5.00; Treatment: OR=3.23, 95% CI: 1.25-8.33) among men. We found no difference in infertility or infertility care measures between non-Hispanic black, Hispanic, and non-Hispanic white Veterans.

CONCLUSIONS: The prevalence of lifetime infertility was high among Veterans compared with their limited receipt of infertility care. The prevalence and associated sociodemographic characteristics also varied depending on whether TTP accounted for fertility intentions. Regardless of the type of infertility measure applied, we found few differences by race/ethnicity, contrasting with other U.S. studies. Overall, these findings have broader implications for identifying infertility that may be under-recognized (for couples without clear fertility intentions), gaps in access to infertility care services, and the differential effect of infertility on female and male Veterans.

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DOES RACE IMPACT EMBRYO MORPHOKINETICS? Luce A. Kassi, MD,[1] Dana B. McQueen, M.D., M.A.S.,[2] Rafael Confino, BS,[3] John Zhang, PhD,[4] Mary Ellen Pavone, MD, MSCI,[4] Dana Kimelman, MD.[4] [1]Northwestern University Feinberg School of Medicine, Chicago, IL; [2]Northwestern University, Chicago, IL; [3]Northwestern Feinberg School of Medicine, Chicago, IL; [4]Northwestern University Feinberg School of Medicine, Department of Obstetrics and Gynecology. Division of Reproductive Endocrinology and Infertility, Chicago, IL.

OBJECTIVE: To assess the relationship between race and embryo morphokinetics on time lapse microscopy (TLM).

DESIGN: Retrospective Cohort Study.

MATERIALS AND METHODS: Institutional Review Board approval was obtained. All IVF cycles between June 2015 and April 2017 were included. Racial groups included Black, Hispanic, Asian, White and other/unknown. Embryo morphokinetic parameters were assessed with TLM and included time to syngamy (TPNf), time to 2 cells, time to 3 cells, time to 4 cells and time to 8 cells. A generalized linear mixed model was used to control for potential confounders and multiple embryos resulting from a single IVF cycle.

RESULTS: 589 IVF cycles were included in the analysis. There were no significant differences in the median maternal age, anti-Mullerian hormone (AMH), days of stimulation, total gonadotropin, number of oocytes retrieved, number of mature oocytes or number fertilized oocytes between groups (Table). There were significant differences in body mass index (BMI) between groups and this was adjusted for in the final model. There was a total of 2,185 embryos assessed by TLM: 100 from Black women, 90 from Hispanic women, 281 from Asian women, 1460 from White women and 254 from women of unknown race. After adjusting for BMI, there was no significant difference in time to time to syngamy, time to 2 cells, time to 3 cells, time to 4 cells or time to 8 cells between racial groups.

CONCLUSIONS: There was no significant association between embryo morphokinetics by TLM and race. Despite the racial disparities observed

	Black (N=25)	Hispanic (N= 28)	Asian (N= 67)	White (N= 404)	Other/Unknown (N=65)	p-value
Age (yr)	36.4 (33.5, 38.4)	36.0 (34.6, 40.4)	35.1 (33.1, 38.5)	35.0 (32.7, 38.4)	36.0 (32.8, 40.2)	0.61
BMI	27.2 (23.7, 30.7)	28.4 (26.3, 35.6)	23.2 (21.5, 25.1)	23.4 (21.2, 27.6)	25.0 (21.9, 27.8)	$<.0001$
AMH (ng/ml)	3.2 (1.5, 3.8)	2.5 (1.4, 4.2)	2.8 (1.4, 3.9)	2.3 (1.1, 4.2)	2.5 (1.1, 4.7)	0.90
Days Stimulation	10.5 (9.5, 11.5)	10.0 (9.0, 11.0)	10.0 (9.0, 11.0)	10.0 (9.0, 11.0)	10.0 (9.0, 11.0)	0.82
Total IU Gonadotropin	2887.5 (2325.0, 4500.0)	3000.0 (2700.0, 4537.5)	2700.0 (2025.0, 3750.0)	3300.0 (2400.0, 4500.0)	3000.0 (2437.5, 4087.5)	0.22
Oocytes	12.0 (9.0, 21.0)	12.0 (7.0, 17.5)	14.0 (10.0, 22.0)	14.0 (10.0, 20.0)	14.0 (10.0, 19.0)	0.64
Mature Oocytes	9.0 (7.0, 16.0)	9.0 (6.0, 17.0)	12.0 (8.0, 16.0)	11.0 (7.0, 16.0)	10.0 (7.0, 13.0)	0.72
Fertilized Oocytes	7.0 (5.0, 14.0)	8.0 (5.0, 13.0)	9.0 (6.0, 13.0)	8.0 (6.0, 12.0)	7.5 (5.5, 11.0)	0.96
% ICSI	24 (96.0)	26 (92.86)	66 (98.51)	384 (96.73)	63 (98.44)	0.36

Data presented as Median(Q1-Q3) or %(N).

in IVF, this study demonstrates that race does not impact embryo development as observed on TLM.

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SINGLE PARENT BY CHOICE CONTENT ON FERTILITY CLINIC WEBSITES IN THE WESTERN REGION. Kajal Verma, MD,[1] Christopher de Haydu, MD,[2] Melody A. Rasouli, MD, MBA,[1] Angela H. Liu, MD,[1] Janelle M. Jackman, MBBS,[3] Sriram Eleswarapu, MD, PhD,[4] Cindy M. Duke, MD, PhD.[5] [1]University of Nevada, Las Vegas, Las Vegas, NV; [2]University of Miami, Miami, FL; [3]New Hope Fertility Center, New York, NY; [4]University of California, Los Angeles, Los Angeles, CA; [5]University of Nevada, Las Vegas and Nevada Fertility Institute, Las Vegas, Las Vegas, NV.

OBJECTIVE: Information on fertility clinic websites is a primary and critical component of the shared decision-making process between patients and physicians. Single men and women comprise a growing subgroup of patients seeking fertility care to help build their families, via use of donor sperm, donor eggs, or donor embryos. The goal of this study is to assess the association of regional demographic factors of fertility centers, with the online information provided by these centers' websites, to patients seeking information on single parenting by choice (SPC) in the Western Region of the United States (WRUS).

DESIGN: Cross-sectional analysis.

MATERIALS AND METHODS: A survey was developed and two independent investigators assessed clinic websites from WRUS clinics included in the 2017 Society for Assisted Reproductive Technology (SART) database. Websites were assessed for content related to single parents seeking fertility services and SPC. The responses were ordered by county level data obtained from the US Census (2010 and 2014-2018) for demographic information including race, income/poverty, and insurance status. Descriptive statistical analyses performed included Chi-square and t-tests.

RESULTS: 100 SART-reporting fertility clinics are located in WRUS and 31% of those clinic websites had discussed SPC for single men and/or women seeking fertility services. 18% of these websites featured standalone pages describing SPC. Compared to the lower three quartiles, there was a positive association between the detail of SPC information provided and the highest quartile of median household income (MHI) ($p = 0.02$), highest quartile of income per capita (IpC) ($p = 0.005$), and the lowest quartile of persons without insurance ($p = 0.01$). This trend was significant and the same for the question regarding websites having a standalone page for SPC ($p<0.05$ for MHI, IpC, and persons without insurance). Regarding race, the quartile of counties with the largest percentage of white persons ($p = 0.01$) or the quartile with the largest percentage of Asian persons ($p = 0.002$) had significantly more information on SPC or standalone SPC pages ($p=0.042$) in relation to the counties with the quartiles with the smallest percentage of those populations (respectively).

CONCLUSIONS: 31% of SART fertility clinics in the WRUS include SPC content on their websites with 18% of them having standalone pages dedicated to this important issue. Using the fertility center's county as a geographic proxy to estimate population demographic variables, there is an association with MHI, IpC, and increased insurance level with the center's websites containing SPC information or standalone pages. Having SPC information is also positively associated with increasing percentages of white or Asian populations; raising questions regarding associations between socioeconomic or racial factors behind this uneven access to SPC information on clinic websites. Overall, this data shows that more clinics need to include SPC information on their websites. Further study to expand this analysis across all US demographic regions is ongoing.

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BASIC FERTILITY INVESTIGATION IN A LOW RESOURCE SETTING IS VALUABLE AS A MARKER FOR OVERALL HEALTH. Ramya Sethuram, MD,[1] Lina Fouad, BS,[1] Alexandra E. Flessel, BS,[1] Ahmad Arabi, MD,[1] Kazuhiko Shinki, Ph.D,[2] Sana Salih, MD.[1] [1]Wayne State University School of Medicine, Detroit, MI; [2]Wayne State University, Detroit, MI.

OBJECTIVE: Infertility is considered a harbinger of overall health and future morbidity and cardiovascular mortality. However, the vast majority of couples in low resource settings do not seek infertility treatment in a timely fashion due to lack of insurance coverage. While the Medicaid plan does not cover for infertility treatment in Michigan, it does cover the initial infertility workup for few visits.

DESIGN: Retrospective, cohort study at a university hospital infertility clinic comparing the results of the infertility workup in low resource settings on Medicaid vs private insurance groups.

MATERIALS AND METHODS: We performed a retrospective chart review of patients after IRB approval. New patients who visited a university health clinic at from 07/2019 –02/2020 were studied. A total of 117 patients were studied (Medicaid = 79; Private =38). All patients had infertility workup inclusive of preconception labs (TSH, Rubella immunity), hormonal profile (AMH, day 2 E2, FSH, and for PCOS, if indicated), day 2-4 TVUS and follicle count and day 4-12 SIS. We collected data on new non-infertility diagnosis that resulted from the workup. The new non-infertility diagnosis studied included ones with long term health implications: hypertension, diabetes, pre-diabetes, thyroid disease, endometrial hyperplasia and cancer, hydrosalpinx, PCOS, and Vitamin D deficiency. Statistical analysis was performed with SPSS V24.0.

RESULTS: The demographics of the patients in Medicaid vs Private groups were not significantly different. The mean age in years was 33(±6.2) ; mean BMI was 32.8 (±8.5). The results of the new non-infertility diagnosis in the two groups is represented in Table 1.

Table 1

New non-infertility diagnosis	Medicaid (n =79)	Private (n =38)	P-value
Diabetes/ Pre -diabetes	25.3% (n=20)	23.6% (n=9)	1
PCOS	24.0% (n=19)	13.1% (n=5)	0.26
Premature ovarian failure	1.2% (n=1)	0.02% (n=1)	1
Hydrosalpinx	5% (n=4)	0%	0.52
Endometrial hyperplasia ± cancer	2.5% (n=2)	0%	0.81
Vitamin D Deficiency	65.8% (n=52)	47.3% (n=18)	0.08

There was no significant difference in the newly diagnosed morbidities between the groups. The findings are still important in that 93.1% of all patients received a non-infertility diagnosis. Among them, 55% had at least two such diagnoses which carried a future health implication. This analysis did not take into account the diagnoses of obesity/ smoker and the weight loss and smoking cessation counseling that are a part of our infertility work up.

CONCLUSIONS: Infertility is not a unique disease of the reproductive axis but is often linked with metabolic diseases. Hence, a basic infertility workup should be undertaken in all patients with infertility, irrespective of their ability to afford fertility treatment post work-up.

SUPPORT: n/a

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SOCIOECONOMIC STATUS IS NOT ASSOCIATED WITH DONOR OOCYTE RECIPIENT SUCCESS: A PAIRED ANALYSIS UTILIZING SIBLING OOCYTES. Kelly McCarter, MD,[1] Robert Setton, MD,[2] Alice Chung, BA,[2] Zev Rosenwaks, M.D,[2] Steven Spandorfer, MD.[2] [1]Weill Cornell Medicine, New York, NY; [2]The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: Lower socioeconomic status has been associated with worse perinatal outcomes; however, the literature is limited, especially in cases of IVF. These studies have also been unable to control for factors that can affect oocyte quality, including psychological stress and environmental exposures that are often associated with lower socioeconomic status. ART using sibling-oocyte recipients (oocytes from the same donor stimulation transferred to two different recipients) offers a unique model that allows a more precise assessment of the endometrial aspect of implantation, as it controls to the greatest degree possible for oocyte quality. We sought to determine if socioeconomic status affects endometrial receptivity by analyzing outcomes in sibling-oocyte recipients.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients who underwent donor egg recipient (DER) cycles who received oocytes from a donor whose oocytes from a single controlled ovarian hyperstimulation cycle were split between two recipients were included. The recipients were categorized into four quartiles based on mean income by zip code. Only paired recipients who were in discrepant quartiles were included. Patients with uterine and severe male factor infertility were excluded. The primary outcome was implantation rate. Secondary outcomes included positive pregnancy and delivery rates. Statistical analysis included paired t-test, and $p<0.05$ was deemed statistically significant.

RESULTS: A total of 1,013 patients who underwent DER cycles between January 2010 and December 2016 were screened for inclusion, of which 408 patients had received oocytes from a split donor oocyte cycle. There were 32 pairs (64 recipients) who had discrepant income quartiles that were analyzed. The two income groups compared were the lowest income quartile (mean income less than $80,025) and the highest (mean income greater than $126,107). Quartile cutoffs were determined from the patient cohort. Mean income of the entire cohort was $107,795. The groups were similar for recipient age, gravity, parity, body mass index, peak endometrial stripe thickness, and number of embryos transferred. The implantation rates (57.8% ± 7.8 vs. 53.6% vs. 7.4, p=0.72), pregnancy rates (75% ± 7.7 vs. 84.3% ± 6.5, p=0.37) and live birth rates (53.1% ± 8.9 vs. 68.75% ± 8.3, p=0.26) were found to be similar amongst the lowest and highest income quartiles. In subsequent analysis, the implantation, pregnancy, and live birth rates were also found to be similar when other income quartiles were compared, such as the lower two quartiles to the highest quartile and the lower three quartiles to the highest quartile. Additionally, no significant difference was found when quartile cutoffs were determined based on the national census data.

CONCLUSIONS: In this idealized model that controls to the greatest degree possible for oocyte quality, by using paired recipients from the same donor from the same stimulation cycle, we found that differing socioeconomic status based on mean income did not affect implantation, positive pregnancy, or delivery rates.

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CLINICAL BARRIERS AND FACILITATORS THAT INFLUENCE AFRICAN AMERICAN WOMEN TO INITIATE TREATMENT FOR INFERTILITY: A MIXED METHODS STUDY. Morine Cebert, Ph.D., RN,[1] Rosa Gonzalez-guarda, PhD, RN,[2] Susan G. Silva, PhD,[2] Peggy A. Shannon-Baker, PhD,[3] Renee E. Hart, MS,[4] Samad Jahandideh, PhD,[4] Eleanor Stevenson, PhD, RN.[5] [1]University of Pennsylvania & Philadelphia VA Medical Center, Philadelphia, PA; [2]Duke University School of Nursing, Durhan, NC; [3]Georgia Southern University, Statesboro, GA; [4]Shady Grove Fertility Center, Rockville, MD; [5]Duke University School of Nursing, Durham, NC.

OBJECTIVE: African American women in the United States have a high prevalence of infertility; yet are least likely to initiate treatment for infertility. This study sought to explore clinical facilitators and barriers to initiating treatment for infertility among African American women who completed an a reproductive endocrinology evaluation.

DESIGN: We conducted a convergent parallel mixed methods study that combined quantitative data from a retrospective chart review and semi-structured interviews discussing clinical perspectives associated with treatment initiation of African American women seeking treatment at a large infertility clinic in northeastern United States between January 2015 and September 2019.

MATERIALS AND METHODS: We analyzed retrospective chart review data using bivariate and logistic regression analyses on a random sample of electronic medical records of African American women to examine the association of clinical factors to treatment initiation. A sample of African American women completed a one-time interview and interview transcripts were transcribed verbatim and a thematic analysis was performed. Joint data displays were used for integration analyses of clinical influences on treatment initiation.

RESULTS: The analysis sample included 391 records of African American women patients. Of the 391, clinical workups revealed half the sample had abnormal female imaging 52% and 36.7% had one of more abnormal hormonal level. The majority (77.2%) experienced primary infertility and 45.6% female factor only. The most common treatment plan presented was IVF (77.0%), followed by IUI (21.5%). Of the total treatment seeking sample, 72.5% initiated treatment. Clinical workup, fertility type, and final treatment plan were not statistically significantly associated with initiating treatment (p>0.05). Among the 13 women who completed interviews, 6 (46.1%) initiated treatment for infertility. Four themes emerged relating to clinical influences: 3 barriers and 1 facilitator. Barriers included concerns for treatment plan complexity and applicability, desire for empathetic staff and holistic assessments, and fears of racial discrimination. The facilitator to treatment initiation was having good understanding of the treatment plan and procedures. The quantitative and qualitative findings diverged. Although clinical factors were not significantly associated with initiation, women discussed several salient clinical barriers to treatment.

CONCLUSIONS: A high proportion of the African American women initiated treatment; however, African American women reported several clinical barriers when considering whether or not to initiate proposed treatment plans. The complexity and invasiveness of the treatment plan along with interactions with staff seem to influence initiation. A staff that provides clarity in the treatment plan with holistic delivery options may further enhance treatment uptake. Nurses play a critical role in communicating treatment plans to patients and along with assessing other treatment needs and concerns.

SUPPORT: None.

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WOMEN ≥40 YEARS OLD UNDERGOING IVF WITH FRESH EMBRYO TRANSFER HAVE DIFFERENTIAL CYCLE OUTCOMES BASED ON THEIR RACE. Stephanie Willson, MD, Pietro Bortoletto, MD, Phillip A. Romanski, MD, Owen Davis, M.D., Zev Rosenwaks, M.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To determine if women ≥40 years old undergoing IVF with fresh embryo transfer have differential cycle outcomes based on their race.

DESIGN: Retrospective cohort study conducted at a university-affiliated center.

MATERIALS AND METHODS: Women ≥40 years old undergoing their first IVF cycle at our center with fresh embryo transfer were stratified by race: 1) minorities (black, Asian, white [Hispanic]) and 2) white (non-Hispanic). Pregnancy and live birth rates per transfer were the primary outcomes. Multivariable logistic regression analysis was performed to examine the association between racial group and cycle outcomes while controlling for confounders identified through the construction of directed acyclic graphs A multivariate logistic regression was created controlling for age, BMI, parity, infertility diagnosis, AMH, number of mature oocytes, and embryos transferred. Odds ratios (OR) with 95% confidence intervals (CI) for cycle outcomes were estimated.

RESULTS: A total of 2,007 cycles in women ≥40 years old were analyzed, of which 576 were racial minorities and 1,431 where white (non-Hispanic) women. The mean (SD) age, 41.7 (1.6) years, was the same for both groups.Women of racial minorities had higher AMH levels than those in the white (non-Hispanic) group (1.57 vs. 1.27 ng/ml; p=0.001). The minority group also had a larger proportion of tubal and uterine factor infertility compared to white (non-Hispanic) women (6.4% vs. 4.1% and 2.6% vs. 1.3%, respectively; p=0.022). The pregnancy rate was 35.2% versus 44.1% (p=<0.001) for women in the minority group and white (non-Hispanic) group, respectively. Age >41 years old (OR 0.48, CI 0.36-0.63), having <4 mature oocytes retrieved (OR 0.63, CI 0.42-0.93), and being a racial minority (OR 0.58, CI 0.43-0.78) were all associated with reduced odds of clinical pregnancy. An AMH >0.87 ng/mL (OR 1.62, CI 1.20-2.20), retrieval of >9 mature oocytes (OR 1.45, CI 1.04-2.03), and the transfer of >3 embryos (OR 1.33, CI 0.98-1.81) were associated with increased odds of clinical pregnancy. Once pregnancy was achieved, there were no differences in live birth rates when comparing patients in the racial minority group versus white (non-Hispanic) women (17.9% vs. 18.9%, p=0.379).

CONCLUSIONS: Women ≥40 years old undergoing IVF with fresh embryo transfer have differential cycle outcomes based on their race. Women from racial minorities, even after controlling for potential confounders, are about 40% less likely to achieve a clinical pregnancy. However, once they are pregnant, their live birth rates do not differ compared to white (non-Hispanic) women. We hypothesize that the increased incidence of tubal and uterine factor infertility in racial minority patients may explain the lower pregnancy rate observed in these patients.

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SALINE ULTRASOUND VERSUS OFFICE HYSTEROSCOPY FOR UTERINE CAVITY EVALUATION PRIOR TO IVF: A RANDOMIZED CONTROLLED TRIAL. Sarah M. Moustafa, MD, Gina Silverstein, MD, Steven L. Young, M.D., Ph.D., Linnea R. Goodman, MD. University of North Carolina, Raleigh, NC.

OBJECTIVE: Saline infusion sonography (SIS) and hysteroscopy are commonly employed methods for uterine cavity evaluation prior to fertility treatment. We aim to compare SIS and office hysteroscopy with respect to patient and provider satisfaction, and to evaluate the capability of office hysteroscopy to manage intra-uterine pathology at the time of diagnosis to reduce delays and supernumerary procedures.

DESIGN: Prospective randomized controlled trial.

MATERIALS AND METHODS: Sixty women undergoing routine cavity evaluation prior to in vitro fertilization (IVF) were randomized to either SIS or office hysteroscopy without use of anesthetic. The LiNAscope disposable 4.2mm hysteroscope with operative port was used, with employment of hysteroscopic graspers as indicated. Abnormalities on SIS were subsequently managed by hysteroscopy. Management of abnormalities on hysteroscopy was attempted within the same screening procedure. Patients and providers completed surveys with findings and Likert rating scales for satisfaction and pain scores, respectively. The sample size was based on a power analysis to detect in the primary outcome of patient satisfaction scores. Statistical comparisons were performed with t-test or Mantel-Haenszel chi-square as applicable.

RESULTS: The study groups did not differ in age, race, body mass index, indication for IVF, or history of uterine pathology. Pain scores (10 point scale) did not differ between SIS and hysteroscopy (respectively, 2.70 $\pm$1.84 vs. 3.32 $\pm$1.89; $p = 0.20$). Time to complete the procedure, patient and provider satisfaction scores, and incidence of pathology did not differ between groups (Table 1). Of the 11 patients with abnormalities in the hysteroscopy group, 10 underwent immediate attempt at operative management (one with unicornuate uterus diagnosed), with 9/10 experiencing complete resolution of pathology.

CONCLUSIONS: Office hysteroscopy and SIS were similar with respect to patient satisfaction, tolerability, and time to complete. Both can be considered well-tolerated screening tools. However, office hysteroscopy often allowed for immediate management of abnormalities detected during uterine cavity evaluation, reducing the need for additional procedures.

Table 1. Comparison of results and management between SIS and office hysteroscopy

	SIS (n = 30)	Hysteroscopy (n = 30)	P-Value
Time to complete (min)	3.69 ($\pm$1.49)	4.22 ($\pm$2.12)	0.27
Patient satisfaction (1-5)	4.83 ($\pm$0.59)	4.77 ($\pm$0.68)	0.69
Provider satisfaction (1-5)			
Uterine cavity evaluation	4.73 ($\pm$0.52)	4.80 ($\pm$ 0.76)	0.69
Perception of pain	4.76 ($\pm$0.63)	4.70 ($\pm$ 0.60)	0.67
Overall satisfaction	4.6 ($\pm$0.77)	4.73 ($\pm$ 0.83)	0.52
Pathology found	6 (20%)	11 (36.7%)	0.15
Second procedure needed	6 (20%)	1 (0.03%)	0.04

SUPPORT: None

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ADENOMYOSIS IN MAGNETIC RESONANCE AND POOR REPRODUCTIVE OUTCOME. Alejandra Aguilar Crespo, doctor, Enrique Tormo Crespo, licensed in medicine, Juana Crespo Simó, MD. Equipo Juana Crespo, Valencia, Spain.

OBJECTIVE: Non-invasive diagnostic methods for adenomyosis have emerged such as the Magnetic Resonance imaging (MRI). Nevertheless, there are no universal criteria for diagnosing adenomyosis on MRI and radiologists have difficulty describing lesions and often interpret it as a trivial finding.

Adenomyosis cause implantation failure and a decrease in clinical pregnancy rate. The treatment must be individualized according to age, gestational desire and clinical symptoms.

There is no study linking adenomyosis lesions on MRI and implantation failure so, our aim is to find out the relationship between adenomyosis lesions on MRI and poor reproductive outcome (PRO) of strictly uterine origin.

The primary objective is to determine adenomyosis lesions on MRI that could be associated with a PRO. With this, we might be able to know in front of which lesions an embryo transfer would not be recommended before a treatment. The second objective is to determine what treatment (surgical, medical or both) improves the prognosis. The third aims to describe which endometrial preparation presents a higher gestational rate.

DESIGN: Descriptive and retrospective study on a single-center, non-homogeneous and unmasked. The study population consists of 389 patients who attended our center after previous embryo failures from egg donation in other centers, between 2015 and 2019 to receive an egg donation treatment.

MATERIALS AND METHODS: Inclusion criteria were applied to select patients with implantation failure or abortion of exclusively uterine cause. We included patients with 6 o more embryos failed from egg donation. After applying those criteria, 58 patients were selected.

The MRI of all of them were analyzed according to the five Bazot criteria, together with the fibrosis criterion proposed by Khaund. In total 9 variables were described and analyzed on each MRI.

RESULTS: All study patients met at least 1 criterion of adenomyosis on the MRI.

A junctional zone more than 12mm followed by uterine fibrosis were the findings that had the worst pregnancy rate (60%). 80% of patients underwent an hysteroscopy and 14% an hysteroscopy with laparoscopy. 62% of women received a treatment based on GnRh agonists.

Regarding the MRI adenomyosis criteria, those who fulfilled only one criteria had a gestational rate of 77%, while those who met all was 7%. 77% of women conceived and 52% of them did it after our first embryo transfer. 91 embryo transfers were performed, 23 following a natural cycle and 68 a substituted one. The pregnancy rate was 52.2% and 39.7 respectively.

CONCLUSIONS: All the patients in this study met at least one criterion suggestive of adenomyosis.

The more criteria are met, the worse is the gestational rate although no specific lesion could be found involving a poor outcome.

There is not a gold-standard treatment and it has not been possible to analyze the differences between medical, surgical or combined treatment, so, it must be individualized according to the patient characteristics to enhance the chances of pregnancy. The trend is towards natural cycles as it has shown a higher pregnancy rate than the substituted ones.

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DOES STANDING ULTRASOUND IMPROVE THE DETECTION OF CLINICALLY IMPORTANT VARICOCELES. Nahid Punjani, MD MPH,[1] Gal Wald, BA,[1] Omar Al Hussein Alawamlh, MD,[1] Vanessa L. Dudley, MSHS,[2] Marc Goldstein, M.D.[2] [1]Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY; [2]Center for Male Reproductive Medicine and Microsurgery, Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY.

OBJECTIVE: To assess the role of a standing vs supine assessment in scrotal ultrasound (SUS) during varicocele assessment by evaluating differences in clinical outcomes.

Figure 1. Clinical Outcomes of Men with Discordant Ultrasound Assessments

	Right				Left			
	N	Pre-Op	Post-Op	*p-value*	N	Pre-Op	Post-Op	*p-value*
Cut-off 2.5mm								
SC	26	37.2 ± 30.6	42.4 ± 40.3	0.72	16	38.1 ± 37.9	39.3 ± 31.9	1.00
TUNEL	7	15.1 ± 8.5	12.9 ± 9.1	0.40	9	16.3 ± 9.6	11.3 ± 5.4	0.26
T	26	336.8 ± 115.4	402.3 ± 164.6	0.17	12	308.8 ± 81.9	490.3 ± 267.5	<0.01
Cut-off 3.0mm								
SC	35	30.2 ± 28.4	39.4 ± 38.7	0.19	33	31.0 ± 22.6	41.0 ± 30.6	0.04
TUNEL	9	14.4 ± 7.5	15.7 ± 9.8	0.44	13	12.5 ± 6.0	9.7 ± 5.8	0.07
T	32	350.6 ± 119.7	451.6 ± 187.2	<0.01	29	324.9 ± 99.1	439.5 ± 157.8	<0.01
Reversal								
SC	16	30.7 ± 30.9	49.7 ± 36.1	<0.01	24	41.4 ± 36.5	43.5 ± 35.7	0.68
TUNEL	4	23.4 ± 10.7	16.2 ± 9.5	0.14	12	20.1 ± 10.3	11.2 ± 8.1	0.02
T	13	345.0 ± 129.5	318.2 ± 119.9	0.86	22	324.0 ± 107.3	399.0 ± 159.8	0.01

DESIGN: Retrospective data collection.

MATERIALS AND METHODS: Men from 2008-2020 diagnosed with varicocele were reviewed. We included men with documented SUS with both supine and standing assessments including measurements with and without Valsalva. Clinical outcomes, including sperm concentration (excluding azoospermia) (SC), TUNEL and testosterone (T) levels were compared among men who had varicoceles diagnosed based on ultrasound characteristics (vein size >2.5mm, vein size >3.0mm and reversal of flow) to those that would have been missed on supine ultrasound who underwent microsurgical varicocelectomy.

RESULTS: 761 men were included. Median age was 38 (IQR 32-44). On orchidometer assessment, median testis size was 18cc (IQR 15-22) on the right and 15cc (IQR 12-18) on the left. Of these men, 396 (52.0%) underwent varicocelectomy (right: 8 (2.0%); left: 136 (34.4%); bilateral: 252 (63.6%)). Agreement between supine and standing SUS for a 2.5mm cut-off were: 79.5% on the right and 88.1% on the left; for a 3.0mm cut-off: 76.3% on the right and 79.8% on the left; for flow reversal: 81.5% on the right and 75.3% on the left. Disagreement between those with abnormal standing vs normal supine for vein size >2.5mm was: 63 men (15.9%) on the right and 34 men (8.6%) on the left, for vein size >3.0mm was: 75 men (18.9%) on the right, and 62 men (15.6%) on the left, and for flow reversal was: 35 (12.2%) on the right and 44 (15.1%) on the left. In Table 1, with a 2.5mm cut-off, only T had significant improvement on the left ($p<0.01$). With a 3.0mm cut-off significant differences were seen for SC on the left ($p=0.04$) and T on the left and right ($p<0.01$). For flow reversal, significant differences were seen for SC on the right ($p<0.01$) and T on the left ($p=0.01$).

CONCLUSIONS: Our results suggest that standing SUS identifies a greater number of men who would have been missed using supine ultrasound only.

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ULTRASONOGRAPHY HAS BETTER PERFORMANCE THAN MAGNETIC RESONANCE IMAGING IN DIAGNOSING DEEP ENDOMETRIOSIS RECURRENCE. Simone Ferrero, MD PhD,[1] Carolina Scala, MD,[2] Ennio Biscaldi, MD,[3] Fabio Barra, MD.[1] [1]IRCCS Ospedale Policlinico San Martino, Genova, Italy; [2]Istituto G. Gaslini, Genova, Italy; [3]Department of Radiology, Galliera Hospital, Genova, Italy.

OBJECTIVE: Transvaginal ultrasonography (TVS) and magnetic resonance imaging (MRI) have similar performance in diagnosing deep endometriosis (DE). The diagnosis of DE recurrence may be more challenging because of the presence of postoperative fibrosis and adhesions (such as those causing obliteration of the pouch of Douglas). The objective of this study was to compare the performance of TVS and MRI in diagnosing DE recurrence.

DESIGN: Prospective study.

MATERIALS AND METHODS: This prospective study enrolled women who underwent a second surgery after surgical excision of deep endometriosis because of suspicion of DE recurrence. TVS was performed by an experienced ultrasonographer. MRI was performed within two months from TVS by a radiologist blinded to the results of TVS. Laparoscopy was performed within four months from MRI; all DE lesions were excised. The findings of TVS and MRI were compared with histological results.

RESULTS: The study included 164 women. The median interval between the first and second surgery was 7 years (range, 2-24 years). 103 patients (62.8%; 95% CI 54.9%-70.2%) had a histological diagnosis of DE after the second surgery. 69 women underwent a hysterectomy, 41 excisions of ovarian endometriomas, 23 unilateral adnexectomies, and 8 bilateral adnexectomies (some patients underwent come than one surgical procedure). The McNemar's test demonstrated that TVS has higher performance than MRI in diagnosis recurrence of DE ($p = 0.007$). The performance of MRI was: accuracy 80.5% (95%CI, 73.6-86.3), sensitivity 83.5% (74.9-90.1), specificity 75.4% (62.7-85.5), positive predictive value (PPV) 85.2% (78.6-90.0), negative predictive value (NPV), 73.0% (63.1-81.0), positive likelihood ratio (LR+) 3.40 (2.17-5.31), negative likelihood ratio (LR-) 0.22 (0.14-0.35). The performance of TVS was: accuracy 88.4% (82.5-92.9), sensitivity 86.4% (78.3-92.4), specificity 91.8 (81.9-97.3), PPV 94.7% (88.5-97.6), NPV 80.0 (71.0- 86.8), LR+ 10.54 (4.54-24.50), and LR- 0.15 (0.09-0.24).

CONCLUSIONS: TVS is superior to MRI in diagnosing postoperative recurrence of DE. MRI has poor specificity in diagnosing DE recurrence, possibly because of postoperative fibrosis.

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CORRELATION BETWEEN CT VIRTUAL HYSTEROSALPINGOGRAPHY FINDINGS WITH THOSE OF HISTEROSCOPY AND LAPAROSCOPY, IN PATIENTS WITH PREGNANT DESIRE. Débora Cristina Siqueira, MD,[1] Natália Fontoura Vasconcelos, Ms,[2] Andrey Cechin Boeno, MD, Msc,[2] Gabriela Buchner, MD,[2] Rayane Felippe Nazário, MD,[2] Angela Figueiredo Pinto Agostini, MD,[2] Marta Ribeiro Hentschke, MD, PhD.[2] [1]Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, Brazil; [2]■■■.

OBJECTIVE: Correlate CT Virtual Hysterosalpingography findings with those of histeroscopy and laparoscopy in patients with pregnant desire.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The study included patients who were submitted to CT-HSG from january/2019 to february/2019, in a university hospital in Brazil, and subsequently were submitted to laparoscopy and hysteroscopy according to medical indication. The data collection was based on the hospital's electronic medical records. The study analyzed clinical characteristics of patients, imaging and surgeries findings, regarding uterine tubes,

TABLE 1. Clinical pregnancy rate by percentage of compaction

Compaction cutoff, %	Compacted n/N (%)	Not Compacted n/N (%)	P-value	Sensitivity %	Specificity %	Positive predictive value %	Negative predictive value %
5	88/116 (75.9%)	167/290 (57.6%)	0.0006	34.5	81.5	75.9	42.4
10	53/71 (74.6%)	202/335 (60.3%)	0.023	20.8	88.1	74.6	39.7
15	34/46 (73.9%)	221/360 (61.4%)	0.098	13.3	92.1	73.9	38.6
20	13/16 (81.3%)	242/390 (62.1%)	0.12	5.1	98	81.3	37.9

uterine cavity and ovaries. The study was approved by the University Research Ethics Committee. The CT-HSG was indicated for infertility investigation, and for the evaluation of tubal stump in patients who were planning the tubal reversal surgery. The image exam followed the protocol established by the hospital gynecology and radiology service. Data were analyzed using SPSS version 22.0, and presented as mean± SD and percentage. Pearson's correlation test was applied considering p< 0.05.

RESULTS: The CT-HSG examination was performed on 204 women in reproductive age, seeking for pregnancy. Women and partners mean age was 32.7±3.4 and 33.2±6.4 years old, respectively, and women mean BMI was 26.0± 3.4. From those who underwent CT-HSG, 12 were submitted to hysteroscopy and 11 to laparoscopy (9 due to infertility investigation and 3 due to reverse tubal desire). The mean time between CT-HSG and the surgery was 6.4±2.6 months. The findings related to the uterus presented 75% of compatibility (r=0.556; p=0.061). Regarding tubal findings between CT-HSG and surgical findings, including 11 patients, a statistically positive direct correlation was seen (r=0.498; p=0.018), which was mainly due to the the right tube (90% of compatibility). In all exams the data regarding the ovaries were in agreement (r=1.00; p<0.0001).

CONCLUSIONS: The present study showed a positive correlation between CT-HSG and laparoscopy/hysteroscopy findings for tubes and ovaries. For the uterus, although no statistical significance was observed, seems to have a clinical correspondence. Hence, CT-HSG seems to be an option for evaluation, not only the tubes, but also the uterine cavity and ovaries. The 3D image can be created, as well as the virtual navigation for better clinical evaluation. The discordant findings are open to discussion considering the time between the exam and the surgery, and the possible false positives and negatives in both situations, which shows the importance of the study follow-up.

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ULTRASOUND IMAGING PREDICTS ENDOMETRIAL RECEPTIVITY – A DECREASE IN ENDOMETRIAL THICKNESS (COMPACTION) PRIOR TO EMBRYO TRANSFER IS ASSOCIATED WITH AN INCREASE IN CLINICAL PREGNANCY RATE IN SYNTHETIC FROZEN EUPLOID IVF CYCLES.

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OBJECTIVE: Two recently published studies demonstrated that pregnancy rates were higher among patients whose endometrium compacted (became thinner) during secretory transformation in both frozen euploid and non-PGT-A embryo transfer cycles (1, 2). An important limitation of these studies was that transabdominal ultrasound images were utilized. This study seeks to assess whether endometrial compaction (a decrease in endometrial thickness) after progesterone treatment as measured by transvaginal ultrasound (TVUS) in synthetic cryopreserved euploid IVF cycles prognosticates clinical pregnancy rates.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All patients completing a synthetic euploid cryopreserved embryo transfer during 2018 and 2019 were reviewed. Patients who had a TVUS completed within two days prior to starting PIO injections and had a second TVUS on day five of progesterone exposure prior to embryo transfer were selected. Ultrasound images were reviewed while blinded to the pregnancy outcomes and the change in endometrial thickness calculated. The primary outcome was clinical pregnancy rate. Comparison of continuous variables between the two groups was conducted using the Student's t test. Chi-square was used for comparison of categorical variables. Logistic regression was used for multivariate analysis. P < .05 was considered statistically significant.

RESULTS: Images from 406 cycles met inclusion criteria. A 10% or greater decrease of endometrial thickness (compaction) resulted in an ongoing clinical pregnancy rate of 74.6% versus 60.3% if there was no compaction (p = 0.023). The sensitivity and specificity of using a 10% cut off were 20.8% and 88.1%, respectively (Table 1). There was no significant difference in age, BMI or embryo quality when comparing those that compacted by at least 10% versus those that did not. Logistic regression controlling for age and BMI found that endometrial compaction of 10% or greater significantly increased the rate of ongoing clinical pregnancy (OR 1.99, 95% CI, 1.05- 3.36, p =0.032).

CONCLUSIONS: A decrease in endometrial thickness after initiating progesterone resulted in a higher ongoing pregnancy rate in our study. Our findings support the recent studies on endometrial compaction as a potential non-invasive marker of endometrial receptivity.

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UTILITY OF THREE-DIMENSIONAL ULTRASOUND (3D-US) IN WOMEN WITH ARCUATE UTERI SCHEDULED FOR INVITRO-FERTILIZATION (IVF): A SCENARIO ECONOMIC ANALYSIS.

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OBJECTIVE: Subtle septae have been reported in women with hysterosalpingography (HSG) diagnosis of arcuate uterus who had prior failed IVF. The optimal diagnostic tool and definition for arcuate uterus diagnosis, that behaves benignly from implantation perspective, is an area of debate. This study is a scenario economic analysis to determine whether implementation of 3D-US after HSG to screen for subtle septae in women with arcuate uterus anomaly prior to IVF treatment could be cost-effective.

DESIGN: A decision-analytic-model

MATERIALS AND METHODS: A decision-analytic-model was developed to compare 2 screening strategies utilized in daily practice. Modeled women were 100 infertile women, indicated for IVF with HSG diagnosis of arcuate uterus. The first strategy (3D strategy) offers 3D-US screening of subtle septum in IVF women with arcuate uterus diagnosis based on initial HSG. The second strategy (NO-3D strategy) is the reference standard that

adopts proceeding to IVF without 3D-US screening in similar cohort; widely practiced in low resource settings. ASRM-2016 defining criteria for uterine septum were followed to categorize modeled women. Model endpoints were cumulative costs and live birth (LB) after 3 successive IVF cycles. The incremental cost-effectiveness ratio (ICER) was calculated. Baseline input probability data were obtained utilizing the best available evidence concerning the effect of uterine septum incision before IVF therapy and the prevalence of missed septum in a population of arcuate uterus. Medicare 2019 National Fee Estimates were considered for costs assumptions. Costs were reported in US dollars. USA population based LB for year 2017 was also used. For modeling and analysis, we used TreeAge Pro Healthcare 2020 software. Sensitivity analysis was conducted.

RESULTS: Base-case analysis revealed that 3D-US screening strategy prior to IVF was more cost effective than NO-3D strategy. After 3 IVF cycles, 3D-US screening resulted in cumulative LB of 73.2% with $ 2,203,250 total costs compared to 58.9 % cumulative LB and $ 2,255,000 total costs in NO-3D strategy. 3D-US implementation would cause initial costs of $142,250 for diagnosis of missed septae and their accompanying metroplasty procedure; however, this would yield cost saving of $ 3620 per live birth gained after 3 IVF cycles. Even in the worst-case-scenario of sensitivity analysis, when low probability of missed septate was evaluated, 3D strategy was still cost effective with extra-costs and more benefits (ICER: $1160 per LB) utilizing $50,000/QALY willingness-to-pay threshold. The higher the probability of missed septum detection in arcuate IVF population and the higher the increase in LB after septum resection, the more would be the cost effectiveness of 3D-startegy. Sensitivity analyses were robust.

CONCLUSIONS: Adoption of 3D-US prior to IVF, to reevaluate arcuate uteri initially diagnosed by HSG, could minimize the financial burden due to failed cycle caused by missed septum. This strategy may be helpful, since randomized controlled trials in IVF women with uterine septum face recruitment challenges.

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SONOGRAPHIC OBSERVATION OF ENDOMETRIAL COMPACTION AS A POTENTIAL PREDICTOR OF ENDOMETRIAL RECEPTIVITY.

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OBJECTIVE: Two recent reports of a correlation between changes in endometrial thickness after progesterone (P4) exposure and outcome after thawed embryo transfer suggest a potential relationship with endometrial receptivity. However, these studies had opposite findings, with one associating endometrial compaction with improved outcome, while the other associated endometrial expansion with improved outcome. This study investigates any correlation between the percent change in endometrial thickness and outcome after transfer of single vitrified-warmed blastocysts.

DESIGN: IRB-approved retrospective cohort study of single vitrified-warmed blastocyst transfers at a private fertility center.

MATERIALS AND METHODS: There were 232 autologous vitrified-warmed single-blastocyst transfers following transvaginal ultrasonographic (TVU) measurement of endometrial thickness on the day of P4 start and 5 days later, on the day of transfer. Vitrified-warmed blastocysts were transferred on the 6th day of P4 injection (100 mg/day) in cycles of artificial endometrial preparation with exogenous estradiol. Outcomes were pregnancy (+hCG in serum) and ongoing pregnancy (fetal heart tone at 10 weeks gestation). Logistic regression was used to determine if the percent change in endometrial thickness from the day of P4 start until 5 days later correlated with pregnancy (+hCG in serum) and ongoing pregnancy (fetal heart tone at 10 weeks gestation). Also included in the model were blastocyst morphology (diameter, inner cell mass size, trophectoderm cell count), patient age at egg collection, and the use of PGT-A (yes/no). $P<0.05$ was considered significant. Ranges of endometrial thickness change were then used to show the magnitude of the effect across these ranges.

RESULTS: Of the available variables, significant predictors of pregnancy (+hCG) were the percent change in endometrial thickness (P=0.0031) and blastocyst diameter (P=0.0060). Lesser percent change in endometrial thickness (including compacting endometria) and larger blastocyst diameter were associated with increased chance of pregnancy. Significant predictors of ongoing pregnancy were percent change in endometrial thickness (P=0.0202), age at retrieval (P=0.0243), and the use of PGT-A (P=0.0039). Lesser percent change in endometrial thickness, younger age at retrieval, and the use of PGT-A were associated with increased chance of ongoing pregnancy. To convey the magnitude of this effect, pregnancy rates were 89.5% when endometria compacted by more than 10%, 83.2% when there was between 10% compaction and 10% expansion, and 73.7% when there was $\geq$10% expansion. Ongoing pregnancy rates were 63.2%, 64.2%, and 54.2% in these respective groups.

CONCLUSIONS: Pregnancy and ongoing pregnancy had negative associations with TVU-observed endometrial expansion after progesterone exposure, and a positive association with endometrial compaction. This association suggests an optimal endometrial response to exogenous P4, and perhaps optimal endometrial receptivity, might be sonographically identifiable in artificial cycles of thawed blastocyst transfer.

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SUPPORT: None.

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THREE-DIMENSIONAL ULTRASOUND GUIDANCE: THE NEW FRONTIER OF EMBRYO TRANSFER?

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OBJECTIVE: A systematic review and meta-analysis to assess the value of using transabdominal, transvaginal or 3D ultrasound guidance during embryo transfer.

DESIGN: Systematic review and meta-analysis of randomized controlled trials evaluating the effectiveness of transabdominal, transvaginal or 3D ultrasound guided embryo transfer.

MATERIALS AND METHODS: Cochrane Collaboration methods were used. Summary estimates and 95% confidence intervals were calculated using random-effects methods.

RESULTS: Twenty-eight randomised trials involving 9,907 women were included. Compared to transfer performed without simultaneous ultrasound (clinical touch method), transabdominal ultrasound guided transfers were associated with a significantly higher live birth rate (OR 1.74, 95% CI 1.04-2.89), pregnancy rate (OR 1.46, 95% CI 1.25-1.70), and biochemical pregnancy rate (OR1.20, 95%CI 00.86-1.68). Transvaginal ultrasound guided transfers were associated with significantly higher live birth rate when compared with transabdominal ultrasound guided transfers (OR 2.56, 95% CI 1.02-6.56). There was no significant difference in pregnancy rate when comparing transabdominal 3D ultrasound with 2D ultrasound guided transfer (OR 0.98, 95% CI 0.75-1.21). Live birth outcomes were poorly reported for this comparison.

CONCLUSIONS: Ultrasound should be routinely used during embryo transfer as it improves clinical outcomes. Other ultrasound modalities, including transvaginal and 3D ultrasound, appear to improve live birth and pregnancy rates respectively. Transvaginal ultrasound should be offered to women during embryo transfer. Further research is required to evaluate the effectiveness of transvaginal and 3D ultrasound. Clinicians and professional societies should champion the routine use of ultrasound during embryo transfer.

SUPPORT: No financial support.

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AUTOMATED 3D (SONOAVC) VERSUS 2D ULTRASONOGRAPHY IN OVARIAN FOLLICLES COUNT IN PATIENTS WITH LARGE OVARIAN ENDOMETRIOMA UNDERGOING IN VITRO FERTILIZATION. Simone Ferrero, MD PhD,[1] Carolina Scala, MD,[2] Giulio Evangelisti, MD,[1] Michele Altieri, MD,[1] Fabio Barra, MD.[1] [1]IRCCS Ospedale Policlinico San Martino, Genova, Italy; [2]Istituto G. Gaslini, Genova, Italy.

OBJECTIVE: To compare the performance of bidimensional ultrasonography (2D-TVS) and three-dimensional automated volume calculation (SonoAVC) in calculating ovarian follicle count in patients with large endometriomas undergoing in vitro fertilization (IVF) cycles.

DESIGN: Prospective single centre study.

MATERIALS AND METHODS: This study included patients with ovarian endometrioma with largest diameter $\geq$ 5 cm undergoing IVF. Exclusion criteria for the study were: previous unilateral ovariectomy, premature ovarian failure, non-endometriotic ovarian cysts. The exams were performed by using a Voluson E10 machine. The number and mean diameter of follicles were measured manually using 2D ultrasound. 3D data were then acquired and analyzed using Sono-AVC. Only ovaries with endometriomas with largest diameter $\geq$ 5 cm were considered in the analysis.

RESULTS: This study included 173 patients and 176 ovaries. 170 women had unilateral endometrioma with diameter $\geq$ 5 cm; three patients had bilaterale endometriomas with diameter $\geq$ 5 cm. The mean diameter of the large endometrioma was 7.0 ($\pm$1.4) cm. 33 patients had other endometriomas with diameter $<$ 5 cm, which were located in the ovary with the large endometrioma in 13 cases, in the contralateral ovary in 18 cases and in both the ovaries in 2 cases. The mean follicular count per ovary was significantly lower when measured manually than with SonoAVC ($p<0.001$). There was no significant difference in the number of follicles with mean diameters $\geq$ 17 mm measured by 2D-TVS and SonoAVC. SonoAVC identified significant more follicles with mean diameters $\geq$ 9 mm ($p=0.003$) and $\geq$ 13 mm ($p=0.036$) than 2D-TVS. There was no significant difference in the diameter of the leading follicle measured manually or by SonoAVC ($p=0.804$). There was a good correlation between the number of oocytes retrieved and the number of follicles detected by 2D-TVS (Pearson correlation coefficient, 0.836) or by SonoAVC (0.906).

CONCLUSIONS: This large prospective study demonstrates that, when large ovarian endometriomas are present, SonoAVC may improve the detection of follicles with diameter $<$ 17 mm.

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TO REMOVE OR NOT TO REMOVE? THAT IS THE QUESTION - THE DILEMMA OF DILATED TUBES. Stephanie R. Brownridge, M.D., Arielle Yeshua, MD, Randi H. Goldman, M.D., Susan Maxwell, MD, Gerald Scholl, MD, Nicole Noyes, MD. Northwell Health Fertility, North Shore University Hospital/Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: Hysterosalpingograms (HSGs) are integral to fertility care. We looked to determine whether surgical removal of dilated fallopian tubes improves pregnancy outcome.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: All HSGs performed at our academic center by a single practitioner from 1/2015-12/2019 were assessed. Reports were reviewed for the following terms: “tubal dilation” (TD) & “hydrosalpinx” (HS). A discussion took place regarding surgery at the time of diagnosis. Pregnancy rates of the TD/HS subset were compared between patients who had surgery (salpingectomy/proximal occlusion, $\pm$ adhesiolysis) vs. those who did not. A sub-analysis was done for patients with patent (PAT) vs. occluded (OCC) tubes. Statistical analysis: Fisher’s exact tests with $p<0.05$ as significant.

RESULTS: TD or HS was diagnosed in 72/1,398 (5%) HSGs. Of these, 6 patients were excluded: 3 - insufficient data, 2 - high FSH, 1 - planned egg freeze, leaving 66 (Table). 35/66 (53%) achieved a pregnancy. 20/66 (30%) patients had surgery and 46 (70%) did not. Of those that had surgery, 18/20 (90%) had a salpingectomy, 1 had laparoscopic proximal occlusion due to disease severity & 1 had adhesiolysis. Of surgical patients who underwent salpingectomy, all had pathologic confirmation of tubal disease. Notably, pregnancy rates were similar in patients with TD/HS whether they had surgery (11/20, 55%) or not (24/46, 52%). Within the Surgery group, 10/11 (91%) conceived with IVF vs. 9/24 (34%) in the No-Surgery group. 0% of Surgery & 4% of No-Surgery patients had ectopic pregnancies. On subgroup analysis comparing TD/HS-PAT vs. TD/HS-OCC, there was a significantly higher likelihood of pregnancy after tubal removal in the OCC group.

Table Pregnancy rates relative to tubal patency & whether surgery was performed.

	Pregnancy (n, %)	Pregnancy (n, %)	
	Surgery (n=20)	No Surgery (n=46)	p-value
Patients with TD or HS (n=66)	11/20 (55%)	24/46 (52%)	NS
PAT (n=30)	25%	65%	NS
OCC (n=36)	75%	35%	0.02
Pregnancy Outcome			
Delivery (n=22)	73%	58%	NS
Ongoing (n=6)	18%	17%	NS
Biochemical/Spontaneous ab (n=2)	9%	4%	NS
Ectopic (n=1)	0%	4%	NS
Unknown (n=4)	0%	17%	NS

CONCLUSIONS: Surgical intervention for TD/HS has been recommended since the 90s when trials suggested a HS negatively impacted ART outcomes. This is from an era of cleavage-stage embryo transfer, and less accurate venereal disease testing. Our data demonstrates pregnancy & live birth can be achieved with a TD in vivo, especially if PAT. Thus, patients should be counseled regarding the option of conservative management for TD. Surgery should still be encouraged in the case of TD/HS-OCC. Our HSG data was obtained from a single provider, decreasing variations in diagnostic criteria. This study was limited by its small sample size and retrospective design.

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IMPACT OF ULTRASOUND DIAGNOSIS OF ADENOMYOSIS ON PREGNANCY RATE AND OUTCOME IN IVF CYCLES WITH DONATED OOCYTES: A PROSPECTIVE STUDY. Caterina Exacoustos, MD, PhD,[1] Martina Cosentino, MD,[1] Luisa Loiudice, MD,[2] Francesco Giuseppe Martire, MD,[1] Daniela Galliano, MD, PhD,[3] Antonio Pellicer, M.D., Ph.D.[3] [1]University of Rome ’Tor Vergata’, Italy; [2]IVI Istituto Valenciano de Infertilidad in Roma and Valencia, University of Valencia affiliated Infertility clinic, Roma, Italy; [3]IVI Istituto Valenciano de Infertilidad in Roma and Valencia, University of Valencia affiliated Infertility clinic, Italy.

OBJECTIVE: The aim of this prospective study was to evaluate in patients who underwent embryo transfer (ET) in an oocyte donation cycle, the impact of adenomyosis, diagnosed by transvaginal sonographic (TVS), on the implantation rate. Also type and degree of adenomyosis scored by TVS were correlated to the implantation rate and pregnancy outcome.

DESIGN: All the patients undergoing their first IVF with oocyte donation were evaluated before ET by TVS to assess presence or absence of adenomyosis. Type and grade of the disease was correlated to pregnancy rate and outcome.

MATERIALS AND METHODS: All the patients aged $\leq$ 45 years old undergoing, for several personal problems, their first oocyte donation at IVI center Rome from June 2019 were included in this study. All had as usual an accurate workup which included history, pelvic exam and 2/3D TVS scan which was saved as images, videoclips and volumes and stored. The off line evaluation of the stored TVS was performed blind to IVF indication and outcomes by expert sonographer of the University of Rome Tor Vergata, who assessed the presence or absence of TVS signs of adenomyosis. Patients were divided into 2 groups according to findings on a baseline pre-treatment TVS: patients with and without adenomyosis. Any medical treatment was given for adenomyosis. In the patients with adenomyosis, the disease was further classified according to type (diffuse,focal), localization (inner and

outer myometrium) and extension inside the uterus (mild, moderate, severe) and correlated to pregnancy rate and outcome

RESULTS: A total of 51 patients were included in this study: 24 with adenomyosis and 27 without adenomyosis. Those with TVS signs of adenomyosis showed a lower pregnancy rate (62.5%) compared to those in the control group (74.1%). Women with adenomyosis that infiltrated only the external myometrium showed a lower pregnancy rate (50%) compared to those who had the involvement of only the inner myometrium (71%). The presence of ultrasound findings of focal disease was associated with a lower pregnancy rate (66%) compared to the diffuse disease (70%); We observed a slightly higher miscarriage rate in the first trimester in patients with adenomyosis in particular in the diffuse type

CONCLUSIONS: The presence, type and degree of adenomyosis showed an important correlation to embryo implantation rate and early miscarriage. Results of this study may be used to evaluate the impact of different medical or surgical treatment in women with adenomyosis undergoing IVF.

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IMAGE GUIDED TRANSVAGINAL & TRANSABDOMINAL DRAIN PLACEMENT FOR SURGICAL NAVIGATION IN A PATIENT WITH TUBO-OVARIAN ABSCESS AND OBSTRUCTED HEMIVAGINA WITH UTERUS DIDELPHYS. Pamela B. Parker, M.D., M.P.H.,[1] Jared Ray Edwards, MD,[2] Teodora Bochnakova, MD,[1] David Lee, MD.[1] [1]Oregon Health & Science University, Portland, OR; [2]Naval Medical Center San Diego, San Diego, CA.

OBJECTIVE: To highlight a minimally invasive, image-guided technique to treat obstructed hemivagina in ipsilateral renal anomaly (OHVIRA) syndrome complicated by tubo-ovarian abscess (TOA)

DESIGN: Case Report

MATERIALS AND METHODS: A case of a 15-year-old female with history of uterine didelphys and longitudinal vaginal septum deviated to the left with concomitant left-sided renal agenesis presented with TOA. MRI of the abdomen and pelvis demonstrated a 13 centimeter loculated, fluid-filled, pelvic mass as well as a complex, fluid-filled structure near the obstructed left hemivagina. She underwent hysteroscopy, cystoscopy, and attempted excision of the vaginal septum and neosalpingostomy. Excision of the vaginal septum was unsuccessful because prior spontaneous drainage from the left vagina to the right through a tract, perhaps partially involving the bladder, left all of the vaginal septal tissue infected and unable to optimally hold suture. Similarly, after extensive robotic lysis of abdominal and pelvic adhesions, surgical planes remained ill-defined given the extensive purulent tissue. Ultimately interventional radiology (IR) was consulted intraoperatively for placement of a transabdominal drain under direct visual guidance through a laparoscopic port. The patient subsequently underwent transperineal ultrasound-guided placement of a transvaginal drain into the hemivaginal collection and CT-guided transabdominal drain placement in the IR suite 8 days following initial surgery. After a cool-down period receiving broad spectrum IV antibiotics, she underwent cystoscopy, vaginoscopy, successful excision of the vaginal septum, drainage and excision of left TOA, removal of drains, and creation of left neosalpingostomy. Placement of the transvaginal drain allowed for subsequent intraoperative identification of the correct anatomy to safely resect the transvaginal septum of the previously obstructed hemivagina. Additionally, placement of the transabdominal drains allowed for successful identification of the abscesses. She was discharged home the following day.

RESULTS: At her 1-week and 3-month follow-up visits, the patient was symptom-free without evidence of vaginal stenosis nor evidence of recurrent infection.

CONCLUSIONS: Patients with OHVIRA syndrome, with and without TOA, can be managed with minimally invasive techniques. In this case, a joint approach allowing for successful placement of a TOA drain placed laparoscopically and a transvaginal catheter placed under image-guidance allowed for the correct incision site into the vaginal septum. Given the anatomic complexity, preoperative measures that aid in intraoperative anatomic navigation are critical in ensuring successful treatment. Collaboration with interventional radiology and pediatric gynecology is particularly helpful for treatment of complicated mullerian and vaginal variants.

SUPPORT: none

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FOLLICULAR TRACKING WITH ULTRASOUND DOES NOT IMPROVE PREGNANCY RATE IN LETROZOLE-INTRAUTERINE INSEMINATION (IUI) CYCLES. Kristy Cho, MD, FRCSC,[1] Jason K. M. Au, MSc,[2] Rachel N. J. Sen-Laurenz, BA,[3] Arianne Y. K. Albert, PhD,[4] Jon C. Havelock, MD, FRCSC, DABOG,[2] Caitlin Dunne, MD, FRCSC.[5] [1]Division of Reproductive Endocrinology and Infertility, University of British Columbia, Vancouver, BC, Canada; [2]Pacific Centre for Reproductive Medicine, Burnaby, BC, Canada; [3]University of British Columbia, Vancouver, BC, Canada; [4]Women's Health Research Institute, Vancouver, BC, Canada; [5]Division of Reproductive Endocrinology and Infertility, University of British Columbia, Burnaby, BC, Canada.

OBJECTIVE: The use of letrozole for ovarian stimulation in intrauterine insemination (IUI) has increased in popularity in recent years due to its efficacy for patients with PCOS and the current shortage of the alternate medication, clomiphene. However, much of the evidence guiding cycle management has been based on clomiphene IUI cycles. This study aimed to determine if the probability of pregnancy was associated with ultrasound monitoring or human chorionic gonadotrophin (HCG) trigger in letrozole IUI cycles.

DESIGN: A retrospective cohort study.

MATERIALS AND METHODS: This study included letrozole IUI cycles performed at two Canadian university-affiliated fertility centers from 2016 to 2019. Exclusion criteria included anovulatory cycles, tubal factor infertility, or total motile sperm < 1 million. The patients were divided into 2 groups: ultrasound-monitored and unmonitored. The associations between pregnancy rate and ultrasound use, lead follicle size at last ultrasound, or HCG use were determined using regression analysis, Fisher's exact test, or Wilcoxon rank-sum test.

Letrozole 2.5-7.5 mg was administered from cycle day 3-7 or day 1-9. In the unmonitored group, patients used ovulation predictor kits (OPK) daily starting on cycle day 10. In the ultrasound-monitored group, patients presented for an ultrasound at baseline, on day 10-12, and as needed until ovulation. HCG 10,000 IU was given for ovulation trigger when clinically indicated. The IUI was performed on the same day as a positive OPK or the day after the HCG trigger.

RESULTS: Out of the 2678 cycles undertaken by 1,397 patients, 351 cycles (13%) were monitored with ultrasound. Overall, the pregnancy rate was 12% per cycle. In this cohort, the cumulative pregnancy rate, up to 6 cycles of IUI, was 53% (95% CI 34% to 66%). Compared to patients who did not conceive, a higher proportion of the patients who achieved pregnancy utilized letrozole $\geq$5mg on cycle day 3-7. The use of letrozole on cycle day 1-9 was associated with a lower rate of pregnancy compared to cycle day 3-7 (9.4% vs 12.6%, $P< 0.05$). Ultrasound monitoring was not associated with an increased pregnancy rate in letrozole IUI treatments ($p= 0.09$).

Adjusting for age and body mass index, there was no relationship between lead follicle size and the odds of pregnancy (OR 0.95, 95% CI 0.85 to 1.05, $p= 0.35$). Multi-follicular response was also not associated with a significantly increased pregnancy rate; the presence of 2 or more lead follicles $\geq$18mm had 1.27 adjusted odds of pregnancy ($p= 0.5$). For those who underwent ultrasound monitoring, 12% required HCG to trigger ovulation. There were no statistically significant differences in pregnancy rates between those who utilized HCG trigger and those who did not ($p= 0.14$).

CONCLUSIONS: The use of ultrasound monitoring was not associated with an improved pregnancy rate in letrozole IUI cycles.

No financial support.

SUPPORT: The abstract has been previously accepted for an e-poster presentation at ESHRE 2020. However, this updated abstract submitted here contains data from an additional study site compared to the previously accepted abstract Â.

POSTER SESSION: INFERTILITY AND CANCER

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EFFECT OF DISTAL CANCER ON THE TELOMERIC LENGTH OF OVARIAN CORTEX CELLS. Lucía Chico-Sordo, MSc,[1] Inmaculada Soler, MD,[2] Jose M. Mateu-Pascual, MSc,[1] Isabel Córdova-Oriz, MSc,[1] Alba M. Polonio, MSc,[1] Marta Medrano, Lab Technician,[3] María J. Soriano, MSc,[1] Juan A. Garcia-Velasco, MD, PhD,[3] Elisa Varela, PhD[3] [1]IVI Foundation, IIS La Fe, Valencia,

Spain; [2]Gynecology, Hospital de Xativa Lluis Alcanyis, Valencia, Spain; [3]IVI-RMA Madrid, Rey Juan Carlos University, Madrid, Spain.

OBJECTIVE: Telomeres are tandem repeats of hexanucleotides which, together with the shelterin protein complex, protect the ends of chromosomes, to preserve genomic integrity. However, over organismal lifetime telomeres shorten on each cell division. Harsh erosion of telomeres compromises chromosome structure with consequences for aging and cancer. In the cancer context, unprotected telomeres promote cell transformation by a process called telomere crisis that leads to numerous genomic alterations including chromosome rearrangements, areas susceptible of mutations and tetraploidization. The aim of the study is to determine whether breast cancer can exert telomere damage in a distal organ as the ovary reducing women's fertility, even before they have undergone any cancer therapy.

DESIGN: Analytic and prospective cohort study.

MATERIALS AND METHODS: Women who participated in this study were recruited between April 2013 and May 2014 from Hospital La Fe (Valencia). Ovarian biopsies from 46 individuals, serum from 44 women and leukocytes from 49 participants were collected. Samples of ovarian tissue and blood from healthy women and cancer patients, prior to cancer treatment, were collected and analyzed. Blood samples were collected before the surgical procedure. Serum and leukocytes were obtained by centrifugation using a Ficoll gradient. Samples of ovarian tissue were obtained at the time of surgery to preserve patients' fertility, and during tubal ligation surgery in controls. Telomere length was measured by Quantitative Fluorescent In Situ Hybridization (Q-FISH) followed by image acquisition using high resolution confocal microscopy.

RESULTS: A total of 57 women have participated, 29 cancer patients (mean 27.92 $\pm$ 7.54 years) and 28 controls (mean 36.78 $\pm$ 4.32 years). From controls, 11.1% were smokers, and 21.7% of cancer patients. The mean AMH values were 1.50 $\pm$ 1.43 and 2.60 $\pm$ 3.08 ng/mL (controls and cancer patients, respectively). Telomere length (TL) was similar between cancer patients and healthy controls, when all cell types of the ovary were analyzed (21.85$\pm$ 0.079 and 22.45 $\pm$ 0.123 a.u., respectively). Granulosa cells of cancer-diagnosed women bore shorter telomeres (TL = 22.34 $\pm$ 8.86 a.u.) compared to control group (TL = 26.37 $\pm$ 9.85 a.u.). In oocytes, a lower mean telomeric length was observed in cancer patients (21.03 $\pm$ 8.64 a.u.) compared to control women (24.54 $\pm$ 12.73 a.u.).

CONCLUSIONS: The telomere length of ovarian cortex cells is altered in cancer patients, indicating a systemic effect of breast cancer on the ovaries, which are known to be very sensitive to toxic insults. The systemic effect of distal cancers has effected mainly to granulosa cells and oocytes, suggesting that these cell types are more susceptible than ovarian stroma cells. All these alterations in telomere biology have been observed before women had undertaken cancer therapy. Collectively, these results remark the urgency of ovarian cortex cryopreservation once the cancer has been diagnosed, in women who wish to became pregnant.

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FERTILITY PRESERVATION IN BREAST CANCER PATIENTS: A LONGITUDINAL STUDY OF RETRIEVAL AND OOCYTE/EMBRYO UTILIZATION. Sydney Chang, MD,[1] Susan Finch, MD,[1] Joseph A. Lee, BA,[2] Alan B. Copperman, MD,[1] Christina Weltz, MD[1] [1]Icahn School of Medicine at Mount Sinai, New York, NY; [2]Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Breast cancer is the most commonly diagnosed malignancy for women living in the United States and more than 26,000 newly diagnosed patients per year are under the age of 45.[1] Given that most chemotherapeutic agents and hormonal therapies used for adjuvant treatment of breast cancer are gonadotoxic and/or teratogenic, fertility preservation is critical prior to initiating treatment. Increased awareness of the need to preserve fertility, timely referral to infertility specialists, and development of ovarian stimulation protocols that are safe in breast cancer patients have increased rates of fertility consultation and treatment among women diagnosed with breast cancer. The objective of this study is to describe the frequency with which breast cancer patients who consulted with fertility experts underwent retrieval procedures and also the rate of utilizing cryopreserved oocyte/embryos.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: Patients with breast cancer who were identified within the center's electronic medical between 2002-2019 were included in the study. Demographic information, cycle characteristics, use of preserved oocyte and embryos, pregnancy outcomes and length of follow-up were collected.

RESULTS: A total of 215 patients with a breast cancer diagnosis (196 invasive, 19 in situ) presented for consultation. The majority of the study population (78.6% [169/215]) saw a REI specialist prior to chemotherapy and/or radiation. Of patients who presented for a consultation, 44.2% (95/215) decided to proceed with an oocyte or embryo freezing cycle, and 2.8% (6/215) pursued oocyte donation. The average age of patients undergoing cryopreservation was 35.9 $\pm$ 5.6 (22-47). 50.5% (48/95) of patients underwent retrieval to freeze oocytes; 47.3% (45/95) underwent retrieval to freeze embryos; 2.1% (2/95) were cancelled prior to retrieval. 33.7% (32/95) of patients had their retrieval within 4 weeks of their initial consultation.

Of patients who underwent cryopreservation, 25.3% (24/95) returned to utilize their oocytes/embryos either at our center (n=12) or at an alternative center (n=12). Of patients undergoing a transfer at our center, 58.3% (7/12) achieved a pregnancy and 50% (6/12) achieved a live birth. From this cohort, there were 3 singleton and 3 twin deliveries. 12.5% (3/24) created embryos for future transfer into a gestational carrier. Mean follow up time was 4.8$\pm$3.3 years, median was 4.5 years. Many patients (43.7% [31/71]) who have yet to return and use their oocytes/embryos underwent cryopreservation $<$3 years ago.

CONCLUSIONS: With 5-year breast cancer survival rate at 90%1, fertility preservation in patients of reproductive age is of paramount importance. Of 215 breast cancer patients who presented for discussion of fertility preservation, 95 underwent retrieval procedures and 24 have returned to utilize their oocytes/embryos. Further research will seek to identify individual patient's decision making relevant to fertility preservation and treatment with the goal of optimizing breast cancer patients' chances of achieving live birth.

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SUPPORT: None

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HEREDITARY BREAST CANCER AND FERTILITY PRESERVATION OUTCOMES. Suha Arab, MD, MS,[1] William Buckett, M.D.[2] [1]Doctor, Montreal, QC, Canada; [2]Division of Reproductive Endocrinology and Infertility, McGill University Health Care Centre, Montreal, QC, Canada.

OBJECTIVE: BRCA mutations are the most common genes linked to hereditary breast cancer, but other inherited genes are also associated with breast cancer. While several studies have evaluated the impact of BRCA gene mutations on response to ovarian stimulation, albeit with conflicting results, few have assessed the impact of other related genes. The objective of this study was to determine the prevalence of hereditary breast cancer associated with different mutated genes as well as the respective fertility preservation outcomes in young patients with active breast cancer presenting for fertility preservation.

DESIGN: A retrospective cohort study of breast cancer patients with known genetic testing results who underwent fertility preservation at a university teaching hospital ART center from 2005-2019.

MATERIALS AND METHODS: All breast cancer patients $<$ 40 years old who had a genetic testing result and underwent fertility preservation before starting gonadotoxic therapy. The total number of oocytes retrieved, number of MII oocytes, number of embryos (where appropriate), and the number of cryopreserved oocytes and/or embryos from genetically positive and negative were compared. Age, stage of cancer, parity, BMI and ovarian reserve were also compared.

RESULTS: Of 244 breast cancer patients, 40 patients tested genetically positive (16%). 31 (77.5%) patients had a BRCA mutation, 3(7.5%) had ATM, 2 (5%) had CHK2 and one (2.5%) for each of the following genes: PALP2, NF, MUTYH.c.536A ,and TP53. A total of 127 patients were $<$ 40 years old: 87 patients were genetically negative; 40 patients were genetically positive. Patients in the hereditary breast cancer group were significantly younger than patients in the non-hereditary group (30.7+/-4.3 vs 32.4+/-3.9) (P=0.034). Both groups were similar regarding ovarian reserve, BMI, parity, and stage of cancer. Proportion undergoing IVF or IVM were similar and IVM outcomes were similar in the two groups. Total gonadotrophin dose and days of stimulation were also comparable. In terms of reproductive outcome, there was no significant difference between the groups in the total number of eggs retrieved overall, the number of MII oocytes

collected, and the number of cryopreserved oocytes. Interestingly the number of fertilized oocytes (5.15+/-6.6 vs 2.90+/-4.2)(P=0.054), and the number of cryopreserved embryos (3.35+/-3.7 vs 1.9+/-2.8)(P=0.046) were borderline significantly higher in hereditary than the non-hereditary group. Sub-analysis showed no difference between the different genes. Outcomes following IVF and IVM were similar.

CONCLUSIONS: 16% of all breast cancer patients and 31% of those under 40 years old were genetically positive to 7 different mutated genes. More than 77% of positive mutated genes were BRCA. Patients with hereditary breast cancer, including BRCA, have similar fertility preservation outcomes to those with non-hereditary breast cancer and should be encouraged to consider fertility preservation.

SUPPORT: No financial support.

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HAVE ONCOFERTILITY INFORMATION FOR PATIENTS IMPROVED? OBJECTIVE ASSESSMENT OF INTERNET BASED FERTILITY PRESERVATION RESOURCES AT NCI CANCER CENTERS FROM 2015-2020.

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OBJECTIVE: Fertility preservation is a critical patient counseling component following cancer diagnosis. The aim of this study was to compare change and quality of fertility preservation information available to patients on the websites of National Cancer Institute (NCI) designated cancer centers over five years (2015 to 2020) for both women and men.

DESIGN: Longitudinal observational study.

MATERIALS AND METHODS: All NCI designated cancer center (and the Cleveland Clinic) websites were queried in a systematic fashion for information on oncofertility in 2020 publicly available to patients. The methodology and rubric were previously employed by this group, in 2015, to establish minimum content quality standards for the validation process. Two investigators collected the data from NCI cancer center (NCICC) websites and a third member from a separate institution reviewed the data for discrepancies. Specific questions included: 1) Does the web site discuss the effects of cancer and cancer treatment on fertility? 2) Are options for fertility preservation discussed? 3) Is there a standalone page dedicated to educating patients on fertility preservation? 4) Was parenting-related cancer survivorship addressed. 5) Does the web site discuss the effects of cancer and cancer treatment on fertility, particularly male fertility? Descriptive statistical analysis and chi-squared testing were performed. Data was then compared with the same data points from 2015 to see the effect of time on availability of oncofertility information.

RESULTS: All 65 websites of NCICC (and the Cleveland Clinic) were evaluated; 92% were affiliated with academic institutions. The risk of cancer treatment on fertility was mentioned by 86% of centers and 83% discussed fertility preservation, which were not significantly different from 2015. Among NCICC, significantly more centers have a standalone page for fertility preservation in 2020 compared with 2015 ($p = 0.004$). Survivorship information on family building significantly increased from 32% in 2015 to 82% in 2020 ($p= 0.0077$). Among all cancer centers, there was a significant increase in information on fertility preservation specifically directed toward men, such as sperm cryopreservation; an increase from only 60% in 2015 to 70% in 2020 ($p= 0.0140$). In counties in the United States with an above average number of people living in poverty, there were significantly fewer NCI centers that discussed the effect of cancer treatment on male fertility ($p=0.012$).

CONCLUSIONS: There was a significant increase in standalone pages for fertility preservation, survivorship information and information on fertility preservation specifically directed toward men on NCI CC websites over the past five years. Sixteen percent of centers still do not discuss any options for male fertility preservation, and these centers are disproportionately located in lower socioeconomic counties. Given the increasing recognition of the importance of oncofertility in cancer survivorship, more education should be available about options for fertility preservation, particularly among men in lower socioeconomic areas.

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LIKELIHOOD OF WOMEN ACHIEVING MORE THAN ONE LIVE BIRTH AFTER VARIOUS TYPES OF CANCERS.

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OBJECTIVE: Future family building is an important concern for many cancer survivors and many may hope for more than one child after cancer treatment. Much of the focus in cancer survivorship research has been on whether a single pregnancy can be achieved, rather than on how many children might be born. Limited data is available about the impact of various cancer types and their treatment on the fertility and reproductive window of cancer survivors.

DESIGN: Population-based cohort study

MATERIALS AND METHODS: The Utah Population Data Base (UPDB) was used to identify female cancer survivors at age 18-45 years in Utah state with first time cancer diagnosed between 1952 to 2014. We identified first and last live births of cancer survivors (n= 6,317) in various cancer types and reported these relative to the timing of their cancer diagnosis. Descriptive statistics and chi-square testing were used where appropriate. Poisson regression models for the number of live births after cancer diagnosis were estimated which adjusted for number of live births prior to cancer diagnosis.

RESULTS: The most common cancer types among the cohort were breast cancer in 23%, neurological cancers 4%, lymphomas in 4%, leukemia in 2% and soft tissue cancers less than 1%. Based on the cancer staging, 43% of women had localized disease, 25% had carcinoma In-situ, 11% had involvement of regional lymph nodes, and 8% had distant metastases. When compared with general population, women with breast cancer were least likely to have more than one child after cancer treatment and those Hodgkin's lymphoma appeared most likely to do so, as reflected in the table below.

CONCLUSIONS: Live births after cancer treatment vary by cancer treatment type. This is likely a reflection of treatment type and average age of diagnosis associated with each cancer type. With the exception of survivors of Hodgkin's lymphoma, fewer than 25% of female cancer survivors had two or more children after their cancer diagnosis. This type of information can be used to assist patients in understanding their chances of achieving a desired family size after cancer treatment, and this may impact decisions on fertility preservation treatments.

SUPPORT: None

Table: Estimated effect of being diagnosed with cancer on parity

Number of live births after cancer treatment	Breast (N=4145)	GI (N=129)	Leukemia (N=322)	CNS (N=763)	Non- Hodgkin's lymphoma (N=393)	Soft tissue (N=166)	Hodgkin's lymphoma (N=399)
0	3950 (95%)	122 (94%)	291 (90%)	646 (85%)	331 (84%)	137 (82%)	270 (68%)
1	137 (3%)	4 (3%)	26 (8%)	73 (10%)	31 (8%)	16 (10%)	56 (14%)
2	47 (1%)	3 (2%)	4 (1%)	30 (4%)	16 (4%)	7 (4%)	48 (12%)
≥ 3	11 (0.2%)	0	1 (0.3%)	14 (2%)	15 (0.3%)	6 (3%)	25 (6%)
p-value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

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FERTILITY PRESERVATION (FP) IN BREAST CANCER PATIENTS: PREDICTORS AND OUTCOMES.

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OBJECTIVE: In breast cancer patients, there is often concern regarding the safety of the increased estradiol (E2) levels and potential delays in treatment associated with ovarian stimulation for FP. The primary objective of this study was to compare recurrence and survival in breast cancer patients who pursued FP to those who did not (no-FP). Secondary outcomes were predictors for utilizing FP, utilization of cryopreserved specimens, and pregnancy outcomes. We hypothesized there would be no difference in cancer outcomes between the 2 groups, regardless of receptor status.

DESIGN: Retrospective Cohort Study

MATERIALS AND METHODS: We reviewed charts of women with breast cancer who contacted the FP patient navigator (PN) at a single institution from 01/2005-01/2018. Cancer stage, estrogen receptor (ER) status, date of initial contact with the PN, subsequent cancer treatment dates, relapse, and mortality data were collected. Ovarian stimulation and pregnancy outcome data were also examined. Data were analyzed by chi-square test or regression, as appropriate. Kaplan-Meier curves were used to examine cancer recurrence and survival. Power analysis indicated 140 patients were required per group to detect 10% difference in disease-free survival with 80% power. Statistical analyses were performed with SPSS IBM Statistics 26.0 for Windows.

RESULTS: 332 patients were included, of which 157 (47.3%) underwent ovarian stimulation for FP. Median age (years) was 33.1 for FP patients and 37.29 for no-FP (NS). Median follow up time (years) was 4.22 for the FP group and 6.19 for no-FP (NS). Median days to cancer treatment after consulting the PN was 35 in the FP group and 21 in no-FP ($P<0.05$). Cancer recurrence was noted in 10 (6.4%) FP and 15 (8.6%) no-FP patients (NS), and mortality in 5 (3.2%) FP patients and 7 (4.0%) no-FP patients (NS). Within the FP group, no significant differences were found in recurrence or mortality based on ER status, age, BMI, peak E2 level or total gonadotropin dose. We modeled decision to pursue FP based on age, race, and parity and found the log odds of choosing FP was related to lower age (OR=1.13, 95%CI=1.08, 1.19) and parity (OR=1.76, 95%CI=1.25, 2.47). Cancer stage did not affect likelihood of pursuing FP. Of FP patients who underwent oocyte retrieval (8 cycles were cancelled), median peak E2 was 1460 pg/ml, median days of stimulation was 10, and median number mature oocytes was 8. To date, 22 (14.0%) have used cryopreserved specimens, and 13 (59.1%) had a live birth. 13% used a gestational carrier. Median time from FP to return was 831 days. There were no differences in age or AMH between patients who returned and those who have not. To date, 5.7% FP and 5.1% no-FP patients had a live birth from spontaneous pregnancy.

CONCLUSIONS: FP is safe and effective in breast cancer patients, regardless of receptor status; E2 elevations and the 2-week delay in treatment start are unlikely to be clinically significant. The findings are unique in that our institution does not use letrozole during stimulation to minimize E2 elevations in breast cancer patients. FP choice was primarily a function of age and parity, and was not affected by cancer stage.

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ONCOFERTILITY AND THIRD PARTY REPRODUCTION: ANALYSIS OF PATIENT DIRECTED INFORMATION AND REGIONAL BARRIERS.

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OBJECTIVE: Third party reproduction is often overlooked in patient counseling following cancer diagnosis, when discussing future fertility. However, for some patients, this may be the only option due to the extent of their disease. The aim of this study was to investigate the availability and quality of patient directed information, on third party reproduction, on the web sites of National Cancer Institute (NCI) designated cancer centers.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: All NCI designated cancer center web sites were queried in a systematic fashion for patient directed information on oncofertility. A rubric was employed to establish minimum content quality standards for the validation process. Descriptive statistical analysis and chi-square tests were performed. Specific questions included: 1) Are options for fertility preservation discussed? 2) Are options for future fertility with donor oocytes and sperm discussed? 3) Is the option of gestational surrogacy discussed? Data were then evaluated based on each cancer center's state income to test whether there was a demographic effect on oncofertility information. State surrogacy laws were reviewed, and each state was categorized in two groups, states where surrogacy is permitted for all parents and states where there are any restrictions on surrogacy.

RESULTS: All NCI designated cancer center (and the Cleveland Clinic) websites were evaluated; 94% were affiliated with academic institutions. Among NCI cancer centers (NCICC's), 86% discuss the risk of cancer treatment on future fertility. Of all NCICC's fertility preservation websites, 60% do not mention the option of donor oocytes or sperm for future fertility and 69% do not discuss the option of gestational surrogacy for future pregnancy. Only 24% of all NCI designated cancer centers discuss both donor gametes and gestational surrogacy. NCICC's in states with the top 50% of medium income were significantly more likely to discuss future fertility with donor gametes ($p=0.01$) and gestational surrogacy ($p=0.003$). Discussion of gestational surrogacy was found to be significantly more likely on NCI cancer centers in states where surrogacy is permitted for all parents ($p=0.002$). There were no differences observed when similar adjustments & analyses were performed by race or percentage of population insured.

CONCLUSIONS: Fifty percent of NCI designated cancer center web sites do not discuss options for any third party reproduction and only 24% discuss both donor gametes and gestational surrogacy. Third party reproduction is less likely to be discussed in states with lower medium income and in states with any regulation on gestational surrogacy. Given the increasing recognition of the importance of oncofertility in cancer survivorship, more education should be available about options for fertility preservation, particularly through third party reproduction.

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THE IMPACT OF LETROZOLE ON OVARIAN STIMULATION RESPONSE IN CANCER PATIENTS WITHOUT BREAST CANCER UNDERGOING FERTILITY PRESERVATION.

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OBJECTIVE: Letrozole had been introduced initially to reduce estrogen level exposure in women with estrogen-sensitive cancer undergoing ovarian stimulation (OS) for fertility preservation. The impact of letrozole on ovarian stimulation response in non-breast cancer oncofertility cases has been inadequately investigated. Some studies suggested that adding letrozole to the gonadotropins yield more mature oocytes at lower estradiol levels compared to gonadotropins alone, some studies found patients who had OS with letrozole would reduce the oocyte maturation, and some studies found no significant differences between OS with and without letrozole. Most of these studies compared the impact of OS with letrozole in breast cancer to OS without letrozole in non-breast cancer patients. The purpose of our study is to investigate whether using letrozole has an influence on the ovarian stimulation response for fertility preservation (FP) within non-breast cancer patients and evaluate if it will modify the risk of ovarian hyperstimulation syndrome (OHSS).

DESIGN: A retrospective cohort study on 209 cancer patients who underwent fertility preservation with and without letrozole supplementation during OS at a university teaching hospital ART center between 2009 -2019.

MATERIALS AND METHODS: Our study included all non-breast cancer patients who presented for FP with an antagonist protocol, no previous chemotherapy, at or $<$ 40 years old, no other ovarian disease, and both ovaries were present at the time of treatment. Of the total of 209 patients, the first group underwent OS with letrozole supplementation (n=18) and the second group underwent OS without letrozole (n=191). Primary outcomes were the total number of oocytes retrieved, number of MII oocytes, and the number of oocytes and/or embryos (where appropriate)

cryopreserved between both groups. Secondary outcomes were the number of cases of mild, moderate,and severe OHSS.

RESULTS: Age, BMI, and AFC were similar between both groups. Compared to OS without letrozole, OS with letrozole had higher numbers of oocytes retrieved (18.9 vs 12.8, p=0.006), MII oocytes (12.7 vs 8.2, p=0.02) and a lower level of serum estradiol (1695.2 vs 4675.8 IU/L, p<0.001). In multivariate regression, AFC, rather than the addition of letrozole supplementation, was associated with a higher number of MII oocytes (OR=1.1, CI 95% (1.053-1.155), p<0.001) vs OR 0.371, CI 95% (0.112-1.234), p=0.106). A total of 12 out of the 209 patients developed OHSS 5.7%, 11 cases were mild and only one was severe OHSS. In a multivariate logistic analysis, the odds to develop OHSS was slightly lower in OS with letrozole supplementation (OR=0.210, CI 95% (0.034-1.311), p=0.095). As expected, AFC was the strongest predictor of OHSS (OR 1.087, CI(1.006-1.173), p=0.035).

CONCLUSIONS: Letrozole supplementation to OS in fertility preservation in non-breast cancer patients does not seem to have an important effect on OS response, although there was an insignificant tendency to decrease the odds of OHSS. This deserves further investigation. Larger prospective studies would be able to determine whether there is any real benefit.

SUPPORT: No financial support.

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OUTCOMES OF FERTILITY PRESERVATION AMONG CANCER PATIENTS UNDERGOING OOCYTE AND EMBRYO CRYOPRESERVATION.

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OBJECTIVE: To compare the outcomes of ovarian stimulation in oncology patients undergoing fertility preservation to outcomes of age and AMH-matched controls.

DESIGN: A matched retrospective cohort study

MATERIALS AND METHODS: All oncology patients who underwent embryo or oocyte cryopreservation at our institution 1/2019 through 2/2020 were included (n=42). We identified a comparison group matched by age (within 1 year), AMH (within 0.5 ng/mL), and cycle type (oocyte cryopreservation or IVF/ICSI). Primary outcomes were number of oocytes retrieved, maturity and fertilization rates, and blastocysts frozen. Patients with estrogen-receptor positive tumors (n=23) received letrozole (5 mg/day) during stimulation. Univariate comparisons between cases and controls were performed using the Fisher's exact or Wilcoxon rank sum test as indicated; a p-value of $\leq .05$ was considered statistically significant. Analyses were performed using online calculators available at http://astatsa.com.

RESULTS: Among both cases and controls, the mean age was 31 years (range 16-42, Table) and mean AMH was 3.0 ng/mL (range 0.1-11.8). The distribution of oncologic diagnoses was breast (n=19, 45%), hematologic (n=9, 21%), ovary (n=6, 14%), colorectal (n=2, 5%), and 1 of each of the following: Bone, brain, cervical, renal, uterine and vulvar. Thirty three oncology patients (79%) had random start stimulations, and all cycles utilized an antagonist protocol. In both groups, final oocyte maturation was achieved using hCG (71%), a GnRH-agonist (17%), and a combination (12%). While total oocyte yield was similar between cases and controls (14.6 vs 15.7, respectively, p>0.05), mean oocyte maturity rate was significantly lower (65% vs 77%, respectively, p=0.01). In stratified analysis according to letrozole use, mean oocyte maturity remained lower among cases (62% with, 70% without, p>0.05). Among patients who underwent embryo cryopreservation (n=12), fertilization rates and numbers of blastocysts frozen were similar (p>0.05).

CONCLUSIONS: Studies debate whether oncology patients have worse outcomes than the general population in oocyte and embryo cryopreservation, including lower egg yield and/or maturity.[1,2] In the present study, when compared to healthy age and AMH matched controls, oncology patients had similar numbers of oocytes retrieved, but a lower proportion were mature. Fertilization rate and blastocyst number were similar, though numbers were small. The effect of letrozole use on final oocyte maturity warrants further investigation in future studies.

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POST CHEMOTHERAPY AMH DOES NOT PREDICT MENSTRUAL CYCLE RESUMPTION IN CANCER SURVIVORS.

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OBJECTIVE: To assess post chemotherapy AMH as a predictor of menstrual cycle resumption in cancer survivors

DESIGN: Retrospective chart review and phone survey at a tertiary care enter

MATERIALS AND METHODS: A retrospective chart review was performed of women registered in our institution's Oncofertility Database from May 2013 to July of 2016. Inclusion criteria was women of reproductive age (18-45 years) that underwent gonadotoxic chemotherapy for cancer and had a pre and/or post chemotherapy AMH assessment. Exclusion criteria was menopausal status prior to chemotherapy, hysterectomy or bilateral oophorectomy as part of their cancer treatment and deceased status at time of phone interview. Patients that met inclusion criteria were contacted by phone to review menstrual and reproductive history. Demographic and clinical variables of interest were compared to menstrual cycle resumption status using t-test, Mann-Whitney test, chi-squared, or Fisher's exact test depending on the underlying distribution of the data. Logistic regression models were conducted to estimate the odds of menstrual cycle resumption status. This is considered an exploratory analysis and statistical significance was defined at the 0.05 level.

RESULTS: Of 281 records evaluated, 56 patients (mean age 29.3, SD 6.5) met inclusion criteria and menstrual cycle interview data was obtained on 44 of the 56 (76%). Fifty-five patients had baseline AMH values (98%), 28 patients had post chemotherapy AMH values (50%), and 27 had both (48%). The median post chemotherapy AMH was 0.1 (range 0.03-6.40), and average time of AMH collection post chemotherapy was 21 months. Menses resumed following chemotherapy in 75% (95% CI: 60 – 87) of women, and 45% of those with resumed menses reported having regular menses. There was insufficient evidence that either post chemotherapy AMH or the change in post chemotherapy AMH from baseline was associated with resumption of menses.

CONCLUSIONS: The American Society for Clinical Oncology recommends that "health care providers should address the possibility of infertility with patients treated during their reproductive years and be prepared to discuss fertility preservation options" (1). Despite these recommendations however, the data regarding predictors of future fertility is limited. Predicting fertility function post treatment is critical as it impacts fertility treatment options and likelihood for success. AMH testing after chemotherapy however does not accurately predict resumption of menses, nor does the change in AMH from baseline.

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THE EFFICACY OF ONCO-TESTICULAR SPERM EXTRACTION (ONCO-TESE): A SINGLE-CENTER ANALYSIS.

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OBJECTIVE: Although sperm cryopreservation is recommended before cancer therapy to preserve fertility in adolescent and young adult patients with malignancy, it is not always achieved owing to various causes such as azoospermia or ejaculatory dysfunction. Onco-testicular sperm extraction (Onco-TESE) is an efficient salvage option for such patients; however, only few studies have investigated its efficacy. The aim of this study was to analyze the efficacy of Onco-TESE.

DESIGN: A retrospective study in a single center

MATERIALS AND METHODS: Between June 2012 and May 2020, 373 patients visited our reproductive health center for sperm preservation. Of these patients, 57 (15.3%) could not achieve preservation mainly because of azoospermia at the time of introduction. Among these 57 patients, we retrospectively

evaluated those who underwent Onco-TESE and analyzed their data on background disease, operation time, and sperm retrieval rate (SRR).

RESULTS: Among the 57 patients, 12 (mean age: 26.8 years) underwent Onco-TESE (21.1%). The background diseases were hematological malignancy in 6 patients; testicular cancer in 3; and colon cancer, bladder cancer, and spinal cord tumor in 1 each. Overall, 10 patients showed azoospermia; 2 showed necrospermia, and 2 showed ejaculatory dysfunction. All 6 patients with hematology malignancy were introduced after the initiation of chemotherapy. In patients with testicular cancer, TESE was performed ex vivo simultaneously with orchiectomy. The mean operation time was 71.5±30.7 min. Sperm retrieval was successful in 8 patients (SRR: 66.7%). No postoperative complications occurred.

CONCLUSIONS: Onco-TESE can be considered an efficient and safe option for preserving fertility in cancer patients with azoospermia and ejaculatory dysfunction.

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DOSE DENSE CHEMOTHERAPY PROTOCOLS RESULT IN HIGH RATES OF POI (PREMATURE OVARIAN INSUFFICIENCY) IN YOUNG WOMEN WITH BREAST CANCER. Alexandra Gannon, M.D.,[1] Terri L. Woodard, M.D.,[2] Laurie J. McKenzie, M.D.[2] [1]Baylor College of Medicine, Houston, TX; [2]The University of Texas MD Anderson Cancer Center, Houston, TX.

OBJECTIVE: To assess the reproductive impact of dose dense chemotherapy protocols in breast cancer survivors

DESIGN: Retrospective chart review

MATERIALS AND METHODS: 142 reproductive aged (18-45 years) women were identified at our institution that underwent treatment for a new diagnosis of breast cancer from May 2013 to May 2016. Thirty women received a dose dense schedule of chemotherapy administration and had follow up menstrual data. Dose dense chemotherapy was defined by chemotherapy administration every two weeks as opposed to every three weeks (1). Premature ovarian insufficiency was defined by the absence of spontaneous menses for at least twelve months following completion of chemotherapy. Exclusion criteria was age >40 years, irregular menses or diminished ovarian reserve prior to chemotherapy, zoladex use, premature ovarian insufficiency at onset of chemotherapy, and lack of ovarian reserve testing prior to treatment.

RESULTS: Twenty-one patients met inclusion criteria. Average age of the patients that received the dose dense protocol was 32 (range ages 25-40). All patients received an alkylating agent treatment protocol with a dose-dense administration schedule. All 23 patients received treatment with cyclophosphamide, doxorubicin and a taxane. Five patients also utilized a monoclonal antibody (trastuzumb, atezolizumab, or pertuzumab) and two utilized talazoparib. All patients demonstrated normal ovarian reserve testing prior to the administration of chemotherapy. Average baseline AMH was 4.02 ng/mL (range 1-13 ng/mL) and normal menstrual cycles (range 21-35 days). Premature ovarian insufficiency was reported in 7 of 21 patients (33%) that received dose dense scheduling as defined by absence of spontaneous menses for 12 months or greater.

CONCLUSIONS: Dose dense chemotherapy regimens have recently demonstrated increased disease-free survival in women with high-risk breast cancer compared to conventional dosing schedules (2). However, it is uncertain if this more aggressive regimen of chemotherapy administration would further decrease future fertility in breast cancer survivors. Our findings indicate that dose dense chemotherapy regimens exhibit a high rate of premature ovarian insufficiency in reproductive aged women even in this exceedingly young cohort of women. These findings are important to communicate during fertility counseling of future patients.

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TYPE OF CANCER AND OVARIAN STIMULATION PARAMETERS IN ONCOFERTILITY PATIENTS. Reda S. Hussein, MD, Zaraq Khan, MD, Yulian Zhao, Ph.D. Department of Obstetrics and Gynecology, Mayo Clinic, Rochester, MN.

OBJECTIVE: To evaluate the influence of type of cancer and cancer itself on the ovarian response during controlled ovarian stimulation (COS) for fertility preservation (FP).

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: This was a retrospective cohort study performed at a single academic tertiary-care infertility center. Women diagnosed with cancer who underwent COS with GnRH antagonist protocol between January 2009 and December 2018 were included in this study. Patients were categorized into three groups; breast/gynecologic, hematologic, and other cancers. We secondarily compared the COS parameters and ovarian reserve markers in oncofertility cases against non-cancer patients who pursued FP for deferred reproduction. The primary outcome was number of mature oocytes. Secondary outcomes included oocyte yield (number of retrieved oocytes/number of follicles aspirated at time of retrieval) and oocyte-maturity index, defined as number of mature oocytes/total oocytes retrieved.

RESULTS: A total of 96 cancer patients were referred for FP counseling before starting their anti-cancer therapy. Clinical characteristics and ovarian response parameters were comparable between the three groups. Type of cancer was not a predictor for number of mature oocytes (p=0.33), oocyte-maturity index (p=0.630), or oocyte yield, (p=0.087) after adjustment to cycle covariates. Moreover, cancer did not have impact on the number of mature oocytes (p=0.699), oocyte-maturity index (p=0.251) and oocyte yield (p=0.094).

CONCLUSIONS: There is no difference observed in outcomes of ovarian stimulation based on primary cancer diagnosis in oncofertility patients undergoing FP. Interestingly, no significant impact for cancer itself was observed on ovarian reserve or response to gonadotrophins stimulation.

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CHANGES IN SPERM CONCENTRATION AND TOTAL MOTILITY, BEFORE AND AFTER THAWING IN CANCER PATIENTS COMPARED TO SPERM DONORS. Irving Olaf Morales, M.D.,[1] Roberto Santos, M.D.,[2] Jose I. Obeso Montoya, PhD,[2] Jesus A. Roiz Castro, MD,[3] Karla Alejandra Cantú, M. Sc.[2] [1]IECH-Biología de la Reproducción Humana, Monterrey, NL, Mexico; [2]IECH, Monterrey, NL, Mexico; [3]IECH, Mexico, Monterry, NL, Mexico.

OBJECTIVE: To determine the changes in sperm concentration and total motility, before and after thawing in post-pubertal patients diagnosed with cancer (PDC) compared to a group of semen donors (DS).

DESIGN: Retrospective, comparative, cross-sectional study

MATERIALS AND METHODS: A total of 153 semen samples (DS=85 and PDC=68) from men attending Fertility Center (IECH), Monterrey, Mexico fertility preservation from 2000 to 2018, were evaluated. Sperm analysis was performed according to the World Health Organization (WHO) criteria. Post-thaw differences in concentrations and total motile sperm were determined and the Student's t-test was used for statistical analysis, considering the p value <0.05 to be significant.

RESULTS: Significant differences were recorded in the sperm concentration after thawing: 18.43% vs 9.67%, p <0.05 (from 27.46 to 22.24 million / mL and from 90.54 to 81.78 million / mL, in the PDC versus DS, respectively) and in total motility: 49.30% vs. 36.17%, p <0.05 (from 67.35% to 34.14% and from 94% to 60.75% in PDC versus DS, respectively).

CONCLUSIONS: Patients diagnosed with cancer have a greater reduction in sperm concentration and total motility after thawing compared to the group of semen donors. This finding is important for counseling patients planning sperm cryopreservation.

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ALTERNATIONS OF SPERM PROTEIN PROFILES TO ELUCIDATE THE MECHANISM OF IMPAIRED SPERMATOGENESIS BY CANCER CHEMOTHERAPY. Teppei Takeshima, M.D., Ph.D., Shinnosuke Kuroda, M.D., Yasushi Yumura, M.D., Ph.D. Yokohama City University Medical Center, Yokohama, Japan.

OBJECTIVE: This study aims to analyze alterations in proteomic profiles and validate selected protein biomarkers of spermatozoa in men with history of undergoing cancer chemotherapy.

DESIGN: This research is a cross-sectional research of control versus treatment. A group of patients with a history of anticancer drug

administration in cancer diagnosis was assigned as "cancer group"(n=3), and a fertile donor group was assigned as "control group"(n=3). Written informed consent was obtained from all patients and this study design was approved by institutional review board of Yokohama City University Medical Center.

MATERIALS AND METHODS: The original diseases of cancer group were non-Hodgkin malignant lymphoma(n=2) and malignant soft tissue tumor(n=1). Measuring the total sperm count by CASA, they were adjusted to 6 million in all specimens, and protein concentration was adjusted by BCA assay. After trypsin digestion and desalting, the expressed proteins in spermatozoa were analyzed by LQ-MS/MS and database searching was performed in two groups. Validation was performed for the proteins with different expression levels by Western-blotting.

RESULTS: A total of 1,152 proteins and 5,268 peptides were identified by global proteomics in both groups. Sorted by max fold change of expressions (>5 folds) and ANOVA ($p<0.01$), 29 proteins were identified. Of these identified proteins, we focused on a few proteins, one is cancer-associated protein highly expressed in digestive tract and urinary tract. In sperm of patients with cancer, this protein was overexpressed 54.8-folds more than that of fertile donor. This protein co-works with other protein of T-cell proliferation factor. Regimens of cancer chemotherapy patients in cancer group received were ABVD and IFM, ADM, and VCM therapy, respectively. It was speculated that T cell proliferation was induced by protein interaction after induction of cancer chemotherapy. By the Western-blotting, expression of this protein was validated. Moreover, oxidative stress-associated proteins with different expression levels compared to control were identified, which supported our previous study.

CONCLUSIONS: It was speculated that T cell proliferation was induced by interaction between these proteins after induction of cancer chemotherapy. Moreover, cancer chemotherapy could induce oxidative stress apoptosis in spermatozoa. Functional analysis of these proteins would provide clue to the mechanisms of impaired spermatogenesis after cancer chemotherapy.

SUPPORT: This study was supported by JSPS KAKENHI Grant Number 18K16739.

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FERTILITY-SPARING SURGERY FOR CERVICAL CANCER IN REPRODUCTIVE-AGED WOMEN.

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OBJECTIVE: Historically, radical abdominal hysterectomy with pelvic lymphadenectomy has been the surgical mainstay in nulliparous women of childbearing age with early stage cervical cancer. A number of surgical approaches, have been proposed to allow fertility preservation while still ensuring adequate oncological outcomes. Based on this, our objective is to evaluate if conservative treatment could be an option for patients with cervical cancer who wish to preserve their fertility.

DESIGN: retrospective observational study

MATERIALS AND METHODS: Patients with a histopathological diagnosis of cervical cancer, FIGO stages IA with lymphovascular space invasion through IB3, were included. All patients received conservative surgical treatment between January 2010 and March 2018 with reproductive counseling prior to surgery. Patients with stage Ib3 treated with neoadyuvant chemotherapy needed a reduction in tumor size, demonstrable by magnetic resonance imaging, to less than 2cm in order to be included. A follow-up period of at least 12 months was required. Clinical and oncological leave for pregnancy was only given after one year of disease-free survival.

RESULTS: Nineteen patients were included. Disease-free survival and overall survival during a 5-year period were 94.4% and 100% respectively, with a median follow-up of 45 months. Eleven patients attempted pregnancy after conservative surgery. Pregnancy rate was 63.6%; of these, four (36.3%) were spontaneous pregnancies and three (27.3%) were achieved through in-vitro fertilization, one of which was preformed with cryopreserved ovocytes.

CONCLUSIONS: The results suggest that is possible to offer fertility-sparing surgery in selected patients with cervical cancer. Pregnancy after treatment achieved either spontaneously or through assisted fertilization. Conservative surgery associated with reproductive counseling is an acceptable treatment course for patients wishing to preserve their fertility.

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FERTILITY PRESERVATION WITH IN VIVO OOCYTE RETRIEVAL AMONG YOUNG WOMEN WITH OVARIAN CANCER: A CASE SERIES.

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OBJECTIVE: To examine outcomes of controlled ovarian hyperstimulation (COH) with in vivo transvaginal oocyte retrieval (TVOR) for fertility preservation among young women with ovarian cancer.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: Six patients (mean age 26.3, range 23-31 years) diagnosed with ovarian cancer (endometrioid carcinoma, mucinous epithelial carcinoma, yolk sac tumor, immature teratoma, mixed germ cell tumor (MGCT), and recurrent serous borderline ovarian cancer, n=1 of each) underwent fertility preservation with COH and TVOR at our academic center from 2018-2020. Four patients had stage I disease, and two had stage III germ cell tumors. Five patients had prior unilateral salpingo-oophorectomy, and one (stage I MGCT) underwent prior chemotherapy (4 cycles of cisplatin/bleomycin, vincristine [1 cycle] and etoposide [3 cycles]). Patient and cycle demographics were collected and descriptive statistics were reported.

RESULTS: Five patients underwent oocyte cryopreservation and one elected to freeze embryos. The mean AMH was 2.5 ng/mL (range 0.4-6.4, Table). All cycles used antagonist protocols with hCG trigger; half were random start stimulations. A mean of 11 oocytes were retrieved (range 1-19), with mean 76% maturity. There were no complications or delays in oncology treatment.

CONCLUSIONS: Nearly 12% of ovarian cancers are diagnosed in women <45 years, and ovarian cancers are increasingly managed with fertility preserving surgery when possible.[1,2] This is the first series reporting in vivo TVOR in women with ovarian cancer, whereas prior reports have focused on ex-vivo retrieval or borderline tumors only.[3,4]. Clinicians may discourage in vivo TVOR in ovarian cancer due to risk of tumor spread. In this series, patients either had stage I tumors post-oophorectomy with no residual tumor (n=3), or had known tumor spread (due to cystectomy, or confirmed metastases, n=3); in each case, gynecologic oncologists agreed that TVOR did not confer significant risk of recurrence or upstaging disease. Patients responded well despite prior oophorectomy (mean 13 oocytes, range 4-19). COH with in vivo TVOR can be considered for young women with ovarian cancer following fertility sparing surgery, specifically those for whom TVOR is deemed unlikely to impact their overall cancer prognosis

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FERTILITY PRESERVATION COUNSELING IN REPRODUCTIVE AGED WOMEN WITH LOCALIZED GYN CANCERS AT AN URBAN SAFETY NET HOSPITAL: A PILOT STUDY.

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OBJECTIVE: To determine whether women diagnosed with GYN cancers at an urban safety net hospital, which represents a predominantly African American population, were made aware of the potential impact treating their cancer may have on their future fertility. Specifically, we sought to determine if they were counseled for fertility preservation.

DESIGN: Investigator administered questionnaire via telephone survey.

MATERIALS AND METHODS: Data from The Tumor Registry for Grady Memorial Hospital in Atlanta, GA was sorted by patient age, cancer

type, and tumor staging. Women included were between 18-40 years old with cervical, endometrial, ovarian, and uterine cancer with date of first contact in 2016-2018. We also chose to limit our study population to those with stage 0 or 1 as these patients are more likely to benefit from fertility sparing interventions. All women with prior permanent sterilization were excluded. Currently, there is no formally validated survey on patient satisfaction of fertility counseling in gynecologic cancer patients. As a result, a 6-question survey was created using the American Society of Clinical Oncology and the American Society for Reproductive Medicine counseling guidelines for physicians and was administered to patients.

RESULTS: After review of Grady Memorial Hospital's Tumor Registry, 53 patients met all inclusion criteria. Of these patients, 8 were unable to be reached due to incorrect or disconnected telephone services. An attempt of 2 times was made to contact patients before we deemed them lost to follow up. Of the remaining 45 patients who were able to be contacted, 8 declined to participate in the study. Ultimately, we were able to obtain responses from 9 patients; 6 received some form of counseling informing them of potential effects on their reproductive ability; 3 of 9 were offered resources for fertility preservation; 2 out of 9 were formally referred to a reproductive endocrinologist.

CONCLUSIONS: Unfortunately, our study had a poor response rate and there may be an overestimation of the results applicability to our population. The results of our pilot study showed that a majority of patients receive counseling on the effects of cancer treatment on their future reproductive capabilities. However, although patients may receive adequate counseling, efforts to provide appropriate resources and referrals to patients appear insufficient. Nevertheless, we believe this initial study showed our hospital may be lacking in our efforts to refer patients for appropriate fertility intervention. As a hospital without REI services and a patient population with an income predominately at or below poverty level, there is substantial difficulty in providing for their reproductive potential. This study may highlight the need for more efforts and partnerships with REI offices and safety-net hospitals. The next steps are to sample prior years to better investigate and interpret patient fertility counseling. Also, we aim to evaluate GYN/ONC physicians on the priority of fertility in their decision-making and self-reported average of referrals as compared to GYN/ONC providers in non-urban settings.

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POSTER SESSION: INFERTILITY TREATMENT OUTCOMES

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HOSPITALIZATIONS IN THE 8 YEARS FOLLOWING DELIVERY IN ART-TREATED AND SUBFERTILE WOMEN.

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OBJECTIVE: To investigate hospitalizations up to 8 years after livebirth among women who utilized ART or non-ART medically assisted reproduction (MAR) or who were subfertile with no fertility treatment, compared to women who conceived naturally.

DESIGN: Retrospective cohort

MATERIALS AND METHODS: Massachusetts deliveries among privately-insured women ≥18 years old between 2004-2017 from state vital records were linked to the Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS), and hospital observational/inpatient stays. We compared ART, MAR, and unassisted subfertile (USF) delivery to fertile delivery. Post-delivery hospitalization information was derived from most prevalent ICD codes for discharges and were combined by type. The relative risks (RR) and 95% confidence intervals (CI) of hospitalization for the first 8 years post-delivery were modeled using generalized estimating equations with a log link and a Poisson distribution with person-months as the offset term. Models were adjusted *a priori* for maternal age, parity, year of delivery, and plurality.

RESULTS: Among 492,515 deliveries, 5.6% used ART, 1.6% used MAR, 1.8% were USF, and 91% were fertile.Compared to fertile women, ART, MAR and USF women were more likely to have inpatient or observational hospitalizations for a variety of conditions including conditions of delivery, the cardiovascular system, overweight/obesity, the reproductive tract, the

Indication for hospitalization up to 8 years after livebirth	Fertile	ART	MAR	USF
		RR(95% CI)	RR(95% CI)	RR(95% CI)
Any condition	1.00(Ref)	1.30 (1.26-1.35)	1.21(1.14-1.29)	1.19 (1.12-1.25)
Delivery	1.00(Ref)	1.49 (1.38-1.60)	1.50 (1.33-1.70)	1.22 (1.05-1.42)
Cardiovascular	1.00(Ref)	1.35 (1.24-1.46)	1.31 (1.13-1.51)	1.17 (1.02-1.33
Infection	1.00(Ref)	1.37 (1.19-1.57)	1.21 (0.95-1.54)	1.17 (0.93-1.48)
Overweight/Obesity	1.00(Ref)	1.35 (1.22-1.49)	1.53 (1.29-1.80)	1.44 (1.26-1.65)
Reproductive tract	1.00(Ref)	1.63 (1.48-1.80)	1.54 (1.30-1.84)	1.24 (1.05-1.46)
Digestive tract	1.00(Ref)	1.41 (1.32-1.51)	1.27 (1.12-1.43)	1.31 (1.19-1.46)
Thyroid	1.00(Ref)	2.04 (1.82-2.29)	2.03 (1.67-2.47)	1.62 (1.34-1.97)
Respiratory	1.00(Ref)	1.15 (1.04-1.26)	1.22 (1.03-1.44)	1.24 (1.09-1.42
Diabetes	1.00(Ref)	1.40 (1.17-1.67)	2.11 (1.63-2.74)	1.48 (1.10-1.99)
Cancer	1.00(Ref)	1.40 (1.18-1.65)	1.38 (1.02-1.89)	1.18 (0.90-1.53)

digestive tract, the thyroid, the respiratory system, diabetes, and cancer (Table).

CONCLUSIONS: Women who utilized ART or MAR or who experienced subfertility without treatment were at an increased risk for subsequent hospitalization up to 8 years after delivery because of a variety of chronic and acute conditions.

SUPPORT: NIH R01HD067270

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PUBLIC REPORTING OF CLINICAL OUTCOMES IN ASSISTED REPRODUCTIVE TECHNOLOGY IN THE US FOR 2014-2017: REPORTING TO CDC ONLY IS ASSOCIATED WITH FEWER CANCELLATIONS AND LOWER SUCCESS RATES.

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OBJECTIVE: Reporting of IVF outcomes in the US is mandated by law to the Center for Disease Control (CDC). The Society for Assisted Reproductive Technology (SART) provides a voluntary reporting platform for additional cycle-specific public information. SART submits reported data to the CDC for its members to minimize duplication. Guidelines for both SART and CDC were changed in 2015 and 2016, respectively. We sought to compare outcomes between the reporting platforms prior to and following guideline changes.

DESIGN: Retrospective.

MATERIALS AND METHODS: Publicly available IVF outcomes published by the CDC for autologous oocytes in 2014-17 were compared between mandatory ("CDC only") vs. voluntary clinics ("SART member clinics") using Wilcoxon rank sum tests.

RESULTS: Cancellation was reported more frequently for voluntary reporting clinics (SART members) for both fresh and frozen embryo cycles (Table). Among all fresh cycles, pregnancy rates were lower among SART members vs CDC only clinics for 2014-2016. In contrast, among all frozen embryo cycles, pregnancy rates were higher among SART members vs CDC only clinics for 2014-2016. Similarly, live birth rates were lower for SART member clinics among fresh cycles but higher than CDC only clinics among frozen cycles for 2015-2016. In 2017, fresh and frozen embryo outcomes were combined and SART member clinics had higher success rates.

CONCLUSIONS: Among CDC only clinics, cancellation was less frequent and success rates appeared higher among all fresh cycles. However, success rates were higher for SART member clinics when fresh and frozen cycles were considered together, potentially due to the varying differences in cancellation reported between the two platforms. Increasing transparency in public ART reporting should be encouraged to ensure accurate reporting of all initiated cycles.

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A LONG-TERM FOLLOW-UP STUDY OF HEALTH OUTCOMES OF FAST TRACK AND STANDARD TREATMENT TRIAL (FASTT) PARTICIPANTS COMPARED TO U.S. WOMEN.

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OBJECTIVE: To compare the long-term health of women with unexplained infertility who participated in FASTT to those of U.S. women as reported in NHANES.

DESIGN: Long-term follow-up of randomized controlled trial (RCT) participants.

MATERIALS AND METHODS: In FASTT, from 2001-2006, 503 couples with women aged 21-39 years and unexplained infertility were randomized to 3 cycles of clomiphene citrate (CC)/IUI, 3 cycles of gonadotropin/IUI, then IVF or 3 cycles of CC/IUI prior to IVF. Between March 2019-February 2020 a 22-question telephone survey with branching logic was administered to couples who were enrolled in FASTT. National Health and Nutrition Examination Survey (NHANES, 2017-2018) data for women aged 40-56 years were used to compare data from the current study to the U.S. general population. With regard to mental illness, the NHANES questionnaire asked whether participants had seen a mental health professional in the past year. Analysis was performed using SAS v9.2. Categorical variables were analyzed using chi-square and Fisher's exact tests while continuous variables were analyzed with two-sample t-tests with $P<0.05$ considered significant.

RESULTS: Of the 503 women enrolled in FASTT, 311 (61.8%) were contacted during the current study and 286 (56.9%) consented to participate with an average age of 49.5 ±3.4 years. 120 (42.0%) women reported being diagnosed with a medical condition since FASTT: 45 (15.7%) thyroid disease, 10 (3.5%) diabetes, 5 (1.8%) joint problems, 21 (7.3%) heart disease, 1 (0.4%) stroke, 11 (3.9%) cancer, and 52 (18.2%) mental illness including 40 (14.0%) with anxiety and/or depression. There were no statistically significant differences in development of long-term medical conditions in patients who did or did not have a live birth during FASTT, those who ever conceived a live birth and those who did not, and those who underwent IVF and/or gonadotropin cycles and those who did not. Patients in FASTT were statistically less likely than women in the general U.S. population to report diabetes ($P=0.0001$), joint problems ($P<0.0001$), stroke ($P=0.002$), and cancer ($P=0.005$), and reported a significantly higher incidence of mental illness ($P=0.02$) and heart disease ($P<0.0001$). Women who underwent IVF and/or gonadotropin cycles were less likely than women in the general U.S. population to report a cancer diagnosis (3.3% vs. 8.9%, $P=0.006$).

CONCLUSIONS: The long-term follow-up of women from FASTT demonstrated that patients with unexplained infertility reported more heart disease and consultations with mental health professionals but less diabetes and cancer compared to women in the general U.S. population.

Table 1. Mandatory ("CDC only") vs. Voluntary ("SART members") clinics

	2014		2015		2016		2017≠	
	CDC n=83	SART n=370	CDC n=89	SART n=372	CDC n=82	SART n=375	CDC n=81	SART n=367
Cancellation rate	5.9 (7.5)*	10 (6.9)*	4.9 (6.5)*	11.7 (9.1)*	5 (5.5)*	12.5 (9.4)*	4.9 (5.3)*	7.7 (4.1)*
Pregnancy rate								
Fresh cycles	31.8 (14.4)	33.7 (12.1)	33.7 (18.7)*	29.5 (13.4)*	33.3 (20.8)*	26.1 (12.9)*		
Fresh transfers	40.5 (15.4)*	46.3 (12.5)*	42.6 (18.7)	46 (13.8)	46 (21.3)	45.3 (14.7)		
Frozen cycles	45.7 (22.5)	49 (14.9)	46.3 (23.2)*	51.5 (14.6)*	47.9 (19.4)*	52.8 (12.6)*		
Live birth rate								
Fresh cycles	25.2 (13.4)*	27.9 (11.3)*	26.2 (17.9)	24.4 (11.9)	27.2 (20.5)	21.5 (11)		
Fresh transfers	31.8 (14.8)*	38.1 (12.4)*	32.9 (18.7)*	38.1 (13.3)*	37.2 (21.1)	37.4 (13.8)		
Frozen cycles	34.2 (21.4)*	39.7 (14.2)*	34.6 (21.2)*	42 (13.9)*	37.2 (19.2)*	43 (11.8)*	32.1(14)*	35.9 (10.5)*

Mean (standard deviation). ≠combined fresh and frozen cycles. * denotes $p<0.05$.

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INTRA CAVITY FLUID WITH PREVIOUS CAESAREAN SECTION COMPROMISED CLINICAL PREGNANCY AFTER IVF/ICSI TREATMENT. Xing Yang, Ph.D.,[1] Mei-hong Cai Master.[2] [1]The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; [2]Guangzhou First People's Hospital, School of Medicine, South China University of Technology, Guangzhou, China.

OBJECTIVE: Caesarean section (CS) rates are rising worldwide, the scar is considered to have impact on the subsequent pregnancy. Researchers reported a lower pregnancy rate in patients with a previous CS compared to a previous vaginal delivery, but the potential causes are still to be determined. Lawrenz et al. reported the relationship between intra cavitary fluid (ICF) with uncompromised clinical outcomes on frozen embryo transfer (FET) cycles[1]. The goal of this study was to explore whether the presence of ICF influence the pregnant outcome of patients with CS in fresh embryo transfer cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A total of 1643 women with at least one previous delivery undergoing the first in vitro fertilization / intracytoplasmic sperm injection (IVF/ICSI) cycle and had their fresh embryo transferred during January 2015 to August 2019 in a university-based hospital were enrolled for analysis. According to the previous delivery method and the ultrasound monitoring results——ICF detected on day of embryo transfer, women were separated into three subgroups, cesarean group with intra cavity fluid (CS-ICF, n=114), cesarean group without intra cavity fluid (CS-noICF, n=572) and another 957 patients without ICF were included in vaginal delivered group (VD, n=957). Main outcome was clinical pregnancy rate. Baseline characteristics data, controlled ovarian hyperstimulation procedures and pregnancy outcomes were extracted from medical databases and were compared among three groups. Potential confounders were adjusted by multivariate logistic regression analyses, including age, previous delivery times, body mass index (BMI), failed attempts of IVF, endometrium thickness, embryo quality and stage of development.

RESULTS: Baseline characteristics and the quality of embryos transferred in the three groups were comparable. Less number of embryos were transferred in CS groups than VD group influenced by clinicians' preference($P<0.05$). There was significantly lower clinical pregnancy rate (33.3% vs 45.2%, P=0.015) and twin pregnancy rate (7.9% vs 24.5%) in CS-ICF group compared with VD group, while the rates were comparable between CS-noICF group and VD group. There is a tendency that the live birth rate in VD group is higher than that in CS-ICF group. After adjusted for all the confounding factors listed above, the presence of ICF was an independent factor associated with lower clinical pregnancy rate (OR 0.586, 95%CI 0.375-0.914, P=0.018). Age and ratio of good quality embryos were also associated with clinical pregnancy rate.

CONCLUSIONS: It is the presence of ICF but not the isthmocele per se that significantly compromised the clinical pregnancy rate in patients with CS. CS interferes with the integrity of uterine, ICF may accompany with inflammatory cytokines and potentially pathogenic bacteria, which further disrupt the endometrial receptivity. Large prospective cohort study is required to better understand the potential mechanism and explore effective therapeutic scheme.

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DEVELOPING A MINIMUM DATA SET FOR INFERTILITY RESEARCH. James M. N. Duffy, DPhil MRes PG HCL MBChB BSc (Hons),[1] Cindy Farquhar, FRANZCOG FRCOG MD MPH.,[2] COMMIT: Core Outcomes and Outcome Measure for Infertility Trials[1]Institute for Women's Health, University College London, Greater London, United Kingdom; [2]University of Auckland, Auckland, New Zealand.

OBJECTIVE: To develop a minimum data set, known as a core outcome set, for infertility research.

DESIGN: Consensus development study.

MATERIALS AND METHODS: ***Identifying potential core outcomes:*** Potential core outcomes were identified by extracting outcomes previously reported in infertility trials.

Determining core outcomes: Potential core outcomes were entered into a three-round eDelphi survey. Professionals, researchers and people with infertility were asked to score the importance of each outcome. Based on their feedback, potential core outcomes were prioritised, and subsequently discussed during a consensus development meeting. Using the modified Nominal Group Technique, a minimum data set for infertility was agreed.

Determining how core outcomes should be defined: A long list of potential definitions was developed by identifying definitions which had been reported by formal definition development initiatives, clinical practice guidelines and Cochrane systematic reviews. Potential definitions were discussed in a consensus development meeting. Using a formal consensus development method consensus definitions were developed.

RESULTS: ***Identifying potential core outcomes:*** A long list of 101 potential core outcomes was developed by extracting outcomes reported in infertility trials.

Determining core outcomes: When considering the Delphi survey, 372 participants, from 41 countries, responded. Twenty-eight consensus outcomes were identified and discussed during the consensus development meeting. Thirty participants, from 27 countries, engaged in the consensus development meeting. A minimum data set for infertility research was agreed (Table 1).

Figure 1 A core outcome set for infertility research.

Viable intrauterine pregnancy confirmed by ultrasound accounting for singleton pregnancy, twin pregnancy, and higher multiple pregnancy
Pregnancy loss accounting for ectopic pregnancy, miscarriage, stillbirth, and termination of pregnancy
Live birth
Gestational age at delivery
Birth weight
Neonatal mortality
Major congenital anonmly
When applicable: time to pregnancy leading to live birth

Determining how core outcomes should be defined: Forty-four potential definitions were identified. Twenty-seven participants, from 11 countries, took part in the consensus development meeting and agreed consensus definitions for individual core outcomes.

CONCLUSIONS: Embedding the core outcome set within future infertility research should ensure the comprehensive selection, collection, and reporting of core outcomes, including live birth. Research funders, the SPIRIT statement, and over 80 speciality journals, including *Fertility and Sterility,* have committed to implementing this core outcome set.

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LONG TERM FOLLOW UP OF REPRODUCTIVE OUTCOMES IN FASTT PARTICIPANTS. Denis A. Vaughan, MD,[1] Marlene B. Goldman, ScD,[2] June L. Fung, PhD,[2] Katherine G. Koniares, MD,[3] Carleigh B. Nesbit, DO,[4] Thomas L. Toth, MD,[5] Richard H. Reindollar, MD.[2] [1]Beth Israel Deaconess Medical Center, Boston, MA; [2]Geisel School of Medicine at Dartmouth, Hanover, NH; [3]Tufts Medical Center, Boston, MA; [4]Dartmouth Hitchcock Medical Center, Lebanon, NH; [5]Boston IVF, Waltham, MA.

OBJECTIVE: To evaluate reproductive outcomes in couples who were enrolled in a large randomized controlled trial (RCT, FASTT[1]) that studied optimal treatment for unexplained infertility.

DESIGN: Long term follow up of RCT participants.

MATERIALS AND METHODS: Between March 2019 and February 2020, a telephone survey was administered to women who had been enrolled in FASTT, an RCT conducted from 2001-2006 that evaluated optimal treatment for unexplained infertility in women ages 21-39 years (3 cycles of Clomiphene/IUI and 3 cycles of gonadotropin/IUI prior to proceeding to IVF) versus a fast track (3 cycles of Clomiphene/IUI before proceeding to IVF). All women enrolled in FASTT had a basal FSH <15 mIU/ml. Statistical analyses were performed using SAS v 9.2. Categorical variables were compared between groups using chi-square and Fisher's exact tests and continuous variables with two-sample t-tests and analysis of variance with P<0.05 as significant.

RESULTS: Of the 503 women originally enrolled in FASTT, 311 (61.8%) were contacted of whom 286 (56.9%) consented to participate in the survey. Mean age and mean FSH at enrollment in FASTT was 33.1 ± 3.2 years and 6.8 ± 2.2 mIU/ml respectively, for those who participated in the follow up survey. Mean age at follow-up was 49.5 ± 3.4 years. 194 (67.8%) women delivered a live birth during the trial and 225 (78.7%) continued to try to conceive after FASTT. There were a total of 360 clinical pregnancies, by all methods, with 251 (69.7%) live births. Of those who tried to spontaneously conceive (157), 101 (64.3%) had a successful live birth while a further 12 (5.3%) delivered a live birth via IUI and 82 (36.4%) via autologous oocyte IVF. Overall 182 women (80.9%) achieved a live birth following FASTT with a mean time to conception of 1.4 years (95% CI 1.2-1.6) following the trial. 113 women (77.4%) who had a live birth during FASTT had another live birth after, compared to 69 (87.3%) of those who hadn't had a live birth during FASTT (P=0.08). A higher proportion of those who had a history of smoking did not achieve a live birth in FASTT compared to those who did not have a history of smoking (24/92, 26.1% vs 31/194, 16.0%, (P=0.05), however there was no difference between those who had a history of smoking and those who did not in terms of ever delivering a live birth (4/18, 22.2% vs 50/267, 18.7%, P=0.75. Controlling for age at enrollment to FASTT, a higher basal FSH was noted in those women who never had a live birth (7.9 ± 1.5 vs 6.6 ± 2.2, P=0.05). The time to conception after the trial for those who hadn't had a live birth during the trial was 0.8 (95% CI 0.5-1.2) years compared to 1.6 years (95% CI 1.4-1.9) for those who had a live birth during the trial (P=0.01).

CONCLUSIONS: The majority of couples in FASTT were able to achieve a live birth following the trial with a large proportion of those achieved spontaneously. Independent of age, those women who never had a live birth had a higher FSH at enrollment to FASTT.

Neither the delivery of a baby during FASTT nor the method by which a live birth was achieved determined the couples' ability to achieve a live birth following the trial.

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SUPPORT: None

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LONGITUDINAL FAMILY BUILDING SATISFACTION IN COUPLES ENROLLED IN THE FAST TRACK AND STANDARD TREATMENT TRIAL (FASTT). Carleigh B. Nesbit, DO,[1] Marlene B. Goldman, ScD,[2] June L. Fung, PhD,[2] Katherine G. Koniares, MD,[3] Denis A. Vaughan, MD,[4] Thomas L. Toth, MD,[5] Richard H. Reindollar, MD.[2] [1]Dartmouth Hitchcock Medical Center, Lebanon, NH; [2]Geisel School of Medicine at Dartmouth, Hanover, NH; [3]Tufts Medical Center, Boston, MA; [4]Beth Israel Deaconess Medical Center, Boston, MA; [5]Boston IVF, Waltham, MA.

OBJECTIVE: To investigate factors contributing to long term family building satisfaction in couples enrolled in FASTT from 2001-2006.

DESIGN: Long term follow-up of randomized controlled trial (RCT) participants.

MATERIALS AND METHODS: From March 2019 to February 2020, a telephone survey was administered to couples who had been enrolled in FASTT, an RCT which investigated time to conception and cost effectiveness of conventional treatment for unexplained infertility vs a fast track approach in women ages 21-39 years. The survey contained questions pertaining to long term health and fertility outcomes and was administered by one of three physicians. Statistical analyses were performed using SAS v 9.2. Categorical variables were compared between groups using chi-square and Fisher's exact tests and continuous variables with two-sample t-tests with $P < 0.05$ as significant.

RESULTS: Of the 503 couples enrolled in FASTT, 311 (61.8%) were able to be contacted of whom 286 (56.9%) consented to participate in the telephone survey. The mean age of female participants at enrollment in FASTT was 33.1 ± 3.2 years and mean age at follow-up was 49.5 ± 3.4 years. The majority of couples surveyed reported satisfaction with their current family size (62.1%). Three couples (1.1%) reported continued attempts to expand their family. Couples who reported family building satisfaction were more likely than those who did not to have two (55.7% vs 41.9%), three (27.6% vs 10.5%), four (5.2% vs 0.0%), or five children (0.6% vs 0%) ($P < 0.0001$). Couples who were not satisfied were more likely than those who were satisfied to have one child (40.0% vs 10.9%) or no children (7.6% vs 0%) (P<0.0001). Time to conception was not significantly different between these two groups ($P = 0.28$). Seven couples (2.4%) achieved a live birth using donor oocytes and 14 (4.9%) adopted children. There were no statistically significant differences between couples who were satisfied with their family size and those who were not in terms of number who conceived using donor oocytes (55.6 vs 44.4%, $P = 0.73$) or adopted children (57.1% vs 42.9%, P= 0.95). Family building satisfaction, ultimate family size, and time to conception did not differ between couples enrolled in the conventional or fast track arm. Couples who achieved a live birth through FASTT reported a higher incidence of family building satisfaction than those who did not (66.7% vs 52.8%, P=0.02) and were more likely than those who did not to have two (53.1 % vs 42.9%), three (25.3% vs 11.0%), or four children (4.1% vs 1.1%). Couples who did not achieve a live birth during FASTT were more likely than those who achieved a live birth to have one child (34.0% vs 17.5%) or no children (9.9% vs 0%) (P<0.0001).

CONCLUSIONS: In this long term follow up of 286 couples enrolled in FASTT between 2001 and 2006, the majority reported current satisfaction with their family size. Predictive factors were the achievement of a live birth during FASTT and having $\geq$ 2 children regardless of how families were built.

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LIVE BIRTHS AFTER UTERUS TRANSPLANTATION: REPORT OF THE FIRST SIX DELIVERIES AT A SINGLE CENTER—DUETS (DALLAS UTERUS TRANSPLANT STUDY). Liza Johannesson, MD, PhD,[1] J. Michael Putman, MD,[2] Lilly Zhang, PhD,[2] E. Colin Koon, MD, PhD,[1] Zachary S. Rubeo, MD,[3] Greg McKenna, MD,[1] Johanna Bayer, MD,[1] Jackie York, MD,[1] Giuliano Testa, MD,[1] Anthony Gregg, MD.[1] [1]Baylor University Medical Center, Dallas, TX; [2]Fertility Center Dallas, Dallas, TX; [3]Obstetrix Medical Group of Texas, Fort Worth, TX.

OBJECTIVE: Uterus transplantation is the only treatment that allows women with absolute uterine-factor infertility to experience gestation and childbirth. This is the first detailed report of a series of live births after uterus transplantation from a single center. We describe aggregated pregnancy outcomes including maternal factors and fetal/newborn factors after uterus transplantation.

DESIGN: Retrospective review.

MATERIALS AND METHODS: Twenty women received a uterus transplant at Baylor University Medical Center in Dallas (a tertiary referral center) from 2016 to 2019 (NCT02656550). Data were reviewed retrospectively for pregnancy outcomes, maternal factors, and fetal/newborn factors for the first six patients who reached 20 weeks' gestation.

RESULTS: Among the first six patients who carried pregnancies past 20 weeks' gestation, all uteri were from nondirected living donors. In this

cohort, all recipients underwent uterus transplantation due to congenital agenesis of the uterus (Mayer Rokitansky Kuster Hauser syndrome).

In vitro fertilization was performed before transplantation, and the first attempt at embryo transfer was successful in five of these six recipients (83%) at 15 to 31 weeks postsurgery. The immunosuppression protocol was modified to reduce fetal exposure to medications and allow a shorter transplant-to-embryo-transfer time. No organ rejection was detected during pregnancy. Fetal growth was not impaired, and the median birthweight was 2890 g (range 1770-3140 g [>25th percentile]). Maternal weight gain was higher than Institute of Medicine recommendations. Maternal medical complications were observed in two recipients (elevated creatinine and gestational diabetes). In two recipients, complications led to early delivery (33w1d, elevated creatinine; 30w6d, preterm labor). The median gestational age at delivery was 36w3d (range 30w6d–37w2d). All infants born were healthy, with Apgar scores ≥7 at 1 and 5 min.

CONCLUSIONS: Pregnancy outcomes after uterus transplantation once pregnancy reaches 20 weeks' gestation appear to be favorable. Pregnancy complications that lead to early delivery can occur. Fetal growth and development are expected to be normal, and low birthweight does not appear to a concern in uterus transplantation as in other solid organ transplantations. Uterus transplantation should only be performed at centers with the capability of assembling a multidisciplinary team that can identify and respond to unforeseen complications during pregnancy.

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INTRAVAGINAL EMBRYO CULTURE AFTER LETROZOLE (LTZ) / GONADOTROPIN MILD STIMULATION AND IMMEDIATE ICSI: SINGLE-CENTER OUTCOMES OF 339 AUTOLOGOUS CYCLES IN 252 COUPLES. Karen R. Hammond, DNP, CRNP,[1] Lisa J. Ray, MS, HCLD,[2] Nicholas A. Cataldo, MD, MPH,[1] Cecil A. Long, MD.[1] [1]America Institute for Reproductive Medicine, Birmingham, AL; [2]ART Labs Unlimited, Streamwood, IL.

OBJECTIVE: To describe outcomes in our practice of a novel ART protocol combining mild ovarian stimulation with immediate ICSI and 5-day intravaginal embryo culture.

DESIGN: Practice cohort of all 252 women with 339 cycle starts on this protocol from 6/2018 to 12/2019 planning fresh transfer, who comprised nearly all our ART cycles.

MATERIALS AND METHODS: Couples desiring lower-cost ART, mostly self-referred to our practice. LTZ x5 days, started 4 days after oral contraceptives were stopped, was overlapped on the 5th day with customized dose gonadotropins. No GnRH analogs were used. Cycle monitoring was repeated if necessary before hCG trigger; retrieval was 35 h later under mild sedation in a hospital office. Metaphase (M) oocytes were immediately treated by ICSI and placed with media into an INVOcell (INVO Biosciences, Sarasota, FL), which was secured in the upper vagina by a diaphragm. The device was typically removed after 5 days, and if found, 1-2 blastocysts (blasts) were transferred; otherwise, cleavage-stage embryos were transferred. We calculated descriptive statistics from prospective data including 87 repeat cycles. Ongoing pregnancy includes reaching 24+ weeks' gestation or live birth as of 5/15/2020.

RESULTS: Mean female age was 34.3 (±4.5) yr; 25% had AMH <1.0 ng/mL, 68% were nulliparous, and 43% had prior pregnancy loss(es). Stimulations used 2.5–10 mg/day LTZ (5 mg in 62%) plus 1100 ± 591 units FSH total over a median of 4 days (range 1-10). Only one follicle scan was needed in 78% of cycles. Cancellation rate was 15%. Successful retrievals, defined as obtaining M-stage oocyte(s), were 94% of attempts (M-2 oocytes in 77% of attempts), with a mean of 1.8 M-2 and 1.4 M-1 oocytes. Transfer [of blast(s)] followed 78% [58%] of 272 successful retrievals, with 97% of transfers done on Day 5.

Of 94 pregnancies [pregnancy rate (PR) 32.8% of attempted retrievals], 14 were biochemical, 2 ectopic, and 14 miscarried, with 64 ongoing pregnancies. In women aged 41+ yr, there were 9 retrievals but 0 pregnancies. In women aged less than 41 yr (319 cycles), PR [and ongoing pregnancy rate (OPR)] were 29.5% [20.1%] per cycle start, 35.7% [24.3%] per successful retrieval, and 43.5% [29.6%] per transfer. At least 1 blast was found in 59% of retrieved INVOcell devices. When exactly 1 blast was transferred, sometimes along with an earlier-stage embryo, PR [OPR]/transfer was 49.4% [35.3%] (85 cycles); after 2-blast transfer, PR [OPR] was 61.4% [41.4%] (70 cycles). When only cleavage-stage embryos were found after 5-day culture (N=49), PR [OPR] was 10% [4%]. Twins were 12% of ongoing pregnancies; there were no higher-order multiple pregnancies and there was no ovarian hyperstimulation syndrome. The cost to patients was about 1/3 of typical US ART cycles.

CONCLUSIONS: Our low-cost ART protocol, which includes a LTZ-based mild ovarian stimulation, few monitoring visits, and intravaginal embryo culture, is a promising regimen that also limits excess embryo production and cryostorage needs. These aspects give our protocol the potential to bring about increased access to IVF care.

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IMPACT OF PRE-IVF TSH LEVELS ON PREGNANCY OUTCOMES. Maria Bustillo, M.D,[1] Ineabelle Collazo, BS,[2] Katherine L. Palmerola, MD,[1] Sabrina A. Gerkowicz, MD,[2] Juergen Eisermann, M.D,[1] Nicholas Hendon, BS,[2] Himanshu Arora, PhD.[3] [1]IVFMD, South Florida Institute for Reproductive Medicine, Miami, FL; [2]IVFMD, South Florida Institute for Reproductive Medicine, Miami, FL; [3]University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: Serum thyroid-stimulating hormone (TSH) levels are routinely screened in women with infertility given the negative impact of thyroid disease on ovarian function. Women with clinical hypothyroidism (TSH levels > 4.2 uIU/mL) are treated with thyroid replacement. However, it is unclear whether subclinical hypothyroidism, defined as TSH levels > 2.5 uIU/mL (and </= 4.2 uIU/mL), affects pregnancy outcome. In the present study, we evaluated the IVF treatment/pregnancy outcomes in euthyroid women and in those with subclinical hypothyroidism (both untreated and treated with low dose thyroid replacement) in the years 2016-2017.

DESIGN: A retrospective cohort study

MATERIALS AND METHODS: Patients were categorized into three groups. Group 1, euthyroid, consisted of women who had pre-IVF TSH levels < 2.5 uIU/mL. Individual practitioners decided whether or not to give low dose thyroid supplementation (treatment) to women with TSH levels > than 2.5 but ≤4.2 uUI /mL (subclinical hypothyroidism, SCl hypoT). For that reason, group 2 included women with SCl hypoT who were **not treated,** and Group 3 included women who were **treated**. All women underwent standard IVF protocols following usual individualized practice in our IVF clinic. The relative pattern of IVF outcomes was compared between the three groups. GraphPad Prism (GraphPad Software) was used for statistical analysis. Chi-square test was used to evaluate the differences between the patient cohorts.

RESULTS: A total of 1,160 patients were categorized into Group 1, euthyroid, with 919 women who had pre-IVF TSH levels < 2.5 uIU/mL, Group 2 included 74 women with SCl hypoT who were **not treated,** and Group 3 included 167 women who were **treated**. The overall pregnancy rate was significantly lower in women with SClhypoT without treatment (compared to Euthyroid (p=0.015). However treated women with SClhypoT, group 3 showed no significant differences compared to Euthyroid, group 1 (p=0.237).

* p= 0.015, # p=0.237

CONCLUSIONS: Our findings suggest that subclinical hypothyroidism may impact IVF success and pregnancy outcomes. Low dose thyroid supplementation may be beneficial in patients with sub-clinical hypothryoidism. Further in-depth studies are ongoing considering parameters such as the presence of TPO antibodies, BMI and other specific treatment strategies which may have an additional effect on successful IVF outcomes..

SUPPORT: This work was supported in part by the *IVFMD, South Florida Institute for Reproductive Medicine*

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DAY 7 EMBRYO CULTURE INCREASES BLASTOCYST YIELD FOR DIFFERENT AGED FEMALE PATIENTS. Nancy L. Bossert, PhD,[1] Rebecca L. Krisher, PhD,[2] William B. Schoolcraft, MD,[2] Hannah Van Der Geest, BS,[1] Jason E. Swain, PhD, HCLD.[3] [1]CCRM Minneapolis, Edina, MN; [2]CCRM Colorado, Lone Tree, CO; [3]CCRM IVF Network, Lone Tree, CO.

OBJECTIVE: Traditional embryo culture systems grow embryos for up to 6 days to reach the blastocyst stage. The assumption is that after this point, the potential for good quality blastocyst (GQB) development is minimal. However, studies have recently shown that blastocysts with the ability to support live birth can develop in vitro on Day 7. The objective of this study was to determine whether an extra day of embryo culture may be a source of additional GQBs and if this varied by female age.

DESIGN: Retrospective data analysis.

Female Age	# Patients	Day 5 Total Bast Rate	Day 5 GQB	Day 5/6 Total Blast Rate	Day 5/6 GQB	Day 5/6/7 Total Blast rate	Day 5/6/7 GQB	% Increase in GQB from D7
<30 yrs	22	63.7%[a]	29.5%[ac]	72.2%[ab]	51.6%[ab]	76.2%[a]	52.7%[ab]	1.1%[ab]
30-34	166	61.1%[a]	28.5%[a]	69.7%[a]	50.4%[a]	74.5%[a]	51.1%[a]	0.7%[a]
35-37	152	51.0%[b]	23.5%[bc]	63.4%[bc]	42.7%[bc]	73.0%[ab]	45.2%[bc]	2.5%[b]
38-40	149	47.8%[bd]	19.4%[be]	59.8%[cd]	39.6%[cd]	71.9%[ab]	41.1%[cd]	1.5%[ab]
41-42	61	42.8%[bd]	11.6%[d]	54.4%[df]	31.1%[df]	68.9%[ab]	32.9%[df]	1.8%[ab]
>42	40	36.9%[cd]	12.3%[de]	45.0%[ef]	22.7%[ef]	63.9%[b]	25.6%[ef]	2.88%[ab]

Different superscripts within a column indicicate significant, differences between age groups p<0.01.

MATERIALS AND METHODS: All embryos were cultured in the same fashion, utilizing a sequential culture media system with 10% SPS protein under ~6% CO2, 5% O2. GQBs of grade 3BB or better were cryopreserved on D5 and D6. In an effort to balance desire for additional embryos with laboratory logistics and impact on incubator capacity, any patient with remaining morulae or early stage blastocysts on D6 were kept in culture for one more day to determine if additional blastocysts were available. Blastocyst conversion was compared between various female age groups using one way ANOVA and Bonferroni multiple comparison test.

RESULTS: The number of GQBs decreased as female age increased. In general, each age group was significantly different from all others except for the age group immediately younger in regard to GQB produced on days 5 and 6, as well as days 5, 6 and 7. One extra day of culture increased GQB in all age groups (1.1% <30yrs, 0.7% 30-34yrs, 2.5% 35-37yrs, 1.5% 38-40yrs, 1.8% 40-42yrs, 2.8% >42yrs), although not significantly (p=0.12 overall). However, the increase in GQB obtained from day 7 culture was higher in women 35-37 yrs than 30-34 yrs.

CONCLUSIONS: Female patients in any age group may obtain extra useable blastocysts from a seventh day of embryo culture**.** While this does not mean that every individual patient may result in more blastocysts after culture to day 7, use of an extra day of culture may help obtain extra embryos. The practice of culturing embryos to day 7 may be useful for any patient who has no or lower than expected blastocysts by day 6, to further increase their reproductive potential following IVF.

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WITHDRAWN

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INCIDENCE OF MULTIPLE BIRTHS IN RELATION TO CURRENT REGULATIONS IN TURKEY REGARDING EMBRYO TRANSFER. Semra Kahraman, MD, Prof., Ipek Nur Balin Duzguner, MD, Soner Duzguner, MD, Yucel Sahin, MD. Istanbul Memorial Hospital, Istanbul, Turkey.

OBJECTIVE: The aim of our study is to evaluate the 2010 regulations in Turkey regarding the number of embryos which can be transferred.

DESIGN: This retrospective single center study evaluated single versus multiple births before and after the introduction of 2010 Turkish regulations.

MATERIALS AND METHODS: The study is based on data from Istanbul Memorial Hospital, ART and Genetics Center used to evaluate the 2010 regulations, which restricts the number of embryos to be transferred. According to the regulation; double embryo transfer (DET) is allowable after two unsuccessful attempts in cases up to maternal age of 35 and in any one cycle in cases ≥35.

For the period from March 2003 to June 2019, a total of 31,459 cycles were analyzed to evaluate the overall effect of 2010 regulations.

For the period from January 2014 to July 2019, a total of 4450 cycles were evaluated according to two different ages groups, patients <35 and patients from 35-42 years of age with single or double blastocyst transfer performed in compliance with current regulations.

First the overall effect of the introduction of the regulations on multiple births was evaluated regardless of previous ART attempts and maternal age. Secondly, the clinical results of fresh and frozen-thawed single or double blastocyst transfer in patients <35 years with a history of 2 or 3 previous unsuccessful ART attempts and in patients ≥ 35 (35-42) years with a history of either no previous attempts or 1,2 or 3 attempts were evaluated.

RESULTS: In the first study groups (March 2003 to July 2019), the parameter most significantly affected by the introduction of the regulations was the number of the embryos transferred. The percentage of single embryo transfer (SET) cycle increased dramatically from 14% to 56.6%. However, despite a fall from 32.4%, the incidence of twin births remained high at 15.5%. In the second study groups from January 2014 to July 2019, in young patients <35 years with 2 or 3 previous cycles, the twin birth rate was very high at 47.26 % in the double blastocyst group whereas it was only 1.75% when a single blastocyst was transferred (p=0.0001). In patients ≥ 35 years (35-42) with zero,1,2 and 3 previous cycles, in the double blastocyst transfer group, the twin birth rate was again high at 28.4% whereas in the single blastocyst transfer group it was only 1.8% (p=0.0001). Importantly, there was no statistically significant difference in clinical pregnancy rates between these two groups (67.4% vs 67.5% in the <35 group, and 59.1% vs 54.1% in the ≥ 35 year group) (p=0.846 and p=0.055). Thus, in DET, there was a high risk of twin births and no advantage in terms of pregnancy rates.

CONCLUSIONS: As a result of the wording of the current regulations, there has been a high demand for DET in both young and older patients. Our study strongly suggests that, especially in the light of the success of blastocyst transfer, the Turkish regulations should be amended to limit the use of DET and encourage the use of SET apart from in exceptional cases and particularly in women under 35 years old.

SUPPORT: No financial support

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CESAREAN SECTION: RISK FOR ECTOPIC IN SUBSEQUENT PREGNANCY. Alixandra Domney, M.D., M.P.H.,[1] Stephanie R. Brownridge, M.D.,[2] Christine Mullin, M.D.[2] [1]Department of OBGYN, North Shore University Hospital/Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY; [2]Northwell Health Fertility, North Shore University Hospital/Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: To determine whether history of cesarean section increases the risk of ectopic pregnancy in assisted-reproductive technology (ART) cycles.

DESIGN: Retrospective, case-control study.

MATERIALS AND METHODS: We reviewed all ART cycles at a single academic institution from 2008-2020. Of the 12,000 cycles reviewed, 105 ectopic pregnancies (cases) and 316 intrauterine pregnancies (controls) were identified. Controls were selected by timing of diagnosis of intrauterine gestation in relation to timing of diagnosis of ectopic pregnancies (cases) to ensure laboratory and clinic practice were similar for that time period. Patient characteristics, cycle type, and previous mode of delivery were compared between the two groups using the Student's unpaired t-test and Fisher's exact test as appropriate, with statistical significance set at a p value of <0.05.

RESULTS: No differences amongst the case and control groups were seen in regard to age, FSH, average number of embryos transferred (ET), history of tubal disease, or smoking. As our primary outcome, history of cesarean section bared no significant difference when comparing cases (21%) to controls (21%). Fresh transfers were more likely to result in an ectopic pregnancy when compared to those undergoing a frozen ET (65% vs. 35%, p= 0.0002). An increase in ectopic pregnancy rate was not seen in patients who had a prior cesarean section regardless of embryo transfer type.

Table 1. Comparison of patient and cycle characteristics in Ectopic vs. Intrauterine Pregnancies

	ECTOPIC (N=105)	INTRAUTERINE (N=316)	P-VALUE
AGE (YEARS)	35.0	35.0	NS
MAX FSH (IU/mL)	7.0	8.0	NS
AVERAGE #ET	2.0	2.0	NS
%TUBAL DISEASE	10.0	8.0	NS
%SMOKER	22.0	24.0	NS
%FRESH ET	65.0	43.0	0.0002
%FROZEN ET	35.0	57.0	0.0002
%PRIOR C/S	21.0	21.0	NS
%PRIOR C/S + FRESH ET	10.5	6.0	NS
%PRIOR C/S + FROZEN ET	10.5	15.0	NS

CONCLUSIONS: A history of prior cesarean section does not appear to be a risk factor for subsequent ectopic pregnancy. Moreover, there was not a higher percentage of patients with a history of tubal disease or smoking in women with an ectopic versus an intrauterine pregnancy. However, patients undergoing a fresh ET had a significantly increased chance of an ectopic pregnancy as compared to those undergoing a frozen transfer. Frozen embryo transfers are a potential treatment strategy to lower the risk of ectopic pregnancy in women undergoing ART.

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DOES JUNCTIONAL ZONE (JZ) THICKNESS EFFECT IMPLANTATION AND IN VITRO FERTILIZATION (IVF) SUCCESS RATES IN UNEXPLAINED INFERTIL PATIENTS? Temel Ceyhan, M.D., Professor,[1] Murat Ozekinci, M.D., Associate Prof,[2] Cem Korkmaz, M.D., Professor,[1] Mehmet Sakinci, M.D., Associate Prof,[3] Baris Baykal, M.D.[1] [1]University of Health Sciences, Ankara, Turkey; [2]Memorial Antalya Hospital, Antalya, Turkey; [3]Akdeniz University Hospital, Antalya, Turkey.

OBJECTIVE: To assess the sonographic changes in JZ anatomy during IVF cycles in unexplained infertility and to observe whether sonographic findings are prognostic for IVF outcomes.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: In this prospective study, patients with unexplained infertility were prospectively recruited between January 2012 and December 2012. Exclusion criteria were presence of known cause of infertility including tubal factor, endometriosis, male factor, and decreased ovarian reserve; history of irregular menses, pelvic or uterine surgery, myoma utery or adenomyosis.

JZ anatomy was evaluated with serial transvaginal ultarsonographic meausurements.Transvaginal ultrasound scans of endometrium and JZ were performed on the day of initiation of ovulation induction(day 2), day 7 of ovulation induction, the day of HCG injection, and the day of oocyte retrieval. Measurements of the JZ were done as anterior,posterior and fundal dimensions in sagittal plane. At the end of the treatment, patients who conceived and who did not were compared for junctional zonal changes.

RESULTS: A total of 56 subjects were included in the study. Twenty three pregnant women (mean age: 32,1 $\pm$ 4.1, range 25 to 38) and 33 non-pregnant women (mean age: 30, 1 $\pm$5.0, range 24 to 38) were analysed in the final comparisons. Basic characteristics of the groups in terms of age, duration of ovulation, total dosages of gonodotropines used, number of oocytes retrieved, quality of embryo and number of embryos transferred were similar.

Anterior, posterior, fundal, maximum and mean JZ diameters were meausured. Mean anterior diameter measured on the initiation day among pregnant women was significantly lower compared to non-pregnant women (3.88 $\pm$ 0.77 vs. 4.47 $\pm$ 0.96, p=0.024), JZ thickness on the initiation day was markedly lower and consistently increased during the cycle among women who achieved pregnancy. However, non-pregnant women had higher initial JZ thickness which remained almost similar thereafter. Posterior, fundal, maximum and the mean of all four JZ diameters were similar on the initiation day, Day 7, day of HCG injection and day of oocyte retrieval measurements of these for diameters were all similar in pregnant and non-pregnant women.

CONCLUSIONS: Anterior JZ thickness at the initiation of ovulation induction has some influences on ivf outcomes in unexplained infertile patients. Randomised controlled trials including more patients are required to elucidate the complexity of the 'enigmatic JZ' and its potential effects on reproduction

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EFFECT OF AN ISTHMOCELE ON IVF OUTCOME IN INFERTILE PATIENTS UNDERGOING STIMULATED IVF TREATMENT. Chung-Hoon Kim, M.D., Ph.D., Jei-Won Moon, M.D., Shin Yong Moon, M.D., Ph.D. M Fertility Center, Seoul, Korea, Republic of (South).

OBJECTIVE: This study was performed to investigate the effect of an isthmocele after previous cesarean section delivery on IVF outcome in infertile women undergoing IVF in stimulated cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A total of 104 infertile patinets who underwent IVF in controlled ovarian stimulation (COS) cycles between May 2018 and April 2020 was included in this study. Of 104, sixty-one patients had no isthmocele, a cesarean scar (group 1) but forty-three had an existing isthmocele. Twenty-three patients of 43 had a small isthmocele with residual myometrial thickness (RMT) of 3mm or more (group 2) and 20 had a large isthmocele with RMT less than 3mm (group 3). COS results and IVF outcome were compared among the three groups. Analysis of variance (ANOVA) was used to compare the mean values among three groups. Chi-square test and Fisher's exact test were used for the comparisons of fraction. Statistical significance was defined as $P<.05$.

RESULTS: The demographic characteristics of subjects were comparable among the three groups. There were also no differences in the three groups with respect to the number of oocytes retrieved, mature oocytes retrieved, fertilized oocytes and grade 1 or 2 embryos. However, intracavitary fluid (ICF) in the day of oocyte retrieval was more frequently developed in group 3 (large isthmocele group), compared with group 1 or 2 ($P = .005$ vs group 2, and $P < .001$ vs group 1). Clinical pregnancy rate (CPR) in group 3 was significantly lower than in group 1 ($P = .028$) and also lower than in group 2 with a borderline significance ($P = .080$). Miscarriage rate was similar in three groups. CPR was significantly lower in IVF treatment group with developing ICF than in group without development of ICF ($P < .001$).

CONCLUSIONS: Large isthmocele was associated with developing ICF and had an adverse effect on the IVF outcome in infertile patients undergoing IVF in COS cycles.

SUPPORT: None

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DOES A HISTORY OF UNEXPLAINED INFERTILITY INCREASE THE RISK OF COMPLICATIONS IN SUBSEQUENT PREGNANCIES? A FOLLOW-UP STUDY OF FAST TRACK AND STANDARD TREATMENT TRIAL (FASTT) PARTICIPANTS. Katherine G. Koniares, MD,[1] Marlene B. Goldman, ScD,[2] June L. Fung, PhD,[2] Carleigh B. Nesbit, DO,[3] Denis A. Vaughan, MD,[4] Thomas L. Toth, MD,[4] Richard H. Reindollar, MD.[2] [1]Tufts Medical Center, Boston, MA; [2]Geisel School of Medicine at Dartmouth, Hanover, NH; [3]Dartmouth Hitchcock Medical Center, Lebanon, NH; [4]Boston IVF, Waltham, MA.

OBJECTIVE: To compare pregnancy complications and birth outcomes of live births conceived by couples with a history of unexplained infertility.

DESIGN: Long-term follow-up of randomized controlled trial (RCT) participants.

MATERIALS AND METHODS: In FASTT, from 2001-2006, 503 couples with women aged 21-39 years and unexplained infertility were randomized to 3 cycles of clomiphene citrate (CC)/IUI, 3 cycles of gonadotropin/IUI, then IVF or 3 cycles of CC/IUI prior to IVF. Between March 2019-February 2020 a 22-question telephone survey with branching logic was administered to couples who were enrolled in FASTT. Analysis was performed using SAS v9.2. Categorical variables were analyzed using chi-square and Fisher's exact tests while continuous variables were analyzed with two-sample t-tests with $P<0.05$ considered significant.

RESULTS: Of the 503 women enrolled in FASTT, 311 (61.8%) were contacted during the current study and 286 (56.9%) consented to participate with an average age of 49.5 ±3.4 years. Participants reported a total of 251 live births conceived after participation in FASTT. Of the 251 live births, 129 (51.4%) were conceived spontaneously, 8 (3.2%) via COH without IUI, 13 (5.2%) via COH with IUI, 90 (35.9%) via IVF with fresh or frozen embryos, and 11 (4.4%) via IVF with donor eggs. Among these methods of conception, there were no statistically significant differences in incidence of preterm delivery, low birth weight, gestational hypertension, preeclampsia, gestational diabetes, placental abruption, abnormal placentation, fetal growth restriction, or postpartum hemorrhage. Pregnancies conceived via IVF with fresh or frozen embryos were more likely to result in twins (22.2%) compared with spontaneous conception (2.3%), COH without IUI (0%), COH with IUI (15.4%), and IVF with donor eggs (9.1%), overall $P<0.0001$. However, the number of embryos transferred in pregnancies conceived via IVF is unknown. Survey respondents reported that 27/251 (10.8%) live births conceived after FASTT resulted in a child that is not alive and well today. 18/27 respondents provided diagnoses and although the numbers are small, the most common abnormalities included asthma (n=6), allergies (n=5), autism (n=3), ADHD (n=3), and trisomy 21 (n=2).

CONCLUSIONS: Women with a history of infertility treated with ovarian stimulation with or without IVF are not at increased risk of developing gestational hypertension, preeclampsia, gestational diabetes, abnormal placentation, fetal growth restriction, postpartum hemorrhage, or having a preterm delivery in subsequent pregnancies.

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THE CHANGE IN ANTRAL FOLLICLE COUNT EFFECT ON PREGNANCY RATE IN CONSECUTIVE CONTROLLED OVARIAN STIMULATION AND INTRAUTERINE INSEMINATION CYCLES. Melissa A. Mathes, MD, Elizabeth A. Kastrick, MD, Stephanie Gustin, MD. The University of Nebraska Medical Center, Omaha, NE.

OBJECTIVE: Various methods of measuring ovarian reserve exist, including antral follicle count (AFC). Ovarian reserve tests, as they relate to pregnancy rates, have mostly been studied in IVF populations (1-3). In the few articles available, an AFC minimum of 5 to 7.5 are cited to improve pregnancy outcomes in IUI cycles (4, 5). In addition, there is limited knowledge regarding the change in ovarian reserve tests, specifically AFC, with consecutive cycles of ovarian stimulation for IUI cycles. The aim of this study was to determine if there was a change in AFC in consecutive cycles of patients undergoing controlled ovarian stimulation with IUI and how this impacts pregnancy rate.

DESIGN: A retrospective cohort study of all IUI cycles at a private practice infertility center from June 2014 to May 2018.

MATERIALS AND METHODS: We obtained female characteristics including age, gravida, parity, BMI, AMH, AFC, tubal patency, stimulation medication, number of dominant follicles, endometrial thickness, post-wash semen parameters, and clinical pregnancy rate. Clinical pregnancy was defined by fetal cardiac activity on ultrasound. Our primary outcome of interest was to determine the change in AFC in consecutive cycles and the impact this had on the pregnancy rate. Consecutive cycles were defined as two IUIs <35 days apart. A secondary outcome was the pregnancy rate correlation with AFC. Cycles with no ovarian stimulation medication were excluded when evaluating the effect of consecutive cycles. Cycles greater than 90 days apart were removed from the analysis of consecutive cycles as to decrease the impact of declined ovarian reserve with time. A mixed effects model including AFC change and days between cycles was used.

RESULTS: A total of 999 women with a total of 2169 IUI cycles were included. Over 92% of IUIs were less than 180 days apart. Although not significant, there was a trend of improved pregnancy rate with cycles beginning with AFC >5. Clinical pregnancy OR for AFC 0-5, 6-10, 11-15, and 16-20 were 0.41, 0.79, 0.75 and 0.88 respectively with p-value 0.003, 0.159, 0.068 and 0.443 respectively. Overall, the AFC decreases overtime, approximately 0.006 per day. The AFC change between cycles <35 days apart was -0.6 and in cycles 35-90 days apart was -0.7 with p-value 0.851. The consecutive cycles that did have a decline in AFC had improved pregnancy rates. Clinical pregnancy OR for AFC change -1 to -5, -6 to -10, and -11 to -15 were 1.43, 1.12 and 1.04 respectively with p-value 0.269, 0.756, 0.940 respectively.

CONCLUSIONS: In this study, we sought to determine if there was an effect of AFC change on pregnancy outcomes in consecutive cycles of controlled ovarian stimulation and IUI. We did find an improved pregnancy rate with AFC >5. The small decrease in AFC of 0.006 per day is likely an impact of a decline in fertility with age. There does not appear to be a significant change in AFC when comparing consecutive stimulated cycles to cycles that have greater time between them. Although insignificant, there was a trend in improved pregnancy rates with a decrease in AFC in consecutive cycles. A prospective analysis is needed to further characterize this trend.

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SUPPORT: None

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EFFICACY ANALYSIS OF LETROZOLE AS CO-TREATMENT AGENT IN PROGESTIN-PRIMED OVARIAN STIMULATION PROTOCOL ON PREDICTED NORM/HIGH RESPONDERS. Xiaolan Li, M.D.,[1] Jiawei Cai, M.D.[2] [1]The Sixth Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China; [2]■ ■ ■.

OBJECTIVE: We aimed to evaluate efficacy of Letrozole co-treatment with PPOS in predicted norm/high responders undergoing in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI).

DESIGN: A retrospective cohort analysis.

MATERIALS AND METHODS: Patients adopting PPOS with 5-day Letrozole in our unit between January 2018 and December 2019 in were included in this retrospective study. Inclusion criteria were as follows: ①basal FSH<10IU/L ; ②basal AFC>7 ; ③ basal AMH≥1.1ng/ml ; age <40 years old. For comparison, we enrolled patients using PPOS only as control group. All patients administered Gn () and medroxyprogesterone acetate (MPA) (10mg/d; Shanghai Xinyi Pharmaceutical Co., Shanghai, China) or Utrogestan () from cycle day 3 onward. In study group, 2.5-5mg Letrozole for 5 days were administered daily beginning on cycle day 3. The final stage of oocyte maturation was triggered was triggered with a GnRH agonist or co-triggered by GnRH agonist and hCG, when at least two follicles with ≥18

mm in diameter was observed. ICSI was performed if the concentration of motile sperm was $<1\times10^6$/mL, otherwise a conventional IVF was used. The cycle outcomes were compared between groups. All statistical analysis were conducted using SPSS 25.0. A $P<0.05$ was considered statistical significance.

RESULTS: In total, 267 patients were recruited in study group and 352 in control groups. There were no significant differences in demographic characteristics between groups, such as age, etiologies of infertility, BMI, antimullerian hormone and antral follicles counts ect.. We found similar Gn dose, Gn stimulation day and number of oocyte retrieval (10(9) vs. 10(9), P = 0.178) between two groups. Although estrogen level on trigger day was significantly lower in study group (947.5(910.4)) vs. 604(2712.5) , P<0.001), patents in two groups had comparable incidence of moderate to severe OHSS (2.25% vs. 1.14% for study group and control group respectively ,P =0.341). The percentage of women with profound pituitary suppression (LH level on trigger day < 1 IU/L) was significantly lower in the study group than in the control group ((1.50% vs 7.67%, P < 0.001). In addition, the LH level on trigger day was higher in study group than in the control group (P<0.001), but comparable percentage patients in two groups exhibited a premature LH surge (4.49% vs. 3.13%, P= 0.372). As for laboratory outcomes, 2pn rate was significantly lower in study group (52.90% vs.58.24%, P<0.001)). But no statistical significance were observed in viable embryo rate (P=0.08), rate of top-quality embryo(P=0.358) and blastulation rate (0= .613) between groups.

CONCLUSIONS: For predicted norm/high responders, Adding 2.5-5 mg of Letrozole for 5 days to PPOS protocol could not increase ovarian response and reduce incidence of moderate to severe OHSS. Although Letrozole supplementation in the PPOS protocol effectively alleviated profound pituitary suppression from progesterone administration without interfering with its LH surge blockade effect, it might compromise fertilization of oocyte.

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COST ANALYSIS OF ESTROGEN PRIMING VS MICRODOSE LEUPROLIDE FLARE PROTOCOLS FOR WOMEN WITH DIMINISHED OVARIAN RESERVE UNDERGOING IVF. Nicole D. Ulrich, MD,[1] Nicholas S. Raja, MD,[2] Charley Jiang, MS,[3] Molly B. Moravek, MD, MPH.[2] [1]Reproductive Endocrinology and Infertility, University of Michigan, Ann Arbor, MI; [2]University of Michigan, Ann Arbor, MI; [3]MD/MSCR candidate, Ann Arbor, MI.

OBJECTIVE: Previous studies comparing E2 priming and leuprolide flare IVF protocols report that E2 priming protocols result in longer cycles and higher total gonadotropin dose with similar oocyte yield, fertilization, and pregnancy rates; though, one report suggests a trend toward higher quality embryos in E2 priming cycles. We aimed to compare cost effectiveness between these two cycle types in women with DOR and hypothesized that a leuprolide flare protocol would be more cost effective.

DESIGN: Retrospective cost effectiveness analysis.

MATERIALS AND METHODS: We reviewed all IVF cycles in women diagnosed with DOR with E2 priming protocol or microdose leuprolide flare protocol in an academic fertility clinic by retrospective chart review from January 2016 through February 2020. We included only the first cycle of either type and excluded any cycles cancelled before retrieval. Variables assessed included patient age at retrieval, markers of ovarian reserve, total dose of gonadotropins, cycle length, number of mature oocytes (M2) retrieved, and number of 2 pronuclear embryos (2PN). We calculated total cost based on charge data from number of monitoring visits, estimated medication cost, and relevant procedure codes. The effectiveness was calculated as total M2 per cycle and total 2PN per cycle. We performed a separate cost effectiveness analysis for each measure, M2 and 2PN. Descriptive statistics, cost effectiveness, and t-test analysis were conducted using SAS 9.4. P values <0.05 were considered statistically significant.

RESULTS: We evaluated a total of 182 cycles (149 E2 priming, 33 leuprolide flare). Mean age was 36.8 years in the E2 priming group, and 37.97 years in the leuprolide flare group. There was an average of 6.95 monitoring visits in the E2 priming groups and 6.18 visits in the leuprolide flare group. The cycle length was shorter (p value=0.013) and the total dose of gonadotropins was lower (p value=0.0026) in the leuprolide flare group (11.0 days, 4536.3 IU) vs E2 priming (12.3 days, 5301.7 IU). The mean number M2 per cycle was higher in the E2 priming group (7.06) vs leuprolide flare (5.0) (p value=0.035). The mean number of 2PN per cycle was also higher in the E2 priming group (5.46) vs leuprolide flare (3.48) (p value=0.002). The total cost per cycle was $24,156 in the E2 priming groups and $22,112 in the leuprolide flare group. The cost per both M2 and 2PN was lower in the E2 priming group ($3,209 and $4,424, respectively) than the leuprolide flare group ($4,134 and $6,345, respectively).

CONCLUSIONS: Despite a longer cycle, higher total gonadotropin dose, and higher overall cost per cycle, patients treated with E2 priming protocol in our cohort had a greater mean number of M2 and 2PN, resulting in significantly lower cost per M2 and 2PN. Based on these data, E2 priming appears to be more cost effective than leuprolide flare in women with DOR. Cost effectiveness of medical care is becoming increasingly important in health systems, and application of this type of analysis in the field of reproductive medicine can help increase treatment success, improve allocation of resources, and ultimately increase access to infertility care.

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THE CORRELATION BETWEEN SALINE INFUSION SONOGRAM FINDINGS AND HISTOPATHOLOGY IN THE MANAGEMENT OF INTRAUTERINE FILLING DEFECTS IN INFERTILE PATIENTS. Ramya Sethuram, MD,[1] Alexandra E. Flessel, BS,[1] Lina Fouad, BS,[1] Damla C. Gonullu, MD,[1] Abhijit Mandal, PH.D,[2] Sana Salih, MD.[1] [1]Wayne State University School of Medicine, Detroit, MI; [2]Wayne State University, Detroit, MI.

OBJECTIVE: In infertile patients, the natural course of endometrial polyps remains unclear and the current evidence on their management is mixed. Surgical resection of endometrial polyps is recommended prior to infertility treatment in order to increase natural conception or assisted reproductive pregnancy rates. Hysteroscopic polypectomy remains the gold standard for surgical treatment. However, there is scarcity of literature examining the correlation between ultrasound findings of small polyps or intrauterine filling defects and histology in patients treated for infertility. Our objective is to study the correlation between polyps identified on saline infusion sonogram (SIS) + 3-dimensional transvaginal ultrasound (3D TVUS) with hysteroscopy and histology.

DESIGN: Retrospective study at a university hospital infertility center.

MATERIALS AND METHODS: We performed a retrospective chart review after IRB approval. All patients who underwent surgery at a university health infertility center from July 2019 to Feb 2020 were included. These patients had a diagnosis of filling defect on SIS + 3D TVUS during their infertility work-up. Patients who had prior hysteroscopic intrauterine surgeries were excluded. A total of 33 patients were studied. We compared the results of the SIS + 3D TVUS with the intra operative and histopathology results in patients who underwent hysteroscopic surgery. All the polyps were resected with Truclear device. Statistical analysis was performed with SPSS V24.0

RESULTS: The mean age of the study group was 34 years (±6.2). The mean BMI was 31.8 (±6.3). Of the total of 33 patients studied, 30 patients had an ultrasound diagnosis of polyp based on appearance and vascularity. Of these, 25 (83%) patients we determined to have a polyp < 1cm, rest (n=5, 17%) had a polyp > 1 cm but $\leq$ 2 cm on ultrasound. On hysteroscopy, findings included: intrauterine polyp in 24 (80%) patients; uterine synechiae in 2 (6%); partial uterine septum in 1 patient (3%); (PPV=80% for polyps). Of the 30 patients, 21 (70%) patients had a positive histological correlation for polyp/ fibroid (PPV =70%). Larger polyp sizes did not correlate better with intra operative and histological correlation of findings a polyp (p = 1 for polyps $\leq$ 1 cm diameter and p = 0.9 for polyps > 1 cm but < 2 cms diameter).

CONCLUSIONS: The diagnosis of a polyp using a combination of SIS and 3D TVUS is a good predictor for finding a polyp intraoperatively and in histology. Most of the polyps studied were sub-centimeter polyps. A polyp size larger than 1 cm diameter but < 2cms, as determined by ultrasound, is not a better predictor for finding a polyp intraoperatively and in histology, when compared to sub-centimeter polyps.

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THE APPLICATION OF DROTAVERINE IN IVF-ET FRESH CYCLE: AN ANALYSIS OF 840 CYCLES. Tingting Li, Doctor,[1] Panyu Chen, Master,[2] Cong Fang, PHD, MD.[2] [1]Reproductive Medicine Research Center, Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; [2]The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: To investigate the clinical value of drotaverine in in vitro fertilization-embryo transfer (IVF-ET) for fresh embryo transfer.

DESIGN: A retrospective study.

MATERIALS AND METHODS: A retrospective study was conducted with clinic-based data in the Reproductive Medicine Research Centre of the Sixth Affiliated Hospital of Sun Yat-sen University from May 2017 to May 2018. Patients aged below 40 years old underwent their first or second IVF-ET cycle and transferred 1-2 good embryos with AMH≥1.1ng/ml are involved. A total of 840 cycles were analyzed. All the cycles were divided into 2 groups according to whether they use drotaverine 80 mg bid 1 day before embryo transfer: cycles with drotaverine (Group A, n=352) , cycles without drotaverine (Group B , n=488).

RESULTS: There were no significantly differences with regard to age, BMI, AMH, and number of transferred embryos between 2 groups. Chemical pregnancy rate (64.77% VS 60.71 %) and implantation rate (42.81% VS 36.71 %) of group A and group B was statistically significant different (P<0.05).

CONCLUSIONS: Drotaverine can significantly improve embryo implantation and pregnancy rate for D3 embryo transfer in fresh cycle.

	Group A (n=352)	Group B (n=488)	*P*
Age(y)	31.61±3.736	31.57±3.705	0.987
BMI(kg/m^2)	22.07±3.170	21.93±3.011	0.218
Basal FSH(IU/L)	6.91±1.925	6.91±2.206	0.776
Basal LH(IU/L)	6.625±4.325	5.917±4.255	0.131
Basal E_2(pg/ml)	34.584±12.905	33.941±13.390	0.504
AMH(ng/ml)	3.5±2.035	3.46±3.025	0.904
Number of oocytes retrieved	10.67±4.26	10.85±4.43	0.548
2PN fertilized oocytes	6.92±3.25	7.23±3.52	0.054
Number of transferrable embryo	5.11±2.89	5.32±2.90	0.180
Number of embryo transferred	1.95±0.221	1.95±0.235	0.760
Chemical pregnancy	64.77%(228/352)	60.71%(272/488)	**0.008***
Clinical pregnancy	62.50%(220/352)	54.10% (264/488)	**0.002***
Implantation rate	42.84% (293/684)	36.71% (348/948)	**0.012***

Chemical pregnancy rate=number of biochemical pregnant cycle/number of embryo transfer cycle; Clinical pregnancy rate=number of clinical pregnant cycle/number of embryo transfer cycle; Embryo implantation rate=number of gestational sac/number of embryo transferred; * *P* values < 0.05

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A PILOT STUDY INCLUDING A RETROSPECTIVE ANALYSIS OF DEMOGRAPHIC, CLINICAL, LABORATORY DATA AND PREGNANCY OUTCOMES OF PATIENTS PRESENTED TO OUR ART CLINIC TO ESTABLISH A SUITABLE NATIONALLY AVAILABLE DATABASE. Elif Ece Inceli, Medical Doctor,[1] Nafïye Yilmaz, PROFESSOR,[1] Aytekin Tokmak, Assoc. Prof.[2] [1]Health Science University Turkey, Ankara City Hospital, Ankara, Turkey; [2]Health Science University Turkey, Mersin City Hospital, Mersin, Turkey.

OBJECTIVE: The aim of this study is to present the analysis of demographic, clinical, laboratory datas and pregnancy results of the patients admitted to our hospital's ART clinic for 3 years as an example for the creation of a database in accordance with international standards.

DESIGN: Our study was planned for retrospective analysis of demographic, clinical and laboratory findings and pregnancy outcomes of 1294 cycles of oocyte pick up (OPU) treated at the ART Clinic of Zekai Tahir Burak Women's Health Education and Research Hospital between January 2015 and December 2017. Age, duration of infertility, BMI, indication of ART, basal hormone levels, basal AFC, number of previous IVF cycles, primary or secondary infertility, previous pregnancy, stimulation protocol, number of oocytes collected and studied, number of embryos obtained, transferred, embryo grade, transfer day, TESE application, total progressive motile sperm count (TPMSS), Kruger morphology, pregnancy outcome, delivery type, sex, birth week, birth weight and complication rates of the cycles were evaluated.

MATERIALS AND METHODS: Informed consent was obtained from the patients about ART treatment options, complications and results before treatment. For controlled ovarian hyperstimulation, agonist and antagonist protocols were applied. The data were separated according to age groups and indications. The number of embryos transferred, the day of embryo transfer and the quality of the embryo transferred were grouped and pregnancy outcomes were analyzed.

RESULTS: It is important to present our results in order to collect and access ART data in our country with the parameters included from the international ART data. Overall pregnancy rate per cycle was 28.6% and pregnancy rate per ET was 32.7%. The live birth rate was 20.5% per cycle and 23.4% per ET. A significant correlation was found between patient age and live birth rates, live birth rates decreased with increasing age of women (p: 0.004). When the live birth rates were examined according to the indications, live birth rates per ET were significantly higher (37.3%) in the ovulatory disfunction group compared to the other groups (p <0.001). In the male factor group, there was a statistically significant difference between the rates of live birth between cycles with TESE procedure (17.9%) and cycles without TESE procedure (27%) (p <0.001). There was a significant difference between twin live birth rates according to the number of transferred embryos, 0.2 % in single ET group and 5.2 % in double ET group (p: 0.001). Clinical pregnancy and live birth rates were similar in transfers of D4 and D5 embryos. Live birth rates were higher in D5 embryo transfer cycles (32.3%) compared to embryos at other stages (p: 0.004). The clinical pregnancy and live birth rates were significantly higher in Grade 1 group (31.2%) compared to Grade 2 group (18%). (p <0.001).

CONCLUSIONS: Pregnancy results of our clinic were observed to be highly similar to the literature. In order to establish a standardized national database in the centers that applying ART in our country, datas of the clinics should be analyzed with international standards.

SUPPORT: None.

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OUTCOMES AFTER ADJUNCT GROWTH HORMONE TREATMENT WITH A LOW, INTERMEDIATE, OR HIGH DOSE PROTOCOL IN IVF CYCLES WITH POOR RESPONDERS. Reeva B. Makhijani, MD,[1] Stephanie M. Hallisey, MD,[1] Prachi N. Godiwala, MD,[2] Chantal Bartels, MD,[1] Daniel R. Grow, MD,[1] Lawrence Engmann, MD,[1] John Nulsen, MD,[1] Claudio A. Benadiva, MD.[1] [1]University of Connecticut Health Center, Center for Assisted Reproductive Services, Farmington, CT; [2]University of Connecticut Health Center, Center for Advanced Reproductive Services, Farmington, CT.

OBJECTIVE: Adjunct growth hormone (GH) is used in poor responders to improve IVF cycle and pregnancy outcomes. There is no consensus on the ideal GH protocol. We compared the extended low, intermediate, and high dose GH protocols used at our center to determine if there was a difference in IVF and pregnancy outcomes.

DESIGN: Retrospective cohort study of women age 26-46 who underwent IVF with adjunct GH from 2013-19 at our center.

MATERIALS AND METHODS: Patients were divided into three groups according to GH protocol: 1) extended low (0.35 IU GH daily for ~30 days before IVF stimulation and with stimulation until day of trigger); 2) intermediate (4.7 IU GH daily for 10 days with stimulation); or 3) high (8.7 IU GH daily for 10 days with stimulation). Primary outcome was ongoing pregnancy or live birth rate (OPR/LBR) per cycle start for fresh transfer or primary frozen-thawed embryo transfer (FET) following a freeze-all cycle. Secondary outcomes were implantation rate (IR), clinical pregnancy rate (CPR), multiple pregnancy rate (MPR), and clinical loss rate (CLR). Subgroup analysis was done for primary euploid blastocyst FET cycles. One-way ANOVA and chi-square tests were used to compare continuous and categorical variables, respectively. A two-sided p-value of 0.05 was considered statistically significant.

RESULTS: 267 patients were included for analysis (low, n=71; intermediate, n=123; high, n=73). There was no significant difference in baseline or IVF cycle outcomes including age, BMI, AMH, number of previous cycles, number of oocytes retrieved, fertilization rate, number of day 3 embryos or blastocysts, use of PGT, number of freeze-all cycles, or cancellation rate between groups. There was no significant difference in OPR/LBR, IR, CPR, MPR, or CLR for fresh transfer or primary FET of euploid or non-PGT tested embryos (Table 1). Subgroup analysis of primary euploid blastocyst FET also showed no difference in OPR/LBR or proportion of cycles with euploid embryos available for transfer between groups.

Table 1. Overall Cycle and Pregnancy Outcomes

Pregnancy Outcomes	Extended low Dose	Intermediate Dose	High Dose	p-value
No. oocytes retrieved (n ± SD)	7.3 ± 2.8	7.7 ± 5.4	8.0 ± 5.5	0.81
No. day 5 blastocysts (n ± SD)	1.4 ± 1.5	1.4 ± 1.8	1.4 ± 1.8	0.97
Cancellation rate (%, n)	23.9 (17/71)	26.0 (32/123)	17.8 (13/73)	0.42
IR (%, n)	30.4 (21/69)	25.6 (31/121)	23.2 (16/69)	0.61
CPR (%, n)	26.1 (18/69)	24.0 (29/121)	20.3 (14/69)	0.72
OPR/LBR (%, n)	26.1 (18/69)	20.7 (25/121)	15.9 (11/69)	0.34
MPR (%, n)	16.7 (3/18)	17.2 (5/29)	21.4 (3/14)	0.93
CLR (%, n)	0.0 (0/18)	13.8 (4/29)	21.4 (3/14)	0.15

CONCLUSIONS: There was no significant difference in IVF cycle or pregnancy outcomes between GH protocol groups. Low dose protocols may be preferred to reduce the additional cost of adjunct GH.

SUPPORT: None.

POSTER SESSION: THIRD PARTY REPRODUCTION

P-400 4:30 PM Sunday, October 18, 2020

CYTOMEGALOVIRUS IMMUNOPOSITIVITY DOES NOT CORRELATE WITH ABNORMAL SPERM PARAMETERS WITHIN A LARGE SPERM DONOR POPULATION.

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OBJECTIVE: Studies have shown that cytomegalovirus (CMV) can be detected in sperm samples [1-3]. CMV infected cultures of human testes have been shown to have decreased number of precursor sperm cells when compared to uninfected cultures [4]. However, there is conflicting evidence about the association between CMV infection, sperm quality, and reproductive potential [2, 5-7]. This study aimed to assess the association between CMV immunopositivity in sperm donors and sperm quality.

DESIGN: Retrospective study.

MATERIALS AND METHODS: The study included male sperm donors between November 2007 and December 2017. Group A included donors who tested CMV IgG+ within a month of first donation. Group B included donors who tested IgG- for the duration of all donations. The following sperm parameters were collected at donation: BMI, age, total sperm count (M), total motile sperm (M), average motility (% of total sperm, motile), and average concentration (M/mL). The association between IgG status and donor parameters was calculated with Student's t-tests or Wilcoxon rank-sum tests. The association between IgG status and sperm quality was evaluated using a general estimate equation (GEE) model to account for the repeated donations per donor.

RESULTS: A total of 1310 sperm donors participated in the study. CMV IgG+ donors (n=394) were compared to CMV IgG- donors (n=916). Demographic factors and sperm parameters at the initial visit are shown (Table 1). CMV IgG status did not affect sperm parameters when accounting for all of a donor's donations: total sperm count (β=-8.89, p=0.16), total motile sperm (β=-5.79, p=0.25), average motility (β=0.47, p=0.36), and average concentration (β=2.68, p=0.18). Controlling for age and BMI, the effect sizes trended upwards but did not reach statistical significance: total sperm count (β=-10.02, p=0.12), total motile sperm (β=-6.44, p=0.21), average motility (β=0.55, p=0.28), and average concentration (β=2.92, p=0.15).

CONCLUSIONS: This study of sperm donors demonstrated that immunological evidence of prior CMV infection does not significantly correlate with sub-optimal sperm parameters. Reproductive medicine practitioners can be reassured that CMV IgG+ status does not significantly impact sperm parameters when compared to CMV IgG- status.

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SUPPORT: None

P-401 4:30 PM Sunday, October 18, 2020

MOTIVATIONS OF SPERM DONORS.

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Table 1. Donor Parameters at Initial Visit

Donor Parameters	Total	CMV lgG+	CMV lgG-	p-value
Age	26 (23,29)	26 (24,30)	25 (23, 29)	0.002
BMI	24.3 (22.5, 26.1)	24.3 (22.4,26.4)	24.3 (22.5, 26)	0.35
Total Sperm Count (M)	245 (171, 340.2)	232.6 (156, 335.8)	250.4 (177.4, 346.8)	0.02
Total Motile Sperm (M)	183.7 (124.3, 253.4)	173.2 (112.9, 247.5)	186.5 (129, 259.9)	0.02
Average Motility (%)	75 (69, 82)	76 (69, 81)	75 (69, 82)	0.92
Average Concentration (M/mL)	80 (62, 103)	77 (61, 99)	80 (62.5, 104)	0.18

OBJECTIVE: The limited knowledge base on sperm donors' motivations includes mostly international studies with small sample sizes [1-6]. In the decades since its inception, sperm donation has shifted from an anonymous physician-led process for infertile heterosexual couples to a holistic process led by the prospective parents, including single mothers by choice and the LGBTQ community, who often request a better understanding of a sperm donor's motivations [7]. The objective of this study was to investigate the association between sperm donor motivations and demographic factors such as age, decade of birth, and highest level of education.

DESIGN: Multi-center, retrospective cohort study.

MATERIALS AND METHODS: The motivations of U.S. sperm donors aged 18-39, from 2008-2010 and 2016-2018, were coded according to the following four categories: financial, desire to pass on genes, general altruism, and personal altruism (i.e. a personal experience inspired the donor). Primary, secondary, and tertiary motivations were included when multiple reasons were cited. Donors were excluded if their motivation did not fit within one of the four categories. Data on age, decade of birth (1970's, 1980's, and 1990's), and highest level of education (Undergraduate/Associate's, Bachelor's, Master's, Doctorate degrees) at the time of donation was also collected. Continuous and categorical measures were compared using a Kruskal-Wallis test and Fisher's exact test, respectively.

RESULTS: A total of 586 sperm donors aged 26.90 $\pm$ 4.54 participated in this study. The most commonly cited motivations were financial and general altruism. 65.02% (n= 381) of donors cited financial as their primary, secondary or tertiary reason, while 27.65% (n=162) of donors selected general or personal altruism as their primary reason with no other reason. Age was significantly associated with primary motivation with a median age of 26 for financial, general and personal altruism, while 30 was the median age for the desire to pass on genes (p=0.0002). Financial and general altruism were the most cited motivations for every decade of birth; general altruism decreased in frequency and financial increased in frequency with every decade (p=0.0026). The highest level of education was not significantly associated with the primary motivation among all ages (p=0.017).

CONCLUSIONS: This robust study of sperm donors demonstrated that financial and general altruism were the most commonly cited motivations, though financial was a prominent motivating force for approximately 2/3rd of donors (65.02%), whereas altruism was the only motivating force for less than 1/3rd (27.65%) of donors. We also noted a generational gap, wherein older generations appeared more altruistic as compared to younger generations. Additionally, donors who expressed a primary desire to pass on genes were significantly older (30.00 (26.00,34.00); p=0.0002). In conclusion, our study is part of ongoing longitudinal research into the sociology surrounding sperm donation — research that is crucial as modern families become more common and donor-conceived offspring come of age.

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SUPPORT: None

P-402 4:30 PM Sunday, October 18, 2020

DOES SHIPPING IMPACT CRYO-SURVIVAL OR USABLE EMBRYO RATES DERIVED FROM VITRIFIED DONOR OOCYTES?. Jenna Friedenthal, MD,[1] Joseph A. Lee, BA,[2] Wayne Caswell, MS,[3] Melissa O. Stratton, BA,[4] Christine Briton-Jones, PhD, HCLD,[2] Alan B. Copperman, MD.[1] [1]Icahn School of Medicine at Mount Sinai, New York, NY; [2]Reproductive Medicine Associates of New York, New York, NY; [3]Donor Egg Bank, USA, Rockville, MD; [4]Donor Egg Bank, USA, Rockville, NY.

OBJECTIVE: Over the last decade, there have been significant advancements in oocyte cryopreservation (OC) and increased utilization of vitrified oocytes (VOs) within modern assisted reproduction technology (ART). While donated oocytes (DOs) have for decades been utilized to treat patients who cannot produce viable oocytes, access was limited by local availability. However, with the expansion of DO banks nationwide resulting from improvement in OC technology, women may now select DOs from across the country. The advantages of a nationwide DO bank rely upon shipping VOs between centers. Concern has been raised regarding the potential impact of temperature fluctuations in the process of shipping on VOs [1], with evidence suggesting that temperature fluctuations may be detrimental to the spindle complex and oocyte integrity[2,3]. The objective of this study was to evaluate the impact of shipment on the clinical potential of donated VOs.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The study included VOs from a DO bank network from 2012-2019. Following oocyte retrieval, oocytes were vitrified and allotted into cohorts of 6 or 7 eggs (oocyte lots). VOs were categorized as Internal or External. Internal: warmed and utilized in the same laboratory. External: transported to a second location where warming, fertilization, embryo culture, embryo transfer and embryo vitrification occurred. Internal oocytes were stored in standard liquid nitrogen storage dewars at -196 ^{o}C until warming; external oocytes underwent 1-2 days of shipping, held in vapor-based dry shippers and monitored to alert if temperatures rose above -150^{o}C until they were transferred into standard liquid nitrogen dewars at recipient laboratory. Baseline demographics were obtained:donor age, number of oocytes retrieved, and number of metaphase II (MII) oocytes retrieved. The primary outcome was oocyte thaw survival rate (OTSR). Secondary outcomes were fertilization rate (FR), total number of usable embryos (UEs), and usable embryo rate (UER). UEs were defined as embryos available for transfer or cryopreservation based on developmental stage and a given fertility center's standard operating procedure. Data were analyzed using t-tests and Wilcoxon signed-rank test, with P<0.05 considered significant.

RESULTS: 248 internal oocyte lots and 5,202 external lots were thawed during the study time and were included in analysis. No significant differences were observed in donor age, number of oocytes retrieved, number of MII oocytes retrieved, or maturation rate. There was no difference in OTSR between Internal and External cohorts (91.41% vs 89.72%, P=0.12). There were also no differences in FR, the total number of UE, or UER.

CONCLUSIONS: Shipping of donated VOs does not adversely affect oocyte cryo-survival. Additionally, we found that shipping had no impact on either FR or the number of UEs. Our results indicate that vapor-based dry shippers maintain VOs in a comparable state to liquid nitrogen for the period they are in transit. Future studies should aim to investigate the impact of transport on precise molecular markers for oocyte integrity.

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SUPPORT: None

P-403 4:30 PM Sunday, October 18, 2020

OCCURRENCE OF SECONDARY FINDINGS DURING UNIVERSAL CARRIER SCREENING FOR EGG DONOR CANDIDATES. Amber Gamma, MS, CGC, Mary Rausch, MD, Jeanette Tomasino, Ph.D., Marie Marella, RN, BSN, Marianne Farkas, RN, BSN. Northwell Health Fertility, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: Describe the frequency of secondary findings, specifically risks to autosomal recessive disease carriers, during genetic screening of candidate egg donors at one academic fertility clinic.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: All fresh egg donor candidates or repeat fresh egg donors presenting for donation between August 1st, 2018 and February 1st, 2020 underwent genetic screening, including three-generation pedigree, hemoglobinopathy evaluation, karyotype and universal carrier screening. Universal carrier screening included >100 conditions and was performed at one of two commercial laboratories. Results were evaluated

Table 1. Secondary findings identified in potential fresh egg donors undergoing genetic screening

Gene	Associated Disorder	Associated Carrier Risks	# of Identified Donors
ATM	Ataxia-telangiectasia/hereditary susceptibility to breast cancer	Increased risk for female breast cancer. Possible increased risk for pancreatic, prostate and ovarian cancers.	1
LDLR	Familial hypercholesterolemia	Significantly increased cholesterol levels and risk for heart attack prior to 50	2

by the genetic counselor and communicated to the candidate by phone with follow-up documentation sent by mail. Those candidates carrying X-linked conditions or with secondary findings were excluded from donation. Appropriate medical follow-up was recommended as necessary.

RESULTS: A total of 44 fresh egg donor candidates began or completed genetic screening during the study time period. Three candidates were excluded based on family history and one candidate did not complete blood draw for genetic testing. Forty candidate donors completed universal carrier screening. 26 of 40 candidate donors (65%) were a carrier of at least one condition. 4 of 40 (10%) were excluded based on their universal carrier screening with 3 of these individuals (11.5%) having secondary findings that included increased risk for cancer(s) and increased risk for cardiovascular disease (see Table 1). Two of these three individuals reported no family history of associated disease symptoms.

CONCLUSIONS: When performing universal carrier screening for fresh egg donor candidates, secondary findings are not uncommon and may not be readily apparent from family history information. These results must be taken into account when evaluating donor screening and choosing to accept a donor. Candidate donors must also be counseled about the potential health information that could be discovered on universal carrier screening and should be informed of appropriate follow-up.

P-404 4:30 PM Sunday, October 18, 2020

EXAMINING PREDICTORS OF PREGNANCY-RELATED COMPLICATIONS AMONG GESTATIONAL CARRIERS. Erika L. Fuchs, PhD, MPH, Abbey B. Berenson, MD, PhD. University of Texas Medical Branch, Galveston, TX.

OBJECTIVE: The purpose of this study was to examine associations between demographic characteristics and pregnancy-related complications in gestational carriers.

DESIGN: A cross-sectional online survey was conducted.

MATERIALS AND METHODS: From November 2015-February 2016, women ≥18 years living in the United States who delivered at least one baby in 2009 or later as a gestational carrier (n = 204) completed an online survey. Potential predictors of labor, delivery, and postpartum complications were examined using chi-squared tests, Fisher's exact tests, t-tests, and multivariable adjusted logistic regression. Logistic regression models were adjusted for age at delivery, race, Hispanic ethnicity, relationship status, household income, type of health insurance, and whether a third-party reproduction agency was used throughout the process. Statistical analyses were conducted using Stata SE Version 16.1 with α=0.05.

RESULTS: Pregnancy-related complications were reported by 53% of participants. Over one third (36.8%) of participants delivered by cesarean section. The most common complications were preterm labor (14.7%), preterm premature rupture of membranes (9.3%), postpartum hemorrhage (7.8%), high blood pressure (7.4%), and gestational diabetes (6.4%). In bivariate analysis, there were few associations between health outcomes and demographic characteristics. In multivariable analysis, increased age was associated with self-reported gestational diabetes (odds ratio 1.14, 95% confidence interval 1.01-1.28).

CONCLUSIONS: Demographic characteristics were infrequently associated with pregnancy-related complications among gestational carriers.

SUPPORT: Dr. Fuchs is a scholar supported by a research career development award (K12HD052023: Building Interdisciplinary Research Careers in Women's Health Program –BIRCWH; Principal Investigator: Berenson) from the Office of the Director at the National Institutes of Health.

P-405 4:30 PM Sunday, October 18, 2020

CLINICAL FACTORS ASSOCIATED WITH EGG DONORS UNDERGOING ADDITIONAL OOCYTE DONATIONS AFTER THEIR FIRST DONOR CYCLE. Diane Tober, PhD,[1] Kevin S. Richter, PhD,[2] Shannon Kokjohn, MSc,[3] Natalia Villegas, BS,[4] Katarina Cook, BS,[4] Raquel Cool, BA,[5] Kezia Mostak, MS,[4] Cristina Garibaldi, MS,[4] Cris Zubizarreta, BA,[4] Said Daneshmand, MD.[3] [1]UCSF Institute for Health and Aging, San Francisco, CA; [2]Fertility Science Consulting, Silver Spring, MD; [3]San Diego Fertility Center, San Diego, CA; [4]University of California, San Francisco, San Francisco, CA; [5]We Are Egg Donors, Santa Cruz, CA.

OBJECTIVE: To examine how experiences of adverse effects related to oocyte donation affect egg donors' decisions to donate again.

DESIGN: Survey.

MATERIALS AND METHODS: Oocyte donors (n=318) in the US were surveyed regarding adverse clinical events associated with their first donation, and the subsequent probability that they undergo additional donations after their first. Donors providing eggs to a friend or relative were excluded.

RESULTS: Patient-reported severity of ovarian hyperstimulation syndrome (OHSS) experienced during egg donors' first oocyte donation cycle was significantly associated with the frequency of donors opting to undergo additional donor cycles after their first. The proportion of egg donors choosing to undergo additional donations declined with increasing severity of OHSS in their first donor cycle; 89.1% for no OHSS (n=64), 83.8% for mild OHSS (n=142), 73.2% for moderated OHSS (n=82), and 66.7% for severe OHSS (n=30) (p=0.0015, Kendall's test for significant association). Donors reporting migraine/headaches, missed work due to complications associated with their donation, insufficient anesthesia during oocyte retrieval, or surgical complications during their first donation were all significantly less likely to undergo a second donation (Table).

	Proportion of patients undergoing repeat cycle(s) according to presence or absence of adverse events during first donation		
Adverse Event	Yes	no	*P*-value (C^2)
Migraine/headaches (n=51)	62.7%	83.9%	0.00048
Missed work due to complications (n=41)	58.5%	83.8%	0.00014
Insufficient anesthesia (n=12)	50.0%	81.7%	0.0065
Surgical complications (n=14)	42.9%	82.2%	0.00028

CONCLUSIONS: Experiences of adverse effects related to oocyte donation reduce the likelihood that an egg donor will donate again. The lowest frequency of second donations was observed among egg donors who experienced surgical complications or who reported insufficient anesthesia during the oocyte retrieval, both of which were associated with a repeat donation rate of 50% or less.

SUPPORT: This study was supported by the University of California, San Francisco, Institute for Health and Aging; UCSF Individual Investigator Grant (#7501159); and funding from the National Science Foundation (#1828783).

P-406 4:30 PM Sunday, October 18, 2020

PERINATAL OUTCOMES IN RECIPROCAL VS. ANONYMOUS DONOR OOCYTE IVF CYCLES. Devora Aharon, MD,[1] Lucky Sekhon, MD,[2] Joseph A. Lee, BA,[2] Jeffrey Klein, MD,[2] Matthew A. Lederman, MD,[2] Beth McAvey, MD,[1] Alan B. Copperman, MD.[1] [1]Icahn School of Medicine at Mount Sinai, New York, NY; [2]Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Pregnancies in donor egg recipients are associated with a higher risk of adverse perinatal outcomes, potentially due to immunologic reactions to a foreign oocyte resulting in impaired placentation.[1-3] Reciprocal IVF in same-sex female couples involves the use of a patient's oocyte to create an embryo that is transferred to the their partner to conceive a pregnancy.[4] In reciprocal IVF (Co-IVF), the oocyte comes from a familiar source to which the recipient may have developed a level of immune tolerance. Whether Co-IVF might mitigate perinatal risks seen with donor oocyte IVF has never been studied. The objective of this study was to compare the perinatal outcomes of pregnancies conceived from Co-IVF in same-sex female couples and anonymous donor oocyte IVF.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Oocyte recipient transfer cycles from January 2011 to June 2019 were included in the study. Co-IVF recipient cycles were compared to anonymous donor (AD) oocyte recipient cycles. Demographic and cycle characteristics including recipient age, oocyte age, parity, endometrial thickness, fresh vs. frozen embryos, fresh vs. frozen oocytes, euploid transfer, and high quality embryo transfer were compared between the groups. Primary outcomes were gestational age at delivery, preterm birth, birth weight, low birth weight (<2500g), and macrosomia (>4000g). Comparative statistics and adjusted logistic and linear regression were used for analysis.

RESULTS: A total of 2620 oocyte recipient cycles were identified and included in the study, of which 108 were reciprocal IVF cycles and 2512 were anonymous donor cycles. Recipient age was significantly lower among Co-IVF compared to AD recipients, while oocyte age was significantly higher. Co-IVF recipients had significantly lower parity and thicker endometrial lining at transfer, and were less likely to use frozen oocytes and to transfer a high-quality embryo. The groups had similar rates of frozen embryo and euploid embryo transfers. Live birth rate was similar between the groups. Gestational age at delivery was significantly higher among Co-IVF recipients compared to AD recipients. No significant differences were seen in preterm birth rate, birth weight, low birth weight, or macrosomia. On multivariate logistic regression, no significant differences were seen in gestational age at delivery (β=0.217, p=0.64), preterm birth (OR 0.84, 95% CI 0.15-4.74, p=0.84), birth weight (β=120.84, p=0.72), low birth weight (OR 0.95, 95% CI 0.16-5.59, p=0.86), or macrosomia (OR 1.18, 95% CI 0.95 0.19-7.41, p=0.86) when controlling for confounders.

CONCLUSIONS: Our study demonstrates similar perinatal outcomes among Co-IVF and AD oocyte recipients. This data suggests that the non-autologous oocyte induces a similar immunologic reaction within the recipient even when derived from a familiar source. Further study should investigate the mechanism behind adverse perinatal outcomes in donor oocyte recipients. Identification of markers associated with immunological acceptance and compatibility may serve as the basis for optimizing anonymous donor selection.

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SUPPORT: None

P-407 4:30 PM Sunday, October 18, 2020

ATTITUDES OF OOCYTE DONORS AND NON-DONORS TOWARDS THEIR GENETIC MATERIAL. Julia Taylor Woodward, PhD,[1] Katherine E. MacDuffie, PhD.[2] [1]Duke University Health System, Durham, NC; [2]University of Washington, Seattle, WA.

OBJECTIVE: The decision to donate gametes is distinct from other donations such as blood or organs given the permanent genetic link created between the donor and any resulting offspring. As the demand for donated oocytes continues to outpace the available supply, efforts to recruit and retain donors would benefit from a more precise understanding of how women conceptualize the donation of their genetic material. The goal of the current study was to explore sociodemographic and psychological factors related to women's willingness and intention to donate oocytes.

DESIGN: A quantitative survey was developed and administered online to a group of women who applied to be oocyte donors ($n = 104$) and a demographically-matched comparison sample ($n = 104$).

MATERIALS AND METHODS: A novel 8-item measure—the Beliefs About Oocytes Scale—was developed for the purpose of measuring specific attitudes towards oocytes. Exploratory factor analysis revealed that the scale generated two distinct, anticorrelated factors: 1) conceptualizing eggs as future offspring, or 2) conceptualizing eggs as an ample or generous biological resource to be shared with others. Existing validated scales were included to measure other factors hypothesized to relate to intention to donate including religiosity, attitudes towards parenthood, belief in the importance of genetic link towards children, knowledge of family of origin, adult attachment style, self-esteem, and altruism. Stepwise logistic regression was used to predict intention to donate.

RESULTS: Intention to donate oocytes was most strongly predicted by the belief that oocytes are a generous resource. Prospective oocyte donors were also characterized by higher altruism scores, more secure attachment style, lower self-esteem, and emphasis on the importance of family and parenthood, regardless of the genetic link between parent and child.

CONCLUSIONS: These data suggest women who choose to donate oocytes value childrearing and family, regardless of genetic relatedness, and do not view their eggs as future offspring. These findings have implications for the recruitment, retention, and counseling of potential egg donors, and may be usefully extended to explore donation of gametes and embryos in other contexts and cultures.

P-408 4:30 PM Sunday, October 18, 2020

UTILIZING A STRUCTURAL SUMMARY APPROACH IN THE PSYCHOLOGICAL INTERPRETATION OF PAI PROFILES OF EGG DONOR AND GESTATIONAL CARRIER CANDIDATES. Mary P. Riddle, Ph.D.,[1] John E. Kurtz, Ph.D.[2] [1]Penn State University, Park, PA; [2]Villanova University, Villanova, PA.

OBJECTIVE: The structural summary approach is a method of data integration that aids clinicians in psychological profile interpretation of the Personality Assessment Inventory (PAI). Study objectives were to conduct both a positive distortion analysis and a Self/Other Issue Cluster interpretation for PAI profiles of egg donor (ED) and gestational carrier (GC) candidates to determine the clinical utility of using a structural summary approach for assessment purposes.

DESIGN: This study is a combined analysis of retrospective chart data and prospectively collected test data.

MATERIALS AND METHODS: 80 de-identified PAI test protocols of gestational carrier (n = 58) and egg donor (n = 22) candidates were examined. Mean scale scores on clinical scales and validity indicators were calculated for each group and Self/Other Issue Clusters were explored. Positive distortion configural analyses were calculated and compared between groups using SPSS statistical software.

RESULTS: Self/Other Cluster analysis shows high levels of self-efficacy, average levels of self-esteem, and high stability in self-concept for both groups. Interpersonally, EDs show a warm, dominating style compared to a more warm, submissive style among GCs. Consistent with previous research, EDs had significantly higher scores than GCs on mean scale scores of Dominance ($p < .05$), Grandiosity ($p < .05$), Egocentricity ($p < .05$), and Stimulus Seeking ($p < .05$). EDs also scored significantly higher than GCs on

the subscale score of PAR-R (Resentment) ($p < .05$) which has not been previous reported. Most significantly, the Defensiveness Index (DEF) is significantly higher ($p < .05$) among EDs although additional validity scale scores (PIM; CDF) did not differ significantly. This, in turn, appears to have influenced noticeable differences in the positive distortion configural analysis with EDs having higher rates of effortful (conscious) distortion (64%) than GCs (53%).

CONCLUSIONS: The PAI is a self-report personality inventory commonly used in psychological screening of ED/GC candidates and no research has examined utilizing a structural summary analysis of either group. Interpersonally, both groups showed high levels of self-efficacy and stability in self-concept. GCs appear to have a more warm/submissive interpersonal style associated with higher levels of dependency and emphasis on maintaining attachments. This study showed significant differences in mean scale scores (Dominance, Grandiosity, Stimulus Seeking, Egocentricity, and Resentment) which contribute to significantly higher Defensiveness Index scores among EDs. Positive distortion analyses show a higher percentage of EDs engaging in "effortful" positive distortion (64%) as opposed to GCs (53%). This study shows that there are likely differences in interpersonal styles between groups that impact tendencies towards more effortful attempts by EDs to present favorably on self-report. A structural summary approach to PAI data interpretation may have clinical utility for an in-depth consideration of self-concept/self-presentation of EDs/GCs presenting for psychological evaluation.

SUPPORT: N/A

P-409 4:30 PM Sunday, October 18, 2020

RACIAL AND ETHNIC DISPARITIES AMONG DONOR OOCYTE BANKS IN THE UNITED STATES. Shelun Tsai, MD,[1] Esther H. Chung, MD,[1] Tracy Truong, MS,[2] Jeremy M. Weber, MS,[2] Amanda S. Farrell, BS,[1] Jenny Wu, BS,[1] Onyinye Ohamadike, BA,[1] Jennifer L. Eaton, MD, MSCI.[1] [1]Division of Reproductive Endocrinology and Infertility, Duke University Medical Center, Durham, NC; [2]Department of Biostatistics & Bioinformatics, Duke University Medical Center, Durham, NC.

OBJECTIVE: Donor oocyte banks offer databases of profiles for people seeking third party reproduction. Minorities face challenges in finding donors concordant with their identified race or ethnicity. Our objective was to determine whether the racial and ethnic distribution of oocyte donors contributing to United States (US) oocyte banks differs from the demographics of the US population and those of donor oocyte recipients.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: "Donor egg bank" and "donor oocyte" were used as Google search terms to identify US donor oocyte banks. Publicly available demographic data on donors was entered into a REDCap database. Only cryopreserved donor oocyte profiles were included. The proportions of women in each race/ethnicity category were compared between oocyte donors, the US population of women based on the 2018 census, and US women undergoing IVF with cryopreserved donor oocytes from 2012-2015 as reported to the Society for Assisted Reproductive Technologies Clinical Outcomes Reporting System (SART CORS). Chi-square or Fisher's exact tests were used for analyses.

RESULTS: 12 donor oocyte banks were identified, encompassing 1,574 donors (Table). Compared to the population of the US and cryopreserved donor oocyte recipients, a significantly higher proportion of donors identified as Hispanic (24.1% vs. 17.9% vs. 8.9%, $P<.001$) or as two or more races (16.1% vs. 2.2% vs. 0.5%, $P<.001$). In contrast, Black donors were significantly underrepresented compared to the US population (8.9% vs. 12.9%, $P<.001$) and recipients of cryopreserved donor oocytes (8.9% vs. 10.3%, $P=.047$). While Asian donors were overrepresented when compared to the US population (7.7% vs. 5.9%, $P=.003$), they were underrepresented when compared to the donor oocyte recipients (7.7% vs. 10.6%, $P=.001$).

CONCLUSIONS: The race/ethnicity distribution of oocyte donors differs significantly from the demographics of the US population and recipients of cryopreserved donor oocytes. These data suggest a need for targeted recruitment of Black and Asian oocyte donors.

P-410 4:30 PM Sunday, October 18, 2020

FRESH EMBRYO TRANSFER IMPROVES LIVE BIRTH RATE OVER FROZEN EMBRYO TRANSFER IN FRESHLY RETRIEVED DONOR EGG CYCLES. Iris Insogna, MD, MBE, Andrea Lanes, PhD, Malinda S. Lee, MD, MBA, Elizabeth S. Ginsburg, MD, Janis H. Fox, MD. Brigham and Women's Hospital, Boston, MA.

OBJECTIVE: To test the hypothesis that in cycles using embryos derived from freshly retrieved donor eggs, a fresh embryo transfer (fresh ET) is more likely to result in a clinical pregnancy and live birth compared to a cryopreserved-thawed embryo transfer (CET).

DESIGN: Retrospective cohort study using national data from the Society for Assisted Reproductive Technology (SART).

MATERIALS AND METHODS: Donor egg cycles in the SART database from 2014-2017 were collected. Only cycles using freshly retrieved eggs from anonymous donors were included. Cycles in which eggs were previously frozen, a known donor was used, or recipient age at time of transfer was over 55 years were excluded. All included cycles had at least one embryo available to transfer at either the cleavage or blastocyst stage. Using log binomial regression, relative risks and 95% confidence intervals were calculated for clinical pregnancy rate (CPR), live birth rate (LBR) and miscarriage rate. Crude and adjusted analyses were performed, controlling for donor age.

RESULTS: Of a total of 51,942 donor egg cycles, 15,308 (29.5%) were fresh ET cycles and 36,634 (70.5%) were CET cycles. Both groups were similar in terms of age, gravidity, parity, BMI, infertility diagnosis, and race/ethnicity. A majority of recipients had blastocyst(s) transferred (92.4% of fresh ETs and 96.5% of CETS), with a similar mean number of embryos transferred: 1.52 ± 0.52 in the fresh and 1.39 ± 0.53 in the CET groups.

Both CPR and LBR were lower after CET compared to fresh ET (CPR 54.2% vs 66.7%, aRR 0.78 [95% CI 0.76-0.79]; LBR 44.0% vs 56.6%, aRR 0.74 [95% CI 0.72-0.75]), controlled for donor age. Miscarriage rate was similar for both (9.4% following CET vs 9.3% following fresh ET, aRR 1.02 [95% CI 0.96-1.10]).

CPR and LBR following transfer of fresh non-PGT-A embryos were statistically significantly higher than following transfer of PGT-A embryos (either fresh or frozen) with no difference in miscarriage rates (Table).

Race and ethnicity distribution

	Oocyte Donors	US Population		Donor Oocyte Recipients	
Race/Ethnicity	N=1,574	N=166,038,755	P[a]	N=4,650	P[a]
White	678 (43.1%)	100,127,799 (60.3%)	<.001	3,234 (69.6%)	<.001
Black/African American	140 (8.9%)	21,342,200 (12.9%)	<.001	479 (10.3%)	.047
American Indian/Alaska Native	1 (0.1%)	1,227,668 (0.7%)	<.001	3 (0.1%)	1.000
Asian	121 (7.7%)	9,809,751 (5.9%)	.003	493 (10.6%)	.001
Hawaiian/Pacific Islander	1 (0.1%)	291,352 (0.2%)	.537	8 (0.2%)	.464
Two or more races	253 (16.1%)	3,602,424 (2.2%)	<.001	21 (0.5%)	<.001
Hispanic	380 (24.1%)	29,637,561 (17.9%)	<.001	412 (8.9%)	<.001

[a] Comparing to the oocyte donor group using Chi-square or Fisher's exact tests

	Fresh non-PGT-A N = 15044	Fresh and frozen PGT-A N = 2327	Frozen PGT-A N = 2063	RR (95% CI)	aRR (95% CI)*	RR (95% CI) ‡	aRR (95% CI) * ‡
Clinical pregnancy	10026 (66.6%)	1420 (61.0%)	1237 (60.0%)	0.92 (0.88-0.95)	0.89 (0.85-0.94)	0.90 (0.87-0.93)	0.84 (0.79-0.90)
Live birth	8505 (56.5%)	1191 (51.2%)	1031 (50.0%)	0.91 (0.87-0.94)	0.89 (0.83-0.95)	0.88 (0.84-0.93)	0.82 (0.75-0.89)
Miscarriage	1396 (9.3%)	203 (8.7%)	183 (8.9%)	0.94 (0.82-1.08)	0.94 (0.76-1.17)	0.96 (0.83-1.11)	1.01 (0.80-1.29)

* adjusted for donor age. ‡ relative risk for only frozen PGT-A compared to fresh non-PGT-A

CONCLUSIONS: Both CPR and LBR following the use of fresh donor eggs are over 10% higher after a fresh rather than frozen embryo transfer. This study suggests that recipients should be encouraged to undergo fresh donor egg embryo transfer without PGT-A.

SUPPORT: None.

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THE EFFECT OF DONOR AND RECIPIENT RACE ON OUTCOMES OF ASSISTED REPRODUCTION USING DATA FROM A VITRIFIED DONOR OOCYTE BANK.

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OBJECTIVE: A growing literature suggest that minority races, particularly Black women, have a lower probability of live birth and a higher risk of perinatal complications after autologous assisted reproductive technology (ART); however, questions still remain as to whether racial disparities are associated with differences in oocyte/embryo quality, an impaired uterine environment, or a combination of the two. To investigate this question further, we evaluated how oocyte donor and recipient race is associated with ART outcomes using data from a large, racially diverse vitrified donor oocyte bank.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Our study included 327 oocyte donors and 899 oocyte recipients who underwent a total of 1601 embryo transfer cycles between 2008 and 2015 at a private fertility clinic in Georgia. All embryo transfer cycles included in this study used oocytes that were cryopreserved via vitrification for an oocyte bank and later thawed for recipients' use. Self-reported race of the donor and recipient and clinical endpoints were abstracted from medical records. We used multivariable cluster weighted generalized estimating equations to evaluate the associations between donor and recipient race and probability of live birth adjusted for donor age and BMI, recipient age and BMI, tubal and uterine factor infertility, and year of oocyte retrieval. Secondary outcomes included the percentage of oocytes that survived warm, fertilized, and developed into usable embryos.

RESULTS: The overall racial profile of our donors and recipients were similar: 73% White, 13% Black, 4% Hispanic, 8% Asian, and 2% Other. There was a high concordance of race between oocyte donors and recipients (96% for White, 73% for Black, 62% for Asian, and 32% for Hispanic recipients). The percentage of warmed oocytes that developed into usable embryos was significantly higher for Black (56.9%) and Hispanic (64.5%) donors in comparison with White donors (40.9%). Women who received oocytes from Hispanic donors had significantly higher probability of live birth (adjusted relative risk (aRR) 1.20, 95% CI 1.05, 1.36) compared with women who received oocytes from White donors. Among Hispanic recipients, however, there was no significant difference in probability of positive pregnancy test or live birth compared with White recipients. Embryo transfer cycles with oocytes from Black donors (aRR 0.86, 95% CI 0.72, 1.03) and Black recipients (aRR 0.84, 95% CI 0.71, 0.99) had a lower probability of live birth compared to White donors and recipients, respectively. There was no significant difference in the probability of live birth among Asian and Other race female donors and recipients compared with White donors and recipients.

CONCLUSIONS: Our study corroborates and extends previous literature showing that Black women have less favorable ART outcomes even when using oocytes from young healthy oocyte donors. In contrast, women who utilized Hispanic oocytes had better ART outcomes regardless of recipient race.

SUPPORT: Dr. Gaskins is supported by a career development grant, R00ES026648, from the National Institute of Environmental Health Sciences (NIEHS). REDCap support was provided by UL1 TR000424 at Emory University.

P-412 4:30 PM Sunday, October 18, 2020

OUTCOMES OF FROZEN OOCYTE DONOR IN VITRO FERTILIZATION (IVF) CYCLES USING FRESH VERSUS FROZEN SPERM.

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OBJECTIVE: To compare outcomes of frozen oocyte donor IVF cycles with intracytoplasmic sperm injection (ICSI) when fresh versus frozen sperm is used for insemination.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We identified patients who underwent their first IVF with ICSI cycle using frozen donor oocytes between 2013 and 2019 at Mayo Clinic Rochester. Oocytes were selected from one of two commercial egg banks and either frozen or fresh sperm was used for ICSI. The primary outcome was live birth rate (LBR). Secondary outcomes included fertilization rate (FR), blastocyst development rate (BR), and clinical pregnancy rate (CPR). Patient characteristics, sperm parameters, and outcomes were compared using chi-square tests and two-sample t-tests, as appropriate.

RESULTS: A total of 52 patients underwent an embryo transfer following a frozen donor oocyte IVF with ICSI cycle. Seven patients were excluded due to a semen total motile sperm (TMS) count of less than 20 million. Of the included 45 patients, the mean age was 40.5 (SD 6.1). Fresh sperm was used by 26 patients and frozen sperm was used by 19 patients. There were no differences noted between the groups in regards to infertility diagnosis, use of specific egg bank, mean patient age (41.5 vs. 39.7 years), mean partner age at sample collection (39.1 vs. 39.8 years), median semen TMS count (92.1 vs. 101.1 million), or average sperm morphology (9.3% vs. 7.3%). In regards to outcomes, there were no differences observed between frozen versus fresh sperm on the mean FR, mean BR, or CPR (Table 1). Additionally, the difference in the LBR was not statistically significant (52.6% vs. 61.5%, p = 0.55).

CONCLUSIONS: Although other studies have examined the effects of various male factors on IVF outcomes, this is the first study to examine the impact of using a fresh versus frozen sperm sample in frozen donor oocyte IVF with ICSI cycles. Our study did not find statistically significant differences when fresh versus frozen sperm were used. These results may reassure providers that using a frozen sample will not negatively impact cycle success. However, further study may be warranted with a larger cohort of patients to adjust for additional covariates when comparing outcomes.

Table 1. Comparison of Outcomes According to Type of Sperm Used for Insemination

	Type of sperm			
Outcome measure	Frozen (N=19)	Fresh (N=26)	Total (N=45)	$P^{\dagger}$
Primary Outcome				
LBR *(n)*	52.6% (10)	61.5% (16)	57.8% (26)	0.55
Secondary Outcomes				
FR *Mean (SD)*	77.5% (21.7)	82.2% (13.2)	80.2% (17.2)	0.37
BR *Mean (SD)*	55.3% (35.8)	49.1% (29.1)	51.7% (31.9)	0.52
CPR *(n)*	57.9% (11)	65.4% (17)	62.2% (28)	0.61

†Comparisons between groups were evaluated using the chi-square test for CPR and LBR; the two-sample t-test was used for FR and BR.

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WHAT PATIENT FACTORS AFFECT SUCCESS IN WOMEN UTILIZING FROZEN DONOR EGGS? A SART DATABASE ANALYSIS.

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OBJECTIVE: To determine patient factors that predict success in embryo transfer (ET) cycles utilizing cryopreserved donor oocytes to intended parent recipients

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The SART database was used to identify cryopreserved donor oocyte cycles that resulted in fresh ET from 2014 to 2015. An initial univariate analysis was performed to identify patient factors associated with live birth rate. These included history of prior: full term birth (FTB), preterm birth (PTB), spontaneous abortion (SAB), biochemical pregnancy; as well as fertility diagnosis, age, race, BMI, smoking status, and number of embryos transferred. Factors with a p-value <0.2 in our primary univariate analysis were included as potential predictors in the final model. The final model was performed via multiple logistic regression. A two-sided p value <0.05 was considered significant in our multiple regression model.

RESULTS: A total of N= 5001 cryopreserved donor oocyte fresh ET cycles were analyzed. Overall livebirth rate was 40.6% in this population. On average, patients were 41.6 (Standard Deviation (SD): 4.88) years old, primarily of white (36.6%) or other (46.5%) race with BMI 26 (SD: 5.56). 6.2% of patients were identified as African American, and 3.8% of the total cohort were defined as smokers. The average number of embryos transferred was 1.54 (SD 0.56). The univariate analysis demonstrated no association of live birth rate with the following factors: history of FTB, PTB, SAB, biochemical pregnancy, number of embryos transferred, or fertility diagnosis, with the exception of tubal factor (p<0.5). After controlling for covariates in the regression model, race was the most significant finding, with African-American race associated with a decreased live birth rate compared to white race (OR 0.73 95% CI 0.55 -0.98). Older patients were found to have lower live birth rate compared to younger recipients (one year increase in age OR 0.98 95% CI 0.97 – 0.99). Higher BMI was negatively associated with live birth rate (OR 0.99 95% CI 0.97 to 0.99). Women with a history of smoking had a higher live birth rate compared to those who did not smoke; however, the total number of smokers was small in the sample 188 (3.8%) (OR 1.34 95% CI 1.00 – 1.86). Patients with tubal factor did not have an appreciable difference in live birth rate in the final model (OR 0.99 95% CI 0.7 – 1.14).

CONCLUSIONS: More patients are choosing cryopreserved donor oocytes in donor egg cycles, yet data is scarce as to how to best counsel patients regarding best prognosis for an individual patient. Our study suggests that cryopreserved donor oocyte outcomes are associated with race, age, and BMI. Smoking does not appear to be negatively associated with live birth.

SUPPORT: none

P-414 4:30 PM Sunday, October 18, 2020

PREGNANCY OUTCOMES WITH GESTATIONAL SURROGACY COMPARED TO NON-SURROGACY FOR IN-VITRO FERTILIZATION CONCEPTION.

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OBJECTIVE: In vitro fertilization (IVF) often requires a gestational carrier (surrogate) to achieve parenting for intended couples. Our objective was to study the characteristics and outcomes of pregnancies with a designated gestational surrogate compared to non-surrogate IVF conceptions.

DESIGN: Retrospective case series.

MATERIALS AND METHODS: Designated gestational surrogate pregnancies managed in a single maternal fetal medicine center from January 2011 to March 2020 were eligible. Age matched IVF pregnancies were selected as controls in a 2:1 fashion. Comorbidities of surrogates, gravidity, parity, singleton vs twin gestation, estimated fetal weight (EFW) and abdominal circumference (AC) percentiles in second and third trimesters, fetal anomalies, abnormal ultrasound findings, cervical length, gestational age at delivery, mode of delivery and perinatal complications were reviewed. Descriptive statistical analysis, Fisher's test and chi-square were performed with a p value of <0.05 considered significant.

RESULTS: Thirty gestational surrogate IVF pregnancies were compared with 60 IVF controls. Gestational surrogates had higher mean gravidity than non-surrogacy IVF pregnancies, (4.75 vs 1.86, p= 0.0001). The rate of twin gestation was 60% among surrogacy pregnancies compared to 40% of controls (p= 0.3295). There were two monochorionic gestations after single embryo transfer in each group. Surrogates had a 17.6% rate of fetal cardiac and central nervous system anomalies identified on prenatal ultrasound compared to 5.8% of non-surrogacy IVF pregnancies (p= 0.1901). There was a significantly higher rate of abnormal placental ultrasound findings in the gestational surrogacy group compared to non-surrogacy IVF pregnancies (placenta previa, placental cysts, and presence of multiple placenta lakes) (p= 0.027). Among gestational surrogacy IVF pregnancies there was a trend towards a higher rate of pre-term delivery at 37% vs 21%, however not statistically significant (p= 0.06). Cesarean delivery among gestational surrogacy IVF pregnancies was 77%, compared to 41% of non-surrogacy IVF pregnancies (p = 0.018). Despite antepartal assessment, fetal demise was found at 35 weeks and 36 weeks in the gestational surrogacy IVF group (11.7%), while there were no losses in the non-surrogacy IVF group (p= 0.021).

CONCLUSIONS: In this case series, gestational surrogacy IVF pregnancies had high rates of twinning, abnormal ultrasound findings, cesarean delivery and intrauterine fetal demise. Our data suggests that pregnancies for intended parents through gestational carriers have an increased rate of adverse perinatal outcomes compared to age matched IVF controls in autologous gestations. This requires modified counseling and additional management over typical IVF pregnancies alone.

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PROMISING LIVE BIRTH RATES ARE SEEN WITH UNTESTED DONOR EMBRYOS.

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OBJECTIVE: To describe the characteristics and reproductive outcomes of patients choosing to utilize donated embryos at a single infertility practice.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: A chart review was performed on patients who presented to a single infertility practice and utilized donated embryos from 2016-2018. Practice criteria for embryo donation included: embryos vitrified onsite at blastocyst stage on day 5 or 6, egg age <40 years old, sperm age <50 years old, no PGT-M/SR; however PGT-A euploid embryos were accepted. Embryos with an estimated 40-45% odds of LB per embryo, based on records review, and assuming no uterine factor, were permitted for donation. Descriptive statistics were used to evaluate patient characteristics and outcomes.

RESULTS: 198 donated embryo FET cycles with planned transfer to 141 unique patients were initiated. Mean recipient age at cycle start was 40.5 years. Mean number of previously completed IUI, IVF and FET cycles per recipient was 0.6, 0.7, and 0.7, respectively, with a mean of 2.1 (SD = 2.79) total prior treatment cycles per recipient. 13 cycles were ultimately cancelled, 10 of which were cancelled due to inadequate endometrial response. Another patient had no transfer because the single thawed embryo did not survive. 184 (93%) of the initiated donated embryo cycles were completed, and the mean egg age at the time of embryo creation was 29.8 years (range 22-38 years). The most common primary infertility diagnosis for recipients was diminished ovarian reserve (36.4%) with the second most common listed as "other" (27.2%). 1.6% of recipients had a diagnosis of uterine factor infertility. 28.4% of the 141 patients using donated embryos were single females and another 7.1% were same sex couples. Patients mostly identified as Caucasian (68.5%) or Black/African American (14.1%). A mean of 1.2 embryos were transferred each cycle. 14.7% of transfers were double embryo transfers, and 9.8% of clinical pregnancies were twin gestations. One patient with a singleton pregnancy underwent a therapeutic abortion at 11 weeks with no reason provided. Livebirth and ongoing pregnancy per transfer were 42.9%, and transfers were performed with mostly PGT untested embryos (95.7%). Mean age at delivery was 37.3 weeks gestation.

CONCLUSIONS: Use of donated embryos can provide a successful means to parenthood, particularly for those with diminished ovarian reserve. In the absence of PGT-A, FET of donated embryo was associated with a high live birth rate. Single embryo transfer should be recommended in order to minimize twin gestations.

P-416 4:30 PM Sunday, October 18, 2020

DOES ELEVATED PROGESTERONE ON DAY OF TRIGGER ASSOCIATE WITH BLASTOCYST PLOIDY IN EGG DONOR CYCLES? Priscilla Caldeira, MD,[1] Aline R. Lorenzon, PhD,[2] Ana Paula Aquino, MD,[3] Bruna Barros, BSc,[3] Eduardo L. A. Motta, MD, PhD,[4] Thais S. Domingues, MD, PhD.[5] [1]School of Medicine - University of São Paulo, Brazil; [2]Scientific Coordinator, Huntington Medicina Reprodutiva, Sao Paulo, Brazil; [3]Huntington Medicina Reprodutiva, São Paulo, Brazil; [4]Department of Gynecology, Paulista School of Medicine, Federal University of São Paulo, São Paulo, Brazil; [5]Huntington Medicina Reprodutiva, Sao Paulo, Brazil.

OBJECTIVE: Evaluate if high progesterone levels on day of trigger influences blastocyst ploidy and embryo quality parameters in egg donors cycles.

DESIGN: Retrospective cohort study from ICSI cycles using frozen donated oocytes that underwent embryo biopsy at blastocyst stage performed between April/2013 and February/2019 at Huntington Medicina Reprodutiva. Two groups were set according to progesterone (P4) level on day of trigger: group A if P4 <1.5 ng/mL (n=75 cycles: 57 donors – 69 recipients) and group B if P4 ≥1.5 ng/mL (N=184 cycles: 115 donors – 163 recipients).

MATERIALS AND METHODS: Donors were women under 35 years old, with regular menstrual cycles, no gynecological or other health diseases, IMC under 30 Kg/m^2 and normal karyotype. They received standard ovarian stimulation protocol with GnRH antagonist. Clinical parameters such as antral follicular count, FSH basal, total gonadotrophins dose and estradiol (E2) at trigger were analyzed. Number of eggs retrieved, mature oocytes (MII), number of ICSI, fertilization rate, number of blastocysts, number of top quality blastocyst, number of euploid/aneuploid blastocysts, euploid/aneuploid embryo rate and clinical pregnancy were compared between group A and B. T and Fisher tests were used for statistical analysis.

RESULTS: Group A mean age was 25.15±3.59 and group B 24.46±3.73 years old (p=0.19). Total gonadotropins used and basal FSH were not different between group A and B (2777.83±526.02 vs 2814.54±538.78, p=0.7363; 5.19±1.51 vs 5.22±1.47, p=0.3035). Antral follicular count was higher in group B than in A (22.95±10.65 vs 19.60±7.08, p=0.0301) and estradiol at trigger was higher in group A than in B (5255.00±6405.77 vs 5252.83±4346.33 vs, p=0.0340). Number of eggs retrieved, MII and number of ICSI performed were higher in group B than A (33.96±1.76 vs 28.01±11.78, p=0.0014; 24.84±11.74 vs 21.12±10.56, p=0.0082; 8.08±1.74 vs 7.61±1.63, p=0.0025). There were no differences between groups in oocytes post-thaw survival rate, fertilization rate, number of blastocysts and number of top-quality embryos (0.95±0.10 vs 0.98±0.17, p=0.2626; 0.83±0.14 vs 0.82±0.13, p=0.854; 3.60±1.52 vs 3.68±1.52, p=0.6671; 2.27±1.59 vs 2.28±1.43, p=0.8019). The mean of blastocyst biopsied per group were similar (3.15±1.33 versus 3.06±1.29, p=0.6998; n=236 group A and 563 group B). There was no difference between groups when comparing number of euploid embryos and euploid embryo rate (1.92±1.25 vs 1.92±1.13,p=0.9542; 0.31±0.20 vs 0.30±0.18, p=0.6257). Number of aneuploid embryos and aneuploid embryo rate were not different between groups (1.23±1.01 vs 1.14±0.94,p=0.5927; 0.21±0.19 vs 0.18±0.15, p=0.4363). There was no difference in clinical pregnancy rate (0.73 vs 0.82, p= 0.4765). Seminal parameters were similar between groups.

CONCLUSIONS: Our data showed that elevated progesterone levels on trigger's day is not associated with blastocyst aneuploidy rates or worst embryo quality parameters in egg donors cycles, in which the cofounder of maternal age is excluded from the analysis.

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PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY IN DONOR OOCYTE IVF CYCLES: A MATCHED, SIBLING OOCYTE COHORT STUDY. Devora Aharon, MD,[1] Dmitry Gounko, MA,[2] Joseph A. Lee, BA,[2] Tanmoy Mukherjee, MD,[1] Alan B. Copperman, MD,[1] Lucky Sekhon, MD[2] [1]Icahn School of Medicine at Mount Sinai, New York, NY; [2]Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: The use of preimplantation genetic testing for aneuploidy (PGT-A) has been shown to improve live birth rate per embryo transfer (ET) and reduce pregnancy loss.[1] Whether PGT-A is beneficial in donor oocyte recipient cycles, with lower expected rates of aneuploidy, is less clear.[2-4] A major concern is the possible lower positive predictive value of PGT-A when the technology is used to screen young donor-oocyte derived embryos, which may reduce the number of healthy embryos available for transfer and/or cryopreservation. This study aims to compare the overall IVF cycle efficacy and efficiency in recipients of sibling donor oocytes who did and did not utilize PGT-A.

DESIGN: Retrospective, matched cohort study.

MATERIALS AND METHODS: The study included single embryo transfers in recipients of sibling oocytes from the same donor in which one recipient utilized PGT-A ("PGT-A" group) and the other recipient did not ("unscreened" group) from September 2016 to March 2020. Donors underwent controlled ovarian hyperstimulation and the retrieved oocytes were divided equally among the recipients. PGT-A was performed using Next Generation Sequencing. Baseline characteristics including age, BMI, endometrial thickness, use of donor sperm, fresh vs. frozen embryo transfer, embryo age, and embryo quality were compared between the groups. Outcomes included cycle efficiency, defined as percentage of fertilized oocytes that were transferred and/or cryopreserved, as well as clinical pregnancy, live birth, and pregnancy loss rates. Comparative statistics and linear and logistic regression were used for analysis.

RESULTS: The study included a total of 50 matched pairs, or 100 oocyte recipient cycles. Average oocyte age was 26.5±2.7 years. The groups were similar in terms of recipient age and BMI. The PGT-A group had a significantly lower endometrial thickness, lower rate of donor sperm use, higher proportion of frozen-thawed embryo transfers, and lower proportion of day 5 vs. day 6 embryos transferred compared to the unscreened group. With regards to embryo quality, the PGT-A group had significantly higher expansion grades, similar inner cell mass morphology grade, and a higher proportion of trophectoderm grade B. Cycle efficiency was similar between the groups (60.7±0.2% vs. 56.5±0.2%, p=0.44). On multivariate logistic regression, no significant differences were seen between the PGT-A and unscreened groups in clinical pregnancy rate (OR 0.85, 95% CI 0.26-2.73, p=0.79), live birth rate (OR 1.93, 95% CI 0.51-7.35, p=0.33), or pregnancy loss rate (OR 0.65, 95% 0.11-3.69, p=0.63) when controlling for confounders.

CONCLUSIONS: Our study which utilized a sibling donor oocyte matched model failed to demonstrate alterations in cycle outcome in cases with embryos that had undergone PGT-A. We did not observe a reduced number of embryos available for transfer or cryopreservation, suggesting that the use of PGT-A does not reduce treatment efficiency. Recipients who desire the use of PGT for sex selection or aneuploidy screening can be reassured that this technology is safe and will not reduce the number of embryos available for treatment.

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SUPPORT: None

P-418 4:30 PM Sunday, October 18, 2020

UNDERSTANDING SELF-PERCEPTIONS AND RISK EXPERIENCES OF GESTATIONAL SURROGATE MOTHERS IN GESTATIONAL SURROGACY ARRANGEMENTS, THAILAND. Jutharat Attawet, PhD candidate. University of Technology Sydney, Sydney, NSW, Australia.

OBJECTIVE: This study aims to explore gestational surrogate mothers' self-perceptions and risk experiences during the process of gestational surrogacy arrangements in Thailand.

DESIGN: Qualitative descriptive design

MATERIALS AND METHODS: Fifteen Thai women who had gestational surrogacy experience were interviewed by telephone. An approximately 30-minute semi-structured interview was conducted per individual. During the interview, audio tape was used to record the conversation for the purpose of transcription and translation. Thematic analysis was applied to analyze the translated interviews.

RESULTS: 'Womb for work' was an overarching theme for Thai women deciding to become gestational surrogate mothers. Thai women perceived that their wombs could be turned into money and simultaneously assist a childless couple to complete their family. In doing this, Thai women were able to justify the exchange of 'womb for work.' For entry into commercial surrogacy arrangements, Thai women had to sign a contract, which they perceived as outlining their obligations and having to be followed without deviating. Thai women mostly entered the surrogacy process through a surrogacy agency, who they called a 'big boss.' Thai women perceived that the 'big boss' was a powerful person in the surrogacy arrangement, with whose instructions they had to comply during the process of the gestational surrogacy arrangement. The women reported that they mainly communicated with the 'big boss' and obtained surrogacy treatment information from the 'big boss.' Communicating between the Thai women and fertility professionals could be described as a 'triangle communication,' meaning they received surrogacy treatment information from the 'big boss' rather than directly communicating with the fertility professionals. Through the process, it was identified that some details, such as risks associated with multiple or potential infected embryo transfer, or complications of multiple pregnancy, were omitted. According to cultural norms, asking questions of a powerful person, such as the 'big boss' or fertility professionals, was an inappropriate behavior. Consequently, these self-perceptions of being inadequately empowered to ask questions about surrogacy treatment and their own health among the Thai women were creating a barrier to further knowledge about potential health risks involved in gestational surrogacy arrangements. It was therefore found that Thai women had limited understanding and knowledge of potential health risks involved in the process of gestational surrogacy arrangements, which could possibly have contributed to their experiences of making decisions regarding surrogacy treatment and accepting risks unintentionally.

CONCLUSIONS: Self-perceptions were found to be the barrier limiting gestational surrogate mothers from further seeking information from reliable sources—fertility professionals—which affected their understanding of health risks and decision-making in the process of surrogacy treatment.

SUPPORT: N/A

P-419 4:30 PM Sunday, October 18, 2020

SUBJECTIVE PSYCHOLOGICAL FACTORS ASSOCIATED WITH EGG DONORS UNDERGOING ADDITIONAL DONATIONS AFTER THEIR FIRST OOCYTE DONOR CYCLE.

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OBJECTIVE: To determine psychological factors that influence egg donors' decisions to undergo repeat donation cycles.

DESIGN: Survey.

MATERIALS AND METHODS: Oocyte donors (n=318) in the US were surveyed regarding subjective psychological assessments of their experience as first-time donors, and the subsequent probability that they undergo additional donations after their first. Donors providing eggs to a friend or relative were excluded.

RESULTS: Egg donors were more likely to donate oocytes again if they considered their first experience with donation to be rewarding, if their expectations regarding egg donation were met, if potential short-term and long-term risks of donation were adequately explained by their clinic before treatment, and if they were satisfied with their clinic (Table). Donors who reported feeling regret (53.5% vs 84.8, $p<0.0001$, C^2), fear or anxiety (63.2% vs 87.9%, <0.0001, C^2), depression (61.4 vs 85.9%, <0.0001, C^2), or mood swings (68.3 vs 84.7%, $p=0.0012$, C^2) during or after their first donation were significantly less likely to undergo a second oocyte donation.

Proportion of egg donors choosing to do additional oocyte donations after their first donation, according to their subjective experiences of their first donation rated on a Likert scale, assessed using Kendall's test for significant association

CONCLUSIONS: Oocyte donors reporting comprehensive informed consent and high satisfaction with patient care were more likely to donate again.

SUPPORT: This study was supported by the University of California, San Francisco, Institute for Health and Aging; UCSF Individual Investigator Grant (#7501159); and funding from the National Science Foundation (#1828783).

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6 YEARS OF DONOR OOCYTE TRANSFERS IN A SINGLE PROGRAM: WHAT HAVE WE LEARNED?.

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OBJECTIVE: Advances in IVF & oocyte cryopreservation technology have allowed for newer modalities in the field of donor oocyte (DE) such as the use of frozen oocytes purchased from banks (COM-O) & genetic testing of resultant embryos. The objective of our study was to analyze our program's DE data over a 6-year period to assess DE usage efficiency & trends over time & whether these changes have positively impacted pregnancy outcomes.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: From 2014-2019, our program completed 462 DE transfers in 241 recipients (REC; avg 2-embryo ET/REC) using embryos derived from a total of 163 donors. We analyzed the data for the following: freshly-retrieved oocytes (FRESH-O) vs. COM-O, FRESH-ET (in retrieval or egg-thaw cycle) vs. FROZEN-ET of resultant frozen thawed embryos; SOLE (all oocytes to 1 REC) vs. SHARED (oocytes split between 2 REC) cycles, & usage of PGT-A or not. In addition, donor age & duration of freeze were analyzed. Primary outcome was ongoing pregnancy (>8 wks) + live birth rate (OP/LB). Chi Square was used with significance at $p< .05$.

RESULTS: A total of 368 FRESH-O (80%) and 94 COM-O (20%) were performed. Overall, FRESH-O ETs yielded a significantly higher OP/LB compared to COM-O ETs (44% vs. 30%, $p= .01$). Within the FRESH-O group, OP/LB was not different when comparing FRESH-ET vs. FROZ-ET (51% vs 41%, $p= .08$). Within FRESH-ETs, those using FRESH-O had a higher OP/LB compared to COM-O (51% vs. 27%, $p= .0007$). When comparing SOLE ETs (n= 169; avg # eggs: 17 MII) vs. SHARED ETs (n= 147; avg # eggs: 10 MII), OP/LB rates were 53% vs. 40% ($p= .02$); of note, 60/75 (80%) SOLE & 28/30 (93%) SHARED donors produced at least 1 OP/LB. The use of PGT-A did not positively impact OP/LB in DE cycles as a whole ($p= .9$). When excluding PGT-A cycles, SOLE ETs yielded a significantly higher OP/LB than SHARED (59% vs. 40%, $p= .002$). Length of freeze as well as donor age (21-32y) did not impact OP/LB outcomes ($p= .15$ and $p= .3$, respectively).

	Strongly agree	Somewhat agree	Neutral	Somewhat disagree	Strongly disagree	*P*-value
Donation was rewarding	87.1%	76.1%	75.0%	40.0%	40.0%	<0.0001
Expectations were met	88.5%	81.0%	73.3%	72.3%	40.9%	<0.0001
Short-term risks explained	89.0%	77.9%	70.6%	78.0%	64.7%	0.0009
Long-term risks explained	91.7%	87.0%	76.9%	78.3%	70.7%	0.0005
Satisfaction with clinic	90.1%	78.1%	77.3%	65.7%	56.7%	<0.0001

CONCLUSIONS: As judged by OP/LB, the use of SOLE, FRESH-O with FRESH-ET without PGT-A remains superior to newer DE treatment combinations. Specifically, the use of COM-O & PGT-A did not improve success. Young oocytes yield sufficient-quality embryos for LB without requiring genetic evaluation. DE considerations now go beyond OP/LB & include enhanced DE choice (COM-O), easier scheduling & coordination (FROZ-ET and COM-O) and lower cost (SHARED). That 32yo and 21yo DEs yield similar OP/LB is important when counseling women pursing fertility preservation to be their own "donors" in the future. Although changing DE practices may enhance patient experience and affordability, patients & providers must be cognizant that choices may not always favorably impact pregnancy outcome and may cause other longer-term ramifications.

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A COMPARISON OF THE CHANCE OF A SECOND LIVE DELIVERED PREGNANCY FROM DONATED OOCYTES BEFORE UTILIZING ALL EMBRYOS FORMED ACCORDING TO WHETHER THE SOURCE OF EGGS WERE INFERTILE DONORS OR PAID POTENTIALLY FERTILE DONORS. Laura X. Zalles, MD,[1] Jerome H. Check, M.D., Ph.D.,[2] Jung Choe, M.D.,[2] Carrie K. Wilson, B.A.,[3] Donna Summers, M.S.[3] [1]Cooper University Hospital, Camden, NJ; [2]Cooper Medical School of Rowan University, Camden, NJ; [3]Cooper Institute for Reproductive Hormonal Disorders, P.C., Mt. Laurel, NJ.

OBJECTIVE: Certain states that have mandated coverage for in vitro fertilization-embryo transfer (IVF-ET) will pay for the whole IVF cost for donor oocyte cycles with the exception of actual payment to the donor or payment for frozen donor oocytes. If a recipient receives one half of the retrieved eggs from an infertile donor undergoing IVF, the recipient cost is zero. The question is whether this comes at a sacrifice for success rates compared to donated oocytes from a paid donor. We previously determined that there was no difference in live delivered pregnancy rates resulting from infertile donor oocytes following fresh transfer. However, it is possible that the initial fresh transfer would select the best quality embryos, and thus result in decreased success in a subsequent frozen (F) ET (FET) in those women trying for another baby. The purpose of this study was to compare pregnancy outcomes according to source of donated eggs in FET's after a successful delivery with fresh donated oocytes.

DESIGN: Retrospective comparative.

MATERIALS AND METHODS: We reviewed FET outcomes of women delivering a live baby on their fresh transfer using one of three sources of donor oocytes: infertile donor sharing half the eggs collected, paid donor with all eggs to one recipient, and paid donor with eggs split between two recipients. Infertile donors receive no payment but only pay for the ET. The category pregnancy rate/retrieval includes the pregnancy rate potentially using all embryos (fresh or frozen) and thus possibly several transfers from embryos formed in the first successful donor-oocyte cycle.

RESULTS: Live delivered pregnancy rates per transfer and retrieval in attempt for a second baby from embryos formed in first donor egg recipient cycle.

CONCLUSIONS: Power analysis found that for the 40% increased live delivered pregnancy rate to be significant the study would need to have 1.5 x more patients. If this difference is found to be true a couple would have to decide if this extra benefit is worth the increased expense.

SUPPORT: None

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AN IMPROVED METHOD FOR ZIKA VIRUS SCREENING IN A GAMETE BANK SETTING. Corey Andrew Burke, BSc, CLS,[1] Dixie Howell, MHA,[1] Julio Cortes, BS,[2] Anne-Bine Skytte, MD,[1] Ruth Fernandez, AAS,[2] Suzy Pixley, BS.[2] [1]Cryos International - USA, Orlando, FL; [2]Unilab of Dade, Fort Lauderdale, FL.

OBJECTIVE: Can the use of an Emergency Use Authorized (EUA) test for Zika IgM antibodies strengthen FDA screening for Zika virus?

DESIGN: Prospectively collected Zika-virus IgM antibody tests have been analyzed during the out-break of the epidemic and the period thereafter for sperm and egg donors donating at Cryos International -USA between August 2016 and January 2020.

MATERIALS AND METHODS: Screening of Sperm donors for Zika IgM by InBios ZIKV Detect™ 2.0 IgM Capture ELISA was carried out at the beginning and closure of each batch of ten ejaculates or every 8 weeks. Egg donors were screened prior to beginning their cycle and again on the day of oocyte pick-up. Zika IgM levels are variable over the course of the infection and may be detectable near day four post onset of symptoms and persist up to approximately 12 weeks following initial infection. Testing was performed at Unilab of Dade.

RESULTS: One-thousand-three hundred-seventy-six tests were performed on one-hundred-forty-six donors. A total of sixteen donors tested positive or reactive. Eight donors (6 sperm, 2 egg) were reported as presumptive positive for Zika IgM. The remaining eight donors (7 sperm, 1 egg) were presumed to have a positive result due to interference from West Nile Virus or Dengue virus however none of these donors were confirmed positive to West Nile Virus or Dengue virus.

CONCLUSIONS: Zika virus infection during pregnancy may cause serious birth defects and developmental disability, including a condition called microcephaly. Other signs and symptoms of congenital Zika virus syndrome (CZVS) may appear later in infancy including seizures, irritability, problems swallowing, as well as hearing and sight abnormalities.

There is also strong scientific evidence that a Zika infection during pregnancy can cause Guillain Barre Syndrome (GBS). Symptoms of GBS include weakness of the arms and legs and, in severe cases, can affect the muscles that control breathing.

When the Zika outbreak first began in the United States in 2016 the FDA issued a screening policy requiring that a series of travel and lifestyle questions be asked of sperm and egg donors. At the same time Cryos International instituted a policy of using an EUA screening test for the Zika virus. Between August 2016 and January 2020 sixteen donors were found to be positive or possibly positive for Zika virus, one of these was confirmed by the state department of health by rt-PCR to have the virus. The remaining fifteen could not be confirmed to be positive or negative for the virus.

None of the donors tested answered yes to FDA questionnaires regarding travel to an infected area, sex with an infected. This raises concern about the effectiveness of using only lifestyle questions to screen for Zika virus. Due to the emerging nature of this virus, the testing methodology has not been fully validated. This study addresses the urgent need of ART facilities including gamete banks for reliable, clinically significant, accurate and accredited methods to screen gamete donors for Zika virus in order to the safety of donor gametes.

	Egg Donor Type		
	Infertile donor	Paid donor, 1 recipient	Paid donor, split between 2 recipients
Avg. age (yrs) of donor	31	29.5	28.7
No. of initial FET cycle*	27	57	56
No. of all subsequent FET cycles*	35	88	68
% live delivered/1st FET	40.7% (11/47)	43.9% (29/57)	35.7% (22/56)
% live delivered/all subsequent FET	51.8% (14/27)*	70.1% (40/57)	46.4% (26/56)

*p=.0837 comparing infertile donor source vs. paid donor 1 recipient, chi-square.

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INFANT BIRTH WEIGHT AND MATERNAL BMI: GENETIC VS EPIGENETIC CONTRIBUTIONS.

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OBJECTIVE: The prevalence of obesity is increasing worldwide. Obesity has been shown to have a negative effect on reproductive outcomes in both spontaneous and IVF pregnancies. Studies on the effect of maternal BMI on pregnancy success rates in donor oocyte IVF cycles are conflicting. Few studies have examined the effect of maternal BMI on neonatal outcomes. While increasing maternal BMI is associated with increased infant birth weight in both spontaneous and autologous IVF pregnancies, it is unclear whether this is primarily a genetic or epigenetic phenomenon. To our knowledge, this is the first study to examine the effect of donor BMI on infant birth weight in donor oocyte IVF cycles. The purpose of this study is to assess the relationship between infant birth weight and recipient and donor BMI in donor oocyte IVF cycles in order to determine the relative genetic (oocyte) and epigenetic (endometrial) contributions.

DESIGN: IRB-approved retrospective cohort study.

MATERIALS AND METHODS: We conducted a retrospective cohort study of 130 donor oocyte IVF cycles resulting in a singleton live birth at a single IVF center from 2012-2018. Pearson correlation coefficients were calculated to examine the relationship between recipient and donor BMI and infant birth weight. ANOVA was conducted to compare infant weight among various BMI subgroups. Linear regression was used to adjust for the type of embryo transfer (fresh vs frozen), diabetes or gestational diabetes status, hypertension in pregnancy, gestational age, and infant sex.

RESULTS: Recipients were >35 years of age on average and predominantly Caucasian. Decreased ovarian reserve was the most common etiology of infertility diagnosis. Forty-four percent of recipients were normal weight and 56% were overweight or obese. The mean age of oocyte donors was 26.7 ± 3.15 (Range 20-39) years. Seventy-eight percent of oocyte donors were normal weight and oocyte donors were predominantly Caucasian. There was no correlation between recipient BMI and infant birth weight (r=0; p=0.99). In contrast, there was a weakly positive, but non-significant, correlation between donor BMI and infant birth weight (r=0.02; p=0.76). This relationship persisted after adjusting for potential confounders.

CONCLUSIONS: Several studies have shown a clear association between maternal BMI and infant birth weight in autologous IVF cycles. In this study we examined the relative contribution of donor and recipient BMIs to infant birth weight in donor oocyte IVF cycles. The lack of correlation observed between recipient BMI and infant birth weight along with the weak although not significant correlation between donor BMI and infant birth weight suggests that oocyte or genetic components may play a greater role in infant birth weight compared to epigenetic or endometrial factors. This study is limited by the relatively small sample size and lack of information on paternal BMI. Future studies aim to examine metabolic health outcomes in oocyte donor-conceived children.

P-424 4:30 PM Sunday, October 18, 2020

THE EVOLVING LANDSCAPE OF DONOR EGG TREATMENT: SUCCESS, WOMEN'S CHOICE AND ANONYMITY.

Alexandra Peyser, M.D., Mary Rausch, MD, Stephanie R. Brownridge, M.D., Nicole Noyes, MD. Northwell Health Fertility, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: 40K+ babies are born in the US annually from the use of donor gametes; ∼¼ are eggs (DE). Notably, in 2017, ∼¼ of the women > 40y that succeeded using ART did so with DE. DE is thus, common practice today as more women delay childbirth in lieu of professional/personal pursuits, causing them to "age-out" of traditional ART. DE has evolved from synching a recipient's (REC) endometrium to a donor's fresh retrieval (FRESH-O) + multi-embryo FRESH-ET to; (non-synchronized) frozen-embryo transfers (FROZ-ET) &/or the use of commercially-bought, frozen DE (COM-O) ± the use of PGT-A; all meant to optimize DE outcomes. We sought to examine trends over time re: psychology, cost, choice, genetics and ease.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: From 1/2014-12/2019, we completed 462 DE transfers in 241 REC using a total of 163 donors (avg: 2-emb ET/REC). We analyzed donor characteristics & cycle repeats, &, over time, FRESH-O vs. COM-O, SOLE (1 REC) vs. SHARED (2 REC), FRESH-ET vs. FROZ-ET, PGT-A or not, single (SET) vs. double (DET) ET. Primary outcome was ongoing (> 8 wks) pregnancy + live birth rate (OP/LB). Stats: Chi Square was used.

RESULTS: Of donors, 98 (60%) were FRESH-O; 65 (40%) were COM-O. 29 (30%) FRESH-O donated greater than once (REPEAT) with embryos transferred to a total of 108 REC. On average, REPEATs had 3 retrievals (range 2-6), went to 4 REC (range 2-9) & their donations resulted in 7 ETs (range 2-23) creating 84 OP/LB; 3 per donor (range 1-9). A total of 74 "genetic half-siblings" were born to 76 REC from 23 donors. Assessing oocyte & ET type, FRESH-ETs using FRESH-O compared to COM-O yielded a higher OP/LB rate (51% vs. 27% p=.0007). In FRESH-O, OP/LB rates were similar in FRESH-ET & FROZ-ET (50% vs 41%, p=.08). For all DE cycles, PGT-A use increased over time (2014-16: 0.2%, 2018-19: 13%) with no OP/LB improvement (p=.9). 2-ETs led to a higher OP/LB compared to SET (50% vs. 37%, p=.007) but had a 15% twin rate. The program trended from 2-ET to SET over 6y (2014-2019), decreasing from 42% to 19% (p<.05); SET continues to dominate. As years progressed, we trended toward SOLE over SHARED and less COM-O due to SOLE's superior OP/LB per ET. Of note, 60/75 (80%) SOLE (17 eggs/REC) & 28/30 (93%) SHARED (10 eggs/REC) donors made at least 1 OP/LB.

CONCLUSIONS: ART continues to evolve. As OP/LB successes have become universally acceptable, primary treatment emphasis has expanded from best-pregnancy-rate-only to include healthy baby (and mother) & meeting patient concerns: cost, timing, ease, non-family genetic siblings. Trends in practice require continuous reevaluation. Moving away from 2-ET in favor of SET is mandatory. PGT-A's role in DE appears unnecessary except for carrier-state issues. The combo of SOLE, FRESH-O + readied REC continues to provide the best absolute OP/LB but COM-O and FROZ-ET add choice and convenience. Sharing donors, whether through FRESH-O or COM-O decreases cost & the # of supernumerary embryos but also increases the number of REC per donor, and therefore genetically-related offspring in the background of consumer testing unraveling anonymity. Donors and intended parents require full & appropriate counseling.

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SURVIVAL RATE OF MATURE DEVITRIFIED OOCYTES IN A DONOR PROGRAM.

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OBJECTIVE: To analyze the number of mature oocytes that survive devitrification classified into three groups by number of aspirated oocytes in a donor program

DESIGN: Retrospective, Observational.

MATERIALS AND METHODS: A retrospective, observational study was carried out between the period of 2014 to 2019 that includes 224 cycles of donors aged between 18 and 25 with antimulleriana hormone > 2.5 ng/ml, patients with polycystic ovary syndrome were excluded. A long protocol of agonist Leuprorelin 5UI d21 was administered, for ovarian stimulation FSHr was used, doses of 200 to 225 IU, final maturation was carried out with choriogonadotropin alfa 250 μg, follicular aspiration was performed 35 hours post trigger. Subsequently, they were classified by number of ovules in <15, 16-30 and 31 or more.

RESULTS: In the group of <15 oocytes, 510 were aspirated, being 401 MII (78.6%) and after devitrification 341 were recovered; Survival rate was 85%. In the group of 16-30 oocytes 2415 were aspirated, of which 1237 MII (51.2%) and 1047 were recovered; the survival rate was 84%. In the group of 31 or more, 990 oocytes were aspirated, of which 475 are MII (47.9%) and 371 were recovered; the survival rate was 78%.

CONCLUSIONS: In donor cycles for vitrified oocytes with a long agonist protocol, aspiration of 15 or fewer oocytes has the best survival rate, as well as a better percentage of usable mature eggs.

P-426 4:30 PM Sunday, October 18, 2020

EGG DONOR PERCEPTIONS OF LONG-TERM ADVERSE OUTCOMES.

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Number of donation cycles and average number of oocytes per donation cycles

Potential long-term risk of oocyte donation	Number of donors reporting condition	Frequency in oocyte donor population	Mean donation cycles with vs without condition	P-value (t-test)	Mean eggs per cycle with vs without condition	P-value (t-test)
Menstrual irregularities	73	30.0%	3.6 vs 3.5	NS	25.4 vs 25.0	NS
Hormonal irregularities	52	21.4%	3.5 vs 3.6	NS	28.3 vs 24.3	NS
Endometriosis	12	4.9%	2.5 vs 3.6	NS	24.6 vs 25.1	NS
PCOS	18	7.4%	3.3 vs 3.6	NS	27.4 vs 25.0	NS
Reproductive or other cancers	11	4.5%	2.5 vs 3.6	NS	21.6 vs 25.3	NS
Post-donation infertility	23	9.5%	3.1 vs 3.6	NS	25.7 vs 25.1	NS

OBJECTIVE: To examine egg donor self reports of perceived long-term adverse outcomes in relation to number of donation cycles and eggs produced per cycle

DESIGN: Survey.

MATERIALS AND METHODS: Oocyte donors (n=243) in the US were surveyed a year or more after their last oocyte donation regarding potential long-term risks associated with repeated oocyte donations. Potential risks evaluated included menstrual irregularities, hormonal irregularities, endometriosis, polycystic ovary syndrome (PCOS), reproductive cancer, and post-donation infertility. The mean number of donation cycles per donor was compared between egg donors reporting the occurrence, or not, for each potential risk and evaluated by t-test.

RESULTS: Past oocyte donors completed the survey from one to as many as 27 years (mean = 7.2, SD = 6.6, median = 4, interquartile range = 2 to 10) following their last oocyte donation cycle. Mean number of donation cycles and mean number of eggs retrieved per donation cycle did not differ significantly between those experiencing vs those not for each of the potential risks evaluated (Table).

CONCLUSIONS: Perceived experiences long-term adverse effects were higher than anticipated, but reports of long-term effects do not appear to be related to number of cycles or number of eggs produced per cycle.

SUPPORT: This study was supported by the University of California, San Francisco, Institute for Health and Aging; UCSF Individual Investigator Grant (#7501159); and funding from the National Science Foundation (#1828783).

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PRE-TREATMENT PREDICTORS OF EGG DONORS WHO WILL UNDERGO ADDITIONAL OOCYTE DONATIONS AFTER THEIR FIRST.

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OBJECTIVE: To assess corresponding factors on probability an oocyte donor will undergo additional donations after their first donation.

DESIGN: Survey.

MATERIALS AND METHODS: Oocyte donors (n=318) in the US were surveyed regarding pre-donation characteristics, and the probability that they undergo additional donations after their first. Donors providing eggs to a friend or relative were excluded.

RESULTS: The frequency of second cycles after a first donation declined from 89% among women aged 18 to 22 years to 56% among women aged 30 to 36 years. The frequency of second cycles after a first donation declined from 91% among women with a high school, GED, or vocational education to 70% among women with a post-graduate degree (Master's or Ph.D.). Reported income and degree to which they were financially motivated to donate were not related to repeat donation. However, donors who were paid more were more likely to undergo multiple donations. Reported prior psychological conditions including anxiety, depression, and mood swings were unrelated to the frequency of repeat donation.

Probability of donors undergoing a second cycle after their first oocyte donation according to age, academic education level, and monetary compensation, assessed using Kendall's test for significant association.

Age at first donation	Sample size	Repeat donation	*P*-value
Less than 23 years	76	89.5%	0.0003
23 to 25 years	117	82.9%	
26 to 27 years	64	81.3%	
28 to 29 years	27	74.1%	
30 years or older	34	55.9%	
Academic education level	Sample size	Repeat donation	0.0007
High school, GED, or vocational school	77	90.6%	
Bachelor's degree	118	80.8%	
Graduate degree	87	70.1%	
Monetary compensation (inflation adjusted)	Sample size	Repeat donation	<0.0001
None	22	22.7%	
Less than $5,000	20	70.0%	
$5,000 to $6,999	120	84.2%	
$7,000 or greater	154	87.0%	

CONCLUSIONS: Higher monetary compensation was correlated with decisions to undergo repeat donation cycles.

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RECIPIENTS RECEIVING EGGS FROM INFERTILE DONORS SHARING HALF OF THE EGGS COLLECTED HAVE NO LESS CHANCE OF HAVING A LIVE DELIVERY COMPARED TO RECIPIENTS RECEIVING EGGS FROM A PAID DONOR.

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OBJECTIVE: Certain states that have mandated coverage for in vitro fertilization-embryo transfer (IVF-ET) will pay for the whole IVF cost for donor oocyte cycles with the exception of actual payment to the donor or payment for frozen donor oocytes. If a recipient receives one half of the retrieved eggs from an infertile donor undergoing IVF, the recipient cost is zero. The question is whether this comes at a sacrifice for success rates compared to fresh oocytes from a paid donor or frozen eggs from an egg bank. The purpose of this study was to compare pregnancy outcome according to source of donated eggs.

DESIGN: Retrospective comparative.

MATERIALS AND METHODS: We reviewed IVF cycle outcomes of women using one of four sources for donor oocytes: infertile donor sharing half the eggs collected, paid donor with all eggs to 1 recipient, paid donor with eggs split between 2 recipients, and frozen eggs from an egg bank.

	Egg Donor Type			
	Infertile donor	Paid donor, 1 recipient	Paid donor, split between 2 recipients	Thawed frozen from egg bank
Avg. age (yrs) of donor	31	29.5	28.7	25.5
No. of fresh transfers	356	473	506	26
No. of fresh and frozen transfers	614	979	892	41
% implantation	32.2%	33.1%	33%	31.1%
% live delivered/1st fresh transfer	47.5% (164/356)	47.4% (224/473)	48.2% (244/506)	38.5% (10/26)
% live delivered/retrieval	70.0% (249/356)	85.2% (403/473)	55%	46.2%

There was a trend for a significantly higher pregnancy rate per retrieval comparing source infertile donors vs. paid donor, 1 recipient (p= .064, chi-square).

Infertile donors receive no payment but only pay for their own embryo transfer. The category pregnancy rate/retrieval includes the pregnancy rate potentially using all embryos (fresh or frozen) and thus possibly several transfers from embryos formed in the first donor-oocyte cycle.

RESULTS: Live delivered pregnancy rates per transfer and retrieval according to source of donated eggs.

CONCLUSIONS: A couple receiving mandated coverage for donor egg cycles would have to decide if the 20% increased chance of a live baby using all embryos formed from a paid donor keeping all oocytes is worth the cost compared to an infertile donor source, which is free. Though the frozen egg group is small, it was least likely to result in a live delivery before having to pay for another group of frozen-thawed eggs, and thus was by far the most expensive option for couples with mandated coverage with paid donor recipient costing half of frozen-thawed eggs and paid split with 2 recipients ¼ the cost.

SUPPORT: None

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BIRTH OUTCOMES AMONG GESTATIONAL SURROGATES ACCORDING TO SURROGATE CHARACTERISTICS: THE INFLUENCE OF SURROGATE AGE AND PARITY.

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OBJECTIVE: To investigate whether commonly measured characteristics of gestational surrogates can be predictive of neonatal outcomes

DESIGN: Retrospective chart review

MATERIALS AND METHODS: Singleton and twin births among parous gestational surrogates from a single infertility treatment center were retrospectively reviewed. Gestational age at birth, birth weight, and frequency of caesarean section were evaluated according to surrogate age, height, body mass index (BMI), parity, and endometrial thickness. Potential associations were evaluated by linear or logistic regression analysis as appropriate.

RESULTS: Singleton gestational age at birth decreased by approximately 2 days with each additional previous birth (268.9 days, 265.3 days, 263.3 days, 262.2 days, and 259.1 days for 1, 2, 3, 4, and 5 previous births respectively, p=0.0025). There were weak trends toward greater gestational age and birth weight with increasing surrogate BMI that approached but did not reach statistical significance (p=0.11 and p=0.07). Twin birth weight per child declined significantly with increasing surrogate age (p=0.042), from 100 oz at 22 years down to 70 oz at 40 years (30% relative reduction in birth weight). Neither surrogate height nor endometrial thickness were associated with gestational age, birth weight, or frequency of caesarean section for either singletons or twins.

CONCLUSIONS: Gestational age of singleton births declined with increasing parity, although to a small extent likely to be of little clinical importance. Birth weight among a small cohort of twin surrogate births decreased substantially with increasing surrogate age, suggesting caution be exercised when considering transfer of multiple embryos to older surrogates. Larger studies of the influence of surrogate parity and age on neonatal outcomes are warranted.

Table. *P*-values for tests of association between surrogate characteristics and birth outcomes.

Singleton Births (n=127)					
Birth Outcome	Surrogate age, mean = 30 ± 5 years	Height, mean = 64.5 ± 2.3 inches	BMI, mean = 26.7 ± 4.2 kg/m^2	Parity, mean = 2.5 ± 1.5 births	Endometrial thickness, mean = 9.6 ± 1.8 mm
Gestational age at birth, mean = 265 ± 20 days	0.55	0.27	0.11	0.0025	0.63
Birth weight, mean = 123 ± 22 oz	0.72	0.71	0.07	0.30	0.42
Caesarean section frequency = 26%	0.20	0.18	0.66	0.46	0.81
Twin Births (n=20)					
Birth Outcome	Surrogate age, mean = 30 ± 6 years	Height, mean = 65.0 ± 2.2 inches	BMI, mean = 27.2 ± 3.2 kg/m^2	Parity, mean = 2.2 ± 1.2 births	Endometrial thickness, mean = 9.6 ± 2.2 mm
Gestational age at birth, mean = 244 ± 20 days	0.24	0.45	0.70	0.68	0.68
Birth weight, mean = 87 ± 20 oz	0.042	0.64	0.85	0.16	0.44
Caesarean section frequency = 71%	0.98	0.67	0.54	0.63	0.68

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ROUTINE ENDOMETRIAL RECEPTIVITY ARRAY IN FIRST EMBRYO TRANSFER CYCLES DOES NOT IMPROVE LIVE BIRTH RATE.

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OBJECTIVE: To report the rate of displacement of the window of implantation (WOI) in an infertile population without a history of implantation failure, and to compare the rates of live birth between patients who undergo personalized embryo transfer (pET) after ERA versus FET with standard timing.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: All patients who underwent their first single euploid programmed frozen embryo transfer at a private IVF center between January and December 2018 were assessed for inclusion. Natural cycle and min-stim FET cycles as well as cycles using egg donation were excluded. All patients were offered ERA prior to their first FET and the decision was made jointly with their physician. In those who elected, an endometrial biopsy with ERA was performed in a programmed mock cycle on day P+5. Results were interpreted as pre-receptive, receptive or post-receptive. In patients with pre-receptive or post-receptive biopsies, the duration of progesterone exposure was accordingly adjusted per manufacturer recommendations. FET cycle outcomes were compared between patients who underwent ERA with a subsequent pET and those who had FET with standard timing. The primary outcome was live birth rate. Secondary outcomes included positive hCG, clinical pregnancy, ongoing pregnancy, biochemical and miscarriage rates.

RESULTS: Of the 229 patients who underwent their first single euploid programmed FET during the study period, 147 (64.2%) elected to do ERA and 82 (35.8%) chose to proceed with FET with standard timing. ERA was receptive in 60/147 (40.8%) and non-receptive in 87/147 (59.2%). Non-receptive ERAs were pre-receptive in 81/87 (93.1%) and post-receptive in 6/87 (6.9%) of patients. Patients who opted to have ERA performed were significantly older (36.9 years vs 34.9 years, p=0.0001) and had fewer euploid embryos available for transfer (2.9+/-2.0 vs 4.3+/-2.4, p<0.0001). There were no differences in BMI, endometrial lining thickness or progesterone route used between the two groups.

Comparison was made between patients who underwent FET with standard timing to those who underwent biopsy and ERA, regardless of whether the duration of progesterone was changed based on ERA results. There were no differences in LBR (56.1% vs 56.5%, p=0.96), clinical pregnancy rate (65.9% vs 67.4%, p=0.82), rate of positive hCG (75.6% vs 79.6%, p=0.48), biochemical rate (14.5% vs 15.4%, p=0.88) or miscarriage rate (13.0% vs 15.2%, p=0.71) between groups. A subgroup analysis of only patients who had an ERA was performed to see if there was a difference in outcomes between patients who had receptive and non-receptive ERA results. Patients with receptive ERA results did not significantly differ from those with non-receptive ERA results with regards to LBR (50.0% vs 60.9%, p=0.19), clinical pregnancy rate (65.0% vs 69.0%, p=0.61), rate of positive hCG (78.3% vs 80.5%, p=0.75), biochemical rate (19.1% vs 14.3%, p=0.48), or miscarriage rate (23.1% vs 10.0%, p=0.08).

CONCLUSIONS: Our data does not support the routine use of ERA in an unselected patient population undergoing first programmed single euploid embryo transfer.

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CLINICAL FACTORS ASSOCIATED WITH MONOZYGOTIC TWINNING AFTER SINGLE EMBRYO TRANSFER.

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OBJECTIVE: The current study aimed to identify clinical factors associated with monozygotic splitting after SET.

DESIGN: Retrospective case-control study

MATERIALS AND METHODS: Patients who underwent IVF with SET from 2002 to 2020 that resulted in monozygotic twinning (MZT) were compared to singleton gestations. Cycles with more than one embryo transferred were excluded. Student's t-test, chi-squared test and multivariate logistic regression were used for the analysis.

RESULTS: 3.1% (n=205) of pregnancies after SET resulted in MZT pregnancies. Patient age, BAFC, stimulation protocol, GND dose, E2 and P4 levels, number of oocytes retrieved and day of embryo development did not differ significantly between MZT and singleton pregnancies. Both groups had similar rates of utilizing donor oocytes, frozen transfer, ICSI, PGT-A, repeat trophectoderm biopsy and repeat vitrification-warming. Controlling for relevant confounders, embryos with increased TE grade (A vs. C: OR 3.11, CI 1.39-6.94) and female sex (OR 1.73, CI 1.09-2.72) had increased odds of MZT.

	MZT pregnancy (n=205)	Singleton pregnancy (n=6404)	p value
Patient age	37 ± 5.1	36.6 ± 5.1	.21
AMH	3.4 ± 3	3.8 ± 4.3	.36
BAFC	13.2 ± 8.1	13.4 ± 8	.75
BMI	24 ± 4.9	24.1 ± 4.5	.85
Stimulation protocol (%)			.55
GnRH antagonist	144 (75.4)	4546 (76)	
GnRH agonist	2 (1)	142 (2.4)	
Microflare	16 (8.4)	414 (6.9)	
OCP/Lupron	4 (2.1)	129 (2.2)	
Synthetic	17 (8.9)	596 (10)	
Other	8 (4.2)	155 (2.6)	
GND dose	3379.9 ± 1344.5	3372.8 ± 1297.5	.94
Donor oocyte (%)	26 (12.7)	816 (12.7)	.98
IVF cycle			.22
Fresh	47 (22.9)	1246 (19.5)	
Frozen	158 (77.1)	5158 (80.5)	
E2	2426.6 ± 1220.3	2446.4 ± 1210.2	.83
P4	.9 ± .5	.9 ± .5	.81
Eggs retrieved	16.5 ± 10.3	17.2 ± 9.8	.33
Fertilization method (%)			.06
Conventional	18 (9.1)	813 (13.3)	
ICSI	176 (89.3)	5282 (86.2)	
Split	3 (1.5)	36 (.6)	
PGT-A (%)	137 (66.8)	4246 (66.3)	.88
Day of embryo development (%)			.92
3	6 (2.9)	168 (2.6)	
5	128 (62.4)	3961 (61.9)	
6	69 (33.7)	2216 (34.6)	
7	2 (1)	59 (.9)	
Number of TE biopsies (%)			.54
1	139 (98.6)	4259 (98)	
2	1 (.7)	67 (1.5)	
3	1 (.7)	21 (.5)	
Number of times vitrified and warmed (%)			.97
1	156 (98.7)	5901 (98.7)	
2	2 (1.3)	67 (1.3)	
Expansion grade (%)			<.01
3	8 (4)	141 (2.3)	
4	92 (46.2)	3321 (53.4)	
5	67 (33.7)	1419 (22.8)	
6	31 (15.6)	1296 (20.8)	
ICM grade (%)			.16
A	141 (71.6)	4624 (75.9)	
B	45 (22.8)	1287 (21.1)	
C	11 (5.6)	179 (2.9)	
TE grade (%)			<.01
A	107 (54.3)	2695 (44.2)	
B	73 (37.1)	2418 (39.7)	
C	17 (8.6)	966 (15.9)	
Embryo sex			<.01
F	90 (63.8)	2267 (52.2)	
M	51 (36.2)	2080 (47.8)	

CONCLUSIONS: Our study showed that female embryos and blastocysts with favorable TE grade are more likely to split. Monozygotic splitting could be related to the rate of proliferation and differentiation of TE cells. Future studies are needed to determine the epigenetic drivers of monozygotic splitting and the molecular basis for the sexual dimorphism found in our study.

SUPPORT: None

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P-432 4:30 PM Monday, October 19, 2020

ARTIFICIAL INTELLIGENCE MACHINE LEARNING MODELING TO PREDICT SINGLE EUPLOID BLASTOCYST TRANSFER OUTCOMES.

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OBJECTIVE: An evidence-based algorithm for the probability of predicting successful live birth has significant clinical utility in counseling infertility patients regarding embryo transfer outcomes. Towards this objective, we examined an artificial intelligence (AI), machine learning classification model using patient clinical measurements and IVF cycle characteristics to assess the prognostic value in estimating treatment outcomes including live birth.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: In total, 3,368 consecutive, single, autologous, euploid frozen blastocyst transfers that occurred from 2009-2019 were included. Decision tree algorithms constructed classification models based on 17 clinical measurements (including ovarian reserve, BMI, embryo grade) and transfer outcomes: negative serum β-hcG (10 days after transfer), biochemical (consecutive positive serum β-hcG 10-12 days after transfer), non-viable implantation (visualized gestational sac and no fetal pole), miscarriage (visualized fetal heart tone followed by loss) and live birth. Data was randomly allocated, with 70% applied to training the AI machine learning model and 30% for prediction testing. Fisher's exact, Kruskal-Wallis, pairwise Wilcoxon, and Benjamini-Hochberg p-value adjustment were used to calculate statistical significance of individual parameters where appropriate, $p < 0.05$.

RESULTS: In the absence of β-hcG, no classification models were significant. Modeling β-hcG alone demonstrated an overall accuracy of 87.5% ($p < 0.0001$) and investigation of β-hcG distribution demonstrated significant pairwise differences between all outcomes ($p < 0.0001$ for all pairwise comparisons). Individual parameter evaluation of miscarriages revealed monozygotic twinning was 2.5x more likely to end in a miscarriage than any other outcome ($p < 0.05$). The addition of maternal age did not result in an increase in model predictive accuracy, emphasizing that the age-related reduction in reproductive efficiency is predominantly overcome with a euploid embryo transfer. Blastocyst quality increased accuracy to 88.0% ($p < 0.0001$), and together with β-hcG distributions, were stratified to create a live birth outcome probability table for clinical utilization. Analysis of blastocyst quality by outcome revealed 2.1x enrichment of high-grade blastocysts with a live birth (day 5 biopsy, Grade 3-5, AA or BA; p-adj < 0.0001). Negative, biochemical, and non-viable implantation outcomes had 2.1x, 1.9x and 1.8x fewer high-grade blastocysts respectively (p-adj < 0.0001, 0.001, 0.05) and negative outcome alone had 4.7x more day 7 biopsied blastocysts (p-adj < 0.0001).

CONCLUSIONS: Overall, clinical measurements evaluated in AI machine learning had poor predictive value in stratifying single, euploid blastocyst transfer outcomes, emphasizing the heterogeneity and biological complexity of infertility patients and their treatment. Nevertheless, classification using β-hcG distributions and blastocyst quality together displayed high predictive accuracy for live birth following a single euploid embryo transfer.

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SEX-SPECIFIC EMBRYO CLEAVAGE KINETICS AND PERINATAL OUTCOMES AFTER BLASTOCYST TRANSFERS.

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OBJECTIVE: Extended embryo culture during in-vitro fertilization (IVF) is associated with an increased risk of adverse perinatal outcomes such as preterm delivery in fresh cycles. While utilization of vitrified/warmed blastocyst embryo transfers (FET) has increased, the impact of subtle differences in embryo development kinetics on perinatal outcomes is unknown. In addition, increasing evidence supports sex-specific variations in early human embryo development, suggesting the impact of extended embryo culture on perinatal outcomes may be dimorphic. Our objective was to determine the sex-specific association of embryo culture duration and adverse perinatal outcomes in FETs.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: All autologous vitrified/warmed blastocyst transfers from 1/1/2015-4/18/2020 at an urban academic center were identified. Cycles with previously frozen oocytes and mixed fresh/frozen transfer cycles were excluded. Embryos were cultured in CSCM media (Fujifilm Irvine Scientific) and cycles were analyzed according to days of embryo culture prior to vitrification: Day 5 (D5ET) vs Day 6 (D6ET). Logistic regression modeling was used to determine the association between duration of embryo culture and preterm delivery considering effect modification by fetal sex and adjusting for relevant confounders as appropriate. Secondary outcomes include rates of clinical pregnancy, live birth, preeclampsia, and low birth weight.

RESULTS: Of 1820 cycles in 1120 patients, there were 1345 D5ET (73%) and 475 D6ET (23%). D6ET patients were slightly older (D5ET 35.3 years vs D6ET 36.3 years, $p<0.05$) and PGT utilization was lower in D5ET compared to D6ET (28% vs 37%, $p<0.05$). There were no differences in race, ethnicity, maternal body mass index, and >80% were single embryo transfers in both groups. D5ET had a higher clinical pregnancy rate (D5ET 60.2% vs D6ET 47.6%, $p<0.001$) and of those who have delivered, a higher live birth rate compared to D6ET (D5ET 42% vs D6ET 32%, $p<0.0001$). Sex ratios were similar between the two groups (M:F D5ET 49:51 vs D6ET 45:55, $p=0.4$). There were no differences in gestational age at delivery, birth weight, or preeclampsia overall ($p>0.05$). Amongst singleton deliveries, D6ET had a higher incidence of preterm delivery (OR 1.85, 95% CI [1.04-3.27]). Moreover, fetal sex was an effect modifier in the relationship between duration of embryo culture and preterm delivery such that a lower incidence of preterm delivery was observed in D5ET females (10% D5ET for males vs 5% D5ET for females) whereas a higher incidence was noted in D6ET females (11% D6ET for males vs 17% D6ET for females).

CONCLUSIONS: Improvements in embryo culture and vitrification have revolutionized IVF success. However, the optimization of perinatal outcomes in pregnancies conceived after IVF remains elusive. Our data suggest that duration of culture may impact embryo development and perinatal outcomes in singletons, and this effect may be sexually dimorphic. Further studies are needed to understand the etiology for these observations and define modifiable factors that may improve pregnancy and perinatal outcomes.

SUPPORT: NIH P50HD068157

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P-434 4:30 PM Monday, October 19, 2020

DOES TROPHECTODERM BIOPSY FOR PREIMPLANTATION GENETIC TESTING AFFECT FETAL BIRTH WEIGHT OR RATE OF PRETERM DELIVERY? A SART CORS STUDY.

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OBJECTIVE: Preimplantation genetic testing for aneuploidy (PGT-A) is used as part of IVF treatment to select euploid embryos, and involves trophectoderm biopsy of blastocysts. The effects of possible trauma caused by biopsy of the blastocyst and implications on placental development are unknown. Therefore, the goal of our study was to evaluate if PGT-A is associated with adverse neonatal birth outcomes, including birthweight, small for gestational age (SGA), and preterm birth (PTB).

DESIGN: Retrospective study.

MATERIALS AND METHODS: Using the data from the national Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS), we identified 6,352 cycles which had single embryo transfer leading to a singleton live birth following frozen embryo transfer (FET) between 2014 and 2015. Our study group included cycles with PGT-A confirmed euploid embryos used for transfer, and our control group included all other FETs where non PGT-A tested embryos were used. We assumed that in the PGT-A group, euploid embryos were transferred and embryos with mosaicism or inconclusive results were discarded. The demographic and IVF cycle information were obtained from the corresponding linked fresh stimulation cycles. PTB was defined as delivery before 37 weeks' gestation and SGA was defined as birth weight less than 10th percentile for gestational age. Depending on the outcome, multivariable logistic or linear regression were used to estimate the association between SGA, PTB, or birthweight and PGT-A. Models were adjusted for patient's age, gravidity, history of PTB, smoking, infant sex, gestational age and number of oocytes retrieved.

RESULTS: From the initial cohort of 31,751 cycles, 6,352 cycles which had a singleton live birth following FET were included in the final cohort. A total of 3,482 (54.8%) had PGT-A confirmed euploid embryos and 2,870 (45.2%) had embryos selected based on morphology for transfer. No difference in birthweight (grams) was noted when FET was performed using PGT-A confirmed euploid embryos compared to non-tested morphologically selected embryos (3370.7 vs. 3354.5 grams, adjusted regression coefficient 11.4; 95% CI: -12.6; 35.3). As compared to morphologically selected embryos, performance of PGT-A did not increase the risk of SGA (3.9% vs. 4.1%, OR: 1.13; 95% CI: 0.86-1.50), low birth weight (1500-<2500 g) (5.8% vs. 5.5%, OR: 0.90; 95% CI: 0.66-1.21), or very low birthweight (1.3% vs. 1.0%, OR: 0.44; 95% CI: 0.44 (0.18-1.10). There was no increased risk of PTB associated with pregnancy resulting from PGT-A embryos vs. non PGT-A embryos (15.8% vs. 16.4%, OR: 0.94; 95% CI: 0.81-1.09).

CONCLUSIONS: In our study, trophectoderm biopsy for PGT-A did not increase the risk of adverse neonatal outcomes, including SGA or PTB in IVF pregnancies.

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ORAL CONTRACEPTIVE PRETREATMENT DOES NOT ALTER LIVE BIRTH RATES IN PGT-A SCREENED FROZEN EMBRYO TRANSFER CYCLES.

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OBJECTIVE: Oral contraceptives pills (OCPs) have been a long-standing adjuvant used for multiple purposes during ART treatment. Despite a widespread adoption of OCPs in many clinical settings, some studies have suggested that OCP utilization might exhibit a deleterious effect on IVF outcomes. Opponents have proposed the progesterone compound of OCPs may negatively affect endometrial receptivity[1]. Recently, one study showed pregnancy rates were negatively associated with OCP usage[2]. Furthermore, the utilization of OCPs has been associated with increased pregnancy loss rates in frozen embryo transfer (FET) cycles[3]. The majority of available published evidence about OCPs use has included data derived from fresh IVF cycle outcomes; however, data regarding the effect of OCPs pretreatment in euploid FETs is scarce. The objective of this analysis is to assess the effect of OCPs pretreatment on pregnancy rates in single euploid FET cycles.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: The study included patients who underwent a FET cycle from 2016-2020. PGT-A with *NGS was* performed in all cases. Cohorts were segregated in two groups based on OCPs pretreatment during the FET cycle: Group 1: OCP pretreatment; Group 2: Endometrial preparation cycles without OCP utilization. Patient demographics and IVF cycle outcomes were assessed. Comparative statistics, multivariate regression and an adjusted mixed model with a GEE were utilized for statistical analyses. A sample size of 388 FET's per group was calculated to ensure an 80% power to detect a difference of 10% on live birth rates (LBR) (α=0.05).

RESULTS: 1,405 single euploid FET cycles with OCP pretreatment were compared to 4,622 control cycles. Significant differences were found in patient and oocyte ages between cohorts. No differences were found in AMH, BMI, and endometrial thickness at FET among cohorts. Also, no differences were found in number of good quality embryos transferred, implantation, clinical pregnancy (CPR), LBR, and clinical loss (CLR) rates. Gestational age and birth weight at delivery were similar among groups. After adjusting for confounders there was no correlation between the days of OCP utilization and lower LBR (R2=0.06, p=0.15). Finally, after adjusting for age, BMI, AMH, embryo quality and endometrial thickness, no association was found between OCP utilization and lower odds of implantation (OR 1.22 CI95% 0.9-1.6, p=0.18); CPR (OR 0.76 CI95% 0.5-1.1, p=0.17); LBR (OR 0.81 CI95% 0.6-1.1, p=0.26) or CLR (OR 1.07 CI95% 0.6-1.6, p=0.73).

CONCLUSIONS: OCPs can safely be used for patient planning and to ensure that NGS results on analyzed embryos is available to support embryo selection decisions. Based on our findings, OCP pretreatment does not appear to affect implantation or live birth rates after the transfer of a euploid embryo within a synthetically prepared endometrium. Further studies focusing on endometrial genetic transcription patterns and their interactions with different hormonal preparations during the peri-implantation period should be performed in order to optimize and personalize the endometrial molecular microenvironment.

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SUPPORT: None

P-436 4:30 PM Monday, October 19, 2020

PERINATAL OUTCOMES IN BABIES BORN FOLLOWING BLASTOCYST VERSUS CLEAVAGE STAGE EMBRYO TRANSFER - A RETROSPECTIVE ANALYSIS OF 113,764 IVF/ICSI CYCLES.

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OBJECTIVE: To compare perinatal outcomes in babies born following blastocyst (Day 5) versus cleavage stage (Day 2 or 3) embryo transfer.

DESIGN: A population-based cohort study using cycle to woman linked data from 2000 to 2017 in the United Kingdom Human Fertilisation and Embryology Authority register.

MATERIALS AND METHODS: In babies conceived through in-vitro fertilisation (IVF), we investgated the association between the day of embryo transfer (blastocyst versus cleavage stage) and gestational age, birth weight, congenital abnormality and healthy baby rate ($\geq$37 weeks, normal birth weight and no congenital abnormalities). Generalized Estimating Equation (GEE) models with robust standard errors were used to account for women

with more than one live birth episode while a log-binomial model was used for binary outcomes and multinomial model for birthweight outcomes.Maternal (age, cause of infertility, previous live birth status) and treatment factors (IVF versus ICSI, number of eggs collected and number of embryos transferred) were considered as confounders in multivariable models. Relative Risk (RR) and 95% Confidence Intervals (CI) were estimated. The analysis was repeated for twins and for singleton siblings conceived through either blastocyst or cleavage stage embryos. Comparison of siblings allowed us to assess the influence of day of embryo transfer whilst minimising the confounding effect of maternal factors.

RESULTS: There were 86, 630 singleton live births (28, 814 following blastocyst versus 57, 816 following cleavage stage ET), 21,940 twin live births (5,194 vs 16,746) and 5,384 sibling pairs. Singletons born following blastocyst transfer were more likely to be born preterm (<37 weeks) compared to those conceived from cleavage stage embryos (aRR 1.13; 95% CI 1.06, 1.19). However, they were more likely to be a healthy baby (aRR 1.01; 95%CI 1.01, 1.02), with a lower risk of having a congenital abnormalilty (aRR 0.63; 95%CI 0.57, 0.71) and high birth weight (>4500g) (aRR 0.92; 95%CI 0.87, 0.99). Twins born following had an increased risk of preterm birth (aRR 1.19; 95%CI 1.12, 1.28) and low birthweight (<2500g) (aRR 1.11; 95%CI 1.05, 1.17) compared to twins born following cleavage stage transfer. However, they had a decreased risk of congenital abnormality (aRR 0.80; 95%CI 0.67, 0.95) and being a healthy baby (aRR 0.85; 95%CI 0.82, 0.90) . There was no statistically significant difference in the risk of between siblings conceived from blastocyst and cleavage stage embryos.

CONCLUSIONS: Babies (both singleton and twins) born following blastocyst ET are more likely to be born preterm but are at a decreased risk of having a congenital abnormality compared to those following cleavage stage ET. However, these differences were not present when siblings were compared suggesting that maternal factors may be a greater influence than the day of embryo transfer. This provides reassurance to the default position of embryo transfer at blastocyst stage.

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WEIGHING IN ON LIVE BIRTH RATE AFTER A SINGLE EUPLOID TRANSFER. Jill Karten, M.D.,[1] Baruch Abittan, M.D.,[2] Weiwei Shan, MS PhD,[3] Randi H. Goldman, M.D.,[2] Christine Mullin, M.D.[2] [1]Department of OBGYN, North Shore University Hospital/Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY; [2]Northwell Health Fertility, North Shore University Hospital/Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY; [3]Northwell Health Department of Biostatistics, New Hyde PArk, NY.

OBJECTIVE: Prior studies have evaluated the effect of body mass index (BMI) on outcomes following euploid frozen embryo transfer (FET) with varying results, and have been limited by small sample sizes[i][ii][iii]. The purpose of this study was therefore to investigate whether BMI impacts pregnancy outcomes following euploid FET using a larger population that contains a greater proportion of patients with obesity.

DESIGN: Retrospective cohort study at an academic fertility center.

MATERIALS AND METHODS: Patients undergoing euploid FET between 2015 and 2019 were included. Preimplantation genetic testing for aneuploidy was performed by either array comparative genomic hybridization or next generation sequencing. Patients were stratified by BMI (kg/m^2) category according to WHO criteria. Differences in clinical outcomes, stratified by BMI, were initially compared using Chi square, Fishers exact tests or ANOVA where indicated. Logistic regression was then performed, controlling *a priori* for maternal age and history of miscarriage.

RESULTS: Most (78%) of the 1,421 patients included were normal or overweight BMI. No differences in outcomes were observed between patients with normal BMI vs. overweight BMI. When adjusted for other variables including age and previous miscarriage, there was a significant reduction in live birth (LBR) among patients with obesity compared to patients with normal or overweight BMI. In general, for every 1-unit increase in BMI above 30, the LBR following euploid FET decreased by 3.7% (with other variables held constant). Patients with obesity had a 40% lower likelihood of LBR following transfer of a euploid embryo compared to patients with normal weight (OR: 0.58 (CI: 0.39-0.86)).

CONCLUSIONS: Obesity is associated with a decreased likelihood of LBR following euploid FET and suggests that the negative impact of BMI on live birth may be independent of embryo genetics.

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A DROP IN ESTRADIOL LEVELS POST-TRIGGER IN FRESH TRANSFER CYCLES DOES NOT NEGATIVELY IMPACT LIVE BIRTH OUTCOMES. Pietro Bortoletto, MD,[1] Phillip A. Romanski, MD,[1] Nigel Pereira, MD,[2] Zev Rosenwaks, M.D.[1] [1]The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY; [2]Ronald O. Perlman and Claudia Cohen Center for Reproductive Medicine, New York, NY.

OBJECTIVE: To determine if a post-trigger drop in estradiol (E2) level negatively impacts live birth outcomes in women undergoing IVF with fresh embryo transfer (ET).

DESIGN: Retrospective cohort study conducted at a university-affiliated center.

MATERIALS AND METHODS: Inclusion criteria included women ages 18-44 years undergoing their first IVF cycle using a GnRH antagonist protocol followed by a fresh day 3 or 5 ET at our center between 2008 and 2018. We excluded women who received a pure GnRH agonist trigger. Women were stratified into groups based on change in their E2 level from day of trigger to post-trigger: E2 rise (>0 pg/mL difference) versus E2 drop ($\leq$ 0 pg/ml difference). Live birth rate was the primary outcome. Multivariable logistic regression was used to examine the association between the two E2 groups and live birth while controlling for confounders. Odds ratios (OR) with 95% confidence intervals (CI) for live birth were estimated.

RESULTS: A total of 7,660 women were included, of whom 7,076 (92.4%) had a rise in their post-trigger E2 level and 584 (7.6%) had a drop. The mean ($\pm$SD) E2 change was 34.7% (23.2) for those with a rise in their post-trigger E2 and 8.6% (7.2) for those with an E2 drop. An hCG only ovulatory trigger was used in 84.3% versus 87.5% of the patients in the E2 rise versus drop group, respectively. Cleavage stage embryo transfer was performed in 74% versus 84% of patients, respectively. The live birth rate was 37.8% versus 32.4% (p=0.009) for women with an E2 rise versus drop, respectively. In the regression model, women over the age of 37 had reduced odds of live birth compared to women <37 years of age (OR 0.48, CI 0.42-0.854). Those with a diagnosis of diminished ovarian reserve had reduced odds of live birth when compared to women with partners diagnosed with male-factor infertility (OR 0.81, CI 0.70-0.94). After controlling for the above factors, in addition to the number of mature oocytes retrieved and the number and developmental stage of embryos transferred, there were no

	Normal weight (BMI 18.5-24.9)	Overweight (BMI 25-29.9)	Class 1 obesity (BMI 30-34.9)	Class 2/3 obesity (BMI >35)	P value
N	767	343	190	121	
Age	35.3	36.6	36.7	36.8	<0.01
%Biochemical	9.6	7.6	10.0	10.7	0.63
%SAB	7.3	6.7	11.6	9.9	0.23
%Live Birth	52.4	49.6	38.9	38.0	<0.01

differences in the odds of live birth when comparing patients with an E2 rise versus drop (OR 1.0, CI 0.83-1.21). Using the same regression model, there was no percent E2 drop (-5% to -35%) threshold identified in which the live birth outcome would have been negatively affected.

CONCLUSIONS: A drop in E2 level post-trigger does not negatively impact the live birth outcome in women undergoing fresh embryo transfer during an IVF cycle after controlling for relevant clinical and cycle level variables.

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A COMPARATIVE EVALUATION OF NOVEL SUB-ENDOMETRIAL AND INTRAUTERINE PLATELET RICH PLASMA TREATMENT FOR WOMEN WITH RECURRENT IMPLANTATION FAILURE (RIF).

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OBJECTIVE: Sub endometrium is considered as the niche area for growth factor (GF) & cytokine production[1] . Aim of the study was to compare the effectiveness of treatment with autologous activated platelet rich plasma (PRP), administered either to sub-endometrium (SE-PRP) or to endometrial surface (intrauterine; IU-PRP) against controls.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: The study was undertaken from Jan 2019-20. Women aged <40 years with history of unexplained RIF undergoing Frozen Embryo transfer (FET) were recruited. **Exclusion criteria** included women with BMI ≥ 30 kg/m2, untreated uterine abnormalities, untreated hydrosalpinges, low ovarian reserve, thrombophilia, uncontrolled endocrinopathy , severe male factor infertility, difficult embryo transfer, only poor quality embryos available & couple with chromosomal abnormalities.

INTERVENTION: SE-PRP- 4 ml PRP was injected into the sub endometrial space trans vaginally via Embryo transfer catheter under ultrasound guidance in the luteal phase of previous cycle of FET (n=33). **IU-PRP**- Intrauterine infusion of 1 ml PRP was done during FET cycle when endometrium was 7 mm (n=109). **Controls** underwent standard FET with no intervention (n=154).

All patients were given the option to choose either SE- PRP, IU-PRP or no intervention with an informed consent.

PRP PREPARATION : Both SE-PRP and IU-PRP groups were given colony stimulating factor (G-CSF) 300 μg subcutaneous for 3 days to boost WBC & GF production[2]. The next day 60 ml blood was drawn & PRP was prepared using by double centrifugation (FDA approved Regen kit) . Post PRP preparation platelets rose to a range of 10-15 L/μl. Activation of PRP was done with freeze thaw technique using liquid nitrogen[3] . PRP was prepared at 20-22°C & infused within 10 min of preparation to maintain efficacy.

For the FET-Endometrium was prepared by hormone replacement treatment (HRT) protocol. Estradiol valerate was started on day 2/3 of cycle at dose of 6mg & once endometrium was ≥8mm progesterone vaginal pessary 400 mg twice daily was offered for luteal support.

Statistical analysis was done with SPSS (version 20) using ANOVA (bonferroni test) & chi-square tests.

Main outcome measures : Ongoing pregnancy or live birth rate (OPR/LBR); Clinical pregnancy rate (CPR), and miscarriage rate (MR).

RESULTS: Baseline characteristics (Age , BMI , AMH, NUMBER OF FET ATTEMPT, NUMBER AND QUALITY OF EMBRYOS TRANSFERRED[4]) were similar in all the groups. OPR/LBR was higher (P<0.01) in the SE-PRP (13/33; 39.4%) and IU-PRP (45/109; 41.3%) than in the control group (34/154; 22.1%). OPR/LBR was similar between SE-PRP vs IU-PRP (P=0.85). CPR showed a similar trend (P<0.01) with a higher rate in the SE-PRP (17/33; 51.5%) and IU-PRP (57/109; 52.3%) than the controls (52/154; 33.8%). There was no statistical difference in the CPR between SE-PRP vs IU-PRP (P=0.94). MR was similar in all three groups (4/33; 12.1%, 12/109; 11% and 18/154 ; 11.7% respectively).

CONCLUSIONS: In women with history of RIF, PRP treatment appears to improve FET outcome with increase in OPR/LBR. However, SE-PEP treatment do not offer any advantage over lesser invasive IU-PRP treatment.

SUPPORT: Nothing to disclose.

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SEARCHING FOR THE OPTIMAL NUMBER OF OOCYTES TO REACH A LIFE BIRTH AFTER *IN VITRO* FERTILIZATION: A SYSTEMATIC REVIEW WITH META-ANALYSIS.

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OBJECTIVE: Several lines of evidence indicate that number of oocytes represents a key point for in vitro fertilization (IVF) success. However, consensus is lacking regarding the optimal number of oocytes for expecting a live birth. The present study aims to investigate the relationship between the number of oocytes and both the live birth rate after fresh embryo transfer (LBR) and cumulative live birth rate (CLBR).

DESIGN: A systematic review and independent meta-analyses.

MATERIALS AND METHODS: Literature search in MEDLINE, EMBASE and Cochrane Library was performed for studies published between January 01, 2004 and August 31, 2019, combining the Medical Subject Headings and text words for 'IVF', 'ICSI', 'fertility preservation' 'oocytes number' and 'live birth'. Studies that only reported results on infertile couples undergoing Prenatal Genetic Screening cycles, or oocyte donation cycles, were excluded. Two independent reviewers carried out study selection, quality assessment using the adapted Newcastle-Ottawa Quality Assessment Scales, bias assessment using ROBIN-1 tools, and data extraction according to Cochrane methods. Independent analyses were planned according to the type of oocytes (retrieved and mature) and to the outcome (LBR and CLBR). Mean-weighted threshold of optimal oocyte number was estimated from documented thresholds followed by a one-stage meta-analysis, using R software, dosresmeta package and restricted cubic splines, on articles with documented or estimable relative risks.

RESULTS: After review of 843 records, 62 full-text articles were assessed for eligibility. A total of 35 studies were available for the quantitative syntheses. Sixteen and 15 studies were included in the meta-analyses evaluating the relationship between the number of retrieved oocytes and LBR or CLBR, respectively. Given the limited number of investigations considering mature oocytes, association between the number of metaphase II oocytes and IVF outcomes could not be investigated.

Concerning LBR, 7 (35.0%) studies reported a plateau effect, corresponding to a weighted mean of 14.4 oocytes. The pooled dose-response association between the number of oocytes and LBR showed a non-linear relationship with a plateau beyond 15 oocytes.

For CLBR, 4 (20.0%) studies showed a plateau effect, corresponding to a weighted mean of 22.9 oocytes. The meta-analysis on the relationship between the number of oocytes and CLBR also found a non-linear relationship, with a slight but sustained increase in CLBR beyond 14 oocytes.

All analyses showed a statistically significant deviance criterion (p<0.01) and a high coefficient of determination (R^2 > 90% for all meta-analyses). Sensitivity analyses were not able to decrease deviance.

CONCLUSIONS: This first meta-analysis on the topic indicates a non-linear relationship between the number of retrieved oocytes and both LBR and CLBR. Above a threshold of 15 oocytes, the LBR following fresh transfer plateaus. On the contrary, for CLBR, our findings suggest a slight increase beyond 14 oocytes. Sub-groups analyses are currently performed in order to assess the influence of female age.

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THE PREDICTIVE VALUE OF ESTRADIOL LEVEL IN EUPLOID NATURAL CYCLE FROZEN EMBRYO TRANSFER PREGNANCY OUTCOMES. Brindha Bavan, MD,[1] Jasmyn K. Johal, MD, MS,[2] Wendy Y. Zhang, BS,[3] Matthew J. Sahagun, BS, MA,[4] Amin A. Milki, MD,[1] Anna Sokalska, MD, PhD,[1] [1]Stanford Fertility and Reproductive Medicine Center, Sunnyvale, CA; [2]Stanford University, Dept of Obstetrics & Gynecology, Stanford, CA; [3]Stanford University School of Medicine, Stanford, CA; [4]California State University East Bay, Dept of Statistics & Biostatistics, Hayward, CA.

OBJECTIVE: To determine whether estradiol (E2) level on the day of LH surge/hCG trigger in euploid natural cycle frozen embryo transfers (NC-FET) is associated with pregnancy outcomes

DESIGN: IRB-approved retrospective cohort study.

MATERIALS AND METHODS: All NC-FET with euploid blastocysts performed at a single academic institution from May 2016 to March 2019 were reviewed. Demographic data including age, BMI, parity, race, smoking status, and SART diagnosis were collected. All patients underwent uterine cavity evaluation with correction if needed prior to NC-FET. Standard protocol for NC-FET included hCG trigger when the dominant follicle was $\geq$18 mm and the endometrial lining was $\geq$7 mm. NC-FET was performed 6 days after spontaneous LH surge (augmented with hCG trigger) or 7 days after hCG trigger alone. E2 (pg/mL) was evaluated on the day of hCG trigger. Vaginal progesterone was started 3 days before NC-FET. NC-FET with E2 $<$200 were compared to NC-FET with E2 $\geq$200. The primary outcomes of interest were clinical pregnancy rate (CPR, defined as intrauterine gestation with positive fetal cardiac activity) and live birth rate (LBR). *The R Project for Statistical Computing* was used to complete independent t-tests for continuous variables, chi-square tests for categorical variables, and logistic regressions for outcome variables.

RESULTS: A total of 441 NC-FET were analyzed. Mean age at transfer was 36.5 $\pm$SD 3.8 years, and mean BMI was 25.0 $\pm$SD 4.8 kg/m^2. The majority of patients were nulliparous (63%), Asian (51%) or White (39%), and never smokers (95%). Mean E2 on the day of spontaneous LH surge/hCG trigger was 274 $\pm$SD 121. The overall CPR was 65%, and the overall LBR was 61%. There were 134 NC-FET with E2 $<$200 and 307 NC-FET with E2 $\geq$200. Demographic variables did not significantly differ between the 2 groups, except for mean BMI, which was 26.2 in the E2 $<$200 group vs. 24.4 in the E2 $\geq$200 group, p$<$0.01. CPR was 58% for cycles with E2 $<$200 vs. 68% for cycles with E2 $\geq$200, p=0.04; LBR was 52% for cycles with E2 $<$200 vs. 65% for cycles with E2 $\geq$200, p=0.01. In a logistic regression controlling for age at transfer, BMI, parity, race, smoking status, endometrial thickness, and embryo grade, E2 $\geq$200 still predicted an increased CPR (OR 1.74 [CI 1.11, 2.72]) and an increased LBR (OR 1.94 [CI 1.25, 3.03]).

CONCLUSIONS: The focus before proceeding with NC-FET has traditionally been dominant follicle size and endometrial thickness. E2 level may also play an important role in preparing the endometrium for implantation and pregnancy, as suggested by a study of 101 untested, cleavage-stage NC-FET (1). The strength of our study lies in its larger cohort size and inclusion of only NC-FET with euploid blastocysts. In our patient population, E2 $\geq$200 at the time of hCG trigger in NC-FET predicted an increased CPR and LBR, both with statistical significance. These findings support delaying hCG trigger if E2 $<$200 in the absence of an LH surge, even when criteria for dominant follicle size and endometrial thickness are met. When an LH surge occurs and delaying hCG trigger is not possible, providers may consider postponing NC-FET to another cycle when E2 level might be more optimal.

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SUPPORT: There was no financial support for this research study.

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MINIMAL STIMULATION USING GONADOTROPIN-RELEASING HORMONE ANTAGONIST IS ASSOCIATED WITH HIGHER LIVE BIRTH RATES: A NATIONAL STUDY OF 13,050 CYCLES. Emily G. Hurley, MD,[1] Fangbai Sun, MPH,[2] Heping Zhang, PhD,[2] Alex J. Polotsky, M.D., M.S.,[3] Julie Sroga Rios, MD,[1] [1]University of Cincinnati, West Chester, OH; [2]Yale University School of Public Health, New Haven, CT; [3]University of Colorado Anschutz Medical Campus, Aurora, CO.

OBJECTIVE: Minimal stimulation for in vitro fertilization (IVF) is advocated for reduced costs and lower rates of side effects. However, the preferred clinical protocol remains undetermined. In order to optimize patient outcomes, it is necessary to establish if the use of gonadotropin-releasing hormone (GnRH) antagonist during minimal stimulation IVF cycles improves live birth rate.

DESIGN: Historical cohort study from the Society for Assisted Reproductive Technology Clinic Online Reporting System.

MATERIALS AND METHODS: The database was queried for all fresh autologous oocyte cycles designated as minimal stimulation from 2014-2016. Cycles were categorized by the use of GnRH antagonist vs. no suppression. Cycles were excluded if an agonist flare or agonist suppression was used or if live birth was not reported. Live birth was the primary outcome. Secondary outcomes included total dose of gonadotropin, number of cryopreserved embryos and cycle cancelation rate. Wilcoxon's rank-sum test was used for continuous variables, and Chi-square test was used for categorical variables. P$<$0.05 was considered significant.

RESULTS: A total of 6,750 patients undergoing 13,050 cycles were included. Patient age ranged from 19-54 years, median 41 (IQR 37, 44) and anti-mullerian hormone (AMH) ranged from undetectable (0) to 40 ng/mL, median 0 (IQR 0.0-0.2). GnRH antagonist use was associated with a significantly higher total gonadotropin dosage (median 975.0 [IQR 600.0, 1575.0] vs. median 660.0 [IQR 375.0, 975.0]), p$<$0.001, lower cycle cancelation rate (11.3% vs. 13.6%), p$<$0.001, and higher live birth rate (4.3% vs. 2.1%), p$<$0.001, when compared to no antagonist suppression. GnRH antagonist use was associated with a significantly higher live birth rate in women 35 years or age or older and AMH $<$1 (Table). Overall, as historically reported, the live birth rate with minimal stimulation was dramatically lower than that of conventional IVF, regardless of the use of suppression.

	With Antagonist Suppression (n=5984)	Without Antagonist Suppression (n=7066)	P value
Dosage of FSH	975.0 (600.0, 1575.0)	660.0 (375.0, 975.0)	<0.001
Embryos cryopreserved	1.0 (0.0, 2.0)	0.0 (0.0, 1.0)	<0.001
Cycle canceled	11.3%	13.6%	<0.001
Live birth			
Overall	4.3%	2.1%	<0.001
AMH < 1	4.9%	2.6%	0.004
AMH ≥ 1	10.7%	11.9%	0.512
Age < 35	12.3%	12.4%	0.989
Age ≥ 35	2.7%	0.9%	<0.001

CONCLUSIONS: The use of GnRH antagonist suppression during minimal stimulation IVF cycles is associated with an improved live birth rate, especially in older women and in women with diminished ovarian reserve. Although GnRH antagonist use may increase medication costs, it significantly decreases cancelation rate and increases number of embryos cryopreserved and should be encouraged for all minimal stimulation IVF cycles.

SUPPORT: Clinical Research/Reproductive Scientist Training Program (CREST), National Institute of Child Health and Human Development (R25HD075737).

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SIMILAR OVARIAN RESPONSE WITH INDIVIDUALIZED FOLLITROPIN DELTA DOSING REGIMEN IN JAPANESE AND NON-JAPANESE IVF/ICSI PATIENTS. Osamu Ishihara, MD, PhD,[1] Anders Nyboe Andersen, MD, PhD,[2] Scott M. Nelson, MD, PhD,[3] Joan-Carles Arce, MD, PhD,[4] [1]Saitama Medical University, Saitama, Japan; [2]Rigshospitalet, Copenhagen, Denmark; [3]University of Glasgow, Glasgow, United Kingdom; [4]Ferring Pharmaceuticals, Copenhagen, Denmark.

OBJECTIVE: To compare across populations from different geographies the ovarian response associated with the individualized follitropin delta dosing regimen.

DESIGN: Post-hoc analysis of two randomized, controlled, assessor-blind, multi-center, efficacy trials with follitropin delta (Rekovelle, Ferring

Pharmaceuticals) in IVF/ICSI patients conducted in Japan and outside Japan (11 countries in Europe, North- and South America) (NCT03228680; NCT01956110).

MATERIALS AND METHODS: A total of 170 and 665 women, respectively, underwent controlled ovarian stimulation with follitropin delta in the trials in Japan and outside Japan. The two trials had similar eligibility criteria, and the Japanese and non-Japanese patients were comparable in age (mean 34.2 vs 33.4 years) and serum AMH (mean 20.9 vs 19.4 pmol/L) but not in body weight (mean 54.5 vs 64.7 kg). In both trials, the follitropin delta dosing regimen was individualized by the woman's serum AMH and body weight (AMH <15 pmol/L [<2.1 ng/mL]: 12 μg; AMH $\geq$15 pmol/L [$\geq$2.1 ng/mL]: 0.10-0.19 μg/kg; maximum 12 μg; minimum 6 μg for the Japanese trial), and the daily dose was fixed throughout stimulation. Elecsys® AMH / AMH Plus, Roche Diagnostics was used. Stimulation was carried out in a GnRH antagonist cycle, with identical triggering criteria. Mean values and proportions were compared between trials using t-tests and Fisher's exact tests.

RESULTS: Stimulation with the individualized follitropin delta dosing regimen resulted in a comparable number of oocytes retrieved in Japanese and non-Japanese IVF/ICSI patients, with a mean of 9.3±5.4 and 9.6±5.8, respectively, among all patients who started stimulation. Cycle management parameters were not significantly different between populations, with cycle cancellation due to poor ovarian response occurring for 1.2% and 3.8% in the Japanese and non-Japanese population, and excessive ovarian response leading to triggering with GnRH agonist in 1.2% and 1.5%, respectively. Among patients with AMH <15 pmol/L, the mean number of oocytes retrieved with follitropin delta was 7.2±3.7 in the Japanese population and 7.5±4.6 in the non-Japanese population, and the proportion of patients with <4 oocytes was 11.6% and 11.8%, respectively, with no significant differences between populations. Among patients with AMH $\geq$15 pmol/L, the average oocyte yield with follitropin delta was comparable with 10.8±5.9 and 11.2±6.2 in the Japanese and non-Japanese women, respectively. In this population, 22.0% of the Japanese women and 27.9% of the non-Japanese women had $\geq$15 oocytes, and 8.0% and 10.1%, respectively, had $\geq$20 oocytes, with no significant differences between populations.

CONCLUSIONS: The performance of the individualized follitropin delta dosing regimen in terms of ovarian response was consistent across trials conducted in Japan and outside Japan. This investigation documents that personalizing the follitropin delta dose based on AMH and body weight provides a predictable ovarian response among different populations, with very comparable results between Japanese and non-Japanese IVF/ICSI patients across AMH levels.

SUPPORT: Ferring Pharmaceuticals

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PREGNANCY OUTCOMES IN LETROZOLE OVULATION INDUCTION FROZEN-THAWED EMBRYO TRANSFER CYCLES AS COMPARED TO NATURAL AND PROGRAMMED CYCLES.

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OBJECTIVE: The optimal endometrial preparation for frozen-thawed embryo transfer (FET) cycles is controversial and variable among IVF centers. Our aim is to compare pregnancy outcomes between letrozole ovulation induction FET cycles, natural FET cycles and programmed FET cycles in a US-based population.

DESIGN: Single academic center retrospective cohort study.

MATERIALS AND METHODS: 2310 cycles consisting of patients <43 years utilizing embryos created from autologous oocytes between 2015-2020 were included. Blastocyst embryo transfer occurred 6 days after a natural LH surge to >20 mIU/mL in natural and letrozole cycles, or 6 days after the initiation of intramuscular progesterone in programmed cycles. The primary outcome was the ongoing pregnancy rate (OPR), and secondary outcomes included pregnancy rate (PR), implantation rate (IR), clinical pregnancy rate (CPR), and clinical loss rate (CLR). Chi-square test for categorical data and one-way ANOVA for continuous data was used with Bonferroni correction for multiple comparisons. Multiple logistic regression analysis was performed adjusting for age, BMI, anovulation diagnosis, number of embryos transferred and utilization of preimplantation genetic testing for aneuploidy (PGT-A). A two-sided p-value of <0.05 was considered statistically significant.

RESULTS: There was a higher proportion of patients with a diagnosis of anovulation in both letrozole and programmed FET cycles compared with natural cycles ($p < 0.01$). Patients undergoing programmed FET cycles were more likely to be younger, have a higher BMI, and to have more embryos transferred compared to patients undergoing natural FET and letrozole FET cycles ($p < 0.01$). The OPRs and CPRs were similar between the groups, while the CLRs were higher in the programmed compared with natural and letrozole FET cycles. After adjusting for potential covariates, the probability of clinical loss was still significantly higher in programmed cycles compared with natural and letrozole FET cycles (aOR 1.58; 95% CI, 1.15-2.12; $p < 0.01$).

Outcome	Natural FET (n = 1135)	Letrozole FET (n = 88)	Programmed FET (n = 1087)	p value
PR (%, n)	77.8 (883/1135)	78.4 (69/88)	79.9 (869/1087)	0.46
IR (%, n)	62.1 (877/1413)	63.4 (64/101)	62.1 (903/1455)	0.96
CPR (%, n)	68.8 (781/1135)	67.0 (59/88)	69.5 (755/1087)	0.87
OPR (%, n)	60.4 (686/1135)	59.1 (52/88)	56.9 (619/1087)	0.25
CLR (%, n)	11.5 (90/781)	11.9 (7/59)	17.5 (132/755)	<0.01

CONCLUSIONS: Letrozole ovulation induction may be a better alternative to programmed FET cycles particularly for anovulatory patients in view of the lower clinical loss rate.

SUPPORT: None

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THE ASSOCIATION OF ENDOMETRIAL THICKNESS AND ENDOMETRIAL TYPE WITH IVF OUTCOMES IN A SHARED OOCYTE DONOR-RECIPIENT MODEL.

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OBJECTIVE: The effect of endometrial thickness and type on pregnancy outcomes of ART cycles is controversial.[1-2] A challenge in evaluating the role of the endometrial characteristics is the inability to completely control for the impact of egg quality in patients who have difficulty achieving an "adequate lining."[2] Assessing transfer outcomes among shared recipients of the same oocyte donor allows for a more precise assessment of the role of endometrial characteristics in embryo transfer outcomes. The objective of this study is to evaluate the impact of endometrial thickness and type on ART cycle outcomes among shared oocyte donor recipients.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Shared recipients of the same oocyte donor cycle from July 2002 through May 2019 were included in the study. Endometrial thickness and type at progesterone start were analyzed. Demographic and cycle characteristics and outcomes were compared among recipients with an endometrial thickness of < 7 vs. ≥ 7mm, and among recipients with an endometrial type of 1 compared to types 2 and 3. Comparative statistics were used to compare the groups. Mixed effects logistic regression was used to analyze the impact of endometrial thickness and endometrial type on clinical pregnancy (CP) and live birth (LB) rate among shared recipients of the same donor cycle, accounting for repeated recipients and donors. Potential confounders considered were recipient age, donor age, days of estradiol administration, embryo quality, frozen embryo, euploid embryo, number of embryos transferred, and embryo age. A threshold value for endometrial thickness associated with improved odds of LB was calculated using an area under the curve model.

RESULTS: A total of 2075 oocyte recipient transfer cycles from shared donors were identified and included in the study. 468 donors and 1364 recipients were included in the analysis. Recipients with endometrium $<$7mm (N=73) had a significantly lower LB rate compared to recipients with lining $\geq$7mm (N=2000) (31.5% vs. 48.7%, p=0.0039). There were no significant differences in CP and LB rates among type 1 (N=947) compared to type 2/3 (N=1055) endometrial lining. Increased endometrial thickness was significantly associated with CP (OR 1.08, 95% CI 1.02-1.14, p=0.004) and LB rates (OR 1.07, 95% CI 1.02-1.13, p=0.008) after controlling for confounders. The thickness threshold that simultaneously maximized sensitivity and specificity for LB was 10 mm, with an average probability of LB of 0.48 and sensitivity and specificity of 0.59 and 0.62, respectively. The model AUC was 0.65.

CONCLUSIONS: When controlling for the oocyte factor using a shared donor model, patients with endometrial thickness of $\geq$7mm had increased LB rate, however a thicker lining was associated with better outcomes, with LB rate optimized at a threshold of 10 mm. This data will be used to generate a multi-dimensional model to optimize synchronization and endometrial preparation to maximize the likelihood of implantation and positive reproductive outcome.

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SUPPORT: None

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CHANGE IN PROGESTERONE LEVEL DURING IVF STIMULATION PREDICTS LIVE BIRTH RATE FOLLOWING FRESH EMBRYO TRANSFER.

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OBJECTIVE: Prematurely elevated progesterone levels at time of hCG/GnRH agonist trigger can lead to a developmentally advanced endometrium relative to the fresh embryo that is subsequently transferred. Embryo implantation may be compromised in the setting of this asynchrony. Our objective is to examine the peak progesterone level at the time of trigger in addition to the change in progesterone levels (ΔP) between baseline and trigger to determine optimal cutoff values for progesterone and ΔP as well as to assess their effects on pregnancy outcome following IVF with fresh embryo transfer.

DESIGN: Single-center prospective cohort study

MATERIALS AND METHODS: A total of 292 patients $<$42 years of age undergoing fresh IVF cycles with an antagonist protocol were included in the study. Exclusion criteria included patients using donor oocytes, gestational carriers, and patients who had preimplantation genetic testing of embryos. The peak progesterone level and ΔP were modeled in relation to prediction of clinical pregnancy rate (CPR) and live birth rate (LBR), controlling for age, BMI, number of embryos transferred, and endometrial thickness. Data was analyzed using the Python Statsmodels library to build a multivariable logistic regression model after standard scaling the data and classifying ΔP as high or low.

RESULTS: The CPR and LBR in the dataset were 53.4% and 46.3 %, respectively. Comparative models demonstrated that a ΔP cut-off of 0.9 ng/ml was more predictive than using peak progesterone level alone in predicting CPR (p=0.025, 95% CI -5.27, -0.035) and LBR (p=0.026, 95% CI -0.564, -0.036). Patients who had a $<$0.9 ng/ml rise in progesterone were 2.5 times and 2.7 times more likely to achieve clinical pregnancy and live birth, respectively.

CONCLUSIONS: The relative change in progesterone level from baseline to trigger (ΔP) is more predictive in determining pregnancy outcome following fresh ET as compared to peak progesterone level alone. As progesterone assays vary between laboratories, the threshold for an optimal serum progesterone level may also vary. Therefore, incorporating the ΔP level may be helpful in assessing hormone levels prior to making the decision to proceed with fresh embryo transfer.

	CPR	LBR
Overall Outcome	53.4%	46.3%
Odds Ratio for pregnancy outcome ΔP$<$0.9	2.5	2.7
Outcome ΔP$>$0.9	66.6%	73.4%
Logistic Coefficient p-value ΔP$>$0.9	0.025	0.026
Logistic Coefficient 95% Confidence Interval ΔP$>$0.9	(-5.27, -0.035)	(-0.564, -0.036)

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IMPACT OF IN VITRO FERTILIZATION AND PREIMPLANTATION GENETIC TESTING ON THE SEX RATIO IN THE UNITED STATES.

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OBJECTIVE: The sex ratio (SER) is defined as the ratio of males to females in the population. In vitro fertilization (IVF) and preimplantation genetic testing (PGT) have each been shown to increase the probability of delivering a male offspring. We sought to investigate the impact of increasing

Table 1Simulation results of SER at birth and SER in the population at 10, 20, and 30 years with varying IVF and PGT rates

% IVF Births	% PGT	US SER at birth	US SER at 10 years	US SER at 20 years	US SER at 30 years
1%	50%	1.050343	0.9785819	0.9862770	0.9931707
1%	75%	1.050416	0.9785894	0.9862912	0.9931910
1%	100%	1.050488	0.9785969	0.9863054	0.9932114
2%	50%	1.050686	0.9786173	0.9863443	0.9932669
2%	75%	1.050831	0.9786322	0.9863728	0.9933076
2%	100%	1.050977	0.9786472	0.9864013	0.9933483
3%	50%	1.051030	0.9786527	0.9864117	0.9933631
3%	75%	1.051247	0.9786751	0.9864544	0.9934242
3%	100%	1.051465	0.9786975	0.9864971	0.9934852
4%	50%	1.051373	0.9786880	0.9864790	0.9934594
4%	75%	1.051664	0.9787180	0.9865360	0.9935407
4%	100%	1.051954	0.9787479	0.9865930	0.9936221

utilization of IVF and PGT on the sex ratio in the United States (US) population.

DESIGN: Simulation model.

MATERIALS AND METHODS: Population data, population SER, SER at birth, and birth and death rates for 2017 were obtained from the Central Intelligence Agency, Centers for Disease Control and Prevention, and the US Department of Health and Human Services. Based on an analysis of Society for Assisted Reproductive Technology (SART) data from 2014-2016, the sex ratio at birth for IVF with PGT was calculated as 1.10 and without PGT as 1.07. The simulation was conducted while varying the IVF and PGT utilization in the US to predict the SER at birth as well as the population SER after 10, 20, and 30 years.

RESULTS: In 2017, the population SER was 0.97, and the SER at birth was 1.05. The simulation results are shown in Table 1. Increasing utilization of IVF and PGT had minimal impact on the SER at birth. However, over time the SER in the population increased from 0.97 to 0.99, or 2 more males for every 100 persons.

CONCLUSIONS: Increased utilization of IVF and PGT would have minimal impact on the population SER at birth but would significantly alter the population SER in the US over time.

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SUPPORT: None

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EVALUATING THE ABILITY OF AN OOCYTE TO REPAIR FRAGMENTED SPERM CHROMATIN.

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OBJECTIVE: To assess the ability of human oocyte repair mechanisms to fix sperm chromatin defects following intracytoplasmic sperm injection (ICSI) insemination in relation to cytoplasmic maturity.

DESIGN: From 2006-2020, ejaculates from 246 men were assessed for sperm chromatin fragmentation (SCF). These men underwent ICSI with their female partners using ejaculated spermatozoa. To understand the impact of nuclear maturity on oocyte repair mechanisms, the proportion of metaphase-II (MII) oocytes obtained at retrieval was used to infer cytoplasmic readiness. We then assessed clinical outcomes according to the proportion of mature oocytes at the time of denudation.

MATERIALS AND METHODS: Samples from consenting couples were screened for SCF levels by terminal deoxynucleotidyl dUTP transferase nick-end labeling (TUNEL) using a commercial kit. A minimum of 500 spermatozoa were assessed per patient, and an SCF of $<15\%$ was considered normal. From the retrieved cohort, the proportion of MII oocytes at the time of ICSI was reported and used for this assessment. ICSI was performed in the standard fashion. Female age was limited to ≤ 37 years to control for confounding female factors. A clinical pregnancy was defined as the presence of a fetal heartbeat.

RESULTS: A total of 259 couples underwent 445 ICSI cycles. Of these, 134 couples underwent 234 cycles yielding an optimal ($\geq 80\%$) oocyte maturity, and 125 couples underwent 211 cycles with a suboptimal ($<80\%$) maturity. The average SCF was $9.3\pm3\%$ within threshold and $24.1\pm10\%$ above threshold ($P<0.0001$).

Characteristics of SCF did not affect clinical outcome within the optimal oocyte maturity cohort in terms of fertilization (74.2% vs. 71.0%), implantation (23.4% vs. 23.1%), and clinical pregnancy rates (CPR; 34.4% vs. 39.3%).

However, in the suboptimal maturity cohort, an abnormal SCF yielded compromised implantation compared to those within threshold (10.7% vs. 20.2%; $P<0.05$).

To validate our findings, we looked only at men with abnormal SCF. The suboptimal oocyte cohort had comparable fertilization rates (71.0% vs. 72.5%) but compromised embryo implantation (23.1% vs. 10.7%; $P<0.05$) and CPRs (39.3% vs. 20.0%; $P<0.05$). No differences were observed in couples with normal SCF independent of oocyte maturity levels.

CONCLUSIONS: This study describes the role of the oocyte in repairing fragmented sperm chromatin in relation to cytoplasmic maturity. Oocyte DNA repair is a dynamic process that, rather than being intrinsic to the oocyte, is linked to the particular ovarian superovulation protocol used.

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RATIO OF HUMAN MENOPAUSAL GONADOTROPIN (HMG) TO RECOMBINANT FOLLICLE STIMULATING HORMONE (RFSH) DOSAGE PREDICTS PREMATURE PROGESTERONE ELEVATION AND LIVE BIRTH RATE IN FRESH IVF CYCLES.

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OBJECTIVE: Premature progesterone rise during IVF stimulation reduces endometrial receptivity and is associated with decreased pregnancy rates following embryo transfer (ET). To our knowledge, no data exists regarding the appropriate ratio of hMG (which has 1:1 LH:FSH activity) to rFSH (which has FSH activity alone) to improve pregnancy outcomes. Our objective is to determine if an optimal ratio of hMG:rFSH can be identified that best predicts a reduced risk of elevated serum progesterone levels and change in progesterone (ΔP) during IVF stimulation, and to determine whether this ratio can also predict pregnancy outcomes following fresh ET.

DESIGN: Single-center prospective cohort study

MATERIALS AND METHODS: A total of 292 women between the ages of 21-42 years undergoing fresh antagonist IVF cycles were included. Exclusion criteria were use of donor oocytes, gestational carriers, and preimplantation genetic testing cycles. The ratios of hMG to rFSH were modeled in relation to prediction of peak progesterone level on day of hCG administration (peak P), clinical pregnancy rate (CPR), live birth rate (LBR), and miscarriage rate. Since we have recently shown that a greater increase in serum progesterone level (ΔP) between stimulation start and time of hCG trigger negatively influences pregnancy outcomes, we also analyzed hMG:rFSH ratios in relation to ΔP. Our analysis controlled for age, BMI, number of embryos transferred, and endometrial thickness. Data was analyzed using the Python Statsmodels library to build a multivariable logistic regression model after standard scaling the data and classifying hMG:rFSH as "within" versus "outside" the "optimal" ranges identified.

RESULTS: Overall CPR, LBR and miscarriage rates were 53.4%, 46.3 %, and 7.9% respectively. Comparative models demonstrated that an hMG:rFSH ratio of 0.6-1.4 was predictive of both peak P (p=0.014, 95% CI -0.259, -0.029) and ΔP (p=0.022, 95% CI -0.228, -0.017) during IVF stimulation. Additionally, for CPR, the best outcomes were seen within the range of hMG:rFSH ratios 0.3-0.4 [75.6% vs 62.5% within and outside of the range, respectively, (p=0.032, 95% CI 0.069, 1.505)]. For LBR, the best outcomes were seen within the ratio range of 0.3-0.6 hMG:rFSH, LBR of [55.4% vs 41.4% (p=0.023, 95% CI 0.081, 1.079)]. Miscarriage rates outside of the ratio range of 0.3-0.6 were significantly higher, [17.7% vs 6.7% (p=0.049, 95% CI 0.099, 0.110)].

CONCLUSIONS: We have shown that the relative dosing of hMG:rFSH in fresh IVF cycles predicts subsequent progesterone levels (both peak P and ΔP), and that the use of an optimal hMG:rFSH dosing ratio is associated with the highest likelihood of CPR, LBR, and lowest miscarriage risk. Thus, use of an appropriate ratio of hMG:rFSH, and specifically incorporating LH activity, should be considered in all fresh IVF cycles in order to achieve optimal outcomes.

SUPPORT: None

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SYSTEMIC CATEGORIZATION OF OOCYTE GRANULATION PATTERNS AND THEIR PREDICTIVE VALUE FOR IVF OUTCOMES.

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OBJECTIVE: Since oocyte quality sits upstream from embryo quality and, therefore, may be a superior predictor of embryo quality, to investigate for the first time in oocytes as potential predictors IVF outcomes4 patterns of cytoplasmic granulations.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Based on size and distribution of cytoplasmic granules of MII oocytes in IVF cycles with intracytoplasmic sperm injection in years 2017-2019, we systematically categorized cytoplasmic granulation of oocytes after assigning them to 4 granulation patterns: (i) fine; (ii) central; (iii) dispersed; and (iv) a pattern we termed uneven. We then statistically assessed their association with fertilization (2PN, <2PN, >2PN), final disposition (usable rates), pregnancy, and live birth rates. Analyses were done in fresh autologous oocytes, for *in vitro*matured autologous oocytes, as well as fresh and thawed donor oocytes. In fresh oocytes, fertilization analysis was also performed in age groups (<=30, 31-35, 36-39, 40-42, ≥43 years) to verify reliability and independence of this categorization system. Two methods, embryos/oocytes count-based method and a more stringent scoring-based method, were used to determine the contribution of embryos/oocytes that resulted in pregnancy.

RESULTS: In fresh autologous MII oocytes, fine granulation demonstrated highest normal fertilization (2PN, 90.3%, n=620); central granulation was the most uncommon pattern and demonstrated slightly lower 2PN rate (85.6%, n=312, P<0.05 vs. fine granulation); Uneven granulation had a lower 2PN rate (76.3%, n=1135, p<0.001, with increased <2PN and >2PN rates vs. fine granulation); Strikingly, dispersed granulation demonstrated the lowest 2PN rate (56.4%, n=543, P<0.001 compared to all other patterns). Fertilization rates showed similar trends among age different groups, suggesting that granulation patterns were relatively (butnot absolutely) independent of age. In fresh autologous oocytes, dispersed granulation had the lowest pregnancy rate [9.1% (14/154), vs. 21.3% (60/282) in fine granulation,P=0.001; vs. 19.8% (82/415) in uneven granulation,P=0.002] and the lowest live birth rate [3.9% (6/154), vs. 12.8% (36/282) in fine granulation, P<0.01; vs. 10.0% (12/120) in central granulation, P<0.05; vs. 12.8% (53/415) in uneven granulation, P<0.0].Similar differences were also found in fresh and thawed donor oocytes.

CONCLUSIONS: Systemic categorizationof cytoplasmic granulation in human oocytes appears to represent a reliable, and in fresh, thawed, even *in vitro*matured oocytes by fertilization rates validated method of ultimate embryo selection and, potentially, pregnancy and live birth prediction, mostly independent of age. Two follow-up studies are underway: (i) On a physiological level, a determination of what these granulations represent; and on a clinical level how they relate to pregnancy and live birth rates at different ages?

SUPPORT: Intramural funds from The Center for Human Reproduction and Foundation for Reproductive Medicine.

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GNRH ANTAGONIST-INDUCED HYPOTHALAMIC SUPPRESSION AS A PREDICTOR OF SUBOPTIMAL RESPONSE TO GNRH AGONIST TRIGGER.

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OBJECTIVE: To determine if iatrogenic hypothalamic suppression during a GnRH antagonist IVF cycle is a risk factor for suboptimal response to GnRH agonist trigger.

DESIGN: Retrospective cohort study of GnRH antagonist IVF cycles triggered with 4 mg GnRH agonist alone or in combination with hCG. Hypothalamic suppression was defined as an LH level <1.0 (mIU/mL). Patients were stratified based on the following LH levels: >1.0 at cycle start and at trigger (control), <1.0 only at trigger (iatrogenic suppression), <1.0 at cycle start and at trigger (moderate endogenous suppression), and <1.0 only at cycle start (mild endogenous suppression).

MATERIALS AND METHODS: The primary outcome was the proportion of patients with post-trigger LH levels <15. The secondary outcome was the proportion of patients with post-trigger LH levels <50. Logistic regression, adjusted *a priori* for age and use of oral contraceptive priming for the IVF cycle, was used to estimate the odds ratio with a 95% confidence interval among the groups (OR (CI)). The timing of the trigger administration was determined by the treating physician.

RESULTS: A total of 5,702 cycles were included (control group: 2,492; iatrogenic suppression: 2,653; moderate hypothalamic suppression: 434; and mild hypothalamic suppression: 123). The mean ± standard deviation post-trigger LH levels (mIU/mL) for each group was: control 110.4 ± 49.8; iatrogenic suppression 100.9 ± 47.0; moderate hypothalamic suppression 54.7 ± 35.0; and mild hypothalamic suppression 81.2 ± 47.1. When evaluating the proportion of patients with a post-trigger LH <15, there were no differences between the control and iatrogenic suppression groups (0.6 vs. 0.5%; OR 0.90; 0.43-1.90). However, there was a significant difference in the proportion of patients with post-trigger LH <50 between these two groups (9.5 vs. 12.6%; OR 1.45; 1.21-1.74). When compared to the control group, the moderate endogenous suppression group was significantly more likely to have a post-trigger LH <15 (0.6 vs. 9.7%; OR 17.87; 9.48-33.66) and post-trigger LH <50 (9.5 vs. 51.4%; OR 10.62; 8.36-13.50). When compared to the control group, the mild endogenous suppression group was also significantly more likely to have a post-trigger LH <15 (0.6 vs. 3.4%; OR 4.51; 1.28-15.93) and a post-trigger LH <50 (9.5 vs. 32.5%; OR 4.46; 2.98-6.66).

CONCLUSIONS: Patients with evidence of hypothalamic suppression at the start of an IVF cycle are at high risk for a suboptimal response to GnRH agonist trigger. In patients who become iatrogenically suppressed during the IVF cycle, the risk of post-trigger LH <15 is similar to non-suppressed patients. Therefore, GnRH agonist-only trigger should be approached with caution in patients with an LH <1.0 at cycle start. Gonadotropin dosing in such cycles should be carefully dosed in order to mitigate ovarian hyperstimulation risk.

SUPPORT: None.

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USE OF PROPENSITY SCORE MATCHING TO ASSESS THE ENDOMETRIAL RECEPTIVITY ASSAY (ERA) IN OPTIMIZING EMBRYO TRANSFER OUTCOMES.

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OBJECTIVE: The increasing utilization of frozen embryo transfer (FET) has intensified the need to assess outcomes and refine protocols. The timing of embryo transfer is of paramount importance, with commercially available endometrial transcriptomic profiling (Endometrial Receptivity Assay, ERA) purported to improve FET outcomes. The primary objective of this study was to utilize propensity score matching to compare FET outcomes in patients who had undergone ERA biopsy to a control group.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All cycles with FET between January 2014 and March 2019 at a university-affiliated IVF center were reviewed. Data from 163 and 5671 patients with and without ERA assessment, respectively, were assessed. Propensity score matching (PSM) was performed based on the following variables: age at oocyte retrieval, number of oocytes retrieved, total number of prior cycles, preimplantation genetic screening, number of embryos transferred, FET protocol, infertility diagnosis, gravidity, body mass index, age at FET, oocyte retrieval date, use of ICSI. 161 ERA patients were successfully matched to 320 of the 5671 non-ERA patients in a 1:2 matching ratio. A conditional logistic regression was performed on the matched data to compare the live birth rates in each group.

RESULTS: After propensity score matching, there was no significant difference in patient characteristics between the groups, creating similar cohorts. For example, the frequency of PGT-A use was significantly different between groups initially (76.7% vs 33.5% in PGT-A vs controls respectively, P =<.0001). Following propensity score matching the use of PGT-A was similar in both groups (Table 1). The overall propensity score had a mean difference of 0.021 between groups. A total of 100/161 (62.1%) ERA patients and 200/320 (62.5%) non-ERA patients achieved live birth over the course of their treatment. 76/161 patients (47.2%) were noted to be non-receptive on ERA.

CONCLUSIONS: In this study, overall live birth rates were similar, irrespective of ERA use. While propensity score matching is a useful tool to match patients in a retrospective setting, there may be inherent differences between groups that cannot be controlled for. Further studies are required to define the patient cohort who may benefit from ERA prior to embryo transfer.

Table 1Example of Patient Characteristics before and after PSM

	Before PSM			After PSM		
	ERA (n=163)	Non-ERA (n=5671)	P value	ERA (n=161)	Non-ERA (n=320)	P value
Age at Retrieval, Mean (SD)	36.2 (3.7)	35.0 (4.0)	0.0002	36.2 (3.7)	36.4 (3.9)	0.44
Cycle Number, Mean (SD)	5.5 (2.5)	3.4 (1.9)	< .0001	5.4 (2.5)	5.2 (2.6)	0.35
PGT-A, n (%)	125 (76.7)	1900 (33.5)	< .0001	124 (77.0)	242 (75.6)	0.74

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SUPPORT: None.

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THE EFFECT OF ENDOMETRIAL THICKNESS ON LIVE BIRTH OUTCOMES IN WOMEN UNDERGOING HORMONE REPLACED FROZEN EMBRYO TRANSFER (HR-FET).

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OBJECTIVE: Endometrial development is an important factor in healthy placentation. Recent evidence demonstrates that endometrial thickness may correlate with live birth (LB) outcomes after In Vitro Fertilization cycles with a fresh embryo transfer [1]. Our objective was to determine the impact of endometrial thickness on LB outcomes and obstetric complications after HR-FET.

DESIGN: Retrospective cohort study of all patients with a singleton LB from a single euploid HR-FET cycle between 1/2017 and 12/2018.

MATERIALS AND METHODS: All patients with a singleton LB after single euploid embryo transfer (by array CGH or Next Generation Sequencing) in a HR-FET cycle in the study period were reviewed. HR-FET cycles were defined by treatment of oral estradiol (E2) daily until E2 >150pg/mL and the endometrium measured a goal of at least 7mm, followed by progesterone; either 50-75mg intramuscular in oil or vaginal suppository. Embryo transfer was performed on the 6th day of progesterone administration. Patients with missing data were excluded from analysis**.** Primary outcomes were 1) birthweight and 2) obstetric complication rate. The composite obstetric complication outcome was defined by inclusion of any of the following: pre-eclampsia or gestational hypertension, HELLP syndrome, abnormal placentation and umbilical cord anomalies, or intrauterine growth restriction. SPSS (v 25.0) was used for statistical analysis including Students t-test, Mann-Whitney U for non-parametric variables, chi-squared, Spearman's rho correlation and logistic regression where appropriate, with $p<0.05$ considered significant.

RESULTS: 492 patients were included. The mean age of patients at HR-FET was 37.14 ±4.49 years and 86.8% of patients had no or minor medical conditions. Median endometrial thickness prior to transfer was 8.6 mm (range 6.0 – 20.0). The mean gestational age (GA) at LB was 38.8 ±2.2 weeks with a mean birthweight of 3,287±590.5 grams. Endometrial thickness was significantly correlated with birthweight ($p<0.03$). When patients were dichotomized into two groups, those with endometriums below or above 7mm, babies born from endometriums <7mm were 1) born earlier (257 ±24.6 vs 273.0±15.0, $p<0.001$) and 2) born at lower birthweights (2455±770.5 vs 3307.2±572.3, $p<0.001$). Notably, in a subgroup analysis of all babies born at term (> 37 weeks), endometrial thickness was not significantly associated with being small for gestational age ($p=0.318$). 7.7% (n=38) of patients had an obstetric complication. Endometrial thickness was not significantly associated with obstetric complications ($p=0.205$), even with adjustments for age and medical history ($p=0.274$). Furthermore, there was no difference in complication rate between patients with an endometrial thickness under as compared to over 7mm (10% vs 8.3%, $p=0.591$).

CONCLUSIONS: Endometrial thickness may be a valuable predictor of placental health and birthweight. Further study is needed to examine the relationship with individual obstetric complications as well as the relationship to endometrial thickness in natural frozen embryo transfer cycles.

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SUPPORT: none.

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LOW EUPLOIDY RATE DOES NOT AFFECT CLINICAL OUTCOMES IN IVF PGT CYCLES WITH SINGLE EMBRYO TRANSFER (SET) - A 2391 SETS REVIEW.

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OBJECTIVE: Recent publications have demonstrated significant improvement in IVF treatment outcomes by implementing NGS/SNP-based preimplantation genetic testing (PGT) while transferring fewer embryos. Euploidy rates can vary significantly even for the same patient from cycle to cycle. The objective of this study was to evaluate clinical pregnancy rates in IVF cycles with low euploidy rates.

DESIGN: A retrospective study of IVF PGT outcome data from blastocysts biopsied on day 5 or day 6 was conducted to identify differences in clinical pregnancy rates.

MATERIALS AND METHODS: 1646 cycles (13869 embryos, 6.2 ± 3.81 per cycle) of IVF PGT treatment where at least one euploid embryo was available between January 2013 and January 2020 were included in the study. 2391 single embryo transfers (SET) were performed (average maternal age – 36.2 ± 4.7). All SETs were divided in 4 groups based on euploidy rates: 1-25% (192 SETs), 26-50% (819 SETs), 51-75% (774 SETs), and 75-100% (606 SETs). All embryos were vitrified after biopsy, and selected embryos were subsequently thawed for a hormone replacement frozen embryo transfer cycle. Clinical pregnancy rate (PR) was defined by the presence of a fetal heartbeat at 6 - 7 weeks of pregnancy.

RESULTS: Analysis of the data showed no statistically significant difference in clinical pregnancy rates between the group with lowest (1-25%) and the group with highest euploidy rates (76-100%): 65.63% (126/192) vs 65.18% (395/606), respectively, $\chi^2 = 0.013$, OR = 1.02, CI = 0.725 – 1.435, $p<0.05$. Even in the group of patients with 100% euploidy rate (average age 34.4 ± 4.9) the clinical pregnancy rate was not statistically different – 63.5% (233/367, $p<0.05$). For some patients low euploidy rates were manifested also in a small number of euploid embryos available for transfer – 29.7% (489/1646) of patients in our study had only one euploid embryo. At the same time, no statistically significant difference was found in the clinical pregnancy rates in the cycles where only one euploid embryo was available versus IVF PGT cycles where four or more euploid embryos were available for a transfer: 65.24% (319/489) vs 66.96% (675/1008), respectively, $\chi^2 = 0.507$, OR = 0.926, CI = 0.737 – 1.162, $p<0.05$.

CONCLUSIONS: Analysis of the data proved that low euploidy rate does not affect clinical outcomes in IVF PGT cycles with single embryo transfer.

Single embryo transfer should be imperative in PGT cycles regardless of the euploidy rate or the total number of euploid embryos available for transfer.

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THE PRESENCE OF CESAREAN SECTION SCAR DIVERTICULUM IS DETRIMENTAL TO THE REPRODUCTIVE OUTCOME OF FRESH AND FROZEN EMBRYO TRANSFER AFTER IN VITRO FERTILIZATION/INTRACYTOPLASMIC SPERM INJECTION. Ling Huang, MD,[1] Sunxing Huang, MD,[1] Yubin Li, Professor,[1] Minghui Chen, Professor,[1] Lingli Long, MD,[2] Canquan Zhou, Professor,[1] [1]Reproductive Medicine Center, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; [2]Translation Medicine Center, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: The primary purpose of our study was to investigate the influence of cesarean scar diverticulum on the reproductive outcome of fresh and frozen embryo transfer after in vitro fertilization/intracytoplasmic sperm injection. The secondary aim of our study was to assess the impact of endometrial cavity fluid on the reproductive outcome of embryo transfer among patients with an existing cesarean scar diverticulum.

DESIGN: This was a retrospective cohort study. 1275 patients who had a history of cesarean delivery between January 2013 and December 2018 at our Institute of Reproductive Medicine were included. The study included 847 cycles of fresh embryo transfer and 1213 cycles of frozen embryo transfer. According to the results of transvaginal gynecological ultrasound, the patients were divided into two groups: cesarean scar diverticulum group(n=169) and cesarean delivery without diverticulum group(n=1106). According to the presence of endometrial cavity fluid during the endometrial preparation process of frozen embryo transfer, patients with the cesarean scar diverticulum were divided into two subgroups: endometrial cavity fluid group(n=36) and non-endometrial cavity fluid group(n=108).

MATERIALS AND METHODS: The basic characteristics, pregnancy outcome and delivery outcome of the included patients were collected from the database of our institute and compared. Binary logistic regression analysis was performed to adjust confounding factors when the baseline demographic variables of two groups of patients were significantly different. The propensity score was computed by accounting for the effect of confounding factors. Propensity scores were matched 1:1 using the nearest neighbor matching method. The matched data set was used in logistic regression.

RESULTS: There were no significant differences in the baseline variables between the cesarean scar diverticulum group and the control group. The implantation rate, clinical pregnancy rate and live birth rate of fresh embryo transfer in the cesarean section diverticulum group was significantly lower than the control group(19.6% vs 32.5%,p=0.001; 25.7% vs 43.0%,p=0.001; 17.8% vs 31.6%,p=0.004). The implantation rate, clinical pregnancy rate and live birth rate of frozen embryo transfer in the cesarean section diverticulum group was also significantly lower than the control group(27.1% vs 34.5%,p=0.015; 32.7% vs 41.2%,p=0.021; 23.5% vs 31.4%,p=0.021). 21.20% cycles of frozen embryo transfer among the cesarean section scar diverticulum group developed endometrial cavity fluid during endometrial preparation. The baseline variables were similar between the endometrial cavity fluid and non-endometrial cavity fluid group after propensity score matching. The odds of clinical pregnancy and miscarry were similar between two subgroups before and after adjustment for covariates (adjusted OR0.45(0.18-1.12), P=0.086; adjusted OR 0.75(0.14-3.95), P=0.736).

CONCLUSIONS: The presence of cesarean section scar diverticulum was detrimental to embryo implantation and had a bad impact on reproductive outcomes of fresh and frozen embryo transfer.

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THE DEGREE OF BLASTOCYST EXPANSION POST-WARMING STRONGLY PREDICTS CLINICAL OUTCOMES IN SINGLE FROZEN EMBRYO TRANSFER CYCLES (SFET). Ahmad Morsi Abu Maizar, M.Sc,[1] Diane Wright, PhD,[2] Richard Marrs, MD,[1] Guy E. Ringler, MD,[1] Kelly J. Baek, MD,[1] Karine Chung, MD,[1] Matthew David VerMilyea, PhD,[3] [1]California Fertility Partners, Los Angeles, CA; [2]Ovation Fertility, Houston, TX; [3]Ovation Fertility, San Antonio, TX.

OBJECTIVE: To determine whether the degree of blastocyst re-expansion post warming affects the Clinical Pregnancy Rate (CPR) in PGT-A tested Embryo Transfer cycles.

DESIGN: Retrospective analysis of data from a single private fertility clinic

MATERIALS AND METHODS: CPR of 519 frozen PGT-A tested euploid blastocyst was evaluated for sFET cases during 2018-2019. CPR was determined by the presence of a positive fetal heartbeat (FHB) at 7 weeks. As a standard lab protocol, all fertilized oocytes underwent uninterrupted extended culture in FujiFilm Irvine Scientific Media CSCM-NXC and CSCM-NX until biopsy on day 5, 6 or 7. Transfers were performed using vitrified/warmed blastocysts. Blastocyst warming was performed on the day of the sFET and re-expansion was checked at the time of transfer. A standardized expansion guide was created, and embryologists were trained to use it to examine and document the degree of re-expansion post warming. Re-expansion evaluations were subdivided into five intervals; 0%, 25%, 50%, 75% and 100%. Data was analyzed by mean time difference for blastocyst re-expansion (time difference between the first and the second check), the patients' age, the egg source (donor vs patient) and the embryo recipient (gestational carrier vs patient). Statistical analysis was performed using Chi-square ($P < 0.05$). A multivariable linear regression analysis was also performed to adjust for confounders such as age.

RESULTS: Our data show that embryos with > 50% re-expansion post warming have a significantly higher CPR when compared to embryos with < 50% re-expansion (63% vs 21% respectively, P= 0.002). Furthermore, the difference was more substantial with embryos with < 25% re-expansion compared to embryos that achieved >= 50% re-expansion (25% vs 71%, p=0.001) Table 1. There was no correlation between patients' age and the degree of re-expansion (P=0.995). In addition, there was not an association between the degree of expansion and the egg source (P= 0.913) or embryo recipient (P= 0.879) categories. Finally, the mean time difference from thaw did not influence the CPR when correlated with the degree of expansion (P=0.824).

CONCLUSIONS: Our data suggest that the degree of embryo re-expansion post warming could serve as a strong predictor of clinical pregnancy in frozen embryo transfers of euploid blastocysts. Furthermore, our data suggests that a minimum of 25% of re-expansion may be a good indicator to predict the embryo's implantation potential.

TABLE 1. The clinical pregnancy rate in each expansion interval. Each subscript letter denotes a subset of Expansion (%) categories that do not differ significantly from each other at the 0.05 level.

Expansion (%)	Transfer Count(n)	FHB(n)	CPR
0	14	2	$14\%_{a}$
25	20	5	$25\%_{a,b}$
50	28	20	$71\%_{c}$
75	49	30	$61\%_{c}$
100	408	256	$63\%_{c}$
Total	519		

SUPPORT: None.

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EAST ASIAN WOMEN EXPERIENCE LOWER RATES OF LIVE BIRTH THAN CAUCASIAN WOMEN AFTER SINGLE FRESH BLASTOCYST TRANSFER BUT HAVE SIMILAR OUTCOMES AFTER FROZEN TRANSFER. Anne E. Martini, DO,[1] Samantha Kodama, MD, MPH,[2] Tommy Na, BS, BA,[3] Samad Jahandideh, PhD,[4] Micah J. Hill, DO,[5] Alan H. DeCherney, MD,[1] Kate Devine, MD,[4] Frank E. Chang, MD,[4] [1]National Institute of Child Health and Human Development, NIH, Bethesda, MD; [2]Medstar Washington Hospital Center/Georgetown University Hospital, Washington, DC; [3]University of Richmond, Richmond, VA; [4]Shady Grove Fertility Center, Rockville, MD; [5]Walter Reed National Military Medical Center, Bethesda, MD.

OBJECTIVE: To compare live birth rates after autologous fresh or frozen single embryo transfers (SET) in East Asian and Caucasian women.

DESIGN: Retrospective cohort

MATERIALS AND METHODS: Autologous SETs of fresh or vitrified/warmed blastocysts in East Asian and Caucasian patients from 2015-2018 were analyzed. Fresh and frozen transfers were analyzed separately.

	East Asian	Caucasian	P-value	P-value (adjusted)
Fresh				
Cycles (n)	265	4359		
Age (y)	36.3 ± 4.7	34.5 ± 5.1	<0.001	
E2 on day of trigger (pg/mL)	2862.1 ± 1658.2	2421.1 ± 1409.4	<0.001	
Follicles >14mm on day of trigger	8.5 ± 5.7	9.1 ± 6.4	NS	
E2/follicle (pg/mL)	329.8 ± 115.3	258.4 ± 95.2	<0.001	
Oocytes retrieved	15.0 ± 9.4	17.2 ± 10.3	0.001	
Fertilization (%)	76.0	78.0	NS	
Positive hCG/transfer (%)	50.6	63.0	<0.001	0.008
Clinical pregnancy/transfer (%)	42.6	54.3	<0.001	0.001
Live birth/transfer (%)	34.0	45.4	<0.001	0.001
Frozen				
Cycles (n)	280	7482		
Age (y)	38.3 ± 4.0	36.2 ± 4.9	<0.001	
E2 at last lining check (pg/mL)	734.16 ± 619.35	755.69 ± 782.58	NS	
Cycles using PGT-A (n (%))	260 (92.9)	2985 (39.9)	<0.001	
Positive hCG/transfer (%)	74.3	67.4	0.02	NS
Clinical pregnancy/transfer (%)	64.6	58.1	0.03	NS
Live birth/transfer (%)	47.5	45.5	NS	NS
Live birth/euploid transfer (%)	47.3	48.1	NS	NS

Mean ± SD unless otherwise stated

Unadjusted comparisons were evaluated by t-test or chi-square. Generalized estimating equations (GEEs) were used to account for repeat cycles and to adjust for age, body mass index (BMI), diagnosis, cycle number, and use of preimplantation genetic testing for aneuploidy (PGT-A).

RESULTS: In fresh and frozen cohorts, East Asians were older (P<0.001 for each), had more prior IVF cycles (P=0.009 and P<0.001), and lower BMI (P <0.001 for each). In fresh cycles, estradiol (E2) on day of trigger was higher in East Asians (P <0.001) despite similar numbers of follicles ≥14mm and fewer oocytes retrieved (P=0.038). Live birth per fresh transfer was significantly lower in East Asians in both unadjusted and adjusted analyses (P<0.001). There was no difference in the odds of live birth from FET between East Asians or Caucasians, whether or not PGT-A was used; however, it is notable that 93% of FETs in East Asians used PGT-A compared with 40% in Caucasians (P<0.001).

CONCLUSIONS: East Asians were 10% less likely to achieve a live birth after transfer of a single fresh (untested) blastocyst. Data revealed no difference in live birth from single blastocyst FET; however, 93% of blastocysts transferred among East Asians were PGT-A normal. While prior data have indicated no difference in rates of aneuploidy in this population[1], the current study suggests that embryo quality may contribute to worse fresh ART outcomes observed among East Asians. The impact of higher estradiol concentration on the endometrium may also play a role.

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SIMILAR DOSE-RESPONSE PROFILES FOR FOLLITROPIN DELTA IN JAPANESE AND NON-JAPANESE IVF/ICSI PATIENTS. Osamu Ishihara, MD, PhD,[1] Joan-Carles Arce, MD, PhD,[2] [1]Saitama Medical University, Saitama, Japan; [2]Ferring Pharmaceuticals, Copenhagen, Denmark.

OBJECTIVE: To compare the ovarian response to different doses of follitropin delta between the Japanese and non-Japanese population.

DESIGN: Post-hoc analysis of two randomized, controlled, assessor-blind, multi-center, dose-response trials with follitropin delta (Rekovelle, Ferring Pharmaceuticals) in IVF/ICSI patients conducted in Japan and Europe (NCT02309671; NCT01426386).

MATERIALS AND METHODS: The two trials had similar eligibility criteria. A total of 117 Japanese women (mean 33.8 years) were randomized to one of three fixed daily doses of follitropin delta – 6 μg (low), 9 μg (medium) or 12 μg (high) – in the Japanese trial, and 222 non-Japanese women (mean 32.7 years) were randomized to one of five fixed daily doses of follitropin delta – 5.2 μg (low), 6.9 μg, 8.6 μg (medium), 10.3 μg or 12.1 μg (high) – in the European trial. In both trials, randomization was stratified according to AMH (5.0-14.9 pmol/L [0.7-<2.1 ng/mL]; 15.0-44.9 pmol/L [2.1-6.3 ng/mL]). The dose-response relationship between the two populations was compared using ANCOVA with Japanese/non-Japanese and AMH strata as factors, and log(dose) as covariate.

RESULTS: A significant (p<0.01) dose-response relationship between follitropin delta dose and number of oocytes retrieved was established for both Japanese and non-Japanese patients, including for each AMH strata. The dose-response relationship was not significantly different between populations, and a doubling of the follitropin delta dose was estimated to lead to an increase of 4.7 oocytes [95% CI: 2.60-6.76] in Japanese patients and 5.5 oocytes [95% CI: 3.95-7.06] in non-Japanese patients. The number of oocytes retrieved was higher for AMH ≥15 pmol/L than AMH <15 pmol/L, with an average difference of 3.4 and 4.0 oocytes, respectively, in the Japanese and non-Japanese patients. Regarding excessive response, there was no significant difference between the Japanese and non-Japanese populations with respect to the proportion of patients having ≥15 oocytes retrieved after stimulation with follitropin delta at low (5% vs 5%), medium (15% vs 14%) or high (28% vs 32%) doses. Concerning the ovarian hormone response, a doubling of the follitropin delta dose in the Japanese patients led to estimated increases of 1.6-fold [95% CI: 1.29-2.03] in inhibin B on stimulation day 6 as well as 1.8-fold [95% CI: 1.33-2.55] in estradiol and 2.0-fold [95% CI: 1.42-2.71] in inhibin A at end of stimulation. Comparable observations were made in the non-Japanese patients with increases of 1.8-fold [95% CI: 1.51-2.09], 1.8-fold [95% CI: 1.48-2.15] and 1.8-fold [95% CI: 1.50-2.16], respectively, for inhibin B on stimulation day 6, and estradiol and inhibin A at end of stimulation.

CONCLUSIONS: The ovarian dose-response to follitropin delta was comparable for Japanese and non-Japanese IVF/ICSI patients. The number of oocytes retrieved vary substantially in Japanese patients depending on AMH level. Therefore, serum AMH levels should be considered when selecting gonadotropin doses for Japanese patients, as already introduced with the individualized follitropin delta dosing regimen outside Japan.

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SUPPORT: Ferring Pharmaceuticals.

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DOES CRYOPRESERVATION AFFECT THE IMPLANTATION POTENTIAL OF BLASTOCYSTS DERIVED FROM VITRIFIED/WARMED OOCYTES?. Hadi Ramadan, M.D.,[1] Tarita Pakrashi, MD, MPH,[1] Andrea Ries Thurman, MD,[1] Kimball O. Pomeroy, Ph.D.,[2] Gerard Celia, Jr., PhD,[3] [1]Eastern Virginia Medical School, Norfolk, VA; [2]The World Egg Bank, Phoenix, AZ; [3]EVMS, Norfolk, VA.

OBJECTIVE: Vitrified, or "frozen", donor eggs (VDE) can either be fertilized and cultured for fresh transfer (group 1), or fertilized and cryopreserved for transfer in a "frozen embryo transfer" cycle (FET, group 2). This study compared implantation rates between the two groups.

DESIGN: A retrospective cohort study analyzing 800 frozen donor egg cycles from a commercial egg bank. Cycles were limited to single embryo transfers (ET) without preimplantation genetic testing (PGT).

MATERIALS AND METHODS: The data was analyzed using the Chi-squared test for categorical variables and the Wilcoxon-Mann-Whitney test for non-parametric continuous variables. P-values <0.05 were regarded as statistically significant. SAS version 9.4 was used for the analysis.

RESULTS: 600 cycles met the inclusion criteria (200 were excluded due to PGT or multiple embryo transfers). There were 409 cycles in group 1 and 191 cycles in group 2. Implantation rate was not significantly different between the two groups (38.63% vs 32.46% p=0.14). Mean embryo age was higher in group 2 (5.1 vs 5.4 days, p< 0.01).

CONCLUSIONS: Contrary to experiences with slow-cooling, a growing body of evidence shows vitrification to have no negative effect on embryo potential, even when subject to multiple vitrify/thaw cycles. To date, however, no investigation has looked at the possible compounding effect of vitrification when applied at two distinct stages: oocyte and embryo. In this study we compared implantation of VDE cycles transferred in fresh versus FET cycles to determine if such an effect exists. Although embryos used in FET cycles were statistically older, as would be expected due to extended culture, no difference was detected between the groups in terms of implantation. Unexpectedly, the data demonstrated a trend toward lower implantation in the FET group, which stands contrary to trends observed with fresh oocyte/FET cycles. While not significant at this power, a larger study should be undertaken to determine the validity of this effect and whether it represents a clinical concern when planning patient cycles.

SUPPORT: No financial support.

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USING SPERM DOUBLE-STRANDED DNA TO PREDICT EMBRYO PLOIDY. Derek Keating, B.A., Alessandra Parrella, M.Sc., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To demonstrate how the presence of double-stranded DNA breaks (dsDNA) in spermatozoa can be used to predict embryo ploidy.

DESIGN: Over the last 12 months, a prospective pilot study was carried out on semen samples to assess dsDNA levels. These samples were also concurrently assessed to determine total DNA damage. A correlation between the two assays was established. Couples were divided into two groups according to the adopted dsDNA threshold, and clinical outcomes were recorded and compared.

MATERIALS AND METHODS: Consenting men had their ejaculates screened for dsDNA rates utilizing an in-house protocol of the neutral Comet assay, assessing at least 200 spermatozoa. Concurrently, samples were assessed by terminal deoxynucleotidyl dUTP transferase nick-end labeling (TUNEL) with a commercial kit, screening at least 500 spermatozoa. ICSI was performed in the standard fashion. Resulting blastocysts were biopsied on day 5 or 6 post-insemination for preimplantation genetic testing for aneuploidy (PGT-A) using next-generation sequencing.

RESULTS: The initial pilot study reported an average total DNA fragmentation by TUNEL of 11.3±6% and a dsDNA average of 2.2±3% by neutral Comet assay. The results of TUNEL and dsDNA presented with a linear correlation (R^2=0.96; P<0.05), and dsDNA values were extrapolated. After establishing a threshold of 3%, 231 couples treated in 381 ICSI/PGT-A cycles were compared according to above or below threshold.

A total of 173 couples (maternal age, 37.2±4 years; paternal age, 38.9±5 years) with normal dsDNA levels underwent 296 ICSI cycles, yielding a fertilization rate of 76.9%; 1,562 embryos were screened by PGT-A. This resulted in 574 normal (36.7%), 827 abnormal (52.9%), and 161 mosaic embryos (10.3%). There have been 171 frozen embryo transfers (FET) of euploid blastocysts thus far, with a 51.6% implantation rate and a 55.6% clinical pregnancy rate (CPR).

A total of 48 couples with abnormal dsDNA levels underwent 85 ICSI cycles. They had a comparable maternal age of 38.0±5 years, but a much older male partner (43.2±8 years; P<0.0001). They achieved a fertilization rate of 72.7% (P<0.01), with 375 embryos biopsied for PGT-A. A total of 115 were euploid (30.7%; P<0.05), 222 were aneuploid (59.2%; P<0.05), and 38 were mosaic (10.1%). Interestingly, FET cycles from these cases trended toward lower implantation (43.9%) and CPRs (47.4%).

CONCLUSIONS: This study confirmed the relevance of dsDNA on structural chromosomal abnormalities and therefore the proportion of euploid embryos. Examining dsDNA of the male gamete can provide important information on the prospects of successful embryo implantation.

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CLINICAL PARAMETERS AND PREDICTORS OF MONOZYGOTIC TWINS (MZT) AFTER SINGLE FROZEN EMBRYO TRANSFER (FET). Amelia G. Kelly, MD, Jennifer K. Blakemore, MD, Caroline McCaffrey, PhD, James A. Grifo, MD, PhD NYU Langone School of Medicine, New York, NY.

OBJECTIVE: FET and lab protocols regularly evolve, which may impact rates of MZT. We evaluated clinical factors in single embryo FET and rates of MZT.

DESIGN: Retrospective cohort study of all patients who underwent a single embryo FET between 1/2016 and 12/2018.

MATERIALS AND METHODS: All FETs in the study time-period were reviewed, and all documented clinical intrauterine pregnancies were included. The primary outcome was the number of MZT. Independent variables included use of Eglue (culture media with increased hyaluronon introduced in the lab on 7/17/17), cycle type, use of ICSI, use of PGT, embryo expansion, inner cell mass (ICM) and trophectoderm (TE) grades, day of blastocyst biopsy/vitrification (B/V), patient age and endometrial thickness (EE). Cycle type was defined as: 1) programmed (PRG) - daily oral estradiol for ≥10 days or until the EE measured greater than 7mm, followed by intramuscular progesterone in oil or 2) natural (NAT) - monitoring until a dominant follicle reached 18mm and ovulation was confirmed and/or triggered with the use of a compounded hCG. Statistical analyses included comparison of means, chi-squared, and multivariate logistic regression with p<0.05 considered significant.

RESULTS: 1621 cycles met inclusion criteria, and 31 resulted in MZT pregnancies (1.9%). Overall, Eglue was used in 877 (54.1%) cycles. 1386 (85.5%) cycles were PRG and 236 (14.4%) were NAT. PGT and ICSI were used in 1425 (87.9%) and 579 (35.7%) of cycles, respectively. The mean patient age at FET was 37.4±4.5 and the mean EE was 9.1±3.0cm and neither patient age (37.5±4.7 MZT vs 37.2±4.5 No MZT, p=0.90) nor EE (9.3±1.8 MZT vs 9.1±2.9 No MZT, p=0.60) were different between groups. The ICM grade (p=0.93), TE grade (p=0.56), expansion (p=0.74), and day of blastocyst B/V (p=0.93) were similar between the groups. Table 1 shows the MZT rate by clinical parameter. After controlling for age, EE, cycle type, embryo grade, day of B/V, ICSI and PGT, the use of Eglue still resulted in fewer MZT (B 1.2, p<0.01). Interestingly, PGT was no longer statistically significant (B -17.6, p=1.0). A regression using the same parameters with PGT only cycles showed that Eglue was still associated with a reduction in MZT (B-1.2, p<0.01), independent of all other unassociated parameters.

CONCLUSIONS: The rate of MZT after FET is reduced by the use of Eglue and is not affected by cycle type or other clinical parameters. The use of PGT needs to be further investigated as a risk factor for MZT.

TABLE 1. MZT after FET by Clinical Parameter

	No MZT (n=1590)	MZT (n=31)	p
Eglue	866 (54.5%)	11 (35.5%)	0.04
No Eglue	724 (45.5%)	20 (64.5%)	
PRG Cycle	1361 (85.6%)	25 (80.6%)	0.44
NAT Cycle	228 (14.3%)	6 (19.4%)	
ICSI	567 (35.7%)	12 (38.7%)	0.73
No ICSI	1023 (64.3%)	19 (61.3%)	
PGT	1394 (87.7%)	31 (100%)	0.04
No PGT	196 (12.3%)	0 (0%)	

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DISPARITIES IN ART LIVE-BIRTH OUTCOMES FOR HISPANIC AND ASIAN WOMEN COMPARED TO WHITE NON-HISPANIC WOMEN. Alexander Kotlyar, MD,[1] Burcin Simsek, Ph.D.,[2] David B. Seifer, MD,[3] [1]Yale School of Medicine, Oange, CT; [2]University of Pittsburgh, Pittsburgh, PA; [3]Yale University, Orange, CT.

OBJECTIVE: To determine if disparities exist in ART outcomes for Hispanic and Asian women compared to white, non-Hispanic (WNH) women.

DESIGN: Retrospective, cohort study and comparison of reported outcomes in the SARTCORS database for 2014-2016.

MATERIALS AND METHODS: Analysis of 2014-2016 SARTCORS database for member clinics that performed at least 50 cycles of ART and reported race/ethnicity in more than 95% of cycles. 60,657 cycles using autologous, fresh, non-donor embryo cycles were analyzed of which 4,544 cycles were from Hispanic women, 11,987 cycles were from Asian women and 44,126 cycles were from WNH women.

RESULTS: In comparison to cycles in WNH women, cycles in Hispanic and Asian patients were generally in older women ($p<0.001$). Concerning causes of infertility, cycles from Hispanic women were more often associated with a history of endometriosis compared to those in WNH women ($p=0.033$). Additionally, Hispanic patients were more than twice as likely to exhibit tubal factor infertility compared WNH women ($p<0.001$). Cycles in Asian women were not associated with greater tubal factor infertility; however, diminished ovarian reserve (DOR) was greater in cycles with Asian women compared to WNH women ($p<0.001$). ART cycles in Asian and Hispanic women, exhibited lower rates of clinical intrauterine gestation (CIG) ($p<0.001$) and live birth (LB) per cycle-start ($p<0.001$) compared to cycles in WNH women. Multivariate logistic regression demonstrated that cycles from Asian and Hispanic women were less likely to have a LB than white women for their initial cycle (OR 0.86; $p=0.004$, OR 0.69; $p<0.001$, respectively). These findings were independent of age, parity, BMI, etiology of infertility, use of ICSI or number of embryos transferred.

CONCLUSIONS: Race/ethnicity continues to be an independent prognostic factor for LB for ART. Substantial outcome disparities exist among ART cycles in Asian and Hispanic women compared to WNH women. This may be in part due to the increasing proportion of older age in Asian and Hispanic women which may be accompanied by DOR as compared to WNH women. Additional analysis of trends among Asian and Hispanic patients is warranted to eventually remedy disparities in outcomes in ART treatment.

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ENDOMETRIAL BCL6 EXPRESSION IS NOT ASSOCIATED WITH IMPLANTATION OUTCOMES. Amber M. Klimczak, MD,[1] Nola S. Herlihy, MD,[1] Cynthia S. Scott-,[2] Brent M. Hanson, MD,[3] Julia G. Kim, MD, MPH,[3] Ashley W. Tiegs, MD,[3] Emily K. Osman, MD,[3] Shiny Titus, PhD,[2] Emre Seli, M.D.,[3] Richard Thomas Scott, Jr., MD,[3] [1]IVI-RMA New Jersey, Basking Ridge, NJ; [2]Foundation for Embryonic Competence, Basking Ridge, NJ; [3]IVI RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: B-cell CLL/lymphoma 6 (*BCL6*) is a proto-oncogene that is overexpressed in the secretory endometrium of women with endometriosis. It has been postulated that BCL6 may serve as a surrogate marker for occult endometriosis, as well as a predictor of endometrial dysfunction and poor implantation. Therefore, BCL6 expression has been proposed as an adjunct test for women undergoing IVF. However, this test has not yet been validated in the general IVF population. The aim of this study was to determine whether increased endometrial BCL6 expression is associated with implantation failure in women undergoing IVF.

DESIGN: Case-control study.

MATERIALS AND METHODS: Endometrial biopsies were collected from women (n=50) undergoing ART, during the mid-secretory phase. In vitro fertilization was performed followed by trophoectoderm biopsy, preimplantation genetic testing for aneuploidy, embryo cryopreservation, and a warmed euploid embryo transfer in a subsequent cycle. Samples underwent paraffin embedding and sectioning, followed by immunohistochemistry for BCL6 using mouse monoclonal primary antibody (GI191E/A8, Sigma) and goat anti-mouse secondary antibody (Sigma). Lymph nodes served as positive controls, while slides stained with only secondary antibody served as negative controls. Two independent investigators blinded to cycle outcome performed semi-quantitative analysis of immunohistochemical staining intensity. Each slide was given a mean HSCORE calculated using the formula $= \sum Pi\ (i+1)/100$ where i= staining intensity ranging from 0-4 (not present-very strong) and Pi= percentage of stained epithelial cells for each intensity (0-100%). BCL6 expression was deemed positive if the HSCORE was >1.4 as previously defined by ROC curve analysis for the diagnosis of endometriosis (1). Additionally, an overall fluorescence intensity of each section was calculated using ImageJ software.

RESULTS: Twenty-seven patients with sustained implantation and 23 patients that failed implantation were included. Patient age, day 3 FSH, AMH, BMI, day of blastulation, and embryo grade did not significantly differ between the two groups. Mean HSCOREs did not significantly differ between the groups ($P=0.75$). Using the previously established BCL6 expression cut-off of positive >1.4, 8/15 samples were positive for BCL6 in the no implantation group, while 7/20 were positive in the sustained implantation group (OR: 1.52 CI [0.45-5.14]). A chi-square test showed that there was no significant association between BCL6 expression and implantation $x^2(2, N=50) = 0.46$, $p=0.49$. Overall fluorescence intensity did not significantly differ between the two groups ($P=0.33$).

CONCLUSIONS: The proportion of patients with BCL6 positivity did not differ between those who achieved sustained implantation and those who did not. While the odds of having aberrant BCL6 expression is increased in patients with no implantation, the confidence interval is wide. Physicians should take caution when implementing BCL6 expression as a diagnostic tool for clinical decision-making.

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DICHORIONIC TWINS WITH PREECLAMPSIA CONCEIVED VIA ASSISTED REPRODUCTIVE TECHNOLOGY DO NOT YIELD HIGHER RATE OF FETAL GROWTH RESTRICTION. Evelina Manvelyan, MD,[1] Baruch Abittan, M.D.,[2] Matthew Blitz, MD,[3] Randi H. Goldman, M.D.[2] [1]Northwell Health at Southside Hospital, Bay Shore, NY; [2]Northwell Health Fertility, North Shore University Hospital/Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY; [3]Northwell Health Fertility, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: Pregnancies complicated by preeclampsia are more likely to result in fetal growth restriction (FGR). Twin gestations increase the likelihood of obstetric complications and are independently associated with FGR. Preeclampsia complicates dichorionic twin gestations conceived using in vitro fertilization (IVF) nearly twice as often as spontaneous dichorionic twins.

We previously reported significant placental differences in dichorionic twin pregnancies impacted by preeclampsia based on whether the pregnancy was achieved using IVF or spontaneously conceived. The objective of this study was to determine whether rates of FGR and fetal growth discordance (FGD) differ in dichorionic twin pregnancies complicated by preeclampsia if conceived using IVF.

DESIGN: A retrospective cohort study of dichorionic twin gestations complicated by preeclampsia conceived spontaneously and with IVF at a tertiary care university hospital from 2011-2016.

MATERIALS AND METHODS: Patients aged 18-45 years with dichorionic twin gestations complicated by preeclampsia who conceived spontaneously or with IVF (+/- ICSI) were evaluated. Patients with chronic hypertension, pre-gestational, or gestational diabetes were excluded. Two tailed student's t-tests and Welch's tests were used for data analyses.

RESULTS: Of 423 twin gestations, 122 pregnancies were suitable for analysis after application of inclusion/exclusion criteria. Sixty patients spontaneously conceived pregnancies (non-IVF group) and 62 conceived via IVF. Patients in the IVF group were significantly older and less parous. No significant differences were found in fetal weight or APGAR scores of either fetus A or B. There were no differences in FGD or FGR for fetus A. More than twice as many fetus Bs had FGR in the non-IVF vs. IVF group, a nearly significant difference (Table).

CONCLUSIONS: Dichorionic twin pregnancies conceived using IVF and complicated by preeclampsia do not demonstrate higher rates of FGD or FGR compared with spontaneously-conceived pregnancies, despite the differences in placental morphology. There was a higher rate of FGR for fetus B

in the non-IVF group that approached significance. This should be further studied.

	IVF GROUP	NON-IVF GROUP	P VALUE
AGE	35.2±5.0	33.0±5.6	0.020
PARITY	0.1±0.5	0.6±1.0	0.005
BMI	27.30+6.6	26.9±6.6	NS
SMOKING(%)	14	8	NS
GESTATIONAL AGE	35.5±2.5	35.6±2.4	NS
BABY A APGAR 1MIN	8.2±1.0	8.0±1.6	NS
BABY A APGAR 5MIN	8.8±0.7	8.8±0.5	NS
BABY B APGAR 1MIN	8.0±1.2	8.1±1.1	NS
BABY B APGAR 5MIN	8.8±0.4	8.8±0.6	NS
BABY A WT(GRAMS)	2412±637	2382±599	NS
BABY B WT(GRAMS)	2333±579	2286±585	NS
FGD (%)	19	22	NS
BABY A FGR(%)	13	8	NS
BABY B FGR(%)	11	25	0.051
OVERALL FGR(%)	21	30	NS

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INCREASING MICROBIAL DIVERSITY AND LACTOBACILLUS DOMINANCE OF GENITOURINARY, GASTROINTESTINAL, AND REPRODUCTIVE TRACTS DO NOT ASSOCIATE WITH REPRODUCTIVE OUTCOMES AFTER EUPLOID SINGLE EMBRYO TRANSFER. Nola S. Herlihy, MD,[1] Xin Tao, Ph.D,[2] Yiping Zhan, Ph.D,[2] Chaim Jalas, N/A,[2] Amber M. Klimczak, MD,[3] Brent M. Hanson, MD,[3] Julia G. Kim, MD, MPH,[3] Emily K. Osman, MD,[3] Ashley W. Tiegs, MD,[3] Emre Seli, MD,[3] Richard Thomas Scott, Jr., MD,[3] Jason M. Franasiak, MD,[3] [1]IVI-RMA New Jersey, Basking Ridge, NJ; [2]Foundation for Embryonic Competence, Basking Ridge, NJ; [3]IVI RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: To analyze preliminary data from a large scale observational study seeking to characterize the global microbiome of infertile patients, including the oral cavity, urinary tract, gastrointenstinal tract, vagina and cervix, and determine its relationship with pregnancy outcomes following euploid single embryo transfer (SET).

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Patients met inclusion criteria if they were undergoing IVF with pre-implantation genetic testing (PGT-A) with plans for euploid SET. Those who had recently used antibiotics and who had failed more than one previous IVF cycle were excluded. Patients underwent ovarian stimulation and oocyte retrieval according to standard practice. Five samples, buccal, vaginal, cervical, and rectal swabs, as well as a urine sample were obtained on the day of retrieval. Patients underwent euploid SET in a subsequent cycle and pregnancy outcomes were recorded, with sustained implantation (fetal heartbeat at discharge) serving as the primary outcome. All samples underwent DNA isolation and next generation sequencing of the V4 region of the bacteria-specific 16S rRNA gene with the Illumina NextSeq. Operational taxonomic units (OTUs) were assigned using the RDP classifier with confidence cutoffs of 0.8. Shannon Diveristy Index (SDI) was calculated for each sample and SDI values were compared for those with and without on-going implantation. For each of the five sample types, logistic regression was used to test the top genera assigned for association with sustained implantation. Samples were characterized as Lactobacillus dominant (LBD, $\geq$ 90%) and not (NLBD), and logistic regression was performed to test for association with sustained implantation.

RESULTS: Sixty patients who underwent euploid SET were included, of which OTUs were assigned for 35 buccal, 53 urine, 36 GI, 60 vaginal, and 59 cervical samples. SDI was highest for the GI tract samples, and was not significantly correlated with sustained implantation for any of the five sample types. The top genera calls for the urine, vaginal, and cervical samples were Lactobacillus, while the top call for the buccal and GI tract samples were Streptococcus and Prevotella respectively. The top fraction of genera calls for each sample type did not correlate with sustained implantation. Samples characterized as LBD (27 urine, 40 vaginal, and 35 cervical samples) did not demonstrate positive correlation with sustained implantation.

CONCLUSIONS: This is the first large scale study to analyze the global microbiome of infertile patients with respect to pregnancy outcomes. Preliminary data do not demonstrate correlation between microbial diversity and sustained implantation or reveal any specific bacterial dominance pattern correlated with sustained implantation, however our ability to detect a difference is limited by a small initial sample size. Recruitment for the study is ongoing.

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PROGESTERONE LEVEL ON THE DAY OF TRIGGER AND FRESH EMBRYO TRANSFER. Mohamad Irani, MD,[1] Brandon Maddy, MD,[2] Simone C. Elder, MD,[3] Fabiana Kreines, MD,[4] Vinay Gunnala, MD,[5] Daylon James, PhD,[6] David Reichman, MD,[6] Zev Rosenwaks, M.D.[6] [1]Advanced Fertility Center of Chicago, Chicago, IL; [2]Mayo Clinic, College of Medicine and Science, Rochester, MN; [3]New York Presbyterian/Weill Cornell Medicine, New York, NY; [4]New York University, New York, NY; [5]Southwest Fertility Center, Phoenix, AZ; [6]The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: There is no consensus on whether serum progesterone (P4) levels should be measured during IVF cycles. Studies that have suggested the benefit of measuring P4 have identified different thresholds above which there may be a reduction in implantation rates (IRs). However, the majority of these studies did not adjust for critical confounding factors. Therefore, we investigated whether serum P4 levels on the day of trigger influence the implantation potential of embryos by including only young women who had transfers of good-quality blastocyst(s) on day 5. Of note, progesterone levels did not influence the decision to proceed with embryo transfer because it was measured after the completion of cycles using stored serum collected on the day of trigger.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All fresh IVF-ET cycles performed at our center between January 2014 and December 2017 were reviewed. We included women $\leq$35 years who had transfers of good-quality blastocysts on day 5. Good-quality was defined as $\geq$2BB (2-6BB, 2-6AA, 2-6AB, 2-6BA) according to Gardner's grading system. The IR and live birth rate (LBR) were compared between patients at different P4 thresholds on the day of trigger. χ^2 and Fisher's exact tests were used for categorical variables. Student's *t* test was used for parametric data. Odds ratios (OR) with 95% confidence intervals (CI) were calculated. Values were expressed as mean $\pm$ standard deviation.

RESULTS: A total of 739 fresh IVF cycles for women who had a transfer of 1 or 2 good-quality blastocysts on day 5 were included. Their mean age was 31.7 $\pm$ 2.8 years, their body mass index was 23.5 $\pm$ 3.8 kg/m^2, and the number of oocytes retrieved was 16.9 $\pm$ 7.0. Women who had a serum P4 level $\geq$2 ng/mL on the day of trigger had a significantly lower LBR (10% vs. 58.2%; P=0.003) and IR (15% vs. 59.6%, respectively; P=0.002) compared to women whose P4 levels were <2 ng/mL. The difference in LBR remained significant after adjusting for the number of embryos transferred (adjusted OR = 12.5; 95% CI = 1.7-91.2). A P4 level <1.5 ng/mL was associated with a comparable LBR (58.5% vs. 52.6%, respectively; P=0.4) and IR (60.3% vs. 47.4%, respectively; P=0.2) to those of women with P4 levels of 1.5-2 ng/mL. Of note, women with a P4 $\geq$2 ng/mL had a comparable estradiol level on the day of trigger (1947 $\pm$ 711 vs. 2224 $\pm$ 865 pg/mL, respectively; P=0.3) and number of oocytes harvested (14.4 $\pm$ 6.4 vs. 16.9 $\pm$ 7.1, respectively; P=0.2) to those of women with a P4 <2 ng/mL.

CONCLUSIONS: An elevated serum P4 level ($\geq$2 ng/mL) on the day of trigger decreases embryo implantation potential during fresh transfer. Elevation of the P4 level during stimulation does not correlate with the estradiol level or the number of oocytes retrieved. Therefore, these parameters do not predict elevation in the P4 level, which should be measured to identify women who may benefit from freeze-all embryos due to embryo–endometrium dyssynchrony.

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DOES TROPHECTODERM BIOPSY NEGATIVELY IMPACT OBSTETRIC OUTCOMES IN WOMEN <35 YEARS OF AGE?. Ruth Moges, MS,[1] Pietro Bortoletto, MD,[2] Phillip A. Romanski, MD,[2] Glenn Schattman, MD,[1] [1]Weill Cornell Medicine, New York, NY; [2]The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To describe if trophectoderm biopsy for PGT negatively impacts obstetric outcomes in women under the age of 35 transferring a single embryo in the natural cycle.

DESIGN: Retrospective cohort study conducted at a university-affiliated center.

MATERIALS AND METHODS: We included women under the age of 35 undergoing their first IVF cycle at our center who then underwent a natural cycle FET of a single embryo which resulted in a live birth beyond 24 weeks. We excluded twin gestations. Women were stratified into two groups: PGT-A versus no PGT-A testing. The primary outcomes were gestational age (weeks) and weight (grams) at birth. The secondary outcomes were late preterm birth (34 to under 37 weeks) and mode of delivery. Chi-square and students t-test were performed. A p-value of <0.05 denoted statistical significance.

RESULTS: In total, 205 live births were included, n=116 in the PGT group and n=89 in the non-PGT group. Patient and cycle characteristics are displayed in table 1. There were no differences in mean gestational age at birth between the non-PGT and PGT group (38.7 versus 38.8 weeks, p=0.671). The birth weight was significantly higher in the PGT group compared to the non-PGT group (3379.3 versus 3191.8, p=0.020). The rate of late preterm birth was similar between the non-PGT and PGT group (5.7 versus 7.8%, p=0.338). The cesarean section rate was similar between the non-PGT and PGT group (31.8 versus 40.7%, p=0.199).

CONCLUSIONS: In women under the age of 35 who have a singleton live birth following single embryo transfer in the natural cycle, trophectoderm biopsy does not appear to portend detrimental obstetric outcomes. Further studies are needed to elucidate the relationship between trophectoderm biopsy on maternal complications in a cohort of young women in which a corpus luteum is present.

	Non-PGT N=89	PGT N=116
Age years mean (SD)	31.6 (2.3)	31.6 (2.4)
BMI (kg/m2) mean (SD)	21.4 (5.9)	22.1 (4.9)
AMH level (ng/ml) mean (SD)	4.1 (3.3)	3.8 (2.9)
Protocol type n(%)		
Antagonist	77 (86.5)	107 (92.2)
Trigger day E2 (pg/ml)	2360.7 (924.7)	2320.1 (1080.5)
ICSI n (%)	72 (81)	116 (100)
Day of surge E2 level in transfer cycle (pg/ml) mean (SD)	321 (94)	370 (149)
Peak endometrial thickness (mm) mean (SD)	8.9 (1.8)	8.8 (2.0)

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PREDICTING SUCCESSFUL CONVENTIONAL *IN VITRO* FERTILIZATION WITH A MACHINE LEARNING APPROACH BASED ON MARKERS OF CAPACITATION. Stephanie Gunderson, MD,[1] Nicholas C. Spies, MD,[2] Lis C. Puga Molina, PhD,[2] Emily S. Jungheim, MD, MSCI,[3] Joan Riley, PhD, HCLD,[4] Celia M. Santi, PhD MD,[2] [1]Washington University, St Louis, MO; [2]Washington University In Saint Louis, Saint Louis, MO; [3]Northwestern Feinberg School of Medicine, Chicago, IL; [4]Washinton University School of Medicine, St. Louis, MO.

OBJECTIVE: To fertilize an oocyte, spermatozoa must capacitate, during which their membrane potential (Em) becomes hyperpolarized and their intracellular pH (pHi) increases. In normospermic males, absolute values of sperm Em and pHi positively correlate with conventional *in vitro* fertilization (IVF) success rates. The objective of this study was to develop a machine learning algorithm using spermatozoa Em and pHi as well as other clinical parameters to predict success of conventional IVF in normospermic couples.

DESIGN: This was a single-institution, Institutional Review Board-approved study of normospermic couples undergoing IVF from September 12, 2018, to September 23, 2019. Couples were excluded if they used frozen sperm, had known male factor infertility, or underwent intracytoplasmic sperm injection only. Data from 76 participants were included in the analysis.

MATERIALS AND METHODS: After being capacitated in commercial IVF media, sperm were incubated with the pH-sensitive fluorescent probe BCECF-AM and with the Em-sensitive probe DISC3 5-AM. Fluorescence was detected by flow cytometry (FACSCanto II TM cytometer). Data from single, live sperm were analyzed with FACS Diva and FlowJo software. Sperm pHi and Em were obtained by linearly interpolating the median fluorescence values to calibration curves. A gradient boosted machine (GBM) classifier was trained with clinical data including age, body mass index, gravidity/parity, and clinical diagnoses, as well as sperm Em and pHi from 58 patients. The classifier was trained to identify patients who would have successful conventional IVF, defined as a fertilization ratio (number of fertilized oocytes [2 pronuclei]/number of mature oocytes) greater than 0.66. The classifier was then validated on an independent set of data from 18 patients.

RESULTS: Couples with a fertilization ratio <0.66 had similar demographic characteristics as couples with a fertilization ratio >0.66, except that female partners in the >0.66 group were significantly older than those in the <0.66 group (34.7±4 years, n=45, vs. 32.7±4.1, n=31, P=0.04) and patients in the >0.66 group had more living children. In receiver operator characteristic analysis of the prediction algorithm, the area under the curve for predicting successful conventional IVF was 0.831. The algorithm had an accuracy of 0.833, sensitivity of 0.857, and specificity of 0.818. The two parameters that were most predictive of conventional IVF success were sperm Em and pHi.

CONCLUSIONS: A machine learning algorithm could be trained to use clinical parameters and sperm capacitation markers to accurately predict success of conventional IVF in normospermic couples.

References: None.

SUPPORT: None.

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GESTATIONAL CARRIER PREGNANCY OUTCOMES FROM FROZEN EMBRYO TRANSFER (FET), DEPENDING ON THE NUMBER OF EMBRYOS TRANSFERRED AND PRE-IMPLANTATION GENETIC TESTING: A RETROSPECTIVE ANALYSIS. Amalia Namath, M.D.,[1] Samad Jahandideh, PhD,[2] Kate Devine, MD,[2] Jeanne E. O'Brien, MD, MSc,[3] [1]Georgetown University School of Medicine, Washington, DC; [2]Shady Grove Fertility, Washington D.C., DC; [3]Shady Grove Fertility Center, Rockville, MD.

OBJECTIVE: Economic and social factors may motivate intended parents (IPs) to request pre-implantation genetic testing for aneuploidy (PGTA) and/or two embryo transfers when using a gestational carrier (GC). We sought to compare gestational age (GA), birth weight (BW), and live-birth rates (LBR) in GCs after the transfer of one or two frozen embryo(s) (FET) with and without PGTA.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: All blastocyst transfers to GCs at our center from 2009-2018 were included. All transferred blastocysts were graded BB or better, vitrified and warmed. Primary outcome was live birth ($>$24 weeks) per transfer with and without PGTA. Secondary outcomes were GA and BW per live-birth. Statistical analysis using Chi Square test and t test were used, with a $p<0.05$ considered statistically significant.

RESULTS: 583 GC cycles were available for analysis. Mean GA and BW were significantly greater from single embryo transfer (SET) live-births (LB) versus double FET ($p<0.001$ for both). However, LBR was greater with double FET ($p<0.001$) (Table). The rate of multiple births was 1.9% for SET compared to 20.0% for double FET. Only 3.8% of LB from SET had low BW and only 0.6% had very low or extremely low BW. In comparison, 12.5% of double FET LB were low BW (p=0.02). Only 13.4% of SET LB were preterm, compared with 40% in double FET ($p<0.001$).

A total of 194 PGTA-tested cycles and 389 cycles without were available for analysis. Overall, LBR was not significantly different between PGTA and no PGTA groups (41.2% vs. 43.7%, p=0.9).

CONCLUSIONS: Economic factors and a desire for 'efficient' family building may incentivize two embryo transfers when the IPs' treatment plan involves a GC. This data indicates that transfer of two embryos to a GC was associated with a significant reduction in GA and BW, with more preterm and lower BW LB compared to SET. The outcomes of low BW and preterm birth are not justified by the observed modest increase in LBR.

The use of PGTA did not appear to improve LBR. This analysis must be interpreted with caution owing to the small sample of patients using

PGTA. Even if no benefit in terms of LB per transfer, PGTA may have value in the setting of GC FET, given that it may encourage elective SET and assist in GC recruitment.

Clinical Outcomes	One FET	Two FET	P value
BW (grams) (Mean ± SD)	3468 ± 559	2945 ± 750	<0.001
Low BW (<2500g)	3.8%	12.5%	0.02
Very low BW (<1500g)	0.6%	5%	0.08
Extremely low BW (<1000g)	0.6%	3.8%	0.2
GA (weeks)* (Mean ± SD)	37.87 ± 1.75	36.29 ± 3.25	<0.001
Preterm (<37 weeks)	13.4%	40%	<0.001
Very preterm (<32 weeks)	0.6%	6.3%	0.03
Extremely preterm (<28 weeks)	0.6%	3.8%	0.2
LBR	157 (36.8%) N: 427	80 (51.3%) N: 156	<0.001

LBR	PGTA	Non-PGTA	P value
Single and two blastocyst FET, combined	80 (41.2%) N: 194	157 (43.7%) N: 389	0.9

N=number of transfers, *of live births

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THE USE OF COMBINED HORMONAL CONTRACEPTIVE FOR IN-VITRO FERTILIZATION CYCLE PRIMING IS NOT ASSOCIATED WITH DECREASED PREGNANCY RATE IN FROZEN EMBRYO TRANSFER CYCLES. Kristy Cho, MD, FRCSC,[1] Chen Jing, MSc,[2] Niamh Tallon, MB BCh BAO, FRCSC,[3] [1]Division of Reproductive Endocrinology and Infertility, University of British Columbia, Vancouver, BC, Canada; [2]Biostatistic, Olive Fertility Centre, Vancouver, BC, Canada; [3]Division of reproductive endocrinology and infertility, University of British Columbia, Vancouver, BC, Canada.

OBJECTIVE: Oral contraceptive pills (OCP) and luteal phase estradiol are frequently used prior to GnRH-antagonist protocols for better cycle scheduling (1). The recent ESHRE guideline on ovarian stimulation stated that priming before IVF with estrogen or progesterone was acceptable, but discouraged the use of OCP due to reduced live birth rate (2).

The study objectives are to evaluate the cycle outcomes from IVF preceded by OCP priming compared to estradiol pretreatment and to determine if there is a role for OCP priming for those undergoing frozen embryo transfers.

DESIGN: A retrospective cohort study from a university-affiliated fertility centre. Inclusion: all IVF antagonist cycles with ICSI from Jan 2016 to Jun 2019. Exclusion: protocol deviation or treatment cancellation.

MATERIALS AND METHODS: The most common indications for OCP priming included ovulatory dysfunction and endometriosis. In the OCP group, patients utilized 30 mcg ethinyl estradiol and 150 mcg desogestrel daily starting in the preceding cycle for 21-35 days followed by a 5 days pill-free period. In the estradiol group, 17β-estradiol 2 mg was taken twice a day for 7-10 days starting in the luteal phase. Gonadotrophin dose was individualized. Follicular maturation was achieved with HCG, agonist, or dual trigger when >/=3 follicles had mean diameters of >/= 17 mm. Retrieval was performed at 36 hours. Embryos were biopsied on day 5-7. A single euploid embryo was replaced on day 5-7 of progesterone. Differences between groups were compared using a Mann-Whitney-Wilcoxon or Chi-square test.

RESULTS: There were 2237 cycles by 1958 patients; 27% of cycles utilized OCP priming. The average age in the OCP group was 34 years old compared to 36.5 in the estradiol group (P<0.01). AMH was reported in 43% of patients and was higher in the OCP group (3.7 vs 2.2 ng/mL, P<0.01). The gonadotrophin dose was higher in the estradiol group (P<0.01). However, the number of oocytes (15.2 vs 12.5), normal fertilization (72% vs 70%), blastulation rate (50% vs 44%), and number of blastocysts (4.6 vs 3.3) were higher in the OCP group (P all< 0.01). After adjusting for age and AMH with linear regression for the 978 cycles with recorded AMH (24% with OCP prime), significantly higher number of oocytes (13.8 vs 11.9, P=0.002) and mature oocytes (11.3 vs 9.3, P=0.05) were still noted in the OCP group. There were no longer differences in the number of embryos, the normal fertilization rate, or the blastulation rate (p> 0.2).

There were 866 euploid embryo transfer cycles (28% with OCP prime). There were no significant differences in implantation (77% vs 76%) or ongoing pregnancy rates (56 vs 54%) between those who had a transfer after OCP compared to estradiol primed stimulation cycles (p all >0.6).

CONCLUSIONS: There were no differences in pregnancy outcomes from euploid embryo transfer after OCP primed antagonist cycles compared to estradiol pretreatment. In fact, the use of OCP pretreatment was associated with increased oocyte yield, keeping in mind demographics differences. Thus, OCP priming should still be considered in specific populations, such as those with oligoovulation or adequate ovarian reserve.

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SUPPORT: No financial support.

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THE TRANSFER OF EUPLOID COMPLETELY HATCHED BLASTOCYSTS IS ASSOCIATED WITH POORER CLINICAL OUTCOMES. Carlos A. Guerrero, Ph.D., Jennifer A. Rodriguez, B.Sc., Daniel Skora, M.D., Rebecca A. Chilvers, M.D., Satin S. Patel, M.D., Jerald S. Goldstein, M.D. Fertility Specialists of Texas, Frisco, TX.

OBJECTIVE: The handling, use and transfer of completely hatched blastocysts is becoming more common due to an increased demand for aneuploidy screening. The objective of this study was to evaluate clinical outcomes for single frozen embryo transfers using euploid completely hatched blastocysts versus euploid expanded/hatching blastocysts.

DESIGN: Retrospective analysis of data collected from January 2017 through January 2020. Patients were divided into two treatment groups based on the developmental stage prior to frozen embryo transfer. Group A) Expanded/Hatching blastocysts (ExBL/HgBL) and B) Completely hatched blastocysts (HBL). Clinical and laboratory end points were analyzed using t-test and Chi-square test as appropriate.

MATERIALS AND METHODS: Patients ≤38 years old (n=835) undergoing single frozen embryo transfer with euploid blastocysts were used in this study. Blastocysts were biopsied on days 5/6 and aneuploidy testing was performed via NextGen Sequencing. Blastocysts were warmed and cultured for 2-4h before embryo transfer. Low quality euploid blastocysts (<BB) were excluded from this study.

RESULTS: There was a lower positive β-hCG, clinical pregnancy and live birth/ongoing pregnancy rate when transferring HBL compared with ExBL/HgBL (Table 1). No difference was noted between treatment groups for patient age and blastocyst quality. Furthermore, no significant difference in clinical outcomes was noted when transferring Day 5 or Day 6 blastocysts.

TABLE 1. Effect of blastocyst developmental stage on clinical outcomes.

Blastocyst Stage	N	Avg. Age	Positive β-hCG Rate	Clinical Pregnancy Rate (+ heartbeat)	Live Birth/Ongoing Pregnancy Rate
ExBL/HgBL	633	32.2 [a]	480/633 (76%) [a]	416/633 (66%) [a]	390/633 (62%) [a]
HBL	202	32.1 [a]	137/202 (68%) [b]	112/202 (55%) [b]	102/202 (50%) [b]

[a,b] Different superscripts within columns indicate significant differences (P<0.05)

CONCLUSIONS: These findings suggest that euploid completely hatched blastocysts have lower clinical success rates than euploid expanded/hatching blastocysts. Completely hatched blastocysts may be more susceptible to the vitrification/warming process and more prone to mechanical damage during the embryo transfer procedure due to the absence of the zona pellucida. Protocols may need to be tailored to reduce the risk of damage during the embryo transfer procedure when transferring fully hatched blastocysts.

SUPPORT: n/a.

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IS THERE A CRITICAL ENDOMETRIAL LINING THICKNESS FOR SUCCESSFUL IMPLANTATION IN A PROGRAMMED CYCLE?.

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OBJECTIVE: The relationship of endometrial thickness to implantation rates has been debated since 1989 [1,2]. Some studies have suggested a specific cutoff of 7- 8 mm or greater correlates with a statistically significant improvement in pregnancy rates [3,4 5]. A meta-analysis including only fresh cycles concluded that current data indicates that endometrial thickness has a limited capacity to predict implantation rates[6]. Programmed cycles with a different hormonal milieu than fresh cycles might offer a different implantation potential. This study was undertaken to determine the optimal endometrial thickness in a programmed cycle.

DESIGN: An IRB approved retrospective cohort study from a single private IVF center.

MATERIALS AND METHODS: 909 autologous first frozen embryo transfer cycles with a single euploid embryo (euSFET) were analyzed from January 2014 to February 2020. The first objective was to determine if euSFET removes the age-related decline in sustained implantation rate (SIR) defined as ongoing pregnancy rate >20 weeks gestation. SIRs were compared between SART age groups (< 35, 35-37, 38-40, and > 41) using a Chi-Square test or a Fisher's exact test, if assumptions were not met. Logistic regression was used to determine the odds ratios for SIR between endometrial thickness and SIR. Endometrial thickness was divided into the following groups: < 7mm, 7-8mm, 9-12mm, and > 12mm. A receiver operating curve (ROC) was created to identify the optimal endometrial thickness for implantation.

RESULTS: The effect of age on SIR with euSFET was not found to be significant at any level: 60% < 35 group (n=361), 60% in 35-37 group (n=220), 56% in 38-40 group (n=223), and 55% in >41 group (n=105), respectively.

Increasing endometrial thickness appears to have a positive effect on SIR: 46.67%, < 7mm (n=30), 51.5%, 7-8mm (n=266), 62.02% 9-12mm (n=445), and 63.9% > 12mm (n=168). Odds of implantation were 1.21 (95%CI: (.57, 2.59)) times higher in the 7-8mm group, 1.87 (95%CI: (.89, 3.92)) times higher in the 9-12mm group, and 2.00 (95%CI: (.92, 4.39)) times higher in the > 12mm group. Endometrial thickness over 12mm demonstrated a marked improvement in SIR (p = .08). ROC shows 8.35 mm to be the optimal thickness for a successful SIR.

CONCLUSIONS: This data demonstrates that endometrial thickness has a positive effect on SIR in euSFET in programmed cycles. Carefully controlled trials are needed to further demonstrate the effect of endometrial thickness on SIR.

Table 1

Effect of age on SIR			
Age group	N	SIR	P
< 35	361	60%	0.84
35-37	220	60%	0.85
38-40	223	56%	0.33
> 41	105	55%	0.37

Effect of endometrial thickness on SIR				
ET group	N	SIR	P	OR (95% CI)
< 7 mm	30	46.40%	0.72	.88 (.43, 1.79)
7-8mm	266	51.50%	0.62	1.21 (.57, 2.59)
9-12mm	445	62.02%	0.1	1.87 (.89, 3.92)
> 12mm	168	63.90%	0.08	2.00 (.92, 4.39)

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SUPPORT: None.

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OVERCOMPENSATING? THE USE OF ICSI FOR NON-MALE FACTOR INFERTILITY DOES NOT IMPROVE LIVE BIRTH RATE IN A MATCHED PATIENT POPULATION.

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OBJECTIVE: The current ASRM guidelines recommend the utilization of ICSI be confined to couples with male factor infertility. ICSI should not be used routinely, but commonly is. Due to potential increases in complications from ICSI, such as increased handling of gametes, it is imperative to analyze if outcomes differ with the use of ICSI for non-male factor infertility (NMF).

TABLE #1. Contingency Tables

	<35 y/o (n=154)		35-38 y/o (n=72)		>38 y/o (n=56)	
	LBR, (n)	No LBR, (n)	LBR, (n)	No LBR, (n)	LBR, (n)	No LBR, (n)
ICSI	47.4% (36)	52.6% (40)	61.1% (22)	38.9% (14)	34.5% (10)	65.5% (19)
IVF	55.1% (43)	44.9% (35)	47.2% (17)	52.8% (19)	37.0% (10)	63.0% (17)

The primary hypothesis was that there is an association between the treatment (IVF/ICSI) and outcome (LBR) for NMF.

DESIGN: A propensity-matched cohort study comparing fresh NMF cycles utilizing ICSI versus IVF in a single academic institution from 2015-2018.

MATERIALS AND METHODS: A bi-directional selection process through optimization Akaike Information Criterion was used to match the ICSI and IVF groups. The number of embryos transferred, number of two pronuclei, diminished ovarian reserve status, and age were highly influential and thus included in a propensity-match across the two cohorts. Our analysis was then stratified by age-group (<34, 35-38, and >39 years).

RESULTS: The propensity-matched dataset found the best-matched 141 ICSI versus 141 IVF patients. The Cochrane-Mantel-Haenszel test showed no significant effect of ICSI when stratified across the three age groups (P = 0.840). The Breslow-Day test showed no significant effect between the three age groups (P=0.313; Table 1). The difference in fertilization rates from total oocytes retrieved, as well as the total number of usable embryos were not significant (P=0.54, P=0.23, respectively).

CONCLUSIONS: We conclude that ICSI does not significantly alter LBR when utilized for NMF, as the results provide insufficient evidence to reject the null hypothesis. The major strength of this study is the use of a propensity-matched population. Other strengths include a multi-year analysis and reduced confounders by isolating to fresh cycles. Limitations include the low number of matched cycles, patient factors not included in the analysis, such as cycle number or IVF protocol, and the non-randomized nature. However, a power calculation determined that a randomized control trial would require over 2000 participants, which is not practical. It is also pertinent to highlight the apparent statistical equivalence in LBR with the use of ICSI for NMF. Therefore, the use of non-essential ICSI puts unnecessary financial burden on the patient, extra demand on the embryology lab, and incurs potential adverse effects of ICSI without a significant alteration in LBR.

References: None

SUPPORT: None.

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OVARIAN RESERVE, RESPONSE, BLASTOCYST DEVELOPMENT AND PREGNANCY RATES IN OPERATED AND NON-OPERATED ENDOMETRIOMA CASES: A COMPARISON WITH AGE MATCHED UEI CASES. Beril Yuksel, MD, Assoc. Prof., Semra Kahraman, MD Prof. Istanbul Memorial Sisli Hospital, Istanbul, Turkey.

OBJECTIVE: The aim of this study was to evaluate the effect of endometriosis on cycle characteristics in operated and non-operated cases when compared with age matched UEI cases.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We retrospectively analyzed 2500 patients with endometriosis who attended to Istanbul Memorial Hospital, ART and Genetics Center between January 2011 and December 2019. We compared cycle characteristics and ovarian reserve of operated (OE) and non-operated endometrioma (NOE) cases. The control group was comprised of age-matched (<35, 35-37, 38-40) unexplained infertile (UEI) cases.

RESULTS: A total of 2500 OE and NOE cycles, with 2140 cycles, age ≤40 were compared with 2353 cycles of UEI in the same age group. The mean AMH levels and the number of retrieved, mature and fertilized oocytes were significantly lower in OE and NOE cases when compared to UEI. The maturation (MR), fertilization (FR) and blastulation rates (BR) were comparable between NOE and OE cases. However, MR and BR were higher than in UEI controls between the ages of 35-40, both in overall and NOE cases (Table 1). Top - good quality (TQ-GQ) blastocyst rates were also higher in NOE patients when compared to UEI (47.8% vs 47.2%, p<0.05). However, the rates of TQ-GQ blastocysts were lower in NOE when compared to OE cases (47.8% vs 48.9%, p<0.05). The biochemical (BPR) , clinical (CPR) and ongoing pregnancy rates (OPR) were comparable between overall endometriosis, NOE and UEI controls, but the rates were significantly lower in OE when compared to NOE cases (BPR: 50.8% vs 45.2; CPR: 45.9% vs 38.7% and OPR: 38.3% vs 33.2%, p<0.05).

CONCLUSIONS: Endometriosis, even in NOE cases, results in significant reduction in ovarian reserve and ovarian response compared to UEI. However, neither the TQ-GQ blastocyst nor the pregnancy rates are affected.

SUPPORT: None.

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IVF OUTCOMES AFTER BARIATRIC SURGERY. Katherine M. Baker, MD,[1] Laura E. Dodge, Sc.D., M.P.H.,[2] Kim L. Thornton, MD,[3] [1]Beth Israel Deaconess Medical Center, Boston, MA; [2]Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA; [3]Boston IVF, Waltham, MA.

OBJECTIVE: Increasing numbers of obese reproductive-age women are undergoing bariatric surgery to achieve and sustain weight loss to improve fecundability and in vitro fertilization (IVF) outcomes. Despite this, limited data is available regarding IVF outcomes in patients undergoing bariatric surgery. The aim of this study was to describe a cohort of patients who underwent IVF after pursuing bariatric surgery. This information will serve to counsel patients who have undergone or are contemplating undergoing bariatric surgery to improve their IVF outcomes.

DESIGN: Retrospective cohort study from the reproductive endocrine division at our academic teaching hospital.

MATERIALS AND METHODS: Patients whose first IVF cycle at our center began between 2008 and December 2013 and who underwent bariatric surgery before starting infertility treatment were included; outcomes were assessed through 2019. Patient characteristics and cycle details were obtained from electronic medical records. Descriptive statistics were used to describe patient demographic and treatment characteristics and IVF outcomes.

TABLE 1. Maturation (MR), fertilization (FR) and blastulation rates (BR) in cases of endometriosis, OE and NOE compared to UEI controls (**p<0.05 is considered statistically significant, Mann-Whitney U test*)

	MR			FR			BR		
Age	Endometriosis (n=2140)	UEI (n=2353)	P	Endometriosis	UEI	p	Endometriosis	UEI	p
< 35 y	0.84 ± 0.1	0.82 ±0.1	*ns*	0.82 ± 0.2	0.81 ±0.1	*	0.51 ± 0.3	0.52 ±0.2	*ns*
35-37	0.84 ± 0.1	0.78 ± 0.1	*	0.80 ± 0.2	0.84 ± 0.1	*ns*	0.53 ± 0.3	0.40 ± 0.3	*
38-40	0.87 ± 0.3	0.79 ± 0.1	*	0.78 ± 0.2	0.87 ± 0.2	*	0.54 ± 0.3	0.29 ± 0.2	*
	NOE	**UEI**		**NOE**	**UEI**		**NOE**	**UEI**	
< 35 y	0.83 ± 0.1	0.83 ±0.1	*ns*	0.83 ± 0.2	0.81 ± 0.1	*	0.50 ± 0.3	0.52 ±0.2	*ns*
35-37	0.85 ± 0.1	0.78 ± 0.1	*	0.81 ± 0.2	0.84 ± 0.1	*ns*	0.52 ± 0.3	0.40 ± 0.3	*
38-40	0.87 ± 0.1	0.79 ± 0.1	*	0.77 ± 0.2	0.87 ± 0.2	*	0.54 ± 0.3	0.29 ± 0.2	*
	NOE	**OE**		**NOE**	**OE**		**NOE**	**OE**	**p**
< 35 y	0.82 ± 0.1	0.84 ± 0.1	*	0.83 ± 0.2	0.80 ± 0.2	*ns*	0.50 ± 0.3	0.52 ± 0.3	*ns*
35-37	0.85 ± 0.1	0.84 ± 0.1	*ns*	0.81 ± 0.2	0.79 ± 0.2	*ns*	0.52 ± 0.3	0.55 ± 0.3	*ns*
38-40	0.87 ± 0.1	0.88 ± 0.1	*ns*	0.77 ± 0.2	0.82 ± 0.2	*ns*	0.54 ± 0.3	0.59 ± 0.3	*ns*

RESULTS: Forty-five eligible patients underwent 151 cycles (median: 2.0, interquartile range [IQR]: 1.0–4.0). Eighty-percent of patients had undergone gastric bypass, 7 (15.5%) had undergone gastric banding, and 2 (4.4%) had undergone a gastric sleeve procedure. At the start of their first cycle, median age was 38.6 years (IQR: 35.9–40.8), and median BMI was 33.6 (IQR: 29.0–39.3). At the time of the first IVF cycle, the median time since surgery was 3.9 years (IQR: 2.0–7.2), and the median weight loss was 100.0 pounds (IQR: 70.0–137.5). Among all cycles, pregnancy was achieved in 55 (36.4%), with 35 of 45 (77.8%) patients achieving at least one pregnancy, and 27 (17.9%) resulted in live birth, with 20 patients (44.4%) achieving at least one live birth. Of the 55 pregnancies, there were 16 (29.1%) biochemical pregnancies, 9 (16.4%) miscarriages, and 3 (5.5%) ectopic pregnancies. Of those who were known to be anovulatory prior to surgery (n=18), 27.8% regained ovulatory function following surgery. Pregnancies were similar between people who lost <100 pounds (n=13; 14 pregnancies among 43 cycles [32.6%]) and those who lost ≥100 pounds (n=23; 28 pregnancies among 80 cycles [35.0%]). Among all cycles, compared to people who lost <100 pounds, people who lost ≥100 pounds were less likely to experience biochemical pregnancy (21.4% vs. 28.6%, respectively) and miscarriage (10.7% vs. 21.4%, respectively) and more likely to experience ectopic pregnancy (10.7% vs. 0%, respectively) and live birth (57.1% vs. 50.0%).

CONCLUSIONS: At our center, patients who have undergone bariatric surgery prior to infertility treatment had favorable IVF outcomes. Our existing cohort is currently being expanded to allow for more robust analysis of outcomes with regards whether the type of surgery, timing of surgery relative to IVF, or absence or presence of comorbidities impacts IVF outcome.

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MITOCHONDRIAL DNA COPY NUMBER OF CUMULUS CELLS IS NOT LINKED TO EMBRYO IMPLANTATION IN GOOD PROGNOSIS IVF PATIENTS. Weiwei Liu, MD, Chongqing, China.

OBJECTIVE: To explore the mitochondrial DNA (mtDNA) copy number of cumulus cells (CCs) could be used as a biomarker of the potential of embryo implantation in good prognosis IVF patients?

DESIGN: This was a prospective cohort study on good prognosis IVF patients from a large reproductive medicine centre. A total of 392 embryos from 61 cycles (including 31 implanted and 30 non-implanted cycles) were enrolled in the study.

MATERIALS AND METHODS: The corresponding CCs mtDNA copy number of embryos was tested by real-time quantitative PCR. The corresponding CCs mtDNA copy numbers were compared between implanted and non-implanted embryos and also compared between high-quality and poor-quality embryos. Then, mitochondrial membrane potentials of the corresponding CCs were compared between high-quality and poor-quality embryos to verify the above experiment's findings.

RESULTS: For the same population, the mean CCs mtDNA copy numbers for implanted and non-implanted embryos were 255.61±81.02 and 254.50±73.29, and those for high-quality and poor-quality embryos were 266.02±98.56 and 295.71±70.64, respectively. There was no difference in CCs mtDNA copy number between implanted and non-implanted embryos or between high-quality and poor-quality embryos. The mitochondrial membrane potential assay was assessed by JC-1, and the quantitative analysis revealed that the ratio of red to green fluorescence did not differ significantly between high-quality and poor-quality groups.

CONCLUSIONS: Measurement of CC mtDNA copy number might not provide any advantage to embryo prioritisation in good prognosis IVF patients. Any suggested link between CCs mtDNA copy number and embryo implantation requires further validation.

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FOLLICLE FLUSHING DOES NOT IMPROVE LIVE BIRTH AND REDUCES OOCYTE YIELD: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS (RCTS). Anne E. Martini, DO,[1] Ariel Dunn, MD,[2] Lauren Wells, BS,[3] Nanette Rollene, MD,[2] Rhiana D. Saunders, MD,[2] Mae W. Healy, DO,[2] Nancy Terry, BS, MLS,[4] Alan H. DeCherney, MD,[1] Micah J. Hill, DO,[2] [1]National Institute of Child Health and Human Development, NIH, Bethesda, MD; [2]Walter Reed National Military Medical Center, Bethesda, MD; [3]Uniformed Services University of the Health Sciences, Bethesda, MD; [4]National Institutes of Health Library, Bethesda, MD.

OBJECTIVE: To determine whether follicle flushing during oocyte retrieval improves live birth or secondary outcomes in ART.

DESIGN: Systematic review and meta-analysis

MATERIALS AND METHODS: Literature searches were performed for RCTs evaluating follicle flushing in ART (PubMed, EMBASE, Cochrane Database, Web of Science). Inclusion criteria were full-text, English language RCTs published from 1989-2020 comparing follicle flushing with conventional oocyte retrieval. Primary outcome was live birth. Secondary outcomes were clinical and ongoing pregnancy, total and mature oocytes (MII) retrieved, and operating time. Dichotomous and continuous outcomes were reported as risk ratio (RR) and mean difference (MD) respectively. Funnel plots were used to assess publication bias. Random effect models were utilized due to significant clinical heterogeneity between studies. Sensitivity analyses were performed to account for differences in patient population (normal vs poor responders), stimulation protocol, ovulation trigger type, number and volume of flushes, infertility diagnosis, flushing needle type, and random vs fixed effects models.

RESULTS: Ten RCTs met inclusion criteria totaling 922 subjects. Funnel plots revealed no publication bias. Five studies with 734 subjects reported live birth. No difference in live birth was demonstrated between follicle flushing and direct aspiration (RR 1.01, 95% CI 0.78-1.32, I^2=0%). Clinical pregnancy (RR 1.04, 95% CI 0.77-1.40) and ongoing pregnancy (RR 1.08, 95% CI 0.75-1.57) were also not improved with flushing. Total oocyte (MD -0.57, 95% CI -0.95 to -0.20) and MII yield (MD -0.36, 95% CI -0.71 to -0.01) were lower with flushing compared to direct aspiration. Sub-analysis of poor responders also demonstrated lower MII yield with flushing (MD -0.34, 95% CI -0.75-0.08). Procedure time was increased with flushing by 2 minutes in poor responders and 9 minutes in normal responders (P<0.05). Other sensitivity analyses did not reveal any changes.

CONCLUSIONS: Follicle flushing during oocyte retrieval increases procedure time and does not improve live birth or secondary ART outcomes. Oocyte yield is significantly reduced with flushing, although by less than one oocyte. The randomized data do not support the use of follicle flushing as an intervention in ART.

Effects of Follicle Flushing on Live Birth

		Flushing		No Flushing			
Study	Year	Events	Total	Events	Total	Weight (%)	Risk Ratio (95% CI)
Haydardedeoglu	2011	56	149	45	125	62.7	1.04 (0.76-1.43)
Mok-Lin	2013	1	25	5	25	6.4	0.20 (0.03-1.59)
Haydardedeoglu	2017	9	40	10	40	12.8	0.90 (0.41-1.98)
Von-Horn	2017	3	39	1	39	1.3	3.00 (0.33-27.60)
Calabre	2020	15	127	13	125	16.8	1.14 (0.56-2.29)
Total		**84**	**380**	**74**	**354**	**100**	**1.01 (0.78-1.32)**

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THE ASSOCIATION BETWEEN TYPE OF PROGESTERONE SUPPLEMENTATION AND MISCARRIAGE RISK IN WOMEN WITH A POSITIVE PREGNANCY TEST FOLLOWING EMBRYO TRANSFER: A RETROSPECTIVE COHORT STUDY. Talya Shaulov, MD, MSc,[1] Nadège Zanré, MSc,[2] Simon Phillips, PhD,[1] Louise Lapensée, MD[1] [1]Ovo Clinic, Montréal, QC, Canada; [2]University of Montreal, Montreal, QC, Canada.

OBJECTIVE: The aim of this study was to investigate the association between type of progesterone supplementation after a positive pregnancy test and miscarriage in in vitro fertilization (IVF), and to determine if switching from intramuscular (IM) progesterone to vaginal progesterone after a positive pregnancy test is associated with higher miscarriage risk.

DESIGN: Retrospective cohort study in a private university-affiliated fertility clinic in Montreal, Canada.

MATERIALS AND METHODS: Women aged 18 to 50 at the time of embryo transfer (ET), with a positive pregnancy test following ET between 2013 and 2016, were included. Only first IVF pregnancies were included. Biochemical pregnancies as well as pregnancies from oocyte donor, surrogacy, natural fresh or natural frozen cycles were excluded. A total of 1988 women with complete data on exposure and outcome were included in the analysis. The two groups of women studied are those who stayed on IM progesterone following a positive pregnancy test and those who switched to vaginal progesterone after a positive test. The main outcome measured was the risk of miscarriage < 24 weeks gestation as a proportion of non-biochemical pregnancies after fresh or frozen ET.

RESULTS: Among baseline characteristics, a higher number of prior miscarriages, as well as a higher number of prior failed embryo transfers and frozen cycles (vs fresh) were associated with continued IM progesterone use (p values 0.006, <0.001, 0.011, respectively). With regards to the primary outcome, miscarriage risk < 24 weeks, 22.4% (274/1221) of patients in the IM progesterone group experienced a miscarriage compared with 20.7% (159/767) in the vaginal progesterone group. A univariate analysis revealed an unadjusted OR of 0.90 (95%CI 0.73 to 1.13, p=0.369) for the association between progesterone type and miscarriage. A multivariable logistic regression model adjusting for potential confounders (age at oocyte retrieval, body mass index, ovarian reserve, parity, prior miscarriages, duration of infertility, cause of infertility, prior failed ETs, number of good quality embryos produced in fresh IVF cycle, type of ET cycle (fresh or frozen), number of embryos transferred and stage of embryo(s) transferred) revealed an adjusted OR (aOR) of 1.00 (95%CI 0.79 to 1.23, p=0.974). There was evidence for an effect modification by antral follicle count: among patients with <13 antral follicles, users of vaginal progesterone had a lower odds of miscarriage compared to users of IM progesterone (aOR 0.64, 95%CI 0.43 to 0.97, p=0.036).

CONCLUSIONS: This study suggests that switching from IM progesterone to vaginal progesterone after a positive pregnancy test following an ET is not associated with a change in miscarriage risk. Considering that IM progesterone imposes substantial discomfort, this study offers clinicians and patients comforting results and some flexibility in treatment protocols. Further prospective studies are necessary to corroborate results of this study, and to investigate this association in different patient or cycle subgroups, such as by fresh or frozen cycles or by level of ovarian reserve.

References: none.

SUPPORT: none.

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THE EFFECT OF ANTIBIOTIC ADMINISTRATION ON NATURAL CYCLE FROZEN EMBRYO TRANSFERS. Jasmyn K. Johal, MD, MS,[1] Isabel Beshar, MPhil,[1] Brindha Bavan, MD,[2] Amin A. Milki, MD,[2] [1]Stanford University, Dept of Obstetrics & Gynecology, Stanford, CA; [2]Stanford Medicine Fertility and Reproductive Health Services, Sunnyvale, CA.

OBJECTIVE: To assess whether withholding antibiotics prior to transfer impacts the success of natural cycle frozen embryo transfers (NC-FET)

DESIGN: IRB-approved retrospective cohort study

MATERIALS AND METHODS: All NC-FET with euploid blastocysts performed by a single provider at an academic institution from 3/2017- 3/2020 were reviewed. Standard protocol for NC-FET included hCG trigger when the dominant follicle was ≥18 mm and endometrial lining was ≥7 mm to time the transfer. NC-FET performed after 1/2019, which did not include antibiotic administration, were compared to a similar number of NC-FET performed prior to 1/2019, which included routine administration of doxycycline 100 mg BID starting two days prior to transfer through the evening of ET. Our three outcomes of interest were +bHCG, clinical pregnancy rate (CPR, defined as the presence of a gestational sac on ultrasound), and live birth (LB) or ongoing pregnancy rate (OPR, defined as pregnancies >13 weeks). Based on an a priori power analysis, our sample size was sufficient to detect a 5% difference. Demographic information and pregnancy outcomes were recorded in a secure database and analyzed in SAS with Wilcoxon ranked sum tests for non-parametric continuous data, chi-squared statistical analyses for categorical variables, and logistic regressions for outcome variables.

RESULTS: 125 NC-FET were included in each group. The overall mean age at transfer was 36.3 years and mean BMI was 24 kg/m2. Baseline characteristics, including age, BMI, and SART diagnosis, were similar between the two groups. Most patients were nulliparous (60%) women of Asian or Caucasian descent (93.4%). We found no significant difference in +bHCG (74% vs. 72.8%, p=0.83), CPR (65.9% vs 68%, p=0.72), and LB-OPR (62.6% vs 64%, p=0.82) for NC-FET with antibiotic administration and those without, respectively. After controlling for patient age, BMI, race, parity, SART diagnosis, endometrial thickness, and embryo grade in a logistic regression model, antibiotic administration still had no effect on +bHCG (OR 0.62[0.27, 1.40], CPR (OR 0.55[0.25, 1.23]), or LB-OPR (OR 0.56[0.26, 1.21].

CONCLUSIONS: While antibiotics had commonly been administered prior to ET to reduce microbial contamination, the effect on pregnancy outcomes in previous retrospective studies and randomized control trials has been inconsistent (1-3). The strength of our study is that it compared very similar populations using euploid frozen embryos in natural cycles, all performed by the same physician using the same technique. We found that withholding antibiotics does not reduce pregnancy success. Given the risks of antibiotics, including side effects and widespread antibiotic resistance, our findings support the current policy of withholding their use in frozen embryo transfer.

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SUPPORT: None.

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REPEATED IMPLANTATION FAILURE AND WINDOW OF IMPLANTATION TESTING: A WINNING DUET TO IMPROVE LIVE BIRTH RATE. Frida Entezami, MD,[1] Delphine Haouzi, PhD,[2] Alice Ferrieres-Hoa, MD,[2] Sophie Brouillet, PharmD, PhD,[3] Claire Vincens, MD,[4] Sophie Bringer-Deutsch, MD,[4] Emmanuelle Vintejoux, MD,[3] Samir Hamamah, MD, PhD,[3] [1]American Hospital of Paris, Neuilly-sur-Seine, France; [2]Inserm U1203, CHU Montpellier, St-Eloi Hospital, Montpellier, France; [3]Arnaud de Villeneuve Hospital, CHU Montpellier, Montpellier, France; [4]ART-PGD department, Arnaud de Villeneuve Hospital, CHU Montpellier, Montpellier, France.

OBJECTIVE: Outcome benefits on live birth rate in patients with repeated implantation failure (RIF) after customized embryo transfer based upon identification of endometrial receptivity window by transcriptomic approach.

DESIGN: This is a french prospective multicenter trial. Endometrial biopsies were performed during the implantation window 7-9 days after the LH surge in natural cycle or 5-9 days after progesterone administration under HRT. According to transcriptomic testing result of the biopsy, blastocysts were transferred in the subsequent frozen embryo transfer cycle (FRET), at the specific day where endometrium was identified as receptive. For cleavage stage D2/D3 embryos transfers were performed 72/48 hours before the specific cycle day where endometrium was identified as receptive.

MATERIALS AND METHODS: From 2015 to 2018 a total of 217 RIF patients (4.4±1.9 failed fresh/frozen transfers of 6.4±3.6 embryos) were enrolled. Genomic testing of endometrial biopsies was performed under natural/HRT cycles and mRNA expression of genes predictive of receptivity was established by RT-qPCR. Customized embryo transfer (n=157 patients) was

performed in a subsequent FRET cycle based upon these results. Clinical pregnancy and live birth rates (LBR) were compared to control RIF patients with standard FRET in natural/HRT cycles (n=60 patients).

RESULTS: Customized embryo transfer using the genomic testing strategy yielded spectacular increase in outcome for 157 RIF patients (age 37.2±4.3 years). Comparison of the results between the study group and the control group showed significantly higher rates for implantation (22.7% vs 7.2%, p=0.0001), clinical pregnancy (38.8% vs 15.0%, p=0.0006), ongoing pregnancy (36.3% vs 8.3%, p=0.00002) and live birth rates (31.8% vs 8.3%, p=0.0002). Analyses of endometrial receptivity status revealed mostly a delay both in natural and HRT cycles, between 1 to 3 days. Most patients achieved pregnancy after the first customized FRET (70%). Better clinical pregnancy and live birth rates were obtained with blastocyst transfer compared to cleavage stage transfers (respectively 36.3% vs 22.5% and 29.5% vs 14.0%). Whatever the day of transfer, results were significantly higher in the study group compared to the control group, with ongoing pregnancy rate for transfer of cleavage-stage embryos of 21.1% compared to 4.5% in the control group (p=0.03). In blastocyst transfer group ongoing pregnancy rate of 33.9% was significantly higher than 8.6% in the control group (p=0.003).

CONCLUSIONS: In RIF patients customized embryo transfer according to endometrial transcriptomic testing improves dramatically the clinical outcome by increasing almost four-fold the LBR. In our study, the majority of RIF patients displayed a delay in their receptivity window of 1 to 3 days, revealing a potential cause for their previous implantation failures. The transcriptomic window of implantation testing alone, and without any embryo genetical testings for aneuploidy, is able to enhance significantly the clinical outcome and should be advised to rescue LBR for patients with multiple RIF.

SUPPORT: This work was partially supported by a grant from Gedeon Richter Pharmaceutical Company. The authors of the study have no competing interests to report.

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IDENTIFYING THE GAMETE RESPONSIBLE FOR ICSI FERTILIZATION FAILURE. Stephanie Cheung, B.S., Philip Xie, B.S., Alessandra Parrella, M.Sc., Derek Keating, B.A., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To identify and effectively treat the gamete responsible for complete ICSI fertilization failure.

DESIGN: A total of 114 couples treated at our center during the last 20 years who had a ≤10% ICSI fertilization rate were identified. Seventy-six men were screened for the presence of PLCζ. Those with a PLCζ presence were considered to have oocyte-related oocyte activation deficiency (o-OAD; n=52) and were treated by standard ICSI with a tailored stimulation protocol. Men with PLCζ absence were further screened by a mouse oocyte activation test (MOAT) and were considered to have sperm-related OAD (s-OAD; n=24). Some of these men (n=4) underwent a genomic evaluation by NGS. These couples then underwent subsequent ICSI cycles with assisted gamete treatment (AGT). ICSI outcome was compared between the study cohort and historical cycles from the same couple.

MATERIALS AND METHODS: Consenting couples with female partners ≤37 years of age and male partners with a sperm concentration of ≥1x10^6/ml who had a ≤10% fertilization rate, despite injecting ≥3 oocytes, were included (IRB 0712009553). PLCζ assessment was performed, confirmed by MOAT and DNA/RNAseq. In subsequent cycles, couples with o-OAD were treated by modulating *in vivo/vitro* maturation time, while s-OAD cases were treated by exposing both gametes to calcium ionophore. Clinical outcomes were compared.

RESULTS: A total of 114 couples (maternal age, 33.8±4 yrs; paternal age, 36.9±5 yrs) with a 9.1% ICSI fertilization rate were identified. Of all men screened for PLCζ, 52 were identified as having o-OAD. These 52 couples underwent subsequent ICSI cycles with tailored superovulation, yielding significantly higher fertilization (59.0% vs. 2.1%; P<0.0001) and clinical pregnancy (28.6% vs. 0%; P<0.0001) rates compared to their respective historical cycles. Thirty clinical pregnancies resulted in 25 deliveries and 5 pregnancy losses. A total of 32 babies were born, 15 boys and 17 girls, with no congenital malformations.

Twenty-four couples (maternal age, 35.6±5 yrs; paternal age, 39.8±6 yrs) in which the male partners had the absence of PLCζ were then screened by MOAT and considered to have s-OAD. In some of these men, DNAseq identified a PLCZ1 deletion, corroborating the initial screening results. Deletions of genes associated with spermiogenesis and embryo development (PIWIL1, BSX, NLRP5), as well as the absence of the subacrosomal perinuclear theca (PICK1, SPATA16, DPY19L), were found. For these couples, AGT provided higher fertilization (42.1% vs. 9.1%; P<0.05) and clinical pregnancy rates (36% vs. 0%; P<0.05) compared to their historical cycles. Six patients have successfully delivered, with children currently displaying normal development at 3 years of age.

CONCLUSIONS: This is the first attempt to identify a gamete-specific OAD in couples with complete ICSI fertilization failure. Couples with o-OAD can be successfully treated in a subsequent cycle by modifying the superovulation protocol, thus preventing AGT overuse. For couples with s-OAD confirmed by detailed genomic analysis, AGT treatment proved paramount in fulfilling their desire to have a child.

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THE EFFECT OF THE ORAL OXYTOCIN ANTAGONIST, NOLASIBAN, ON PREGNANCY RATES IN WOMEN UNDERGOING EMBRYO TRANSFER FOLLOWING IVF. Georg Griesinger, MD, PhD,[1] Jacques Donnez, PhD, MD,[2] Andrew Humberstone, PhD,[3] Paul Terrill, PhD,[4] Oliver Pohl, DVM, MPH, MSc,[5] Elizabeth Garner, MD, MPH,[6] Ernest Loumaye, MD, PhD,[3] [1]University Hospital Schleswig-Holstein, Lübeck, Germany; [2]Catholic University of Louvain, Brussels, Belgium; [3]ObsEva SA, Plan-les-Ouates, Switzerland; [4]Cytel Inc, London, United Kingdom; [5]ObsEva, Plan-les-Ouates, Switzerland; [6]ObsEva Inc, Boston, MA.

OBJECTIVE: To summarize data from three randomized clinical trials in women undergoing IVF and a mechanism of action (MoA) study in healthy volunteers of nolasiban, an oral oxytocin receptor antagonist, being developed to improve pregnancy and live birth rates in women undergoing fresh embryo transfer following IVF.

DESIGN: The first clinical trial was a randomized, double-blind, parallel group, dose-ranging Phase 2 trial comparing single oral doses of 100, 300 and 900 mg nolasiban to placebo in women undergoing fresh Day 3 embryo transfer (ET) following IVF or ICSI. The subsequent two Phase 3 trials were randomized, double-blind, parallel group, trials comparing a single oral dose of 900 mg nolasiban to placebo in women undergoing fresh single embryo transfer on Day 3 or Day 5 post-OPU. A meta-analysis of ongoing pregnancy rate in the nolasiban 900 mg vs placebo groups in all three trials was performed.

MATERIALS AND METHODS: For the clinical trials, IVF patients (≤37 years and ≤ 1 previous failed cycle) were recruited from 60 fertility centers in 11 European countries between 2015 and 2019. In the clinical trials, a single dose of nolasiban or placebo was administered four hours before embryo transfer. Key clinical endpoints in the clinical trials were pregnancy test (14 days post-oocyte pick-up), clinical pregnancy (6 weeks post-ET), ongoing pregnancy (10 weeks post-ET), pregnancy loss, and live birth. Population pharmacokinetics of nolasiban were also assessed. The MoA study assessed the effect of single doses of 900 and 1800 mg in healthy female volunteers on measures of endometrial receptivity including uterine contractions, endometrial blood flow and endometrial gene expression.

RESULTS: A significant increase in ongoing pregnancy and live birth rates was observed in the 900 mg nolasiban group compared to placebo in the first Phase 3 trial but not confirmed in the second study. A meta-analysis of all the clinical trials showed an absolute increase of 5% (p=0.029) in ongoing pregnancy rate with nolasiban 900 mg versus placebo. There was a similar magnitude of effect with Day 3 compared to Day 5 ET (increases of 6.18% and 4.54%, respectively), although statistical significance was not achieved for either ET day when considered separately. Comparison of population PK results to pregnancy outcomes indicated a correlation between higher nolasiban exposures and pregnancy. In the MoA study, nolasiban showed effects suggesting an improvement in endometrial receptivity, including changes in gene expression associated with endometrial receptivity with the higher dose.

CONCLUSIONS: A single oral dose of 900 mg nolasiban administered 4 h before ET increased ongoing pregnancy rate by an absolute 5% (p=0.029) (i.e., a 15% relative increase) in a meta-analysis of 3 clinical trials. The overall clinical data, including pharmacokinetic modeling and evidence from the MoA study, support future evaluation of higher doses and/or alternate regimens.

SUPPORT: The trials were funded by ObsEva SA.

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ASSOCIATION BETWEEN ESTRADIOL LEVELS AND OBSTETRIC OUTCOMES IN LETROZOLE-STIMULATED FROZEN EMBRYO TRANSFER CYCLES. Wendy Y. Zhang, BS,[1] Maya K. Ramachandran, BS,[1] Gayathree Murugappan, MD,[2] Lusine Aghajanova, MD PhD,[2] Ruth Bunker Lathi, MD,[2] [1]Stanford University School of Medicine, Stanford, CA; [2]Stanford University, Stanford, CA.

OBJECTIVE: Letrozole-stimulated frozen embryo transfer (LTZ-FET) cycles are increasingly utilized due to growing evidence of improved success rates in multiple populations, including patients with polycystic ovary syndrome, diminished ovarian reserve, tubal factor, or unexplained infertility. The degree of estrogen suppression is variable between patients, and the impact of low estradiol (E2) levels in the follicular phase is unknown. Thus, the goal of this study was to assess the impact of low estradiol on outcomes of LTZ- FET cycles.

DESIGN: Retrospective cohort

MATERIALS AND METHODS: We studied all LTZ-FET cycles at an academic center from 1/2018 to 8/2019 (n=220). 5 mg of letrozole was administered daily for 5 days from cycle day 3. Ovulation was triggered with HCG when the lead follicle was ≥18 mm and endometrial thickness (EMT) was >7 mm. FET was performed 7 days after trigger or 6 days after LH surge, and micronized progesterone was given vaginally twice daily 2 days after ovulation. Peak serum E2 levels were measured on the day of trigger, with low E2 defined as <10th percentile (E2<104.4 pg/mL). The primary outcomes including EMT, clinical pregnancy rate (presence of fetal cardiac activity), and LBR were compared using t- and chi-squared tests between low and normal E2 groups.

RESULTS: There were no differences in age, BMI, race, distribution of infertility diagnoses, gravidity, parity, number of embryos transferred, and use of PGT between groups. The mean E2 level for the normal E2 (control) group was 738.7±878.7 pg/mL compared to 77.6±19.3 in the low E2 group. Cycle characteristics, pregnancy rates, and biochemical miscarriage rates were similar between groups. However, the low E2 group had a significantly higher miscarriage rate and a significantly lower LBR.

	Controls n=186	Low estradiol n=34	P-value
Baseline characteristics			
Age (y)	36.1 ± 4.2	36.0 ± 3.6	0.98
BMI	24.0 ± 4.8	24.1 ± 6.8	0.92
Cycle characteristics day of trigger			
Peak estradiol (pg/mL)	738.7 ± 878.7	77.6 ± 19.3	0.0001
Progesterone (ng/mL)	0.57 ± 0.45	0.64 ± 0.46	0.41
LH (IU/L)	22.4 ± 21.0	22.1 ± 18.5	0.93
Endometrial thickness (mm)	8.6 ± 1.2	8.9 ± 1.4	0.19
# of follicles >14mm	1.6±0.9	1.4 ± 0.8	0.42
Clinical Outcomes			
Progesterone at first BHCG (ng/mL)	39.5 ± 15.1	41.5 ± 16.6	0.46
Pregnancy rate, n(%)	121 (65.1)	19 (55.9)	0.31
Biochemical miscarriage rate, n(%)	20 (10.8)	4 (11.8)	0.86
Miscarriage rate, n(%)	18 (14.9)	7 (36.8)	0.02
Live birth rate, n(%)	103 (55.4)	12 (35.3)	0.01

CONCLUSIONS: In LTZ-FET cycles, low E2 levels were associated with a significantly higher miscarriage rate and lower live birth rate. Our data suggest that E2 levels in the follicular phase may have an effect on cycle outcomes, but further studies are needed to confirm our findings and understand the mechanisms behind these differences.

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ENDOMETRIAL COMPACTION DOES NOT PREDICT ONGOING PREGNANCY RATE IN PROGRAMMED SINGLE EUPLOID EMBRYO TRANSFER CYCLES. Carrie Riestenberg, MD,[1] Molly M. Quinn, MD,[1] Alin Lina Akopians, MD, PhD,[2] Hal Danzer, MD,[2] Mark Surrey, MD,[2] Shahin Ghadir, MD,[2] Lindsay Kroener, MD,[1] [1]University of California, Los Angeles, Los Angeles, CA; [2]Southern California Reproductive Center, Beverly Hills, CA.

OBJECTIVE: To evaluate whether endometrial compaction using sequential transvaginal ultrasound is associated with improved ongoing pregnancy rate in programmed single euploid FETs.

DESIGN: Retrospective observational study.

MATERIALS AND METHODS: All single euploid FET cycles between January and December 2018 were assessed for eligibility. Natural cycle and controlled ovarian stimulation FETs as well as gestational carrier cycles were excluded. Patients were also excluded if their endometrial thickness was <7 mm at the initiation of progesterone. All patients received the same exogenous hormones for endometrial preparation per clinic protocol. Endometrial thickness was measured with transvaginal ultrasound after an average of 9-10 days of estrogen. Progesterone in oil 50mg daily and endometrin 100 mg TID were started within two days of the final lining measurement if the endometrium was ≥7 mm and trilaminar in appearance. Patients returned the day prior to embryo transfer for reassessment of the endometrial lining using transvaginal ultrasound. All FETs were performed on the sixth day of progesterone. The primary outcome was ongoing pregnancy rate defined as the presence of fetal cardiac activity at 10 weeks. We grouped patients by percentage of endometrial compaction, defined as the difference in endometrial thickness at the end of the estrogen-only phase and the day before embryo transfer, divided by the thickness at the end of estrogen-only phase. Cycles in which the percent compaction was less than +/-5% were considered unchanged.

RESULTS: A total of 294 single euploid FETs were included in the analysis. Only 17.3% (51/294) of the cycles demonstrated ≥5% compaction, whereas 82.7% (243/294) either expanded or were unchanged. Of those without any compaction, 30.0% (73/243) had no change in compaction and 70.0% (170/243) expanded ≥5%. Ongoing pregnancy rate did not significantly differ between cycles with compaction, no change, or expansion (69.8% vs 57.5% vs 58.8%, p=0.94) (Table 1). When considering only those

TABLE 1. Ongoing pregnancy rate (any compaction vs no change vs any expansion)

	Any Compaction	No Change	Any Expansion	p-value[a]
Ongoing Pregnancy Rate	31/51 (69.8%)	42/73 (57.5%)	100/170 (58.8%)	0.94

[a]chi-squared

TABLE 2. Ongoing pregnancy rate by percent compaction

	No Change	5-9%	10-14%	≥15%	p-value[a]
Ongoing Pregnancy Rate	42/73 (57.5%)	12/17 (70.6%)	9/15 (60%)	10/19 (52.6%)	0.72

[a]chi-squared

cycles in which the endometrium compacted, no difference was seen in ongoing pregnancy rates at different levels of compaction (p=0.72) (Table 2).

CONCLUSIONS: Endometrial compaction is not associated with ongoing pregnancy rate in single euploid FETs in our cohort.

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PREGNANCY AND BIRTH OUTCOMES ASSOCIATED WITH MATERNAL AGE AND EUPLOID EMBRYO GRADE AFTER NATURAL CYCLE FROZEN TRANSFER. Wendy Y. Zhang, BS,[1] Jasmyn K. Johal, MD, MS,[2] Brindha Bavan, MD,[3] Amin A. Milki, MD,[4] [1]Stanford University School of Medicine, Stanford, CA; [2]Stanford University, Dept of Obstetrics & Gynecology, Stanford, CA; [3]Stanford Fertility and Reproductive Medicine Center, Sunnyvale, CA; [4]Stanford Medicine Fertility and Reproductive Health Services, Sunnyvale, CA.

OBJECTIVE: As aging decreases female fertility due to diminished oocyte quality and increased aneuploidy risk, it similarly impacts IVF success via diminished embryo quality. However, data are lacking with regards to the effect of maternal age when euploid embryos of similar grade are used. Thus, we examine whether age – when aneuploidy and embryo quality are accounted for - still influences IVF outcomes.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: We studied all natural cycle frozen embryo transfers (NC-FET) with one euploid blastocyst from 2016 to 2019 (n=516 cycles). Blastocysts were graded from AA to DD based on their inner cell mass and trophectoderm morphology; CC or better embryos were biopsied. To minimize confounding by poor quality embryos, our study included only embryos of grade BB or better. We also performed a subanalysis stratifying by embryo grade. The outcomes studied were viable pregnancy (presence of fetal cardiac activity), miscarriage, live birth, preterm delivery, and birth weight. We compared three age groups: <35, 35-39, and ≥40. ANOVA and chi-squared tests were used for continuous and categorical variables, respectively.

RESULTS: Patients had similar baseline characteristics including BMI, race, smoking rate, and endometrial lining thickness. As expected, women age ≥40 had significantly lower antral follicle counts and AMH levels. Among women who transferred euploid embryos of similar grade, advanced maternal age (≥35) was still associated with significantly decreased rates of viable pregnancy (p=0.0002) and live birth (p=0.0008). However, once viable pregnancy was confirmed, there were no significant differences in miscarriage rate, preterm delivery rate, and mean birth weight. Upon stratification by embryo grade, this significant pattern persisted for embryo grade AA, with a similar trend for grades AB, BA, and BB.

CONCLUSIONS: Despite the use of euploid embryos of similar quality, advanced maternal age is still associated with significantly decreased rates of viable pregnancy and live birth. This remains true even if the best quality (AA) embryos are used. These findings may help further guide age-based counseling for women seeking IVF treatment.

Maternal Age Groups (y)	<35	35-39	≥40	P-value
Outcomes for all embryo grades				
	N=155	*N=248*	*N=113*	
Viable pregnancy n(%)	121 (78.1)	150 (60.5)	65 (57.5)	*0.0002*
Live birth n(%)	115 (74.2)	142 (57.3)	56 (49.6)	*0.0008*
Miscarriage n(%)	6 (3.9)	8 (3.2)	9 (7.9)	*0.1*
Preterm delivery n(%)	8 (7.0)	8 (5.6)	4 (7.1)	*0.8*
Birth weight (grams)	3258 ± 505	3321 ± 556	3337 ± 684	*0.3*
Outcomes for embryo grade AA				
	N=64	*N=92*	*N=30*	
Viable pregnancy	52 (81.3)	58 (63.0)	17 (56.7)	*0.01*
Live birth	50 (78.1)	55 (59.8)	13 (43.3)	*0.003*
Miscarriage	2 (3.8)	3 (3.3)	4 (13.3)	*0.06*
Birth weight	3244 ± 428	3251 ± 669	3336± 309	*0.3*

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LIVE BIRTH RATE AND ORAL CONTRACEPTIVES PRETREATMENT IN IVF CYCLES: WHO TO CONSIDER FOR A FRESH EMBRYO TRANSFER?. Yao Lu, M.D.,[1] Steven R. Lindheim, M.D.,[2] Yun Sun, M.D.[1] [1]Center for Reproductive Medicine, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China; [2]Wright State University, Dayton, OH.

OBJECTIVE: Concern regarding the use of pretreatment of oral contraceptives (OC) in IVF cycles has been debated. We investigated for factors that may have been associated with live birth rate (LBR) in fresh embryo transfer cycles after OC pretreatment.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: From January 2014 to June 2017, all normo-ovulatory patients (defined as regular menstrual cycles between 21–35 days), aged 20–35 years and a basal FSH < 10IU/L who were undergoing their first autologous IVF or intra-cytoplasmic sperm injection (ICSI) cycle followed by fresh cleavage embryo transfer were reviewed. All patients who used gonadotropin releasing hormone (GnRH) antagonist (ant) or long GnRH-agonist (a) protocol for ovarian stimulation after OC pretreatment were included. Excluded were cycles those diagnosed with PCOS, uterine abnormalities, untreated hydrosalpinges and those undergoing preimplantation genetic testing (PGT).

RESULTS: 814 patients were included in the analysis. Multivariate logistic regression analysis demonstrated that GnRH-ant protocol was significantly associated with lowered LBR (adjusted OR 0.70, 95% CI 0.52-0.94), while endometrial thickness on day of hCG trigger was associated with increased LBR (adjusted OR 1.16, 95% CI 1.06-1.28). Despite patients' age, duration of infertility, BMI, primary/secondary infertility and basal FSH were all comparable between GnRH-a and GnRH-ant groups, the GnRH-ant group resulted in significantly lower LBR compared to the GnRH-a group (48.5% vs. 37.4%, p=0.002). Using ROC analysis and a cut-off endometrial thickness < and ≥9.5mm, those <9.5mm in the GnRH-ant group result in a significantly lower LBR than GnRH-a group (28.5% vs. 43.4%, p=0.004),

while no differences were noted with an endometrial thickness ≥9.5mm (49.6% vs.51.1%, p=0.78).

CONCLUSIONS: Live birth was significantly impacted in OC pre-treated GnRH-ant cycles with an endometrial thickness <9.5mm on day of hCG trigger. Cryopreservation of all embryos in these cycles when using GnRH-ant protocols should be considered.

SUPPORT: This study was supported by National Key R&D Program of China (No. 2017YFC1001403), the National Natural Science Foundation of China (No. 81771648) , Shanghai leading talent program, Innovative research team of high-level local universities in Shanghai (No. SSMU-ZLCX20180401), Shanghai Municipal Education Commission-Gaofeng Clinical Medicine Grant Support (No. 20161413), Program of Shanghai Academic Research Leader in Shanghai Municipal Commission of Health and Family Planning (No. 2017BR015), Shanghai Technological Innovation Plan (No. 18140902400) and Shanghai Commission of Science and Technology (No. 17DZ2271100).

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FACTORS ASSOCIATED WITH IMPLANTATION OF EMBRYOS NOT ABLE TO BE BIOPSIED UNTIL DAY 7.

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OBJECTIVE: Recent studies have demonstrated that extended culture of blastocysts to day 7 leads to satisfactory pregnancy outcomes in patients with slow-growing embryos.[1,2] However, even when confirmed to be euploid by preimplantation genetic testing for aneuploidy (PGT-A), day 7 embryos have lower rates of implantation, clinical pregnancy, and live birth compared to day 5 or day 6 embryos.[1] Prior studies assessing factors associated with implantation of euploid embryos only assessed embryos biopsied on day 5 or 6.[3,4] The objective of this study was to identify patient, cycle, and embryo characteristics associated with successful implantation of euploid day 7 embryos by comparing day 7 embryos resulting in clinical pregnancy to those that did not.

DESIGN: Case control study.

MATERIALS AND METHODS: The study included single, euploid, vitrified-warmed day 7 embryo transfers (FET) from September 2016 through March 2020. We compared day 7 embryo transfer cycles resulting in clinical pregnancy (cases), defined as the presence of a gestational sac on ultrasound, to those where clinical pregnancy was not achieved (controls). PGT-A was performed using Next Generation Sequencing. Demographic and cycle characteristics were evaluated among the cohorts and included: age, oocyte age, BMI, AMH, endometrial thickness, use of PGT for single gene disorder (PGT-M), fresh vs. frozen oocytes, availability of supernumerary euploid day 5 and 6 embryos for transfer, and morphology grading for embryo expansion, inner cell mass, and trophectoderm (TE). Comparative statistics and adjusted logistic regression were used for analysis.

RESULTS: A total of 228 single euploid day 7 FETs were identified, of which 72 resulted in clinical pregnancy and 156 did not result in clinical pregnancy. The groups were similar in terms of age, oocyte age, BMI, AMH, endometrial thickness, use of PGT-M, presence of supernumerary day 5/6 embryos, and fresh vs. frozen oocytes. Embryos resulting in clinical pregnancy had a significantly higher proportion of ICM grade A (54.2% vs. 32.1%, p=0.001) and a significantly lower proportion of ICM grade C (12.5% vs. 26.9%, p=0.015). Expansion and TE grade were similar between the groups. On multivariate logistic regression, when controlling for age, oocyte age, AMH, BMI, endometrial thickness, PGT-M, fresh vs. frozen eggs, supernumerary D5/6 embryos, expansion, and TE grade, ICM grade A vs. C was significantly associated with increased odds of clinical pregnancy (adjusted OR 3.56, 95% CI 1.41-9.0, p=0.0071).

CONCLUSIONS: The subset of day 7 embryos that successfully implant have a more robust inner cell mass, as defined by Gardner's score of A vs. C, than those that do not. Our study indicates that the same morphologic criteria shown to predict reproductive competence of euploid day 5 and 6 embryos is associated with the success of day 7 embryos, despite the lower overall implantation rate of these slower-growing embryos. As emerging data demonstrate the feasibility of day 7 embryo transfer, this study can inform recommendations regarding selecting an embryo for transfer to assist patients in achieving their family building goals.

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SUPPORT: None.

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DETERMINING THE OPTIMAL FOLLICLE SIZE AT TRIGGER IN PATIENTS UNDERGOING OVARIAN STIMULATION WITH A CLOMIPHENE CITRATE PLUS GONADOTROPIN ANTAGONIST PROTOCOL FOR IN VITRO FERTILIZATION.

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OBJECTIVE: To investigate the optimal follicle size at the time of ovulatory trigger in clomiphene citrate plus gonadotropin/antagonist IVF protocols.

DESIGN: Retrospective cohort study at a single academic center. Patients who underwent their first IVF cycle with a clomiphene citrate plus gonadotropin/antagonist protocol at our center between 01/01/2013 and 3/31/2019 were included. Patients were stratified into two groups by the median size of the three largest follicles on the day of trigger: <20 mm (Group A) and ≥20 mm (Group B). Patients were excluded if they did not have at least 3 follicles >12 mm at the time of trigger.

MATERIALS AND METHODS: On cycle day 2, patients received 100 mg clomiphene citrate for 5 days, with gonadotropins starting on cycle day 5 and continuing until the night before trigger. Patients were triggered with either hCG alone or in combination with GnRH agonist. The timing of trigger administration was determined by the treating physician. The primary outcome was the number of mature oocytes retrieved; secondary outcomes were the number of oocytes retrieved and the number of zygotes. Poisson regression was used to estimate RR (95% CI) adjusted *a priori* for patient age for oocyte and zygote development outcomes. A subgroup analysis was performed for women in the upper quartile for age (≥41.7 years).

RESULTS: A total of 635 patients were included (399 patients in the <20 mm group and 236 patients in the ≥20 mm group). The median (IQR) of the three largest follicles was 18.5 mm (18-19) in Group A and 21 mm (20.2-22) in Group B. Among the entire cohort, the mean number of oocytes retrieved was significantly higher in Group B (9.9 ± 6.5; RR 1.08; 1.03-1.14) compared to Group A (9.2 ± 6.3). Otherwise, when Group B was compared to Group A, the number of mature oocytes (7.3 ± 4.8 vs. 7.0 ± 4.9; OR 1.04; 0.98-1.11) and the number of zygotes (5.2 ± 4.3 vs. 4.9 ± 4.0; OR 1.07; 0.99-1.15) were similar. In the subgroup analysis of patients in the upper quartile for age (≥41.7 years), Group B was observed to have statistically significantly more oocytes retrieved (8.1 ± 5.9 vs. 6.7 ± 4.5; OR 1.23; 1.10-1.38), more mature oocytes retrieved (6.0 ± 4.0 vs. 5.2 ± 3.4; OR 1.16; 1.02-1.33), and more zygotes (4.7 ± 3.5 vs. 3.6 ± 2.8; OR 1.32; 1.13-1.55).

CONCLUSIONS: In clomiphene citrate plus gonadotropin/antagonist IVF protocols, patients who were triggered at larger follicle sizes yielded more oocytes retrieved, but a similar number of mature oocytes and zygotes when compared to patients triggered at smaller follicle sizes. However, in older patients, waiting to administer the ovulatory trigger until the median of the three largest follicles was ≥20 mm yielded more mature oocytes and zygotes per cycle. Based on these findings, we conclude that the ideal time to administer the ovulatory trigger in clomiphene citrate-based IVF cycles is when the median of the three largest follicles is ≥20 mm, particularly in patients of advanced maternal age.

SUPPORT: No financial support, funding or services were obtained for this study. The authors do not report any potential conflicts of interest.

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A SINGLE-CENTER RCT DATA ANALYSIS OF UROFOLLITROPIN PRECONDITIONING TO IMPROVE THE EFFICACY OF ICSI THREAPY IN MEN WITH MODERATE TO SEVERE OLIGOSPERMIA AND ASTHENOSPERMIA. Tingting Li, Doctor Reproductive Medicine Research Center, Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: To evaluate the possibility of urofollitropin preconditing to improve the sperm quality of infertility patients in ICSI treatment cycle in male patients who were diagnosed with moderate to severe oligospermia and asthenospermia, as well as the effect of treatment on fertilization rate and embryo quality.

DESIGN: Prospective clinical controlled trial.

MATERIALS AND METHODS: By analyzing the data of the experimental group, which 24 patients were intramuscularly injected uFSH(urofollitropin) 150U every three days before the ICSI period for 12 consecutive weeks, whilst other 8 patients didn't injected as the blank control group and the ratio was 3 to 1, we compared the 2PN fertilization rate, the available embryo rate, the high-quality embryo rate and the blastocyst formation rate between the experimental group and the blank control group.

RESULTS: There was no differences in the basic conditions inside the experimental group and the blank control group, such as the age of the male and female. The 2PN fertilization rate between the two groups was83.47% vs 81.69%, and the available embryo rate and blastocyst formation rate were 66.83 % vs 74.40 %, 54.95 % vs 67.74%, respectively .

CONCLUSIONS: ontinuous use of uFSH 150U Q3D for 12 weeks before ICSI entry in patients with moderate to severe oligospermia and asthenospermia did not improve or increase the subsequent ICSI oosphere fertilization rate and embryo quality.

OBJECTIVE: Follicle recruitment occurs throughout the cycle and is not limited to the follicular phase. We aim to determine the rate of blastocyst formation in luteal phase stimulation cycles in older women with severe diminished ovarian reserve (DOR) using mild stimulation.

DESIGN: Retrospective study at a large fertility center with a university affiliation.

MATERIALS AND METHODS: Patients over 38 years old with severe diminished ovarian reserve undergoing ovarian stimulation cycles at a single fertility center during the calendar years 2018-2019 were reviewed. Luteal phase stimulation was defined as ovarian stimulation in patients who had already ovulated and had serum progesterone levels > 3.0 ng/mL. Mini stimulation per center protocol was administered without injectable medications and mainly consisted of clomid (50-100 mg) and letrozole (2.5-5 mg) administered orally. Oocyte maturation trigger was performed with Ovidrel (hCG). Mature oocyte (MII) yields, 2PN rate, and blastocyst formation rate per cycle were calculated and stratified by Society for Assisted Reproductive Technology (SART) age groups. Data are presented as mean +- sem.

RESULTS: Two hundred fifty-eight cycles were included in data collection with a total of 483 oocytes retrieved in the luteal phase. In all participants, age was 43.7 ± 0.12 years, body mass index was 23.7 ± 0.5 kg/m2, serum P4 levels were 15.9 ± 0.6 ng/mL, and the menstrual cycle day when oocyte retrieval was performed was 25.1 ± 0.6. The total number of oocytes collected was 1.9 ± 0.1, MII oocytes was 1.4 ± 0.2, 2 PN was 1.0 ± 0.1, and blastocysts cryopreserved was 0.8 ± 0.1. The fertilization rate was 58.59% with a blastocyst formation rate of 42.40%. The table shows detailed results according to SART age group.

CONCLUSIONS: Mild ovarian stimulation is effective in producing blastocysts in women with severe DOR. These data are important for this patient population where time is of essence and can support random start times for infertility treatment. Mild stimulation is also helpful for women who desire to avoid injectable hormonal medications.

	Experimental group	The blank group	P
The number of cases	24	8	
The man age	33.96 ± 1.16 (31.56, 36.35)	31.75 ± 1.88 (27.31, 36.19)	0.404
The man BMI	23.16 ± 0.53 (22.05, 24.26)	25.42 ± 1.14 (22.72, 28.13)	0.113
Woman's age	31.08 ± 0.87 (29.27, 32.89)	30.25 ± 1.42 (26.88, 33.62)	0.454
The woman AMH	3.30 ± 0.32 (2.64, 3.96)	3.28 ± 0.45 (2.22, 4.32)	0.949
E2 on HCG day	3537.00 ± 464.35 (2576.41, 4497.59)	2903.13 ± 249.91 (2312.19, 3494.06)	0.815
Total Gn of the woman	1868.75 ± 78.87 (1705.59, 2031.91)	1906.25 ± 103.70 (1661.04, 2151.46)	0.949
A number of oospheres	14.13 ± 1.72 (10.58, 17.67)	10.63 ± 0.73 (8.90, 12.35)	0.334
2 pn fertilization rate(%)	83.47(202/242)	81.69 (58/71)	0.725
Available embryo rate(%)	66.83 (135/202)	74.14 (43/58)	0.291
Blastocyst formation rate(%)	54.95 (50/91)	67.74 (21/31)	0.212

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OVARIAN STIMULATION WITH ORAL MEDICATIONS IN THE LUTEAL PHASE CAN PRODUCE BLASTOCYSTS IN WOMEN WITH SEVERE DIMINISHED OVARIAN RESERVE. Lana Lipkin, M.D.,[1] Zaher Merhi, MD HCLD,[1] Meir Olcha, MD,[2] Bingyang Hu, MSBA,[2] John Zhang, MD, PhD[1] [1]SUNY Downstate University and New Hope Fertility Center, New York, NY; [2]New Hope Fertility Center, New York, NY.

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SART Age Group	Cycle Count	Total Egg (average per cycle)	Total 2PN	2PN Rate	Total Blastocyst	Blastocyst Rate
38-40	36	80(2.22)	50	62.50%	31	62.00%
41-42	64	155(2.42)	87	56.13%	41	47.13%
>42	158	248(1.57)	146	58.87%	48	32.88%
Total	258	483(1.87)	283	58.59%	120	42.40%

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DOWN REGULATION WITH LUTEAL GONADATROPIN-RELEASING HORMONE AGONIST THERAPY IN EUPLOID EMBRYO TRANSFERS DOES NOT IMPACT PREGNANCY RATES.

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OBJECTIVE: Gonadotropin-releasing hormone (GnRH) agonists have been used during assisted reproductive technology (ART) treatment both for pituitary suppression and stimulation. Some studies have shown benefits to prolonged GnRH agonist therapy prior to IVF and/or embryo transfer.[1,2] It has been suggested that GnRH suppression of toxic peritoneal cytokines and potential direct effect on endometrial tissue could improve pregnancy rates with ART treatment, particularly in patients with endometriosis.[1] Currently, clinical opinion is divided about whether GnRH agonist therapy improves pregnancy rates when used for luteal down-regulation in a frozen euploid embryo transfer (FET) cycle.[2,3] The objective of this study is to evaluate the clinical utility of GnRH agonist down-regulation in single, euploid FET cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A retrospective analysis was performed at a single fertility center, using data from patients who underwent a single, euploid FET cycle from 2012 to 2019. Patients were segregated into two cohorts: Group A: single, euploid FET with down-regulation using GnRH agonist; Group B: single, euploid FET without down-regulation using GnRH agonist. GnRH agonist was started in the mid-luteal phase and continued through the addition of estrogen and progesterone for endometrial lining preparation. The GnRH agonist was stopped prior to a single, euploid FET. Primary outcome included pregnancy rates among study cohorts.

RESULTS: Group A demonstrated a pregnancy rate of 72.92% in 96 single, euploid FET cycles with down-regulation using a GnRH agonist. Group B demonstrated a pregnancy rate of 73.27% in the 5,668 single, euploid FET cycles without a GnRH agonist. There was no difference in pregnancy rates between groups, X2 (2, N = 5764) = 0.0061, p = 0.94. A subgroup of patients (n=5) with endometriosis in the GnRH agonist down-regulation group achieved an 80% (4/5) pregnancy rate.

CONCLUSIONS: Single, euploid FET cycle pregnancy rates were not affected by the use of down-regulation with a GnRH agonist. The increased pregnancy rates found with prolonged GnRH agonist use in other studies was not seen with the short-term use for down-regulated FET cycles in this study. Future research should focus on molecular markers and gene transcription signatures to attempt to define whether there is an ideal population of patients who would benefit from GnRH agonist down-regulation prior to frozen embryo transfer.[2,3] Luteal GnRH agonist for ovarian suppression in FET cycles does not appear to be detrimental to pregnancy rates, and may play a role in personalized reproductive treatment.

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SUPPORT: None.

P-492 4:30 PM Monday, October 19, 2020

DO DIFFERENT LH LEVELS ON GNRH ANALOG TRIGGER DAY AFFECT THE NUMBER OF CRYOPRESERVABLE BLASTOCYSTS?.

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OBJECTIVE: The objective of our study was to discover whether different LH levels on gonadotrophine relasing hormone agonist (GnRHa) trigger day affect the number of mature oocytes and blastocysts suitable for freezing.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Data were collected from Istanbul Memorial Hospital ART and Genetics Center. 2437 GnRHa trigger cycles were evaluated between 2011 and 2020. Cycles were analyzed in three groups according to serum LH levels on GnRHa day: Group A (n=1983) LH level $\geq$ 1 mIU/mL; Group B (n=314) LH level 0.5-1 mIU/mL; Group C (n=140) LH level $\leq$ 0.5 mIU/mL. The numbers and percentages of obtained oocytes (COC), mature (MII) oocytes and fertilized oocytes (with 2PN), the blastocyst/2PN ratio and the number of cryopreservable blastocysts number in the three LH groups were compared.

RESULTS: Baseline characteristic differences between the three groups, including mean age (31,37±5,06 vs. 31,68±5,10 vs. 30,56±4,75 group A, B, C respectively, p:0.92), mean AMH level (5,08±3,52 vs. 4,78±2,72 vs. 5,175±3,08, p:0.339) and mean BMI (25,17±4,89 vs. 24,69±4,91 vs. 24,99±4,1, p:0.537) were not significant. However, some cycle characteristics were significantly different between the groups. In group A, day 2 LH level (7,52±3,47 vs. 6,28±2,64 vs. 6,23±2,97, p:0.0001) and (2,86±2,1 vs. 1,69±1,25 vs. 1,15±0,81 p:0.001) were significantly higher than in group B and in group C. There were no significant differences between group B and group C.

Although, the number of oocytes retrieved was significantly higher in group C than in group A and B (19.09±8.95 vs. 20.5±8.26 vs. 23.54±11.73 group A to C respectively, p:0.003) , the percentage of mature oocyte was significantly lower in group C than in groups A and B (85.3%± 13.9 vs. 85.3%±12.3 vs. 81.5%±13.8, A to C respectively, p:0.002). Despite these results, there were no significant differences between the three groups according to percentage of fertilized oocyte (81.5%±16.8 vs. 81.65±13.4 vs. 79.5%±14.7, p:0.370), the percentage of blastocyst/2PN (54.4%±22.4 vs. 54.5%±20.1 vs. 50.5%±19.9 p:0.121) and mean number of cryopreservable blastocysts (6.98±4.26 vs. 7.51±4.05 vs. 7.18±4.07 p:0.128).

CONCLUSIONS: GnRHa ovulation trigger in a GnRH antagonist protocol significantly decreases the ovarian hyperstimulation syndrome (OHSS) risk. There is a lack of clear information in the literature regarding the effectiveness of GnRHa trigger in cases with low (<1mIU/mL) or very low (<0.5mIU/mL) LH levels. Low and very low LH levels on the GnRHa trigger day have no negative effect on the number of cryopreservable blastocysts. In cases with the risk of OHSS, GnRHa trigger can be used safely regardless of LH level on trigger day.

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FROZEN-THAWED EMBRYO TRANSFERS ARE ASSOCIATED WITH A HIGHER RISK OF LARGE FOR GESTATIONAL AGE NEWBORNS.

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OBJECTIVE: Improvements in cryopreservation techniques associated with the possible impairment in endometrial receptivity due to the supraphysiologic hormonal levels observed during conventional controlled ovarian stimulation (COS) have increased the implementation of frozen-thawed embryo transfers (FET). Perinatal outcomes of fresh embryo transfers (ET) and FET have shown to be similar. However, several studies associate FET with a higher risk of large-for-gestational-age (LGA), thereby, increasing risk of adverse obstetric and neonatal outcomes. This study aims to assess whether FET is associated with a higher risk of large for gestational age newborns, compared with fresh ET in our population.

DESIGN: Retrospective, single center study performed from 2017 to 2019.

MATERIALS AND METHODS: A total of 561 patients who became pregnant after fresh and frozen embryo transfers. A first study group included all IVF cycles where fresh embryo transfer resulted in a singleton live birth (fresh group n=254). A second cohort included FET that led to a singleton live birth (FET group n= 307). All embryos were transferred at a blastocyst stage and vitrification was the only cryopreservation method. In all FET the endometrium was artificially prepared through the administration of exogenous estrogen and progesterone. Data was collected from telephone surveys. We compared the number of LGA newborns and weight differences in both groups. z-test was applied for statistical analysis. A p value <0.05 was considered significant.

RESULTS: The median gestational age in both groups was 38 weeks. The mean adjusted birth weight after FET group was higher by 109.26 g, than the fresh group (3269.32 g vs 3160.13 g respectively, p=0.285). The incidence of newborns that weighted $\geq$ p50 was significantly higher for FET group (142 vs 75 for FET and fresh respectively, p= 0.000048). Moreover, the incidence of LGA livebirths was significantly higher in the FET group (p=0.0226) (23 from the FET group vs 8 from fresh ET). No difference in female to male ratio for LGA newborns or preterm birth rate was identified between groups.

CONCLUSIONS: FET is associated with increased risk of LGA in our population. FET has become an important technique in IVF; however, whether it should be the first choice for ET requires further analysis. An individual approach should remain when deciding between fresh or frozen embryo transfers. Longer-term potential health effects remain to be evaluated.

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OOCYTE MATURITY AS A PREDICTOR OF IVF OUTCOME. Michelle L. Krohn, D.O.,[1] Amy E. Sparks, PhD,[2] Bradley J. Van Voorhis, MD,[3] [1]Monument Health, Spearfish, SD; [2]University of Iowa Center for Advanced Reproductive Care, Iowa City, IA; [3]University of Iowa, Iowa City, IA.

OBJECTIVE: Oocyte maturity after retrieval during IVF can vary significantly and is important in fertilization and development of embryos. Our purpose was to determine if low oocyte maturity from a retrieval cycle is a predictor of poor outcomes from IVF. Secondary objectives were; to identify factors predictive of low oocyte maturity, to assess oocyte maturity across cycles, and to determine if oocyte maturity is affected by the length of ovarian follicular stimulation or the total dose of gonadotropins used.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A total of 1451 autologous IVF cycles from 1/2016- 7/2019 at our center were evaluated. Oocyte maturity was initially assessed upon retrieval (M1 + M2 oocytes/total oocytes). The final oocyte maturity assessment was made 5 hours post retrieval, prior to ICSI (oocytes inseminated at ICSI/total oocytes). As the maturity score at the time of retrieval was correlated with score at ICSI (Pearson's r=.848, $p \leq .001$), we used maturity at retrieval as our measure of maturity, allowing inclusion of all cycles. Maturity designation as suboptimal vs. optimal was derived from previously established classifications (1). Statistical tests utilized included Pearson's correlation, independent samples t-tests, and generalized estimating equations.

RESULTS: There was no correlation between female age at retrieval and oocyte maturity (Pearson's r= .131, $p \leq .001$). A diagnosis of polycystic ovarian syndrome (PCOS) was associated with a slightly reduced maturity (81.9% $\pm$ 14.6 vs. 85.5% $\pm$ 14.0, p=.002). There was no association with diminished ovarian reserve (defined as AFC< 10; DOR) and oocyte maturity (p=.172). Increasing oocyte maturity was associated with increased clinical pregnancy rates, age adjusted odds ratio (AOR) 2.5 (1.1-5.8). Oocyte maturity was not found to be associated with miscarriage rates. When cycle 1 was compared to cycle 2 in the same patient, there was a fair correlation between oocyte maturity scores (Pearson's r=.339, $p \leq .001$) with 44% of those classified as suboptimal maturity also classified as suboptimal maturity within their second cycle. In contrast, only 22% of cycles classified as optimal maturity in cycle 1 had suboptimal maturity if a second cycle was performed. There was no evidence of correlation between days of stimulation prior to the trigger shot or total gonadotropins used and maturity scores (Pearson's r=0.43, p=0.149).

CONCLUSIONS: There is no correlation between oocyte maturity and female age or diagnosis of DOR. The diagnosis of PCOS is associated with a slight but statistically significant reduced oocyte maturity at retrieval; however this is unlikely to be clinically significant given that these patients most often have an increased number of total oocytes retrieved. Low oocyte maturity was associated with decreased clinical pregnancy rates but did not impact miscarriage rates. Cycles complicated by low oocyte maturity can be repetitive, and maturity did not appear to correlate with the duration of ovarian stimulation or total gonadotropin dosage used.

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EVALUATION OF DUAL TRIGGER EFFICACY FOR FINAL OOCYTE MATURATION IN HIGH COMPLEXITY ASSISTED REPRODUCTION TECHNIQUES: A SYSTEMATIC REVIEW AND META-ANALISYS. Luciana Carvalho Delamuta, MD, Alexandre LS. Lobel, MD, PhD, Pedro AA. Monteleone, MD, PhD, Jose Maria Soares, Jr., MD, PhD, Edmund Chada Baracat, MD, PhD University of São Paulo, São Paulo, Brazil.

OBJECTIVE: To compare the number of mature oocytes, number of total oocytes and clinical pregnancy rate in assisted reproductive techniques that used dual trigger (gonadotropin releasing hormone agonist + human chorionic gonadotropin) or human chorionic gonadotropin (hCG) alone for oocyte final maturation.

DESIGN: Systematic review an meta-analysis.

MATERIALS AND METHODS: A systematic review was conducted to compare the number of mature oocytes, number of total oocytes and clinical pregnancy rate in assisted reproductive techniques that used dual trigger or human chorionic gonadotropin alone. For this evaluation, randomized clinical trials (RCT) and retrospective cohort studies were included. We comprehensively searched PubMed, EMBASE and Cochrane Library with the last search made in December 2019. Bibliographies of relevant studies identified by the search strategy and relevant reviews/meta-analyses were also searched for identification of additional studies. The following MeSH terms (gonadotropin-releasing hormone, human chorionic gonadotropin, oocyte maturation, in vitro fertilization) and their combinations were searched. Inclusion and exclusion of the studies were completed according strict criteria. The methodological quality of RCT and retrospective cohorts was assessed using the Review Manager software and the modified Newcastle-Ottawa scale respectively. Data from the included studies were extracted to define whether dual trigger improves the number of total and mature oocytes retrieved and the clinical pregnancy rate. The meta-analysis was performed using *software* R 3.6.1 (R Core Team, 2019) and *meta* package (Schwazer, 2013).

RESULTS: A total of 18 studies were included (8 RCT and 10 retrospective cohorts) with a total of 2798 patients in the dual trigger group and 2649 patients in the hCG trigger group. In six of the studies the patients had a prior failure in an assisted reproductive treatment (ART) and in the other 12 studies it was the first treatment. For the pregnancy rate the relative risk (RR) was 1,24 [CI 95% 1,14 – 1,36], for the number of mature oocytes the mean difference (MD) was 1,41 [CI 95% 0,63 – 2,19], and for the number of total oocytes the MD was 1,07 [CI 95% 0,40 – 1,73]. A subgroup analysis separating RCT from retrospective cohorts showed no difference between the types of study for all the outcomes analyzed. Another subgroup analysis separating patients who had the first ART from patients who had prior failure showed pregnancy rate RR 1,31 [CI 95% 1,06 - 1,62] for "previous failure" and 1,23 [CI 95% 1,12 – 1,34] for "first treatment". For the number of mature oocytes MD was 3,15 [CI 95% 2,39 – 3,91] for "previous failure and 0,81 [CI 95% 0,20 – 1,42] for "first treatment". For the number of total oocytes MD was, respectively, 1,60 [CI 95% 0,60 – 2,60] and 0,93 [CI 95% 0,20-1,66].

CONCLUSIONS: We can conclude that dual trigger for final oocyte maturation results in higher pregnancy rate and higher number of total and mature oocytes when compared to hCG alone. Patients who had a previous ART failure seem to be the subgroup that benefits the most from dual trigger use.

SUPPORT: None.

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THE IMPACT OF DOUBLE-STRANDED SPERM DNA BREAKS ON ICSI OUTCOME. Derek Keating, B.A., Alessandra Parrella, M.Sc., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: We sought to evaluate specific sperm DNA damage, double-stranded DNA breaks (dsDNA), and its effect on embryo development and implantation.

DESIGN: Over a year-long period, a prospective pilot study was carried out on sperm samples to evaluate the proportion of dsDNA on samples screened by terminal deoxynucleotidyl dUTP transferase nick-end labeling (TUNEL) to assess total DNA fragmentation. Once a correlation was established, we extrapolated dsDNA values retrospectively onto patients who had their ejaculates screened by TUNEL to evaluate clinical outcome.

MATERIALS AND METHODS: Samples from consenting couples were screened for dsDNA rates by neutral Comet assay using an in-house protocol; 200 spermatozoa were assessed per patient. These samples were also assessed by TUNEL using a commercially available kit, analyzing at least 500 spermatozoa per patient. ICSI was performed in the standard fashion.

RESULTS: The pilot study reported an average total DNA fragmentation of 11.3±6% by TUNEL and an average dsDNA of 2.2±3% by neutral Comet. The results showed a linear relationship between the overall SCF and dsDNA rates (R^2=0.96). This equation was applied to extrapolate the dsDNA levels from 573 normozoospermic men (volume of 2.6±1 mL, concentration of 42.3±33x10^6/mL, 43.1±10% motility, and 4.2±1% normal morphology) with an average SCF of 14.2±8%. Therefore, on the basis of this preliminary test, we established a dsDNA threshold of 3%.

A total of 417 couples (maternal age, 37.0±4 yrs; paternal age, 38.6±5 yrs) underwent 777 ICSI cycles and presented with dsDNA levels of 1.8±0.6%. These cycles had a 73.0% fertilization rate, a 12.7% (123/966) implantation rate, and a 23.2% (102/440) clinical pregnancy rate (CPR), of which 15 were lost (14.7%), leaving a 19.7% (87/440) ongoing/delivery rate.

There were 155 couples with dsDNA levels of 4.2±1%. These couples underwent 268 ICSI cycles with a comparable maternal age of 37.3±5 years, but with older male partners at 41.3±8 years of age (P<0.001). These cycles had a comparable fertilization rate of 71.0%, implantation rate of 11.4% (53/464), and clinical pregnancy rate of 24.3% (44/181). However, these couples were much more likely to lose their pregnancy at 29.5% (13/44; P = 0.03), leaving an ongoing/delivery rate of 17.1% (31/181).

CONCLUSIONS: These findings provide further evidence that dsDNA has an important role in the success of a pregnancy generated by ICSI. dsDNA damage has been linked to aneuploidy and consequent pregnancy loss. The use of an assay in a laboratory setting to screen exclusively for dsDNA would help to identify paternally linked aneuploidy that traditional screening would only report as total SCF.

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PREDICTORS OF EMBRYO ANEUPLOIDY AND MOSAICISM: INSEMINATION METHOD, SPERM AND PATIENT CHARACTERISTICS. Gabriela M. Grant, MSc,[1] Jessica R. Walter, MD,[1] Helena I. Russell, MSc,[2] Dara S. Berger, PhD,[1] [1]University of Pennsylvania, Division of Reproductive Endocrinology and Infertility, Philadelphia, PA; [2]Eastern Virginia Medical School, Norfolk, VA.

OBJECTIVE: Intracytoplasmic sperm injection (ICSI) is often the insemination method used with pre-implantation genetic testing (PGT). We studied the effects of insemination method on aneuploidy and mosaicism rates in a clinical setting.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Embryos created during an IVF cycle and biopsied using next-generation sequencing between 1/1/2016 to 12/21/2019 were included in this study. Embryos were categorized by insemination method, ICSI versus conventional insemination. Age of the patient, infertility diagnosis, stimulation protocol, and biopsy results were examined. Semen analysis performed using Krueger strict criteria to determine morphology (normal morphology defined as $\geq$ 4). Univariate statistical analyses were performed using the student t-test and chi-square test. Multinomial logistic regression with cluster standard error was performed to identify determinants of a normal, abnormal or mosaic biopsy outcome. Euploidy was the base outcome and all results are explained in terms of aneuploidy and mosaicism.

RESULTS: A total of 3522 embryos were biopsied from 818 IVF cycles. 2667 embryos (75.7%) were fertilized by ICSI. Oocytes inseminated by ICSI were from younger patients (36.3 years compared to 38.0 years, p<0.001), with a significantly higher percentage originating from abnormal morphology (32.0 % compared to 13.7%, p<0.001). Couples with ICSI embryos were more likely to have a reported component of male factor infertility (23.7 versus 2.1%, p <0.001). Female diagnoses of ovulatory dysfunction, structural (uterine/tubal disease), and advanced maternal age were more common in the conventionally inseminated group. Among embryos biopsied, 1758 (53.3%) were aneuploid and 530 (16.1%) demonstrated mosaicism. There were higher rates of aneuploidy among ICSI inseminated embryos (55.2% versus 47.6%; p<0.001) and higher rates of mosaicism among conventionally inseminated embryos (20.5% versus 14.8%, p<0.001). ICSI insemination was found to be an independent risk factor for aneuploidy (RR 1.38 95% CI 1.07-1.77, p= 0.01), when adjusting for oocyte age and female infertility diagnosis. Female infertility diagnosis, specifically ovarian pathology (diminished ovarian reserve, ovulatory dysfunction, and endometriosis), not presence or severity of male infertility, demonstrated an increase in the relative risk of mosaicism. Sperm morphology did not influence the relative risk of a specific biopsy results.

CONCLUSIONS: The influence of laboratory techniques and patient characteristics on aneuploidy and mosaicism rates, are not well understood. While semen parameters and male factor infertility were not shown to affect biopsy results irrespective of insemination method, we demonstrate in this large study that aside from oocyte age, ICSI may adversely affect euploid rate when controlling for relevant confounders, but neither meaningfully seem to influence mosaicism. Future studies are needed to examine the potential relationship between infertility diagnosis, specifically of ovarian origin, and mosaicism rates.

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MICROFLUIDIC SPERM SELECTION IS AN EFFECTIVE METHOD FOR IMPROVING EMBRYO DEVELOPMENTAL COMPETENCE IN IVF WITH OLDER PATIENTS. Rie Matsunaga, M.A., Kana Isobe, B.A., Megumi Miura, M.A, Yuki Kobayashi, B.A., Minako Kamihata, B.A., Hiroshi Makino, Ph.D., Kurumi Iwaki, Ph.D., Tomoko Maeda, Ph.D, Toshitaka Horiuchi, Ph.D., Masanori Ochi, Ph.D. OCHI YUME CLINIC NAGOYA, Nagoya, Japan.

OBJECTIVE: Sperm DNA fragmentation can reduce the rate of embryo development and also increase the rate of miscarriage. Various methods have been developed to select and collect sperm with good motility. However, the DNA fragmentation index (DFI) of the collected sperm differs among these methods. The microfluidic sperm selection chamber (ZyMōt™; DxNow) is a selection kit designed to collect low DFI sperm. Although a few reports have suggested a relationship between embryo quality and euploidy rate (assessed by preimplantation testing for aneuploidy after intracytoplasmic sperm injection), there has been little investigation of the efficacy of microfluidic sperm selection (MSS) in IVF. We studied whether MSS can improve the success rate of embryo development in IVF.

DESIGN: The study was conducted between June 2019 and December 2019. Patients were divided into two groups according to the sperm processing method used: DGS (114 patients, 326 oocytes), and MSS (113 patients, 356 oocytes). For both groups, IVF was performed using selected sperm.

MATERIALS AND METHODS: We compared the rates of fertilization, blastulation, and available blastocysts (defined as those with Gardner Grade better than 4BC); we also compared the rates of available blastocyst cycle, defined as the rate of cycles that yielded at least one available blastocyst. IVF was performed using sperm selected by MSS; as a control, 4×10^4 sperm/ml was used for IVF in the DGS group.

RESULTS: The fertilization rates using 4×, 6×, and 8×104 sperm/ml in the MSS group were 44.8%, 55.3%, and 62.4%, respectively; by comparison, the rate in the DGS (control) group was 66.6%. Rates of oocyte fertilization using sperm selected by MSS were significantly lower at 4× and 6×104 sperm/ml than for the DGS control. However, the rate of fertilization improved with increasing sperm concentration in the MSS group and was comparable to DGS at the 8×104 sperm/ml concentration. Embryo development was compared for oocytes from women of different age ranges: under 34 years (A), 35–39 years (B), 40–42 years (C), and over 43 years (D). Blastulation rates did not differ between the DGS and MSS groups in A (76.9% vs. 71.7%), B (65.2% vs. 80.5%), C (70.0% vs. 53.6%), and D (35.3% vs. 62.5%). The rates of available blastocysts and the blastocyst cycle rates for MSS were comparable to DGS in A (49.1% vs. 53.8% and 81.3% vs. 83.3%, respectively), B (53.7% vs. 34.8% and 80.0% vs. 61.9%, respectively), and C (39.3% vs. 36.7% and 50.0% vs. 64.3%, respectively). These rates were significantly higher for MSS than DGS in D (33.3% vs. 5.9% and 53.8% vs. 9.1%, respectively).

CONCLUSIONS: The present study indicates that MSS might enable improvement in the rates of embryo development after IVF of oocytes from women with an advanced maternal age. The use of MSS for sperm

selection resulted in the production of a higher frequency of good quality IVF-embryos with these older patients.

SUPPORT: None.

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NEONATAL AND MATERNAL OUTCOMES IN SINGLETON LIVE BIRTHS (LB) FOLLOWING SINGLE EUPLOID FROZEN EMBRYO TRANSFER (FET): DOES TRANSFER PROTOCOL MATTER?.

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OBJECTIVE: Two FET protocols commonly used for endometrial preparation are programmed (PRG) and natural (NAT). Despite an increasing focus on preimplantation genetic testing for aneuploidy (PGT-A)[1] prior to FET, there are scarce data on outcomes by protocol following transfer of a single euploid embryo. We sought to evaluate the neonatal and maternal outcomes by protocol after single euploid FET.

DESIGN: Retrospective cohort study of all patients with a singleton LB from a single euploid FET (by aCGH or Next Gen Sequencing) between 1/2017 - 12/2018 at our center.

MATERIALS AND METHODS: All patients with a singleton LB after single euploid FET in the study time period were reviewed. Patients with monozygotic twins or whose delivery information was not verified were excluded. Patients were grouped by protocol: PRG or NAT. PRG cycles were defined by treatment of oral E2 daily, followed by progesterone (P4); either 50-75mg intramuscular in oil or vaginal suppository. NAT cycles, with and without with letrozole, were defined by monitoring until a dominant follicle reached >18mm and ovulation was confirmed, followed by supplementation with vaginal P4 suppository. Primary outcomes were 1) preterm birth (PTB) defined as delivery on or before 36w6d and 2) birth weight (BW) and low birth weight (LBW) defined as <2500g. A secondary outcome was a composite complication rate defined by inclusion of any of the following: hypertensive (HTN) disorders of pregnancy, HELLP syndrome, intrauterine growth restriction, oligohydramnios, abnormal placentation or umbilical cord anomalies. Statistical analyses included a Kolmogorov-Smirnov, Mann-Whitney U, chi-squared, and logistic regression where appropriate, with $p<0.05$ considered significant.

RESULTS: 647 cycles were included: 491 PRG and 156 NAT. Mean patient age was 37.2 ± 4.4 years (range 21-59). 7% (n=45) were donor egg (DE) recipients but use of protocol was not different (8.2% PRG vs 3.3% NAT, p=0.05). In this cohort, 7 (1.1%) had HTN, 3 (0.5%) had diabetes, and 81 (12.6%) had depression/anxiety. Mean gestational age (GA) at birth was 39 ± 1.9 wks (range 24w1d-42w4d), and 7.9% had PTB. Mean BW was 3299.4 ± 567.3 grams (range 737.1-5017.9). Infants with LBW and macrosomia (≥ 4000g) occurred in 6.9% and 7.9% of deliveries respectively. There was no difference in patient age (37.5 v 37.0, p=0.91), GA at delivery (39w0d v 38w6d, p=0.96), and BW (3350g v 3283.5g, p=0.50), between PRG and NAT cycles. The PTB (8.8% vs 5.1%; p=0.17) and LBW (8.0% vs 3.3%; p=0.62) rates did not differ by protocol, independent of age, past medical history (PMH) and GA (PTB p=0.99, LBW p=0.13). The overall composite complication rate was 6.3%. PRG cycles had more complications compared to NAT (8.1% vs 0.6%; $p<0.01$) even when controlled for by age, PMH and GA ($p<0.01$). Excluding DE, the complication rate was 6.0%, still higher in PRG cycles (7.8% vs 0.7%, $p<0.01$).

CONCLUSIONS: There is no difference in PTB or LBW rates by cycle protocol after single euploid FET. However, PRG cycles had a higher rate of complications. Further investigation, with larger cohorts, is needed to understand the differences with individual complications.

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SUPPORT: None.

P-500 4:30 PM Monday, October 19, 2020

CAN ERA BIOPSY RESULTS BE PREDICTED BY FET CYCLE PARAMETERS?.

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OBJECTIVE: Successful implantation requires synchronous development of the embryo and endometrium. Euploid embryos fail to implant in about 1/3 of IVF cycles, which may be attributable to a non-receptive endometrium. The endometrial receptivity array (ERA) has emerged as a diagnostic tool to identify receptive endometrium and to guide timing of embryo transfer. While studies have shown the utility of ERA testing in a natural cycle, the impact of endometrial stimulation with exogenous estrogen (E) and progesterone (P) on ERA results are not well understood. The objective of this study was to investigate whether cycle parameters obtained during a programmed endometrial stimulation cycle can predict abnormal ERA results.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We reviewed the records of all women who underwent a mock frozen-thawed embryo transfer (FET) cycle and ERA testing (n= 88) at a university-affiliated IVF clinic from 2017-2019. All women received endometrial preparation with exogenous oral estradiol (E2). Exogenous P was administered once endometrial thickness reached ≥8 mm. Endometrial biopsy for ERA testing was performed on the sixth day of exogenous P. Study measures included patients' age, BMI, number of previous failed embryo transfers, maximum (max) serum P level, max P dose, max endometrial thickness (MET), duration of E exposure, max serum E2 level, and ERA result. Multivariable logistic regression models and resulting odds ratios (OR) with 95% confidence intervals (CI) were used to test for measure association, where stepwise AIC selection criteria was applied to determine the optimal model. All reported p-values are 2-sided and a p-value < 0.05 was considered statistically significant.

RESULTS: Mean (SD) age was 36.3 (4.2) years and median (Q1, Q3) BMI was 26.3 (22.0, 28.5) kg/m^2. Of the 88 ERA tests performed, 21 (23.9%) were receptive and 67 (76.1%) were non-receptive. A full multivariable model for predicting non-receptive ERA results showed that the total number of transfers prior to ERA (OR [95% CI]: 0.81 [0.5, 1.31], p=0.40), MET (OR 0.97 [0.74, 1.27], p=0.83), age (OR 0.98 [0.85, 1.12], p=0.83), and duration of E exposure (OR 1.05 [0.91, 1.21], p=0.51) were not significant factors. Based on the reduced, optimized multivariable model, the odds of having a non-receptive ERA result decreased by 0.54 per 25 mg increase of P dose (OR [95% CI]: 0.46 [0.24, 0.87], p=0.016), increased by 0.31 per 100 pg/ml increase in max E2 level (OR 1.31 [1.03, 1.68], p=0.030) and increased by 0.13 per unit increase in BMI (OR 1.13[1.01, 1.26], p=0.039), when also adjusting for max serum P, max dose of P, max serum E2 level, and BMI.

CONCLUSIONS: Our data suggests total number of transfers prior to ERA, MET, age and duration of E exposure do not predict ERA results. However, when modeled together, serum P level, P dose, serum E2 and BMI can be used to predict ERA results. Since implantation failure may be a result of a non-receptive endometrium in programmed FET cycles, studies with a larger sample size are needed to determine if cycle parameters can help providers determine who may benefit from ERA.

P-501 4:30 PM Monday, October 19, 2020

ELEVATED AMH NOT ASSOCIATED WITH PRETERM DELIVERY IN IVF PREGNANCIES.

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OBJECTIVE: Recent evidence of an association between AMH and preterm birth (PTB) after in vitro fertilization IVF suggests a physiologic effect of AMH on the uterus, particularly among women with polycystic ovary syndrome (PCOS). In order to confirm these preliminary findings and account for additional variables, we examined a large US dataset at an academic fertility center.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We included all autologous (IVF) cycles that resulted in a live, singleton birth from 2015-2019. AMH values were compared in women who had a spontaneous PTB after 20 weeks gestation to those who delivered at full term. We excluded women with uterine and other factors necessitating a preterm delivery (e.g. severe pre-eclampsia, vasa previa, chorioamnionitis). Pregnancies in which delivery information could not be confirmed were not included in the analysis. Chi-square or Fisher's exact tests and t-test or Wilcoxon rank-sum test were used where appropriate. Multivariable logistic regression was used to adjust for age,

body mass index (BMI) and IVF cycle type (fresh vs frozen embryo transfer). $P < 0.05$ was considered statistically significant.

RESULTS: In the 606 unique patients, the median AMH values among women who had a PTB (n=39) was 2.5 ng/mL IQR [1.4-5.3], compared to 2.7 ng/mL IQR [1.3-5.2] among those who had a term delivery (n=567) (p=0.92). Odds of PTB was not significantly different by AMH quartile after adjusting for age, bod and cycle type. Women with AMH in the 2nd, 3rd, and 4th AMH quartiles had an adjusted odds ratio (aOR) for PTB of 0.80 (95% confidence interval (CI): 0.32 – 2.01), 0.50 (95% CI 0.18 – 1.42) and 1.01 (95% CI 0.41 – 2.48), respectively, when compared to the lowest quartile. Among women with PCOS (n=90), there was no difference in odds of PTB (2nd quartile - aOR 1.73, 95% CI: 0.26 – 11.58; 3rd quartile - aOR 0.57, (95% CI 0.18 – 1.42), 4th quartile - aOR 1.03; 95% CI 0.12 – 8.64) compared to the lowest quartile. No differences were also seen when examining AMH quartiles and prevalence of PTB in fresh (n=183) and frozen cycles separately (n=423).

CONCLUSIONS: Our study shows that women with elevated AMH were not more likely to experience a spontaneous PTB after IVF than women with lower AMH values. Women with the diagnosis of PCOS were also not more likely to experience a PTB, however the sample size was limited. Larger cohort studies specifically in women with PCOS are needed to understand the relationship between AMH and preterm birth.

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REPRODUCTIVE OUTCOMES BETWEEN FRESH AND FREEZE ONLY DEFERRED BLASTOCYST TRANSFERS. Fred V. Morgan-Ruiz, MD,[1] Julio C. Rosales, M.D.,[1] Patrizio Pasquale, MD, MBE, HCLD,[2] Pablo Diaz-Spindola, MD,[1] Edelmiro Garza-Padilla, M.D.[1] [1]IECH, Monterrey, NL, Mexico; [2]Yale Fertility Center, Orange, CT.

OBJECTIVE: To compare the reproductive outcomes in patients who undergo fresh transfer vs. freeze only delayed transfers.

DESIGN: Retrospective, cross sectional, comparative study.

MATERIALS AND METHODS: 721 patients who underwent IVF/ICSI at the IECH, Monterrey, México, from January 2014 to December 2019 were studied. Patients were divided into two groups: 228 patients (31.6%) had a freeze only deferred embryo transfer (TED) and 493 patients (68.4%) had fresh transfer (TEF). Both groups were classified into suboptimal, normal and high responders according to the number of eggs obtained. All transfers and cryopreservation were at blastocyst-stage. The variables analyzed were implantation, clinical pregnancy and live birth rates. All the clinical records of infertility patients requiring IVF/ICSI with an age range of 21-40 years were included. In both transfer groups, patients received the same treatment protocols for controlled ovarian stimulation. Oocytes were retrieved vaginally 35 to 36 hours after hCG administration and fertilized using either standard IVF or ICSI. In the TED group, blastocysts were cryopreserved by vitrification and rewarmed few hours before the transfer.

RESULTS: The average age for both groups was 32.93 ± 3.85 for TED and 33.95 ± 4.09 ($p<0.001$) for fresh transfers. Overall, there were significant differences in favor of TED in implantation rate (58.13% vs 29.89%, $p<0.05$; OR: 3.25 95% CI: 2.44-4.33), clinical pregnancy (50% vs 25.08%, $p<0.05$; OR: 2.98, 95% CI: 2.24-3.98) and live birth r (54.26% vs 31.01%, $p<0.05$; OR: 2.63, 95% CI: 1.98-3.50).However, when the results were compared according to the ovarian response, the freeze only deferred embryo transfer maintained superiority over the fresh transfers only in the high ovarian response subgroup. In the TEF group there were no significant differences among the subgroups.

CONCLUSIONS: Deferred frozen embryo transfers offer better reproductive results (implantation rate, clinical pregnancy and live birth) compared to the fresh transfer strategy particularly in patients with high ovarian response.

SUPPORT: None.

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THE CLINICAL USE OF ENDOMETRIAL RECEPTIVITY ANALYSIS (ERA®) AND THE EFFECTS ON IMPLANTATION RATES IN WOMEN WITH PRIOR FAILED TRANSFERS. Grace Z. Lu, B.S., Carolyn Givens, M.D., Liyun Li, M.D. Pacific Fertility Center, San Francisco, CA.

OBJECTIVE: Endometrial receptivity is thought to be an important cause of implantation success or failure. ERA® (Endometrial Receptivity Analysis) analyzes the transcription profile of luteal phase endometrium (in a natural or programmed cycle) to determine its receptivity. ERA® results purport to allow physicians to personalize frozen embryo transfer (FET) protocols to transfer embryos during the "receptive" window, and thus increase implantation (IR) and pregnancy (PR) rates. In this study, we aimed to (1) evaluate the utilization of ERA® in a single large private ART practice, (2) for patients who had "non-receptive" ERA® results, determine if customized modifications of FET protocols according to ERA® results have led to changes in IR and PR in subsequent FETs.

DESIGN: A retrospective cohort analysis.

MATERIALS AND METHODS: We reviewed records of patients who had an ERA® between 2014 to 2019 at our IVF center. All ERA® cycles were programmed cycles with an average progesterone duration of 133 (98-168) hours before the endometrial biopsy. Patient demographics, previous FET data, ERA® results, and outcome of subsequent FETs were analyzed. Data analysis was performed using Excel and MedCalc.org and SciStat.com.

RESULTS: 173 patients completed an ERA®. The age was 39±4.781 years, with 82% of patients having had at least one prior FET (0-7). 8.6% had a chart diagnosis of uterine factor, 7.5% with endometriosis, 11% with adenomyosis, and 15% of patients had fibroids. The average peak endometrial thickness was 9.8±2.0 mm for the ERA® cycle and 9.9±2.1 mm during the first subsequent FET.

Of all ERA®s completed, 40% (N=69) patients were receptive, 43% (N=74) pre-receptive (recommended transfer 24 hrs later), 14.45% (N=25) early receptive (12 hrs later), 2.3% (N=4) late receptive (12 hrs earlier), and one patient was post-receptive. 10% completed a second ERA® due to an invalid biopsy sample, and only one patient completed three ERA®s.

Overall FET PR in this cohort of patients pre-ERA® was only 5% (16/320). The overall PR post-ERA® was 36% (63/171) with an odds ratio of 11.1 (95% CI 6.1-20.0). Pre-ERA® IR of autologous euploid embryos was 6.3% (11/176). The post-ERA® IR of autologous euploid embryos was 42% (47/112) with an odds ratio of 10.8 (95% CI 5.3-22.2).

For the non-receptive groups (both pre- and post-receptive), the pre-ERA® PR was 5.5% (10/180) and post-ERA® PR was 36% (35/97) with an odds ratio of 7.9 (95% CI 3.3-18.8). The pre-ERA® IR of autologous euploid embryos was 8.7% (9/104). The post-ERA® IR was 42% (24/56) with an odds ratio of 9.6 (95% CI 4.5-20.53). For the receptive groups, the pre-ERA® PR was 4.3% (6/140), and post-ERA® PR was 37% (28/74) with an odds ratio of 13.6 (95% CI 5.3-34.9). The receptive group had a pre-ERA® IR of autologous euploid embryos of 2.8% (2/71), and a post-ERA® IR of 41% (23/55) with an odds ratio of 24.8 (95% CI 5.5-111.6).

CONCLUSIONS: 60% of patients had non-receptive ERA®s. While non-receptive patients had increased implantation and pregnancy rates post-ERA®, similar improvements were also seen in receptive patients making it difficult to draw the conclusion that ERA® was clinically beneficial.

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DOES INTRACYTOPLASMIC SPERM INJECTION (ICSI) PROVIDE ANY BENEFIT OVER IN VITRO FERTILIZATION (IVF) ON PREGNANCY OUTCOMES IN NON-MALE FACTOR INFERTILITY CYCLES UNDERGOING PRE-IMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A)?. Jessica N. Tozour, MD, PhD, Alyson Brady, MS, Meredith Akerman, MS, Alicia J. Arnott, BS, Linda Sung, MD, Rani Fritz, DO, PhD, NYU Winthrop Hospital, Mineola, NY.

OBJECTIVE: ICSI is currently the recommended fertilization method for cycles undergoing PGT-A [1]. To our knowledge there are no studies evaluating pregnancy outcomes of PGT-A transferred embryos inseminated by IVF versus ICSI. Our objective is to evaluate whether significant differences exist in pregnancy outcomes from PGT-A transferred embryos fertilized by IVF compared to ICSI.

DESIGN: Retrospective cohort study at a single academic institution.

MATERIALS AND METHODS: All frozen embryo transfers (FET) performed from 1/2016 to 2/2020 that underwent PGT-A from trophectoderm biopsy and tested by next generation sequencing were evaluated. Exclusion criteria included diagnosis of male factor infertility, embryos tested for pre-implantation genetic testing for monogenic disorders, structural rearrangements, or HLA-typing, cryopreserved oocytes, blastomere or polar body biopsy, in vitro maturation, rescue ICSI, and split IVF/ICSI cycles. Patient demographics, infertility diagnoses, cycle characteristics, and pregnancy

outcomes including not pregnant, biochemical pregnancy, miscarriage, ongoing pregnancy (OP), and live birth (LB) were collected. Primary outcome was OP/LB rates. Secondary outcomes included miscarriage and biochemical rates. Chi-square or Fisher's exact test, as appropriate, and Mann-Whiney test were used for categorical and continuous variables, respectively. Outcomes between both groups were compared using a repeated-measures mixed-effects logistic regression model, in which the rates were adjusted for confounding variables attained during the univariate screen. Results were considered statistically significant with a p-value <0.05.

RESULTS: A total of 317 FET's met criteria (IVF-150 [47.3%]; ICSI-167 [52.7%]). Significant difference between the IVF and ICSI cohort existed in age (35.8 y/o vs. 36.8 y/o, respectively, p=0.03), BMI (23.6 vs 25.1, respectively, p=0.005), and ethnicities. LB/OP rates and miscarriage/biochemical rates demonstrated no significant differences in IVF vs. ICSI inseminated groups (Table 1).

CONCLUSIONS: There were no significant differences in pregnancy outcomes in FET's between IVF and ICSI inseminated embryos that underwent PGT-A. The use of ICSI in non-male factor infertility cycles undergoing PGT-A does not provide an advantage for LB/OP rates over IVF.

TABLE 1.

	IVF (150)	ICSI (167)	p-value
Not pregnant	35.7%	37.3%	0.79
Biochemical	12.1%	14.8%	0.62
Miscarriage	11.4%	7.8%	0.43
Live birth	37.3%	35.0%	0.69
Biochemical/Miscarriage	23.6%	22.5%	0.85
Live birth/Ongoing	39.8%	38.3%	0.74

References: Practice Committees of the American Society for Reproductive Medicine and Society for Assisted Reproductive Technology. Intracytoplasmic sperm injection (ICSI) for non-male factor infertility: a committee opinion.Â *Fertil Steril*. 2012;98(6):1395-1399.

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PERINATAL AND MATERNAL OUTCOMES AFTER FROZEN VERSUS FRESH EMBRYO TRANSFER CYCLES IN WOMEN OF ADVANCED MATERNAL AGE. Xinyi Zhang, PhD, Jichun Tan, PhD Shengjing Hospital of China Medical University, shenyang, China.

OBJECTIVE: The delay of childbearing age in women has become a worldwide issue in recent decades. The application of assisted reproductive technology in women of advanced maternal age (AMA) is increasing. There is still lacking evidence on the safety and outcomes of frozen embryo transfer (FET) compared with fresh embryo transfer (ET) in women of AMA. Therefore, the objective of the present study is to compare perinatal and maternal outcomes after autologous FET and fresh ET cycles in women of AMA.

DESIGN: This was a retrospective study of 1663 FET cycles and 3964 fresh ET cycles in four reproductive medical centers from 2009 to 2014. Women $\geq$35 years of age who had clinical pregnancies after autologous frozen or fresh ET were included.

MATERIALS AND METHODS: Main perinatal outcome measures included birth weight, gestational age, rates of macrosomia, low birth weight (LBW), very low birth weight and preterm birth. Maternal outcome measures included rates of hypertensive disorders of pregnancy, gestational diabetes mellitus and preterm premature rupture of the membranes.

RESULTS: Women who underwent FET had a higher risk of hypertensive disorders of pregnancy [1.1% vs. 0.4%, adjusted OR (95%CI): 2.76 (1.39-5.51); $p = 0.004$]. Singletons born after FET had significantly higher mean birth weight (3388.78 $\pm$ 538.47 vs. 3316.19 $\pm$ 549.08; $p = 0.001$). Furthermore, increased risk of macrosomia [13.5% vs. 10.4%, adjusted OR (95% CI): 1.35 (1.07-1.71); $p = 0.013$] and decreased risk of LBW [3.6% vs. 5.3%, adjusted OR (95%CI): 0.67 (0.45-1.00); $p = 0.048$] were found in singletons born after FET.

CONCLUSIONS: Perinatal risks of AMA patients are higher in FET than in fresh ET, including higher birth weight, risks of macrosomia in singleton births and hypertensive disorders of pregnancy.

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HLA-G LEVELS IN FOLLICULAR FLUID ARE NOT ASSOCIATED WITH FOLLICULAR G-CSF CONCENTRATIONS IN WOMEN UNDERGOING IN VITRO FERTILIZATION. Dimitar Parvanov, PhD,[1] Rumiana Ganeva, MSc,[1] Milena Todorova, MSc,[1] Kristina Nikolova, MSc,[1] Magdalena Vasileva, MSc,[1] Ivaylo Rangelov, MSc,[1] Fabio Scarpellini, MD,[2] Georgi Stamenov, MD/PhD,[1] [1]Nadezhda Women's Health Hospital, Sofia, Bulgaria; [2]Center For Endocrinology And Reproduction, Rome, Italy.

OBJECTIVE: Recently, soluble human leukocyte antigen-G (sHLA-G) and granulocyte colony-stimulating factor (G-CSF) quantified in the follicular fluid have been proposed as non-invasive biomarkers of oocyte competence in both stimulated and natural IVF/ICSI cycles. sHLA-G, G-CSF and their receptors were described in various human fetal tissues and it was suggested that they play an important role in ovulation, oocyte maturation, embryo development and implantation. However, the possible association between these two molecules in the follicular fluid has not been studied yet.

The purpose of the present study was to determine whether the sHLA-G levels are associated with the G-CSF levels in follicular fluid of women undergoing in vitro fertilization.

DESIGN: This is a cohort study of 56 women undergoing stimulated cycles and in vitro fertilization between September 2019 and November 2019 at Nadezhda Women's Health Hospital.

MATERIALS AND METHODS: Follicular fluid from up to six clear follicular aspirates was collected during regular egg collection procedure of 56 patients. Samples were stored at -20°C until measurement. Follicular fluid levels of sHLA-G and G-CSF were evaluated by ELISA kits (Elabscience; E-EL-H1663 and RayBiotech; ELH-GCSF-1, respectively) according to the manufacturer's instructions. The absorption was measured on a microplate reader (Beckman Coulter DTX 880 Multimode detector) at 450 nm. Statistical analysis was performed using SPSS v.21 (IBM Corp., Armonk, NY, USA).

RESULTS: **s**HLA-G was detected in all 56 follicular fluid samples, with a median value of 47.52 IU/ml and a range of 13.85-63.06 IU/ml. Follicular fluid G-CSF was also detected in all samples and ranged between 3 and 116 pg/ml with a median of 16.23 pg/ml.

Measured sHLA-G levels did not show a significant correlation with G-CSF concentration in follicular fluid ($P = 0.63$).

CONCLUSIONS: This is the first report regarding the association between follicular fluid levels of sHLA-G and G-CSF. Although the increased secretion of both sHLA-G and G-CSF usually correlates with better oocyte quality and implantation success, our findings suggest that they are not related to each other.

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EFFECT OF FOLLICLE SIZE AT TRIGGER IN GNRH ANTAGONIST PLUS LETROZOLE IVF CYCLES ON OOCYTE QUALITY OUTCOMES. Phillip A. Romanski, MD,[1] Nirali J. Shah, MD,[2] Pietro Bortoletto, MD,[1] Zev Rosenwaks, M.D.,[1] Glenn Schattman, MD,[1] [1]The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY; [2]Weill Cornell Medicine, New York, NY.

OBJECTIVE: To assess the effect of follicle size at trigger in GnRH antagonist/letrozole IVF cycles on oocyte yield and fertilization rate.

DESIGN: We conducted a retrospective cohort study at an academic center. Patients who underwent their first IVF cycle with a GnRH antagonist/letrozole protocol at our center between 01/01/2012 and 12/31/2019 were included. Patients were stratified into two groups by the size of the second largest follicle on the day of trigger: $\leq$21 mm and >21 mm. Patients with fewer than three follicles >12 mm on the day of trigger (n=23) and patients on continuous letrozole protocols (n=334) were excluded.

MATERIALS AND METHODS: The primary outcome was the number of mature oocytes retrieved; secondary outcomes were the total number of oocytes retrieved and the number of fertilized oocytes. Poisson regression adjusted *a priori* for patient age and AMH level was used to estimate the risk ratio (RR) with a 95% confidence interval (CI) among the study groups. The antagonist/letrozole protocol used was 5mg letrozole daily for five days starting on cycle day two. Gonadotropins were then started on cycle day four

and continued until the night of trigger administration. The timing of trigger administration is determined by the treating physician. The trigger used was either hCG alone or GnRH agonist plus hCG (dual trigger).

RESULTS: A total of 278 GnRH antagonist/letrozole cycles resulting in an oocyte retrieval were included: 140 patients in the ≤21 mm group and 138 patients in the >21 mm group. The mean (mean ± standard deviation) number of oocytes retrieved was significantly lower in the ≤21 mm group (7.6 ± 5.9) compared to the >21 mm group (10.2 ± 5.8; RR 1.15 (95% CI 1.06-1.25)). The mean number of mature oocytes retrieved was significantly lower in the ≤21 mm group (5.4 ± 3.9) compared to the >21 mm group (7.0 ± 4.1; RR 1.12 (95% CI 1.02-1.24)). The mature oocyte rate observed was 73.8% in the ≤21 mm group and 70.7% in the >21 mm group. The mean number of fertilized oocytes in the ≤21 mm group was 3.8 ± 3.2, which was not statistically significant when compared to the >21 mm group (4.8 ± 3.8; RR 1.09 (95% CI 0.96-1.24)). The fertilization rate observed was 63.6% in the ≤21 mm group and 59.0% for the >21 mm group.

CONCLUSIONS: In ovarian stimulation protocols where letrozole is utilized, timing the trigger to when the second largest follicle is >21 mm yields a higher number of total and mature oocytes. Additionally, a mean of one additional zygote per cycle was observed in the >21 mm group. While this was not a statistically significant finding, it is a clinically meaningful outcome. Therefore, we conclude that the ideal time to administer the ovulatory trigger in cycles utilizing letrozole is when the second largest follicle is >21 mm. The optimal size identified in this study is larger than the optimal follicle size that has been identified in traditional GnRH antagonist protocols. We hypothesize that this may be due to alterations in cell signaling and oocyte development as a result of temporary aromatase inhibition and suppression of estradiol formation.

SUPPORT: None.

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PROGESTERONE/ESTRADIOL RATIO HAS A BETTER PROGNOSTIC VALUE THAN PROGESTERONE ALONE IN THE PREDICTION OF PREGNANCY OUTCOMES IN INTRACYTOPLASMIC SPERM INJECTION (ICSI) CYCLES.

Reda S. Hussein, MD,[1] Ihab M. El-Nashar, MD,[1] Ahmed F. Amin, MD,[1] Yulian Zhao, Ph.D.,[2] Ahmed M. Abbas, MD,[1] Ahmed M. Abdelmagied, MD,[1] Osama S. Abdalmageed, MD,[1] Ahmed Youssef, MD,[1] Esraa Badran, MD,[1] Tarek Farghaly, MD,[1] Ahmed Ali Abdelaleem, MD,[1] Mostafa N. Ibrahim, MD,[1] Hisham A. Abou-Taleb, MD, PhD,[1] [1]Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; [2]Department of Obstetrics and Gynecology, Mayo Clinic, Rochester, MN.

OBJECTIVE: To compare the predictive value of progesterone/estradiol ratio (P/E) ratio and absolute progesterone (P) level on the ovulation triggering day for pregnancy outcomes in fresh gonadotropin-releasing hormone (GnRH) antagonist intracytoplasmic sperm injection (ICSI) cycles.

DESIGN: A retrospective cohort study conducted in a university-affiliated IVF center between January 2017 and April 2019.

MATERIALS AND METHODS: The study included women who underwent their first- or second-ranked GnRH antagonist ICSI cycles with day-3 embryo transfer. P/E ratio was calculated as [P (ng/mL) × 1000]/E (pg/mL). Cut-off values of ≥1.5 ng/ml for high P (HP) and ≥0.55 for high P/E ratio were chosen based on literature [1]. A receiver operating curve (ROC) curve was performed to detect the predictability of serum P/E and P for the ongoing pregnancy rate. First, patients were divided according to either P level (low P< 1.5 ng/mL and high P≥ 1.5 ng/mL) or P/E ratio (low P/E< 0.55 and high P/E≥ 0.55). Patients were further divided into four subgroups [Group A: High P (HP) and high P/E ratio, group B: low P and low P/E ratio, group C: HP only, group D: high P/E only]. A multivariate regression analysis models were used to account for the effect of the cycle confounders on the likelihood of pregnancy.

RESULTS: A total of 402 ICSI cycles were analyzed. The area under the curve (AUC) was 0.67 and 0.59 for P/E and P, respectively. P/E showed a significant association with ongoing pregnancy (aOR: 0.409, 95% CI 0.222-0.753, p=0.004) while HP revealed no significant predictive value (aOR: 0.542, 95% CI 0.284-1.036, p=0.064) after the multivariate analysis.

CONCLUSIONS: P elevation may not present as an independent predictor for cycle outcomes. P/E ratio has a better prognostic value than P alone in predicting pregnancy outcomes of GnRH antagonist cycles.

References:

1. Elgindy, E.A., 2011. Progesterone level and progesterone/estradiol ratio on the day of hCG administration: detrimental cutoff levels and new treatment strategy.Â *Fertility and sterility*,Â *95*(5), pp.1639-1644.

SUPPORT: The study was supported by Assiut Faculty of Mediicne Grants' office.

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FROZEN EMBRYO TRANSFER CYCLES MAY OFFER ADVANTAGE IN BOTH PREGNANCY SUCCESS AND REDUCING THE NUMBER OF PATIENTS DISCONTINUING CARE.

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OBJECTIVE: To evaluate pregnancy and discontinuation rates after a single oocyte retrieval, by type of transfer – fresh vs freeze-all – with subsequent frozen embryo transfer (FET).

DESIGN: Non-randomized, observational, retrospective cohort study.

MATERIALS AND METHODS: Electronic medical records of patients from a large US database of fertility clinics (IntegraMed America, Inc.) were analyzed. Patients included had a first treatment cycle in 2015–2017, with a single oocyte retrieval followed by fresh embryo transfer (ET; and subsequent FET, if frozen embryo(s) were available) or freeze-all cycle, with subsequent FET(s). Clinical pregnancy rate (CPR) was defined as clinical intrauterine gestation or later evidence of pregnancy. Patient discontinuation rate was determined by evaluating the proportion of patients with no further cycles after the last ET without a pregnancy.

RESULTS: Of 18,875 patients who had a single oocyte retrieval, 11,784 (62.4%) had a fresh ET (followed by 0–7 FETs) and 7091 (37.6%) had a freeze-all cycle (followed by 1–6 FETs). The overall proportion of cycles that underwent preimplantation genetic testing for aneuploidy was 1.9% for patients who initially had a fresh ET and 22.4% for freeze-all. CPR following a single fresh ET was 75.5%, compared with 82.9% for a single FET in freeze-all cycles, with the elective single ET (eSET) rate for the first fresh ET being 39.0% compared with 68.8% for first FET in freeze-all cycles with subsequent FETs. CPRs were >70% for ≤2 FETs following fresh ET or ≤3 FETs after freeze-all. Rates of eSET decreased with each subsequent transfer attempt and were consistently lower after fresh ET (1st FET 39.0% and 2nd FET 27.9%) than after first FET (2nd FET 60.3% and 3rd FET 43.7%). Patients who had a fresh ET and did not achieve a pregnancy had fewer surplus embryos after the first ET than patients who had their first FET after a freeze-all cycle (mean [standard deviation]: 0.75 [1.99] vs 3.20 [3.73], respectively). Patient discontinuation rate was higher for patients who had started with a fresh ET, with 23.9% discontinuing treatment without a pregnancy, compared with 19.2% who had undergone FET(s) after freeze-all. Among the 23.9% of patients who initially had a fresh ET and discontinued, most stopped after the fresh ET (19.2%) or 1 FET (3.7%); just 3.9% of patients had ≥2 FETs, even with surplus embryos available.

CONCLUSIONS: Elective cryopreservation of all embryos followed by FET resulted in higher CPRs and patient retention rates when compared with fresh ET followed by FET. Rates of eSET were also higher with a freeze-all approach, which minimizes the incidence of multiple pregnancies and associated risks, and reserves surplus embryos for later use without the need for additional retrievals.

SUPPORT: Study sponsored by EMD Serono, Inc., Rockland, MA, USA (a business of Merck KGaA, Darmstadt, Germany).

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TIME FROM OOCYTE RETRIEVAL TO SINGLE EMBRYO TRANSFER IN THE NATURAL CYCLE DOES NOT AFFECT CYCLE OUTCOMES.

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OBJECTIVE: To determine if time from oocyte retrieval to single frozen embryo transfer (FET) in the natural cycle affect reproductive or neonatal outcomes?

DESIGN: Retrospective cohort study conducted at a university-affiliated center.

MATERIALS AND METHODS: Reproductive (pregnancy & live birth rate) and neonatal outcomes (gestational age & weight) between first (n=222) vs. second menstrual cycle (n=354) after oocyte retrieval were compared. Rank-sum, Student's t-test, and Chi-square tests were performed as appropriate. A multivariable logistic regression was performed with adjustment for age, infertility diagnosis, ovulatory trigger type, and pre-implantation genetic testing. Statistical significance was denoted by $p<0.05$

RESULTS: A total of 576 women were analyzed, of which n=222 transferred an embryo during their first menstrual cycle after retrieval and n=354 in a subsequent cycle. Patient and cycle characteristics are provided in Table 1. Prior to adjustment for confounding, we found a significantly different pregnancy rate (72.5 vs. 64.4%, $p = 0.043$) and live birth rates (57.7 vs. 48.6%, $p = 0.034$) for natural cycle FET occurring in the first versus second menstrual cycle, respectively. In a multivariate analysis, performing a natural cycle FET of a single blastocyst in the second, compared to the first menstrual cycle did not statistically impact odds of live birth rate (OR: 0.76, 95% CI: 0.54-1.08). After adjustment for age, diagnosis, and ovulatory trigger type, only PGT testing was associated with significantly increased odds of live birth compared to no PGT testing (OR: 2.46, 95% CI: 1.72-3.52). There were no differences in mean singleton birth weight (3429 vs. 3333 grams, $p = 0.148$) or gestational age at time of delivery (39.0 vs. 38.7 weeks, $p = 0.076$) between both groups.

CONCLUSIONS: Performing a natural cycle FET of a single blastocyst in the second, compared to the first menstrual cycle following ovarian stimulation did not statistically impact odds of live birth. Furthermore, gestational age and birth weight were similar between groups. Patients and providers should feel comfortable selecting a timeline for FET that best suits their clinical and personal needs.

	First Menstrual Cycle N=222	Second Menstrual Cycle N=354
Age years mean (SD)	36.0 (3.7)	35.6 (4.0)
Parity median (IQR)	0 (0-1)	0 (0-1)
Infertility Diagnosis n(%)		
Diminished ovarian reserve	111 (50.0)	150 (42.4)
Male factor	49 (22.1)	105 (29.7)
Uterine factor	24 (10.8)	23 (6.5)
PGT n (%)	151 (68.0)	191 (54.0)
Trigger type n (%)		
HCG only	126 (56.8)	218 (61.6)
Dual Trigger	96 (43.2)	136 (38.4)
Peak endometrial thickness of FET cycle (mm) mean (SD)	9.0 (1.7)	8.8 (1.7)
Cycle day of LH surge of FET cycle	16 (14-18)	15 (13-18)

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IN VITRO PERI-IMPLANTATION DEVELOPMENT OF GOOD QUALITY HUMAN EMBRYOS IS AFFECTED BY BLASTOCYST MORPHOLOGICAL GRADE AND MATERNAL AGE. Deirdre M. Logsdon, M.S., Rachel C. West, PhD, Rebecca Kile, MS, Courtney K. Grimm, MS, Mandy G. Katz-Jaffe, PhD, Sue McCormick, BS, Karen Maruniak, MLS, William B. Schoolcraft, MD, Rebecca L. Krisher, PhD, Ye Yuan, PhD, Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Peri-implantation development during in vitro extended culture may reflect a human blastocysts developmental potential following transfer. The objective of this study was to determine whether blastocyst morphology and maternal age impact peri-implantation developmental potential as determined by extended embryo culture.

DESIGN: Retrospective study.

MATERIALS AND METHODS: Over two years, 653 human blastocysts donated for research (WIRB study #1179872) underwent extended embryo culture for various research projects in our laboratory. Each embryo was assessed for attachment to fibronectin coated microslides on day (D) 2 and D 3 of culture. Where applicable, images were taken of embryos for outgrowth (OG) area measurements, spent media was saved for hCG quantification, and embryos were fixed with 4% paraformaldehyde to determine total (DAPI) and epiblast (POU5F1) cell numbers with fluorescent imaging using a spinning disk confocal microscope and Imaris software. Good quality blastocysts ($\geq$3BB) with the highest morphological grade (high) that typically yield live birth rates above 60 % were compared with those of lower morphological grade (low) that typically result in less than 55% live birth rate, based on our historical data. In addition, blastocysts from advanced maternal age (AMA; $\geq$ 36 years) and younger ($\leq$ 35 years) patients were compared. Measurements were analyzed using one-way ANOVA.

RESULTS: Embryos with high morphological grade had significantly larger OG areas than those with low morphological grade on D 3 (0.17 mm2 n=218 high; 0.12 mm2 n=74 low; $p \leq 0.05$) and D 7 (0.56 mm2 n=28 high; 0.23 mm2 n=11 low; $p \leq 0.05$) of extended culture. There were no significant differences in embryo attachment, total cell number, epiblast cell number or hCG production between these two groups. Embryos from AMA women had significantly lower attachment on D 3 of extended culture (91.3% $\pm$ 1.8% young, 84.5% $\pm$ 2.9% AMA; $p \leq 0.05$). In addition, significantly fewer embryos from AMA women contained POU5F1-positive epiblast cells (62.1% $\pm$ 6.0%, n=66 young; 44.6% $\pm$ 6.2% n= 65 AMA: $p \leq 0.05$), and AMA embryos with POU5F1 positive cells tended to have fewer epiblast cells by D 5 in extended culture (75.3 $\pm$ 11.5, n=24 young; 44.5 $\pm$ 8.1, n=17 AMA: $p \leq 0.06$). There were no significant differences in OG area on D 3, total cell number, or hCG production in extended culture.

CONCLUSIONS: Our data collected from 653 human embryos in extended culture provides valuable information about a time in development that cannot be observed in vivo. Better blastocyst morphology, which in our experience results in higher pregnancy rates after transfer, is also associated with improved extended culture outcomes suggesting that our system is a sensitive method to predict post transfer developmental potential. Advanced maternal age may contribute to decreased developmental potential of morphologically good quality blastocysts, which could result in implantation failure after transfer. Additional studies examining the impact of maternal BMI, stimulation protocol, infertility diagnosis, ovarian reserve, and embryo grade on developmental potential are underway.

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USE OF ADJUVANT HUMAN GROWTH HORMONE DOES NOT IMPROVE BLASTOCYST EUPLOIDY RATES IN PATIENTS UNDERGOING IN VITRO FERTILIZATION. Holly Mehr, MD MSEd,[1] Zain Al-Safi, MD,[1] Carrie Riestenberg, MD,[1] Victoria Lee, BS,[1] Rong Guo, MS,[1] Kathleen Brennan, MD,[1] Lindsay Kroener, MD,[1] UCLA.[1]University of California, Los Angeles, Los Angeles, CA.

OBJECTIVE: To determine if the use of adjuvant human growth hormone (hGH) during in vitro fertilization (IVF) improves euploid rates in patients age <35, 35-38, and $\geq$39.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All patients who underwent autologous IVF with preimplantation genetic testing for aneuploidy at a single academic center between 1/2016 and 12/2019 were screened for inclusion. Patients who received adjuvant hGH 2.32mg/40iu daily from the first day of stimulation until day of trigger were compared to those who were not treated with hGH. Baseline patient characteristics and cycle outcomes were compared between groups. Summary statistics for cycle outcomes were stratified by age at the time of oocyte retrieval (< 35, 35-38, and $\geq$39 yo). Mixed model analysis was performed to examine hGH effect on euploid rate after controlling for possible confounders.

RESULTS: A total of 280 patients underwent 405 IVF cycles during the study period. The hGH and control groups had a comparable percent of cycles resulting in no embryos for biopsy (10% vs 7.6%, p=0.39). The remaining 367 IVF cycles from 258 patients had at least one embryo for biopsy and were analyzed. Compared to the control group, the hGH group had a lower AFC in patients $\geq$ 39 yo (12.7 vs 17.2, p=0.031), a higher FSH dose in patients $\geq$ 39 yo (3509 vs 5182, p=0.007), and more prior IVF cycles in patients <35 yo (0.7 vs 0.16, p <0.0001) and 35-38 yo (0.65 vs 0.17, p=0.006). Baseline characteristics were otherwise similar between groups. Patients $\geq$ 39 yo treated with hGH had fewer embryos to biopsy (3.6 vs 4.9, p=0.043). For all other outcomes, including euploid rate, there was no significant difference between groups prior to adjustment (Table 1). In the multiple mixed model analysis adjusting for age, BMI, prior IVF cycles, AFC, and FSH dose there was no significant effect of hGH on euploid rate (p=0.604).

TABLE 1. Unadjusted IVF outcomes; Mean (SD)

	Age < 35 (n=119)			Age 35-38 (n=102)			Age ≥ 39 (n=146)		
	No hGH (n=63)	hGH (n=56)	p-value	No hGH (n=38)	hGH (n=66)	p-value	No hGH (n=33)	hGH (n=113)	p-value
Oocytes retrieved	19.3 (8.1)	18.8 (10.1)	0.352	19.1 (9.0)	15.7 (7.4)	0.143	17.0 (9.1)	13.6 (7.9)	0.147
Embryos biopsied	6.2 (3.9)	6.0 (3.3)	0.725	6.1 (3.7)	5.5 (3.4)	0.745	4.9 (3.6)	3.6 (2.4)	**0.043**
Euploid embryos	3.8 (2.5)	3.1 (2.1)	0.388	3.0 (2.3)	2.1 (2.0)	0.266	1.2 (1.1)	0.9 (1.2)	0.555
Euploid rate (%)	59 (25)	55 (27)	0.366	4.9 (2.8)	3.9 (24)	0.083	25 (24)	23 (27)	0.750

CONCLUSIONS: Use of adjuvant hGH in IVF did not result in a significant improvement in embryo euploid rates for women of any age group. Our study may have failed to identify and adjust for unmeasured confounders that would lead a physician to offer hGH. Further randomized studies are warranted to determine if there is a unique population who may benefit from adjuvant hGH.

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CLINICAL CHARACTERISTICS SHOULD NOT BE OVERLOOKED WHEN SELECTING EMBRYOS CULTURED IN A TIME-LAPSE INCUBATOR SYSTEM. Amanda Souza Setti, MSc,[1] Daniela Paes de Almeida Ferreira Braga, PhD,[1] Ana Caroline Silva Soares, DVM, PhD,[2] Patricia Guilherme, MSc,[2] Assumpto Iaconelli, Jr., MD,[1] Edson Borges, Jr., PhD.[1] [1]Fertility Medical Group / Sapientiae Institute, Sao Paulo, Brazil; [2]Fertility Medical Group, Sao Paulo, Brazil.

OBJECTIVE: Single embryo transfers (SETs) has become indispensable to maximize live birth rates while avoiding multiple pregnancies. The development of a non-invasive embryo implantation predictor has become crucial for reproductive medicine. Time-lapse imaging systems (TLS) allow for the mapping of morphological changes or events with the exact time-point of occurrence. Analysis of implantation-related morphokinetic characteristics has facilitated the development of algorithms for implantation prediction. The main drawback of most studies is that each embryo is treated as an individual, and clinical and stimulation–related confounding factors are ignored. The aim of this study was to investigate the influence of morphokinetic events and patients and cycles characteristics on embryo implantation.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: This study included 175 embryos cultured in a TLS incubator deriving from ICSI cycles with single day 5 embryo transfers, between Jan-2019 and Dec-2019. The effect of morphokinetic events and patients and cycles characteristics on embryo implantation was evaluated by multiple regression models. Recorded kinetic markers were: pronuclei appearance (tPNa), timing to pronuclei fading (tPNf), timing to two (t2), three (t3), four (t4), five (t5), six (t6), seven (t7), and eight cells (t8), and timing to blastulation (tB). Durations of the second (t3-t2) and third (t5-t3) cell cycles (cc2 and cc3, respectively) and timing to complete synchronous divisions s1 (t2-tPNf), s2 (t4-t3), and s3 (t8-t5) were also calculated. Maternal age, number of follicles, number of retrieved oocytes, number of mature oocytes, and oocyte yield, as well as the presence of endometriosis, male and ovarian factors of infertility were also added to the model. To cross-validate the results, variables which significantly affected embryo implantation were included in a stepwise discriminant analysis for the prediction of grouping variable implantation outcome, defined as positive or negative. Cut-off points for the selected variables were established halfway between averages in both implantation groups.

RESULTS: Multiple regression results showed that female age (OR: 0.813, p=0.041), total dose of FSH (OR: 0.998, p=0.003), longer t8 (OR: 0.938, p=0.040) and s3 (OR: 0.922, p=0.029), and the presence of endometriosis (OR: 0.311, p<0.001) negatively influenced the chance of embryo implantation, while the number of follicles (OR: 1.947, p=0.018) and mature oocytes (OR: 1.133, p=0.001) had a positive influence. The discriminant function correctly classified 77.8% of original cases, best predicting negative implantation (98.8%). Established cut-off points for positive implantation were 37.1 years-old for female age, 2701.2 IU for total dose of FSH, 10.1 follicles, 5.4 MII oocytes, 56.6 hours for t8 and 7.8 hours for s3.

CONCLUSIONS: Our evidences underline the importance of patients individual characteristic for the development of any algorithm for embryo implantation. Ignoring the impact of confounder's factors, as the embryo origin, may weaken the model and its predictive value.

SUPPORT: None.

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ENDOMETRIAL MIRNOME ESTABLISHMENT DURING THE IMPLANTATION WINDOW UNDER HORMONE REPLACEMENT THERAPY FOR FROZEN EMBRYO TRANSFER CAN PREDICT SUCCESSFUL PREGNANCY. Samir Hamamah, MD, PhD,[1] Chloé Baron, PhD, student,[2] Anna Gala, MD,[2] Alice Ferrieres-Hoa, MD,[2] Sophie Brouillet, PharmD, PhD,[2] Frida Entezami, MD,[3] Delphine Haouzi, PhD.[2] [1]Arnaud de Villeneuve Hospital, CHU Montpellier, Montpellier, France; [2]Inserm U1203, CHU Montpellier, St-Eloi Hospital, Montpellier, France; [3]American Hospital of Paris, Neuilly sur Seine, France.

OBJECTIVE: Can endometrial miRNAs profile during the implantation window under the same HRT for frozen embryo replacement cycle, predict successful implantation?

DESIGN: Endometrial biopsies (n=12) were collected during the implantation window from RIF patients (mean ± SD, age: 36.7 ± 6.4 years) under hormone replacement therapy (HRT) for frozen embryo transfer. RNAs were extracted to perform the miRNA expression profile. Then, miRNA expression was analyzed according to following pregnancy outcome: implantation achieved (n=6) or implantation failure (n=6). Successful implantation was defined as both a positive b-hCG and clinical pregnancy and implantation failure as a negative b-hCG.

MATERIALS AND METHODS: Endometrial biopsies were performed during a mock HRT cycle from RIF patients, according to the definition by Polanski *et al.* (RBMonline 2014). Then, miRNA expression profile between the two groups, successful *vs.* implantation failure after frozen embryo replacement was evaluated with the *Affymetrix® miRNA 4.1 Array Strips.* The significant analysis of microarrays (SAM) were used to identify *miRNAs* that were differentially expressed between groups.

RESULTS: *SAM analyses according to a pregnancy successful or implantation failure identified 188, 157, and 163 miRNAs using the ANOVA,* Student's *t-test, and Wilcoxon test, respectively with a fold change (FC) >2 and* false discovery rate (FDR) <5%. *The 136 miRNAs identified according the three statistical analyses were overexpressed in endometrium associated with implantation failure. Supervised hierarchical clustering of these 136 miRNAs showed a good segregation of endometrium samples from patients with and without a successful implantation.* Using the Ingenuity software, we first aimed to identify the potential target genes of these microRNAs. We identified 41 miRNAs that are putative regulators of 13663 genes attached to numerous biological functions including the leukocyte extravasation signaling, the regulation of the epithelial-mesenchymal transition pathway, the epithelial adherent junction signaling and the growth hormone signaling that play a crucial in implantation and maintain of pregnancy. The top-five miRNAs over-expressed in endometrium from patients with implantation failure were miR-1 (x7, FDR<0.0001), miR-2 (x6.3, FDR<0.0001), miR-3 (x4.9, FDR<0.0001), miR-4 (x4.3, FDR<0.0001), miR-5 (x4.2, FDR=0.004). The miR-2 was validated by RT-qPCR in an independent cohort of 23 patients opening new perspectives in the development of a non-invasive test to predict pregnancy outcome (p = 0.002).

CONCLUSIONS: miRNAs profile of endometrial tissues during the implantation window preceding frozen embryo transfer cycle can predict the pregnancy outcome. These data are crucial leading potentially to the

development of a prognostic tool of the attempt, opening news perspectives in the patient care management.

SUPPORT: This study was partially supported by a grant from Gedeon Richter company.

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DOES ENDOMETRIAL COMPACTION ON THE DAY OF FROZEN BLASTOCYST TRANSFER IMPROVE THE OUTCOME OF FROZEN-THAWED CYCLES? INTERIM ANALYSIS.

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OBJECTIVE: To assess whether the occurrence of endometrial compaction (decreased thickness) on the day of frozen blastocyst transfer has a role in optimizing pregnancy outcome in frozen-thawed cycles. Further, to investigate possible interrelationship between the occurrence of compaction and progesterone (P) blood level on the day of transfer.

DESIGN: Observational cohort study.

MATERIALS AND METHODS: According to sample size calculation, 220 patients undergoing good quality frozen blastocyst transfer (GFBT) are to be included. Interim analysis of 120 patients is done. All patients received estradiol valerate (6mg daily) and 100 mg of intramuscular (IM) progesterone (P). Endometrial thickness was measured by transvaginal ultrasound at the end of the estrogen phase and on the day of embryo transfer. Progesterone level was measured on the day of GFBT.

RESULTS: Endometrial compaction occurred in 63 (52.5%) of 120 cases. The ongoing pregnancy rate (OPR) was higher in the endometrial compaction group in comparison to those without compaction (62.5% versus 47.1% respectively); however, it did not reach statistical significance (P= 0.11). Furthermore, the endometrial compaction group had a comparable P level on the day of ET (37.96±16.4 ng/ml to those without compaction (38.3±10.7 ng/ml), where the difference was not statistically significant (P= 0.94).

CONCLUSIONS: Although there was an increase in the OPR in the endometrium compaction group, it is not yet statistically significant in the cases observed so far. In addition, the P level on the day of ET was not found to be different in the compaction group. The validity of these findings will be determined through the observation of the remaining cases.

SUPPORT: None.

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CLINICAL OUTCOMES AFTER SINGLE VERSUS DOUBLE EMBRYO TRANSFERS IN WOMEN WITH ADENOMYOSIS: A RETROSPECTIVE STUDY.

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OBJECTIVE: The single blastocysts embryo transfers policy is an effective strategy known to minimize the risk of multiple pregnancy for non--adenomyosis women. However, little is known about its applicability to women with adenomyosis. The purpose of this study is to compare pregnancy outcomes between single blastocysts embryo transfers (SBT), double blastocysts embryo transfers (DBT), single cleavage-stage embryo transfers (SET) and double cleavage-stage embryo transfers (DET) in the frozen - thawed embryo transfer cycles among adenomyosis patients.

DESIGN: This retrospective study was conducted in all frozen-thawed autologous embryo transfer cycles conducted between 2014 and 2019 in Reproductive Centre of Six Affiliated Hospital of Sun Yat-sen University. A total of 393 frozen-thawed autologous blastocyst or cleavage-stage embryo transfer cycles performed in adenomyosis patients were enrolled. Differences in baseline characteristics between the four groups were assessed. The major clinical outcomes were implantation rate (IR), clinical pregnancy rate (CPR), miscarriage rate (MR), multiple pregnancy rate (MPR) and live birth rate (LBR).

MATERIALS AND METHODS: Among the adenomyosis women, 203 single blastocysts transfers (SBT), 75 double blastocysts transfers (DBT), 13 single cleavage-stage embryo transfers (SET) and 102 double cleavage-stage embryo transfers (DET) were performed.

RESULTS: The SBT and DBT groups achieved higher IR (47.78%, 39.33%, vs 38.46%, 26.96%, $P<0.05$) , CPR (39.90%, 49.33%, vs 7.70%, 33.33%, $P<0.05$), LBR (28.72%, 38.57%, vs 7.69%, 21.88%, $P=0.040$) and lower MR (27.84%, 21.43%, vs 80.00%, 49.90%, $P<0.05$) than the SET and DET groups. But the SBT and DBT groups achieved similar CPR and LBR. The SBT and SET groups achieved lower MPR(0%, 0%, vs 28.57%, 10.20%, $P<0.001$) than the DBT and DET group.

CONCLUSIONS: When performing frozen-thawed embryo transfer cycles among adenomyosis patients, the SBT group has similar IR, CPR, MR, LBR but lower MPR compared to the DBT group. Therefore, SBT might be offered as standard practice.

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CORRELATION BETWEEN ENDOMETRIAL THICKNESS AND PROBABILITY OF LIVE BIRTH IN FROZEN BLASTOCYST TRANSFER CYCLES WITH AND WITHOUT PRE-IMPLANTATION GENETIC TESTING.

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OBJECTIVE: 1) To detect if a correlation exists between endometrial thickness and probability of live birth in PGT-A tested and untested frozen embryo transfer (FET) cycles and 2) To determine optimal endometrial thickness to achieve live birth in PGT-A tested and untested FET cycles.

DESIGN: Retrospective study.

MATERIALS AND METHODS: All FET cycles in 2018 at the Rockville office of Shady Grove Fertility were included. All cycles were autologous elective single-embryo transfer. The generalized estimating equation (GEE) model was used to associate last endometrial thickness measured prior to transfer and the probability of live birth from PGT-A tested and untested FET cycles when controlled for age and body mass index (BMI). Subgroup analysis was performed based on endometrial thickness (<8mm, 8-12mm, and >12mm) with a two-sided chi-square test performed on live birth observations.

RESULTS: A total of 742 PGT-A tested and 689 untested FET cycles were analyzed. The endometrial thickness and probability of live birth showed a positive correlation in PGT-A tested (adjusted odds ratio [aOR] 1.01, 95% CI 0.95-1.08) and a negative correlation in PGT-A untested cycles (aOR 0.99, 95% CI 0.94-1.05); however, these did not reach statistical significance ($p>0.05$). Regression analysis detected a correlation between age and probability of live birth for PGT-A untested, but not PGT-A tested cycles (aOR 0.95, 95% CI 0.91-0.98, $p<0.001$). Sub-analysis did not detect a statistically significant association between endometrial thickness groups of <8mm, 8-12mm, or >12mm and probability of live birth in either PGT-A tested or untested cycles ($p>0.05$).

	Mean (SD)	Adjusted OR (95% CI)	Adjusted p-value
PGT-A Tested (n=742 cycles)			
Endometrial Thickness	9.63 (2.21)	1.01 (0.95-1.08)	0.74
Age	36.20 (3.54)	0.99 (0.95-1.03)	0.68
BMI	25.70 (5.00)	1.00 (0.97-1.03)	0.97
PGT-A Untested (n=689 cycles)			
Endometrial Thickness	9.90 (2.52)	0.99 (0.94-1.05)	0.92
Age	34.20 (4.15)	0.95 (0.91-0.98)	<0.001*
BMI	26.10 (5.64)	0.99 (0.97-1.02)	0.73

CONCLUSIONS: These results did not detect a difference in the probability of live birth with either combined or categorized (<8mm, 8-12mm, or >12mm) endometrial thickness in both PGT-A tested and untested cycles suggesting lack of optimal endometrial thickness to achieve live birth.

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THE IMPACT OF MODE OF DELIVERY ON SUBSEQUENT SINGLE EMBRYO TRANSFER CYCLES IN INFERTILE PATIENTS. Zachary Walker, MD,[1] Emily K. Osman, MD,[2] Ashley W. Tiegs, MD,[2] Julia G. Kim, MD, MPH,[2] Brent M. Hanson, MD,[2] Nola S. Herlihy, MD,[2] Amber M. Klimczak, MD,[2] Emre Seli, M.D.,[2] Richard Thomas Scott, Jr., MD,[2] [1]University of Alabama at Birmingham, Birmingham, AL; [2]IVI-RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: To determine (1) if live birth rates vary between infertile women with a prior cesarean section (CS) versus those with a prior vaginal delivery (VD) and (2) to assess if differences exist in endometrial thickness in frozen thawed embryo transfer (ET) cycles according to previous mode of delivery.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All infertile women that received in vitro fertilization (IVF) treatment resulting in a live birth and returning for a subsequent ET at a single, large infertility center from January 2006 until September 2019 were included. Women with a previous live birth at time of initial presentation for infertility evaluation, use of donor oocyte, gestational carrier, prior uterine surgery, those with intrauterine fluid present during the ET stimulation cycle, double or multiple ET and pregnancies with multiple gestation were excluded. Logistic regression was performed to assess if differences existed in the live birth rates between women with a prior CS versus VD. Differences in mean peak endometrial thickness before and after delivery were analyzed using linear regression with mixed effects modeling. Embryo ploidy, body mass index (BMI), type of uterine stimulation and smoking status were controlled for in all analyses.

RESULTS: In total, 2,026 subsequent ETs of 1,410 patients were analyzed; 687 with prior CS and 723 with prior VD. Of these frozen-thawed ET cycles, 1,678 were synthetic, 301 were natural, and 47 were stimulated. The mean difference in peak endometrial thickness between the ET cycle which resulted in the first live birth and subsequent ET cycles did not differ by the mode of delivery (0.11 ± 2.1 mm VD vs. 0.30 ± 2.0 mm CS, $p=0.53$). Patients with a prior CS had a lower live birth rate (59.1%) with the first ET cycle after initial delivery compared to women with prior VD (67.6%, $p<0.01$; OR 0.69, 95% confidence interval 0.53-0.90).

CONCLUSIONS: Although differences in endometrial thickness did not vary between ET cycles according to the mode of delivery, infertile patients with a prior CS have lower live birth rates in comparison to those that have had a previous vaginal delivery. This may be attributable to the presence of structural uterine abnormalities after CS, such as an isthmocele or mucocele, which could lead to alterations in the endometrium and decreased live birth rates. Further investigation is needed to assess the relationship between uterine abnormalities that may be present after CS and decreased live birth rates in infertile patients. Women with a previous CS should be counseled on these potential implications in future transfer cycles.

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LIVE DELIVERED PREGNANCY RATES ACCORDING TO AGE AND EMBRYO CLEAVAGE RATES IN WOMEN WITH DIMINISHED OOCYTE RESERVE (DOR) HAVING ONLY A SINGLE EMBRYO TO TRANSFER ON DAY 3. Jerome H. Check, M.D., Ph.D.,[1] Donna Summers, M.S.,[2] Carrie K. Wilson, B.A.,[2] Jung Choe, M.D.,[1] Laura X. Zalles, MD,[3] [1]Cooper Medical School of Rowan University, Camden, NJ; [2]Cooper Institute for Reproductive Hormonal Disorders, P.C., Mt. Laurel, NJ; [3]Cooper University Hospital, Camden, NJ.

OBJECTIVE: To determine the confounding effect of age and blastomere number on pregnancy outcome in women whose oocyte reserve was so low that only one embryo cleaved to at least 4 cells on day 3.

DESIGN: Prospective observational comparison study.

MATERIALS AND METHODS: Women were identified who have diminished oocyte reserve (DOR) based on a day 3 serum follicle stimulating hormone (FSH) level >12 mIU/mL who were undergoing in vitro fertilization-embryo transfer (IVF-ET). They agreed to have an ET on day 3 even if there was only 1 embryo to transfer as long as it cleaved to at least 4 cells. For those having only 1 embryo to transfer, the pregnancy outcome was sub-analyzed according to 2 age groups $\leq$35 and 36-39 and according to blastomere number (<6 cells vs. $\geq$6 cells). All patients were treated with a very mild FSH stimulation protocol depending on baseline FSH ranging from completely natural, to a small boost of 75 IU FSH starting in the late luteal phase, to as much as 150 IU FSH from day 3. Cetrorelix or ganirelix was used in most cycles as was human chorionic gonadotropins.

RESULTS: Clinical and live delivered pregnancy rates according to 2 age groups and 2 blastomere number groups is seen in the table below.

	Age $\leq$35		Age 36-39	
Cell stages	$\leq$5 cells	$\geq$6 cells	$\leq$5 cells	$\geq$6 cells
# transfers	14	48	43	113
% clinical preg./transfer	14.3%	31.3%	14.0%	15.9%
% delivered	14.3%	25.0%	7.0%	13.3%

CONCLUSIONS: The results show that for women $\leq$39 years old with such DOR that only one embryo cleaved to day 3, and even if the number of blastomeres is only 4 or 5 cells, live delivered pregnancies are possible. If the trend would continue it would seem that for younger women $\leq$35 years old, an embryo cleaving to at least 6 cells has about twice the chance of producing a live baby following single embryo transfer. This seems to be the case also for women age 36-39. The data show that for women with such DOR that only one embryo cleaves to at least 4 blastomere by day 3, the majority will at least attain a 6-cell embryo (76.4%, 48/62 for women $\leq$35 and 72.4%, 113/156 for women 36-39). Thus, a woman aged $\leq$35 with severe DOR leading to only 1 cleaved embryo to transfer on day 3, has a 22.4% of having a live baby vs. 11.5%, 18/156 in women age 36-39. There does not seem to be any advantage to the patient to freeze the embryo and perform multiple retrieval cycles to get one transfer with several embryos (as is the policy in some IVF centers) or to let the embryo cleave to the blastocyst stage with or without pre-implantation testing for aneuploidy as is performed in some other IVF centers.

SUPPORT: None.

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LIVE BIRTH RATES ARE COMPARABLE BETWEEN MODIFIED NATURAL AND PROGRAMMED FROZEN EMBRYO TRANSFER CYCLES. Elizabeth L. Wolfe, MD,[1] Denis A. Vaughan, MD,[2] Daniel W. Duvall, Jr., BA,[3] Denny Sakkas, PhD,[3] Thomas L. Toth, MD,[2] [1]Maine Medical Center, Portland, ME; [2]Beth Israel Deaconess Medical Center, Boston, MA; [3]Boston IVF, Waltham, MA.

OBJECTIVE: The increasing utilization of frozen embryo transfer (FET) has intensified the need to assess outcomes and refine protocols. Currently, the use of natural, modified natural or programmed FET cycles varies both regionally and internationally. The aim of this study was to compare live birth rates (LBR) between commonly used modified natural and programmed FET protocol regimens.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All FET cycles between January 2014 and December 2017 at a university-affiliated IVF center were reviewed. Modified natural cycles relied on either an hCG trigger or an endogenous LH surge, with supplemental vaginal progesterone (P4). FET was performed 7 days after hCG trigger or 6 days after LH surge with P4 supplementation starting 3 days before FET. Programmed FET cycle protocols included endometrial preparation with oral and/or transdermal estrogen until a satisfactory endometrial thickness was achieved and the use of either vaginal P4, intramuscular (IM), or a combination, with FET after approximately 108-112 hours of P4 exposure. The primary outcome was LBR. Only those aged <38 years, with a single blastocyst transfer, <3 prior miscarriages, <3 prior FETs, and <3 prior IVF cycles were included in this analysis. Chi-squared test was used to compare outcomes.

RESULTS: 703 modified natural and 2131 programmed FET cycles were included, resulting in 1326 total live births (LBR 47%). The mean age was similar in both groups (33 years). Similar numbers of cycles had embryos transferred that were deemed euploid by PGT (23% of modified natural cycles and 24% of programmed cycles). There was a higher clinical pregnancy rate amongst modified natural cycles (423/703, 60%) compared to all programmed cycles (1161/2131, 54%, P=.012). A significantly higher LBR was noted in modified natural cycles compared to all programmed cycles (Table 1). When a sub-analysis was performed comparing modified natural to programmed cycles in which IM P4 was used (alone or in combination with vaginal) no significant difference in LBR was noted.

CONCLUSIONS: Live birth rates are comparable in modified natural FET cycles and programmed hormone replacement cycles with IM P4. Further efforts are needed to standardize and optimize FET protocols. Based on this study, shared decision making between patient and provider is encouraged when selecting FET protocols. Emerging information regarding maternal and perinatal outcomes may influence clinical decision making in the future.

TABLE 1. FET cycle outcomes

Category	Cycles	Live Births	P value*
Modified Natural	703	366 (51%)	-
Programmed (All)	2131	960 (45%)	0.01
Programmed (IM)	791	407 (55%)	0.81

*Live births compared to modified natural cycles

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ASSOCIATION BETWEEN DAY OF TROPHECTODERM BIOPSY AND OUTCOMES OF EUPLOID EMBRYO TRANSFERS. Catherine Gordon, MD, Andrea Lanes, PhD, Ann M. Thomas, PhD, Catherine Racowsky, PhD Brigham and Women's Hospital, Boston, MA.

OBJECTIVE: To compare clinical outcomes following transfer of euploid blastocysts biopsied on day 5 with those of embryos deemed unsuitable for biopsy on day 5 and that were biopsied on day 6.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Warmed NGS-tested euploid single embryo transfers from autologous IVF cycles performed at our center from 10/2015 to 2/2020 were included. Implantation rates (IR) and ongoing pregnancy rates (OPR) beyond 12 weeks gestation were assessed. Transfers were grouped by blastocyst quality (good, fair and poor) and then stratified by day of biopsy. Relative risks (RR) and 95% confidence intervals (CI) were calculated within each blastocyst quality class using log-binomial regression adjusting for age. GEE modeling was used to account for patients contributing multiple cycles.

RESULTS: 237 transfers from 191 patients were analyzed. See table below.

Both the IR and OPR were increased for embryos biopsied on day 5 compared to those biopsied on day 6 when combining all transfers regardless of blastocyst quality (72.4% vs. 63.0%; 62.3% vs. 53.2%). However, these differences were not significant. When stratified by biopsy day and blastocyst quality, a similar trend was noted for good and poor quality embryos. Fair quality Day 5 embryos and good quality Day 6 embryos had equivalent IR and OPR (RR 0.97 95%CI 0.78, 1.20; RR 0.94 95%CI 0.75, 1.17). The IR of poor quality day 5 blastocysts was significantly increased compared with that of poor quality day 6 blastocysts (72.7% vs. 36.0%; RR 0.69 95%CI 0.53, 0.88).

CONCLUSIONS: Although statistically not significant, the approximate 10% increase in IR and OPR between embryos biopsied on day 5 vs. day 6 is clinically significant and is useful for patient counseling. When the choice is available, a euploid embryo that was biopsied on day 5 should be transferred over one biopsied on day 6, regardless of blastocyst quality.

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DO ANDROGENS MAKE STRAIGHT A STUDENTS?: EXPLORING THE LINK BETWEEN HYPERANDROGENISM AND BLASTOCYST GRADE. Nepheli Raptis, B.A., M.A.,[1] Hanna Mandell, M.A.,[1] Lauren Grimm, M.A.,[1] Emma Radley, M.A.,[1] Christy Oso, B.A.,[1] Zoran J. Pavlovic, M.D.,[2] Jessi Anderson, MPH,[1] Roohi Jeelani, MD,[1] Angeline Beltsos, MD[1] [1]Vios Fertility Institute, Chicago, IL; [2]Rush University Medical Center, Chicago, IL.

OBJECTIVE: To determine whether hyperandrogenic-presenting PCOS patients produce blastocysts of different quality compared to classically-presenting PCOS patients.

DESIGN: While polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders of reproductive-age women, researchers have recently established a hyperandrogenic subgroup of PCOS patients who specifically present with the clinical symptoms of adult acne and hair growth. In order to optimally diagnose and treat this subgroup, the clinical implications must be better understood. Previous research determined that endocrine disorders underlying PCOS threaten follicular and oocyte development. Furthermore, hyperandrogenic PCOS patients were found to have a lower blastocyst utilization rate compared to classical PCOS patients, which we hypothesized could be accounted for by a potential difference in blastocyst quality score between these PCOS subgroups.

MATERIALS AND METHODS: Retrospective chart review at a private multi-site infertility center. Patients who underwent in-vitro fertilization (IVF) cycles between April 2017 and September 2019 and who had PCOS were included. A serum anti-mullerian hormone (AMH) level of $>$ 5ng/mL was used as a surrogate marker for PCOS. Hyperandrogenic PCOS and classical PCOS subgroups were defined based on the presence or absence of self-reported adult acne and hair growth. Baseline characteristics were evaluated, and blast quality score (BQS) and pregnancy outcomes were analyzed. BQS was calculated according to the Gardner and Schoolcraft criteria. Two sample t-tests and chi square analysis were used to analyze the data using SPSS (SPSS Inc., Chicago, IL, USA).

RESULTS: A total of 109 IVF cycles were identified as having a cycle resulting in at least 1 blastocyst stage embryo. Baseline characteristics, including age, BMI, and AMH were similar between the two groups. Fifty-three of these cycles were those who presented with hyperandrogenic PCOS, while 56 were those with classical PCOS. There is no statistical difference (p=.59) between the average BQS for the non-hyperandrogenic PCOS group (15.881) compared to the hyperandrogenic group (16.464). Differences in pregnancy outcomes between both groups were also similar (p=0.70).

CONCLUSIONS: While hyperandrogenic PCOS patients may experience a decrease in utilizable embryos following an IVF cycle compared to their classical PCOS counterparts, these results support that this difference may not be caused by a difference in blastocyst quality. Given these results, physicians may counsel their hyperandrogenic PCOS patients to complete more IVF cycles to produce utilizable, high quality embryos in consideration of their patients' family planning objectives. Further research investigating other potential factors that could account for this

Blastocyst quality	Day Biopsy/ET	No. of transfers	IR (%)	RR (95% CI)	OPR (%)*	RR (95% CI)
Good	5	17	15/17 (88.2%)	ref	14/17 (82.3%)	ref
	6	21	15/21 (71.4%)	0.86 (0.67, 1.10)	13/20 (65.0%)	0.85 (0.64, 1.13)
Fair	5	117	82/117 (70.1%)	ref	68/112 (60.7%)	
	6	35	27/35 (77.1%)	1.09 (0.91, 1.31)	21/34 (61.8%)	1.03 (0.86, 1.23)
Poor	5	22	16/22 (72.7%)	ref	12/22 (54.6%)	ref
	6	25	9/25 (36.0%)	0.69 (0.53, 0.88)	8/25 (32.0%)	0.81 (0.63, 1.04)
Any	5	156	113/156 (72.4%)	ref	94/151 (62.3%)	ref
	6	81	51/81 (63.0%)	0.90 (0.74, 1.08)	42/79 (53.2%)	0.88 (0.69, 1.11)

*data missing for 7 patients

discrepancy in blastocyst utilization rate between these two PCOS groups could elucidate the mechanism that leads to classical PCOS patients producing more utilizable embryos than their hyperandrogenic PCOS counterparts.

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EFFECT OF CERVICAL MICROBIOME ON CLINICAL PREGNANCY RATE OF WOMEN UNDERGOING IN VITRO FERTILIZATION.

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1. OBJECTIVE: To investigate if cervical microbiome influences the in vitro fertilization (IVF) outcome.

2. DESIGN: A nested case-control study involving 100 IVF patients.

3. MATERIALS AND METHODS: This study included 100 IVF patients transplanted with two cleavage stage embryos. Divided into 4 groups according to clinical pregnancy outcome and transplantation cycle. Two samples of cervical secretions were collected before all patients underwent embryo transfer. The variable regions 3 and 4 (V3-V4) of the 16S ribosomal ribonuclease acid gene were amplified by polymerase chain reaction and analyzed by Illumina MiSeq sequencing to compare the diversity of the four groups of microbiome.

4. RESULTS: In the fresh cycle, the alpha diversity of the clinical pregnancy group(n=25) was significantly lower than that of the non-pregnancy group(n=26)(P=0.0078), and there were statistical differences between the pregnancy group and non-pregnancy group in the beta diversity (P=0.004). During the thawing cycle, the alpha diversity of the clinical pregnancy group(n=27) was also lower than that of the non-pregnancy group(n=22), but it was not significant, and the two groups were not statistically significant in the beta diversity analysis. For cervical microbiome of fresh cycle patients, we obtained five main different strains by differential analysis, namely Lactobacillus, Akkermansia, Desulfovibrio, Atopobium, and Gardnerella. Among them, Lactobacillus was negatively correlated with other differential strains, and positively correlated with serum E_2 levels. Regression analysis of fresh cycle data showed that the composition of the cervical microbiome on the transplantation day would affect the clinical pregnancy rate of IVF(P=0.030).

5. CONCLUSIONS: The composition of the cervical microbiome can affect the outcome of patients undergoing IVF treatment. The next step should be to clarify the mechanism of non- Lactobacillus -dominated microbiome affecting embryo implantation.

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PREDICTORS OF ENDOMETRIAL COMPACTION PRIOR TO THAWED BLASTOCYST TRANSFER.

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OBJECTIVE: Recent reports of a correlation between changes in endometrial thickness after progesterone (P4) exposure and success rates after thawed embryo transfer suggest a potential relationship with endometrial receptivity. We have found in our center that the change in endometrial thickness after progesterone exposure was correlated with pregnancy and ongoing pregnancy rates, so that those with less expansion (or with compaction) had greater ongoing pregnancy rates than those with more endometrial expansion after progesterone exposure. This study attempts to find factors that are predictive of the change in endometrial thickness.

DESIGN: IRB-approved retrospective cohort study of single vitrified-warmed blastocyst transfers at a private fertility center.

MATERIALS AND METHODS: There were 232 autologous vitrified-warmed single-blastocyst transfers following transvaginal ultrasonographic (TVU) measurement of endometrial thickness on the day of progesterone start and 5 days later, on the day of transfer. Vitrified-warmed blastocysts were transferred on the 6th day of P4 injection (100 mg/day) in cycles of artificial endometrial preparation with exogenous estradiol. Linear regression was used to identify factors that are predictive of the percent change in endometrial thickness from the day of P4 start until 5 days later on the day of planned transfer. Potential predictive factors included patient age, weight, BMI, endometrial thickness on the day of P4 start, and endometrial growth from baseline (E2 start) until P4 start. Also available were serum E2 levels measured before, on the day of, and 2 days after P4 start. P4 levels were also measured 2 days after P4 start and on the day of transfer. Additionally, the E2/P4 ratio measured 2 days after P4 start was available. $P<0.05$ was considered significant.

RESULTS: Only the endometrial growth from baseline to P4 initiation was a significant predictor of the change in endometrial thickness after P4 start ($P<0.001$). A greater degree of growth from baseline until P4 initiation was associated with less expansion (or greater compaction) between P4 initiation and FET.

CONCLUSIONS: These results suggest that endometria that responded most vigorously to exogenous E2 (more growth) are those most likely to have compaction (or less expansion), while those with less vigorous response to E2 (less growth) are those most likely to have greater endometrial expansion after P4 start. Whether this is an inherent property of those endometria, perhaps through biological variation, or is something that can be clinically manipulated is yet to be determined.

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SUPPORT: None.

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DONOR SPERM CANNOT IMPROVE ART OUTCOMES IN WOMEN WITH LOW OVARIAN RESERVE.

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OBJECTIVE: To investigate the efficiency of assisted reproductive technology in patients with low ovarian reserve who choose sperm donor or husband sperm in vitro fertilization-embryo transfer (IVF-ET).

DESIGN: A retrospective analysis.

MATERIALS AND METHODS: A retrospective analysis was carried out on patients with ovarian reserve decline who underwent IVF-ET assisted pregnancy in the Reproductive Center of the Sixth Affiliated Hospital from January 2014 to May 2019. AMH $<$ 1.1 ng/ml and antral follicle count (AFC) $<$ 6 were selected. All the patients divided into 3 groups according to sperm source and sperm quality: Group 1 was IVF group for donor sperm, 73 cycles. SPSS statistical software was used to match the tendentiousness score with the control group, and group 2 was ICSI for 64 cycles due to less severe male infertility. Group 3: husband sperm IVF group, 73 cycles.

RESULTS: There was no significant difference in age, BMI, AMH, basal FSH, AFC, other general data among the three groups.Compared with group 3, group 1 and group 2 had higher non-oocyte cycles, 13 and 10 cycles respectively. The probability of available embryos among the three groups were 64.38%, 57.81%, 76.71% respectively, with no statistical difference. The clinical pregnancy rates in the three groups were 31.03%, 37.5% and 40.91%, respectively, with no significant difference. The miscarriage rate in group 2 increased significantly (50%). As the number of cases was relatively small, there was no significant difference after analysis (P=0.233).

Group	1 (n=73)	2 (n=64)	3 (n=73)	F/X2	P
Age(y)	38.88±5.66	37.09±5.05	36.77±4.93	0.068	0.934
BMI	22.08±2.61	22.41±2.74	22.57±3.35	0.511	0.600
Basal FSH	10.28±5.61	9.33±4.11	9.04±3.64	1.485	0.229
AMH(ng/ml)	0.51±0.28	0.65±0.26	0.79±0.25	1.069	0.303
AFC	3.95±1.61	3.78±1.55	4.14±0.76	1.872	0.134
Number of eggs obtained	2.58±1.90	2.63±1.73	2.73±1.64	1.759	0.165
Number of no eggs obtained cycles	13	10	1		
Ratio of available embryo cycles (%)	64.38 (47/73)	57.81 (37/64)	76.71 (56/73)	5.206	0.074
2PN fertilization rate(%)	67.55(127/188)	60.12(101/168)	59.56(162/272)	3.402	0.183
Available embryo rate(%)	79.53(101/127)	81.19(82/101)	79.63(129/162)	0.121	0.941
D3 high quality embryo rate(%)	77.23(78/101)	78.05(64/82)	81.40(105/129)	0.681	0.711
Clinical pregnancy rate (%)	31.03 (9/29)	37.5 (6/16)	40.91 (9/22)	0.556	0.757
Embryo implantation rate (%)	21.74 (10/46)	20.69 (6/29)	32.35 (11/34)	1.535	0.464
Miscarriage rate (%)	11.11 (1/9)	50 (3/6)	11.11 (1/9)	3.455[a]	0.233[a]
Live birth rate (%)	20.69 (6/29)	18.75 (3/16)	31.82 (7/22)	1.157	0.618

CONCLUSIONS: Assisted reproductive technology for patients with low ovarian reserve can not increase pregnancy rate by donor sperm.

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DOES TRIGGER DAY PROGESTERONE AFFECT THE OUTCOME OF SUBSEQUENT FROZEN EMBRYO TRANSFER?. Ji Yeon Han, Fellow,[1] Soo Jin Han, MD,[1] Se Jin Kim, Fellow,[1] Hye Kyeong Kim, Fellow,[1] Sung Woo Kim, Professor,[1] Hoon Kim, Professor,[1] Seung Yup Ku, Professor,[1] Chang Suk Suh, Professor,[1] Seok Hyun Kim, MD. PhD.[2] [1]Seoul National University Hospital, Seoul, Korea, Republic of (South); [2]Seoul National University College of Medicine, Seoul, Korea, Republic of (South).

OBJECTIVE: To investigate the effect of progesterone level measured at trigger day on subsequent frozen embryo transfer cycle.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The medical records of 123 women who underwent in vitro fertilization (IVF) without fresh embryo transfer were reviewed. Patients were divided in two groups, women with elevated progesterone (EP, $\geq$1.5ng/mL) on trigger day (n=26) and women with other reasons of elective cryopreservation (n=97), such as usage of letrozole, risk of ovarian hyperstimulation syndrome, and poor endometrium condition, etc. The outcome of first frozen embryo transfer was investigated. Mann-Whitney test and Fisher's exact test were used for statistical analysis.

RESULTS: Age, BMI, AMH, basal FSH, and initial antral follicle count (AFC) were similar between two groups. Stimulation days were significantly longer in EP group (10.23 vs. 8.73, p=0.004), and total gonadotropin dose was also higher in EP group (3181.73 vs. 2235.05, p=0.002). The outcomes of COS, such as fertilization rate, and the number of oocytes retrieved, mature oocyte, good embryo, and blastocyst, did not differ between two groups. Clinical pregnancy rate was higher in EP group, but it did not achieve statistical significance (34.6% vs. 17.7%, p=0.062). Miscarriage rate was similar in both groups (EP: 33.3% vs. control: 35.3%, p=0.372).

CONCLUSIONS: Baseline characteristics did not differ according to progesterone level of trigger day, except stimulation days and total gonadotropin doses. Additionally, the outcome of next frozen embryo transfer cycle was similar, regardless of progesterone level on trigger day.

SUPPORT: No external funding was used for this study. None of the authors has any potential conflict of interest.

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DOES GONADOTROPIN DOSAGE AFFECT THE RATE OF ANEUPLOIDY?. Michelle Volovsky, MBBS (Hons),[1] Richard Grazi, M.D.[2] [1]Maimonides Medical Center, New York, NY; [2]University of Washington, Seattle, WA.

OBJECTIVE: Our aim was to investigate whether increased gonadotropin doses during ovarian stimulation affects the rate of aneuploidy in subsequently produced embryos.

DESIGN: This is a retrospective cohort analysis performed using data from a single outpatient assisted reproductive technology (ART) facility.

MATERIALS AND METHODS: A standardized data set spanning 2016-2019 was analysed. This was comprised of 308 cycles in which gonadotropins in the form of follicle stimulating hormone or human menopausal gonadotropin were administered during ovarian stimulation, with pre-implantation genetic testing for aneuploidy being performed on all subsequently produced high-grade blastocysts. The main outcome assessed was the rate of aneuploidy among the tested embryos. Using a logistic regression model controlling for anti-mullerian hormone (AMH) and age, this rate was compared to the total dose of gonadotropins administered. Factors such as prior pregnancy, body mass index (BMI), intracytoplasmic sperm injection, cause of infertility, stimulation protocol, days of gonadotropin administration and type of ovulation trigger were evaluated and found not to affect the aneuploidy rates and hence were not included in the final logistic regression model. A secondary analysis was performed after separating total units of gonadotropin dose administered (Gn) into three groups [low (Gn $<$2000IU), moderate (Gn 2000-3000IU) and high (Gn $>$3000IU)] in order to assess whether a certain dose threshold would produce a statistically significant change in aneuploidy.

RESULTS: In the initial analysis we observed no statistically significant difference in aneuploidy rates with increasing gonadotropin doses when controlling for age and AMH. The secondary analysis, however, demonstrated a statistically significant decrease in the odds of aneuploidy in the moderate dose group by 0.73 ($p < 0.05$), when compared to the low dose group. There was no statistically significant difference between the moderate and high dose groups.

CONCLUSIONS: Previous reports have suggested that high gonadotropin dosing during ART cycles might have an adverse impact on the rate of aneuploidy. Our data suggests that lowering the dosage of gonadotropins might in fact raise the aneuploidy rate, independent of age, ovarian reserve (as measured by AMH), BMI and cause of infertility. The gonadotropin dosage in ART cycles should be appropriate for the patient's age and ovarian reserve, with the goal of safely maximizing the number of blastocysts, as lower doses do not appear to improve the chromosomal integrity of resultant embryos.

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THE INFLUENCE OF OOCYTE MATURATION RATE ON EMBRYO DEVELOPMENT AND PREGNANCY OUTCOMES IN ICSI CYCLES. Tingting Li*, Doctor,[1] Yi Zhou, master,[1] Cong Fang, PHD, MD,[2] [1]Reproductive Medicine Research Center, Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; [2]The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: The aim of this study was to investigate the influence of oocyte maturation rate on embryo development and pregnancy outcomes in intracytoplasmic sperm injection(ICSI) cycles in different age groups.

DESIGN: A retrospective study.

MATERIALS AND METHODS: This was a retrospective study analyzing date from 5442 ICSI cycles in a single reproductive center between January 2015 and December 2019. According to the oocyte maturation rate(OMR),

patients were divided into 3 groups: Group A, OMR ≤ 30%; Group B, 30% < OMR ≤ 60%; Group C, OMR > 60%. Fertilization rate, embryo development and pregnancy outcomes were compared among groups stratified by 40 age cut-point.

RESULTS: The average number of mature oocytes is higher in patients aged < 40 years than patients aged ≥ 40 years(9.70±5.20 vs 6.58±3.42 , P < 0.001), but no significant difference was found in the OMR different age groups. In patients aged < 40 years, the two pronucleus (2PN) fertilization rate is highest in Group C(P < 0.001). The cleavage rate, rate of transferable embryos, rate of good-quality embryos, implantation rate and clinical pregnancy rate were higher with increasing OMR(Group A < Group B < Group C , P < 0.05). The live birth rate is significantly lower in Group A compared with Group B and C(respectively 9.1% vs 40.5% ; 9.1% vs 44.8% , P < 0.05) and is similar in Group B and C. In patients aged ≥ 40 years, though the number of transferable embryos and good-quality embryos is higher with increasing OMR(Group A < Group B < Group C , P < 0.001), no significant difference was found in embryo development and pregnancy outcomes.

CONCLUSIONS: In patients aged < 40 years, increasing OMR is associated with better embryo development and pregnancy outcomes in ICSI cycles. The embryo development competency and pregnancy outcomes significantly decrease when the OMR ≤ 30%.

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THE TROPHECTODERM BIOPSY EXPERIENCE DOES NOT AFFECT PGT OUTCOME. Tuong V. D. Pham, B.S.,[1] Randall Dunn, M.D.,[1] Subodh Chauhan, M.D.,[1] Leah Schenk, M.D.,[1] Rakesh Mangal, M.D.,[1] Audie Co, B.S.,[1] Melissa Pinasco, M.S.,[1] Wan-Song A. Wun, PhD,[2] Aspire Fertility,[1]Aspire Fertility, Houston, TX; [2]Harvest Fertility, Arcadia, TX.

OBJECTIVE: The PGT at the blastocyst stage looks to be a trend worldwide. Trophectoderm biopsy is the first step in performing PGT. There are reports (Aoyama and Kato, 2019; Capalbo et al, 2015; Munne et al, 2017) concerning the technique and the experience of the biopsy practitioner. How newly trained biopsy practitioner affect the outcome of PGT is examined in this study.

DESIGN: Retrospective study.

MATERIALS AND METHODS: All trophectoderm biopsy cases during 2016-2018 are included in this study. A total of 4897 blastocysts had trophectoderm biopsy. An experienced embryologist has performed 4284 biopsies. The newly trained embryologist performed 613 biopsies. There were 20.3% biopsies on day 5, 70% on day 6, and 9.6% on day 7. The trophectoderm biopsy uses the suction approach (no pre-assisted hatching). A Saturn V laser was used to cut the trophectoderm samples to take about 4-6 trophectoderm cells. All biopsies on day 5 and day 6 are at the expanded or hatching stage. A small number of biopsies are done at blastocyst stage on day 7.

This is a retrospective study. Chi-square tests used for statistical analysis.

RESULTS:

CONCLUSIONS: The results show there are no significant difference on the euploid rate, LLM, or NR with an experienced biopsy practitioner and a newly trained biopsy practitioner. This result is similar to the Capalbo et al (2015) observation. The ploidy state seems already inherently determined and the experience of the biopsy practitioner does not have a significant affect on the euploid status. It is interesting finding to see the experienced embryologist had a significantly higher HLM which may be due to selection bias or inherent in a retrospective analysis. Good quality and easy cases are usually targeted to be handled by the new biopsy practitioner in this setting.

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ESTABLISH A NOMOGRAM MODEL TO PREDICT LIVE BIRTH RATE OF PCOS PATIENTS AFTER IVF/ICSI TREATMENT. Xing Yang, Ph.D., Linzhi Gao, Master degree, Lina Wei, Ph.D. The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: The clinical outcome after in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) treatment is diverse in infertility patients with polycystic ovary syndrome (PCOS). The aim of this study was to develop a nomogram model based on patients' characteristics to predict the live birth rate of PCOS patients after IVF/ICSI treatment.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All women in a public university hospital who attempted to conceive by IVF/ICSI for PCOS infertility from January 2014 to October 2018 were included. PCOS was diagnosed according to the Rotterdam criteria. A nomogram was built from a training cohort of 178 consecutive patients and tested on an independent validation cohort of 81 patients. Multivariable logistic regression was used to generate coefficients for each variable and the constant in the equation. The nomogram was constructed to be a graphic representation of the prediction model with the R software. Backward stepwise selection was performed to determine independent covariates.

RESULTS: No significant difference was observed in the patients' characteristics between the two cohorts. 79 patients (44.69%) achieve live birth in the training cohort. According to univariable logistic regression analysis, live birth was significantly correlated with total serum cholesterol (TC) ($p = 0.005$), BMI ($p=0.010$) and basal FSH ($p=0.080$). In multivariable analysis of the training cohort, live birth was significantly correlated with TC > 6.11 ng/ml (odds ratio [OR] 0.209; 95% CI 0.069–0.548; $p=0.003$), BMI > 23.9 (OR 0.478; 95% CI 0.250–0.900; $p=0.023$) and basal FSH (OR 1.291; 95% CI 0.990–1.705; $p = 0.064$). Higher TC, BMI and FSH were associated with a decreased live birth rate. Age and Day of Transfer were not statistically related to the live birth rate but were included in the predictive model due to their clinical relevance. Their inclusion improved the overall quality of the model as well (as measured by the Akaike information criterion).Therefore, this predictive model built on the basis of BMI, TC, basal FSH, Day of Transfer and age showed good calibration and discriminatory abilities, with an area under the curve (AUC) of 0.708 (95% CI 0.632–0.785) for the training cohort. The nomogram showed satisfactory goodness-of-fit and discrimination abilities in the independent validation cohort, with an AUC of 0.686 (95% CI 0.556–0.815).

CONCLUSIONS: Our simple evidence-based nomogram presents graphically risk factors and prognostic models for IVF/ICSI outcomes in patients with PCOS, which can offer useful guidance to clinicians and patients for individual adjuvant therapy.

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OPTIMAL REPRODUCTIVE OUTCOMES OBTAINED FROM VASECTOMIZED MALES UNDERGOING TESE (TESTICULAR SPERM EXTRACTION) AND INTRACYTOPLASMIC SPERM INJECTION WITH OWN OR DONATED OOCYTES. Irene Hervas, MSc,[1] Nicolas Garrido, PhD,[2] Lorena Valls, M.D,[3] Rocio Rivera-Egea, PhD,[4] Maria Gil Julia, MSc, MRes,[1] Jose Maria Martinez-Jabaloyas, M.D,[4] [1]IVI Foundation - IIS La Fe Biomedical Research Institute, Valencia, Spain; [2]IVI Foundation

Item	LLM[a]	HLM[b]	NR	=>4BB[d]	<4BB
Experience incidence/total	112/4284 (2.6%)	192/4284 (4.4%)	58/4284 (1.3%)	1892/3123 (60%)	268/799 (33%)
Newly trained incidence/abnormal	18/613 (2.9%)	11/613 (1.7%)	8/613 (1.3%)	280/443 (63%)	50/133 (37%)
Statistical analysis	n.s.	P<0.005	n.s.	n.s.	n.s.

[a]: low level mosaic; [b] : high level mosaic; [c]: no result; [d]: quality of blastocyst, #euploid/# without mosaic

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OBJECTIVE: Vasectomy is a permanent contraceptive method in males aiming birth control. Studies have shown that 3.4–7.4% regret their decision and request either sterilization reversal or in vitro fertilization treatment. Literature is scarce, series limited, main outcomes reported insufficient and often female contribution to reproductive success neglected. The aim of this study is to better address clinical outcomes of intracytoplasmic sperm injection (ICSI) cycles with testicular sperm after vasectomy in the largest series published so far.

DESIGN: Unicentric retrospective study.

MATERIALS AND METHODS: Data from vasectomized patients who underwent testicular sperm extraction followed by ICSI (TESE-ICSI) were obtained. Main outcome measures included implantation (IR), biochemical (BPR), clinical (CPR), and ongoing pregnancy (OPR) and delivery with live birth (LBR) rates per embryo transfer (ET), per controlled ovarian stimulation (COS) and couple. Proportions were compared with Chi-square tests, while survival curves were constructed with the Kaplan Meier method to estimate cumulative live birth rate (CLBR) per number of embryos consecutively replaced until the first newborn or abandoning.

RESULTS: A total of 513 TESE-ICSI cycles were evaluated, including 390 couples using their own (OE) and 123 donors' eggs (DE), in 497 and 215 embryo transfers respectively. Mean time since vasectomy and male age were 11.7 (CI95% 11.1-12.3) and 39.5 years (CI95% 38.7-40.3) in OE cycles, while in DE were 13.3 (CI95% 12.0-14.5) and 54.8 years old (CI95% 53.1-56.2). When using own's eggs, IR was 29.7% (CI95% 26.2-33.2), BPR 51.4% (CI95% 47.0-55.8), CPR 42.3% (CI95% 37.9-46.7) and OPR 35.0% (CI95% 30.8-39.2). The livebirth rate was 33.9% (CI95% 29.7-38.1) per ET, 23.0% (CI95% 19.8-26.2) per COS and 43.1% (CI95% 38.2-48.0) per couple. On the other hand, considering the 215 ET from donated oocytes ICSI cycles, IR was 33.6% (CI95% 28.1-39.0), BPR 54.2% (CI95% 47.5-60.9), and a CPR and OPR of 45.8% (CI95% 39.1-52.5) and 36.0% (CI95% 29.6-42.4) respectively. The LBR was 34.1% (CI95% 27.8-40.4) per transfer, 44.8% (CI95% 37.2-52.4) per COS and 59.3% (CI95% 50.6-68.0) per couple. Cumulative LBR were 33.6% (CI95% 27.9-39.3) with OE and 39.4% (CI95% 30.6-48.2) with DE when two embryos were transferred, 56.7% (CI95% 49.8-63.6) and 66.0% (CI95% 55.6-76.4) with four embryos replaced, and 75.6% (CI95% 68.2-83.1) *versus* 72.1% (CI95% 60.5-83.7) with seven embryos transferred, respectively. When up to nine embryos were transferred, the cumulative live birth rate was 85.9% (CI95% 79.0-92.8) in own oocytes cycles and 89.5% (CI95% 77.5-101.5) in donated oocytes treatments.

CONCLUSIONS: Clinical outcomes post-vasectomy results show reasonably high success rates, in both, autologous or donated oocytes, as estimated per ET, COS, couple and the cumulative livebirth rates depending on the number of consecutive embryos transferred using the largest series so far, to aid doctors and patients in the decision making process.

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FOLLITROPIN ALFA (OVALEAP®) COMPARED WITH FOLLITROPIN BETA (PUREGON®) IN WOMEN UNDERGOING A FIRST GNRH ANTAGONIST CYCLE FOR ICSI: A RETROSPECTIVE COHORT STUDY. Lien Van den Haute, Specialist degree, Panagiotis Drakopoulos, MD, PhD, Greta Verheyen, PhD, Michel De Vos, MD, Herman Tournaye, MD, PhD, Christophe Blockeel, MD, PhD, University Hospital Brussel, Brussels, Belgium.

OBJECTIVE: Based on published evidence, ovarian stimulation (OS) for IVF/ICSI with follitropin alfa (Gonal-F®) and follitropin beta (Puregon®) is equally efficient .

Although pharmacokinetic studies of Ovaleap®(follitropin alfa, Theramex), a biosimilar to Gonal-F, showed dose-proportional and bioequivalent results compared to the reference follitropin alfa product (Gonal-F®), the efficacy of Ovaleap® and Puregon® has not previously been compared.

The objective of this study was to determine whether cumulative live birth rates (CLBR) after Ovaleap® and Puregon® are similar when used for OS with ICSI in a first-rank GnRH antagonist protocol.

DESIGN: Retrospective single centre cohort study including infertile patients undergoing their first ICSI cycle at a tertiary referral Centre between July 2016 and July 2019.

MATERIALS AND METHODS: In total, 894 patients were included. Of those, 358 patients had used follitropin alpha (Ovaleap®) and 536 patients had received follitropin beta group (Puregon®). The primary outcome was CLBR defined as the delivery of a live born (>24 weeks of gestation) after a fresh or a subsequent frozen–thawed embryo transfer (ET) using solely embryos derived from one OS cycle. Secondary outcomes were gonadotrophin consumption, duration of stimulation, oocyte yield, fertilization rate, number of cryopreserved embryos and live birth rate (LBR).

RESULTS: Patient age was similar in both groups (32.5 ± 4.6y vs 32.9 ± 4.8y, p= 0.1), while AMH was also comparable (2.9 ± 1.9 vs 3 ± 2, p= 0.31)

The cause of infertility was comparable in both groups (p= 0.92).

There was no difference in OS starting dose (171 ± 31.6 IU in the Ovaleap® group vs 173 ± 30 IU in the Puregon® group, p= 0.28), but the duration of stimulation was slightly higher in the Ovaleap ® group (10.6

Oocyte yield was similar (11.3 ± 7.7 vs 11.8 ± 6.6 oocytes, p= 0.06). Fertilization rate (defined as fertilized oocytes/mature oocytes*100) after Ovaleap® (74.7 ± 24.2%) and Puregon® (72.1 ± 23.7%) was significantly different (p= 0.03). The number of cryopreserved embryos was similar in both groups (2.7 ± 2.8 with Ovaleap® and 2.6 ± 2.6 with Puregon®, p= 0,86).

Live birth rate after fresh ET (93/358 (26.0%) vs 142/535 (26.5%), p= 0.85) and CLBR (185/358 (51.7%) vs 249/535 (46.5%), p= 0.13) were not significantly different.

Multivariate regression analysis allowing adjustment for relevant confounders revealed that the type of gonadotropin was not associated with CLBR.

CONCLUSIONS: This retrospective study shows no significant difference in CLBR between Ovaleap® and Puregon® in patients undergoing a first GnRH antagonist ICSI cycle.

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RELATIONSHIP BETWEEN NUMBER OF OOCYTES RETRIEVED AND EMBRYO EUPLOIDY RATE. Jonathan D. Buerger, MD,[1] Jitesh Datla, MS,[2] Shahab Minassian, MD,[3] Michael J. Glassner, MD,[3] John J. Orris, DO,[3] Nicolle Clements, PhD,[2] Alyssa Sheffy, BS,[3] Sharon H. Anderson, PhD,[3] [1]Tower Health Reading Hospital, West Reading, PA; [2]Saint Joseph's University, Philadelphia, PA; [3]Main Line Fertility Center, Bryn Mawr, PA.

OBJECTIVE: Controlled ovarian stimulation (COS) protocols for in vitro fertilization (IVF) cycles for preimplantation genetic testing for aneuploidy (PGT-A) are optimized to obtain the highest number of high-quality, competent embryos while minimizing the chance of ovarian hyperstimulation syndrome. The objective of this study is to determine if higher number of oocytes retrieved affects rate of euploidy in the embryos.

DESIGN: Retrospective, cohort study of data from a private fertility center between 2017-2019.

MATERIALS AND METHODS: Data from 902 patients undergoing COS for IVF-PGT-A was analyzed. Interactive real-time graphing software Tableau was used to plot number of oocytes retrieved (independent variable) and embryo euploidy rate (dependent variable). Three multiple linear regression models were used to evaluate the relationship between number of oocytes retrieved and euploidy rate, where euploidy rate was analyzed per number of biopsied blastocysts, per number of oocytes retrieved, and per number of fertilized oocytes. The independent variables were patient age, anti-Mullerian hormone (AMH) level, PGT-A testing lab, and number of oocytes retrieved. Statistical significance was set at $p<0.05$.

RESULTS: The number of oocytes retrieved ranged from one to 63. A negative trend was observed between the number of oocytes retrieved and embryo euploidy rate when the interactive Tableau graphing software was used for visual analytics, especially when more than 25 oocytes were retrieved. After regression analysis, patient age was the only variable found to have a statistically significant negative effect ($p<0.0001$) on euploidy rate in all three regression models. Number of oocytes retrieved was not found to have a statistically significant effect on euploidy rate when analyzed per number of biopsied blastocysts (p=0.5356), per number of oocytes retrieved (p=0.1025), and per number of fertilized oocytes (p=0.7241). AMH and PGT lab were not found to have a statistically significant effect on euploidy rate in any of the three regression models. Regression models showed negative parameter estimate (-0.000929) for number of oocytes retrieved.

CONCLUSIONS: There was a statistically significant effect found in the regression analyses between patient age and embryo euploidy rate, which is already known. A negative trend in euploidy rate was observed in the Tableau visual analytics graphs, especially when number of oocytes retrieved was greater than 25. There is some evidence to suggest that higher number of oocytes retrieved may negatively impact the number of euploid embryos per number of oocytes retrieved based on the visual analytic graphs, p-value approaching significance, and the negative parameter estimate in the regression

models. Further research on the effect of high egg yields on embryo euploidy rates is needed.

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PREDICTING THE NUMBER OF BIOPSY QUALITY BLASTOCYSTS BASED ON OOCYTES RETRIEVED. Catherine Gordon, MD, Andrea Lanes, PhD, Kimberly W. Keefe, MD, Catherine Racowsky, PhD, Brigham and Women's Hospital, Boston, MA.

OBJECTIVE: To determine the rate of attrition from oocytes retrieved to biopsy-quality blastocysts formed to aid in patient counseling regarding the decision to proceed with preimplantation genetic testing for aneuploidy (PGT-A).

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: Autologous IVF PGT-A cycles performed at our center from 4/2015 to 12/2018 resulting in at least one biopsy-quality blastocyst on either day 5 or 6 were included. Number of oocytes, mature oocytes (MII), zygotes (2PN), blastocysts, and biopsy-quality blastocysts were assessed. Data were stratified by age and adjusted for AMH and BMI. Relative risks (RR) and 95% confidence intervals were calculated using Poisson regression. GEE modeling was used to account for patients contributing more than one cycle.

RESULTS: 886 cycles from 687 patients were analyzed (See table).

	Age					Total
	<35	35-37	38-40	41-42	>42	
# Oocytes	23.16 ±12.46	19.73 ±11.44	15.00 ±9.38	14.84 ±9.79	12.58 ±7.55	18.85 ±11.26
# MIIs	17.63 ±10.07	15.62 ±9.65	11.53 ±7.45	11.45 ±8.13	9.51 ±5.43	14.54 ± 9.40
# 2PNs	14.35 ±8.57	12.54 ±7.99	8.8 ±6.19	9.07 ±6.7	6.67 ±5.02	11.56 ±7.96
# Blastocysts (%)*	10.33 ±6.61 (44.6)	8.26 ±6.02 (41.9)	5.21 ±4.52 (34.7)	5.38 ±4.52 (36.3)	3.27 ±2.97 (26.0)	7.66 ±6.11 (40.6)
# Biopsy quality blastocysts (%)*	6.85 ±5.07 (29.6)	5.67 ±4.26 (28.7)	3.71 ±3.19 (24.7)	3.18 ±2.84 (21.4)	1.73 ±1.40 (13.8)	5.23 ±4.46 (27.7)

Data expressed as mean ±SD. * % of oocytes

Values for all assessed variables decreased with increasing patient age. As age increased the proportion of oocytes that formed blastocysts ($p<0.01$; trend) and biopsiable blastocysts ($p<0.01$; trend) decreased, especially comparing the 41-42y and >42y groups (blastocysts: 36.3% vs 26.0%; $p<0.01$; biopsiable blastocysts: 21.4% vs 13.8%; $p=0.01$). Adjusting for AMH and BMI revealed no significant change in either number of blastocysts or biopsiable blastocysts for 35-37y vs <35y women (RR 0.95, 95%CI 0.87-1.03 and RR 0.94, 95%CI 0.84-1.06, respectively). However, the number of blastocysts was significantly lower in each group of women over 37y compared to <35y (38-40y RR 0.80 95%CI 0.73-0.88; 41-42y RR 0.82 95%CI 0.73-0.92; >42y RR 0.57 95%CI 0.45-0.71). The age-related decline was even more pronounced for biopsiable blastocysts in the adjusted analysis (38-40y RR 0.79 95%CI 0.70-0.91; 41-42y RR 0.66 95%CI 0.56-0.79; >42y RR 0.42 95%CI 0.31-0.59).

CONCLUSIONS: Blastocyst conversion and the number of biopsy quality blastocysts is inversely correlated with age. After adjusting for AMH and BMI, this trend remained significant for patients aged 38y and older. Women over the age of 37y should be counseled on the high rate of blastocyst attrition with advancing age.

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DOES THE ADDITION OF VAGINAL ESTROGEN IN FROZEN EMBRYO TRANSFER CYCLES WITH LOW SERUM ESTRADIOL LEVELS BUT ADEQUATE ENDOMETRIAL LINING IMPROVE CYCLE OUTCOMES?. Joshua C. Combs, MD,[1] Karrie A. Walker, DO,[1] Peter G. Lindner, MD,[1] Micah J. Hill, DO,[1] Alan H. DeCherney, MD,[2] Mae W. Healy, DO,[1] [1]Walter Reed National Military Medical Center, Bethesda, MD; [2]Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD.

OBJECTIVE: To determine, in the setting of an adequate endometrial thickness (≥8mm) prior to progesterone start, if the addition of vaginal estrogen for patients with a serum estradiol level of < 200 pg/mL altered clinical outcomes.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All vitrified blastocyst embryo transfers from September 2016 to December 2018 were included. All patients received oral estrace for endometrial preparation followed by embryo transfer on day 6 of progesterone in oil. Only patients with an adequate endometrial thickness of ≥8mm noted on day 14 to 16 were included. Vaginal estrogen (estrace 1mg daily) was added by some providers if the patient's serum estradiol level was <200 pg/mL on that day. Cycles with an endometrial thickness measuring <8mm, and natural cycle frozen blastocyst transfers were excluded from this study. Chi-squared analysis was performed to evaluate for statistical significance between the two cohorts in respect to biochemical pregnancy loss, clinical miscarriage rates, clinical pregnancy rates, and live birth rates.

RESULTS: 164 patient-cycles met inclusion criteria; 85 with vaginal estrogen added, 79 with no vaginal estrogen added. There was no difference

	n	Biochemical Pregnancy Loss	Clinical Miscarriage Rate	Clinical Pregnancy Rate	Live Birth Rate
Vaginal Estrogen Added	85	12(14%)	5(9%)	54(64%)	48(56%)
No Vaginal Estrogen Added	79	7(9%)	10(19%)	52(66%)	41(52%)
p Value		0.49	0.32	0.99	0.84

in biochemical pregnancy loss, clinical miscarriage rates, and clinical pregnancy rates between the two groups (Table 1). Live birth rate was similar between the two groups (56% versus 52%, p=0.84) (Table 1).

CONCLUSIONS: In a vitrified blastocyst embryo transfer cycle, treating estradiol levels < 200 pg/mL with additional vaginal estrogen, in the setting of an adequate endometrial thickness of ≥8mm, does not improve biochemical pregnancy loss, clinical miscarriage rates, clinical pregnancy rates or live birth rates.

References: None.

SUPPORT: None.

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THIN ENDOMETRIAL LINING DURING FROZEN EMBRYO CYCLES- A CASE-CONTROL STUDY OF RISK FACTORS AND NATURAL HISTORY.

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OBJECTIVE: To identify predictors of thin endometrial lining in the first frozen embryo transfer cycles and to characterize the natural history of this condition over subsequent cycles.

DESIGN: Retrospective case-control study

MATERIALS AND METHODS: Cases were patients who had a standard hormonal endometrial preparation cycle (Estrace 6 mg/day in divided doses for a minimum of 12 days) and had their first frozen blastocyst embryo transfer (FET) delayed or cancelled due to thin endometrium (<6 mm) between the years of 2012 and 2018. Controls were the next two consecutive patients undergoing a standard hormonal preparation who did not have a thin endometrium (≥ 6 mm) and proceeded with their first FET. Medical charts were reviewed and demographic data and pertinent medical history was extracted. Multivariable logistic regression was performed to determine predictors of inadequate endometrium in FET cycles. Types of interventions utilized and subsequent endometrial thickness in additional cycles were recorded and the cumulative delivery rate from the initial attempt at FET onwards was calculated and compared with Fishers exact test and Kaplan-Meier survival analysis.

RESULTS: **Risk factors-** This study included 29 cases and 58 controls. Multiple logistic regression analysis of factors related to thin endometrium indicated thinner fresh cycle endometrium and lower body weight were associated with thin endometrial lining in FET cycles. Specifically, for each additional 5 kilograms of weight, the odds of having an endometrial lining under 6 mm decreased by 0.845 (95% CI: 0.717-0.995), and for every 1 mm increase in endometrial thickness in the fresh cycle, women were 0.659 times less likely to have a thin endometrium in the subsequent FET (95% CI: 0.521-0.835). **Natural History-** The mean endometrium during first FET was 4.9 ± 1.1 mm in cases versus 9.5 ± 2.6 mm in controls (p-value <0.001). During first FET, 18/29 cases had their estrogen dose extended. Subsequently, 10/18 were able to achieve an adequate endometrium (mean 7.14 ± 1.5 mm) and had a FET with a live birth rate of 40%. A second FET occurred in 21 cases and 20 controls. The mean endometrium during second FET was 6.2 ± 1.3 mm in cases versus 9.3 ± 2.6 mm in controls (p-value <0.001). Endometrial thickness for cases undergoing a second FET did not differ clinically based on intervention utilized (6.5 ± 1.1 mm with the addition of vaginal estrogen vs. 5.7 ± 2.2 mm with intramuscular estrogen vs. 6.6 ± 0.8 mm with low dose gonadotropin stimulation). There was no statistically significant difference in cumulative live birth rate between cases and controls (55% vs 72% respectively, p-value 0.148), however cases underwent more cycles to achieve live birth (mean number of cycles 3.0 vs 2.1 in control group, p-value 0.013).

CONCLUSIONS: This study shows that prognosis after a diagnosis of thin endometrium is favorable. Lower weight and thinner fresh cycle lining are predictors of thin endometrium in FET cycles. Most importantly, women with a diagnosis of thin endometrium have similar live birth rates as those with adequate endometrium, although their time to achieve live birth is slightly longer.

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EFFECT OF BED REST FOLLOWING SINGLE EUPLOID BLASTOCYST TRANSFER ON PREGNANCY OUTCOMES.

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OBJECTIVE: Recommending bed rest following embryo transfer was a common practice in ART. More recent publications suggest no positive impact of bed rest and even a possible detriment. Prior studies examined short time periods prior to ambulation and did not utilize a strong model to control for embryo stage or quality. The objective of this study was to examine whether extended bed rest following frozen embryo transfer using a single euploid blastocyst had any impact on subsequent pregnancy rates.

DESIGN: Retrospective data analysis

MATERIALS AND METHODS: Standard laboratory practice entailed 30-60 minutes of bed rest following embryo transfer in the procedure room, with extended bed rest the test of the day once leaving the office. This practice was stopped for 2 months and patients were permitted to ambulate immediately with no bed rest recommendation. Outcomes from frozen embryo transfers using a single euploid blastocyst with no bedrest were compared to the same type of frozen embryo transfers from the preceding 6 months with bed rest, as well as to the same 2 month time period 1 year prior with bed rest. All frozen embryo transfers utilized a single blastocyst of at least 3BB quality. No laboratory culture procedures or transfer procedures were changed during this time and examination of the 2 control time periods with bed rest were selected to try to control for other possible variables. Groups were compared using ANOVA and pairwise comparisons.

RESULTS: No significant differences were apparentl in the examined patient demographics (female age, male age, uterine lining thickness). No significant differences in clinical outcomes were apparent between patients who utilized the bedrest paradigm following single euploid blastocyst transfer compared to those who had no bedrest.

	No Bed Rest	Bed Rest – 1 yr prior	Bed Rest- Prior 6 Months
Not preg	(14/86) 16.3%	(8/50) 16.0%	(25/144) 17.4%
+ hCG	(72/86) 83.7%	(42/50) 84.0%	(119/144) 82.6%
Biochemical	(14/72) 19.4%	(5/42) 11.9%	(18/119) 15.1%
Clinical Preg	(58/72) 80.6%	(37/42) 88.1%	(101/119) 84.9%
Avg. Female Age	35.2	36.1	35.9
Avg. Male Age	37.3	37.2	37.8
Avg. uterine lining	9.88	10.5	9.85

CONCLUSIONS: Stopping the practice of extended bedrest following transfer of a frozen/thawed single, high quality euploid blastocyst had no statistically significant impact on the clinical outcomes measured in this study. This has implications for clinical workflow related to embryo transfer procedures.

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DO INSULIN-LIKE GROWTH FACTOR (IGF-1) LEVELS IN INFERTILITY PATIENTS AFFECT IVF OUTCOMES?.

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OBJECTIVE: Since IGF-1 serves as a major effector of growth hormone (GH)-stimulated somatic growth, to determine whether peripheral IGF-1 levels in infertile women prior to IVF cycle start are predictive of IVF outcomes.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We here report on 978 consecutive patients undergoing 1033 IVF cycles at our center between 2018-2020 who, indiscriminately, had peripheral IGF-1 level determinations at time of initial presentation as part of an initial work-up. IGF-1 was tested immunochemiluminometric by commercial assay (LabCorp, Burlington, NC), with normal range for all ages defined as 78-270ng/mL. Patients on human growth hormone (HGH) supplementation and repeat cycles were excluded from the study. Ultimately, 302 (29.2%) fresh non-donor cycles qualified as final study population. Based on IGF-1 levels, these women were divided into 3 subgroups representing lower 25thpercentile (Group A, <132ng/mL, n=64),

25th-75thpercentile (B, 132-202ng/mL, n=164) and upper 25thpercentile (C, >202ng/mL, n=74). Study endpoints were cycle cancellations, oocytes retrieved, embryos transferred, pregnancies and live births after adjustments for age.

RESULTS: IGF-1 distribution was Gaussian. Patients in the lowest IGF-1 quartile (Group A)) were significantly older (43.0 ±4.8 years) than those in mid-range (Group B, 41.3 ±4.9 years) and highest quartile Group C (40.7 ±5.6 years; P=0.019). IGF-1 levels were age dependent. Linear regression revealed that IGF-1 levels decreased with increasing age 2.2 ±0.65 ng/mL per year (P=0.0007). Though not statistically different, trends of ovarian reserve parameters were the best in B (FSH 17.3 ± 17.8 vs. A, 24.8 ±35.3 and C, 18.1 ± 20.6 mIU/mL; P=0.085; AMH 1.4 ± 3.3 vs. A, 0.7 ±1.2 and C, 1.0 ± 1.6; P=0.200). Cycle cancellations were statistically the lowest in C (11.6%), the highest in A (25.0%) and in mid-range in B (13.5%; P=0.042). Oocytes, transferred embryos, pregnancy and live birth rates did not differ significantly, though oocyte numbers trended the highest in B (5.2 ± 5.4 years) vs. 3.6 ± 5.4 (A) and 4.5 ± 5.0 (C). Adjusting statistical assessments for age, the difference of cancelled cycles remained significant (P=0.021), while all other outcome, likely because of too small patient numbers, remained non-significant.

CONCLUSIONS: This study hints at best effects on outcomes of baseline IGF-1 on IVF at mid-range of 132-202 ng/mL, representing lowest cycle cancellations. The study, thus, warrants further exploration of HGH supplementation in women with low IGF-1 levels, usually mostly older patients. Cautious interpretation of here presented results is, however, advised since they in general reflect patients of very advanced ages. Low pregnancy and live birth rates in such patients, moreover, likely, prevented adequate power to inform on pregnancy and live birth rates.

SUPPORT: Intramural funds from The Center for Human Reproduction and Foundation for Reproductive Medicine.

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COMPARING IVF OUTCOMES AND PROVIDER ASSESSMENT OF PATIENT TOLERANCE DURING OOCYTE RETRIEVAL PROCEDURES USING CONSCIOUS SEDATION VERSUS MONITORED ANESTHESIA CARE.

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OBJECTIVE: As in vitro fertilization becomes more widely utilized to treat infertility, oocyte retrieval has become one of the most common minor surgical procedures. With adequate pain control, complete patient immobilization can be achieved, thus improving provider ease.[1] No previous studies have investigated the differences in IVF outcomes, provider ease and patient tolerance for conscious sedation (CS) with midazolam and fentanyl versus monitored anesthesia care (MAC) with propofol.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: A questionnaire was used to document providers' opinions regarding ease of procedure, patient movement and discomfort during oocyte retrievals at the UC Center for Reproductive Health (CRH). The surveys were utilized for a quality improvement project during the transition from CS to MAC from January 2018 to May 2019. After obtaining IRB approval, data was collected regarding the patient's reported level of pain and nausea post procedure, cycle information, oocyte retrieval outcomes and pregnancy rates. Provider assessments and IVF outcomes were compared between the two groups (CS vs MAC). Statistical analysis was performed using multivariate linear and logistic regression using R software, with $p<0.05$ considered significant.

RESULTS: A total of 101 patients were included in the study. Anesthesia during oocyte retrieval was conducted with either CS (n=48) or MAC (n=53). Patient demographics regarding medical diagnosis, cycle information, BMI and age were similar in both anesthesia groups. No statistical difference was found in the number of oocytes retrieved when comparing anesthesia type (p=0.06) or provider score regarding procedure difficulty (p=0.13). A higher BMI predicted increased procedure difficulty amongst both anesthesia types (p=0.001). However, this trend was mitigated in higher BMI patients when using MAC versus CS (p=0.053). Patient reported postoperative pain and nausea were also similar between the types of anesthesia (p=0.54 and p=0.72, respectively). Lastly, no difference in pregnancy outcome was found between anesthesia groups (p=0.63).

CONCLUSIONS: No differences were found between CS and MAC during oocyte retrieval regarding provider ease, patient tolerance or IVF outcomes. Although many fertility clinics have adopted MAC, CS appears to be a suitable alternative for those without readily available anesthesia providers and may be a more cost-effective option. However, consideration should be given to using MAC in higher BMI patients.

References: Vlahos NF, Giannakikou I, Vlachos A, Vitoratos N. Analgesia and anesthesia for assisted reproductive technologies. Int. J. Gynecol. Obstet. 2009;105 (2009) 201–205.

SUPPORT: None.

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PREDICTIVE FACTORS OF AT LEAST ONE EUPLOID EMBRYO ON CUMULATIVE LIVE BIRTH RATES IN PATIENTS 40 YEARS AND OLDER UNDERGOING PRE-IMPLANTATION GENETIC TESTING FOR ANEUPLOIDY.

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OBJECTIVE: In vitro fertilization (IVF) is the recommended first-line treatment of infertility for patients aged 40 and older. However, patients often have a rapidly-declining ovarian reserve and exponentially increasing rate of aneuploidy embryos. We set out to investigate whether the embryonic ploidy outcome of a patient's first cycle is predictive of her cumulative live birth rate (CLBR) from IVF, and if markers of ovarian reserve can aid in that prediction.

DESIGN: Retrospective cohort study of IVF with preimplantation genetic testing for aneuploidy (PGT-A) at an academic fertility center from 2015-2019.

MATERIALS AND METHODS: 298 women age 40 to 45 undergoing their first autologous IVF cycle with PGT-A were included. Anti-mullerian hormone (AMH) and follicle-stimulating hormone (FSH) levels were measured prior to ovarian stimulation. The cycle protocol was individualized to each patient by their respective physician. PGT-A was performed by one laboratory on trophectoderm biopsies from expanded blastocysts. The study patients' cumulative live birth rate (CLBR) was defined as the probability of a live birth from all cycles (first, and subsequent) during the study period. Descriptive statistics, Mann-Whitney U, and tests were computed; $p<0.05$ was considered significant.

RESULTS: Of the 298 women undergoing IVF-PGT-A, 47% resulted in at least one euploid embryo. Younger age and higher AMH levels were associated with at least one euploid embryo ($p<0.001$ and $p<0.001$, respectively). FSH levels did not have a statistically significant effect on producing an euploid embryo ($p = 0.337$). The CLBR was significantly higher in patients who had at least one euploid embryo compared to patients who did not have any euploid embryos (39.3% vs 5.1%, $p<0.001$).

	No Euploid Embryos	At Least One	p
N	158	140	-
Age	41.84	40.84	< 0.001
AMH	1.88	2.78	< 0.001
FSH	8.22	7.77	0.337
CLBR	5.1%	39.3%	< 0.001

CONCLUSIONS: While IVF is the recommended treatment for patients aged 40 and above, the ability to produce at least one euploid embryo in a patient's first cycle is a good prognostic indicator of ability to achieve live birth through autologous IVF.

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OPTIMIZING FROZEN EMBRYO TRANSFER (FET) SUCCESS: IMPROVED SUCCESS IN NATURAL CYCLES WITH THE USE OF HCG TRIGGER DESPITE SIMILAR OVERALL OUTCOMES WITH GONADOTROPIN STIMULATED, NATURAL, AND PROGRAMMED CYCLES. Rhea Chattopadhyay, MD, Rachel S. Weinerman, MD, James H. Liu, M.D., Rebecca Flyckt, MD, Sung Tae Kim, PhD, HCLD, University Hospitals Fertility Center/Case Western Reserve University, Beachwood, OH.

OBJECTIVE: To evaluate reproductive outcomes in FET cycles following hormonally programmed cycles vs alternate regimens of gonadotropin stimulated cycles or natural or letrozole-induced cycles. Within natural and letrozole cycles, pregnancy rates with and without hCG trigger to induce ovulation were compared.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All programmed, natural cycle, letrozole, and gonadotropin stimulated FETs from a single academic center from 2017 – 2020 were evaluated. Programmed cycles consisted of oral micronized estradiol 2 mg TID starting day 1 of menses followed by intramuscular progesterone. Gonadotropin stimulated cycles consisted of ovulation induction with FSH and/or hMG starting on Day 1-5 of menses followed by hCG injection ("trigger"), with vaginal or intramuscular progesterone in the luteal phase. Natural cycles involved no medication in the follicular phase, whereas letrozole cycles consisted of letrozole 5 mg cycle day 3-7. For both natural and letrozole cycles, transfer was timed either to the patient's own ovulation as measured by serum LH and progesterone or by ovulation induced by hCG trigger. Vaginal progesterone was used for luteal support. For the primary analysis, natural and letrozole cycles were included together in the natural group. One way- ANOVA was performed to compare baseline variables between cohorts. Chi-square was used to compare pregnancy outcome variables. Fisher's Exact test was used to compare two groups when appropriate due to sample size. A p value <0.05 was considered significant.

RESULTS: A total of 784 FETs were included: 728 programmed FETs, 24 natural cycle FETs, and 32 gonadotropin stimulated FETs. No statistical difference was found between all 3 cohorts based on age, BMI, endometrial thickness, or number of embryos transferred. Clinical pregnancy rates (CPR) or implantation rates (IPR) did not differ between programmed, natural/letrozole cycles, or gonadotropin stimulated FETs (54.3% vs 41.7% vs 59.4%, p=0.4) (46.3% vs 42.3% vs 48.8%, p= 0.9) respectively. Live birth/ongoing pregnancy rates were also not different (43.3% vs 41.7% vs 56.3%, p=0.3). Additionally, miscarriage rates did not differ between groups (10.3% vs 0% vs 3.1% p = 0.1). A subset analysis of natural cycle FETs showed no difference in letrozole induction versus spontaneous ovulation CPR (40% vs 42.9%, p=0.99), however natural/letrozole cycles with hCG trigger were associated with an increase in CPR (75% vs 25%, p=0.032).

CONCLUSIONS: Our center utilizes stimulated FET cycles as an alternative for patients who do not achieve appropriate endometrial growth with traditional programmed FET. Our findings suggest stimulated FET cycles can be a successful alternative for patients whose lining is not appropriate in a programmed FET cycle. We use letrozole or natural cycle FETs in patients for whom a programmed or stimulated FET is not appropriate, with similar success rates. However, our study suggests use of an hCG trigger may improve outcomes in natural or letrozole cycles.

SUPPORT: None.

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LESSONS LEARNED FROM A 10 YEARS CRYOEMBRYO VITRIFICATION PROGRAM: THE AGE OF THE OOCYTE MATTERS. Carmen Vidal, M.D., Ph.D.,[1] Juan Giles, M.D., Ph.D.,[2] Guillermo Mollá Robles, M S,[3] Ma José de los Santos, PhD,[1] Jose Remohi, MD PhD,[1] Ana Cobo, PhD,[1] [1]IVIRMA Valencia, Valencia, Spain; [2]IVI-RMA Valencia, Valencia, Spain; [3]IVI Foundation, Health Research Institute La FE, Valencia, Spain.

OBJECTIVE: Embryo vitrification has been a breakthrough in assisted reproduction (ART), allowing higher cost-effectiveness of ART cycles by offering a higher number of embryos to be transferred per cycle, given the high survival rate of these embryos. The best-Known prognostic factor for success in fresh ART cycles is the oocyte's age (OA). Our objective is to analyze the influence of OA in the outcome of cryotransferences (CTs) conducted with vitrified embryos.

DESIGN: Retrospective cohort study in a university- affiliated infertility center.

MATERIALS AND METHODS: Ongoing pregnancy rate (OPR) and live birth rate from n= 9246 women undergoing 14442 CTs from January 2007 and December 2017 (6199 from egg donation, 8243 from own oocytes) involving 22263 Emb vitrified, was analyzed depending on the OA. $\chi 2$ test was used for pregnancy rates comparisons. A logistic regression was performed with live birth rate as the response variable and the OA, adjusting for patient age and BMI as well as for the type of CTs, and special analysis was performed considering only OA less than 36 and considering the origin of the eggs. Data are presented as means or proportions (95% confidence intervals).

RESULTS: Total mean OA the day of fertilization of the embryos was 30.78 y (30.69-30.87), from donated CTs OA was 25,90 (25.79-26.01), own oocytes CTs OA 34,45 (34.37-34.52), and mean receiver's age 38.03 y, embryo survival 97,29 %(97.13-97.46), 1.84 embryos warmed (1.81-1.85), 1.54 embryos transferred (1.53-1.55). Biochemical pregnancies, clinical pregnancy, and OPR/warming cycle were 54,29 %(53.47-55.10), 44.55%(43.74-45.37), and 35.09 %(34.31-35.88).

According to the model, for each year-increase in the OA, the odds of achieving a live birth rate (LBR) decrease by 1.83 % (OR 0.981.95 % CI 0.97-0.99, p< 0.001). In the younger group (until OA 35 y), the change from donated to own oocytes was found to have a statistically significant effect (OR 0.85 CI 95 %; 0.78-0.06, p=0-01), diminishing the odds of having an OPR by 14%.

CONCLUSIONS: OA is a key prognostic factor in the outcome of vitrification CTs program. OA yields a clear annual negative impact on OPR. In younger OA group, the fact that they come from egg donors and not from own oocytes equally affects the results. Increasing the number of embryos transferred should be taken in consideration for elder women according to these data.

SUPPORT: none.

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TROPHECTODERM MORPHOLOGY IN EUPLOID EMBRYOS IS RELATED TO INFERTILITY DIAGNOSIS AND PREGNANCY OUTCOME AFTER TRANSFER. Nicole D. Ulrich, MD,[1] Ashley Hesson, MD, PhD,[2] Anne Waldo, MS,[3] Erin Inman, M.D.,[2] Micaela J. Stevenson, BS,[4] Molly B. Moravek, MD, MPH,[3] Samantha B. Schon, MD, MTR,[1] Min Xu, Ph.D,[3] [1]Reproductive Endocrinology and Infertility, University of Michigan, Ann Arbor, MI; [2]University of Michigan, Obstetrics and Gynecology, Ann Arbor, MI; [3]University of Michigan, Ann Arbor, MI; [4]University of Michigan Medical School, Ann Arbor, MI.

OBJECTIVE: A number of studies have shown that both day 3 and day 5 embryo morphology correlates with ongoing pregnancy rate and live birth rate. However, in the era of single euploid embryo transfer, few studies are available regarding effect of inner cell mass (ICM) and trophectoderm (TE) morphology on pregnancy outcomes after euploid transfer. We aimed to evaluate pregnancy outcomes, including live birth, as they relate to embryo characteristics and morphology.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: We reviewed all single euploid embryos transfers in an academic fertility clinic by retrospective chart review from January 1, 2016 through August 31, 2018. Blastocyst morphology was evaluated by Gardner grading system. PGT-A was performed using a next generation sequencing platform. Variables assessed included blastocyst expansion level (EL), ICM grade, TE grade, patient age at retrieval, number of oocytes retrieved, infertility diagnosis, pregnancy (serum hCG), ongoing pregnancy (fetal cardiac activity) and pregnancy outcome. Logistic and linear mixed models with random intercepts to account for within-patient correlation were used to evaluate association between predictors and outcomes. All models were adjusted for age at retrieval and BMI.

RESULTS: We evaluated embryo morphology in 341 single euploid embryo transfers including EL 3-6 (9 embryos were EL 3, 14 EL 4, 285 EL 5, 32 EL 6), ICM grade (136 A and 205 B), and TE grade (94 A, 222 B, 25 C). Pregnancy rate (positive serum hCG/total transfers) was only correlated with TE grade and was significantly lower in TE grade C (40%) transfers when compared to A and B (67%, 73%); (p=0.003, OR 0.3; 0.1-0.6). There was no difference in pregnancy rate between blastocysts frozen on day 5 vs 6. However, after a positive HCG, transfer of day 6 blastocyst was negatively associated with ongoing pregnancy (p=0.02; OR 0.3; CI 0.2-0.7). TE grade, ICM grade, and EL of blastocyst were not predictive of ongoing pregnancy after positive HCG. When TE grade C embryos resulted in pregnancy, subsequent live births were similar at 60% compared to grades

A and B (71%, 62%). Of 12 spontaneous abortions in our cohort, there were none in the TE grade C group; unsuccessful pregnancies in this group were all classified as biochemical. The mean proportion of TE grade C embryos compared to total embryos created per fresh cycle was 17.4%. Unexplained infertility diagnosis was an independent predictor for a higher proportion TE grade C embryos per fresh cycle (p=0.02). There was no correlation between number of oocytes retrieved and proportion of TE grade C embryos.

CONCLUSIONS: Euploid embryos with poor TE morphology occur more often in unexplained infertility. While pregnancy rate and initial HCG level is lower in embryos with poor TE morphology, ongoing pregnancy rates are similar, and live births occur. Setting appropriate expectations is key when counseling patients prior to single euploid embryo transfer. It is important that we understand subtle differences in expected outcomes based on embryo characteristics and morphology.

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CLEAVAGE STAGE OR BLASTOCYST STAGE - WHAT IS THE OPTIMAL STAGE OF FROZEN EMBRYO TRANSFER IN PATIENTS WITH PREDICTED POOR OVARIAN RESPONSE AFTER UNDERGOING IN VITRO FERTILIZATION WITH MILD OR MINIMAL STIMULATION?.

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OBJECTIVE: To determine outcomes between cleavage versus blastocyst stage frozen embryo transfers (FET) in women with predicted poor ovarian response (POR) after mild/minimal stimulation

DESIGN: Retrospective cohort analysis.

MATERIALS AND METHODS: Women with predicted POR by the Bologna criteria underwent mild/minimal stimulation in vitro fertilization treatment with oocyte retrieval and frozen embryo accumulation, followed by FET at a single academic center from 2012 to 2018. Only first and second FET cycles were assessed. Patients with both blastocyst and cleavage stage transfer across cycles were excluded. 420 FET cycles were reviewed; 88 cycles met inclusion criteria. Statistical analysis was performed using independent t test and χ^2 test as appropriate. $P < 0.05$ was considered statistically significant.

RESULTS: While there was no difference in AMH, the basal FSH was significantly higher, the mean age was significantly older, and the duration of infertility was significantly shorter in the cleavage compared to the blastocyst stage FET group. There was no difference in number of embryos transferred; however, more oocytes were retrieved per stimulation in the blastocyst FET group. There was a 60% live birth rate (LBR) after preimplantation genetic testing (PGT) in the blastocyst FET group, but sample size was small (n=5). Clinical pregnancy rate (CPR) and LBR were higher after blastocyst compared to cleavage stage FET, but differences were not statistically significant. There were no differences in birth weight. Birth defects were not reported in either group.

Table 1

	All cycles	Cleavage stage	Blastocyst stage	*P* value
Age (y)	39.1±3.6	40.6±2.9	38.0±3.7	<0.05 *
BMI (kg/m^2)	26.8±5.0	27.6±5.5	26.1±4.6	NS
AMH (ng/mL)	0.7±0.4	0.7±0.6	0.6±0.3	NS
Basal FSH (IU/mL)	13.2±8.7	17.3±10.8	10.2±4.9	<0.05 *
Gravidity	1.1±1.3	1.0±1.3	1.2±1.3	NS
Months of infertility	41.3±32.8	33.2±15.6	47.1±40.1	<0.05 *
# Oocytes retrieved	3.2±1.7	2.8±1.5	3.6±1.9	<0.05 *
# Embryos transferred	1.7±0.6	1.6±0.5	1.7±0.6	NS
Cycle 1 (n)	67	26	41	
CPR (%)	49.3	34.6	58.5	NS
LBR (%)	41.8	26.9	51.2	NS
Cycle 2 (n)	21	11	10	
CPR (%)	47.6	36.4	60.0	NS
LBR (%)	19.0	9.1	30.0	NS
Birth weight (g)	3351.9±596.5	3537.2±295.8	3283.7±668.4	NS

CONCLUSIONS: There is paucity of data regarding optimal day of FET in POR patients after mild/minimal stimulation due to difficulty in randomization. Counseling should be guided by the patient's age, number of oocytes retrieved, cumulative number of embryos obtained, and other clinical parameters. Although PGT is associated with higher LBR in patients >35, there has been no proven benefit in POR patients. Mild/minimal stimulation remains a useful tool for patients with predicted POR who undertake FET, with acceptable LBR regardless of the stage of embryo transfer.

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EVALUATING THE EFFECTS OF OOCYTE COHORT SIZE AND MATURITY IN ANTAGONIST IVF CYCLES ON FERTILIZATION, CLEAVAGE, BLASTULATION, AND HIGH-QUALITY EMBRYO FORMATION.

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OBJECTIVE: Study aim was to determine whether number of oocytes retrieved and oocyte maturity rate following antagonist protocol IVF cycle affected the following outcomes: fertilization, cleavage, blastulation, and high-quality blastocyst formation rates.

DESIGN: Single center, retrospective study involving 240 infertile women undergoing a total of 261 completed oocyte retrievals in 2018.

MATERIALS AND METHODS: Based upon prior literature we divided our patients into 3 cohorts, grouped by number of oocytes retrieved: Group 1 with <10 oocytes, Group 2 with 10-15 oocytes, and Group 3 with >15 oocytes. Various predictive factors of high-quality blastocyst formation have been reported. For this study we collected the following data variables: age, BMI, baseline AMH level, TSH, total FSH stimulation dose, use of HCG during stimulation, trigger drug used, estrogen level on day of ovulation trigger, number and size of follicles, number of oocytes retrieved, number of mature oocytes, fertilization rate, cleavage rate, blastulation rate, and rate of high-quality blastocysts. For fertilization and cleavage rates, the denominator was total oocytes retrieved. For blastulation and high-quality blastocyst rates, the denominator was total fertilized. Utilizing total fertilized as our dominator eliminated poor fertilization secondary to lower oocyte maturity as a confounder. Kruskal-Wallis test was used to compare the median rate of variables.

RESULTS: Significant differences between the groups with relation to age at retrieval, baseline AMH, estrogen level day of retrieval, total FSH stimulation dose, and trigger drug administered. These differences were anticipated and reflect known variances in IVF stimulation across the ovarian reserve spectrum.

With regards to cohort maturity, group 3 had significantly less mature oocytes, median rate of 74% mature, compared to group 2 with median rate of 81% of oocytes being mature. When comparing fertilization rate, cleavage rate, and blastulation rate there was no difference between the three groups.

There was significant difference in formation of high-quality blastocyst between group 1 and group 3 with a median rate of 63% and 53% respectively. Group 2 formed high-quality blastocyst 62% of the time, similar to Group 1. However, this was not statistically different from Group 3, likely due to population size.

CONCLUSIONS: Cohorts with >15 oocytes have reduced oocyte maturity. This marker for reduced cytoplasmic maturity is manifesting in a 9-10% lower median rate of high-quality blastocyst formation. Interestingly, the fertilization rate, cleavage rate, and blastulation rate are unaltered in these oocytes. However, additional studies on the implantation potential, ongoing pregnancy rates, and live birth rates is needed to understand if reduced cytoplasmic maturity has additional downstream effects aside from high-quality blastocyst formation. Additionally, our data offer reassurance to women who have lower than average oocyte cohort recruitment. While total oocyte yield is suboptimal, the rate of high-quality blastocyst formation remains high with a median rate of 63%.

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BIRTH OUTCOMES FROM ACUPUNCTURE ADDED TO FROZEN EMBRYO TRANSFER (FET) OF AUTOLOGOUS EMBRYOS WITHOUT GENETIC SCREENING: A RETROSPECTIVE COHORT STUDY. Lee Hullender Rubin, DAOM,[1] Carmelo S. Sgarlata, M.D.,[2] Morgan Hogue, MAcOM,[2] Lisa Pate, MAcOM,[2] Elizabeth Richards, MAcOM,[2] Lisa K. Tongel, MAcOM,[2] Hong Jin, DAOM, MD(PRC),[3] [1]Osher Center for Integrative Medicine University of California San Francisco, San Francisco, CA; [2]ORM Fertility, Portland, OR; [3]Oregon College of Oriental Medicine, Portland, OR.

OBJECTIVE: For patients who underwent Frozen Embryo Cycles (FET) of autologous embryos without any genetic screening, our objective was to assess birth outcomes between patients with no known additional therapies compared with the addition of two distinct acupuncture approaches varying in dose (2 sessions or ≥3 sessions) and treatment (standardized or individualized).

DESIGN: Retrospective cohort study of patient charts from a single, private clinic and matched charts from affiliated acupuncturists' clinics.

MATERIALS AND METHODS: The fertility clinic contracted with six acupuncture associates to perform day of embryo transfer acupuncture (ET Acu) onsite. Charts were reviewed of women who completed an FET cycle of autologous embryos with no genetic screening and with or without ET Acu between July 2016 and December 2018. The acupuncturists also extracted data from charts from their community clinics of shared fertility clinic patients who added acupuncture prior to embryo transfer (ET). Data was matched by name and ET date then merged with the fertility clinic database for analysis. Cycles with gestational carriers, donor eggs, no transfer, or embryos with chromosomal screening were excluded. Patient groups were categorized as 1) usual care for women who completed FET alone (UC group); 2) UC and ET Acu of two standardized acupuncture sessions before and after ET (ET Acu group); and 3) UC, ET Acu and acupuncture therapy received in the community prior to ET that included Traditional Chinese Medicine therapies such as diet and lifestyle modifications, warming therapy, or if appropriate, Chinese herbal therapy (TCM group). Comparability between groups was assessed by age and number of embryos transferred. Differences in means were assessed using one-way analysis of variance and proportions by Chi-square analysis. Main outcome measure was live birth.

RESULTS: We identified 275 FET cycles with 181 in UC, 33 in ET Acu, and 61 in TCM. Mean age was not comparable between groups: 35.8 ± 4.6 in UC, 37.6 ± 4.9 in ET Acu, and 37.3 ± 6.0 in TCM (*p=0.04*). The UC, ET Acu and TCM groups were comparable on mean number of embryos transferred (1.48 ± 0.5, 1.42 ± 0.5, and 1.49 ± 0.5, respectively, *p=0.82)*. The proportion of live births by group was 50.5% in UC, 33.3% in ET Acu, and 59.0% in TCM. The association in the proportion of live births between UC and ET Acu groups trended towards significance (*p=0.07*), but there was no difference between UC and TCM (*p=0.25*). However, TCM was associated with more live births when compared with ET Acu (*p=0.02*). Miscarriage rates were 12.5% in UC, 12.1% in ET Acu, and 6.6% in TCM, and no associations were observed with this outcome (UC vs ET Acu *p=0.95*, UC vs TCM *p=0.20*, TCM vs ET Acu *p=0.36)*.

CONCLUSIONS: Three or more acupuncture sessions were associated with more FET live births compared with two sessions in women with unscreened embryos, but not FET alone. These observations are limited by small group numbers of women who differed from those who did FET alone. Future investigations should assess individualized acupuncture in a prospective, randomized trial to determine the appropriate dose of acupuncture needed to support FET.

SUPPORT: No financial support to disclose.

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ELECTIVE DOUBLE EUPLOID EMBRYO TRANSFER IN ADVANCED MATERNAL AGE COUPLES – IS THERE A BENEFICIAL ROLE?. Krishna Mantravadi, Sr., MBBS, PGDHOM, Masters in clinical embryology,[1] Vijay Kumar Sharanappa, Sr., MBBS, MD, MCE,[2] Sarvani Bellala, II, M.S. Biomedical Genetics (Spl. in GC) B.S.(BC, BT & HG),[1] Durga Gedela Rao, Sr., MRCOG,[1] Sandeep Karunakaran, Sr., MS, PGDHM, PGDMLE,[1] [1]Oasis fertility, Hyderabad, India; [2]Oasis Fertility, Hyderabad , Telangana, India.

OBJECTIVE: Is there a beneficial role for elective euploid double embryo transfer(e-DET) in Advanced Maternal Age (AMA) couples to optimize reproductive outcomes?

DESIGN: This retrospective case series study was done from May 2014 to May 2019 at a Private Teaching Fertility Clinic. A total of 51 AMA (Age ≥ 37 years) in our study group and 181 young (Age < 37 years) patients in control group underwent Intracytoplasmic Sperm Injection(ICSI), Trophectoderm(TE) biopsy and Next Generation Sequencing(NGS). Patients who at least had two euploid embryo were considered in this study. Based on the number of embryos transferred in Frozen Embryo Transfer cycle (FET) patients were divided into eSET group and eDET group.

MATERIALS AND METHODS: All In-Vitro Fertilization (IVF) patients who underwent Pre-Implantation Genetic Testing for Aneuploidy (PGT-A) were divided into 2 groups depending on number of embryo/s transferred. Decision on the number of embryos for FET was taken by the couples after discussion with the clinicians about the risks and benefits. A written consent was obtained for the same. Reproductive outcomes of the study group were compared with control group.

Group 1 (eSET) – AMA (n = 32) Vs Young (n = 147)

Group 2 (eDET) – AMA (n = 19) Vs Young (n = 34)

Following reproductive outcomes were compared - Implantation Rate (IR), Clinical Pregnancy Rate (CPR), Miscarriage Rate (MR), Multiple Pregnancy Rate (MPR), Live Birth Rate (LBR)

RESULTS: Mean of the Reproductive outcomes with eSET in Study Vs Control group were as follows:

CPR – 65.63% Vs 65.99% (**P = 0.96**)
IR – 68.75% Vs 67% (**P = 0.84**)
MR – 15.63% Vs 10.88% (**P = 0.45**)
MPR – 0% Vs 0.68% (**P = 0.64**)
LBR – 50% Vs 55.10% (**P = 0.60**)

Mean of the Reproductive outcomes with eDET were as follows:

CPR – 78.95% Vs 82.35% (**P = 0.76**)
IR – 47.36% Vs 53% (**P = 0.57**)
MR – 21.05% Vs 14.71% (**P = 0.57**)
MPR – 15.78% Vs 2.94% (**P = 0.09**)
LBR – 57.89% Vs 67.65% (**P = 0.48**)

When considering Euploid embryos for transfer, AMA women or younger women had comparable reproductive outcomes with eSET or eDET.

In spite of transferring two euploid embryos the IR was still lower in eDET group (when compared with eSET) and there was no statistical significance with LBR. Higher multiple pregnancies in AMA group poses higher risk for maternal morbidity and mortality.

AMA women with euploid embryos should be counselled for eSET as there is no added benefit with eDET.

CONCLUSIONS: Transferring two euploid embryos in advanced maternal age women doesn't optimize reproductive outcomes. Even in AMA women eSET policy is recommended.

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WITHDRAWN

P-549 4:30 PM Monday, October 19, 2020

IS THERE A CORRELATION BETWEEN ENDOMETRIAL THICKNESS AND IVF OUTCOMES?. Magdalena Decia, MD, Dana Kimelman, MD MS-RSM, Lucia Abulafia, MD, Gabriel A. De la Fuente, MD Centro de Esterilidad Montevideo, Montevideo, Uruguay.

OBJECTIVE: Endometrial thickness (ET) has been traditionally used as predictor of reproductive outcomes in fresh and frozen-thawed embryo transfer (FET) cycles in patients undergoing in-vitro fertilization (IVF). Multiple studies have been conducted to evaluate endometrial thickness as an independent predictor of outcomes. Findings have shown conflicting results. Given the discrepancies in the literature, the aim of this study is to evaluate the relationship between endometrial thickness and IVF outcomes with different endometrial preparation protocols. We hypothesized there is an optimal endometrial thickness value to predict pregnancy.

DESIGN: Retrospective, single center study performed from January 2017 to march 2019.

MATERIALS AND METHODS: Autologous and egg donor FET and fresh egg donor ET cycles were included. Both natural and artificial endometrial preparation protocols were used. Women with known intrauterine anomalies, ectopic and biochemical pregnancies were excluded. For the purpose of the analysis, patients were categorized into 3 groups: autologous FET (n=141), egg donor fresh embryo transfers (n=142 patients), egg donor FET (n=99). Data was obtained from medical records. Endometrial thickness (defined as the distance between the echogenic interfaces of the myometrium) was measured the day progesterone supplementation was initiated (5-6 days before ET). The impact of endometrial thickness on pregnancy (hCG $>$ 20 IU/L), live birth and pregnancy loss rates were analyzed. All analyses were conducted using jupyter-notebooks, with python 3.6 as the main tool for the development of descriptive statistics. A p value $<$0.05 was considered significant. Cutoff values of endometrial thickness were proposed every 1mm, from 5 mm to 11 mm. An optimal endometrial thickness value was proposed as a predictor of pregnancy.

RESULTS: A total of 382 patients were included. Mean age was 38.6 $\pm$ 5.4. The overall pregnancy rate was 49,74%, miscarriage rate 19,47% and live-birth rate 39,5%. The mean endometrial thickness was 8.5 mm (SD: 1.95). The optimal cutoff value for the total n was 8.0 mm (p=0.013). For fresh and frozen egg donor cycles endometrial thickness cutoff was $\geq$8.5mm (p=0.036 and p=0.002 respectively). In autologous oocyte FET there was no significant difference in pregnancy (p=0.22), miscarriage or live-birth rates. Our data does not show a cutoff value to predict miscarriage or live birth. When submitted to a multivariate logistic regression analysis in which demographic variables where included (i.e age, number of oocytes retrieved, MII oocytes, number of fertilized oocytes, number of blastocysts available), endometrial thickness no longer remained as an independent predictor of pregnancy rates (p=0.43).

CONCLUSIONS: Our results show pregnancy rates increase when endometrial thickness is $\geq$8.5mm in egg donor cycles. This finding no longer remains significant after controlling for potentially relevant confounders, this finding may be due to the small sample. Further research is needed to elucidate if endometrial thickness is a critical predictor of pregnancy rates and live birth.

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MICROFLUIDIC SPERM SORTING VS. DENSITY GRADIENT: A PRELIMINARY ANALYSIS EXAMINING EMBRYO GRADE AND PREGNANCY OUTCOMES IN IVF-ICSI CYCLES USING VARYING SPERM SELECTION METHODS. Zoran J. Pavlovic, M.D.,[1] Megan R. Sax, MD,[2] Alex Tawa, B.S.,[3] Lauren Grimm, M.A.,[4] Nepheli I. Raptis, B.A., M.A.,[4] Jessi Anderson, MPH,[4] Emma Radley, M.A.,[4] Hanna Mandell, M.A.,[4] Christy Oso, B.A.,[4] Angeline Beltsos, MD,[4] Roohi Jeelani, MD,[4] [1]Rush University Medical Center, Chicago, IL; [2]University of Cincinnati and Cincinnati Children's Medical Center, Cincinnati, OH; [3]Midwestern University Chicago College of Osteopathic Medicine, Downers Grove, IL; [4]Vios Fertility Institute, Chicago, IL.

OBJECTIVE: To determine differences in embryo quality and clinical pregnancy rates in cycles using microfluidic sperm sorting as compared to cycles using density gradient centrifugation.

DESIGN: Male factor infertility is estimated to be the sole cause of infertility in nearly 20% of couples. In the presence of normal semen parameters, male infertility may be overlooked. DNA fragmentation tests have been recently utilized to allow for a more comprehensive analysis of male factor infertility for ongoing unexplained infertility and to evaluate sperm quality. Microfluidic sperm sorting methods may allow for selection of healthy sperm, including those with less DNA fragmentation and reactive oxygen species. This is a promising area of investigation to improve pregnancy rates and clinical outcomes for couples undergoing assisted reproductive technologies (ART).

MATERIALS AND METHODS: A retrospective cohort analysis was performed on patients who underwent density gradient IVF-ICSI cycles followed by microfluidic sperm sorting IVF-ICSI cycles. Baseline characteristics included paternal and maternal age, BMI, primary infertility diagnosis and semen analysis. The primary outcome was embryo grade using the Gardner scale that was organized into high (3-6 AB or AA), medium (2-6 BB or BA) and low grade (any embryo with an Expansion Grade of 1 as well as 2-6 BC, CB or CC) groups. The secondary outcome measured was clinical pregnancy rate. Results were analyzed by chi-square test of association.

RESULTS: Patients that underwent both density gradient and microfluidic sperm sorting IVF-ICSI cycles were identified. Within this patient population, 373 and 376 MII oocytes underwent ICSI with microfluidic and density gradient selected sperm, respectively. 73.5% (274/373) of microfluidic IVF-ICSI embryos and 74.2% (279/376) of density gradient IVF-ICSI embryos developed to day 4 of incubation before being classified as either arrested/morula or receiving a grade. All embryos that did not incubate past day 3 were excluded from analysis. There was no significant difference in the quantity of embryos that developed beyond a day 4 morula/arrested classification and achieved blastocyst status between the two groups. Similarly, there was no significant difference between the two groups in terms of the number of embryos that were cryopreserved (34.3% vs. 30.0%), transferred (4.7% vs. 5.0%) or discarded (65.7% vs. 70.0%), respectively. When comparing embryo quality there was no significant difference between the number of blastocysts rated as high (29.4% vs. 25.2%), medium (36% vs. 29.5%) or low

(34.6% vs. 45.3%) quality between the two groups. Finally, out of the embryos that were transferred, only 23% (3/13) in the microfluidic group and 7.1% (1/14) in the density gradient group achieved a clinical pregnancy which was not a statistically significant difference.

CONCLUSIONS: There is no significant difference in embryo quality or clinical pregnancy rate between microfluidic sperm sorting IVF-ICSI vs. density gradient selected IVF-ICSI cycles. Both methods are promising options to improve clinical outcomes for patients undergoing ART.

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SUPPORT: This study received no financial support.

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THE EFFECT OF MODIFIABLE RISK FACTORS ON IMPLANTATION SUCCESS FOLLOWING IN-VITRO FERTILIZATION: A RETROSPECTIVE COHORT.

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OBJECTIVE: The objective of this study was to examine how modifiable factors, specifically Body Mass Index (BMI) and smoking status, impact the ability to generate a serum detectable pregnancy following in-vitro fertilization (IVF) treatment.

DESIGN: This is a retrospective cohort study over nine years of IVF data from a fertility clinic in Lexington, KY.

MATERIALS AND METHODS: Over 1200 patients with age range 24-44years old and BMI range 17-47 were analyzed over 9 years. They were divided into current smoker and current non-smoker. Both fresh and frozen embryos were used, and the number transferred in each cycle was 1-3 embryos. Pregnancy was defined as a positive serum beta human chorionic gonadotropin (hCG) greater than 5mIU/mL at 2 weeks after egg retrieval. Those who used egg donors, had Ovarian hyper-stimulation syndrome, or lacked data on the factors of interest were excluded. A logistic regression model, including BMI, smoking status, and age as potential explanatory variables was used with p-value of less than 0.05 considered significant. All analyses were completed in SAS 9.4

RESULTS: As expected, there was an effect of age on pregnancy success as defined by a positive beta hCG and was included in the final data. However, the results show no significant impact of BMI or smoking status on pregnancy success following IVF. The results are summarized in the table below:

Factor	Test Statistic (Degrees of Freedom), p-value	Odds Ratio Estimates, with 95% confidence interval
BMI	$X^2(1) = 0.00$, (p= 0.9530)	1.000 (0.981, 1.020)
Smoking	$X^2(1) = 1.39$, (p= 0.2384)	1.296 (0.842, 1.992)
Age	$X^2(1) = 25.02$, (p= <0.0001)	0.938 (0.915, 0.962)

CONCLUSIONS: There are numerous factors that influence the fertility potential for a woman. Many of these are out of their control including; ovarian reserve, tubal factor, uterine factor, and male factor. However, there are also modifiable lifestyle factors that have been previously shown to impact fertility, including Body Mass Index and smoking status. The fact that both elevated BMI and smoking has resulted in altered follicular fluid contents with increased leptin and cotinine levels respectively, suggests that this could also impact the molecular ability of the oocyt to function and implant. However, because no significant difference was found between BMI nor smoking status on the resulting early pregnancies following IVF, this suggests that these modifiable lifestyle factors may have greatest impact on maintaining a pregnancy, but not necessarily as important for actual implantation and establishment of a pregnancy.

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A MODIFIED PROGESTIN PRIMED OVARIAN STIMULATION PROTOCOL FOR PREDICTED POOR RESPONDERS IN IVF/ICSI.

He Cai, M.D., Li Tian, M.D., Ting Wang, M.D., Juanzi Shi, M.D., Ph.D. Northwest Women's and Children's Hospital, XI'AN, China.

OBJECTIVE: A novel modified progestin primed ovarian stimulation (mPPOS) protocol (administrating medroxyprogesterone acetate (MPA) in the late follicular phase) has been described to adequately prevent premature ovulation and yield comparable number of retrieved and vitrified oocytes in oocyte donor cycle. The aim of the study was to test the hypothesis that a low-cost regimen of mPPOS is similarly effective or only slightly worse than GnRH-antagonist regimen in predicted poor ovarian responders.

DESIGN: A prospective cohort study associated with a cost-effectiveness analysis.

MATERIALS AND METHODS: Infertile women with less than 10 antral follicles undergoing planned freeze-all cycles were recruited. Ovarian stimulation was started with 150-225IU of gonadotropin on the second day of cycle. Each eligible patient could choose whether to undergo either a single cycle of the mPPOS or GnRH antagonist regimen. MPA (10 mg) or GnRH antagonist (0.25 mg) (mPPOS group/GnRH antagonist group) was given daily when the leading follicle reached 14 mm and continued until the day of ovulation trigger. Viable embryos were cryopreserved for later frozen-thawed embryo transfer in both groups. Multiple linear regressions analysis was performed to search for a correlation between individual characteristics and the number of retrieved oocyte. Primary outcome was the number of oocytes retrieved. Secondary outcomes included the incidence of premature LH surge, duration of stimulation, total gonadotropin use, embryological laboratory outcomes and direct medical costs.

RESULTS: We included 53 eligble women who had stimulation cycle performed with either a mPPOS (n=26) or an antagonist (n=27). The number of oocytes retrieved and viable embryos were similar between two groups (5.0±4.0 vs 4.8±3.6; 2.9±2.7 vs 2.4±2.1; P>0.05). No significant differences were observed in the duration of stimulation and total gonadotropin consumption. No premature LH surge occurred in either group. Only female age ($p = 0.001$) was associated with the number of retrieved oocytes in the multiple regression model. In the cost-effectiveness analysis, the mPPOS protocol was strongly dominant over the antagonist protocol.

CONCLUSIONS: Progestin used later is feasible and effective in ovarian stimulation for predicted poor ovarian responders without intent to fresh embryo transfer. Current GnRH antagonist and mPPOS protocols were associated with similar results but the economic analysis was in favor of latter one. There was no statistically significant difference might be due to the sampling size. Large randomised controlled trials are needed to further confirm.

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ROLE OF BLASTOCYST MORPHOLOGY IN PREDICTING CLINICAL OUTCOMES IN SINGLE FROZEN BLASTOCYST TRANSFERS. Gaurav Majumdar, MCE, PhD, Sonal Sehgal, MBBS, MD, Sir Ganga Ram Hospital, New Delhi, India.

OBJECTIVE: To assess the value of individual blastocyst morphological parameters in predicting clinical outcomes in single frozen blastocyst transfers.

DESIGN: A retrospective cohort study in which, 1046 frozen embryo transfers (FETs), performed between June 2015 and June 2019, were analyzed.

MATERIALS AND METHODS: Only autologous, single, frozen blastocyst transfers with female age $\leq$ 38 years were included in the analysis. Those FET cycles were excluded in which, either, partially damaged blastocysts or blastocysts that failed to show any re-expansion post warming, were transferred. All frozen thawed blastocysts included in the analysis were originally graded prior to vitrification, on day 5 or 6 of culture, on the basis of morphology and individual scores were assigned to each blastocyst in terms of degree of expansion, inner cell mass (ICM) and trophectoderm (TE) cells using the Gardner and Schoolcraft scoring system. Multi-collinearity test and logistic regression analysis was used to study the relationship between blastocyst morphology and FET cycle outcomes.

RESULTS: Univariate analysis showed that there is very little correlation between blastocyst morphology and the likelihood of implantation or that of a pregnancy loss, subsequently. Multivariate analysis showed that implantation rates were highest when a blastocyst with the following combination, having degree of expansion = 5, ICM = A and TE = A, was transferred. For all other combinations, little or no association was observed with both, implantation rates and pregnancy loss rates. Outcome prediction using logistic regression showed that grade 5 hatching blastocyst was the only statistically significant variable in predicting implantation. Prediction accuracy of 55.1% and 33.8% was observed for implantation and pregnancy loss, respectively.

CONCLUSIONS: Our data shows that none of the parameters used to assess morphology were predictive of implantation for frozen blastocysts. The pregnancy loss rates were also found to be same irrespective of morphology or degree of expansion. Prediction accuracy of 33% for pregnancy loss showed that blastocyst morphology in no way governed the clinical likelihood of a pregnancy loss.

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PLATELET RICH PLASMA (PRP) CAN IMPROVE PREGNANCY OUTCOME IN PATIENTS WITH RECURRENT IMPLANTATION FAILURE (RIF) AND THIN ENDOMETRIAL LINING. Janelle M. Jackman, MBBS,[1] Shelena Ali-Bynom, M.D., M.P.H,[2] Alex Amberg, M.D.,[2] John Zhang, MD, PhD,[3] Lana Lipkin, M.D.,[3] Meir Olcha, M.D.,[3] Zaher Merhi, MD, HCLD,[3] [1]New Hope Fertility Center, New York, NY; [2]The Brooklyn Hospital Center, Brooklyn, NY; [3]SUNY Downstate University and New Hope Fertility Center, New York, NY.

OBJECTIVE: Autologous PRP has recently had a considerable attention as a new modality in assisted reproductive technology. PRP contains many chemicals such as growth factors, cytokines, chemokines, adhesive proteins, and integral membrane proteins that contribute to cell growth and proliferation. This study aimed to report the efficacy of autologous intrauterine PRP on clinical pregnancy rate (CPR) in patients with history of recurrent implantation failure and in women with persistently thin endometrial lining thickness (EMT) following frozen single embryo transfer (ET)

DESIGN: Retrospective data analysis at a large fertility center with university-based affiliation.

MATERIALS AND METHODS: Women (n=16) with recurrent implantation failure (3 or more failed ET) or with more than two cancelled ET cycles due to thin EMT (<7 mm) were included. Women with any known endometrial problem such as Asherman's syndrome, congenital uterine anomalies or any known causes of implantation failure were excluded from the study. The PRP (0.5- 1 mL) was prepared from the patient's own peripheral blood using centrifugation techniques and infused by catheter inside the uterus 2-3 days prior to the ET. Vaginal progesterone was used for luteal phase support. CPR was calculated following the PRP infusion with clinical pregnancy defined as the presence of a fetal heartbeat at 6-7 weeks of gestation. Data are expressed as mean $\pm$ sem. Chi-square test was performed for comparison of CPR before and after PRP infusion.

RESULTS: The 16 patients who met the inclusion criteria had CPR of 0% in the cycle treatment before PRP intrauterine infusion. The age of all the participants was 41.8 $\pm$ 1.3 years. 13 patients had ET at the blastocyst stage and 3 patients had ET at the cleavage stage of embryo development. The EMT on the day vaginal progesterone was started ranged from 5-10 mm (7.3 $\pm$ 0.4 mm). Of the 16 patients, 31.2% had positive serum b-HCG levels; 80% of which had an ongoing clinical pregnancy ($p<0.05$ compared to CPR before PRP) and 20% had an early spontaneous miscarriage or a chemical pregnancy.

CONCLUSIONS: These preliminary data suggest that PRP intrauterine infusion can improve pregnancy outcome in women with recurrent implantation failure or persistently thin EMT. Larger randomized clinical trials are needed to confirm our findings and further basic science research is needed to determine the exact mechanism by which PRP improves endometrial receptivity.

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ASSOCIATION BETWEEN AGE AND ESTRADIOL/ PROGESTERONE INDEX WITH GOOD QUALITY BLASTOCYSTS. Marianna Pérez-Vargas, M.D.,[1] Jose I. Obeso Montoya, PhD,[1] Roberto Santos, M.D.,[1] Patrizio Pasquale, MD, MBE, HCLD,[2] Arnoldo Gonzalez, M.D.,[3] Salomon Alvarado, MD,[1] Edelmiro Garza-Padilla, M.D.[1] [1]IECH, Monterrey, NL, Mexico; [2]Yale Fertility Center, Orange, CT; [3]RESIDENTE SEGUNDO AÑO, MONTERRY, NL, Mexico.

OBJECTIVE: To determine if female age and the estradiol/progesterone index measured on the day of hCG administration is a predictive factor for blastocyst quality.

DESIGN: A retrospective, cross-sectional, and descriptive study.

MATERIALS AND METHODS: Patients attending our private fertility clinic between January 2018 and December 2019 were included and factors as female age (up to 39 years old), AMH, number of MII oocytes, fertilization rate, number and quality of blastocyst-stage embryos (using the Istanbul Consensus scoring system) were evaluated. Male factor and women with diminished ovarian reserve were excluded. The estradiol/progesterone index was determined on the day of hCG administration by calculating the progesterone value multiplied by one thousand and dividing the estradiol value over the progesterone result. The analysis used a multivariable regression model and receiver operator curve to evaluate the association between the clinical parameters.

RESULTS: Seventy-four cycles and 181 blastocyst-stage embryos were evaluated. The proportion of the cases were 39 ICSI (53%), 17 IVF (23%), and both 18 (24%). The factors associated with the presence of two or more optimal embryos in the sample were patient age under 35 years (ROC = 0.6243), estradiol over 1895 ng/dL (ROC = 0.6511), and an estradiol / progesterone index greater than 5.4 (ROC = 0.6194). Including the variables mentioned above, using a multivariate logistic regression model (ROC = 0.7107, SPE 79.31%, SEN 63.93%) it was possible to predict those patients that would have at least two good quality embryos. AMH after the logistic regression model had a non-relevant, low positive correlation.

CONCLUSIONS: Patient's age, the estradiol, as well as the estradiol/progesterone index, measured on the day of hCG administration, can provide a valid indicator to predict blastocyst development and embryo quality. To validate this model a prospective study is currently planned.

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GNRH ANTAGONIST AND LETROZOLE CO-TREATMENT IN NORMAL OVARIAN RESERVE PATIENTS. Tingting Li, Doctor Reproductive Medicine Research Center, Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: To investigate the clinical value of letrozole in IVF-ET for normal ovarian reserve patients who were treated using GnRH antagonist protocol.

DESIGN: A retrospective study.

MATERIALS AND METHODS: Patients underwent firs or second IVF-ET cycle, with age between 22-38 years old, AMH between 1.1-3.6ng/ml, FSH<10U/L, AFC>6, were involved. The 867 cycles were analyzed. All the cycles were divided into 2 groups based on whether use letrozole 5 mg qd*5 in GnRH antagonist protocol: cycles with letrozole (Group A, n=462), cycles without letrozole (Group B, n=405). We compared the basic status of patients and clinical outcomes of the 2 groups.

RESULTS: There were no significantly differences found in age, BMI, AMH, and basal FSH between 2 groups, Group A had significantly lower Gn doses, E_2 levels on trigger day, numbers oocytes retrieved, higher rate of LH increase and progesterone advance. Most importantly, Group A had significantly lower rate of oocyte maturation, 2PN fertilization, high quality embryo, clinical pregnancy. But positive aspects is that Group A had lower OHSS incidence rate (1.93% vs 4.44%).

CONCLUSIONS: Combination of letrozole in antagonist protocal for patients with normal ovarian reserve may have adverse effects on pregnancy rate, oocyte maturation and fertilization. Positive effects are to reduce Gn usage and OHSS incidence.

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LOW LUTEAL SERUM PROGESTERONE LEVELS ARE ASSOCIATED WITH LOWER ONGOING PREGNANCY AND LIVE BIRTH RATES IN ART: SYSTEMATIC REVIEW AND META-ANALYSES. Noemie Ranisavljevic, M.D., Ph.D.,[1] Stephanie Huberlant, M.D., Ph.D.,[2] Marie Montagut, M.D.,[3] Pierre Marie Alonzo, PharmD,[4] Bernadette M. Darné, MD,[5] Solene Languille, PHD,[5] Tal Anahory, M.D., Ph.D.,[1] Isabelle Cedrin-Durnerin, M.D.[6] [1]CHU and University of Montpellier, Montpellier, France; [2]University hospital of Nimes, Nimes, France; [3]Clinique La Croix du Sud, Quint-Fonsegrives, France; [4]Gedeon Richter France, Paris, France; [5]Monitoring Force, Maisons Laffitte, France; [6]Jean Verdier Hospital, bondy, France.

OBJECTIVE: To determine whether ongoing pregnancy (OP), live birth (LB) and miscarriage rates are associated with luteal serum progesterone levels according to the number of corpus lutea (CL): none (artificial cycle for frozen-thawed embryo transfer (FET)), one or few (ovulation induction, intra-uterine insemination, natural cycle for FET) or several (fresh embryo transfer).

DESIGN: Systematic review and meta-analysis prospectively registered (PROSPERO CRD42019139019).

MATERIALS AND METHODS: A systematic review was performed using the following key words: 'ART', 'IVF', 'ICSI', 'IIU', 'ovulation induction/stimulation', 'embryo transfer', 'progesterone', 'follicular phase', 'live birth', 'pregnancy'. Searches were conducted on MEDLINE, EMBASE and the Cochrane Library, from 1990 up to 2019. This study was restricted to published research articles that reported serum progesterone level determined during luteal phase and clinical outcomes (OP or LB). Two independent reviewers carried out study selection, quality assessment using the adapted Newcastle-Ottawa Quality Assessment Scales, bias assessment using ROBIN-1 tools and data extraction according to Cochrane methods. Original author was contacted if required to complete information/data. Using Review Manager 5, independent random-effect meta-analyses were performed according to the number of CL.

RESULTS: Overall 2,366 non-duplicate records were identified, of which 20 relevant studies were available for quantitative analysis. In artificial cycles with no CL (n=7 studies), OP and LB rates were significantly decreased when progesterone level is low compared to optimal progesterone level (risk ratio [RR] 0.63; 95% Confidence interval [CI] 0.49-0.81 and 0.61; 95% CI 0.43-0.86, respectively). The RR for miscarriages was 1.62 (95% CI 1.06-2.47). Only two studies were related to cycles with one or few CL, hence meta-analysis was not conducted. In cycles with several CL, RR of OP and LB rates could not be evaluated neither (n=2 studies). However, in cycles with several CL, mean progesterone levels were displayed in OP and no OP groups (n=5 studies) and in LB and no

	Group A (n=462)	Group B(n=405)	*P* values
Age (year)	35.010 ± 5.168	34.610 ± 2.980	0.710
BMI	23.128 ± 3.166	22.997 ± 3.085	0.082
Basal FSH (U/L)	6.764 ± 1.461	6.685 ± 1.284	0.553
AMH (ng/ml)	3.757 ± 3.608	3.807 ± 0.539	0.241
Gn days	8.640 ± 1.672	8.820 ± 1.623	0.164
Gn doses	1735.673 ± 607.855	1880.786 ± 615.408	<0.001
Em thickness (mm)	9.988 ± 2.187	11.041 ± 2.114	<0.001
E2 on HCG day (pg/ml)	738.061 ± 478.824	2196.872 ± 1065.920	<0.001
LH on HCG day (U/L)	4.517 ± 3.502	3.130 ± 2.354	<0.001
P4 on HCG day (ng/ml)	0.625 ± 0.322	0.671 ± 0.322	0.094
No. retrieved oocytes	8.250 ± 4.125	10.470 ± 4.386	<0.001
progesterone advance rate on trigger day (≥1.5pg/ml)%	11.69 (54/462)	7.16 (29/405)	0.024
LH increased rate on trigger day (>10U/L)%	9.96 (46/462)	3.95 (16/405)	0.001
oocyte maturation rate (ICSI)%	64.30 (913/1420)	73.64 (1084/1472)	0.000
2PN fertilization rate (%)	52.63 (2004/3808)	59.23 (2657/4486)	0.000
available embryo rate (%)	76.40 (1531/2004)	77.00 (2046/2657)	0.627
high quality embryo rate (%)	78.12 (1196/1531)	81.48 (1667/2046)	0.013
embryo transplant ratio (%)	38.74 (179/462)	44.69 (181/405)	0.076
Clinical pregnancy rate (%)	35.75 (64/179)	46.96 (85/181)	0.031
Miscarried rate (%)	16.13 (10/62)	19.75 (16/81)	0.578
ectopic pregnancy rate (%)	3.13 (2/64)	4.71 (4/85)	0.627
incidence of moderate and severe OHSS	1.95 (9/462)	4.44 (18/405)	0.035

LB groups (n=3 studies). Means of progesterone level were significantly lower in no OP and no LB groups than in OP and LB groups [difference in means 68.8 (95% CI 45.6-92.0) and 272.4 (95% CI 10.8-533.9), ng/ml, respectively].

CONCLUSIONS: Low luteal progesterone concentrations are related to lower OP and LB rates in cycles with absence of CL or iatrogenically induced luteal phase defect suggesting that standard luteal support might not be effective for optimizing outcomes in ART. These results support the requirement of luteal serum progesterone level monitoring in order to individualize progesterone administration.

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THE EFFECT OF GROWTH HORMONE ON CLINICAL OUTCOMES OF POOR OVARIAN RESPONDER UNDERGOING IN VITRO FERTILIZATION/INTRACYTOPLASMIC SPERM INJECTION TREATMENT: A RETROSPECTIVE STUDY BASED ON POSEIDON CRITERIA. Xing Yang, Ph.D.,[1] Mei-hong Cai Master,[2] [1]The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; [2]Guangzhou First People's Hospital, School of Medicine, South China University of Technology, Guangzhou, China.

OBJECTIVE: Poor ovarian responder (POR) had been dramatically increased among patients require assisted reproductive technology. The effect of growth hormone (GH) adjuvant in POR had been widely discussed. The novel POSEIDON criteria could better differentiate patients with minor heterogeneity[1]. The aim of this retrospective analysis is to explore whether GH treatment is beneficial for POR patients undertaken in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) treatment.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: POR meet the POSEIDON criteria were recruited and stratified into the 4 subgroups according to ovarian reserve and patients age [1]. Patients in each subgroup were further divided into GH adjuvant group (GH+ group) and the counterpart without GH pretreatment (GH- group). One-to-one case-control matching was performed to adjust essential confounding factors between GH+ group and GH- group in two layers, normal ovarian reserve and poor oavarian reserve. Conventional ovarian stimulation protocols were applied for IVF/ICSI treatment. The demographic data, cycle characteristic and clinical outcomes between GH+ group and GH- group in each subgroup were compared separately.

RESULTS: A total of 1104 patients were included in this study, among which 428 with normal ovarian reserve and 676 with poor ovarian reserve. GH adjuvant showed a beneficial effect on the ovarian response and live birth rate in poor ovarian reserve subgroups (PG3 and PG4). The further stratification revealed that in the PG4, the number of good-quality embryos were significantly increased in the GH+ group than in the GH- group (1.58±1.71 vs. 1.25±1.55, P =0.032), the miscarriage rate (6.7% vs. 13.8%, P=0.173) and live birth rate (29.89% vs. 17.65%, P =0.028) were also greatly improved, these effects failed to been detected in patients with normal ovarian reserve(PG1,PG2) or in poor ovarian responder younger than 35 (PG3).

CONCLUSIONS: In conclusion, GH pretreatment is beneficial for promoting ovarian response and live birth rate, further decreasing miscarriage rate in poor ovarian reserve patients older than 35 (PG4).

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IMPROVEMENT OF PREGNANCY OUTCOME BY TARGETING A CUSTOMIZED TIMING OF FROZEN EMBRYO TRANSFER IN PATIENTS FOR DONOR EGG RECIPIENTS. Delphine Haouzi, PhD,[1] Frida Entezami, MD,[2] Charlotte Mauries, MD,[1] Alice Ferrieres-Hoa, MD,[1] Anna Gala, MD,[3] Emmanuelle Vintejoux, MD,[3] Cecile Brunet, MD,[3] Claire Vincens, MD,[4] Sophie Bringer-Deutsch, MD,[3] Sophie Brouillet, PharmD, PhD,[3] Samir Hamamah, MD, PhD,[3] [1]Inserm U1203, CHU Montpellier, St-Eloi Hospital, Montpellier, France; [2]American Hospital of Paris, Neuilly sur Seine, France; [3]Arnaud de Villeneuve Hospital, CHU Montpellier, Montpellier, France; [4]ART-PGD department, Arnaud de Villeneuve Hospital, CHU Montpellier, Montpellier, France.

OBJECTIVE: The aim of this study was to optimize pregnancy outcome using customized embryo transfer according to the evaluation of endometrial receptivity of patients included in eggs donation program.

DESIGN: Endometrial biopsies are performed during the implantation windows 5-9 days after progesterone administration under hormone replacement therapy. Then, the transfer strategy consists in performing cET of blastocysts according the endometrium receptivity day identified using the Win-Test. Therefore, frozen day 2/3 embryos were transferred 72/48 hours before this specific receptivity day, respectively. When the endometrial sample was defined as non-receptive, a second evaluation was performed later, according to transcriptomic result.

MATERIALS AND METHODS: 45 patients in eggs-donation program due to an advanced age (n=36) or premature ovarian failure (n=9) were included. RNAs from biopsies were extracted and the Win-Test gene expression was assessed by qRT-PCR. Positive pregnancy test was defined as at least two consecutive positive b-hCG serum concentration. Clinical pregnancy, implantation rate and live birth rate were recorded after cET according to the transcriptomic results.

RESULTS: Analyses of endometrial receptivity status (n=108 biopsies) in patients in oocyte donation program (age mean ± SD: 41.2 ± 3.8 years) revealed a strong inter-patient variability of the moment of the opening of the receptivity window within the implantation window. Majority of patients (84%) present a delay of their receptivity window compared to the classical timing for blastocyst transfer (16% at Pg+5/Pg+6). This delay was mainly between 1 (40%) to 2 days (33%), or more (11%). Then, a cET can to be perform during a subsequent cycle according the endometrium receptivity day and in the respect of the synchronization of the fœto-maternal dialogue. Using this strategy, the positive b-hCG and clinical pregnancy rate per patient were 73.3% and 60%, respectively. The implantation and live birth rates after cET were 50% and 48.9%, respectively.

CONCLUSIONS: This finding demonstrated that customized embryo transfer according to the specific cycle day where endometrium is receptive improves both implantation rate and live birth rate in patients in oocyte donation program.

SUPPORT: This work was partially supported by a grant from the Gedeon Richter Pharmaceutical Company.

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ESTABLISHING THE FOLLITROPIN DELTA DOSE PROVIDING COMPARABLE OVARIAN RESPONSE AS 150 IU/DAY FOLLITROPIN ALFA FOR CONTROLLED OVARIAN STIMULATION. Joan-Carles Arce, MD, PhD, Per Larsson, PhD, Ferring Pharmaceuticals, Copenhagen, Denmark.

OBJECTIVE: To determine the daily follitropin delta dose (μg) providing similar ovarian response as 150 IU/day follitropin alfa.

DESIGN: Post-hoc analysis of ovarian response in 1,591 IVF/ICSI patients undergoing controlled ovarian stimulation in two randomized, assessor-blind, controlled, multi-center trials in the development program for follitropin delta (NCT01426386; NCT01956110). Ovarian response was evaluated in terms of number of oocytes retrieved as well as number of follicles by size and hormone response.

MATERIALS AND METHODS: The phase 2 dose-response trial included 265 IVF/ICSI patients who were randomized to receive a daily dose in the range 5.2-12.1 μg of follitropin delta (Rekovelle, Ferring Pharmaceuticals) or 150 IU (11 μg) of follitropin alfa (Gonal-F, Merck Serono) with no dose adjustments of either follitropin during stimulation. The phase 3 efficacy trial included 1,326 IVF/ICSI patients who were randomized to an individualized follitropin delta dose (determined for each woman based on her serum AMH level and body weight) that was fixed throughout stimulation or to a starting dose of 150 IU (11 μg) follitropin alfa for the first five days followed by potential dose adjustments as per the investigator's judgement. Dose-response relationships for follitropin delta dose and ovarian response parameters were approximated by log-linear functions. For the phase 3 trial, follitropin delta was compared to follitropin alfa by stratifying follitropin alfa patients

according to the dose they would have received if randomized to follitropin delta. Analyses were made for these patient populations: all, AMH $\geq$15 pmol/L, no dose changes, and AMH $\geq$15 pmol/L and no dose changes.

RESULTS: Mean follitropin delta doses of 10.0 [95% CI 7.9; 12.8] μg and 10.3 [95% CI 9.7; 10.8] μg yielded the same number of oocytes retrieved as 150 IU follitropin alfa for all patients in the phase 2 and 3 trials, respectively. When analyzing patients with normal/high ovarian reserve (based on serum AMH $\geq$15 pmol/L) and with no dose changes during stimulation, the same number of oocytes retrieved was obtained with 150 IU follitropin alfa and mean doses of follitropin delta of 9.7 [95% CI 7.5; 12.4] μg in the phase 2 trial and 9.3 [95% CI 8.6; 10.1] μg in the phase 3 trial. Evaluation of additional ovarian response parameters besides number of oocytes retrieved provided consistent findings. Mean follitropin delta doses in the range 9.4-10.1 μg were estimated to correspond to 150 IU follitropin alfa in terms of number of follicles $\geq$10 mm, $\geq$12 mm and $\geq$17 mm at end of stimulation, across all analysis populations in the phase 3 trial. Further, for serum estradiol, progesterone and inhibin A at end of stimulation, mean follitropin delta doses in the range 9.4-10.6 μg were estimated to correspond to 150 IU follitropin alfa.

CONCLUSIONS: In IVF/ICSI patients, a daily follitropin delta dose of 10 μg provides a similar ovarian response as 150 IU/day follitropin alfa. The establishment of this equivalence factor will facilitate the use of follitropin delta in both dosing algorithms and conventional dosing and will also ease patient transition between protocols.

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SUPPORT: Ferring Pharmaceuticals

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IN-UTERO ANDROGEN EXPOSURE CHANGES NEONATAL OVARIAN GENE EXPRESSION IN A LEAN PCOS MOUSE MODEL. Jamie Merkison, MD, Chellakkan Selvanesan Blesson, PhD. Baylor College of Medicine, Houston, TX.

OBJECTIVE: To investigate the role of prenatal androgen exposure on the neonatal ovary by analyzing gene expression and mitochondrial structure.

DESIGN: Prospective cohort study investigating the role of androgens in fetal ovarian development by analyzing gene expression in neonatal ovary exposed to dihydrotestosterone (DHT).

MATERIALS AND METHODS: Pregnant mice were treated with DHT (250μg/day) or vehicle (sesame oil) on days 16 -18 of gestation. Ovaries from pups were micro-dissected at birth (day 0) and RNA and protein were sent for RNA sequencing, bioinformatics, and qPCR. Relevant genes were further studied via Western blot analysis. *t*-tests and one-way ANOVA were used to analyze the differences when appropriate.$P < 0.05$ was considered statistically significant.

RESULTS: The neonatal ovaries of DHT treated group had 287 upregulated and 95 downregulated genes compared to untreated group.Upregulated genes were associated with infertility, abnormal follicle development and altered hormonal signaling.Top 20 up and downregulated genes were validated with qPCR – 26 were differentially expressed. These 26 genes were found to be related to mitochondrial dysfunction, oocyte maturation, ovarian cell cycle regulation, and PCOS. Of the 26 genes, 8 had been previously described to be related to reproduction physiology. From those genes that have been previously described within the literature, 3 genes showed a statistically significant difference in the amount of protein expressed on Western blot analysis.

CONCLUSIONS: Prenatal androgen exposure altered transcriptional pathways in ovarian gene expression, with resulting differences in the amount of protein produced in affected mice. Data suggests that PCOS development occurs prior to birth with alterations in gene expression evident during the neonatal period.

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CUMULUS CELL TRANSCRIPTOMIC PROFILES OF OOCYTES THAT RESULT IN WHOLE CHROMOSOME 21 MONOSOMY AND TRISOMY ARE SIGNIFICANTLY DIFFERENT. Ashley W. Tiegs, MD,[1] Shiny Titus, PhD,[2] Sameet Mehta, PhD,[3] Rolando Garcia-Milian, MLS, AHIP,[3] Emre Seli, M.D.,[2] Richard Thomas Scott, Jr., MD[2] [1]IVI-RMA New Jersey, Basking Ridge, NJ; [2]IVI RMA New Jersey, Basking Ridge, NJ; [3]Yale School of Medicine, New Haven, CT.

OBJECTIVE: To determine if the transcriptomic profile of cumulus cells (CCs) from oocytes that resulted in embryos diagnosed to be whole chromosome aneuploid for chromosome 21 by preimplantation genetic testing for aneuploidy (PGT-A) differs from that of CCs of oocytes that resulted in euploid embryos.

DESIGN: Prospective experimental study.

MATERIALS AND METHODS: Cumulus cells from individualized oocytes were obtained prospectively from consenting patients undergoing in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) with PGT-A (August 2018 - December 2019). Embryos were individually cultured to enable accurate correlation with trophectoderm PGT-A results. The CC transcriptomic profiles from 22 non-sibling embryos were evaluated and compared: 7 monosomy 21, 8 trisomy 21, and 7 euploid. RNA sequencing was followed by ingenuity pathway analysis (IPA) for assessment of overrepresented pathways in differentially expressed genes in trisomy 21 and monosomy 21 as compared to euploid embryos. Real-time polymerase chain reaction (PCR) was then performed to confirm differential gene expression as specifically indicated by the IPA results.

RESULTS: RNA sequencing revealed significant differences in CC gene expression between PGT-A euploid and whole chromosome 21 aneuploid embryos. Specifically, a total of 3122 genes in CCs associated with monosomy 21 and 19 genes in CCs associated with trisomy 21 embryos were differentially expressed as compared to CCs associated with PGT-A euploid embryos. Thirteen of these genes were differentially expressed in both monosomy and trisomy 21 aneuploid as compared to euploid embryos, including disheveled segment polarity protein 2 (DVL2), cellular communication network factor 1 (CCN1/CYR61) and serum response factor (SRF). Such genes have been previously implicated in embryo developmental competence. Additionally, IPA analysis revealed cell-to-cell contact functioning to be significantly altered in CCs associated with both monosomy and trisomy 21 embryos as compared to CCs associated with PGT-A euploid embryos.

CONCLUSIONS: Significantly altered expression of several genes implicated in embryo development was identified upon comparison of CC transcriptomic profiles of embryos with whole chromosome aneuploidy for chromosome 21 (monosomy and trisomy) versus euploid embryos. As a proof-of-concept study, these findings encourage further investigation of CC gene expression analysis for the development of biomarkers evaluating oocyte quality for patients undergoing fertility preservation of oocytes.

SUPPORT: IVI-America, Foundation for Embryonic Competence

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REASSIGNED

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NATURAL COMPOUND METHYL JASMONATE SHOWS PROMISING ANTI-FIBROID EFFECTS IN HUMAN UTERINE FIBROIDS VIA INHIBITION OF EZH2 MEDIATED WNT/B-CATENIN SIGNALING PATHWAY ACTIVATION. Mohamed Ali, B.Pharm, MSc,[1] Ayman Al-Hendy, MD, PhD,[2] Qiwei Yang, PhD[1] [1]University of Illinois at chicago, Chicago, IL; [2]University of Illinois at Chicago, Chicago, IL.

OBJECTIVE: Uterine Fibroids (UFs) are the most common benign tumors in women of reproductive age with subsequent significant quality of life and economic negative impact. EZH2 and Wnt/β-catenin are linked to many diseases pathogenesis including UF. Current treatment options are primarily surgical and no FDA approved medical treatment is available so far. Natural compounds may be beneficial for UFs patients as a safe non-hormonal therapeutic option. Methyl Jasmonate (MJ) is a natural compound isolated from jasmine with a potent anti-EZH2 activity. In this study, we determine the effect of MJ on UFs.

DESIGN: Laboratory research studies using Human uterine leiomyoma (HuLM) and normal uterine smooth muscle cells (UTSM).

MATERIALS AND METHODS: HuLM and UTSM cells were treated with (0.1mM-3mM) of MJ and cell proliferation was assessed by MTT assay after 24 and 72 hr. Protein and RNA levels of several markers were measured in MJ treated or untreated HuLM, including ECM markers collagen type1(-COLL1A) and Fibronectin (FN), proliferation markers Cyclin D1 (CCND1) and (PCNA), tumor related marker (P21, EZH2 and β-catenin) and apoptotic markers {Bax, Cytochrome-c and cleaved caspase 3}. EZH2 overexpression or inhibition was achieved using EZH2-expressing adenovirus or chemical EZH2-inhibitor (DZNep) respectively in HuLM, and protein expression of EZH2, β-catenin and PCNA were measured as well as alterations of gene expression in WNT signaling pathway using 84-gene Prime-PCR array with subsequent confirmation of 9 genes using qRT-PCR. Unpaired student t test was used for statistical significance. ($P< 0.05$) is considered significant.

RESULTS: EZH2 overexpression significantly increased nuclear translocation of β-catenin and PCNA with subsequent many Wnt ligands gene expression increase (PITX2, WISP1, WNT5A, WNT5B and WNT9A), while EZH2 inhibition blocked Wnt/ β-catenin signaling activation where aforementioned genes were significantly decreased as well as PCNA, CyclinD1 and PITX2 protein expression compared to untreated HuLM ($P<0.05$). MJ showed a potent anti-proliferative effect on HuLM cells in a concentration and time dependent manner ($P<0.05$). Interestingly, dose range (0.1-0.5 mM) showed selective growth-inhibitory effect on HuLM not normal UTSM cells. MJ treatment at 0.5 mM for 24 hr. significantly decreased both protein and RNA levels of EZH2, β-catenin, COLL1A, FN, CCND1, PCNA, WISP1 and PITX2, while increased protein levels of p21, Bax, Cytochrome-c and cleaved caspase-3 compared to untreated HuLM ($P<0.05$). MJ treated cells exhibited downregulation in RNA expression of 35 genes including *CTNNB1*, *CCND1*, *Wnt3*, *Wnt5A*, *Wnt5B* and upregulation in expression of 36 genes including Wnt antagonist genes *WIF1*, *PRICKlE1* and DKK1 compared to control.

CONCLUSIONS: Our studies provide a novel link between EZH2 and Wnt/β-catenin signaling pathway in UFs. MJ exhibited a promising anti-fibrotic effect via inhibition of this link. MJ might offer a promising therapeutic option as safe non-hormonal long term and cost-effective treatment against UFs with favorable clinical utility especially for women seeking future fertility.

SUPPORT: NIH grants: RO1 ES028615, U54 MD007602.

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PLASMINOGEN DOES NOT IMPROVE BLASTOCYST HATCHING IN VITRO, BUT MAY IMPROVE BLASTOCYST QUALITY. Heidi J. Engelhorn, MS,[1] William B. Schoolcraft, MD,[2] Rebecca L. Krisher, PhD[1] [1]CCRM Colorado, Lone Tree, CO; [2]CCRM Fertility Network, Lone Tree, CO.

OBJECTIVE: The aim of this study was to determine if the addition of transferrin-selenium-ethanolamine (TSX) and/or plasminogen to mouse embryo culture medium would increase the incidence of blastocyst hatching and cell number. TSX is a commonly used cell culture supplement. Transferrin regulates iron uptake, selenium is a precursor for proteins acting as antioxidants, and ethanolamine supports cell membrane function. Plasminogen is a precursor to the protease plasmin that degrades fibrin and is thought to be a component of blastocyst hatching mechanisms in vivo.

DESIGN: Research study.

MATERIALS AND METHODS: A sequential culture medium was used to prepare four treatments: control, TSX, plasminogen and TSX+plasminogen, which were added exclusively to the final culture step. Mature mouse (CF1, 4 wks) oocytes were collected following PMSG and hCG stimulation, fertilized in vitro, and 2PN embryos selected for culture and randomly allocated to treatments. Blastocyst development and hatching were assessed on days 4 (96 hr) and 5 (112 hr). Forty day 5 hatching and hatched blastocysts per treatment were fixed in 4% paraformaldehyde and stained to determine TE (CDX2) and ICM (SOX2) cell number. Five biological replicates were performed (120-123 embryos/treatment). Data was analyzed by two-tailed t test with a p value for significance of <0.05.

RESULTS: There were no significant differences in blastocyst development on day 4 or blastocyst hatching on day 5. No differences in the number of hatching sites or thickness of the zona pellucida were noted between treatments. Inclusion of plasminogen significantly decreased blastocyst trophectoderm cell number (122 ± 6.1) compared to control (139.4 ± 5.2), TSX (145 ± 4.6) and TSX+plasminogen (147.2 ± 5.9), as well as total cell number (plasminogen, 138.1 ± 6.6; control, 156 ± 5.6; TSX, 162.7 ± 5.1; plasminogen+TSX, 162.3 ± 6.5). However, ICM cell number was not affected by treatment (control, 16.6 ± 0.8; plasminogen, 16.1 ± 0.9; TSX, 17.7 ± 0.9; plasminogen+TSX, 15.1 ± 1.1). As a result, blastocysts cultured with plasminogen had a higher percentage of ICM cells (11.8%) compared to TSX+plasminogen (9.3%), but did not differ from control (10.7%) or TSX (10.9%).

CONCLUSIONS: Although plasminogen is suspected to play a role in blastocyst hatching in vivo, the addition of plasminogen to culture medium did not improve in vitro hatching of mouse blastocysts. Plasminogen may improve in vitro blastocyst quality, as suggested by an increase in the percentage of ICM cells. The combination of TSX and plasminogen provided no overall benefit to embryo development, and may actually be detrimental as the percentage of ICM cells was reduced.

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A REDUCED NUTRIENT CULTURE ENVIRONMENT IMPROVES BOVINE BLASTOCYST DEVELOPMENT AND ALTERS MITOCHONDRIAL METABOLISM AS ELUCIDATED BY SINGLE CELL RNA SEQUENCING. Benjamin B. Goheen, BS,[1] Sandeep K. Rajput, PhD,[1] Deirdre M. Logsdon, MS,[1] Ye Yuan, PhD,[1] Zongliang Jiang, Ph.D,[2] William B. Schoolcraft, MD,[1] Rebecca L. Krisher, PhD[3] [1]Colorado Center for Reproductive Medicine, Lone Tree, CO; [2]Louisiana State University, Baton Rouge, LA; [3]CCRM Colorado, Lone Tree, CO.

OBJECTIVE: To characterize developmental and transcriptomic differences between in vitro embryos produced in standard culture medium (IVC) with those produced using a culture medium with 75% reduced nutrients (25% of the carbohydrates and amino acids of control medium; IVRN).

DESIGN: Prospective Research Study.

MATERIALS AND METHODS: Bovine embryos were cultured to the blastocyst stage and bisected. The portion of the embryo containing both ICM and TE was dissociated using Accumax (Innovative Cell Technologies) into single cells. Single cell RNA sequencing libraries were prepared using the Smart-Seq v2 approach and sequenced with Illumina HiSeq platform. In total, we sequenced 215 single cells and obtained an average of approximately 10 million 150bp paired-end reads per sample. The resulting data underwent pre-processing, alignment, and feature selection before being analyzed for differential gene expression using limma-voom and pathway analysis using Ingenuity Pathway Analysis (Qiagen).

RESULTS: IVRN embryos had improved blastocyst development (49.8% of total oocytes; n=649) compared to control (31.6% of total oocytes, n=637). RNA-seq results revealed upregulation of IGF-1 (z-score: 1.667, p-value: 6.13E-04), AKT (z-score: 1.291, p-value: 3.76E-03), and insulin receptor signaling (z-score: 1.069, p-value: 2.25E-02) pathways involved in glucose transport, suggesting an increase in glucose uptake by IVRN embryos. Increased AMPK signaling (z-score: 2.2524, p-value: 4.98E-05) and expression of CPT1A, CPT1B & CPT2 genes in IVRN blastocyst indicate reliance on fatty acid oxidation (FAO) for ATP production under reduced nutrient conditions. Upregulation of PDK1 and PDK2 enzymes (inhibit PDH/conversion of glycolytic pyruvate to acetyl-coA and entry into the TCA cycle) and increased expression of glutaminase (GLS) in IVRN blastocyst suggests that glucose is diverted into another pathway such as lactate production or the PPP, but that the TCA cycle remains active not only via FAO but also via glutaminolysis. Collectively, these results suggest that

embryos cultured under reduced nutrient conditions switch to a Warburg-like metabolism to maintain energy homeostasis. Supporting this conclusion, ERK/MAPK signaling was upregulated in IVRN blastocysts (z-score: 1.147, p-value: 2.51E-03), suggesting that growth and proliferation are upregulated similar to cancer cells, which also employ Warburg metabolism. IVRN embryos also had elevated levels of mtDNA compared to control (IVRN = 1951.25122.42, IVC= 1530.7357.36, p = 0.003.

CONCLUSIONS: The metabolic strategy adopted by IVRN embryos appears to support increased blastocyst development and quality in vitro, although the ultimate viability of these embryos after transfer has not been evaluated. This study provides novel insight into embryo metabolic strategies that support blastocyst development, as well as potential approaches to manipulate metabolism to improve both the quantity and quality of embryos produced in vitro.

P-567 4:30 PM Monday, October 19, 2020

THE ROLE OF TRYPTOPHAN 2,3-DIOXYGENASE IN HUMAN UTERINE LEIOMYOMA HARBORING MED12 MUTATION. Anne P. Hutchinson, M.D.,[1] Ping Yin, M.D., PhD,[2] John S. Coon V, M.S.,[2] Ilona Neale, BA (expected 2020),[2] Serdar E. Bulun, MD[3] [1]Northwestern University Feinberg School of Medicine, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Chicago, IL; [2]Northwestern University Feinberg School of Medicine, Chicago, IL; [3]250 E Superior, Chicago, IL.

OBJECTIVE: Uterine leiomyomas (fibroids) represent the most common reproductive-age benign tumor in women. Two distinct subtypes, which carry a Mediator complex subunit 12 (MED12) mutation (mut-MED12) or with high mobility group AT-hook 2 (HMGA2) overexpression (ov-HMGA2), comprise 85% of all leiomyomas. A universal feature of all leiomyomas is responsiveness to estrogen and progesterone, which function by activating their cognate nuclear receptors ERα and PR, respectively, to increase their binding to regulatory regions of target genes and control their transcription and function. Using leiomyomas carrying mutant MED12 (G44D), wild type MED12, and over expression of HMGA2, and their corresponding adjacent normal myometrial tissues, we performed RNA-seq and ChIP-seq against PR, ERα, and MED12. Integrative analyses of these data identified that the tryptophan (Trp) 2,3-dioxygenase (*TDO2*) gene expression was significantly upregulated in mutant MED12 leiomyoma. TDO2 protein catalyzes the oxidation of L-Trp to N-formyl-L-kynurenine (Kyn), as the first and rate-limiting step of Kyn production, which plays important roles in tumorigenesis in general. It has been reported that Trp was significantly downregulated in mutant MED12 leiomyoma; however, the underlying mechanism remains unclear and the role of this pathway in leiomyoma tumorigenesis has not been explored. The aim of the present study was to determine the expression levels TDO2 and the other two enzymes that catalyze the same enzymatic step: indoleamine-2,3-dioxygenease 1 (IDO1) and IDO2 in different subtypes of leiomyoma.

DESIGN: Laboratory Study.

MATERIALS AND METHODS: Mutation screening was performed for MED12 exons 1 and 2 and the intronic flanking regions using Sanger sequencing in 48 leiomyoma and matched myometrial tissues (n=24 subjects). Quantitative real-time polymerase chain reaction (qRT-PCRs) was performed in order to estimate the expression of TDO2, IDO1, and IDO2 in leiomyoma samples with or without MED12 gene mutations.

RESULTS: MED12 mutations were detected in 18 (75%) leiomyoma samples, including 6 tissues harboring G44D (131G>A) mutation (the most frequently observed mutation in leiomyomas). TDO2 expression was significantly higher in mutant MED12 leiomyomas not only in comparison with all myometrial samples ($p<0.0001$), but also in comparison with leiomyomas without a MED12 mutation ($p<0.05$). The expression of IDO2 was undetectable using qRT-PCR in all tissues, and the expression of IDO1 was low and not significantly different between leiomyoma and myometrium, suggesting that TDO2 is the key enzyme responsible for Trp metabolism in leiomyoma carrying MED12 mutation.

CONCLUSIONS: We demonstrated that TDO2 expression was dysregulated in leiomyomas carrying MED12 mutation. Therefore, it may serve as a good therapeutic target and provide new insight into understanding the molecular mechanisms responsible for the pathogenesis of the MED12 mutation-specific leiomyoma subtype.

P-568 4:30 PM Monday, October 19, 2020

USING MIRROR COPIES OF PARENTAL GENOMES TO GENERATE DEVELOPMENTALLY COMPETENT EMBRYOS. Philip Xie, B.S., Aysha Trout, B.A., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To create identical copies of parental genomes to generate developmentally competent zygotes.

DESIGN: Mirror copies of parental genomes were created for the male genome by injecting an individual spermatozoon into an enucleated oocyte. For the female genome, parthenogenetic activation was performed. Both constructs were allowed to reach the first embryonic cleavage. A single male pseudo-blastomere was fused with a female counterpart to reconstitute a diploid zygote. The reconstructed zygotes were cultured in a time-lapse incubator up to full preimplantation development compared to zygotes generated by piezo-actuated ICSI that served as a control.

MATERIALS AND METHODS: To generate male pseudo-blastomeres, MII oocytes from superovulated B6D2F1 mice were treated by cytochalasin B, enucleated, injected by a sperm head from the same strain, and allowed to cleave to the 2-cell stage. Female counterparts were generated by exposing unmanipulated oocytes to 10 mM calcium ionophore and allowed to reach the first division. DNA polymerase inhibitor was supplied to culture medium immediately after the first division to synchronize cell cycles before zygote reconstruction. Biparental zygote reconstruction was performed by Sendai virus–mediated fusion of a male pseudo-blastomere with a female counterpart. Reconstructed zygotes were cultured and monitored up to 96h and compared to control ICSI conceptuses.

RESULTS: Enucleation of 60 MII oocytes generated 57 ooplasts; 43 survived subsequent injection (74%), and each developed a single pronucleus. After culturing for 16h, 40 androgenetic embryos reached the 2-cell stage (93%). For the female counterparts, 50 out of 55 MII oocytes (87%) were successfully activated and cleaved. Forty zygote reconstructions were performed, yielding 36 reconstructed biparental zygotes (90%). An additional 35 zygotes were generated by ICSI and served as controls. The control and experimental zygotes were observed in a time-lapse system and maintained up to 96h. Early development of control and experimental conceptuses into 2-cell (86% vs 78%) and 4-cell embryos (80 vs 69%) was comparable. Morula compaction in the control and experimental groups was 77% and 50%, respectively ($P < 0.01$), and further development into blastocysts was 77% and 44%, respectively ($P < 0.01$). The experimental group displayed morphokinetic abnormalities during cleavage and higher instances of fragmentation.

CONCLUSIONS: It is feasible to use mirror copies of parental genomes to generate zygotes, albeit at a lower rate of preimplantation development as compared to zygotes generated by ICSI. This experiment sheds light on the process of syngamy, and the technique has potential for use in genomic editing as well as in screening for inheritable heterozygous genetic disorders.

SUPPORT: None

P-569 4:30 PM Monday, October 19, 2020

HYPOXIA INDUCES TROPHOBLAST MIGRATION AND INVASION GENE PATHWAYS A SUBSET OF WHICH ARE REDUCED IN PREECLAMPSIA CVS. Barry E. Perlman, DO,[1] Audrey Merriam, MD, MS,[2] Alexander Lemenze, PhD,[1] Salma Begum, PhD,[3] Qingshi Zhao, PhD,[1] Carrie J. Shawber, PhD,[4] Nataki C. Douglas, MD, PhD[1] [1]Rutgers New Jersey Medical School, Newark, NJ; [2]Yale University, New Haven, NJ; [3]Rutgers-New Jersey Medical School, Newark, NJ; [4]Columbia University College of Physicians and Surgeons, New York, NY.

OBJECTIVE: At the start of pregnancy, trophoblasts (TBs) migrate and invade into the decidua and remodel the spiral arteries in physiologic hypoxic conditions (1-3% O_2). Persistent hypoxia secondary to a defect in remodeling of the maternal arteries is proposed to lead to a failure to increase oxygen tension, leading to poor placental perfusion and pregnancy complications, such as preeclampsia (PE). The objectives of this study are to determine how exposure to hypoxia impacts gene expression and cellular motility of first trimester TBs, and to assess if expression of migration-associated genes is

dysregulated in 2nd trimester chorionic villous samples (CVS) from PE pregnancies relative to CVS from healthy pregnancies.

DESIGN: Laboratory *in vitro* studies using the first-trimester TB cell line, HTR-8/SVneo (HTR-8). RNA-sequencing (RNA-seq) of HTR-8 cells and CVS.

MATERIALS AND METHODS: HTR-8 cells were exposed to hypoxia (2.5% O_2) or normoxia (21% O_2) for 6hrs and RNA-seq was performed. Significant differentially expressed genes (SDEGs) and upregulated Gene Ontology (GO) cellular pathways were identified. To determine if gene expression changes were associated with changes in cellular response, transwell assays were performed to assess HTR-8 cell migration and invasion after exposure to 2.5% O_2 or 21% O_2 for 6hrs and 24hrs. For transwell migration assays (n=6), number of migrated cells through culture inserts were counted. For invasion assays (n=6), number of cells that invaded into Matrigel and collagen I matrices were counted. Means were compared using unpaired t tests and statistical significance was defined as $p < 0.05$. To determine if changes in gene expression induced by exposure of HTR-8 to 2.5% O_2 were present in 2nd trimester CVS from PE pregnancies relative to healthy pregnancies, CVS were collected and analyzed under an IRB approved protocol. RNA-seq of CVS from PE (n=2) and healthy (n=4) pregnancies was performed and DEGs were identified.

RESULTS: GO analysis showed that exposure of HTR-8 to 2.5% O_2 for 6hrs upregulated cellular migration pathways. SDEGs included genes involved in TB migration and invasion (*MMP9, TIMP1,* and *PAPPA)*, as well as genes involved in tumor migration and invasion (*ACTA2, MFAP4, SNAI2, SLCO4A1, GDF15, KLF5, ZBTB20,* and *ZNF703*). HTR-8 cell migration and invasion, through both collagen I and Matrigel matrices, was significantly increased after exposure to 2.5% O_2 for 24hrs but not 6hrs. Analysis of RNA-seq data from CVS of PE and healthy pregnancies identified 17 significant DEGs, 4 of which (*FAT2, SPON2, RASGRF2*, and *SCLO4A1*) were decreased in CVS from PE pregnancies and are involved in cellular migration and invasion.

CONCLUSIONS: Exposure of 1st trimester TBs to physiologic hypoxic conditions induces expression of genes associated with cellular migration and invasion and increases 1st trimester TB migration and invasion *in vitro*. Decreased expression of migration and invasion genes in CVS from PE pregnancies may impair TB migration and invasion in the 2nd trimester of pregnancy, resulting in inadequate spiral artery transformation and prolonged hypoxia, preceding the development of PE.

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IN VITRO MATURED OOCYTES DERIVED FROM THREE DIMENSIONAL CULTURE (3-D) OF PRE-ANTRAL FOLLICLES IN A HYALURONAN BIO-MATRIX ARE FUNCTIONALLY COMPETENT.

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OBJECTIVE: In vitro culture systems that preserve 3-D follicle architecture and oocyte-granulosa cell interaction may be the key to in vitro oocyte maturation (IVM). Hyaluronan is one component of natural extracellular matrices that provide support to cells in vivo. This report describes the application of hyaluronan for 3-D in vitro follicle culture and the production of developmentally competent metaphase II oocytes.

DESIGN: Pre-antral follicle culture in vitro.

MATERIALS AND METHODS: Ovaries of 14- 16 day old B6D2F1 mouse pups were treated with collagenase. Released pre-antral follicles with 2-3 layers of granulosa cell were collected. The hyaluronan hydrogel (HA) was prepared by mixing 25 μl of the HA gel (3 mg/ml) with 1 μl of 0.03% hydrogen peroxide to initiate cross-linking. Microdrops of HA gel (5-7 μl) were placed in individual wells and rapidly seeded with 4 follicles before gelling was completed. Culture medium (100 μl) was added to each well and the dish was overlaid with oil. Follicle culture was performed in $\propto$-MEM supplemented with 5% FBS, 100 mIU/ml FSH, 10 mIU/ml LH and ITS. Dishes were incubated at 37°C with 6% CO2. Final maturation was triggered with hCG (1.5 IU/ml) and EGF (5 ng/ml) after 12 days of growth. Follicles were monitored daily. Mature oocytes were inseminated with epididymal sperm. Fertilization was assessed the following morning based on presence of 2 pronuclei or cleavage to 2-cell. Outcome parameters monitored were estradiol levels, follicle morphology and survival throughout the in vitro culture interval (IVC), germinal vesicle breakdown (GVBD), oocyte maturation to metaphase II stage, fertilization and development to blastocyst. Cell number in blastocysts was determined by Hoechst staining

RESULTS: Pre-antral follicles measured 121.9 $\pm$ 40.9 μM with oocyte diameters of 61.1$\pm$ 4.1 μM at time of seeding. Mean oocyte diameter, measured after maturation was 90.2 $\pm$ 8.0 μM. IVM data from three experiments were pooled. A total of 402 pre-antral follicles were embedded in HA gel. Antrums were observed in 55% of follicles by day 8. Post-hCG trigger 314 oocyte-cumulus complexes ovulated from the cultured follicles and 84% (264/314) underwent GVBD. The maturation rate to MII was 72.6%. (228/314). The fertilization rate was 82.5% (188/228). The subsequent blastulation rate with IVM oocytes was 46.3% (87/188). Blastocysts were cryopreserved for future transfer experiments to determine their ability to produce live offspring. Seven blastocysts were subsequently thawed and stained with Hoechst to determine cell number. Mean cell number was 55 $\pm$ 7.5.

CONCLUSIONS: HA was an excellent biomaterial for 3-D culture, allowing follicle growth, antrum formation and ovulation of oocyte-cumulus complexes upon hCG trigger. This matrix was easy to use, its rigidity could be adjusted and its transparent nature allowed optimal visualization. Functional competence of HA- matured oocytes was evidenced by their ability to fertilize and continue development to the blastocyst stage. Live birth data are needed to further validate this 3-D culture system. Testing of HA with follicles from larger animal models is warranted.

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SUPPORT: None

P-571

WITHDRAWN

P-572 4:30 PM Monday, October 19, 2020

CORONAVIRUS DISEASE (COVID-19): TRANSCRIPTOMIC AND PROTEOMIC INVESTIGATION OF CELLS OF THE MALE AND FEMALE REPRODUCTIVE SYSTEMS TO EVALUATE SARS-COV-2 INFECTION RISK.

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OBJECTIVE: To identify cell types in male and female reproductive systems at risk of SARS-CoV-2 infection based on expression of viral host entry proteins.

DESIGN: Transcriptomic and proteomic analysis.

MATERIALS AND METHODS: Publicly available single cell RNA sequencing (scRNAseq) data in human testis and non-human primate ovary was analyzed, as well as bulk RNA and proteomic data in human testis and ovary. Additionally, novel RNA sequencing data from 18 samples of human cumulus cells was generated. Tissue- and cell-type specific risk of viral infection was predicted based on the co-expression of host receptor angiotensin-converting enzyme 2 (*ACE2*) and transmembrane serine protease 2 (*TMPRSS2*) which are required for viral binding and cleavage, respectively. Expression of receptor basigin (*BSG*) and cysteine protease cathepsins L (*CTSL*) were also assessed as they are hypothesized to facilitate viral entry.

RESULTS: Based on scRNAseq data in non-human primate ovarian tissue, *ACE2* and *TMPRSS2* co-localize in a sub-population of oocytes in antral follicles (62% of cells, Pearson correlation=0.37), but to a lesser extent in less mature oocytes (Pearson correlation=0.13-.21) and not at all in ovarian somatic cells. While *ACE2* transcripts were detected in human cumulus cells (mean 24.03 transcripts per million), *TMPRSS2* expression was absent in 15/18 samples and low in the others (0.13 TPM). Consistent with these findings, bulk RNA and protein data showed *ACE2* expression in ovarian tissue, but no *TMPRSS2* expression. In testicular cells, including sperm, co-expression of *ACE2* and *TMPRSS2* was not detected (Pearson correlation=-0.01). Bulk RNA and protein data revealed *ACE2* but no *TMPRSS2* expression. *BSG* was more broadly expressed in testis than *ACE2* and was co-expressed with *CSTL* in early (78.7%) and late (90.8%) primary spermatocytes.

CONCLUSIONS: Given that known COVID-19 symptoms are associated with tissues co-expressing *ACE2* and *TMPRSS2* (e.g. lung, heart, kidney, gut), it is conceivable that reproductive function could be effected if constituent cells co-express these genes. Based on these results, testicular cells including sperm are not at risk of *ACE2-TMPRSS2*-mediated viral entry, however low levels of SARS-Cov-2 in human semen have been reported and may suggest alternative routes of entry. The cells predicted to have the greatest susceptibility to infection are antral oocytes which are either ovulated or atrophy within several days of appearance each cycle and are therefore unlikely to have sustained impact on female fertility if infected. Moreover, the lack of *ACE2-TMPRSS2* expression in cumulus cells may act as a barrier to infection. Therefore, procedures in which cumulus cell-enclosed oocytes are collected and fertilized outside the female reproductive tract (e.g. IVF) may not pose a risk. IVF success rates decline with increasing female age and it is therefore imperative that patients are allowed to access fertility treatments if safe to do so. The results presented here are indicative, but ovarian pathology data from women of reproductive age with COVID-19 at time of death is needed for definitive confirmation.

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SEPT12 EXPRESSION IN HUMAN TROPHECTODERM CELLS: INSIGHT INTO EMBRYONIC ARREST.

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OBJECTIVE: *SEPT12*, a member of the Septin gene family, has expression restricted to the testis and is critical for normal spermatogenesis. Septin genes code for polymerizing guanosine triphosphate (GTP) binding proteins whose homologs have been conserved throughout evolution from yeast to humans (1). Roles assigned to Septin genes include cell division, cytoskeletal organization, and membrane-remodeling events including the epithelial-mesenchymal transition in metastatic cancers (2). A study that investigated azoospermia and teratozoospermia in a mouse knockout model demonstrated oocytes fertilized via ICSI with sperm targeted *SEPT12* antisense alleles resulted in embryo arrest by the morula stage (3). The application of RNA sequencing to elucidate the expression profile of *SEPT12* in human preimplantation embryos may unlock insights into the transcriptional events of early embryogenesis.

DESIGN: Prospective cohort study on human, donated embryos.

MATERIALS AND METHODS: The study included patients who donated fresh embryos at the blastocyst stage during an IVF cycle between January, 2016 and June, 2016. Embryos were biopsied, and approximately 2-4 cells were removed for preimplantation genetic testing for aneuploidy (PGT-A) by next generation sequencing (NGS) using the ReproSeq assay to assess copy number variants (CNVs). The remaining cells of the embryo were designated for RNA Sequencing. Read counts per gene were summed across embryo cohorts and normalized using the median of ratios. Differential gene expression between embryo cohorts was calculated using DESeq2, in order to estimate variance-mean dependence and evaluate differential gene expression using a negative binomial distribution. A likelihood ratio test was used to account for heterogeneity due to patient, batch, and ploidy and growth status (arrested/ongoing). The adjusted threshold for significance was $p<0.05$.

RESULTS: 43 blastocysts underwent PGT-A assessment and RNA sequencing. 36 showed expression of *SEPT12*, 6 of the 7 blastocysts that failed to show *SEPT12* expression had poor trophectoderm morphology grade. The expression of *SEPT12* was further examined in 15 embryos, 9 were enriched (>90%) for trophectoderm cells (TE) and 6 enriched (>80%) for inner cell mass cells (ICM). *SEPT12* expression was significantly higher in TE cells than ICM cells, where $P<0.0001$.

CONCLUSIONS: Septins were first discovered nearly fifty years ago however their function remains poorly understood (4). The importance of this gene family has been indicated by the conservation of the functional domains throughout evolution. *SEPT12* has been shown to be critically important in spermatogenesis. This study is the first to characterize *SEPT12* expression in the human embryo. Our data supports the findings that wild type *SEPT12* expression was preferentially associated with blastocyst formation compared to arrest at the morula stage for embryos that contained the antisense *SEPT12* allele (3). Our current studies are focused on characterizing *SEPT12* expression in cleavage and morula stage human embryos to further elucidate this gene's role in early embryogenesis.

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SUPPORT: None

P-574 4:30 PM Monday, October 19, 2020

DIFFERENCES IN METABOLIC SIGNATURES BETWEEN THE INNER CELL MASS AND THE TROPHECTODERM IN DISCARDED HUMAN BLASTOCYSTS. Marta Venturas, M.Sc.,[1] Jaimin S. Shah, M.D.,[2] Tim H. Sanchez, Ph.D.,[3] Will Conway, Bs in Physics and Biology,[1] Denny Sakkas, PhD,[4] Dan Needleman, Ph.D.[1] [1]Harvard University, Cambridge, MA; [2]Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA; [3]None; [4]Boston IVF, Waltham, MA.

OBJECTIVE: To determine whether non-invasive metabolic imaging can detect differences in metabolic profiles between the inner cell mass (ICM) and the trophectoderm (TE) of discarded human blastocysts.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: We used 192 morphologically normal human vitrified blastocysts from 126 patients (mean age 35.5 ±4.75 years) that were discarded and donated for research under an approved institutional review board protocol. These embryos were warmed, cultured for 2h and imaged, to analyze their metabolic signatures. Metabolic function was assessed using Fluorescence Lifetime Imaging Microscopy (FLIM). FLIM enables non-invasive imaging of the autofluorescent endogenous molecules, NADH and FAD+, essential coenzymes for cellular respiration and glycolysis. FLIM yields quantitative information on metabolite concentrations from fluorescence intensity and on enzyme engagement from fluorescence lifetimes. A single measurement provides 9 metabolic parameters (4 for NADH, 4 for FAD and Redox Ratio) which was used to separately analyze the metabolic signatures of the ICM and TE from each embryo. Metabolic parameters from the ICM were compared to those of the TE using paired t-test analyses while a sub analysis of embryo day (5 or 6) was performed using multilevel models.

RESULTS: Our data showed statistically significant variations in all metabolic parameters between the ICM and the TE from discarded human blastocysts. Both NADH and FAD+ intensities, that correlate with the concentration of these coenzymes, were significantly different between the ICM and the TE ($p<0.0001$). Furthermore, the lifetimes of these molecules and the fraction engaged with enzyme were significantly different between the ICM and the TE ($p<0.0001$). These findings are in line with previous evidence in mouse blastocysts showing that the ICM of mouse embryos have a relatively quiescent metabolism compared with that of the TE. Additionally, metabolic signatures from the ICM and the TE correlated with blastocyst day. When comparing day 5 and day 6 embryos, distinct metabolic signatures were visualized in the ICM (6/9 FLIM parameters, $p<0.002$) and also in the TE (6/9 FLIM parameters, $p<0.001$).

CONCLUSIONS: Non-invasive metabolic imaging can detect significant metabolic variations between the ICM and TE of discarded human blastocysts, suggesting different metabolic demands specific to the ICM and TE. Further studies on human embryo samples are planned which will investigate possible correlations between metabolic signatures of both the ICM and the TE with embryo morphology and pregnancy outcomes.

SUPPORT: Supported by the Blavatnik Biomedical Accelerator Grant at Harvard University. Becker and Hickl GmbH, and Boston Electronics sponsored research with the loaning of equipment for FLIM.

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CIRCULATING MIRNAS AS A NON-INVASIVE DIAGNOSTIC TOOL TO PREDICT IMPLANTATION FAILURE. Chloé Baron, PhD student,[1] Delphine Haouzi, PhD,[1] Frida Entezami, MD,[1] Sophie Brouillet, PharmD, PhD,[1] Samir Hamamah, MD, PhD[2] [1]Inserm U1203, CHU Montpellier, St-Eloi Hospital, Montpellier, France; [2]Arnaud de Villeneuve Hospital, CHU Montpellier, Montpellier, France.

OBJECTIVE: Do circulating miRNAs profile during the implantation window under the same hormone replacement therapy (HRT) treatment for frozen embryo replacement cycle,predict successful pregnancy?

DESIGN: Serum (n=14) were collected during the implantation window from repeated implantation failure (RIF) patients (mean ± SD, age: 38.6 ± 5.0 years) under HRT treatment for subsequent frozen embryo transfer. RNAs were extracted to perform the miRNA expression profile. Then, miRNA expression was analyzed according to the following pregnancy outcome: successful implantation (n=7) or implantation failure (n=7). Successful implantation was defined as both positive b-hCG and clinical pregnancy and implantation failure as negative b-hCG.

MATERIALS AND METHODS: Serum were obtained during a mock HRT treatment cycle from 14 RIF patients. Then, miRNA expression profile between groups, successful *vs*. implantation failure after frozen embryo replacement was evaluated by Next Generation Sequencing using the HTG EdgeSeq miRNA Whole Transcriptome Assay (Illumina, Firalis). miRNA sequencing data were normalized using the method recommended by HTG molecular diagnostic. Then, statistical analysis and receiver operating characteristic (ROC) analysis were applied to miRNA sequencing data.

RESULTS: We identified 44 miRNAs differentially expressed between groups with a fold change > 2 and a p-value < 0.05. All miRNAs were overexpressed in serum from patients with successful implantation. Supervised hierarchical clustering of these 44miRNAs showed a good segregation of serum samples from patients with and without a successful implantation. Related to these 44 miRNAs, we note four of them which are members of the let-7 family [miR-1 (x2.4, $p = 0.017$, AUC $= 0.88$), miR-2 (x2.2, $p = 0.004$, AUC $= 0.94$), miR-3 (x2.1, $p = 0.001$, AUC $= 0.90$), miR-4 (x2.1, $p = 0.001$, AUC $= 0.98$)].The microRNA target filter function from Ingenuity software predicted that 1375 mRNAs were targeted by the let-7 family that are involved in cell invasion, proliferation, growth and survival via integrin subunit beta 3 (*ITGB3*), vimentin (*VIM*), B-cell CLL/lymphoma 2 like 1 (*BCL2L1*) that play a central role in endometrial receptivity acquisition and implantation process. These results might have potential clinical applications to develop a non-invasive diagnostic tool to predict successful implantation, to avoid endometrium biopsy and consequently, to increase IVF/ICSI success.

CONCLUSIONS: We identified a miRNA signature in serum during the implantation window that can predict successful implantation. This information is crucial and can lead to the development a prognostic tool of the attempt, opening new perspectives in the patient care management. Further investigations with a larger number of patients are in progress to validate theses results.

SUPPORT: This study was partially supported by a grant from Gedeon Richter company.

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DISRUPTION OF NRF2- MEDIATED STRESS RESPONSE AND DNA REPAIR PATHWAYS ARE ASSOCIATED WITH LIMITED DEVELOPMENTAL POTENTIAL OF TRISOMY EMBRYOS. Jason C. Parks, BS, Mary E. Haywood, PhD, Blair R. McCallie, BS, Sue McCormick, BS, William B. Schoolcraft, MD, Mandy G. Katz-Jaffe, PhD. Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Embryonic chromosomal trisomy is recognized as a leading cause of reproductive failure and pregnancy loss in human reproduction. Interestingly, specific trisomy's have differing implantation potential and only a handful of trisomies (chromosome 13, 18, 21, X and Y) will even develop past the first trimester. The aim of this study was to investigate the association between the embryonic transcriptome and a range of embryonic trisomy with differing implantation potentials.

DESIGN: Research study.

MATERIALS AND METHODS: Surplus, frozen blastocysts (n = 55) were donated to research with IRB and patient consent. Blastocysts underwent micromanipulation to isolate trophectoderm (TE) cells for transcriptome analysis. In addition to euploid blastocysts (n=17), the following trisomies were identified based on differing implantation potential: trisomy 7 (n=11) and trisomy 11 (n=5) that are most likely to result in implantation failure, as well as trisomy 15 (n=11) and trisomy 22 (n=11) which are able to implant but will always result in miscarriage. Individual TE total RNA (n = 25) was isolated for sequencing on the NovaSEQ 6000 (Illumina). Reads were aligned to hg38 using GSNAP and only reads mapping to non-trisomy chromosomes were included in downstream analysis (genes on chromosomes 7, 11, 15, and 22 were excluded in all samples). Differential gene expression was analyzed with edgeR and limma (FDR<5%), and interpreted using Ingenuity Pathway Analysis (Qiagen). Validation was performed on additional individual TE samples (n = 30; 6 per group) with gene expression confirmed using Real-Time PCR (ViiA 7 Real-Time PCR System; $P<0.05$).

RESULTS: An interplay of several biological processes were evident in all trisomy embryo groups compared to euploid, regardless of the specific chromosome involved in the meiotic error, with a total of 389 differentially expressed genes ($P<0.05$). There was no enrichment for chromosome type or cytoband. Pathway analysis identified a globally inhibited NRF2-mediated stress response including validation of the two central players in the pathway, NRF2 and KEAP1 ($P<0.001$) and 8 significantly decreased NRF2 targets

(regulating key antioxidant and metabolic genes; P<0.05). CLPTM1L, also a target of NRF2, was validated showing increased expression that may result in activation of apoptosis (P<0.05). DNA damage response was also significantly associated with embryonic trisomy (P<0.05). Specific validated genes included confirmation of significant increased expression of BRCA2, PALB2 and ATR, all genes that are essential for DNA damage repair pathways (P<0.0001).

CONCLUSIONS: This in-depth molecular characterization of embryonic trisomy concluded that regardless of the individual triploid chromosome, a globally compromised transcriptome was apparent. Significant disruption to the NRF2- mediated stress response and DNA repair pathways were specifically evident in all trisomy embryos, which explains why the vast majority of trisomy conceptions will have limited potential and perish during the early stages of development.

SUPPORT: None

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AGE-EFFECT ON THE FATTY ACID AND LIPIDOMIC PROFILE OF THE FOLLICULAR FLUID DURING IN-VITRO FERTILIZATION CYCLES.

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OBJECTIVE: Compelling evidence suggests that the metabolic profile and lipidomic composition of the human follicular fluid (FF) may play a role in reproductive outcomes. However, there are gaps in current knowledge regarding the follicular environment of aging, which is the main factor affecting female reproductive capacity. Thus, we aimed to evaluate if there is any variability in the fatty acid and lipidomic composition of the FF between oocyte donors and infertile patients with advanced age.

DESIGN: Prospective observational case-control and experimental study.

MATERIALS AND METHODS: Non-targeted lipidomic and fatty acid analysis of the FF from two groups: 17 oocyte donors aged < 35 years *versus* 17 infertile women aged ≥ 38 years that underwent controlled ovarian stimulation with an antagonist protocol between September and October 2018. Women with diseases that could potentially impair ovarian function were excluded. Pooled follicular aspirate from each patient was centrifuged at 800g for 20 min to isolate FF from cells. The supernatant was sterile-filtered using a 0.22 mm pore size membrane filter and stored at -80oC. Lipids were extracted according to the method of Bligh and Dyer, subjected to liquid chromatography-mass-spectrometry and analysed using MassHunter Qualitative Analysis software. Fatty acid groups were analysed as methyl ester derivates by gas chromatography and compared with authentic standards.

RESULTS: We detected 4431 molecular species in the FF. Only those found in at least 70% of samples of the quality-control and presenting a low variability were selected, which resulted in 159 lipid species. Multivariate analysis failed to demonstrate statistically significant differences in the lipidomic profile between groups. Principal component analysis (PCA) and hierarchical clustering revealed that the lipidome does not seem to be an important feature defining the reproductive age. Similarly, partial least square-discriminant analysis (PLS-DA) was applied to identify molecules that could explain variability within samples. Despite the good clusterization between groups, permutation test and cross-validation showed that the model was overfitted. Univariate statistics revealed two lipid species which were substantially increased in the older group. Those were the ones with the highest weight explaining the variability in the PLS-DA model. Unfortunately, only one of them could be identified, the sphinganine. Finally, we analyzed the fatty acid composition of samples, but no differences were found regarding saturated fatty acids, unsaturated fatty acids, monounsaturated fatty acids, and polyunsaturated fatty acids n-3 and n-6 series. Likewise, the double bond index and the peroxidability index were similar between groups.

CONCLUSIONS: The sphinganine was the only lipid specie showing higher concentrations in FF from older patients. Since the sphinganine is a precursor of ceramide, it could be associated with increased apoptotic metabolism and, ultimately, depletion of ovarian reserve and function as women age. Further molecular studies should confirm our findings.

SUPPORT: IVIRMA-Madrid, Spain

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MITOCHONDRIAL STRESS RESPONSE GENE CLPP IS NOT REQUIRED FOR GRANULOSA CELL FUNCTION.

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OBJECTIVE: Mitochondrial unfolded protein response (mtUPR) is a highly conserved mechanism by which cells can maintain their homeostasis in the presence of cellular or metabolic stress. CLPP (caseinolytic peptidase P) plays a key role in this process by promoting degradation of unfolded mitochondrial proteins. We have previously shown that global deletion of *Clpp* in mice results in female infertility and accelerated follicular depletion. However, it is not known whether the infertility phenotype observed in mice with global deletion of *Clpp* results from an impact on oocytes, granulosa cells, or both. In this study, we investigated whether CLPP is required for granulosa cell function.

DESIGN: Experimental study.

MATERIALS AND METHODS: $Clpp^{flox/flox}$ mice were generated and crossbred with *Cyp19a1-Cre* mice in order to generate mice with granulosa cell specific *Clpp* deletion ($Clpp^{-/-}$). Mature (8-week old) $Clpp^{-/-}$ female mice were compared to same age wild type (WT) mice. To assess fertility, $Clpp^{-/-}$ (n=8) were mated with adult WT males with proven fertility for 12 weeks and compared to WT female mice (n=8). To analyze folliculogenesis, serial ovarian sections were obtained and stained with hematoxylin and eosin. Primordial, primary, secondary, early antral and antral stage follicles were counted and numbers were compared between $Clpp^{-/-}$ and WT mice. Mice were injected with of PMSG (5IU) or PMSG and HCG (5IU) to assess generation of germinal vesicle and MII stage oocyte, respectively. ANOVA, student's t-test, and Chi Square analysis were used for statistical analysis as appropriate.

RESULTS: Fertility of mature $Clpp^{-/-}$ female mice was similar to WT females; they produced similar number of pups per litter (9.0±1.0 vs 7.32±0.58, p=0.067). Folliculogenesis was not affect by loss of CLPP in granulosa cells as $Clpp^{-/-}$ and WT mice had similar numbers of primordial (317.80±119.90 vs 278.20±13.08, p=0.69), primary (147.80±88.74 vs 135.30±31.47, p=0.87), secondary (71.0±26.16 vs 83.50±3.54, p=0.57), early antral (54.75±12.37 vs 46.25±13.08, p=0.57), and antral follicles (3.0±2.12 vs 1.75±0.35, p=0.5). Number of GV (32.67±2.52 vs 40.67±6.11, p=0.10) and MII (19.0±8.19 vs 22±2.65, p=0.59) oocytes collected from $Clpp^{-/-}$ and WT female mice were also similar.

CONCLUSIONS: Fertility in female mice is not affected by granulosa cell-specific mtUPR disruption through CLPP deletion even though mtUPR and CLPP have been shown to be required for female fertility and oogenesis. Our findings suggest that oocyte but not granulosa cells require CLPP-mediated mtUPR.

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SUPPLEMENTATION OF CULTURE MEDIUM WITH MELATONIN IMPROVES BLASTOCYST DEVELOPMENT AND REVERSES GLUCOSE INTOLERANCE IN IVF MICE.

Yanping Jia, student, Wenqiang Liu, Research associate, Dandan Bai, student, Kunming Li, professor, Miaoxin Chen, PhD Center for Reproductive Medicine, Shanghai First Maternity and Infant Hospital,Tongji University, Shanghai, China.

OBJECTIVE: This study aimed to determine if the adverse effects of IVF on blastocyst and offspring could be reversed by supplementation of culture medium with melatonin in mice.

DESIGN: A cross-sectional mouse model was utilized, wherein blastocysts were generated by natural mating (control group) or IVF with or without melatonin (10^{-6}M) (mIVF and IVF group respectively) in clinical grade fertilization and culture media. Blastocysts were transferred to pseudo-pregnant ICR females. Cell lineage allocation was assessed for 30-40 blastocysts from each group. Body weight, glucose tolerance, energy expenditure, hepatic gene expression was measured in 6-10 mice from each group.

MATERIALS AND METHODS: C57BL/6 female mice and DBA2 male mice were used to generate blastocysts by natural mating (control group) or IVF with or without melatonin (10^{-6}M) (mIVF and IVF group respectively) in clinical grade fertilization and culture media. Blastocysts were transferred to pseudo-pregnant recipients. Embryo development was recorded for IVF groups. Cell numbers of inner cell mass (SOX2) or trophectoderm (Cdx2+) were determined by immunohistochemistry. Males were weaned at 3 weeks

of age onto a chow diet or a high-fat diet (60% fat) for 8 weeks. Glucose tolerance was assessed by an intraperitoneal glucose tolerance test (2g/Kg). Energy metabolism was examined in metabolic cages. Hepatic gene expression was measured by RNA-Seq and validated by real-time quantitative PCR.

RESULTS: Blastocyst rates were similar in the two IVF groups. Reduced inner cell mass, trophectoderm and total cell number were observed in IVF blastocysts, compared with the control group ($P<0.05$). IVF pups had significantly lower birth weight and body weight before weaning, but exhibited increased body weight and liver weight at 11 weeks of age compared with controls ($P<0.05$), independently of diet. IVF mice were glucose intolerant shown as an increased glucose area under the curve, and had decreased energy expenditure as well as a large number of differentially expressed genes related to metabolic pathways in the liver tissue compared with the control group ($P<0.05$), independently of diet. The mIVF group showed intermediate cell numbers in blastocysts, body weight, liver weight and differentially expressed hepatic genes compared with the IVF group and control group, and normalized glucose tolerance and energy expenditure compared with the IVF group ($P<0.05$), independently of diet. Importantly, there was no significant difference in glucose tolerance and energy expenditure between the mIVF group and the control group.

CONCLUSIONS: The data suggests that supplementation of culture medium with melatonin improved IVF blastocyst differentiation, reduced excessive weight gain after birth and normalized glucose intolerance in adult male offspring of IVF mice.

SUPPORT: The study was funded by two grants from the National Natural Science Foundation of China (81671468, 81871213).

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BREAKDOWN OF FOLLICLE-OOCYTE COMMUNICATION CONTRIBUTES TO AGE-RELATED INFERTILITY: DISRUPTED *TGFB1* SIGNALING IMPAIRS ACQUISITION OF OOCYTE COMPETENCE. Jennifer E. Russ, BS, Mary E. Haywood, PhD, Blair R. McCallie, BS, William B. Schoolcraft, MD, Mandy G. Katz-Jaffe, PhD Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Ovarian aging precedes that of any other mammalian organ, and resultant attenuated oocyte quality and quantity are key limiting factors in female fertility. Our aim is to elucidate the impact of ovarian aging on folliculogenesis and oocyte development as it pertains to reduced female reproductive potential.

DESIGN: Longitudinal research study.

MATERIALS AND METHODS: Outbred female mice were naturally aged to represent young (3-4 months old; Young) and advanced reproductive age (12-15 months old; Aged) populations. Total RNA was isolated from individual follicles (n=6 per age group) and oocytes (n=12 per age group). Sequence libraries were prepared using the NEBNext Single Cell/Low Input RNA library prep kit and sequenced on the Illumina NovaSEQ6000. Differentially expressed genes (DEGs) were generated using edgeR and evaluated by Ingenuity Pathway Analysis (IPA)(Qiagen). Sequencing was validated by RT-qPCR on additional follicles (Applied Biosystems) (n=6 per age group).

RESULTS: A globally decreased transcriptome was observed for the Aged females. In the follicles, 24,373 transcripts were identified, which included 7,388 DEGs in the Aged females (2,921 increased and 4,461 decreased in expression; $p<0.01$). Single-cell RNA sequencing of oocytes identified 12,986 transcripts and 226 DEGs in Aged oocytes (64 increased and 162 decreased in expression; $p<0.05$). Unsupervised hierarchical clustering of DEGs cleanly separated follicles and oocytes according to female age. IPA revealed significant decreased expression of EIF2 Signaling, Cell Cycle Control of Chromosomal Replication, Estrogen-mediated S-phase Entry and G2/M DNA Damage Checkpoint Regulation in Aged follicles ($p<0.0001$), indicating severe impairment of DNA replication, protein translation, cell division and proliferation. In the oocyte, transforming growth factor beta 1 (*Tgfb1*) was identified as the most significant upstream regulator and predicted to be inhibited in Aged oocytes ($p<0.0001$). *Tgfb1* signaling maintains meiotic arrest within the oocyte, and its disruption results in premature meiotic resumption. *Tgfb1* is initially secreted from the follicle as an inactive precursor molecule unable to interact with cellular receptors until activated. We observed increased *Tgfb1* expression in the follicle accompanied by inhibited *Tgfb1* signaling in the oocyte, suggesting that activation of latent *Tgfb1* is prevented in the Aged follicle. Conversion of *Tgfb1* to its biologically active form occurs through various tissue-specific mechanisms, and our data implicates Thrombospondin-1 (*Thbs1*). *Thbs1* is a known activator of *Tgfb1* and exhibited significantly decreased expression in Aged follicles ($p<0.005$).

CONCLUSIONS: Insufficient expression of *Thbs1* required for *Tgfb1* activation could lead to aberrant *Tgfb1* follicle-oocyte signaling resulting in premature meiotic resumption and oocyte incompetence. Collectively, these results provide insight to the molecular mechanisms of ovarian aging and suggest that disrupted intercellular communication between follicle and oocyte contributes to the fertility decline with age.

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OVARIAN TISSUE FROM DECEASED DONORS MAINTAINS NORMAL FOLLICLE VIABILITY DESPITE PROLONGED COLD ISCHEMIA. Yuting Fan, MD, PhD,[1] Colleen L. Flanagan, MSE,[1] Margraret Brunette, MS,[1] Andrea Jones, PhD,[1] Sherman Silber, MD,[2] Ariella Shikanov, PhD[1] [1]University of Michigan, Ann Arbor, MI; [2]Infertility Center of St. Louis, St. Louis, MO.

OBJECTIVE: To evaluate the number and quality of ovarian follicles that can be isolated from young deceased human donors before and after cryopreservation.

DESIGN: Fresh ovaries were obtained from 5 deceased donors aged 18-26 years from the International Institute for the Advancement of Medicine (IIAM) between 1/10/19 and 12/20/19.

MATERIALS AND METHODS: The characteristics of the donors, average cold ischemic time during transportation, volume of the ovaries and follicle density were analyzed. Ovarian cortex tissues were dissected from ovaries and ovarian tissue cryopreservation (OTC) was performed using slow freezing. Follicle morphology and classification were assessed with hematoxylin-eosin staining. DNA fragmentation of follicles and stroma was detected with TUNEL staining. Preantral follicles were enzymatically isolated from fresh and cryopreserved/thawed ovarian tissue. Follicle viability was determined using LIVE/DEAD staining.

RESULTS: Histologically, the mean follicle density in the 5 donors was 1781 ± 2249 follicles/mm^3 (mean $\pm$ SD), ranging from 14-4704 follicles/mm^3. Follicle density negatively correlated with age ($r = -0.943$, $P < 0.05$). A total of 2803 follicles from fresh and 1608 follicles from cryopreserved tissues were classified and analyzed. The average percent of morphologically normal follicles in cryopreserved/thawed and fresh group was 95.88% and 95.67% respectively, while there was no significant difference between the two groups ($P > 0.05$). Analysis of the data obtained from histologic slides stained with the TUNEL assay indicated no significant differences in DNA damage in the follicles and the stroma cells after cryopreservation compared to fresh tissue ($P > 0.05$). Morphologically normal preantral follicles were enzymatically isolated from both fresh and cryopreserved tissue with $88.51 \pm 5.93\%$ (mean $\pm$ SD) of the isolated follicles confirmed viable ($n = 443/490$).

CONCLUSIONS: The quantity and quality of follicles isolated from fresh and cryopreserved ovarian tissue of deceased donors were not affected by ischemia during transport of the organs from the hospital to the laboratory. Follicles at different developmental stages tolerated the cryopreservation process and maintained a high survival rate. The ample source of human ovarian tissues obtained from deceased donors may be applied to promoting research and future clinical applications.

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UNIQUE SUBCELLULAR CO-LOCALIZATION OF FMR1 WITH FIBRILLARIN AND AMH IN GRANULOSA CELLS SUGGESTS NOVEL ROLES IN LOCALIZED REGULATION OF CELL CYCLE PROGRESSION. Jianjun Hu, MD,[1] Min Yang, PHD,[2] Lin Zhang, MD,[1] David F. Albertini, PhD, MS,[1] Emanuela Molinari, PhD,[1] David H. Barad, MD, MS,[1] Norbert Gleicher, MD[3] [1]Center for Human Reproduction, New York, NY; [2]Rockefeller University, New York, NY; [3]Center for Human Reproduction, Foundation for Reproductive Medicine, Rockefeller University, Medical University Vienna, New York, NY.

OBJECTIVE: To explore where and how FMR1 protein, as an RNA-binding protein, plays at subcellular level in granulosa cells multiple roles in regulating ovarian reserve and follicle recruitment.

DESIGN: Experimental human research.

MATERIALS AND METHODS: Granulosa and cumulus cells were in IVF cycles isolated from follicular fluids after oocyte collection and

cumulus-oocyte-complex identification. Primary and selectively cultured granulosa cells were stained after whole mount fixation or chromatin spread for subcellular localization analysis. To characterize the structural nature of unique localization patterns inside the nucleus and the peri-nuclear region, double staining of FMR1-Fibrillarian (nucleolus marker), FMR1-CREST (centromere marker), FMR1-gamma-tubulin (centrosome marker), FMR1-AMH (anti-Müllerian hormone), and AMH-gamma-tubulin, were performed, respectively. Phosphorylated FMR1 (pS1194) antibody was used to verify the novel findings of FMR1 antibody. Puromycin treatment followed by immunostaining was applied to determine whether FMR1, fibrillarin and/or AMH were enriched in active puromycin incorporation sites, suggesting relatively active protein translation regions. Matched secondary antibodies were used as controls for staining background. GAPDH and TOM20 antibodies were used as controls for antibody specificity.

RESULTS: Unique subcellular localization patterns of FMR1 in granulosa cells were observed by nuclear spread and whole mount preparation followed by immunostaining. Interestingly, FMR1 was enriched in the nucleolus as confirmed by double staining of FMR1-Fibirllarian (nucleolar marker). Unexpectedly, FMR1 protein was enriched in centromere (CREST as the marker) in metaphase, but not in any non-metaphase. Strikingly, FMR1 was found in centrosomes (gamma-tubulin as the marker) in both metaphase and non-metaphase. More strikingly, we found that: (i) AMH, previously reported diminished in large antral follicles, was relatively enriched in centrosomes; (ii) Double staining of FMR1-Fibrillarin, FMR1-gamma-tubulin, AMH-Fibrillarin, AMH-gamma-tubulin verified that FMR1, Fibrillarin and AMH were all co-localized in centrosomes in non-metaphase. Puromycin incorporation showed that FMR1, phospho-FMR1 (pS1194), Fibrillarin and AMH were co-enriched with puromycin signals in the nucleolus and centrosomes in many of the stained cells. As controls, GAPDH and TOM20 did not show similar patterns.

CONCLUSIONS: In granulosa cells, FMR1 and its phosphorylated form FMR1(pS1194) localized to the nucleolus and centrosomes in non-metaphase, and to both centromeres and centrosomes in metaphase. FMR1 and AMH were, thus, unexpectedly found co-enriched in centrosomes in non-metaphase, unexpectedly revealing that FMR1 might play roles in regulating nucleolar assembly and disassembly, spindle formation and/or stability as well as chromosome segregation in cell cycles. Further studies identifying FMR1 targets, and characterizations of inter-talk or inter-regulation between FMR1 and AMH are underway.

SUPPORT: Intramural funds from The Center for Human Reproduction and Foundation for Reproductive Medicine.

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ASSOCIATION BETWEEN THE PERCENTAGE OF P16-POSITIVE SENESCENT CELLS AND THE EXPRESSION OF ESTROGEN AND PROGESTERONE RECEPTORS IN HUMAN ENDOMETRIUM DURING THE MID-LUTEAL PHASE. Dimitar Parvanov, PhD, Rumiana Ganeva, MSc, Nina Vidolova, MSc, Georgi Stamenov, MD/PhD. Nadezhda Women's Health Hospital, Sofia, Bulgaria.

OBJECTIVE: Progesterone and estrogen secretion and the expression of their receptors are strongly connected with the cyclic changes in endometrium and its receptivity. We previously reported that the frequency of occurrence of p16-positive senescent cells in human endometrium appear to be also associated with endometrial receptivity and successful embryo implantation. The objective of this study was to analyze the relationship between the percentage of senescent cells and estrogen and progesterone receptors expression in human endometrium during the mid-luteal phase of the menstrual cycle.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: This study includes 383 women who had an endometrial biopsy during the mid-lutheal phase (7 days after LH surge) of the natural cycles. Tissue sections were stained immunohistochemically for ER, PR and p16 using the following monoclonal antibodies: progesterone receptor (PR) (NCL-PGR-312, Leica Microsystems), 1:100 dilution; estrogen receptor (ER) (NCL-L-ER-6F11, Leica Microsystems), 1:100 dilution; p16 ^{ink4a} antibody (MAD-000690QD–7, Master Diagnostica), ready-to-use. The percentage of positively stained p16 cells and the levels of ER/PR expression were evaluated by Image-J software (NIH, Maryland, USA) in multiple endometrial sections. Statistical analysis was performed by Spearman's correlation test using SPSS v.21 (*IBM* Corp., Armonk, NY, USA).

RESULTS: No correlation was found between the frequencies of occurrence of senescent p16-positive stromal, luminal and glandular epithelial cells and PR ($p>0.05$). In contrast, the glandular expression of ER showed low, but a significant correlation with the percentage of p16+ glandular epithelial cells ($R=0.34$; $p=0.03$).

CONCLUSIONS: In conclusion, we found that the increased cell senescence in endometrial glands during the mid-luteal phase is associated with increased expression of glandular ER in the mid-luteal phase of the cycle. These results suggest an estrogen related change of endometrial senescent cells during the period of embryo implantation.

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EARLY EMBRYO INITIATED UTERINE RECEPTIVITY REGULATED BY LOCAL APOPTOTIC CASPASE-3 MEDIATED PROSTAGLANDIN ACTION. Sicily E. Garvin, MD, MSBS,[1] Chandrashekhara Kyathanahalli, PhD,[2] Jeyasuria Pancharatnam, PhD,[2] Jennifer Condon, PhD[2] [1]Wayne State University, Detroit, MI; [2]Wayne State University School of Medicine, Detroit, MI.

OBJECTIVE: We observed a twenty-fold increase in caspase-3 activation in pregnant the mouse uterus on day 1 post coitus (1dpc) which rapidly declined on 2dpc to barely detectable levels. The function of caspase-3 at this early gestational time-point in pregnancy has not been determined. We have previously determined that elevated levels of apoptotic caspase-3 at term regulate uterine prostaglandin synthesis through the cleavage and activation of phospholipase-A2 (iPLA2). Therefore, the primary objective of this current study was to determine if elevated caspase-3 on 1dpc also regulates prostaglandin synthesis very early in pregnancy, which others have demonstrated to play a leuteoprotective role, thereby enhancing uterine receptivity. Our secondary objective was to determine if the conceptus was the trigger for this very early pregnancy surge in uterine caspase-3.

DESIGN: Prospective laboratory animal study using pregnant mouse models.

MATERIALS AND METHODS: Utilizing an inbred strain of non-pregnant mice, the following mouse models were created. Unilaterally ligated and bilaterally ligated mouse models were generated with non-pregnant mice that underwent surgical ligation of uterine horn/horns just proximal to the oviduct. Mice which did not undergo surgical uterine horn ligation, served as controls. All mice were time mated, sacrificed and uteri collected from pregnant control mice on day 1-19 dpc, unilateral and bilateral and control pregnant mouse models on day 1, 3 and 6 of gestation and non-pregnant mice at estrous and diestrous ($n=3$ for each). Uteri were examined for apoptotic indices, including caspase-3 activation and TUNEL staining. Immunohistochemical analysis was performed to identify the site of apoptotic caspase-3 activation. Cytoplasmic and nuclear extracts were prepared and examined for caspase-3 activation, PARP cleavage and the appearance of cleaved iPLA2 by western blot analysis, PDI and NCOA3 served as our loading controls.

RESULTS: Apoptotic caspase-3 and iPLA2 cleavage were isolated to the uterine endometrial compartment in control mice and both uterine horns of unilaterally ligated model solely on 1dpc. Apoptotic caspase-3 and cleaved iPLA2 were absent in the bilaterally ligated uterine horn model on all days examined.

CONCLUSIONS: Our data supports, a novel link for apoptotic endometrial casepase-3 in promoting prostaglandin mediated uterine receptivity in early pregnancy. The absence of apoptotic caspase-3 and iPLA2 cleavage in the bilaterally ligated uterine horn supports that the early conceptus and not coitus acts as the trigger for endometrial caspase-3 in very early pregnancy. We therefore propose that the conceptus releases systemic signals as evidenced by caspase-3 activation and cleaved iPLA2 in both horns of the control and unilateral pregnant model on 1dpc, acting to increase prostaglandin E2 levels thereby supporting corpus luteal progesterone production and endometrial receptivity in very early pregnancy.

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INTERFERON-STIMULATED GENE 15 ENHANCEMENT OF TROPHOBLAST INVASION IS REGULATED BY INCREASED FILAMENTOUS-ACTIN FORMATION AND β1 INTEGRIN EXPRESSION AND DECREASED β4 INTEGRIN LEVELS. Ali E. Wells, MD, A. S. L. I. Ozmen, PhD, Xiaofang Guo, MD, Ozlem Guzeloglu-Kayisli, PhD, Charles J. Lockwood, MD, MHCM, Umit A. Kayisli, PhD. Department of Obstetrics and Gynecology, Morsani College of Medicine, University of South Florida, Tampa, FL.

OBJECTIVE: During early placentation, cytotrophoblasts differentiate to an invasive phenotype associated with increased β1 integrin and decreased β4 integrin expression. We previously showed significantly decreased interferon-stimulated gene 15 (ISG15) expression in interstitial extravillous trophoblasts (EVTs) in the decidua basalis of pre-eclamptic *vs.* gestational-age-matched control specimens. We also showed that silencing ISG15 inhibits trophoblast migration/invasion in an HTR8 cell line (EVT cells). We hypothesize that ISG15 regulates trophoblast invasion by switching integrin types and regulating filamentous- (F-) actin formation. Thus, this study investigates expression of integrin-β4 as a non-invasive hemi-desmosome receptor, and integrin-β1, an extracellular matrix receptor of invasive trophoblasts and F-actin levels as an indicator of focal adhesion and migration in ISG15-silenced HTR8 cells.

DESIGN: Laboratory research, designed to study role of ISG15 in regulation of β1and β4 integrin and F-actin formation in trophoblast cultures**.**

MATERIALS AND METHODS: HTR8/SVNeo cell cultures were grown to confluence and were transfected with either scrambled (control) or ISG15 siRNAs according to the manufacturer's protocols. qRT-PCR analysis was used to amplify the target genes: human β1 integrin (*ITGB1)*, human β4 integrin *ITGB4,* and housekeeping gene human *ACTB*. Phalloidin-conjugated F-actin immunofluorescence staining was performed to compare F-actin formation in ISG15-siRNA versus control-siRNA transfected HTR8 cell cultures. Results were analyzed via *t-test* where $P<0.05$ was considered significant.

RESULTS: We initially confirmed that ISG15 siRNA treatment reduced levels of ISG15 mRNA and protein expression in HRT8 cells analyzed by qPCR and immunoblot analyses. qRT-PCR analysis revealed that ISG15 siRNA silencing led to a significant decrease in *ITGB1* mRNA expression (1.00± 0.00 *vs*. 0.42± 0.11 *P=0.007*, n=3) and a significant increase in *ITGB4* mRNA expression (1.01± 0.01 *vs*. 1.73± 0.15 *P=0.009*, n=3) compared to control siRNA treated group. Moreover, immunofluorescence staining revealed ISG15 silencing in HTR8 cells resulted in reduced F-actin formation compared to controls.

CONCLUSIONS: These results indicate that ISG15 stimulates trophoblast differentiation toward an invasive phenotype and that silencing of ISG15 in trophoblast cultures upregulates β4 integrin and inhibits β1 integrins and F-actin formations, thereby contributing to reduced trophoblast invasion.

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PHTHALATES AND HYPEROSMOTIC STRESS FORCE LOSS OF GROWTH AND PROGRESSION PAST G1 PHASE IN FUCCI EMBRYONIC STEM CELLS. Elizabeth E. Puscheck, MD, MS, MBA,[1] Mohammed Abdulkareem Abdulhasan, Ph.D.,[2] Steven J. Korzeniewski, Ph.D.,[3] Katherine Gurdziel, Ph.D.,[4] Douglas Ruden, Ph.D.,[4] Daniel Rappolee, Ph.D.[3] [1]InVia Fertility, Hoffman Estates, IL; [2]Reproductive Stress 3M, Inc., Grosse Pointe Farms, MI; [3]Wayne State University School of Medicine, Detroit, MI; [4]Wayne State University, Detroit, MI.

OBJECTIVE: Determine whether various stresses including positive control hyperosmotic sorbitol, hormonal cortisol, PFOA (Perfluorooctanoic acid) and phthalates slow growth and suppress cell cycle progression measured by FUCCI (Fluorescence Ubiquitination Cell Cycle Indicator) embryonic stem cells (ESC) to test for effects on growth and stemness/differentiation balance.

DESIGN: Experimental

MATERIALS AND METHODS: FUCCI- ESC were tested for confluence/growth and cell cycle commitment by IncuCyte Zoom by bulk or single cell (sc) RNAseq after 72 hr exposures to 0-300 mM hyperosmotic sorbitol or 1 nM-100uM PFOA (with stemness-maintaining Leukemia Inhibitory Factor, LIF) to quantify stress-forced differentiation. Controls for normal stemness were LIF+ and normal differentiation were LIF-. RNA was isolated by RNAeasy lysis or 10XGenomics Dropseq, RNA quality was checked by Agilent TapeStation, cDNA was synthesized using Lexogen's QuantSeq library kit, and barcoded, multiplexed and sequenced by Illumina NovaSeq 6000. Data were demultiplexed by CASAVA software and FC expression was compared between conditions. In triplicate experiments, significant fold change (FC) genes ($FC\geq 2$; $FDR\leq 0.05$, $P<0.05$) identified affected genes. Validating studies including qPCR.

RESULTS: Hyperosmotic sorbitol and PFOA caused dose-dependent decrease in growth measured by confluence and decreased fraction of fluorescent green cells moving from G1 into cell cycle S-M phase. IC50 for PFOA at approximately 1 uM is consistent with several in vitro and in vivo assays. Significant increases in cell checkpoint gene transcripts in hyperosmotic stressed ESC compared with normally differentiating ESC by p-Value and FDR were observed for TRP53 (2.1fold), Cdkn1c/p57KIP2 (4.1fold), and decreased Cdk5r2 (3.2fold) were observed, although decreases in Cdkn2a/p16/INK4A (3.5 fold) was observed. Like trophoblast stem cells, media change at 24 hr is insufficient to maintain stem cells in asynchronous, rapid growth. After 24 hr media change, there was an immediate 6-10 fold surge in cells entering S-M phase and there were nil S-M phase cells in the last 12 hr after media change. Media change every 12 hr decreased the FUCCI green peaks post-media change.

CONCLUSIONS: FUCCI ESC are useful to perform Quality Control (QC) during high throughput screening and validate cell number, handling and reported PFOA and hyperosmotic induced decreases in cell cycle and cell accumulation. FUCCI ESC showed that media change should be done more frequently and can be used to assess ESC used for high throughput screening for environmental toxicants.

SUPPORT: Funding: NIH 1R41ES028991-01 and NIEHS P30 CURES Pilot grant

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TRANSFER OF DIPLOID SOMATIC CELLS INTO ENUCLEATED OOCYTES TO INDUCE MEIOSIS-LIKE HAPLOIDIZATION. Aysha Trout, B.A., Philip Xie, B.S., Robert Setton, M.D., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: We compared haploidization rates and preimplantation development of embryos generated by somatic cell nuclear transfer using three sources of somatic cells: *cumulus oophorus*, fibroblasts, or mouse embryonic stem cells (mESCs).

DESIGN: Metaphase II (MII) enucleated oocytes isolated from B6D2F1 mice were fused with *cumulus* cells (CCs), fibroblasts, or mESCs. The resulting constructs, identifiable by meiotic-like spindle development, were injected with mouse spermatozoa by piezo-ICSI. A series of unmanipulated oocytes were piezo-ICSI inseminated and served as controls. Successful haploidization by extrusion of a pseudo polar body, the appearance of biparental pronuclei, and full preimplantation development were compared between the experimental and control groups. Whole genome karyotype analysis was performed on the resulting blastocysts.

MATERIALS AND METHODS: MII oocytes were enucleated in the presence of cytochalasin B by extracting the spindle complex and first polar body under Oosight™ visualization. A single CC, fibroblast, or mESC was fused with the ooplast of enucleated oocytes using Sendai virus. After $\geq$2 hours, successful somatic cell fusion and meiotic-like spindle development were assessed. Piezo-actuated sperm injection was executed on the experimental and unmanipulated oocyte controls. Fertilization and preimplantation development were monitored by time-lapse imaging. DNA *seq* was used to assess the karyotype of the resulting blastocysts.

RESULTS: After enucleation of 535 MII oocytes, haploidization by spindle development was verified at a significantly higher rate for those transferred with CCs (56%, $P<$ 0.00001) compared to those with fibroblasts (30%) or mESCs (32%). After injection, the controls had an 86% survival rate, while oocytes reconstituted with CCs, fibroblasts, or mESCs survived at rates of 54%, 53%, and 57%, respectively ($P<0.001$). The control group fertilized at a rate of 74%, while oocytes reconstituted using CCs fertilized at a rate of 52%, fibroblasts at 35%, and mESCs at 55% ($P<0.001$). Finally, 81% of fertilized oocyte controls developed to blastocysts, while only 21% of oocytes reconstituted with CCs, 20% of fibroblasts, and 5% of mESCs reached the blastocyst stage ($P<$ 0.00001). Moreover, experimental conceptuses had morphokinetic developmental characteristics to the blastocyst stage comparable to the controls, as assessed by time-lapse imaging. Preliminary results of 4-8 cells taken from 9 CC-derived blastocysts and 1 mESC-derived blastocyst, sequenced at an independent laboratory, show that 5 CC blastocysts and the 1 mESC blastocyst were euploid.

CONCLUSIONS: While these results indicate that the chances of fertilization and blastocyst development among the different somatic cell sources are lower than the controls, they were still achievable and had comparable morphokinetic characteristics. CCs also appear to be more easily reprogrammed, as shown by a significantly greater rate of haploidization. Once optimized and reproduced in humans, this technique may generate genotyped female gametes to alleviate age-related infertility.

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DEFECTIVE MITOPHAGY IN EGGS FROM WOMEN OF ADVANCED MATERNAL AGE. Shaihla A. Khan, PhD,[1] Deirdre M. Logsdon, MS,[2] Heidi J. Engelhorn, MS,[2] Sue McCormick, BS,[3] William B. Schoolcraft, MD,[3] Rebecca L. Krisher, PhD[2] [1]Post-Doctoral Research Associate, Lone Tree, CO; [2]CCRM Colorado, Lone Tree, CO; [3]Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Both oocyte number and quality decrease as women age; however, the mechanisms underlying these changes remain unclear. Oocyte mitochondrial metabolism is critical for oocyte and subsequent embryo quality. This aim of this study was to investigate the mechanisms involved in the loss of mitochondrial quality and health in oocytes from women of advanced maternal age (AMA).

DESIGN: Research Study.

MATERIALS AND METHODS: Expression of proteins involved in mitochondrial upregulated protein response (UPR^{mt}) and mitophagy was investigated in *in vitro* matured metaphase II (MII) oocytes collected from 10 young (< 32 years old) and 10 AMA (>38 years old) patients. Specific proteins were detected using Jess Simple Western, a modified western blot analysis that allows protein detection from samples containing as little as 300 ng total protein. One MII oocyte per replicate was used to detect Heat Shock Protein 60 (HSP60), Lon Peptidase 1, mitochondrial (LONP1); phosphorylated Parkin (p-Parkin), total Parkin (Parkin), PTEN induced kinase 1 (PINK1) and p62. Total protein concentration in each sample was used to normalize proteins of interest. All protein expression was represented relative to young oocytes, which were set to a value of 1 for comparison. Data is expressed as mean ± SEM of 6-10 independent replicates for each protein. Results were analyzed for significance using Students t- test in GraphPad Prism 6.0.

RESULTS: AMA oocytes had significantly less total (mean= 0.25± 0.1) and phosphorylated (mean= Parkin compared to young oocytes ($p \leq 0.05$). Although not significant, we also observed decreased PINK1 protein in AMA MII oocytes (mean= 0.3± 0.12, p=0.14). There were no significant differences in HSP60, LONP1 and p62 expression between young and AMA MII oocytes.

CONCLUSIONS: We have shown for the first time that Parkin mediated mitophagy is significantly decreased in MII oocytes from AMA women. There was no significant difference in UPR^{mt} between young and AMA MII oocytes, indicating that eggs may not induce this pathway to regulate mitochondrial quality. Functional mitochondria are important to provide energy for cellular processes during maturation, fertilization and embryonic development. In addition, inefficient mitochondria will contribute to elevated ROS. Therefore, mitochondrial quality control is critical for the oocyte, and if compromised may result in decreased developmental competence. We have demonstrated that compromised mitophagy may be responsible, at least in part, for the poor oocyte quality observed in oocytes from AMA women.

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TRANSCRIPTOMIC EVIDENCE OF SEXUAL DIMORPHISM IN EARLY HUMAN BLASTOCYSTS. Christine Briton-Jones, PhD, HCLD,[1] Erkan Buyuk, MD,[2] Sydney Chang, MD,[2] Joseph A. Lee, BA,[1] Sam Steffan, BA Sc.,[3] Amit U. Sinha, PhD,[3] Alan B. Copperman, MD[2] [1]Reproductive Medicine Associates of New York, New York, NY; [2]Icahn School of Medicine at Mount Sinai, New York, NY; [3]Basepair Inc, New York, NY.

OBJECTIVE: Although it is widely accepted that there are differences in early growth, development, and implantation between male and female embryos, few studies have yet to fully circumvent study design obstacles when evaluating the transcriptome of the human embryo (1). The objective of this study was to compare and contrast the transcriptome patterns of sibling male and female euploid blastocysts.

DESIGN: Prospective cohort study on human embryos.

MATERIALS AND METHODS: After receiving IRB consent, eleven sibling embryos were donated for research by an infertile couple. The embryos underwent embryo biopsy for preimplantation genetic testing for aneuploidy (PGT-A) by next generation sequencing (NGS) and vitrification. The blastocysts were thawed and underwent RNA Sequencing. Read counts per gene were summed across embryo cohorts and normalized using the median of ratios. Differential gene expression between embryo cohorts was calculated using DESeq2, in order to estimate variance-mean dependence and evaluate differential gene expression using a negative binomial distribution. A likelihood ratio test was used to account for heterogeneity due to batch. The adjusted threshold for significance was $p<0.05$.

RESULTS: Of the 11 euploid blastocysts, differential gene expression was compared between 5 male and 6 female embryos. 21,417 genes were identified, 357 were up-regulated and 538 were down-regulated in male blastocysts. Of the 10 genes showing the lowest P value for significantly different expression levels between male and female blastocysts, 8 were located on the Y chromosome and 2 on the X. 7 of the 8 Y chromosome genes have paralog genes located on the X chromosome. The majority of the genes showing significantly different expression levels were located on the sex chromosomes, however there were a number located on autosomes. One example is the gene GCK located on chromosome 7. It showed a 7.97 Fold (log2) lower expression in male blastocysts, where $P<0.0003$. 1658 different molecular pathways were active in the two cohorts, while the ranking of the most active pathways was different between males and females, none showed statistical differences. Putative roles for these genes have been described in other tissues and include protein synthesis, cell proliferation, metabolism and cell differentiation.

CONCLUSIONS: At a period in development when there are no obvious morphological or functional differences between males and females, 895 of the 21,417 (4%) of the active genes identified were expressed at significantly different levels in males compared to females. Many of the functions ascribed to the genes showing different levels of expression are related to processes in cellular proliferation and differentiation in adult stem cells and cancers. Most of the genes located on the sex chromosomes have homologous genes on the opposite sex chromosome, thereby correcting for a gene imbalance. Understanding transcriptomic events associated with mammalian sexual dimorphism may provide insights into the etiology of embryo morphokinetics, implantation, and maybe even later behavior patterning.

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SUPPORT: None

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X INACTIVE SPECIFIC TRANSCRIPT (*XIST*) AND ANTISENSE *TSIX* EXPRESSION IN SIBLING EUPLOID HUMAN BLASTOCYSTS: INSIGHTS INTO HUMAN X CHROMOSOME INACTIVATION. Christine Briton-Jones, PhD, HCLD,[1] Alan B. Copperman, MD,[2] Sydney Chang, MD,[2] Joseph A. Lee, BA,[1] Sam Steffan, BA Sc.,[3] Amit U. Sinha, PhD,[3] Erkan Buyuk, MD[2] [1]Reproductive Medicine Associates of New York, New York, NY; [2]Icahn School of Medicine at Mount Sinai, New York, NY; [3]Basepair Inc, New York, NY.

OBJECTIVE: Within a mouse model, X chromosome inactivation has been shown to be tightly regulated in early embryo development (4 cell stage), and remains so throughout adulthood (1). The RNA of two non-coding genes (*Xist* and *Tsix*) coats the X chromosomes within the cell nucleus (2). Mouse *Xist* is expressed by the inactive paternal X, yet, future activity of the X chromosome is protected from *Xist* inactivation by antisense RNA *Tsix* (2). While the human homologs of *Xist* and *Tsix* have been described, their roles in human X chromosome inactivation remains misunderstood. Only studies utilizing human embryonic stem cells and / or placental tissue have attempted to elucidate the roles of *XIST* and *TSIX* in the human embryo. The objective of this study was to compare *XIST* and *TSIX* gene expression in sibling euploid male and female human blastocysts.

DESIGN: Prospective cohort study on human embryos for research.

MATERIALS AND METHODS: After receiving IRB consent, eleven sibling embryos were donated for research by an infertile couple. These embryos had previously undergone embryo biopsy, with approximately 2-4 cells removed for preimplantation genetic testing for aneuploidy (PGT-A) by next generation sequencing (NGS) prior to vitrification. The embryos were derived from an anonymous oocyte donor and the sperm from the couple's male partner. After standard warming procedures, the blastocysts underwent RNA Sequencing. Read counts per gene were summed across embryo cohorts and normalized using the median of ratios. Differential gene expression between embryo cohorts was calculated using DESeq2, in order to estimate variance-mean dependence and evaluate differential gene expression using a negative binomial distribution. A likelihood ratio test was used to account for heterogeneity due to batch. The adjusted threshold for significance was $p<0.05$.

RESULTS: 11 euploid blastocysts, 5 male and 6 female were analyzed. The two embryo cohorts compared were male versus female. Both *XIST* and *TSIX* were expressed in all blastocysts. Male blastocysts showed significantly lower expression of *XIST* than females, -3.36 fold change where p=0.0003. *TSIX* was expressed at significantly lower levels in males compared to female blastocysts, -3.30 fold change where p=0.0005.

CONCLUSIONS: The inherent variability in human embryos makes studying the molecular processes of X inactivation difficult. The strongest feature of this study is the known ploidy status of the sibling embryos derived from a young, healthy oocyte donor. Unlike studies using a mouse model, ours demonstrated expression of both the *XIST* and *TSIX* genes within the human male blastocysts. Our finding suggests the *XIST* and *TSIX* genes are co-expressed allowing expression of both in male blastocysts. Again, we diverge from studies utilizing a mouse model, wherein the *Xist* gene is expressed only from the inactive X and the *Tsix* gene from the active X chromosome only seen in mouse female embryos. Our study shows that *XIST* and *TSIX* are active in both male and female human blastocysts. The expression of both genes in male embryos indicates the roles that these genes play may be different in the human than the mouse.

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SUPPORT: None

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ATOSIBAN AND BARUSIBAN IMPROVED IMPAIRED ENDOMETRIAL BLOOD FLOW IN PREGNANT RABBITS.

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OBJECTIVE: Despite considerable success in generating human blastocytes with artificial reproductive technologies, embryo implantation remains a challenge for unclear reasons. Excessive uterine movements may cause implantation failure while atosiban (ATO), a mixed vasopressin (VP) V_{1A}/oxytocin (OT) receptor antagonist, is used off-label to normalize uterine movements. In addition to inflammation or iatrogenic factors, poor perfusion can contribute to low implantation rates. It is hypothesized that elevating the uterine blood perfusion may increase the quality of the uterine mucosa and thus implantation success. The objective was to quantify whether ATO or barusiban (BAR), a selective OT antagonist, can improve endometrial blood perfusion in a rabbit model of early pregnancy.

DESIGN: In early pregnant rabbits (GD8–10), the endometrial blood flow (EBF) was monitored by laser Doppler flowmetry under propofol anesthesia. Following uterotomy, a laser probe was placed on the luminal site of the endometrium at a blastocyst. Mean arterial pressure (MAP), heart rate (HR) and femoral blood flow (FBF) were monitored. Vehicle or drugs were administered cumulatively via the right jugular vein.

MATERIALS AND METHODS: Five doses of 10-min duration of 2.22–1390 ng/kg/min OT, 634 pg–407 ng/kg/min VP, 4–40,000 ng/kg/min ATO or 0.4–4000 ng/kg/min BAR or vehicle were tested on EBF and cardiovascular parameters (N=6/group). In the ATO, BAR and vehicle groups, an IV bolus of 4170 ng OT was administered at the end of the infusion to test the antagonistic action of ATO and BAR.

RESULTS: EBF at the highest OT infusion dose was markedly reduced by 77% relative to vehicle, and in the VP group by 62% (both $P<0.01$) with similar potency. By contrast, no changes were apparent after infusion of vehicle, ATO or BAR. Similarly to EBF, a decrease in FBF was observed with VP (or OT), whereas administration of vehicle, ATO or BAR did not result in any change. The administration of an OT bolus to the vehicle group resulted in a decrease of EBF. No such decrease was observed following ATO or BAR pretreatment, indicating that the OT-induced EBF reduction by the bolus was antagonized by either ATO or BAR. Both OT and VP induced a large increase in MAP by 93% and 57%, respectively ($P<0.001$) with similar potency. MAP did not display any change in the vehicle, ATO or BAR groups. The OT bolus induced a small increase in MAP in the vehicle, ATO and BAR groups and was not blocked. No relevant changes in HR was observed in the vehicle, OT, VP, ATO or BAR groups.

CONCLUSIONS: ATO or BAR infusions did not influence baseline EBF in the early pregnant rabbit. Indeed, pre-treatment with ATO or BAR prevented OT-induced EBF reduction. This complicated model allowed only a small number of animals. Additionally, it was not possible to elucidate the relative importance of the OT receptor versus the V_{1A} receptor, because no differences were found between the agonists or between the antagonists despite their differences in receptor activity. The study suggests a benefit of OT or VP receptor antagonism in terms of recovery of OT-compromised EBF and thus potentially increases embryo implantation success.

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LOSS OF MIR-29A IMPAIRS PROLIFERATION AND DECIDUALIZATION OF ENDOMETRIAL STROMAL CELLS VIA ENHANCING THE INTERACTION OF TET3 AND COL1A1 DURING PATHOPHYSIOLOGY OF EARLY PREGNANCY LOSS.

Aixia Liu, PH.D., Dimin Wang, M.D., Mengmeng Jin, M.D., Ying Zhou, B.S., Laidi Xie, B.S. School of Medicine, Zhejiang University, Hangzhou, China.

OBJECTIVE: MiR-29a plays an important role in differentiation and proliferation of various uterine cells through regulating downstream target genes. However, whether miR-29a affects proliferation and decidualization of endometrial stromal cells (ESCs), and involves implantation and maintenance of early pregnancy remain unknown.

DESIGN: The expression and significance of miR-29a and TET3 were explored in endometrial or decidual tissues. Isolated primary ESCs were decidualized and exposed to miR-29a antagomir *in vitro*.

MATERIALS AND METHODS: This study protocol was approved by the Ethical Committee of the Women's Hospital. The endometrial tissues collected from patients in proliferative phase (10 cases) or secretory phase (15 cases), and the decidual tissues from patients with early pregnancy loss (EPL) (23 cases) and normal early pregnancy (22 cases) were used to determine the differential expression patterns of miR-29a and TET3. The primary ESCs were isolated from human uterine tissues and used to constructe the *in vitro* decidualized cell model. The miR-29a antagomir, CCK-8, quantitative PCR, western blot, RNA pull-down, immunofluorescence assays and bioinformatics analysis were used to investigate the relationship among miR-29a, TET3 and Col1A1 and their function on the proliferation and decidualization of ESCs.

RESULTS: The increased expression of miR-29a and the decreased expression of TET3 were found in the endometrial tissues of secretory phase compared with the endometrial tissues of proliferative phase. However, the expression of miR-29a was significantly reduced and the protein expression of TET3 was enhanced in the endometrial tissues of EPL in comparison to the normal early pregnancy. To study the significance of the ectopic expression levels of miR-29a and its potential relationship with TET3, miR-29a was inhibited by miR-29a antagomir in decidualized ESCs *in vitro*. Subsequently, we found inhibition of miR-29a significantly suppressed the Human ESCs viability. Moreover, the expression levels of decidualized biomarkers PRL and IGFBP1 were remarkably reduced, and the Col1A1, which involved in TET3 methylation, were downregulated following inhibition of miR-29a. Furthermore, after decidualization of ESCs, TET3 expression levels were decreased significantly, while inhibition of miR-29a promoted a significant increase in TET3 expression levels. Meanwhile, TET3 was predicted to be targeted by miR-29a by bioinformatics analysis. Most importantly, we found the binding capacity of TET3 and Col1A1 was decreased after ESCs decidualization. Interestingly, inhibition of miR-29a was revealed to enhance the interaction of TET3 and Col1A1 in the ESCs. In addition, loss of TET3 reversed the inhibitory effect of miR-29a antagomir on the proliferative activity in decidualized ESCs, as well as the protein expression levels of PRL and IGFBP1.

CONCLUSIONS: Loss of miR-29a suppressed proliferation and decidualization through enhancing the interaction of TET3 and Col1A1 in ESCs, which uncovers the important role of miR-29a/TET3/ Col1A1 in the regulation of decidualization and embryo implantation.

SUPPORT: This work was supported by grants from National Key R&D Program of China (no. 2018YFC1004403).

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HYPERBARIC OXYGEN PRECONDITIONING OF OVARIAN TISSUE BEFORE CRYOPRESERVATION MODULATE GENES INVOLVED IN FOLLICLE ACTIVATION AND ANTI-APOPTOTIC PATHWAYS.

Anders Kjellberg, MD, DESA, EDIC, PhD student,[1] Christina Diakaki, Master student,[2] Xia Hao, PhD student,[2] Amandine Anastácio, PhD, PostDoc,[2] Kenny A. Rodriguez-Wallberg, MD, PhD, Associate Professor[3] [1]Karolinska Institutet, Stockholm, Sweden; [2]Laboratory of Translational Fertility Preservation, Karolinska Institutet, Stockholm, Sweden; [3]Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden.

OBJECTIVE: Our overall hypothesis is that pre-conditioning with **hyperbaric oxygen** (HBO) can promote **survival** by improving **hypoxia tolerance** and modulation of genes in **anti-apoptotic** pathways.

DESIGN: Controlled experimental study, parallel arms.

MATERIALS AND METHODS: Ovaries (n=6) from B6CBA/F1 postnatal day-4 mice, were harvested and randomly assigned to either **pre-conditioning** ex vivo with **hyperbaric oxygen** in HBO chamber at 2.5 ATA for 30 minutes or control (30 minutes in room air). Both groups were kept in cryopreservation buffer on ice. **Cryopreservation** through slow freezing. RNA including miRNA was extracted using miRNeasy Mini Kit (Qiagen). RNA concentration was checked with NanoDrop™ 2000C; integrity and Quality Control were confirmed with Agilent Tapestation 2200®. **Gene expression** and **microRNA interactions**, 3 pooled samples from each group were analyzed using *Affymetrix Clariom D MTA 1.0 and microRNA 4.0 arrays, (performed by BEA core facility service at KI/Huddinge)*. Data analysis was performed using TAC 4.0 software, filter criteria: Fold change > 2 or <-2. The study was approved by the ethics review board for animal experiments in Sweden.

RESULTS: Out of 65956 genes identified in the analysis, 633 genes passed filter criteria, 379 were upregulated and 254 downregulated. Analysis of the 20 most altered genes in the Affymetrix array indicated genes involved in follicle activation. **Gremlin1** was highly downregulated (-6.8-fold change) suggesting that a preconditioning effect was obtained. A number of genes that stimulate growth and differentiation, such as immediate early genes **Fos** (-45.3-fold), **Fosb** (-44.7-fold) and **JunB** (-12.5-fold) were downregulated. Aromatase, encoded by **cyp191a** (-12.4-fold) was also downregulated. The most differently expressed microRNA was miR-714 (-10.89), associated with Fosb.

CONCLUSIONS: **Pre-conditioning** of ovarian tissue from mice with **hyperbaric oxygen** *ex vivo* induced changes in gene expression that are associated with **primordial follicle activation**, **oocyte maturation**, **hypoxia tolerance** and **apoptosis**. MiR-714 may be a useful biomarker for Fosb gene expression that warrant further investigation. The model seems promising for future studies with the **aim** to **improve survival** of **ovarian tissue** post **re-transplantation**. The data suggest a pre-conditioning effect but needs to be confirmed using methods to evaluate functionality of follicle development and maturation.

SUPPORT: The research was funded by grants from The Swedish Cancer Society, The Swedish Childhood Cancer Foundation, The Cancer Research Funds of Radiumhemmet, the Stockholm County Council and Karolinska Institutet (to KRW) and Gösta Franekels foundation (AK).Â We also would like to thank the core facility at Novum, BEA, Bioinformatics and Expression Analysis, which is supported by the board of research at the Karolinska Institute and the research committee at the Karolinska hospital.

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ASSESSMENT OF MITOCHONDRIAL DNA METHYLATION IN HUMAN BLASTOCYSTS.

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OBJECTIVE: Methylation of cytosine residues is a well-characterized epigenetic regulatory mechanism for nuclear genomic DNA (gDNA), affecting gene expression and cellular differentiation. Recent evidence suggests that methylation also occurs in mitochondrial DNA (mtDNA) and plays a role in mtDNA gene expression and replication. In addition, animal studies show that mtDNA methylation is not restricted to CG sites but also occurs at CHG and CHH sites, and may play help regulate programming during gametogenesis. In this study, we characterized mtDNA methylation in human blastocyst stage embryos, and investigated whether mtDNA methylation is affected by euploidy status and maternal age.

DESIGN: Experimental study.

MATERIALS AND METHODS: Two trophoectoderm (TE) biopsies from each of the previously diagnosed euploid (n=10) and aneuploid (n=20) embryos were analyzed using Whole Genome Bisulfite Sequencing (WGBS). Bisulfite conversion was performed using EZ DNA Methylation-Direct Kit (Zymo). Methylome sequencing libraries were constructed using TruSeq DNA Methylation Library Prep (Illumina) with 18 cycles of amplification. Sequencing was performed on Illumina HiSeq 2500 with paired-end 150 bp reads, and sequencing reads were aligned to human mtDNA reference using Bismark software. Duplicates were removed, unconverted reads were filtered, and cytosine methylation at single base resolution was determined. Statistical analysis was carried out using a linear model to assess the relationship of mtDNA methylation levels with ploidy status, maternal age (range 29.5 to 41.1), and time of blastulation (day 5 [n=16] vs. day 6 [n=14]).

RESULTS: Analysis revealed that an average of 1.5% of CpG sites in mtDNA were methylated in TE samples, which was significantly lower than methylation level of gDNA (20-30%; $p<0.0001$). CHH and CHG site methylation were found to be consistent in mtDNA and gDNA (CHH:1%, CHG:1.5%). There was no difference in mtDNA CpG, CHH, or CHG site methylation ratio between aneuploid and euploid embryos. Mitochondrial DNA CpG, CHH, or CHG site methylation levels were not correlated with maternal age. When blastocysts cryopreserved on day 6 were compared to those that were cryopreserved on day 5, mtDNA methylation levels of CpG, CHH, or CHG sites were not different.

CONCLUSIONS: Our findings suggest that mtDNA methylation of TE biopsies from human blastocysts is not associated with ploidy status, embryo growth characteristics, or maternal age. Therefore, it is unlikely that mtDNA methylation status can be used to develop a diagnostic test predictive of embryo viability for women undergoing infertility treatment with IVF.

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MIRNA-92A SUPPRESSES ANDROGEN-PRODUCING STEROIDOGENIC GENES EXPRESSION IN H295R, A HUMAN PCOS IN-VITRO THECA-LIKE CELL MODEL.

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OBJECTIVE: Polycystic ovary syndrome (PCOS) is a heterogeneous disorder, which affects up to 10% of reproductive-age women. The main characteristics are anovulation, hyperandrogenism and presence of polycystic enlarged ovary in reproductive age women. The underlying molecular mechanisms are not still clear. Previous study demonstrated that Mesenchymal stem cells secretes a variety of growth factors, cytokines, and miRNAs (including miRNA-92a) both free and in exosomes. Women with PCOS showed downregulation of miRNA-92a and high gene expression of main androgen-producing steroidogenic pathway genes CYP17A1, CYP11A1 and DENND1A in ovarian theca cells. In this study, we evaluated the effects of miRNA-92a mimic on steroidogenic gene expression using Human adreno-carcinoma cell line (H295R cells) an in-vitro PCOS cell model.

DESIGN: We hypothesize that H295R cells transfected with miRNA-92a mimic will exhibit a decrease in the gene expression of androgen biosynthesis genes in that PCOS cell model.

MATERIALS AND METHODS: The human adreno-carcinoma (H295R) cell line were seeded on 24-well plates at a density of 1×10^6 cells per well and cultured for 24 hours. Cells were transfected with different concentrations 30, 60, 90 pM of mirVana has- miR-92a-3p mimic or negative control-1 mimic using manufacturer protocol. After 24 hours of transfection, H295R cells were trypsinized and collected for analysis. The expression of CYP17A1, CYP11A1, and DENND1A genes were quantified at mRNA level by real-time PCR while DENND1A expression at protein level by western blot. Student t-test was used for statistical analysis and $p<0.05$ is considered as significant.

RESULTS: Human 295R cells transfected with 30pM of miRNA-92a-3p mimic showed significantly decrease CYP17A1, CYP11A1 and DENND1A gene expression ($p<0.05$) at RNA level and at protein level for DENND1A.V2 gene ($p<0.05$).

CONCLUSIONS: The miRNA-92a-3p mimic induced a significant suppression in androgen-producing steroidogenic pathway genes in a human PCOS cell model. Mesenchymal stem cell therapy may be a viable novel treatment option for PCOS patients.

SUPPORT: UIC start up fund

P-596 4:30 PM Monday, October 19, 2020

ENHANCEMENT OF HUMAN GRANULOSA CELLS SELF-RESCUE BY MITOCHONDRIAL TRANSFER VIA TUNNELING NANOTUBES. Chia-Jung Li, Ph.D, Kuan-Hao Tsui, M.D; Ph.D. Department of Obstetrics and Gynecology, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan.

OBJECTIVE: The intercellular transfer of mitochondria through tunneling nanotubes (TNTs) is a novel means of cell-to-cell communication between granulosa cells.

DESIGN: Experimental laboratory study.

MATERIALS AND METHODS: We established a co-culture system for human young GCs (P5) and aged GCs (P50) and found that tunneling nanotubes (TNTs) formed between them. Most of the TNTs initiated from young towards aged GCs. Disruption of TNTs using nocodazole abolished increased proliferation of young GCs initiated by contacts with aged GCs. Using specific fluorescent markers, we identified exchange of mitochondria via TNTs.

RESULTS: Young mitochondria were transferred towards the aged cells via TNTs, and the restoration of mitochondrial fusion between the young and old mitochondria occurred. We also observed that the young GCs exhibited mitochondria highly transfer and increased TNTs connections and lengths in co-cultured with aged GCs. Further morphological and molecular analyses indicated that the transfer of functional mitochondria reduced mitochondrial fission protein Drp1 expression in the aged cells. The transfer of young mitochondria was associated with a significant rescue of impairment of mitochondrial bioenergetics function in aged GCs.

CONCLUSIONS: Our data suggest that TNTs between young and aged GCs facilitate mitochondria transfer and therefore alter the properties, including the proliferation potential, of aged GCs.

P-597 4:30 PM Monday, October 19, 2020

EXPOSURE OF HUMAN BLASTOCYSTS TO SPECIFIC GROWTH FACTORS BASED ON RECEPTOR PRESENCE IMPROVES EPIBLAST FORMATION IN EXTENDED EMBRYO CULTURE. Deirdre M. Logsdon, MS, Sandeep K. Rajput, PhD, Courtney K. Grimm, MS, William B. Schoolcraft, MD, Ye Yuan, PhD, Rebecca L. Krisher, PhD Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Embryos are exposed to multiple growth factors during preimplantation development in vivo. However, inclusion of a variety of growth factors in embryo culture medium has resulted in disparate results between studies and across species, making it difficult to ascertain the potential efficacy of growth factors to improve human embryo culture. Our objective was to identify the presence or absence of specific growth factor receptors in human blastocysts using western blot analysis, and then to determine the effect of exposing embryos to the growth factors for which receptors are present on embryo development and viability.

DESIGN: Research Study

MATERIALS AND METHODS: Western blots were conducted using the Protein-Simple Jess system, with detection of each putative growth factor receptor assessed in a pool of two human blastocysts as well as a positive control (human granulosa cells). Due to the paucity of human zygotes that are available for such research, we used vitrified human blastocysts donated for research, exposing blastocysts to growth factors for 48 hrs prior to placement into an extended embryo culture system (WIRB study # 1179872). After warming, day (D) 5 human blastocysts (n=35) were cultured in the presence (GF) or absence (control) of selected growth factors. After 48 hrs (D7), the zona pellucidae were removed prior to placing blastocysts on fibronectin coated 8 well chambered microslides for extended culture. Embryo outgrowth area was measured on D10, D11, and D12, at which time embryos were fixed and stained with DAPI and antibodies against F-actin and the pluripotency marker POU5F1 to determine the number of epiblast cells and total cells using 3D spinning disk confocal microscopy. Data was analyzed using t-test.

RESULTS: Of the eleven growth factor receptors analyzed, six were found to be present in human blastocysts. Receptors that were not detected included EGFR, ACVR1, ACVR2, IGF1R, and TGFβR2. There were no differences in embryo outgrowth area on D10, D11, or D12 (control, 0.206 ± 0.053 mm2; GF, 0.234 ± 0.046 mm2). More embryos cultured with chosen growth factors formed an epiblast (control, 35.7%; GF, 84.6%; p=0.03). However, there were no differences in the number of epiblast cells as an average of all embryos (control, 27.8 ± 15.4; GF, 38.8 ± 9.4) or as an average of only those embryos with epiblast cells (control, n=5, 77.8 ± 34.3; GF, n=11, 45.9 ± 9.6). There was also no difference in total cell number (control, 344.1 ± 116.0; GF, 413.4 ± 116.8) in the D12 embryo outgrowths.

CONCLUSIONS: In summary, inclusion of growth factors in embryo culture medium at the blastocyst stage, chosen based upon receptor presence, increased the ability of the embryos to form an epiblast suggesting that the presence of these growth factors increased embryo viability. Future work will examine the effect of these growth factors during preimplantation embryo culture on blastocyst development and quality prior to embryo transfer.

SUPPORT: None.

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SIMULATED LONG-TERM EFFECTS OF RELUGOLIX COMBINATION THERAPY ON BONE MINERAL DENSITY AT THE LUMBAR SPINE AS PREDICTED BY A VALIDATED SEMI-MECHANISTIC EXPOSURE-RESPONSE MODEL. Anthe S. Zandvliet, PhD, PharmD,[1] Aziz Ouerdani, PharmD, PhD,[1] Tien-Yi Lee, PhD,[2] Elizabeth M. Migoya, Pharm D,[2] Juan Camilo Arjona Ferreira, MD,[2] Rik de Greef, MSc[1] [1]Certara, Oss, Netherlands; [2]Myovant Sciences Inc., Brisbane, CA.

OBJECTIVE: To address potential concerns of bone mineral density (BMD) loss associated with an endogenous estradiol (E2) suppression by relugolix, an oral, non-peptide gonadotropin-releasing hormone (GnRH) receptor antagonist, a semi-mechanistic, exposure-response model of BMD based on circulating E2 concentrations was developed and validated to predict maintenance of BMD during long-term (> 1 year) treatment with relugolix combination therapy (Rel-CT; relugolix 40 mg / E2 1 mg / norethindrone acetate 0.5 mg), upon which the E2 concentrations during treatment reflect the combined effect of exogenous E2 administration and relugolix-mediated endogenous E2 suppression.

DESIGN: E2 and BMD data from relugolix monotherapy (Phase 2) and Rel-CT (Phase 3) studies in women with uterine fibroids or endometriosis were used to develop the E2 – BMD model.

MATERIALS AND METHODS: The relationship between the % change from baseline in BMD at the lumbar spine based on circulating E2 concentrations over time during relugolix monotherapy or Rel-CT was described by a modified model originally proposed by Riggs et al (CPT Pharmacometrics & Systems Pharmacology, 2012) for approved GnRH receptor modulators. Data from a Phase 3 extension for up to 1-year treatment was used to validate the model-predicted BMD changes. Model-based simulations were performed to extrapolate expected BMD changes with Rel-CT for up to 2 years.

RESULTS: The model well described the BMD percent change from baseline during treatments with relugolix monotherapy up to 6 months or Rel-CT up to 1 year, with the 95% CI of the model-predicted quartiles for BMD change consistent with the corresponding values observed in the Phase 2 and Phase 3 studies and the Phase 3 extension. The model also predicted the plateau achieved in the BMD change upon E2 administration (concurrently with or initiated following 12 weeks of administration of relugolix alone) to be maintained for at least 2 years of Rel-CT treatment. Model-predicted BMD change over a 2-year treatment period was smaller than the clinical relevance bound of -2.2%, with the median (95% CI) of the predicted BMD loss from baseline over 2 years of 1.0% (0.3%, 1.9%) for Rel-CT. Of the women who received Rel-CT in the Phase 3 studies, 87.7% had E2 concentrations $\geq$ 20 pg/mL, an E2 concentration threshold proposed by Riggs et al to prevent the GnRH-modulator-associated BMD loss from baseline of greater than 2.2%.

CONCLUSIONS: A validated semi-mechanistic exposure-response model accurately described BMD change in the lumbar spine over time in women with uterine fibroids or endometriosis upon treatment with relugolix monotherapy (Phase 2) or Rel-CT (Phase 3), enabling prediction of Rel-CT to maintain BMD with long-term treatment for at least 2 years.

SUPPORT: Myovant Sciences Inc.

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THE REPRODUCTIVE SUBJECTS REGISTRY AND SAMPLE REPOSITORY (RSRSR): ESTABLISHING A BIOREPOSITORY FOR THE STUDY OF REPRODUCTIVE HEALTH. Nicholas S. Raja, MD,[1] Samantha B. Schon, MD, MTR,[2] Min Xu, Ph.D,[1] Kun Yang, MD,[2] Jayne Reynolds, BA,[2] Heather G. Cameron, MPH,[2] Erica E. Marsh, MD, MSCI, FACOG[1] [1]University of Michigan, Ann Arbor, MI; [2]Reproductive Endocrinology and Infertility, University of Michigan, Ann Arbor, MI.

OBJECTIVE: Biorepositories are an invaluable resource for conducting population-wide studies into the pathophysiology of complex disease. Despite their utility in translational research, there are very few reports of biobanks dedicated to the fields of reproductive health and infertility. Here we describe our experience establishing a reproductive biorepository and specifically discuss the collection of samples from subjects undergoing in vitro fertilization (IVF) and gynecologic procedures.

DESIGN: Prospective enrollment and collection of biological specimens and clinical information.

MATERIALS AND METHODS: The Reproductive Subjects Registry and Sample Repository (RSRSR) was established in 2017. Collection of samples began in 2018. Consenting individuals presenting for care at the University of Michigan were asked to complete a comprehensive questionnaire collecting demographic information, medical history, and focused gynecologic and fertility history. Patients consented to donate biological samples that would otherwise be discarded after treatment. IVF materials collected include blood, urine, follicular fluid, granulosa cells, cumulus cells, and immature and unfertilized oocytes. Surgical specimens include benign endometrium, myometrium, fallopian tube, ovarian tissue, and cervix. All samples are processed using vitrification, flash freezing, paraffin embedding, or placed in RNAlater© and aliquoted for storage.

RESULTS: There are currently 1169 female patients enrolled in RSRSR. The average age of female participants at the time of enrollment is 42.9 years (range 18.5-80.6 years). The mean BMI is 29.4 (range 15.1-68.9). Participants are predominately Caucasian (80.5%) and Non-Hispanic (89.7%). They are also highly educated, with >65% reporting a Bachelor's degree or higher and >46% reporting an annual household income of >$100,000. 21.4% of female participants reported a history of infertility, and a range of gynecologic disorders were also reported including menorrhagia (21.5%), metrorrhagia (15.1%), fibroids (21.5%), polycystic ovarian syndrome (13.5%), and endometriosis (9.9%). IVF specimens collected to date include 98 unique cycle samples of follicular fluid, granulosa cells, immature oocytes, and cumulus cells. Surgical samples are available from 146 unique patients with aliquots of benign endometrium, myometrium, fallopian tube, ovarian tissue, and cervix.

CONCLUSIONS: Herein, we report our success establishing a reproductive biorepository and subject registry. Additionally, we have created a streamlined process for collection of samples from women undergoing IVF. The collection of these unique biological samples linked with clinical information allows for a comprehensive investigation of women undergoing IVF and gynecologic surgery. Furthermore, these samples are processed and stored using a variety of methods, facilitating multiple downstream analyses. As one of the few existing biorepositories centered on reproductive health and infertility, RSRSR offers tremendous potential for innovative and translational research in reproductive medicine.

SUPPORT: 5K12HD065257-07 (SBS) University of Michigan Department of OBGYN (EEM)

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NITRIC OXIDE SYNTHASE AND AGE RELATED INFERTILITY: THE ROLE OF ARGINASE II. Charalampos Chatzicharalampous, MD, PhD, David Bai, BS, Sana Khan, MD, Robert Morris, MD, Husam M. Abu-Soud, PhD Wayne State University, C.S. Mott Center for Human Growth and Development, Detroit, MI.

OBJECTIVE: Low L-Arginine (L-Arg) may lead to alteration in nitric oxide synthase (NOS) activity shifting from nitric oxide (NO) synthesis to $O_2^{\bullet-}$ generation, a process known as NOS uncoupling. Arginase II, a critical enzyme in the urea cycle, can modulate the availability of L-Arg for NOS, regulating NO release in many types of cells. Based on the relationship between L-Arg and NO modulation, we sought to determine the relationship between differing NO profiles in young and old mouse oocytes and their expression of the arginase gene (ARG1) as well as developmental effects such as fertilization and embryonic development.

DESIGN: This is an experimental case-control study.

MATERIALS AND METHODS: B6D2F1 mice were divided into young (6-10 week) and old (48-60 week) groups. An NO-selective electrode was used for direct NO measurements in ovaries, oviducts, and oocytes. A subset of ocytes were also further exposed to 50 μM Nitro-L-arginine methyl ester (L-NAME), an NOS inhibitor for 20-30 minutes. NO levels in each of those groups were measured using ICSI. *ARG1* expression was assessed in ovarian tissue of young versus old mice with real-time PCR. Ornithine, the final product of arginase II, and L-Arg were also measured in oocytes from young (n=100) versus old mouse (n=100) ovaries via high-performance liquid chromatography (HPLC).

RESULTS: NO levels in the ovaries of young mice were 20 $\pm$ 1.5 nmol. There was a marked reduction, ~60%, in old mouse NO, with similar results among oocytes, ovaries and oviducts. *ARG1* expression was upregulated (threefold) in old versus young mice. Ornithine was significantly increased (fivefold) in old versus young oocytes, while L-Arg levels, in contrast, were markedly decreased (0.25 +/- 0.02 nmol/ml) in old compared to young oocytes (0.50 +/- 0.01 nmol/ml).

CONCLUSIONS: The upregulation of *ARG1*, and therefore increased arginase II activity, in older animals was correlated with higher levels of ornithine, decreased L-Arg, and decreased NO. Therefore, our results suggest that increased activity of arginase II may be an important modulator of NOS activity and thus NO bioavailability in aged animals.

SUPPORT: None

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INFLAMMATORY MACROPHAGES DERIVED EXOSOMAL MIR-222 PROMOTED THECA CELL STEROIDOGENESIS BY MODULATING MYLIP EXPRESSION. Xing Yang, Ph.D., Linzhi Gao, Master degree, Lina Wei, Ph.D. The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: To explore the role of M1 macrophages (M1M) in the linkage between low-grade inflammation and ovarian dysfunction in obesity.

DESIGN: In vitro experimental laboratory study.

MATERIALS AND METHODS: Raw264.7 macrophage was treated with lipopolysaccharide (LPS) to establish a model of M1M. Exosome (Exo) secreted by macrophage was isolated by ultracentrifugation and identified by transmission electron microscopy (TEM), western blot, and flow nanoanalyzer. The primary murine ovary theca cell (TC) was co-incubated with PKH67 fluorescence-labeled Exo to detect whether Exo secreted by macrophage could be uptaken by TC. The expression of CYP11A1 and CYP17A1 were analyzed by qPCR and western blot. Medium testosterone and progesterone level were analyzed. High-throughput sequencing was performed to analyze the expression of exosomal miRNA (miRNA-seq). In order to select key differential exosomal miRNA, the GSE97652 (species: mouse) was downloaded from the GEO DataBases. The data set contains 7 replications in both experimental group and control group. The experimental group is obese mouse adipose tissue macrophage (ATM)-derived Exo, and the control group is control mouse ATM -derived Exo. The overlap between miRNA-seq and GSE97652 differentially expressed miRNA was analyzed according to the Fold change $> 2, p < 0.01$ standard, which determined miR-222 and MYLIP for subsequent experiments. Next, gain-of-function experiments were performed to examine their role in TC steroidogenesis function with the involvement of the cholesterol metabolism pathway.

RESULTS: TEM, Flow NanoAnalyzer and western blot analysis confirmed the successful extraction of Exo. After co-cultured TC with PKH67-labeled Exo, green fluorescence could be detected in TC which demonstrated that TC was able to ingest Exo secreted by the macrophage. M1M increased the expression of CYP11A1 and the production of progesterone in TC which is dependent upon M1-Exo. The result of miRNA-seq showed that there were 30 upregulated miRNA and 112 down-regulated miRNA in M1M derived Exo compared with control Exo according to the standard of Fold change $> 2 (p < 0.05)$. A total of two differentially expressed miRNA, namely miR-222 and miR-155, were selected from the venn diagram of miRNA-seq and GSE97652. QPCR verified that miR-222 in both M1M derived Exo and M1M derived Exo treated TC were significantly upregulated. Subsequently, we predicted the target gene of miR-222 through five different databases. MYLIP, with the highest target score was selected, which has been identified as a key factor promoting LDLR degradation. M1M derived Exo was verified to display a high expression level of

miR-222, and M1M derived Exo mediated TC steroidogenesis depended miR-222. The overexpression of miR-222 resulted in the down-regulation of MYLIP expression and up-regulation of LDLR expression, followed by increased cholesterol influx, CYP11A1 overexpression and progesterone overproduction.

CONCLUSIONS: M1M derived Exo can be ingested by TC. M1M promote TC CYP11A1 overexpression and progesterone overproduction through Exo by delivering miR-222 into TC.

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SIMILAR TO RETINOIC ACID, HYPEROSMOTIC STRESS INDUCES EXPRESSION OF A 2-CELL LIKE SUBSET OF PLURIPOTENT STEM CELLS WHILE ALSO INDUCING A SUBSET OF DIFFERENTIATED 1ST LINEAGE CELLS. Elizabeth E. Puscheck, MD, MS, MBA,[1] Sudipta Dutta, Ph.D.,[2] Mohammed Abdulkareem Abdulhasan, Ph.D.,[3] Katherine Gurdziel, Ph.D.,[2] Steven J. Korzeniewski, Ph.D.,[4] Douglas Ruden, Ph.D.,[2] Daniel Rappolee, Ph.D.[4] [1]InVia Fertility, Hoffman Estates, IL; [2]Wayne State University, Detroit, MI; [3]Reproductive Stress 3M, Inc., Grosse Pointe Farms, MI; [4]Wayne State University School of Medicine, Detroit, MI.

OBJECTIVE: Determine whether various stresses change the expression in embryonic stem cells and their differentiated lineages of a large set of viral receptors and susceptibility genes.

DESIGN: Experimental.

MATERIALS AND METHODS: Rex-1 promoter- ESC were tested by bulk or single cell (sc) RNAseq after 72 hr exposures to 0-300 mM hyperosmotic sorbitol (with stemness-maintaining Leukemia Inhibitory Factor, LIF) to quantify stress-forced differentiation. Controls for normal stemness were LIF+ and normal differentiation were LIF-. RNA was isolated by RNAeasy lysis or 10XGenomics Dropseq, RNA quality was checked by Agilent TapeStation, cDNA was synthesized using Lexogen's QuantSeq library kit, and barcoded, multiplexed and sequenced by Illumina NovaSeq 6000. Data were demultiplexed by CASAVA software and FC expression was compared between conditions. In triplicate experiments, significant fold change (FC) genes ($FC \geq 2$; $FDR \leq 0.05$, $P<0.05$) identified affected pathways. Proliferation or death were assayed by Hoechst staining or Trypan blue staining, respectively. Validating studies including qPCR.

RESULTS: Stress caused expression of 15/17 Warburg anabolic pathway genes and decrease of aerobic glycolysis pathway was highly significant by P value and FDR for 9 genes. Compared with two previous studies 14/21 genes during early XEN and15/18 genes of late ESC XEN during normal differentiation by LIF removal, were upregulated by stress despite LIF presence. But simultaneously with loss of stemness metabolism and gain of several first lineage markers, several markers of the 2-cell like state were significantly and highly; B020031M17Rik and GM8994 by bulk RNAseq analysis. These two genes were amongst 6 others identified by tSNE analysis of scRNAseq that approximately 3% of ESCs were induced into a 2-cell like state previously reported to be induced by retinoic acid as a reversible subpopulation of first lineage XEN cells that revert to 2-cell like stemness.

CONCLUSIONS: Taken together the data suggest that stress induces distinctly different events, an approximate 23% increase in Rex1-GFP-ESCs with stemness loss, and a similar 24% increase in intermediate bright PDGFRA-GFP+ gain indicating XEN, but that bulk RNAseq corroborates XEN subpopulation increase. Morever, like retinoic acid induction of XEN, scRNAseq suggests that stress-forced XEN also induce a small subpopulation of 2-cell like revertants that may reversibly form pluripotent stem cells.

SUPPORT: Funding: 1R41ES028991-01 and NIEHS P30 CURES Pilot grant

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THE HUMAN ENDOGENOUS RETROVIRUS ERVW-1 REGULATES TROPHOBLAST STEM CELL PROLIFERATION. Rachel C. West, PhD, William B. Schoolcraft, MD, Rebecca L. Krisher, PhD, Ye Yuan, PhD Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: The human endogenous retrovirus ERVW-1 drives differentiation of cytotrophoblast into syncytiotrophoblast, the fetal portion of the placenta responsible for secretion of hormones and nutrient exchange. ERVW-1 also presents in cytotrophoblast cells; however, its role in maintaining this undifferentiated population of cells is poorly understood. The objective of this study was to examine the role of ERVW-1 in the maintenance of proliferation of human trophoblast stem cells (TSC). We hypothesized that ERVW-1 regulates undifferentiated trophoblast cell proliferation during placental development.

DESIGN: Prospective research study.

MATERIALS AND METHODS: To assess the role of *ERVW-1*, we used the CT27 line of TSC first described by Okae et al. in 2018. TSC were treated with lentivirus containing either shRNA designed to knockdown *ERVW-1* (KD) or a scramble control (SC). To select successfully transduced cells, we treated wild type (WT), SC, and KD cells with 2 μg/mL puromycin. After 48 hours, all wild type cells treated with puromycin were dead. We continued puromycin selection for 5 additional days to ensure successful selection. After puromycin selection, RNA was isolated from WT, SC, and KD cells. First strand complementary DNA was synthesized using the BioRad iScript Reverse Transcriptase kit and real-time quantitative PCR (RT-qPCR) was performed to confirm knockdown of *ERVW-1*. After confirmation of knockdown, WT, SC, and KD cells were plated at a concentration of 5,000 cells/well of a 12-well tissue-culture treated plate. Cells were collected after 24, 36, 48, and 72 hours and counted to assess cell doubling time (n= 4 replicates). Finally, to assess trophoblast cell proliferation and health, we used RNA to determine gene expression of placental growth factor (*PGF)* in all 3 cell types using RT-qPCR (n= 3 replicates).

RESULTS: Knockdown cells had significantly reduced expression of *ERVW-1* mRNA compared to SC (73.5% reduction, $p<0.05$) and WT cells (80.9% reduction, $p<0.05$). *ERVW-1* knockdown cells had an average doubling time of 26 ± 1.74 hours compared to the 15.43 ± 0.46 and 16.18 ± 0.6 hour doubling time of the SC and WT cells, respectively. These data show that *ERVW-1* KD cells have a significantly ($p<0.005$) longer cell doubling time compared to WT and SC cells. There was no difference in cell proliferation between WT and SC cells. Additionally, mRNA levels of *PGF* were significantly decreased in the KD cells compared to SC control cells ($p=0.05$). As PGF is known to increase trophoblast cell proliferation and reduce apoptosis, these data further suggest that decreased expression of *ERVW-1* causes altered cell proliferation in TSC.

CONCLUSIONS: *ERVW-1* is important in maintaining cell proliferation in undifferentiated TSC. The decreased expression of *PGF* is also interesting as PGF is known to regulate cell proliferation as well as trophoblast vascularization. As reduced *ERVW-1* and *PGF* has been implicated in placental pathologies including preeclampsia, these data provide context for the role of *ERVW-1* in placental cell function outside of its classically understood role in regulating placental cell fusion.

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HYALURONIDASE INHIBITS MIDKINE IN CUMULUS CELLS DURING OOCYTE DENUDATION. Mine Ergüven Assoc.Prof. Dr.,[1] Tülay İrez Prof. Dr.[2] [1]İstanbul Aydın University, Faculty of Medicine, İstanbul, Turkey; [2]İstanbul Yeniyüzyıl University, Faculty of Medicine, İstanbul, Turkey.

OBJECTIVE: Hyaluronidases are applied to break hyaluronic acid found in high levels in the cumulus-oocyte complex at the oocyte denudation for in vitro fertilization (IVF). The purpose of the study was to investigate whether midkine (MK) has a role at the proliferation and viability of cumulus cells (CCs) at the oocyte denudation done by using hyaluronidase.

DESIGN: This was a prospective, randomized study done with 90 females aged 21-40 and diagnosed as a male factor undergoing intracytoplasmic injection (ICSI) from September 2017 to September 2018.

MATERIALS AND METHODS: CCs taken via mechanical applications from patients were cultured. Hyaluronidases at the concentrations of 0.1 IU/ml [The lowest concentration, (n:30)],1 IU/ml (n:30), and 10 IU/ml [The highest concentration, (n:30)] were applied to CCs. Every 24 hours of 72 hours, proliferation and apoptosis indeces (Flow cytometry) of CCs were evaluated with MK levels (ELISA). Ultrastructure of CCs (n:15 per group) was also evaluated by using Transmission Electron Microscopy (TEM). One way-Anova was used and $p<0.05$ was considered statistically significant.

RESULTS: All concentrations decreased the cumulus cell numbers for 72 hours ($p<0.05$). The highest decrease in cell number was detected at the highest concentration ($p<0.05$) at the 72nd h. In concordance with this result, the highest increase in apoptotic and dead cell rates with the lowest viable

cell rate was detected at the highest concentration ($p<0.05$) at the 72nd h. The highest level led to the highest decrease in MK levels at the 72nd h ($p<0.05$). The ultrastructural analysis showed that the number of apoptotic CCs was increased from the lowest concentration to the highest concentration.

CONCLUSIONS: The inhibition of the proliferation and the viability of CCs by hyaluronidase through the inhibition of MK was firstly reported in this study. This may be one of the reason of poor oocyte quality which leads to the decrease in IVF success.

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SINGLE CELL RNA-SEQ ANALYSIS OF THE HUMAN FALLOPIAN TUBE. Nicole D. Ulrich, MD,[1] Yu-chi Shen, Ph.D.,[2] Qianyi Ma, PhD,[2] Kun Yang, MD,[1] Erica E. Marsh, MD, MSCI, FACOG,[2] Jun Z. Li, Ph.D.,[2] Sue Hammoud, Ph.D.[2] [1]Reproductive Endocrinology and Infertility, University of Michigan, Ann Arbor, MI; [2]University of Michigan, Ann Arbor, MI.

OBJECTIVE: Single cell RNA-seq analysis has provided a novel way to characterize cell types through whole transcriptome analysis on the level of the individual cell and has been used to effectively analyze many human organs. Here we use single cell RNA-seq to define major and rare cell types of the human fallopian tube.

DESIGN: Characterizing cellular composition and heterogeneity of human fallopian tube using single cell RNA-seq analysis

MATERIALS AND METHODS: A fallopian tube sample was collected from a perimenopausal female undergoing surgery for a benign indication and was dissected into 3 anatomic segments (isthmus, ampulla, fimbria). Fresh samples from these three anatomic areas were dissociated using our in-house protocols (allowing for > 95 % viability) and analyzed separately. Single cell RNA-seq data were generated using the 10X Genomics Chromium platform. Data analysis was performed using R package Seurat, following our pipeline previously described (Green et al. 2018).

RESULTS: After data processing and QC, we analyzed a high-quality set of 2,338 cells in the isthmus, 5,918 cells in the ampulla, and 4,252 cells in the fimbria. Analysis of the three fallopian tube samples separately identified 11 distinct cell clusters in each. Cluster-cluster correlation across the three segments demonstrated a high degree of correlation of the cell clusters, suggesting that most of the cell types are present over the length of the fallopian tube. We merged the data from the 3 segments (n=12,508 cells) and analyzed together to generate a final cell atlas with 15 recognizable clusters. Using marker gene analysis we annotated the 15 cell clusters as the following cell types: ciliated, secretory (3 sub types), myofibroblast, smooth muscle, pericyte, endothelial, vascular smooth muscle, micro vessel, cytotoxic T/natural killer (two subtypes), mast, and monocyte/macrophage (2 subtypes). The diversity of observed cell types confirms the reliability of our dissociation method and collectively represent a deep census of cell heterogeneity from the fallopian tube. Well known molecular markers based on published literature were used to confirm cell identification.

CONCLUSIONS: Here we present the first comprehensive catalogue of transcriptome-defined cell types of the human fallopian tube. We annotate them to known major cell types and present a foundational reference of functional states and molecular markers for this complex organ. These data provide a new knowledge resource for studies of female reproduction and its disorders, including infertility and ovarian cancer.

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NOVEL CAPA-IVM USING DIBUTYRYL-CAMP (DBCAMP) AND C-TYPE NATRIURETIC PEPTIDE (CNP): BOVINE MODEL STUDY FOR HUMAN IVM OF OOCYTES. Nami Morishita, Ph.D., Kana Shibata, B.A., Rie Matsunaga, M.A., Masanori Ochi, Ph.D., Toshitaka Horiuchi, Ph.D. OCHI YUME CLINIC NAGOYA, Nagoya, Japan.

OBJECTIVE: Spontaneous GVBD is thought to be the cause of the decrease in the development competence of IVM of immature oocytes because of less communication between cumulus cells and oocytes. In vivo, meiosis has been maintained by the action of cAMP and cGMP. CNP is mainly produced by granulosa cells, and the receptor for CNP, Npr2 is mainly located in cumulus cells. The binding of CNP to Npr2 increases cGMP level in oocytes, and it inhibits the hydrolysis of cAMP by phosphodiesterase. There have ever been no reports of CAPA-IVM using dbcAMP and CNP together. Is it effective for higher developmental competence of IVM oocytes in CAPA-IVM when dbcAMP and CNP are supplemented?

DESIGN: The study was conduced between August 2018 and July 2019. We investigated the effect of pre-IVM with dbcAMP and CNP (CAPA-IVM) on developmental competence of bovine IVM oocytes after ICSI. The concentrations of cGMP and cAMP in COCs after CAPA-IVM, GVBD rate 6 h after IVM, GSH and ROS levels in MII oocytes, cleavage rate 27 h after ICSI and blastocyst rate were compared between CAPA-IVM and conventional groups (no CAPA-IVM).

MATERIALS AND METHODS: COCs were obtained from follicles with a diameter of 2 to 8 mm of bovine ovaries. COCs were cultured in pre-IVM medium supplemented with 200 μM dbcAMP and 100 nM CNP for 2 h, followed by standard IVM for 22 h. Oocytes matured by standard IVM with 100 ng/ml Amphiregulin for 22 h (no CAPA-IVM) were used as the control. Developmental competence of IVM oocytes was assessed by ICSI.

RESULTS: First, we detected gene expression of *CNP* and *NPR2* in granulosa and cumulus cells. Second, the optimal concentration of CNP was examined. GVBD rate 6 h after IVM was markedly decreased by the supplementation of 100 nM CNP in the presence of 200 μM dbcAMP (0, 100 and 200 nM CNP: 61.9, 12.5 and 7.7%). In addition, pre-IVM treatment of dbcAMP and CNP for 2 h (CAPA-IVM) increased the levels of cGMP (374.6 vs. 14.8 fmol/COC) and cAMP (473.3 vs. 12.3 fmol/COC) in COCs. After then, CAPA-IVM increased the levels of intra-oocyte glutathione (GSH) and decreased the level of reactive oxygen species (ROS) content in MII oocytes 22 h after IVM. Cleavage rates 27 h after ICSI and blastocyst rates were significantly higher in CAPA-IVM than control groups (cleavage rates: 85.7% vs. 64.3%, and blastocyst rates: 36.4% vs. 18.4%).

CONCLUSIONS: The present study indicates that pre-IVM culture of immature oocytes with dbcAMP and CNP for 2 h significantly improved the rate of embryo developed to 2-cell stage 27 h after ICSI and blastocysts. The use of CAPA-IVM with dbcAMP and CNP resulted in more production of blastocysts after ICSI. Supplementation of CAPA-IVM medium with dbcAMP and CNP delayed germinal vesicle breakdown (GVBD), and levels of GSH increased in MII oocytes, and improved blastocyst rates.

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LIVE MORPHOLOGY IMAGING IS A BETTER APPROACH FOR OBSERVING SPERM HEAD OSMOLALITY-INDUCED MORPHOLOGICAL CHANGES COMPARED WITH DIFF-QUIK STAINING METHOD. George C. Hsu, MSc,[1] Ming-Hsun Wu, MSc, MBA,[2] Miao O. Chien, MBA,[2] Han-Ching Tsai, MSc,[1] Cheng-Teng Hsu, PhD[1] [1]Bonraybio Co., Ltd., Taichung City, Taiwan; [2]Min-Sheng General Hospital, Taoyuan City, Taiwan.

OBJECTIVE: To compare the live morphology imaging technology of LensHooke™ X1 Pro Semen Quality Analyzer with Diff-Quik staining in sperm head morphometric analysis.

DESIGN: A blinded prospective study of osmolality-induced morphological changes (OIMC) of human sperm head exposed to hypo-, iso- and hyperosmotic solutions.

MATERIALS AND METHODS: Semen samples (n=15) were pooled to perform 5 repeated experiments. Pooled samples were first washed then resuspended with ddH_2O, human tubal fluid and 20% Glucose respectively

with or without the addition of 200 ppm $HgCl_2$. Sperms were incubated in room temperature for 2 hours and analyzed using the following methods:

(1) Live imaging: a 4.5μL drop of sample covered with a 22 x 22 mm cover slip. Snapshots were taken by microscopy (1000X, oil immersion, Ph3).

(2) LensHooke™ X1 Pro: images of live sperms were captured by AI-controlled lens automatically.

(3) Diff-Quik: sperms were fixed and stained according to the WHO 5th guideline.

400 sperms were measured in each repeated test. A total of 2000 individual sperms were analyzed in each group. The dimensions of head parameters i.e. length, width and area were measured either by X1 Pro or by using the ImageJ software manually. Statistical analysis included t-test and two-way ANOVA with significance at $p < 0.01$.

RESULTS: Live imaging and X1 Pro showed minor changes in head area after ddH_2O treatment (0.1%, $p = 0.87$; -0.4%, $p = 0.51$). Hyperosmotic exposure showed significant shrinkage (-11.5%, $p < 0.01$; -12.3%, $p < 0.01$). With the addition of aquaporin inhibitor $HgCl_2$, head area were dramatically enlarged upon hypo-osmotic exposure in both live imaging and X1 Pro (9.4%, $p < 0.01$; 8.0%, $p < 0.01$). However, hyperosmotic exposure showed no significant difference (-0.4%, $p = 0.49$; -0.7%, $p = 0.26$). On the contrary, Diff-Quik method displayed inconsistent results of head area with (hypo: -0.3%, $p = 0.67$, hyper: -23.1%, $p < 0.01$) and without $HgCl_2$ addition (hypo: -6.7%, $p < 0.01$, hyper: -7.5%, $p < 0.01$). Moreover, while X1 Pro took less analyzing time compared to microscopic live imaging (5.1 ± 0.3 vs 319.3 ± 27.4 min, $n = 30$, $p < 0.01$), there was no significant difference between head morphometrics ($p = 0.40$) in contrast to Diff-Quik method ($p < 0.01$).

	Osmolality	Parameter	Live	X1 Pro	Diff-Quik
$HgCl_2$ (–)	Iso-	Area (μm^2, Mean ± SD)	12.23 ± 2.47	12.34 ± 2.66	9.23 ± 1.68
	Hypo-		12.24 ± 2.58	12.29 ± 2.52	8.61 ± 1.57
	Hyper-		10.82 ± 2.34	10.83 ± 2.39	8.54 ± 1.75
$HgCl_2$ (+)	Iso-	Area (μm^2, Mean ± SD)	13.20 ± 2.48	13.12 ± 2.53	9.39 ± 1.91
	Hypo-		14.44 ± 3.08	14.17 ± 3.13	9.37 ± 1.91
	Hyper-		13.14 ± 2.50	13.03 ± 2.57	7.22 ± 1.63

CONCLUSIONS: LensHooke™ X1 Pro live morphology imaging technology is fast and applicable in assessing OIMC. Diff-Quik staining method is not recommended for assessing sperm morphology when OIMC occurred.

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IN YOUNG WOMEN WITH POOR OVARIAN RESPONSE (POR), MICRORNA EXPRESSION IN PERIPHERAL BLOOD MONONUCLEAR (PBMN) CELLS IS ALTERED COMPARED TO NORMO-RESPONDER CONTROLS.

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OBJECTIVE: Micro RNAs (miRNAs) are a large family of short (21 nucleotide), evolutionarily conserved, non-coding RNAs. They repress expression of their target messenger RNAs (mRNAs) by causing degradation and/or inhibition of translation. Micro RNAs play a central role in the regulation of gene expression in a number of cell types and tissues, and altered miRNA expression is implicated in the pathogenesis of numerous disorders. The aim of the current study was to determine whether peripheral somatic cell miRNA expression show unique characteristics in women with reproductive disorders associated with abnormal follicular development. We therefore investigated miRNA profile of peripheral blood mononuclear cells (PBMNCs) in young women with polycystic ovary syndrome (PCOS) and poor ovarian response (POR), and compared to normo-responder controls.

DESIGN: Prospective experimental study.

MATERIALS AND METHODS: Young reproductive age women (<35 years old) with PCOS (n=5; selected based on Rotterdam criteria); poor ovarian response (n=5; selected based on Poseidon criteria – group 1a with number of oocytes retrieved <4); and normo-responder controls (n=5) were included in the study. Peripheral blood mononuclear cells (PBMNCs) were collected on the day of retrieval, and total RNA was extracted in the RNeasy Micro kit (Qiagen). The HiSeq sequencing results were annotated and classified by comparing the sequences with those of noncoding RNAs (miRNA, siRNA, piRNA, rRNA, tRNA, snRNA, etc.) in GenBank databases. The identified miRNA sequences were annotated by matching the sequencing results with known miRNA sequences in miRBase 21.0. MiRNAs with log2FC > 2 or <−2 were identified as differentially expressed.

RESULTS: Mean age and number of oocytes retrieved were 32.5 ± 0.7 years and 16 ± 4.9 oocytes for the PCOS group, 34.2 ± 1.4 years and 2 ± 1.5 oocytes for the POR group, and 31.0 ± 2.1 years and 21 ± 3.6 oocytes for controls. In women with POR, 11 miRNAs were differentially expressed compared to controls; 6 showed increased expression (hsa-let-7f-5p, hsa-let-7g-5p, hsa-miR-6130, hsa-miR-98-5p, hsa-miR-1246, hsa-miR-7-5p) and 5 showed decreased expression (hsa-miR-30a-5p, hsa-miR-30d-5p, hsa-miR-139-5p, hsa-miR-425-5p, hsa-miR-199a-5p). No changes were observed in the PBMNC miRNA expression in women with PCOS compared to controls.

CONCLUSIONS: Our findings demonstrate that somatic cells of women with POR have altered miRNA profiles. We found members of the let-7 family of miRNAs, which play important roles in development, cancer, and metabolism to be up-regulated in women with POR. In mice, where targeted deletion of H19 cause elevated let-7, AMH is decreased, and follicle recruitment is accelerated (1). Future studies will be needed to determine whether similar mechanisms are in effect in ovaries of women with POR, and whether these findings can be exploited for diagnostic purposes.

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MATERNAL-TO-ZYGOTIC TRANSITION-RELATED MICRO RNAS ARE INCREASED IN BLASTOCYST CULTURE MEDIUM.

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OBJECTIVE: Maternal-to-zygotic transition (MZT) is associated with transcriptional activation of zygotic genome and degradation of maternally-derived messenger RNAs (mRNAs) carried over from the oocyte. MZT is a crucial step in pre-implantation development and occurs at 4-8-cell stage in human embryos. Degradation of maternal mRNAS during

MZT is mediated by evolutionarily conserved microRNAs (miRNAs), such as miR-430 in zebrafish, miR-427 in Xenopus, and miR290-miR295 in mice. Using a bioinformatic approach, miR371-miR373 were identified as the human orthologues. In the current study, we investigated whether miR371-miR373 are expressed in human cleavage stage and blastocyst embryos and whether they can be detected in spent culture medium (SCM).

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: To assess expression in cleavage stage embryos and blastocysts, discarded embryos (n=4 for each developmental stage) were used. RNA was extracted using single cell RNA purification kit from Norgen Biotech. Additionally, SCM was collected from four different patients' embryos in the cleavage, morula, and blastocyst stages (n=10 per stage). The media was centrifuged at 10,000 rpm for 5 minutes. RNA was extracted using miRNA easy kit and was converted to cDNA by the miRCURY LNA RT kit. Real time quantitative reverse transcription-polymerase chain reaction (qRT-PCR) analysis for miR-371-miR373 was performed using the MiRCURY LNA SYBR Green PCR kit from Qiagen. RNU6B (or U6 snRNA) expression was quantified in each sample for normalization. The fold change was calculated by 2^-(delta delta ct).

RESULTS: The presence of miR371, miR372, and miR373 was confirmed in the embryos. There was no significant difference in their expression between cleavage stage embryos and blastocysts (p=0.88, p=0.85, p=0.83). In contrast, there were differences found in miRNA concentrations with progressive embryonic development. miR371-3p and 372-3p were undetectable at the cleavage stage, but became detectable at the morula stage, with significantly increased levels at the blastocyst stage (miR371-3p ($p<0.01$) and 372-3p ($p<0.001$)). Expression of miR 373-3p in SCM was noted in all three developmental stages and relative concentrations increased from the cleavage stage to the morula stage ($p<0.05$) then further increased at the blastocyst stage ($p<0.005$).

CONCLUSIONS: Our findings demonstrate that miR371, miR372, and miR373 are expressed in human pre-implantation embryos and that their secretion into culture media increases progressively with the stage of embryonic development. Further studies are now indicated to determine if the variability in these increases will prognosticate the ability of embryos to sustain implantation. This simple and inexpensive assessment will now progress to clinical trials.

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APPLICATION OF OMNI-ATAC TO PROFILE CHROMATIN ACCESSIBILITY BEFORE AND AFTER OVARIAN TISSUE CRYOPRESERVATION.

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OBJECTIVE: Recently, ovarian tissue cryopreservation (OTC) was declared non-experimental. Even prior to this, the technique was being rapidly adopted worldwide as a means to both restore ovarian function and preserve fertility. OTC and subsequent transplantation may be limited by "graft burnout," where hypoxia and aberrant follicular activation may play a role. The molecular mechanisms behind follicular activation are not fully defined. Our goal is to apply a new method, omni-ATAC, for chromatin accessibility profiling, both to characterize follicular transcriptional regulation and to determine whether cryopreservation affects follicular transcriptional integrity. Ideally, the cryopreservation technique should not result in significant changes in regulatory element usage after its application.

DESIGN: Ovarian cortical tissue was collected from patients (n = 6) receiving oophorectomy for benign reasons, and was processed following established OTC protocols. Omni-ATAC was applied to both fresh and cryopreserved-thawed tissue.

MATERIALS AND METHODS: Ovarian tissue was collected and transported on ice. The cortex was isolated, with part of the specimen used for fresh evaluation, and part vitrified. Tissue underwent a liberase DH (dispase high) digestion. Follicular isolation was performed under light microscopy. Omni-ATAC was performed. Transposed DNA fragments were column purified, SYBR-PCR amplified, and double-bead purified. Sequencing was performed. Thawed specimens underwent the same protocol for follicular and DNA isolation, with the addition of a nuclear red (NR) viability stain during digestion. Last, histopathology for proliferation (Ki67) and apoptosis (TUNEL) was completed.

RESULTS: Histopathology and NR staining indicate healthy follicles in all specimens. Average correlation is 0.99 among fresh specimens, and 0.92 among thawed specimens. Peak distribution is significantly enriched at promoter regions in both fresh (9.1%) and thawed (11%) data sets. Preliminary peak calling browser tracks appear similar between fresh and thawed specimens.

CONCLUSIONS: We successfully processed fresh ovarian cortical samples from six women, resulting in highly correlated data sets. Further, we compared fresh to cryopreserved-thawed cortex, and demonstrate that these specimens remain highly correlated. These data suggest that cryopreservation itself does not greatly affect transcriptional regulation. Future analysis will focus on gene ontology and motif analysis, as well as differentially expressed gene (DEG) analysis between fresh and thawed specimens. Pathway analysis will proceed via comparison to currently published transcriptome data.

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PROGRAMMED MITOPHAGY IS ESSENTIAL FOR THE GLYCOLYSIS SWITCHING DURING SENESCENCE IN HUMAN CUMULUS CELLS.

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OBJECTIVE: Cumulus granulosa cells, a group of closely associated granulosa cells that surround and nourish oocytes. Here, we show that human cumulus granulosa cell proliferation depends on mitophagy, the programmed autophagic clearance of mitochondria.

DESIGN: Experimental laboratory study.

MATERIALS AND METHODS: In a prospective study, fresh granulosa cells were obtained from 48 women aged 20–40 years who underwent IVF with embryo transfer and who were divided into two groups: the diminished ovarian reserve (DOR) group (n = 20) and the control group (n = 28). Patient characteristics including age, infertility duration, body mass index, FSH, anti-Müllerian hormone (AMH) and cumulus cell, mitophagy, mitochondrial mass were analysed.

RESULTS: The elimination of mitochondria in aged GCs proliferation was coupled to a metabolic shift with increased lactate production and elevated expression of glycolytic enzymes at the mRNA level. Pharmacological inhibition of either mitophagy or glycolysis consistently increased GCs proliferation during aging. Oxidative stress triggered expression of the mitophagy regulator BNIP3L/NIX at peak GCs during aging. Senescent granulosa cells from poor ovarian responder displayed decreased mitochondrial mass, elevated expression of glycolytic enzymes and decreased cell proliferation.

CONCLUSIONS: In summary, developmentally controlled mitophagy promotes a metabolic switch towards glycolysis, which in turn contributes to cellular proliferation in senescent granulosa cells.

REFERENCES: None

SUPPORT: None

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CASE REPORT: RNASEQ ANALYSIS OF BLASTOCOEL FLUID FROM EUPLOID EMBRYOS ORIGINATING FROM THE SAME PATIENT RESULTING IN DIFFERENT IMPLANTATION OUTCOMES REVEAL ALTERED EXPRESSION OF GENES ASSOCIATED WITH DEUBIQUITINATION PATHWAY.

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OBJECTIVE: Is the gene expression profile different between two 46, XX blastocysts, with identical morphology from the same patient? While Preimplantation Genetic Testing for Aneuploidies (PGT-A) allows for identification of ploidy status and morphology scoring provides additional information when selecting an embryo for transfer, euploid embryos with the same morphology do not always result in the same implantation outcome. This study aimed to evaluate global gene expression using RNASeq in

blastocoel fluid-conditioned media from two 46, XX euploid embryos from the same 36-year old infertility patient from the same egg retrieval cycle.

DESIGN: Retrospective analysis of day-5 euploid blastocoel fluid gene expression in two 46, XX embryos with different implantation outcomes from a 36-year old patient.

MATERIALS AND METHODS: Day-5 ICSI-generated blastocysts were scored via the Gardner and Schoolcraft grading system. Blastocoel fluid-conditioned media was obtained following biopsy of the day-5 blastocysts of same morphology grade (5AA). RNA was extracted and libraries prepared using a SMART-Seq Stranded kit followed by Illumina NextSeq500 sequencing performed at the University of South Carolina Functional Genomics Core. Sequences were aligned to the human genome, reads counted and gene expression determined. The resulting data set was then analyzed with the iDEP 9.1 web application to run a PGSEA pathway analysis utilizing Gene Ontology Biological Processes Geneset (Ge et al. BMC Bioinformatics 2018;19:534).

RESULTS: Gene expression associated with various cellular pathways were compared between the blastocoel fluid sample from each blastocyst which revealed a decreased level of gene expression associated with the protein deubiquitination pathway in the positive implantation embryo, and no other analyzed pathway yielded significant difference in gene expression between the two blastocoel fluid samples. Specifically, genes encoding SHMT2, KAT2A, ASXL1 were all downregulated in blastocoel fluid from the embryo associated with successful implantation.

CONCLUSIONS: RNASeq analysis of media samples from two 46, XX embryos with the same morphology from the same patient but associated with different implantation outcomes yielded differences in gene expression. Knowledge of chromosomal status and morphology of a preimplantation blastocyst stage embryo did not provide a complete picture of the underlying biological processes taking place within the embryo, nor could these measures fully predict an embryo's implantation outcome. This case study provides evidence of a detectable difference in gene expression in blastocoel fluid obtained from embryos that would be considered indistinguishable by current methods employed by reproductive specialists. Moreover, this alteration in gene expression is associated with a difference in implantation outcome. While this case study identified the deubiquitination pathway as altered, further study is needed to determine if this difference in these euploid blastocysts is also found in embryos from other patients and/or with the same chromosomal status.

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SUPPORT: University of Texas Health Science Center San Antonio

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IS IMMUNOGLOBULIN IGE RELEVANT FOR PREGNANCY LOSS? David H. Barad, MD, MS,[1] Sarah K. Darmon, PhD,[1] David F. Albertini, PhD, MS,[1] Emanuela Molinari, PhD,[1] Norbert Gleicher, MD[2] [1]Center for Human Reproduction, New York, NY; [2]Center for Human Reproduction, Foundation for Reproductive Medicine, Rockefeller University, Medical University Vienna, New York, NY.

OBJECTIVE: To determine whether IgE levels impact miscarriage risk in association with IVF in view of anecdotal observations at our center in recent years suggesting that IgE levels were changing.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: A complete immunoglobulin profile, including IgG, IgM, IgA and igE has been atour center a routine component of an initial check list obtained on every new patient for over 20 years and we have repeatedly reported on Ig-levels relating to IVF outcomes. Over the last 3 years we, however, anecdotally have noted a significant shift in IgE results in our patient population, in principle characterized by either complete absence or extremely low levels of IgE. In a search of the general literature, we were unable to detects any clinical associations between extremely low IgE and adverse clinical outcomes, except for an association with abnormalities in IgG levels. We, therefore, decided to reinvestigate IgE levels in reference to female infertility. We here report on associations between IgE and pregnancy loss in our center's most recent 1018 new patients. This analysis was, however, restricted to 259 patients presenting for a first IVF cycle who had a previous history of pregnancy. IgE levels were divided into quartiles. The percentages of previous pregnancies lost in each quintile of IgE were then compared, adjusted for age.

RESULTS: Average age of patients was 42.2 ±5.4 years; average gravidity was 2.1 ± 1.3 pregnancies, of which 1.0 ± 1.1 ended in abortion, with 47% of previous pregnancies aborted and 61% of patients having at least one miscarriage. IgE levels ranged from 1 to 700 UI/mL (mean 83.9 ± 134 UI/mL); 66 patients in the lowest quartile (< 13.00) had a previous miscarriage rate of 37%, only nominally lower than miscarriages in other three quartiles (q2 - 47.3%, q3 - 52.7%, q4 – 52.2%). This trend suggested that lowest IgE was associated with fewest past miscarriages a hypothesis further tested by comparing patients with extremely low IgE (< 10 UI/mL) in a general linear model adjusted for age to all others and demonstrating that lowest IgE (n=48) was only associated with 33% pregnancy loss compared to 50% in remaining 211 patients (P = 0.022). Within the latter population, IgE was, however, not a strong predictor of overall pregnancy loss (ROC AUC 0.596 ± 0.36, P= 0.01).

CONCLUSIONS: IgE appears statistically predictive of pregnancy loss in female infertility patients, with very low levels actually appearing potentially protective. Since IgE is functionally associated with allergic and anti-parasitic reactions, its levels can be viewed as a reflection of anti-inflammatory immune activity, thereby, supporting the previously voiced hypothesis that inflammation increases miscarriage risks.

SUPPORT: Intramural funds from The Center for Human Reproduction and grants from The Foundation for Reproductive Medicine.

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ALTERED EXPRESSION OF GENES INVOLVED IN JAK-STAT, ADIPOCYTOKINE AND TOLL-LIKE RECEPTOR SIGNALING PATHWAYS ARE DETECTED IN BLASTOCOEL FLUID CONDITIONED MEDIA FROM EUPLOID EMBRYOS WITH POSITIVE IMPLANTATION OUTCOMES. Arnav Lal,[1] Laura Grace Wolfe, B.S.,[2] Trevor Shull, B.S.,[2] Addison Paige Brandt, B.A.,[2] Carson M. Collins, na,[2] Sammy K. Khalil, n/a,[2] Shawn Zimmerman, PhD, HCLD,[3] T. Arthur Chang, PhD, HCLD, ELD,[4] Randal D. Robinson, MD,[5] J. David Wininger, PhD, HCLD,[6] William E. Roudebush, PhD, HCLD,[2] Alyssa Clay-Gilmour, PhD,[7] Renee J. Chosed, PhD[2] [1]University of Pennsylvania, Philadelphia, SC; [2]University of South Carolina School of Medicine Greenville, Greenville, SC; [3]Vios Fertility Institute, Swansea, SC; [4]University of Texas Health Science Center, San Antonio, TX; [5]University of Texas Health Science Center San Antonio, San Antonio, SC; [6]Atlantic Reproductive Medicine Specialists, Raleigh, SC; [7]University of South Carolina Arnold School of Public Health, Greenville, SC.

OBJECTIVE: Altered gene expression leading to modified expressions of pathways in preimplantation embryos may be a contributing factor in successful embryo implantation outcome. Identification of genes in day-5 blastocysts that are associated with successful uterine implantations would provide reproductive specialists with an additional measure of embryo quality when selecting the most viable embryo for transfer. This study evaluated global gene expression using RNASeq in blastocoel fluid-conditioned media from euploid IVF-generated embryos resulting in successful implantations versus those that failed to successfully implant.

DESIGN: Retrospective analysis of day-5 euploid blastocoel fluid gene expression in seven (three successful; four unsuccessful) euploid embryos.

MATERIALS AND METHODS: Blastocoel fluid-conditioned media was obtained following biopsy of ICSI-generated day-5 blastocysts. RNA extractions, library preparation (SMART-Seq Stranded kit) and Illumina NextSeq500 sequencing were performed at the USC Functional Genomics Core. Standard RNASeq workflow was conducted: 1) removal of adaptor sequences 2) alignment to human Gh38 genome with STAR, and 3) FeatureCount to obtain raw gene count number for each sample. Differential gene expression analysis (DGE) of raw counts was performed using DESeq2 applying negative binomial generalized linear models and taking advantage of the package to generate more accurate shrunken log fold changes and variance stabilizing estimators for data with considerations regarding low counts and high dispersion. Significance was defined as a false-discovery rate (FDR) p-value <0.05 to adjust for multiple testing. Pathway analysis was performed using GAGE, mapping genes to KEGG pathways.

RESULTS: After quality control 21,321 genes were included in the DGE analysis and 36 (FDRp<0.05) were identified as DE (6 up-regulated / 30 down-regulated). Pathway analysis revealed altered expression patterns of genes encoding proteins in the adipocytokine**,** Toll-like receptor and JAK-STAT signaling pathways between blastocoel fluid from embryos associated with successful versus unsuccessful implantation outcomes. Specifically,

gene products of these pathways were up-regulated in blastocoel fluid from embryos associated with successful implantation.

CONCLUSIONS: We identified differential gene expression in blastocoel fluid from euploid embryos associated with successful versus unsuccessful implantation. JAK-STAT pathway members were identified in this study, which is supported by a previous reports that members of this pathway are expressed during blastocyst stage development. Detection of these gene products in blastocoel fluid may represent apoptotic remnants of cells that were selectively eliminated from the developing embryo. One possibility is that the JAK-STAT pathway activates apoptotic gene expression in specific cells within the embryo as a means of embryo self-correction. Future research aims to clarify the roles of identified genes and consider bi-directionally dysregulated genes within a given pathway in the preimplantation embryo.

SUPPORT: University of Texas Health Science Center San Antonio

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KIDNEY TRANSPLANT AND FERTILITY: A RETROSPECTIVE STUDY ON RECIPIENT WOMEN AND LIVING DONORS.

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OBJECTIVE: Compare the reproductive capacity in recipient and donor women against a control group, in kidney recipients before and after transplant and in donors before and after nephrectomy. In addition, the frequency of gynecological alterations in recipients and donors was compared against the control group, in recipients before and after transplant, and in donors before and after nephrectomy.

DESIGN: 146 individuals were divided into 3 groups: transplanted, living donors and control group. The control group consisted on fertile aged women who were neither donor nor recipients.

In order to measure reproductive capacity, biological children, time trying to conceive and performance of assisted reproduction treatments were taken into account.

MATERIALS AND METHODS: Analysis of variance (ANOVA) and Kruskal Wallis test were used to compare populations. Chi-square test was used for the analysis of frequencies between groups.

RESULTS: Transplant patients showed a lower reproductive capacitiy, while living donor's was similar to the control group. Reproductive capacity was higher in kidney patients before transplant, and in living donors before nephrectomy.

No significant differences were found in the frequency of gynecological alterations in transplant patients and living donors, in comparison with the control group. The frequency of these alterations was similar in transplant patients before and after transplant, and in donors before and after nephrectomy.

CONCLUSIONS: Transplant patients would have difficulty conceiving, either as a side effect of the surgery, due to the effect of immunosuppressive medication, or the postponement of motherhood due to emotional, psychological or medical reasons related to the transplant.

It is known that kidney transplants can restore fertility in women with kidney failure, but our study revealed it was easier for patients to achieve pregnancy before transplantation. However, being the same population before and after transplant, the mean age of the post-transplant group was greater than the pre-transplant group, and this could impact on the results. In addition, it is likely that patients had sought pregnancy during early stages of the disease, therefore behaving as a control group.

Living donors would be more likely to conceive before nephrectomy. However, there are some caveats to this study: the sample size was low, and the mean age was greater in the post-nephrectomy group.

The decrease in reproductive capacity in transplant patients is not related to physiology of the reproductive system, since this group did not present a higher frequency of gynecological alterations.

Transplant and nephrectomy neither showed significant impacts on gynecological alterations, which means that surgeries do not involve extra complications at the gynecological level.

Beyond the complications, 86% of recipients managed to have a normal life, and 100% of living donors reported a normal quality of life and being emotionally satisfied with the decision.

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EFFECT OF IL-6 AND TNF ALPHA ON INVASION OF EPITHELIAL AND STROMAL ENDOMETRIAL CELLS IN AN *IN VITRO* MODEL OF HUMAN PERITONEUM.

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OBJECTIVE: Endometriosis is an inflammatory process regulated by cytokines, such as IL-6 and TNF alpha, that are known to be present in higher concentrations in the peritoneal fluid of patients with endometriosis. (1) The purpose of this study was to investigate the effect of IL-6 and TNF alpha on the invasion of immortalized epithelial endometrial cells (iEECs) and human stromal endometrial cells (hESCs) from patients with endometriosis in modeled peritoneum *in vitro*.

DESIGN: *In vitro* study.

MATERIALS AND METHODS: Immortalized cells (hESCs and iEECs) were treated with either IL-6 (1,000 pg/mL,) TNF alpha (8 pg/mL), or the combination; controls were untreated. Invasion assays were completed as previously published. (2) Briefly, cells were labeled with fluorescent dye and incubated in a prepared Matrigel invasion chamber assay with immortalized peritoneal mesothelial cells (LP9). The number of cells invaded per frame was assessed using confocal laser scanning microscopy. The normally distributed data were analyzed by ANOVA with a post-hoc Dunnett's test.

RESULTS: IL-6 and TNF alpha alone did not affect invasion of iEECs. Treatment of iEECs with both IL-6 and TNF alpha resulted in increased cell invasion compared with control (30% vs 23% , p=0.01, n=3). TNF alpha alone decreased invasion of hESCs compared to control (48% vs 88%, p=0.003, n=3). There was no difference in invasion in hESCs with IL-6 or both IL-6 and TNF alpha.

CONCLUSIONS: These findings indicate a synergistic effect of IL-6 and TNF alpha on the invasion of iEECs in an *in vitro* peritoneal model and provide further evidence for the role of these cytokines in the pathogenesis of endometriosis.

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SUPPORT: K23 HD097307 (JFK)

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MITOQ SHIFTS ENERGY METABOLISM TO INCREASE BIOGENESIS IN HUMAN GRANULOSA CELLS.

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OBJECTIVE: The objective of this work was to determine the specific mechanisms by which MitoQ enhance oxidative phosphorylation.

DESIGN: Experimental laboratory study.

MATERIALS AND METHODS: We used excessive oxidative stress to induce cell senescence, and examined the phenotype of aging. HGL5 cells were cultured in hydrogen peroxide medium for 24 h with or without MitoQ. Protein and gene expression of different enzymes related to metabolism in senescent granulosa cells were analyzed by qPCR, protein array or immunofluorescence.

RESULTS: We report that MitoQ causes an increase in the expression and phosphorylation of AMPK and an increase in the expression of acyl-CoA synthetase, of carnitine palmitoyl transferase 1 and of carnitine acylcarnitine translocase, all enzymes involved in lipid catabolism. On the other hand, the levels of acetyl-CoA carboxylase as well as those its product, i.e. malonyl CoA, are decreased.

CONCLUSIONS: The results suggest that MitoQ may be beneficial in protecting human GCs and may provide a useful monitoring tool for clinical studies of oral MitoQ supplements to older patients undergoing IVF treatment.

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MITOCHONDRIAL DNA QUANTITY AND SEQUENCE VARIATION IN HUMAN CUMULUS CELLS ARE ASSOCIATED WITH PATIENT BMI BUT NOT AGE OR ASSISTED REPRODUCTION OUTCOMES. Kishlay Kumar, PhD,[1] Marta Venturas, MSc,[2] Dan Needleman, Ph.D.,[2] Catherine Racowsky, PhD,[3] Dagan Wells, Ph.D.[4] [1]University of Oxford, Oxford, United Kingdom; [2]Harvard University, Cambridge, MA; [3]Brigham and Women's Hospital, Boston, MA; [4]Juno Genetics, Oxford, United Kingdom.

OBJECTIVE: Cumulus cells (CCs) fulfil a vital role in support of oocyte developmental competency. The appropriate function of CCs relies on adequate energy production, which in turn depends on the quantity and genetic competence of mitochondria. We sought to characterize the mitochondrial DNA content of a large number of human CCs samples via a combination of quantitative (relative mtDNA copy number) and qualitative (DNA sequence) analyses. Results were considered in relation to factors of relevance to oocyte reproductive potential, such as female age and body mass index (BMI), as well as to embryo characteristics and assisted reproductive technology (ART) outcomes.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: Human CCs, associated with 347 oocytes from 110 IVF patients, were recruited in the ongoing study. Patient age, body mass index (BMI) (kg/m^2), clinical diagnosis and ART outcomes were recorded with respect to each cumulus complex. Mitochondrial DNA quantity was measured in all the samples with a validated quantitative PCR method and the entire mitochondrial genome was sequenced in a subset of 119 samples using a high-depth massively parallel sequencing approach. Sequence variants in the mtDNA were evaluated using Mitomaster and HmtVar to predict their potential impact. Generalized linear mixed model and other appropriate statistical models were used to assess significance ($P \leq 0.05$).

RESULTS: Mitochondrial genome sequencing of CCs samples showed a total of 952 synonymous (i.e. no amino acid change) single nucleotide variants (SNVs) and another 626 non-synonymous (altered amino acid sequence) SNVs. Most SNVs were homoplasmic and therefore presumed to have been inherited, but 21 were heteroplasmic variants and potentially had a somatic origin. 104 of the homoplasmic variants, detected in 63 samples, were predicted to impact protein function, potentially affecting ATP production. Significant associations were observed between BMI and the number of non-synonymous mtDNA variants ($p=0.037$) and BMI and mtDNA quantity ($P = 0.013$). Moreover, a significant difference was also detected between mtDNA levels in CCs and normal weight (BMI 18.5-24.9) and obesity-class groups (BMI-30.0-34.9, $P=0.023$; ≥ 40.0, $P=0.024$). No significant differences were observed between mtDNA quantity in CCs and oocyte fertilization status or embryo quality.

CONCLUSIONS: No significant associations were detected between cumulus cell mtDNA quantity or sequence variants and clinically relevant endpoints. These findings suggest that, analysis of mtDNA (sequence and quantity) in CCs is unlikely to provide an advantage in terms of improved embryo selection during assisted reproduction cycles. Nonetheless, our data raise interesting biological questions, particularly regarding the interplay of metabolism and BMI.

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PATERNAL SEGMENTAL CHROMOSOME CONFUSION. Susanna McReynolds, PhD, Lauren Henry, BS, Nathan McCubbin, BS, Rachel S. Mann, BS, MS, Rachel Tucci, BS, Sue McCormick, BS, William B. Schoolcraft, MD, Mandy G. Katz-Jaffe, PhD. Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Chromosome segmental deletions and duplications resulting in a recognizable genetic syndrome account for 0.5-1% of prenatal diagnostic testing and are mostly considered random de novo events occurring during gametogenesis. The aim of this study was to identify factors associated with the parental origin, time point and types of chromosome segmental errors in preimplantation embryos.

DESIGN: Prospective blinded cohort study.

MATERIALS AND METHODS: In total, 27 blastocysts (mean maternal age = 35.1 ±3.1years; mean paternal age = 37.9 ±5.3years) were identified following preimplantation genetic testing for aneuploidy (PGT-A) with a ≥5Mb chromosome segmental deletion (n=24) or duplication (n=3). Patient consent and parental DNA were obtained to determine the origin of error using HumanKaryomap-12 BeadChip (Vitrolife). In addition, 54 transferrable quality blastocysts (≥Grade 3BB) with chromosome segmental aneuploidies were donated with patient consent for diagnostic confirmation (mean maternal age = 36.7 ±4.2years; mean paternal age = 38.6 ±5.1years). Each blastocyst underwent dissection into three distinct sections with inner cell mass (ICM) identification, and blindly re-analyzed using the equivalent VeriSeq™ platform (Vitrolife). After un-blinding, the data was compiled, identifying representatives of the ICM and TE, for a complete picture of each individual blastocyst.

RESULTS: The overall incidence of chromosome segmental aneuploidies (≥5Mb) in PGT-A cycles is 3.6% (n=62,564 biopsied blastocysts). Origin of segmental aneuploidy of 27 blastocysts revealed the vast majority of errors were paternal in origin (84%) and of these 95.2% occurred on the metacentric or sub-metacentric larger and medium size chromosomes. In contrast, maternal origin segmental errors were predominantly located on the smaller acrocentric chromosomes as observed with maternally derived whole chromosome aneuploidies (66.7%; $P<0.05$). There were no significant differences in the number of recombination events in association with parental origin or the location of chromosome segmental errors with the majority occurring on the q arm (74.1%). Blinded dissection re-analysis of 54 blastocysts with chromosome segmental aneuploidies validated the original TE diagnosis in 51 (94.4%) embryos and included concordance in all four sections (ICM and TE) for 39 blastocysts, indicating meiotic origin (72.2%). The remaining 12 (22.2%) blastocysts that were concordant, displayed a euploid cell line in ≥1 section and/or the reverse segmental error. These findings support mitotic chromosome segmental aneuploidies occurring during embryo development.

CONCLUSIONS: This study confirms the incidence of chromosome segmental aneuploidies predominantly originating from the male genome. This is in strict contrast to whole chromosome aneuploidies that have been extensively documented to originate from oogenesis. Additionally, our results reveal no association with paternal meiotic recombination events but do involve the q arm of larger to medium size metacentric and submetacentric chromosomes during meiosis or mitosis.

SUPPORT: None

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INCREASED CONCORDANCE RATES BETWEEN EMBRYO CELL-FREE DNA AND TROPHECTODERM BIOPSIES ARE RELATED TO FEMALE AGE INDEPENDENTLY OF CULTURE CONDITIONS. Carmen Rubio, PhD,[1] Luis Navarro-Sánchez, PhD,[1] Carmen Maria García-Pascual, PhD,[1] Olcay Ocali, BS,[2] Danilo Cimadomo, PhD,[3] William Venier, MSc, ELD (ABB),[4] Gerardo Barroso, MD,[5] Laura J. Kopcow, MD,[6] Mustafa Bahçeci, MD,[7] Lourdes López-Yañez, MD, PhD,[8] Marcos Kulmann, MSc,[9] Emilio De La Fuente, MSc,[1] Roser Navarro, MSc,[1] Diana Valbuena, MD, PhD,[1] Denny Sakkas, PhD,[2] Laura Francesca Rienzi, MSc,[3] Carlos Simon, MD, PhD[10] [1]Igenomix, Paterna (Valencia), Spain; [2]Boston IVF, Waltham, MA; [3]GENERA, Center for Reproductive Medicine, Rome, Italy; [4]San Diego Fertility Center, San Diego, CA; [5]Nascere, Mexico City, DF, Mexico; [6]Pregna Medicina Reproductiva, Buenos Aires, Argentina; [7]Bahçeci Health Group-Fulya IVF Centre, Istanbul, Turkey; [8]ProcreaTec, Madrid, Spain; [9]Nilo Frantz Reproductive Medicine, Porto Alegre, Brazil; [10]Professor University of Valencia, INCLIVA, Founder and Head of the Scientific Advisory Board, Igenomix, Paterna (Valencia), Spain.

OBJECTIVE: The presence of embryo cell-free DNA (cfDNA) in spent blastocyst media (SBM) and concordance with trophectoderm (TE) biopsies has been reported in PGT-A patients. However, the impact of different culture media, incubator models and female age on cfDNA detection is still unknown.

DESIGN: Multicenter, prospective study including 1,301 SBM from day-6/7 blastocysts in PGT-A patients aged 20-44 years. Informative results for both cfDNA and TE biopsies were obtained in 1,108 blastocysts. Concordance rates for embryo ploidy between cfDNA and TE biopsies were estimated for each culture media and incubator model at different age ranges (ClinicalTrials.gov; NCT03520933).

MATERIALS AND METHODS: TE biopsies and SBM were collected from April 2018 to September 2019. After IVF or ICSI, embryos were

	Irvine (n=641)	LifeGlobal (n=305)	Vitrolife (n=102)	Sage (n=60)	Minc (n=396)	C-TOP (n=305)	K-Systems (n=254)	Astec (n=102)	Miri (n=51)	TOTAL (n=1108)
<=30 years	71.9	75.0	95.8	100	70.6	75.0	88.9	95.8	100	76.9
31-35 years	74.6	78.9	83.7	80.0	79.0	78.9	53.3	83.7	92.3	77.4
36-38 years	77.9	82.9	83.3	72.7	75.7	82.9	79.0	83.3	80.0	78.4
39-40 years	79.5	87.5	84.6	92.3	68.4	87.5	88.6	84.6	88.9	81.6
41-44 years	83.1	93.3	90.0	92.9	77.9	93.3	92.7	90.0	83.3	85.3
p-value	0.0425	0.0383	NS	NS	NS	0.0383	0.0256	NS	NS	0.0256

cultured using the standard culture conditions of each laboratory up to day 4, with culture media from Irvine Scientific; Life Global; Vitrolife or Sage. Embryo culture was conducted in Minc; C-top; K-Systems; ASTEC or MIRI incubators. On day 4, embryos were individually transferred to a 10μL drop of fresh media. No previous assisted hatching or embryo vitrification was allowed. Individual SBM was collected on day 6/7 and frozen until analysis. TE biopsies and SBM were analyzed by Next Generation Sequencing with proprietary algorithms for cfDNA and TE biopsies.

RESULTS: Concordance rates were similar using different culture media or incubator models. However, female age was a significant variable, with concordance rates showing a significant linear trend with increasing age (p=0.0256, Chi-squared test for trend). This trend for female age was also observed when results were stratified by culture media and incubator model, in most of the cases. The increase in concordance rates was mostly due to the significant decrease in false positive rates, from 15.0% in women below 30 years, to 5.5% in women between 41-44 years (p= 0.0011, Chi-Square). False negative rates were not affected by female age. A summary of the concordance results is shown in the table.

CONCLUSIONS: High concordance rates have been reported for embryo cfDNA and TE biopsies. Female age was positively correlated with increased concordance rates for all the culture media and incubator models tested.

SUPPORT: The study was supported by Igenomix.

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DO SPECIFIC CHROMOSOME ANEUPLOIDIES INCREASE WITH ADVANCING PATERNAL AGE? Katrina Merrion, MS, Dusan Kijacic, MS, Michelle Kiehl, MS Natera, Inc., CA.

OBJECTIVE: Prior literature suggests there may be a chromosome-specific aneuploidy risk for offspring associated with advanced paternal age (PA), mainly trisomy 21 and sex chromosome aneuploidy.[1-5] In this study, we analyze the 24-chromosome preimplantation genetic testing for aneuploidy (PGT-A) results for trophectoderm (TE) samples from a series of men who underwent in vitro fertilization (IVF) using an oocyte donor, broken down by chromosome and PA.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: All PGT-A cases with TE biopsy and an oocyte donor between July, 2010 – April, 2020 were included in the analysis. IVF cycles and TE biopsies were performed according to each clinic's standard procedures. TE and biological parent samples were shipped to a reference lab for genotyping using Illumina Cyto12 SNP-based microarrays and a bioinformatics technique. TE samples were compared to parental samples across multiple SNP loci to determine parental origin of each chromosome and to establish chromosome copy number. Statistical analysis was performed using a two-tailed t-test.

Table 1. Aneuploidy rates of paternal and mixed origin by chromosome number and PA group (years).

Chromosome Number	<35 (%)	35-37 (%)	38-40 (%)	41-42 (%)	43-50 (%)	51-60 (%)	>60 (%)
1	0.7	0.7	1.1	1.3	1.4	1.0	2.0
2	1.1	0.7	1.5	1.3	1.7	1.6	2.0
3	1.2	1.1	1.6	1.5	1.5	1.1	1.2
4	1.2	1.1	1.6	1.4	1.6	1.4	2.0
5	1.7	0.9	1.2	1.1	1.3	0.9	2.0
6	1.7	1.0	1.6	1.7	1.3	1.6	2.7
7	1.1	0.8	1.1	1.2	1.4	1.1	1.6
8	0.9	1.3	0.9	1.4	1.3	1.3	1.2
9	0.6	0.9	1.5	1.5	1.5	1.6	0.8
10	1.0	0.8	1.2	1.1	1.3	1.2	0.8
11	1.2	0.8	1.3	1.2	1.3	1.0	1.6
12	0.8	0.8	1.4	1.9	1.2	1.1	1.2
13	1.4	0.8	1.4	1.9	1.5	1.7	2.3
14	1.4	1.1	1.2	1.6	1.6	1.7	1.6
15	1.0	0.8	1.2	1.6	1.7	1.3	2.0
16	0.8	0.8	1.1	1.7	1.3	1.1	1.6
17	1.0	0.4	1.0	1.1	1.3	0.9	1.6
18	0.8	0.8	1.0	1.8	1.5	1.2	2.0
19	1.1	0.5	1.2	0.6	1.1	1.1	2.0
20	1.2	1.0	1.2	1.2	1.2	1.3	0.8
21	1.2	1.2	1.1	1.4	1.6	1.5	1.6
22	1.0	0.9	1.6	1.1	1.3	1.4	2.0
Sex	1.8	1.6	1.8	2.0	1.8	1.6	2.0

RESULTS: Results were obtained on 14,901/15,371 (97%) of TE samples. The average PA for the patient cohort was 43.6 ± 7.0 years (range 23.1-73.1). Aneuploidy rates by chromosome are broken down using SART age groups, in addition to a further breakdown of men >42 years (Table 1). There was no statistical difference in the paternal aneuploidy rates by chromosome between PA groups (p>.05).

CONCLUSIONS: While previous literature has suggested chromosome-specific aneuploidy risks for offspring may increase with advancing PA, our large dataset shows no correlation.

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SUPPORT: Natera, Inc.

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INCREASED USE OF EXPANDED CARRIER SCREENING (ECS) GENETIC PANELS IDENTIFY MANY TYPES OF FACTOR XI VARIANTS: WHAT DO WE DO WITH THIS INFORMATION FOR INFERTILITY PATIENTS?

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OBJECTIVE: Factor XI deficiency is an autosomal recessive (AR) bleeding disorder frequently seen in the Ashkenazi Jewish population but less common among other ethnicities. Although carriers of AR disorders are typically asymptomatic, Factor XI deficiency carriers can have reduced factor XI levels and experience increased bleeding. Any deficiency in factor XI may lead to propensity to bleed; however, the bleeding risk is unpredictable as there is poor correlation with factor XI level. As ECS becomes more commonplace in the IVF clinic and many ECS panels include the F11 gene, an increasing number of patients are being identified to carry or be affected with factor XI deficiency. Since pregnancy and gynecological surgery are encounters that potentially expose these patients to hemorrhage risk, the objective of this study was to explore how Reproductive Endocrinology and Infertility (REI) physicians might use this information.

DESIGN: Case series of factor XI deficiency identified on ECS genetic panel at a large urban university-based fertility center from 6/2018 to 3/2020.

MATERIALS AND METHODS: All cases of factor XI deficiency were identified from the same ECS panel performed by a single reference laboratory. Patient records were reviewed for medical and surgical history, infertility treatments and outcomes, and hematologic evaluation.

RESULTS: 21 patients were identified with factor XI mutations out of 1501 patients tested for an incidence of 1.4%. Of these, 10 were male. All patients were heterozygotes. No carrier couples of factor XI deficiency were identified. Seven different variants were detected: 45% (10) of patients had variant c.403G>T, a nonsense mutation that is known to be the most common mutation in Ashkenazi Jewish patients; 23% (5) had variant c.901T>C, a missense mutation also common in the Jewish population; 5 other variants were found in the remaining 6 patients. 82% (18) variants were identified as "pathogenic," and 14% (3) as "likely pathogenic." Of the 12 female patients, 5 completed fertility treatments including office-based oocyte retrieval without excessive bleeding; 4 of these patients completed retrievals before their factor XI mutation was known. 8 patients are actively trying for pregnancy via ovulation induction or embryo transfer; all of these patients were either referred to hematology for clearance or had factor XI levels ordered by their REI physician. Of the 6 patients referred to hematology, 2 have been cleared for pregnancy and surgery, while the other 4 have pending consults. 2 patients had factor XI levels available; one was normal (66%, c.901T>C variant) and one low (45%, c.1716+1G>A variant) – both patients had normal coagulation panels (coags) and were cleared for fertility treatments. 3 patients had factor XI level and coags ordered by the REI physician; all are pending results.

CONCLUSIONS: As ECS is more commonly ordered for infertility patients, our knowledge of the implication of different variant types on surgical and pregnancy bleeding risks will grow. REI physicians should establish a standard approach to identify those at increased risk of hemorrhage and adverse outcomes.

SUPPORT: There is no financial support to declare.

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AN EVIDENCE-BASED EVALUATION OF GUIDELINES CRITERIA FOR CONDITION INCLUSION ON ECS PANELS: IDENTIFYING A GUIDELINES-COMPLIANT PANEL.

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OBJECTIVE: The American College of Obstetrics and Gynecology (ACOG) states that expanded carrier screening (ECS) is an acceptable strategy for carrier screening and that conditions selected for inclusion on ECS panels should meet several of the following criteria: 1. have a carrier frequency of 1 in 100 or greater, 2. have a well-defined phenotype, 3. have a detrimental effect on quality of life, 4. cause cognitive or physical impairment, 5. require surgical or medical intervention, 6. have an onset early in life, and 7. can be diagnosed prenatally. These criteria lack specificity, making them difficult to interpret.

DESIGN: We drew from published, quantitative frameworks to clarify and operationalize each criterion, and then identified conditions that unambiguously met the criteria.

MATERIALS AND METHODS: Carrier frequencies were calculated from an internal database of more than 450,000 carriers of condition(s) on a 176-condition panel. "Well-defined phenotype" was defined by the ClinGen categorization of the strength of gene-disease association. The four severity-related criteria (criteria 3-6) were defined by the mapping of disease traits to each criterion by 12 independent board-certified genetics providers (genetic counselors and medical geneticists). The ability to be diagnosed prenatally was considered to be a feature of all monogenic conditions.

RESULTS: It is unclear how many criteria ACOG deems acceptable to adhere to its statement that "several" criteria should be met. Therefore, the two conditions that ACOG currently recommends for panethnic carrier screening, cystic fibrosis (CF) and spinal muscular atrophy (SMA), were used to establish baseline thresholds. Both conditions have carrier frequencies greater than 1 in 100 in any ethnicity, have Definitive gene-disease associations, meet at least one severity-related criterion (CF met one and SMA met four), and can be diagnosed prenatally. 176 conditions were then analyzed using these thresholds: 40 had carrier frequencies greater than 1 in 100 in any ethnicity, 173 had Definitive gene-disease associations, 170 met at least one severity-related criterion, and all 176 could be diagnosed prenatally. Combining these thresholds yields a guidelines-compliant panel of 37 conditions (Table), with a combined carrier detection rate of 30.4% and an ARC detection rate of 1.0%. Relative to a 176-condition panel, the 37-condition panel would detect 84.6% of ARCs.

CONCLUSIONS: Evidence-based application of the ACOG severity criteria resulted in the identification of a guidelines-compliant panel consisting of 37 conditions.

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HOW EFFECTIVE IS UNIVERSAL CARRIER SCREENING TO ENCOMPASS TURKISH POPULATION MUTATION PROFILE?

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OBJECTIVE: According to WHO, 8000 people (in every 100000) are affected with rare diseases and in Turkey 6-8 million people are affected by rare diseases. There are around 8000 rare diseases known in the world and an average of 5 new diseases are described every week. Since the vast majority of genetic diseases cannot be cured, it is of great importance to identify carrier status of partners and prevent affected child births with prenatal or preimplantation genetic methods. Consanguineous marriages have been a major health burden in our country highlighting crucial need of eradication of single gene disorders.

DESIGN: In this study, we investigated the adequacy of carrier panels screening 200-600 different conditions. Our approach was to investigate all pathogenic and likely pathogenic variants in 200 whole exom sequencing (WES) cases without considering the clinical phenotype and combine this data with variant list of all PGT-M cases to obtain rare mutaion profile of Turkish population.

MATERIALS AND METHODS: We compared gene overlap for 2 different commercially available carrier screening tests encompassing 201 and 647 genes and WES mutation results in 301 genes for 200 patients. WES was performed using Twist Human Core Exome Plus kit. Data were analysed using Ingenuity Variant Analysis software according to ACMG guidelines. Variants were filtered according to QC scores (read depth, allel fraction, call quailty), minor allele frequency (%1> in all major databases) and pathogenicity status (in HGMD, Clinvar or predicted pathogenic/likely pathogenic). Additionally, we have included 264 genes from PGT-M data.

RESULTS: 26 out of 965 genes (2.7%) were present in all 4 groups. 360 genes were solely observed in Panel 1, while this number was 13 in Panel 2, 176 for WES and 124 for PGT-M. 304 genes observed in WES and PGT-M cases were not covered by both panels. WES reveals that the variant frequency of the most common genes (top 15 genes) constitute only 34% of all variants detected.

CONCLUSIONS: Carrier screening is an essential public health requirement, especially in countries where high consanguineous marriage is observed. Since commercially available panethnic panels do not fully meet the needs of geographical regions, no panel can be designated as universal. This hypothesis is supported by the comparison results revealing that 360 genes in Panel 1 do not overlap with any other group. The most important reason for this is high consanguinity in our country underlying rare genetic variants and it is noteworthy that 65% of the families applying for PGT-M are carriers of rare diseases. This is also highlighted in the outcome of the study, where variant frequency of the most common genes (top 15 genes) in WES cases constitutes only 34% of all variants detected. Furthermore, since mutation databases are not well-established in our population, especially in rare diseases, variants of uncertain significance (VUS) are frequently encountered. Therefore, these kind of studies constitute an important source of information for the creation of community-specific panels.

P-625 4:30 PM Monday, October 19, 2020

STRUCTURAL AND GENOMIC CHARACTERIZATION OF GLOBOZOOSPERMIC MEN. Alessandra Parrella, M.Sc., Philip Xie, B.S., Stephanie Cheung, B.S., Danielle Rebecca Tavares, B.A., Brianne Barker, B.S., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To characterize the structural abnormalities, genetics, and transcriptomic profile of globozoospermic (GZ) men.

DESIGN: During the last 8 years, 11 GZ men undergoing treatment at our center were screened by ultrastructural analysis and categorized as having partial (PG) or complete (CG) globozoospermia. CG men, according to their ability to sustain a term pregnancy, underwent whole genome karyotyping, gene mutation analysis, and transcriptomic profiling.

MATERIALS AND METHODS: GZ men underwent standard semen analysis, and ultrastructural details were evaluated by transmission electron microscopy (TEM). Aniline blue staining measured histone content (normal threshold $\leq$20%). SCF was performed by TUNEL (normal threshold $\leq$15%). PLCζ was detected with immunofluorescence staining (normal threshold $\geq$30%). Genome and transcriptome analyses were obtained by DNA- and RNA-seq, respectively.

RESULTS: A total of 11 men were diagnosed as PG (N=4) and CG (N=7) by TEM, revealing 98 $\pm$ 1% and 100 $\pm$ 0% occurrence of round heads, respectively (P=0.01).

PG men (32.6±4 years) had a sperm concentration of 31 $\pm$ 42 x10^6/ml, 15 $\pm$ 12% motility, and normal morphology of 0.7 $\pm$ 0.5%; CG men (36.1 $\pm$ 4 years) had a sperm concentration of 36.5 $\pm$ 39 x10^6/ml, 24.4± 21% motility, and 0% normal morphology. Residual histones were 40±19% and 53.8±24% and SCF was 16.3 $\pm$ 2 and 19.5 $\pm$ 12 in PG and CG men, respectively. PLCζ was 34 $\pm$ 4 in PG men and 7.4 $\pm$ 4 in CG men (*P*=0.001). Aneuploidy was 3.6% in PC men and 8.2% in CG men. Genetic analysis of 3 men showed common mutations in DPY19L2, SPATA16, and PICK1 genes, which are all associated with spermiogenesis.

A patient unable to achieve a pregnancy (CG1) was found to have a mutation on NLRP5, which is essential for zygote development. In a patient whose female partner suffered a miscarriage (CG2), exome sequencing revealed a heterozygous deletion on BSX, which is associated with neonatal development. Genetic assessment of a patient whose female partner had a term pregnancy (CG3) showed a single nucleotide insertion on PIWIL1, which is related to sperm phenotype. CG1 had 71 imbalanced genes involved in reproductive processes, with 19 associated with spermatogenesis (*KLHDC3/chr 6, KLHL10/chr 17, MORN2/chr 2, PAPPA/chr 9, UBR2/chr6*), sperm maturation (*ADAM21/chr 14, CNBD2/chr 20, SPEM1/chr17, TXNRD3/chr 3*), DNA condensation (*H1FNT/chr 12, NEK2/chr 1, RNF8/chr 6*), fertilization (*CALR3/chr 19, HSPA1L/chr 6, IQCF1/chr 3*), and embryo development/implantation (*OVGP1/chr 1, STC2/chr 5, WNT9B/chr 17*).

CG2 had 37 imbalanced genes, with 13 down-regulated ones involved with spermatogenesis (*CSF1/chr 1, NAMPT/chr 7, SEMG1/chr 20, SEMG2/chr 20, SMCP/chr 1)*, DNA double-strand break repair *(RMI1/chr 9)*, and embryo development (*ACVR1C/chr 2, CBX2/chr 17, CRHR1/chr 17, TGFB3/chr 14)*. CG3 had only 2 underexpressed genes involved with cell adhesion, migration, and signaling receptor binding: *HAS2*/Chr 8 and *TGFB2*/Chr 19.

CONCLUSIONS: Globozoospermia is a rare but severe form of male infertility that requires extensive structural and genomic analysis to identity treatment options and the ability to support a term pregnancy.

P-626 4:30 PM Monday, October 19, 2020

HUMAN GROWTH HORMONE (GH) AND EMBRYONIC CHROMOSOMAL CHANGES: WHAT WE CAN EXPECT. Michelle Nagai, MD,[1] Larissa Matsumoto, MD,[1] Mariana Moraes Piccolomini, MS,[2] Orcar Duarte, MD,[3] Edson G. Lo Turco, PhD,[4] Carolina Rebello Costa, MD,[1] Ekaterini koutsantonis Pires, MD,[1] Fernanda Imperial Granjo, MD,[1] Lucas Yamakami, MD,[5] Eduardo Hideki Miyadahira, MD[1] [1]MD, São Paulo, Brazil; [2]Senior Embryologist, São Paulo, Brazil; [3]Clinical Chief in Lab For Life Laboratory, São Paulo, Brazil; [4]IonMedicine - Precision Medicine, Sao Paulo, Brazil; [5]Clinical Chief, São Paulo, Brazil.

OBJECTIVE: To evaluate the effect of adjuvant human growth hormone (hGH) on the aneuploid rate in women undergoing IVF PGT-A cycles.

DESIGN: Retrospective chart review at a private infertility center.

MATERIALS AND METHODS: This study includes patients with poor prognosis and low chances for treatment success who underwent IVF-PGT-A with and without hGH as complementary medication. The inclusion criteria are: women were stratified as Poor Responders by Bologna criteria or patients with low rates of blastulation and low rates of euploidy in previous treatment without hGH. It was used 2,66 mg /day of hGH, started on the first day of ovarian stimulation until the trigger. Statistic analysis: ANOVA test was performed to assess the comparison between the groups, with an IC 95%, with a statistical significance of p< 0,05.

RESULTS: A total of 137 cycles were analyzed, of which 103 used hGh and 34 without hGh. There was no significant statistical diference between the groups on the average age (38.44 +- 3.4 vs 38.82 +- 2.96), AMH(1.48 +- 0.80 vs 1.65 +- 1.28, p= 0.115), basal FSH(9.00 +- 5.04 vs 9.01 +- 6.12, p=0.941), basal LH (7.04 +- 6.37 vs 6,43 +- 8.79, p=0,718) and antral follicle count (11.05 +- 4.80 vs 12.31 +- 5.27, p=0.688). Although the blastulation rates are similar(p=0,952), an increase in number of embryo biopsy rate was observed in the hGH group(2,64 +- 1,86 vs. 1,82 +- 1,14 p=0.017) as well as the euploid rate (33.57%) if compared to the group that did not use hGH (16.62%) (p=0.017). However no statistical difference was found between the blastulation and miscarriage rates.

CONCLUSIONS: Despite the advancement of technology, the success rate of IVF remains relatively stable in one group of patients: poor responders, over 40 years old, with a history of failure of previous IVF cycles and/or formation of poor quality embryos. Different strategies have been used to improve the IVF outcome and euploidy rate, including GH as an adjunct treatment. In the present study, the use of GH was related to an increase in the euploidy rate. No significant statistical difference was observed in the miscarriage rate, nevertheless, there is a tendency to be lower in the hGh group. The mechanism by which GH can decrease the rate of aneuploidy is still uncertain.

REFERENCES: no reference

SUPPORT: non

P-627 4:30 PM Monday, October 19, 2020

PRENATAL GENETIC DIAGNOSTICS FOR FAMILIES WITH MITOCHONDRIAL DNA DISEASE. Amy Koski, BA,[1] Nuria Marti-Gutierrez, PhD,[1] Eunju Kang, PhD,[2] Hayley Darby, MS,[1] Ying Li, MS,[1] Crystal Van Dyken, BS,[1] Aleksei Mikhalchenko, PhD,[1] Dan Liang, PhD,[1] Hong Ma, PhD,[1] Sally Shields, BSN,[3] Paula Amato, MD,[1] Shoukhrat Mitalipov, PhD[1] [1]Oregon Health & Science University, Portland, OR; [2]ASAN Medical Center, Seoul, Korea, Republic of (South); [3]Medical University of South Carolina, Charleston, SC.

OBJECTIVE: This study sought to evaluate the feasibility of predicting the 13513G>A mitochondrial DNA (mtDNA) disease causing mutation in newborns by prenatal testing. Reproductive options to prevent or lower the passage of pathogenic mtDNA mutations from carrier parents to children are limited to preimplantation or prenatal genetic diagnostics. However, in vitro fertilization procedures followed by preimplantation genetic testing is accessible to few families due to high cost.

DESIGN: We report our clinical experience with prenatal diagnostic testing and birth of two asymptomatic children for a family with m13513G>A mutation associated with Leigh Syndrome following natural conception.

MATERIALS AND METHODS: Biopsies of a gestational sac and/or chorionic villi (CVS) and amniotic fluid were collected from the first pregnancy at 10 weeks and 16 weeks gestation and subsequently tested for the m13513G>A heteroplasmy using whole mtDNA sequencing (MiSeq platform). This pregnancy was carried to term and resulted in vaginal delivery of an asymptomatic newborn. Cord blood, foreskin, urine, and venous blood samples were collected from newborn 1 and underwent whole mtDNA sequencing as well. Two years following, a second pregnancy conceived by natural conception was evaluated by chorionic villus sampling only. The intended mother opted out of amniocentesis testing.

RESULTS: Mutation load for the first pregnancy was measured at 27.5% in the chorionic villi and 29.5% post amniocentesis; individual cells isolated from the amniotic fluid ranged between 9-48%. Samples collected from newborn 1 had a mutation load of 15% in cord blood, 14% in foreskin, 11.7% in urine and 0.07% in venous blood. Mutation load for the second pregnancy was evaluated solely via CVS at 0.11%. This pregnancy also resulted in the birth of healthy child with undetectable mutation in cord blood, foreskin and venous blood.

CONCLUSIONS: This case study suggests feasibility of predicting 13513G>A mtDNA mutation in newborns by prenatal testing.

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POSTER SESSION: MALE REPRODUCTION

P-628 4:30 PM Tuesday, October 20, 2020

CLARIFYING THE RELATIONSHIP BETWEEN TOTAL MOTILE SPERM COUNTS (TMSC) AND INTRAUTERINE INSEMINATION (IUI) PREGNANCY RATES. Akhil Muthigi, MD,[1] Samad Jahandideh, PhD,[2] Lauren A. Bishop, MD,[3] Firoozeh K. Naeemi, Bs,[2] Sharon K. Shipley, MS,[4] Jeanne E. O'Brien, MD, MSc,[2] Paul Shin, MD,[2] Kate Devine, MD,[2] Cigdem Tanrikut, MD[2] [1]MedStar Georgetown University Hospital, Washington, DC; [2]Shady Grove Fertility Center, Rockville, MD; [3]NIH, Bethesda, MD; [4]Shady Grove Fertility Center, Rockville, MD.

OBJECTIVE: The use of post-wash TMSC in predicting pregnancy outcomes in IUI has been a subject of debate. Limitations of previous reports have been due to small sample sizes and attempts to identify clinically meaningful thresholds rather than define gradual pregnancy rate trends across a continuum of TMSC. To clarify the relationship between post-wash TMSC and IUI outcomes, we provide an updated evaluation of a large single institution sample.

DESIGN: Retrospective review.

MATERIALS AND METHODS: All stimulated clomiphene citrate, letrozole, and/or injectable gonadotropin IUI cycles performed at a single institution from 2002 through 2018 were reviewed. Generalized estimating equations (GEE) analysis was used to account for multiple cycles by individual patients and to adjust for female partner age, body mass index, stimulation protocol, and serum estradiol. Primary outcome was successful clinical pregnancy defined as ultrasound confirmation of an intrauterine gestational sac.

RESULTS: 92,471 insemination cycles were available to evaluate the relationship between TMSC and clinical pregnancy. Pregnancy rates were highest with ≥9 million TMSC, and declined gradually as TMSC decreased (Table 1).

Complete data for the adjusted GEE analysis were available for 62,758 cycles. Adjusted GEE analysis among cycles with ≥9 million TMSC (n=46,557) confirmed that TMSC in this range was unrelated to pregnancy (p=0.46). Conversely, TMSC was highly predictive of pregnancy (Wald χ^2=39.85) in adjusted GEE analysis among cycles with <9 million TMSC (n=16,201), with a statistically significant decline (p<0.001).

CONCLUSIONS: IUI pregnancy is optimized with TMSC ≥9 million, below which rates gradually decline. Although rare, pregnancies were achieved with TMSC <0.25 million. Since the decline in pregnancy is gradual and continuous, there is no specific threshold above which IUI should be recommended. Rather, these more specific quantitative predictions can be used to provide personalized counseling and guide clinical decision making.

Table 1. Clinical pregnancy rates per intrauterine insemination cycle according to post-wash TMSC

Total Motile Sperm Count (millions)	Number of Insemination Cycles	Number of Clinical Pregnancies	Clinical Pregnancy per Cycle
<0.25	263	11	4.18%
0.25-0.49	341	14	4.11%
0.50-0.99	627	23	3.67%
1.00-1.99	1611	120	7.45%
2.00-3.99	4561	462	10.13%
4.00-4.99	2845	331	11.63%
5.00-5.99	3109	400	12.87%
6.00-6.99	3474	484	13.93%
7.00-8.99	6810	976	14.33%
≥9	68830	11496	16.70%

P-629 4:30 PM Tuesday, October 20, 2020

FOXO4-DRI ALLEVIATES AGE-RELATED TESTOSTERONE SECRETION INSUFFICIENCY VIA TARGETING SENESCENT LEYDIG CELLS IN AGED MICE. Guihua Liu, Ph.D.,[1] Xing Yang, Ph.D.,[1] Tingting Li, Doctor[2] [1]The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; [2]Reproductive Medicine Research Center, Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: To investigate the effects and mechanism of targeted inhibition of FOXO4 -p53 interaction on testicular aging in mice.

DESIGN: Animal study was designed.

MATERIALS AND METHODS: Three-month-old and 20-month-old male C57BL/6 mice were used as research objects. The mice were divided into FOXO4-DRI treated group, old control group and young control group, with 10 mice in each group. The FOXO4-DRI treated group were intraperitoneally injected with FOXO4-DRI (5 mg/kg/d) every other day for three administrations, and the old control group and young control group were injected with the same amount of normal saline, and the observation period is 30 days. Upon the endpoint of experiment, assess muscle performance of mice in each group through an upside down suspension test, and analyze

testicular weight/body weight ratio and seminal vesicles weight/body weight ratio. Then, epididymal sperm counts and motility, serum testosterone, myocardial enzymes (CK and CK-MB), liver function (ALT and AST) and renal function (CREA and BUN) were measured. Immunohistochemical staining was performed to detect the expression of FOXO4 in testes. SA-β-Gal staining was performed to assess the quantity of senescent cells in testes. Western blot was performed to measure protein levels of testosterone synthesis-related enzymes (3β-HSD and CYP11A1), senescence-related proteins (p53, p21, and p16) and SASP factors (IL-1α, IL-1β, IL-6, IL-10, TNF-α, and TGF-β) in testes. Immunofluorescence staining was performed to detect the expression of meiotic marker SCP3.

RESULTS: FOXO4 was expressed in LCs of the old mice, but not the young mice. Compared with old control group, the quantity of senescent LCs and expression of aging-related proteins (p53, p21 and p16) in the testes of FOXO4-DRI treatment group were significantly decreased (P <0.05). Levels of SASP factors including IL-1β, IL-10 and TGF-β were decreased (P<0.05). Testicular endocrine function-related indicators including serum testosterone concentration, expression of 3β-HSD and CYP11A1, and muscle performance were significantly improved (P<0.05). Spermatogenic function indicators including epididymal sperm counts and vitality (P<0.05) and expression of SCP3 were also improved. The testicular weight/body weight ratio (P >0.05) showed no significant changes, but the seminal vesicles weight/body weight ratio decreased significantly (P <0.05). Indicators of systemic organ function or injury including CK, CK-MB, ALT, AST, CREA and BUN showed no significant changes (P >0.05).

CONCLUSIONS: Targeted inhibition of FOXO4-p53 interaction can safely and effectively eliminate senescent LCs in testes and repair testicular aging in mice, which may become a new strategy for the treatment of testicular aging.

SUPPORT: no

P-630 4:30 PM Tuesday, October 20, 2020

THE PUBLICATION FATE OF MALE FERTILITY ABSTRACTS PRESENTED AT THE ANNUAL MEETINGS OF THE AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE.

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OBJECTIVE: Approximately 1000 abstracts are presented every year at the annual meeting of the American Society for Reproductive Medicine (ASRM), of which 10% involve male fertility. This study was undertaken to determine the publication rate among these abstracts, time to publication, and factors associated with publication.

DESIGN: Cross-Sectional Study.

MATERIALS AND METHODS: All accepted abstracts related to male fertility that were presented at the 2012-2014 ASRM annual meetings were reviewed. Comprehensive PubMed and internet searches were conducted for evidence of publication in full-length manuscript form up to April 2020. Chi-square analysis was performed to determine predictive factors for publication.

RESULTS: A total of 393 abstracts involving male fertility were presented from 2012 to 2014. By April 2020, 136 (35%) achieved a median time to publication of 15 months (range 0-76 months). Manuscripts were most commonly published in: *Fertility and Sterility* (17%), *Urology* (8%), *Human Reproduction* (7%), and *Journal of Urology* (4%). A higher trend in publication was seen with podium compared to poster presentations (41.4% vs 31.9%, p =0.08). Publication rates by category were: Society for Male Reproduction and Urology (SMRU) Traveling Scholars 75% (12/16), Testis 50% (9/18), Male Reproductive Urology 44% (47/106), Sperm Biology 38% (17/45), Male Reproductive Endocrinology 33% (7/21), Male Factor 31% (49/158), Sperm Preparation 14% (6/43). Most abstracts were submitted by US institutions 52% (205/393), with a 38% (77/205) publication rate. International publication rates were similarly seen from Asian 36% (32/88), South American 33% (16/49), and European 24% (12/51) institutions. Higher publication rates were observed when studies originated from Department of Urology 45% (57/127) or in collaboration with Department of Obstetrics & Gynecology [OB/GYN] 46% (18/39) compared to OB/GYN alone 26% (50/196) [p < 0.01].

CONCLUSIONS: Overall publication rate of 35% for male fertility studies is similar to publication rates of abstracts presented at international urological meetings. SMRU Traveling Scholars had the highest publication rate and should continue to showcase their findings at the ASRM annual meeting. Urology department-only affiliations or collaborations with OB/GYN department were more likely to publish their results after presentation. Continued efforts should be made to increase publication of male fertility related abstracts presented at the ASRM annual meetings.

SUPPORT: None

P-631 4:30 PM Tuesday, October 20, 2020

TRANSPLANTATION OF HUMAN URINE-DERIVED STEM CELLS AMELIORATES ERECTILE FUNCTION AND CAVERNOSAL ENDOTHELIAL FUNCTION BY PROMOTING AUTOPHAGY OF CORPUS CAVERNOSAL ENDOTHELIAL CELLS IN DIABETIC ERECTILE DYSFUNCTION RATS.

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OBJECTIVE: The main mechanism of diabetic erectile dysfunction (DED) is cavernosal endothelial dysfunction, but the origins of cavernosal endothelial dysfunction are unclear. The present study aimed to determine the contribution of autophagy in cavernosal endothelial dysfunction of DED rats, and explain therapeutic effect of urine-derived stem cells (USCs).

DESIGN: Animal study was designed.

MATERIALS AND METHODS: After rat corpus cavernosal vascular endothelial cells (CCECs) were isolated and cultured *in vitro*, CCECs were treated with advanced glycation end products (AGEs) to mimic the diabetic situation. Autophagy flux, proliferation and apoptosis of CCECs were determined by mRFP-GFP-LC3 adenovirus transfection combined with immunofluorescence observation and western blot analysis. USCs were isolated from the urine of six healthy male donors, and co-culture systems of USCs and CCECs were developed to assess the protective effect of USCs for CCECs *in vitro*. The contribution of autophagy to the cellular damage in CCECs was evaluated by the autophagic inhibitor, 3-methyladenine (3-MA). Then, DED rats (n=15 per group) were induced by streptozotocin (50 mg/kg) and screened by apomorphine (100 μg/kg), and another 15 normal rats served as positive controls. In DED rats, USCs or PBS as vehicle was administrated by intracavernous injection. Four weeks after injection, erectile function was evaluated by measuring the intracavernosal pressure (ICP) and mean arterial pressure (MAP). Endothelial function and autophaic activity were examined by western blot analysis, immunofluorescence and transmission electron microscopy.

RESULTS: *In vitro,* AGEs-treated CCECs displayed fewer LC3 puncta formation, and expressed less LC3-II, Beclin1 and PCNA, but expressed more p62 and cleaved-caspase3 than controls (P<0.05). Co-culture of USCs with CCECs demonstrated USCs were able to protect CCECs from AGEs-induced autophagic dysfunction and cellular damage, which could be abolished by 3-MA (P<0.05). DED rats showed lower ratio of ICP/MAP, reduced expression of endothelial markers, and fewer autophagic vacuoles in cavernosal endothelium when compared with normal rats (P<0.05). Intracavernous injection of USCs improved erectile function and endothelial function of DED rats (P<0.05). Most importantly, our data showed the repaired erectile function and endothelial function were result from restored autophagic activity of cavernosal endothelium in DED rats (P<0.05).

CONCLUSIONS: Impaired autophagy is involved in the cavernosal endothelial dysfunction and erectile dysfunction of DED rats. Intracavernous injection of USCs upregulates autophagic activity in cavernosal endothelium, contributing to ameliorate cavernosal endothelial dysfunction, and finally improved the erectile dysfunction induced by diabetes.

SUPPORT: no

P-632 4:30 PM Tuesday, October 20, 2020

TRENDS IN TESTOSTERONE THERAPY.

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OBJECTIVE: Rates of testosterone therapy (TT) prescribing dropped dramatically following the 2014 FDA warning on the potential for cardiovascular morbidity. Since then, prescription rates appear to be increasing in North America[1]. Current database studies tracking these trends suffer from incomplete prescription capture, lack of information on continued use, and confounding from concurrent population growth.

DESIGN: Nova Scotia (NS) is a Canadian province with minimal population growth over the past decade. NS tracks every testosterone prescription and refill through their prescription monitoring program (NSPMP). All testosterone prescriptions must be written on triplicate forms, allowing for comprehensive tracking.

MATERIALS AND METHODS: Data were extracted from the NSPMP database on all prescriptions and prescription refills of androgens for men over 18 years of age from 2007 to 2019. Population statistics were gained using publicly available data from Statistics Canada. Analysis of patterns by patient age decile and by year were examined for number of patients, prescriptions, and prescribers as well as formulation.

RESULTS: The population of Nova Scotia stayed relatively stable throughout the study period (2007: 936,203; 2019: 965,249; population increase of 3.1%) Throughout the study period, a total of 8837 men (0.9% of the population) received a testosterone prescription, and 6005 men (0.6%) remained on TT for longer than 6 months. Men aged 55-64 received the most prescriptions for TT (31%). 25% of men receiving TT were under age 45. There has been a steady decrease in oral formulations prescribed since 2007 (36% in 2007, 13% in 2019) with an increase in injectable esters (34% in 2007, 49% in 2019) and transdermal gels (24% in 2007, 35% in 2019). Primary Care Providers (PCPs) wrote 92% of all prescriptions on average (range 89-93%). Amongst all men, TT rates increased yearly from 2007 until 2014, at which point TT rates plateaued or decreased, depending on age group. The only exception to this trend was in men aged 18-34, in which TT rates have increased every year since 2007.

CONCLUSIONS: In a large Canadian province with stable population growth, prescriptions of testosterone increased until 2014, and then either stabilized or decreased. TT prescriptions in young men have continued to increase yearly. Injectable and gel-based formulations have increased in popularity over the past decade. Future efforts to educate prescribers, especially surrounding the effects on fertility in young men, should be largely focused on PCPs.

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SUPPORT: none

P-633 4:30 PM Tuesday, October 20, 2020

TARGETED ICSI TREATMENT IN GLOBOZOOSPERMIC MEN ACCORDING TO SPERM PLCZ CONTENT.

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OBJECTIVE: We assessed the PLCζ content of sperm from globozoospermic (GZ) men to determine the best treatment protocols for these patients.

DESIGN: Eleven men diagnosed with globozoospermia after morphological and ultrastructural assessment and treated at our center during the last 8 years were included. To identify their fertilization capacity, spermatozoa were screened for PLCζ. Patients were treated by ICSI or by ICSI with assisted gamete treatment (AGT) depending on PLCζ content. Embryological and pregnancy outcomes were compared between the two treatment methods.

MATERIALS AND METHODS: GZ men underwent standard semen analysis and transmission electron microscopy (TEM). Sperm oocyte activation was quantified by a PLCζ test on ≥200 cells per specimen, with a normal threshold of ≥30%. Genome and transcriptome analyses were compared to donor specimens. ICSI was performed in the standard fashion or with AGT by exposing both gametes to calcium ionophore.

RESULTS: Globozoospermia was confirmed by TEM, which showed 93.3 ± 12% occurrence of round heads. Eleven GZ men (34.6 ± 5 years) had the following semen parameters: a concentration of 36 ± 44 x10^6/ml, 20.3 ± 20% motility, and normal morphology of 0.2 ± 0.4%. Of these, 7 men (32.6 ± 4 years) with PLCζ content of 34 ± 4% underwent 17 ICSI cycles with their female partners (31 ± 4 years), achieving a fertilization rate of 24.6% (64/260). The implantation rate was 11.4% (4/35) with a clinical pregnancy and delivery rate of 12.5% (2/16) per cycle. The success rate was 28.5% (2/7) per patient. Men in the remaining 4 couples (men, 34.2 ±7 years; women, 33.2 ± years) had negative PLCζ assays, indicating only 7.4 ± 4% content. These couples underwent 6 ICSI cycles with AGT, achieving 37.5% (24/64) fertilization, 18.7% (3/16) implantation, and 33.3% (2/6) clinical pregnancy rates per cycle, yielding a 16.6% (1/6) delivery rate. The success rate was 25% (1/4) per patient. All treatment outcomes were comparable, except the fertilization rate, which was significantly higher in the cohort treated by ICSI with AGT ($P = 0.04$). Genetic analysis of these men identified mutations in the DPY19L2, SPATA16, and PICK1 genes, confirming the absence of the subacrosomal perinuclear theca. We identified mutations in PIWIL1, which is involved in late spermiogenesis, supporting the use of AGT. The transcriptomic profile showed 1,866 genes significantly imbalanced; of these, 111 were reproductive genes, of which 34 were underexpressed. These downregulated genes are associated with spermatogenesis (*KLHDC3*, *KLHL10*, *MORN2*, *PAPPA*, *UBR2*, *CSF1*, *NAMPT*, *SEMG1*, *SEMG2*, *SMCP*), sperm maturation (*ADAM21*, *CNBD2*, *SPEM1*, *TXNRD3*), DNA condensation and DNA-binding transcription factor activity (*H1FNT*, *NEK2*, *RNF8*, *FOXL2*, *GATA1*, *LHX9*, *RMI1*), fertilization capacity (*CALR3*, *HSPA1L*, *IQCF1*), and embryo development and implantation (*OVGP1*, *STC2*, *WNT9B*, *ACVR1C*, *CBX2*, *CRHR1*, *TGFB3*); *MFSD14A* is known to be found within GZ patients.

CONCLUSIONS: It is difficult to determine the best treatment protocol for GZ men. To avoid overtreatment, we assessed sperm PLCζ content and determined that if it is ≥30%, standard ICSI can be carried out.

SUPPORT: None

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IMPACT OF METABOLIC AGE ON SEXUAL AND ANDROGENIC FUNCTION IN YOUNG PATIENTS.

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OBJECTIVE: Erectile dysfunction is increasingly prevalent with age. Metabolic Age (metAge) refers to the number calculated by comparing Basal Metabolic Rate (BMR) of an individual to BMR average of his chronological age (chAge) group. It hence serves to reflect the metabolic status which is believed to influence sexual function. The aim of this study is to assess the relation between metAge & sexual function in men younger than 40 years of age

DESIGN: Prospective observational study.

MATERIALS AND METHODS: A total of 120 male healthcare workers of a tertiary medical center were randomly selected through computer generated randomization tables. Subjects receiving exogenous testosterone or erectogenic medications were excluded. In addition to providing an early morning serum testosterone (T) sample, subjects were requested to fill the International Index of erectile function questionnaire (IIEF-5) & to undergo Bioelectric Impedance Analysis [BIA] of their metabolic status using TANITA body analyzer (TBF-410GS) (Illinois, USA). Risk factors for erectile dysfunction (ED) such as diabetes mellitus, hypertension, coronary artery disease & dyslipidemia were also assessed. Participants were divided according to their chAge into two groups (<40 & > 40 years).

RESULTS: Ninety subjects were included (< 40 years, n=53; > 40 year, n=37). ED was reported by 48 (53%) subjects, while a low T level was detected in 18 (20%). Risk factors were detected in 41% of subjects. No significant relationship between risk factors & serum T or IIEF-5 results were observed. Participants with ED had significantly lower T levels (12.7 ± 4.6 vs.14.8 ± 3.9, p=0.02) compared to those without ED. Older chAge & metAge were observed in ED vs no ED participants as well, however without statistical significance. 24 (45.3%) subjects < 40 years of age had ED. Significantly lower T levels & significantly higher metAge & BMI were observed in participants <40 years with ED compared with their counterparts without ED (table 1). In this participant group (< 40years), significant correlations were observed between metAge & T (r-0.347, p=0.01), chAge (r0.384, p=0.005), visceral fat (r0.747, p<0.001), fat % (r0.78, p<0.001), weight (r0.524. p<0.001), BMI (r 0.635, p<0.001) & BMR (0.347, p=0.01).

CONCLUSIONS: Metabolic status may significantly influence the sexual & androgenic status of young men. An older metAge is observed in young men with ED & hypogonadism.

Parameters	< 40 years with ED (n=24)	< 40 years without ED (n=29)	P value
Testosterone (nmol/L)	19.8 ± 4.1	14.5 ± 4.1	0.002
metAge (years)	44.6 ± 6.8	39.9 ± 8.5	0.034
BMI (kg/m^2)	30.4 ± 4.2	27.9 ± 4.4	0.044
Fat% (%)	27.5 ± 5.3	24.5 ± 5.9	0.064
Visceral fat (rate)	10.6 ± 3.8	8.7 ± 3.8	0.072
Muscle mass (kg)	63.8 ± 8.8	61.4 ± 8.1	0.296
BMR (Kj)	8413.5 ± 1277.8	8022.0 ± 1128.9	0.242

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DOES SPERM TOTAL NORMAL MOTILE COUNT IMPACT PGT-A AND IVF OUTCOMES?

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OBJECTIVE: Male factor is the sole cause of infertility in about 20% of cases and is at least partially involved in up to 40% of cases. Sperm total normal motile count (TNMC) integrates the semen analysis components of morphology, motility, and total count to yield a single clinical value. The objective of this study is to assess whether a relationship exists between TNMC and preimplantation genetic testing for aneuploidy (PGT-A) as well as *in vitro* fertilization (IVF) outcomes.

DESIGN: Retrospective, observational study.

MATERIALS AND METHODS: In this retrospective, observational study, unidentified data sets were included of couples who visited our fertility center between October 2012 to December 2018 and had PGT-A (N= 1492) and elective single embryo transfer (N=242) performed. Inclusion was limited to those with a semen analysis within 90 days of IVF start. TNMC was calculated by multiplying total sperm count by percent motility and percent normal forms (Kruger's strict criteria). For analyses, we categorized TNMC into three groups: Group 1 (<1 million), 2 (1-4.99 million), and 3 (≥5 million). Primary endpoint was IVF outcomes. Secondary endpoints included embryo quality, morphology, ploidy, and gender. Pearson's chi-squared test was used for statistical analysis with $p<0.05$ considered significant.

RESULTS: A total of 1492 embryos (Group 1 N=395, 2 N=558, and 3 N=539) were analyzed. For all groups, embryos were more likely to be female; however, embryos from the <1 million group had the highest percentage of female embryos (58.5% vs 50.4% and 54.2%; p=0.046), and were more likely to be high-grade (69.1% vs 62.7% and 63.5%; p=0.015), compared to Groups 2 and 3, respectively. Embryos from the 1-4.99 million group were more likely to be low-grade (21.0% vs 14.4% and 15.8%; p=0.015), have a poor inner cell mass grading (14.9% vs 9.6% and 9.8%; p=0.027), and a poor trophectoderm grading (16.8% vs 12.2% and 12.4%; p=0.039), compared to those in Groups 1 and 3, respectively. There was no difference in embryo development (p=0.076), day of blastocyst transformation (p = 0.368) or ploidy status (p=0.324) among the different TNMC groups.

Subpopulation analysis of 242 transferred embryos (Group 1 N=50, 2 N=92, and 3 N=100), showed no statistical difference in implantation (p=0.311), clinical pregnancy (p=0.214), chemical pregnancy (p=0.426), miscarriage (p=0.685), ectopic pregnancy (p=0.417), or ongoing pregnancy rates (p=0.069) between the different TNMC groups.

CONCLUSIONS: This large-scale study is the first to examine the relationship of sperm TNMC to PGT-A and IVF outcomes. While it is possible that TNMC may impact certain embryo characteristics, such as gender, inner cell mass, trophectoderm, and overall grade, TNMC does not appear to impact IVF outcomes. Further studies are needed to further elucidate these relationships.

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NOVEL TREATMENT FOR SPERM CAPACITATION IMPROVES EMBRYO DEVELOPMENT IN MOUSE INTRACYTOPLASMIC SPERM INJECTION (ICSI).

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OBJECTIVE: Ohana has developed a novel *ex-vivo* sperm enhancement treatment designed to mimic sperm capacitation during natural conception. Previous non-clinical data have shown that this approach improves human sperm hyperactivation in samples from men in couples seeking treatment for infertility and from healthy men, as well as sperm hyperactivation, fertilization, and blastocyst development from 2-cell embryos in a mouse *in-vitro* fertilization (IVF) model (Seyb K, et al, ASA 2020; Poster 109). The impact of the Ohana sperm enhancement treatment on mouse embryo development from fertilized eggs indicates that this approach may also improve embryo development when used with ICSI. This study was conducted to evaluate the impact of the Ohana sperm enhancement treatment on embryo development in a mouse model of ICSI-IVF compared with standard mouse sperm activation.

DESIGN: Sperm were processed using the Ohana sperm enhancement treatment and standard control conditions. The percentage of mouse oocytes that developed into 2-cell embryos and blastocysts following ICSI were evaluated and compared between groups.

MATERIALS AND METHODS: Oocytes were collected from superovulated CD1 females and sperm isolated from epididymis of C57Bl/6 males. Sperm were capacitated using either TYH buffer (control) or using the Ohana sperm enhancement treatment. Sperm in both groups were washed in TYH buffer, then sperm tails removed, and sperm heads injected with an ICSI micropipette into oocytes stripped of cumulus cells. Injected oocytes were cultured overnight, and 2-cell embryos were assessed as a measure of successful fertilization. Embryos were then cultured to blastocysts. Data are from 10 experiments, with a total of 562 oocytes per arm. Statistical significance was evaluated by t-test.

RESULTS: The rate of 2-cell embryo formation per mouse oocyte between control (24.4±6.1%) and the Ohana sperm enhancement treatment (25.3±5.1%) were similar, as expected when fertilization is performed using ICSI. However, 2.3x more 2-cell embryos developed into blastocysts when sperm was prepared using the Ohana sperm enhancement treatment compared to control-processed sperm (74.7±11.1 vs 31.8±11.5%, respectively).

CONCLUSIONS: While ICSI prevents failed fertilization in some cases, it does not improve other outcomes such as embryo development, pregnancy, or birth (Boulet SL, et al. JAMA 2015;313:255). The Ohana sperm enhancement treatment significantly increased the probability of a 2-cell embryo developing into a blastocyst compared to control in a mouse ICSI study. These results confirm earlier observations that the Ohana sperm enhancement treatment has an impact beyond fertilization and indicate that the Ohana sperm treatment may improve sperm-mediated oocyte activation and early embryo development. These data suggest that the Ohana treatment for human sperm may also improve embryo development for people undergoing IVF with ICSI. The Ohana sperm enhancement treatment is being tested in an on-going clinical study evaluating fertilization and embryo development in conventional IVF.

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INSIGHTS IN THE MECHANISMS OF DEFECTIVE SPERM MATURATION IN INFERTILE MEN USING A COMPARATIVE PROTEOMICS APPROACH.

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OBJECTIVE: Ejaculated semen harbors not only mature and motile spermatozoa, but also spermatozoa at different stages of maturation, immature germ cells, and morphologically aberrant gametes, and may therefore be utilized to analyze the mechanism behind sperm dysfunction in infertile men. Transcription and translation are silent in post-testicular spermatozoa. Therefore, it is important to focus on alterations of the protein profiles in various phenotypes of spermatozoa present in ejaculated semen from fertile and infertile individuals to identify specific proteomic signatures that may shed light on defective sperm maturation and/or function in infertile men. In the

present study, a comparative proteomic approach was undertaken to understand the mechanism(s) involved.

DESIGN: Semen samples from fertile (n=12) and infertile (n=6) men were subjected to multi-layer density gradient (40%, 60%, and 80%) centrifugation to separate different phenotypes (F1, F2, F3 and F4; F1 least mature and F4 most mature). The proteome profile of each faction was compared between infertile and fertile group.

MATERIALS AND METHODS: Proteomic profiling of sperm phenotypes from both groups was performed using liquid chromatography-tandem mass spectrometry (LC-MS/MS). MASCOT- and SEQUEST-identified sperm proteins were compared and differentially expressed proteins (DEPs) were subjected to ingenuity pathway analysis (IPA) to detect the molecular networks affected. The key proteins of top networks were validated by western blot.

RESULTS: Sperm in the F4 fraction (matured) from fertile and interfile men showed high motility (>60%). A total of 119, 167, 373 and 262 DEPs were identified in the F1, F2, F3 and F4 fractions of fertile men compared with infertile men, respectively. The dysfunctional mTOR signaling with anomalous expression of downstream factors EIF2, eIF4 and p70S6K implies defective protein synthesis and abortive apoptosis in F1 and F2 fractions limiting sperm maturation. Conversely, mitochondrial dysfunction, particularly of oxidative phosphorylation pathways, was more prominent in F3 and F4 sperm fractions of infertile men along with proteins involved in sperm binding function. Validation of key proteins by western blot revealed that oxidative phosphorylation complex and HSPA2 were over-expressed in all sperm fractions of fertile men compared to infertile, whereas ACR was over-expressed only in mature (F4) spermatozoa.

CONCLUSIONS: Our results suggest that abortive apoptosis is responsible for presence of more immature spermatozoa in the ejaculate of infertile men. A decline in mitochondrial function, particularly oxidative phosphorylation in F4 fraction, implies an energy deprived hypoxic state; thus, resulting in impairment of sperm function in infertile men.

REFERENCES: None

SUPPORT: None

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COMPARING EUPLOIDY IN TESE, MESA, AND EJACULATE FROM PATIENTS WITH AND WITHOUT MALE FACTOR INFERTILITY.

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OBJECTIVE: Sperm retrieval via testicular sperm extraction (TESE) or microsurgical epididymal sperm aspiration (MESA) have been used to treat men with obstructive and non-obstructive azoospermia. Here we compare fertilization rates, blastocyst formation, euploidy, and euploidy rates, in IVF cycles with intracytoplasmic sperm injection (ICSI) and preimplantation genetic testing for aneuploidy (PGT-A), with sperm obtained via TESE, MESA and ejaculation.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Patients who underwent IVF or embryo banking with ICSI and PGT-A at NYU Fertility Center from 2/1/15 to 3/31/19, were separated into four groups for comparison based on the method of sperm procurement: TESE, MESA, ejaculate of males with male factor infertility (initial motility < 40% and/or count < 20 M/ml) (Ejac+MF), and ejaculate of males without male factor infertility (Ejac-MF). Demographics, total IUs gonadotropin received, trigger-day estrogen levels, number of oocytes retrieved, number of mature oocytes, fertilization rates, number of blastocysts formed, number of euploid embryos formed, and euploidy rates, were compared by performing a one-way ANOVA using 0.05 as the alpha level, and *a posteriori* testing.

RESULTS: Altogether, 283 patients were compared in the four groups: 56 TESE patients, 5 MESA patients, 160 Ejac+MF patients, and 62 Ejac-MF patients. There were no significant differences in maternal age, total IUs gonadotropin received, trigger-day estrogen levels, number of oocytes retrieved, or number of mature oocytes, between all four groups. TESE patients had significantly lower fertilization rates, blastocyst formation, and euploid embryos (64%, 3.7, 1.1, respectively) than both Ejac+MF (73%, 4.7, 1.4, respectively) and Ejac-MF (78%, 5.8, 2.1, respectively). The euploidy rates (euploid embryos/number of blastocyts) were not significantly different between the three groups (TeSE 23%, Ejac+MF 27%, Ejac-MF 30%). Finally, Ejac+MF patients had a significantly lower number of euploid embryos (1.4) that Ejac-MF patients (2.1).

CONCLUSIONS: In patients undergoing IVF with ICSI and PGT-A, significantly lower fertilization rates, and numbers of blastocysts and euploid embryos, were found when comparing TESE to Ejac+MF and Ejac-MF. However, the euploidy rates were not significantly different, suggesting that the number of embryos formed is the point of distinction. Ejac+MF patients also produced a smaller number of euploid embryos, than Ejac-MF patients.

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USING GENE EXPRESSION PROFILES OF EJACULATES OF NOA MEN TO HELP PREDICT SUCCESSFUL TESTICULAR SPERM RETRIEVAL.

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OBJECTIVE: To use gene expression profiles of ejaculates of non-obstructive azoospermic (NOA) men to determine whether testicular biopsy will yield spermatozoa.

DESIGN: During the last 12 months, a prospective study was carried out on specimens from 10 consenting men who yielded no sperm after extensive semen analysis (ESA). RNA expression analysis was performed and compared to fertile donors and men with obstructive azoospermia (OA). All men consented to undergo testicular biopsy (TESE) to attempt sperm retrieval. Transcriptomic profiling was correlated to successful sperm retrieval.

MATERIALS AND METHODS: ESA was carried out in the andrology laboratory for diagnostic purposes with the same rigor as ICSI for NOA patients. RNA was isolated from ejaculated specimens using a commercial spin column kit. Samples were then made into paired-end libraries; pilot paired-end 76-bp RNA-Seq using Illumina platform (NextSeq 500) was performed and expanded to 60M reads. Expression values were calculated in fragments per kilobase (FPKM) and normalized read counts. Expression with $P<0.001$ and absolute log2fold change >1 were considered significant.

RESULTS: Ten men (37.3±6.0 yrs) were included in this study. All underwent ESA in multiple ICSI dishes searched by several andrologists for about 90 minutes; no spermatozoa was found. After a NOA diagnosis following urological evaluation, the 10 men underwent micro-TESE: spermatozoa was retrieved from 5 (+sTESE). The paternal ages between +sTESE and –sTESE were comparable.

Quantitative analysis of RNA extracted from ejaculated samples averaged a concentration of 2.3±1 ng/ul and RNA integrity of 7.0±1. Compared to the donor, we found 45 significantly imbalanced genes common among all 10 patients. Most were underexpressed (95%) and associated with spermatogenesis (PRM2, SPATA42, CABS1) and spermatid development (KLHL10, H1FNT).

The +sTESE group had 87 significantly imbalanced genes, of which 62% were underexpressed. These included genes related to spermatogenesis (PRM1, ODF1) and spermatid development (CAPZA3). The –sTESE group had 37 imbalanced genes that were mostly underexpressed (89%) and associated with apoptosis (SEPT7P2, MKNK2), DNA repair (RNF138), cell cycle arrest (MLF1, NUPR2), and spermatid development (ADAD1, RBMXL2).

Gene expression analysis was also done between all men in the study and OA controls. There were no common significantly imbalanced genes among all 10 men. Among the +sTESE group, there were 8 underexpressed genes, of which half were non-protein coding. Interestingly, only one common gene (MSMB) was underexpressed in all –sTESE men. MSMB has inhibin-like activity and is secreted into the seminal plasma.

CONCLUSIONS: Gene expression profiling by RNA-seq on the ejaculates of NOA men may help to predict whether spermatozoa will be surgically retrieved. Most interestingly, all men who failed TESE had an underexpression of genes related to apoptosis, DNA repair, and cell cycle arrest compared to fertile donors, and the MSMB gene compared to OA controls.

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A NOVEL ONLINE SYSTEM LINKING AT-HOME SMARTPHONE SEMEN TESTS WITH EMBRYOLOGISTS. Yoshitomo Kobori, MD, PhD, Akiyoshi Osaka, MD, Toshiyuki Iwahata, MD, PhD, Kei-ichiro Uemura, MD, PhD, Hiroshi Okada, MD, PhD. Dokkyo Medical University Saitama Medical Center, Koshigaya, Japan.

OBJECTIVE: Infertility is a serious disease requiring timely treatment. If treatment is delayed, the condition of patients may deteriorate over time. The coronavirus (COVID-19) pandemic has seriously affected couples in need of immediate infertility treatment. Because of stay-at-home guidance, fewer people are visiting medical facilities, and thus it may become necessary to provide online medical services, including infertility treatment. Male-factor infertility contributes to about 50% of the incidence of infertility in couples. Semen analysis is key to diagnosing reproductive potential in men. In current practice, men must visit a clinic or other medical facility for semen analysis. However, there are cases in which visiting a medical facility is problematic, as in the current pandemic. To address this issue, many devices for at-home testing of semen samples have been developed and commercialized. We have developed a service enabling infertility patients to receive medical advice by allowing them to easily share at-home smartphone semen test data with embryologists. To verify the effectiveness of this system, we evaluated the correlation between at-home smartphone semen test data analyzed by embryologists and semen test results measured by computer assisted semen analysis (CASA).

DESIGN: Laboratory investigation.

MATERIALS AND METHODS: We developed an online system that allows sperm videos captured using a smartphone microscope to be uploaded and shared with embryologists. After receiving training on the online system, the embryologists viewed the videos on a large computer screen and recorded motile and static sperm counts. Because the appearance of sperm captured in videos can differ depending on the type of smartphone, the embryologists measured sperm concentration and motility by estimating the size of the sperm head and tail. A total of 45 human semen samples were analyzed using both the developed system and CASA software. Each test was evaluated for compliance with World Health Organization semen testing criteria.

RESULTS: Sperm concentration measured using the online system showed a very strong correlation with CASA results ($P < 0.01$, $r = 0.89$). Sperm motility analyzed by embryologists using the online system were significantly correlated with CASA results ($P < 0.01$, $r = 0.74$).

CONCLUSIONS: Online medical care will likely become increasingly important during the COVID-19 pandemic. The system we developed is a useful service allowing infertility patients to share at-home semen test data with embryologists. Analysis of the test data by embryologists resulted in few mistakes compared with automatic machine analysis. The system enables patients to connect with doctors and receive medical treatment online. Services like this one could be become more common in the future.

SUPPORT: none.

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EPIGENETIC EFFECT OF ABSTINENCE TIME ON THE REPRODUCTIVE POTENTIAL OF INFERTILE MEN. Brianne Barker, B.S., Alessandra Parrella, M.Sc., Sherina Lawrence, B.S., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To perform transcriptomic analysis of spermatozoa from infertile men to determine whether different abstinence times affect embryo development and implantation.

DESIGN: Over the past 2 years, we assessed the semen profiles, sperm chromatin fragmentation (SCF), and transcriptomic profiles of 23 men whose specimens were used for ICSI. Samples were collected from 2 consecutive ART cycles: the first ICSI cycle utilized specimens with an abstinence range of 2-14 days (LongA), and the second used specimens with an abstinence range of 30-120 minutes (ShortA). Semen parameters, SCF, and transcriptomic and clinical outcomes were assessed and compared in relation to the abstinence time.

MATERIALS AND METHODS: Ejaculated spermatozoa from consenting men were analyzed per WHO 2010. TUNEL was used to assess SCF on at least 500 sperm, using a threshold of $\leq$15%. ICSI was done in the standard fashion. Total RNA was isolated from the specimens of consenting men using a commercial spin column kit. Pilot paired-end 76bp RNA-Seq using Illumina platform (NextSeq 500) was performed to 60M reads. Comparisons were made to a fertile donor and between the two specimens from the same individual according to abstinence time.

RESULTS: Twenty-three couples (paternal age, 36.7±6 years; maternal age, 35.8±5 years) underwent 2 ICSI cycles. The initial ICSI cycles (LongA) had an abstinence of 10.9±3 days, a concentration of 66.8±73 10^6/ml, 27.0±15% motility, and an SCF of 23.2±17%. Fertilization and implantation rates were 71% (152/214) and 6.7% (4/60), respectively, and the clinical pregnancy rate was 17.39%. Epigenetic analysis of this group showed a total imbalance of 71 genes, with most underexpressed (74.6%). These included genes associated with fertilization (SMCP, ADAM21), calcium ion concentration (PLCZ1, TRPC1), motility (PGK2), and fetal organ development (ZNHIT2, CA2).

The subsequent cycles (ShortA) had an abstinence period of 51.9±19 minutes. These specimens had a comparable concentration and motility (55.2±64 10^6/ml, 31.2±15%), and a lower SCF (10.2±0.6%; $P<0.05$). There was improved fertilization (162/203; 79.8%; $P<0.03$), implantation (13/53; 24.5%; $P<0.01$), and clinical pregnancy rates (51.7%; $P<0.05$). There were 67 imbalanced genes for this group, with only 26% underexpressed; none of these are associated with fertilization, implantation, or embryo development.

When comparing the LongA and ShortA specimens for each individual, 16-68 genes were imbalanced. For the couples with successful clinical pregnancies, the ShortA had a higher expression of genes associated with DNA repair (CHEK1), fertilization (SPINK2, SERPINA5), and embryo development (ENDOG) compared to couples in the LongA group.

CONCLUSIONS: This analysis shows that specimens with shorter abstinence times yield spermatozoa with higher genomic integrity, leading to enhanced fertilization, implantation, and clinical pregnancy rates. Transcriptomic analysis confirms this finding and indicates that a specific gene imbalance is associated with a better ICSI outcome in couples where the semen sample used has a shorter abstinence time.

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MALE INFERTILITY DIAGNOSES AMONG PATIENTS WHO USED ASSISTED REPRODUCTIVE TECHNOLOGY IN THE UNITED STATES, 2016-2018. Amy Jewett, MPH,[1] Lee Warner, PhD,[2] James M. Dupree, M.D., M.P.H.,[3] Stan Honig, MD,[4] A. J. Nangia, MBBS,[5] Michael L. Eisenberg, M.D.,[6] Jennifer F. Kawwass, MD,[7] James Hotaling, MD,[8] Akanksha Mehta, M.D., M.S.,[9] Dmitry M. Kissin, MD, MPH[1] [1]Centers for Disease Control and Prevention, Chamblee, GA; [2]Centers for Disease Control and Prevention, Atlanta, GA; [3]University of Michigan, Ann Arbor, MI; [4]Yale University, New Haven, CT; [5]University of Kansas Medical Center, Kansas City, NY; [6]Stanford University, Stanford, CA; [7]Emory University (Emory GYN / OB, Emory Reproductive Center), Atlanta, GA; [8]University of Utah School of Medicine Andrology and IVF Laboratories, Salt Lake City, UT; [9]1365 Clifton Road NE, Building B, Atlanta, GA.

OBJECTIVE: To describe patient and treatment characteristics among assisted reproductive technology (ART) cycles with a male infertility diagnosis in the United States (US).

DESIGN: Cross-sectional analysis of the US National ART Surveillance System (NASS).

MATERIALS AND METHODS: We used data from NASS for reporting years 2016-2018 to describe patient and treatment characteristics of ART cycles among patients with diagnosed male factor infertility. Subgroups of male infertility include medical condition, genetic or chromosomal abnormality, abnormal sperm parameters (azoospermia, oligospermia, low motility or low morphology, other abnormal sperm parameters), other male factor (less common diagnoses), and more than one male factor.

RESULTS: Among 596,044 cycles started with the intent to transfer an embryo between 2016 and 2018, 30.9% (n=184,060) reported a diagnosis of male factor infertility as a reason for using ART. Abnormal sperm parameters were the most commonly reported diagnoses for male infertility (58.7%), including low motility or low morphology (34.9%), oligospermia (11.5%), other abnormal sperm parameter (6.3%), and azoospermia (5.9%). Other reasons for male factor infertility included other male factor (35.2%), medical condition (2.9%), genetic or chromosomal abnormality (0.5%), and more than one male factor (2.7%). In nearly 45% of the cycles with male factor infertility, male age was not reported. When reported, the age distribution for males among cycles

with male factor infertility was less than 35 years (18.3%), 35-40 years (20.1%), 41-50 years (14.1%), over 50 years (3.1%). Among cycles with a male genetic or chromosomal abnormality, 67.7% reported male age of 40 or less years. For cycles with reported male factor infertility, 33.0% had a concurrent female factor infertility diagnosis. Sperm donors were used in less than 1% of all cycles reporting male factor infertility, but in 10.0% of cycles with abnormal sperm parameters. Intracytoplasmic sperm injection was the primary method of fertilization in all male factor infertility (80.7%) cycles and for subgroups: abnormal sperm parameters (84.4%), medical condition (77.0%), genetic or chromosomal abnormality (76.7%), and other male factor (75.1%). Preimplantation genetic testing was used in 24.4% of male infertility cycles and varied by infertility diagnosis: genetic or chromosomal abnormality (37.0%), medical condition (28.4%), abnormal sperm parameters (25.0%), and other male factor (22.5%). Single embryo transfer, used in 62.3% in all male infertility cycles, varied by male infertility subgroup: genetic or chromosomal abnormality (74.3%), medical condition (68.8%), abnormal sperm parameters (63.7%), and other male factor (58.9%).

CONCLUSIONS: Male infertility is a substantial contributor to infertility treatments, accounting for nearly one-third of ART cycles. Continued assessment of prevalence and characteristics of ART cycles with male infertility may inform treatment options and improve ART outcomes.

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UTILIZATION OF PREIMPLANTATION GENETIC DIAGNOSIS IN MEN WITH Y-CHROMOSOME MICRODELETION. Danielle Velez, MD, William T. Berg, MD, Rachel Morgan Greenberg, MD, Tsikata Yaovi Apenyo, BS, Mark Sigman, MD, Gabriella Avellino, MD Brown University, Providence, RI.

OBJECTIVE: Y-chromosome microdeletion (YCMD), a genetic cause of male infertility, should prompt genetic counseling and possible pre-implantation genetic testing in those pursuing assistive reproductive technologies (ART). It is unknown whether patients utilize these resources. We sought to characterize how a YCMD diagnosis influences a couple's reproductive decisions.

DESIGN: This was a retrospective cohort study of severe oligo- or azoospermic men for whom a YCMD assay was ordered. Men with a positive YCMD were then prospectively surveyed on their reproductive decision making following their diagnosis.

MATERIALS AND METHODS: All men who presented for fertility evaluation from 2010 to 2020 and were found to have <5 M/mL sperm were included. After excluding men with obstructive azoospermia, 284 male patients were identified that met inclusion and exclusion criteria. Data was collected on ethnicity, semen analysis, karyotype, serum FSH, testosterone, and female partner's age and factor. Patients with a positive YCMD were then contacted and queried on their specific reproductive decisions following their diagnosis. Patients were surveyed on whether they pursued IVF, with or without ICSI, and with or without PGD, or whether they elected for donor sperm insemination, adoption, or nothing. Patients were also queried on what factors influenced these decisions.

RESULTS: Twenty-nine patients (10.21%) were diagnosed with a YCMD, of which 19 (65.5%) were AZFc, two were AZFb, one was AZFa, and the remainder were "other." Sixteen of the YCMD patients identified as Caucasian (55.2%), four African-American, one Hispanic/Latino, and 8 "other" or not available. All patients with YCMD were contacted by our researchers, with a 58.6% response rate. Seven patients (5 AZFc, 1 SRY deletion, 1 p6 single deletion) underwent sperm retrieval. The average number of ART cycles was 1.7, with only one patient pursuing IVF with ICSI and PGD. Commonly cited reasons for not pursuing further fertility treatments were "couple broke up or got divorced, due to the stress of the diagnosis," and "concern about success of microTESE." Of the four patients who used donor sperm, commonly cited reasons were "no other option available" or "failed microTESE." AZFa and b deletion patients were unlikely to be offered genetic counseling. Sixteen patients recalled being referred to genetic counseling, of whom only eight actually saw a counselor.

CONCLUSIONS: In our cohort of YCMD patients, only one patient chose to utilize IVF with ICSI and PGD. Additionally, for this patient population genetic counseling appears to be severely underutilized. Given the high number of relationships that ended after receiving the YCMD diagnosis, providers must be sensitive to the stress this diagnosis can impart on patients and their partners.

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PREDICTORS OF CHANGES IN SEMEN PARAMETERS IN MEN WHO RECEIVED NATESTO IN AN OPEN-LABEL SINGLE CENTER CLINICAL TRIAL. Ruben Blachman-Braun, M.D., M.Sc.,[1] Thomas A. Masterson, III, MD,[1] Ranjith Ramasamy, MD[2] [1]University of Miami Miller School of Medicine, Miami, FL; [2]University of Miami, Miami, FL.

OBJECTIVE: To determine if there are clinical, hormonal characteristics that might predict which men are more likely to have change in sperm concentration after 3 months of treatment with 4.5% nasal testosterone gel (Natesto), a short-acting testosterone replacement therapy.

DESIGN: Post-hoc analysis of a single institution, prospective, single-arm clinical trial conducted between November 2017 and September 2019 at the University of Miami.

MATERIALS AND METHODS: Men aged 18-55 diagnosed with symptomatic hypogonadism (total testosterone < 300ng/dL) and total motile sperm count >5million were enrolled, the participants applied Natesto 3 times a day. We evaluated concentration change between baseline and 3 months follow-up and compared those that had an increase or decrease of more than 20% in sperm concentration. Using the statistical program SPSS 24, we also performed a univariable logistical regression analysis to determinate the association between 20% increase or decrees in sperm concentration and the clinical, demographic, hormonal and semen analysis variables.

RESULTS: A total of 49 men received Natesto three times a day as part of the clinical trial. The median concentration at baseline was 26 million [17.5 –

Table. Variables representation. In addition, to a univariable analysis between the independent variables and increase or decrees in sperm concentration at 3 months follow-up.

	Overall n = 49 (100%)	Concentration decrees by 20% n = 21 (42.8%)			Concentration increase by 20% n = 15 (30.6%)		
		OR	CI 95%	p-value	OR	CI 95%	p-value
Age in years	36.5 ± 7.4	0.97	0.90 - 1.05	0.513	0.99	0.91 - 1.08	0.812
BMI (kg/m^2)	30.2 ± 5.6	0.99	0.89 - 1.09	0.772	1.01	0.91 - 1.13	0.844
Baseline							
Testosterone (ng/dl)	237.5 [199 – 280]	1.00	0.99 - 1.01	0.323	1.01	0.99 - 1.02	0.239
FSH (mIU/mL)	3.2 [2.2 - 4.8]	0.96	0.78 - 1.18	0.709	1.15	0.93 - 1.43	0.204
LH (mIU/mL)	3.2 [2.2 - 4.9]	1.00	0.84 - 1.17	0.975	1.10	0.91 - 1.34	0.310
Concentration	26 [17.5 – 36]	1.06	1.01 - 1.10	**0.014**	0.95	0.90 - 1.00	0.063
Motility	55 [46.8 - 60.3]	1.04	0.98 - 1.10	0.234	0.98	0.93 - 1.04	0.500
TMSC	32.5 [16 - 56.7]	1.02	0.99 - 1.04	0.056	0.99	0.96 - 1.01	0.202

36] and was similar (22 million [13.8 -35]) at 3 months follow up. Overall, after 3 months of treatment 30.6% of the men had a concentration increase by >20%, and 42.8% had decrease by >20%. Higher sperm concentration at baseline predicted a >20% decrease in sperm concentration. No other clinical, demographic, endocrinological, and semen analysis characteristics were associated with change in sperm concentration ($p > 0.05$) (Table).

CONCLUSIONS: Although 43% of men who received Natesto had a decline in sperm concentration, only 5% of them became azoospermic. There does not appear to be any baseline characteristics that can predict who adversely reacts to Natesto.

SUPPORT: This was an investigator-initiated trial sponsored in part by Aytu BioSciences

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SPERM DNA FRAGMENTATION INDEX AND HIGH DNA STAINABILITY DO NOT INFLUENCE PREGNANCY ACHIEVEMENT FOLLOWING ICSI.

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OBJECTIVE: To evaluate the ability of sperm DNA fragmentation index (DFI) and high DNA stainability (HDS) to influence the chance of achieving pregnancy in couples undergoing intracytoplasmic sperm injection (ICSI) cycles.

DESIGN: A retrospective study evaluating couples that underwent an ICSI cycle between 2009 - 2018 at a reproductive center.

MATERIALS AND METHODS: We included all couples who underwent an ICSI cycle and had a semen analysis with subsequent DFI and HDS testing. Clinical and demographic characteristics of the couples were recorded; couples with missing data, those who previously underwent ICSI and those that used donor eggs or sperm. In couples that achieved pregnancy, the number of ICSI cycles were considered until the first clinical intrauterine pregnancy, subsequent pregnancies were not considered in this analysis. Using the statistical software SPSS 24, means or medians were analyzed with U Mann-Whitney or Student T-test as required. We then performed a multivariable-adjusted logistical regression analysis to determine the association between pregnancy and couples independent variables.

Table. Multivariable analysis showing the association between pregnancy and independent variables in the 550 studied couples.

	Multivariable		
	OR	95% CI	p-value
Male age at first cycle (per year)	1.01	0.98 - 1.04	0.514
Male prior fertility			
No (%)	1		
Yes (%)	1.17	0.79 - 1.72	0.436
Male smoking history			
No (%)	1		
Yes (%)	0.98	0.59 - 1.63	0.939
Varicocele history			
No (%)	1		
Yes (%)	2.06	0.81 - 5.23	0.127
TMSC (10^6 motile sperm)	1.00	0.99 - 1.01	0.128
Female age at first cycle (per year)	0.83	0.79 - 0.89	**< 0.001**
Female BMI at first cycle (per kg/m^2)	1.01	0.97 - 1.05	0.727
DFI (%)	1.00	0.98 - 1.01	0.716
HDS (%)	1.01	0.98 - 1.04	0.551
ICSI attempts (per attempt)	0.60	0.49 - 0.72	**< 0.001**

RESULTS: A total of 550 couples who underwent 1050 ICSI cycles were analyzed, 220 couples achieved pregnancy. In couples that achieved pregnancy, females were younger (35.3 ± 3.4 vs. 33.7 ± 3.6 years; $p < 0.001$) and underwent fewer cycles (2 [1 – 3] vs. 2 [1 – 2]; $p = 0.001$). Importantly, the DFI% (no pregnancy: 12.2 [7.1 – 20.2] vs. pregnancy: 12.9 [8 – 20]; $p = 0.735$) and HDS% (no pregnancy: 9.1 [6.7 – 14] vs. pregnancy: 9.3 [6.1 - 14.6]; $p = 0.914$) were similar. A multivariable analysis showed that an increased female age and couples that underwent a greater number of ICSI attempts had a lower probability of getting pregnant. Furthermore, neither the DFI% nor HDS% were associated with an increase chance of achieving pregnancy (Table).

CONCLUSIONS: Neither DFI nor HDS at baseline influence the chances of a couple to achieve pregnancy after ICSI. Increased female age and couples who underwent more ICSI cycles were associated with lower chances of achieving pregnancy.

SUPPORT: No

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CAN REACTIVE OXYGEN SPECIES (ROS) ESTIMATION PREDICT FERTILISATION RATES AND LIVE BIRTH RATES IN OBSTRUCTIVE AZOOSPERMIC MEN WITH SPERMATOCELE?

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OBJECTIVE: To determine whether altered Reactive Oxygen species(-ROS) levels in men with obstructive azoospermia(OA) due to Spermatocele impairs sperm quality leading to poor In-Vitro Fertilisation (IVF) outcome.

DESIGN: Prospective study; sperm isolated from spermatocele of 19 men with OA and Testicular sperm extraction (TESE) sperm from testis of 22 men with other causes of OA served as study cohort and control respectively. 155 oocytes and 140 oocytes were retrieved from women(age<30) with normal hormonal profile in the study group and the control group respectively. Intra-cytoplasmic sperm injection(ICSI) was done in both the groups. The study was conducted from October 2002 to September 2019 at the Institute of Reproductive Medicine, Kolkata, India.

MATERIALS AND METHODS: 19 couples with OA due to spermatocele and 22 couples with OA for other reasons underwent IVF with antagonist protocol using recombinant FSH. Surgical sperm retrieval and ICSI was done . Fertilisation check was done after 17 hours and 2-3 Grade I embryos were transferred in the female partner on Day3. ROS levels were evaluated in the spermatocele fluid and the testicular fluid by chemiluminescence assay using luminol (5-amino-2,3-dihydro-1,4-phthalazinedione; Sigma Chemical Co., St. Louis, MO, USA) as a probe. β-hCG (β-Human chorionic gonadotrophin) was done 2 weeks after embryo transfer. Clinical pregnancy was confirmed using Transvaginal ultrasound. The primary outcome measures are fertilization rate, number of Grade I/II embryos and clinical pregnancy rate. Miscarriage rate and live birth rates are the secondary outcome measures. Statistical significance was set at $p<0.05$ with Pearson's correlation test and student's T-test.

RESULTS: The study group and control group were comparable regarding demographic and cycle characteristics. The fertilisation rate (61.4% vs 79.4%) and number of Grade I/II embryos (53.4% vs 70.9%) was significantly lower in the study group than the control group ($p<0.05$). The pregnancy rate in the two groups (39.1% vs 34.1%) were comparable ($p>0.05$). However the miscarriage rate was higher in the study group than control group(38.8% vs 13.3%)($p<0.05$), hence the live birth rates in the study group were lower than the control group (23.9% vs 29.5%)($p>0.05$), though it did not reach statistically significance. The ROS levels in the spermatocele fluid was also found to be significantly higher in the study group than the control group (92.15 ± 68.73 cps vs 61.39 ± 12.82 cps)($p<0.05$).

CONCLUSIONS: High ROS levels in spermatocele fluid can be the reason behind poor quality sperms in these patients than the sperms retrieved from the testis in the control group. Hence patients with spermatocele and OA show lower fertilization rates, lower number of good quality embryos and lower live birth rates than their counterparts with OA due to other causes.

Thus for patients with spermatocele, it is important to seek reproductive medical help as soon as the fatherhood desire is felt. As sperms collected from spermatocele confers a proinflammatory milieu, sperm collected by TESE from the testicular compartment of OA male is a better option.

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RAISED SPERM DNA FRAGMENTATION –RANDOMISED CONTROLLED TRIAL OF MACS VS TESA TO OPTIMISE REPRODUCTIVE OUTCOMES.

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OBJECTIVE: In Individuals with raised Sperm DNA Fragmentation (SDF), randomization with magnetic activated cell sorting (MACS) or surgical retrieval of testicular sperms (TESA) will it reduce SDF and optimize the reproductive outcomes?

DESIGN: This is an ongoing Randomized Control Trial (RCT) with prior approval from institutional Ethical Committee (IEC) conducted at a Private Teaching ART Clinic. This is preliminary data of the pilot study. Study duration 7months (January – July 2019). Couples undergoing IVF stimulation with raised SDF were randomized into MACS group (n=30) and TESA group (n=30) for sperm selection.

MATERIALS AND METHODS: Couples with history of one failed IVF cycle were offered testing for SDF. Individuals with SDF > 30% were included in the study. SDF testing was done with SCSA method and couples randomized using software into respective intervention groups. TESA was done as per our clinic's Standard Operating Protocol (SOP) and MACS was done as per the instruction from the manufacturer. Intra Cytoplasmic Sperm Injection (ICSI) was the method of insemination in all cases. Extended embryo culture till blastocyst stage was done and a freeze all policy was opted. Two Blastocysts that showed 100% survival were transferred in a Frozen Embryo transfer (FET) cycle. Mean of Implantation Rates (IR) and Clinical Pregnancy Rates (CPR), Miscarriage Rates (MR) & Live Birth Rates (LBR) were compared between both groups.

RESULTS: Mean Reproductive Outcomes for MACS & TESA groups were as follows:

Blastocyst formation rates – 38% Vs 31% (P=0.5717)
CPR – 50% Vs 83% (P= 0.0072)
IR – 43% Vs 72% (P= 0.0243)
MR- 33% Vs 16% (P= 0.1290)
LBR – 17% Vs 67% (P= 0.0001)

Blastocyst formation was comparable between the groups; However, TESA group had significantly higher CPR, IR, LBR and lesser MR.

Testicular sperm seem to have better DNA quality than ejaculated sperm. In couples with failed IVF attempts and raised SDF, we can offer TESA as an active intervention to optimize reproductive outcomes. Poor outcomes in MACS group needs further research.

LIMITATIONS, REASONS FOR CAUTION:

Small sample size. TESA is a surgical intervention.

CONCLUSIONS: TESA seems like a beneficial intervention to optimize sperm selection and reproductive outcomes for Individuals with raised sperm DFI.

SUPPORT: N/A

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SPERM RETRIEVAL RATES AND PREGNANCY OUTCOMES IN MEN WITH KLINEFELTER SYNDROME.

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OBJECTIVE: To report sperm retrieval rates and outcomes from men with Klinefelter Syndrome (KS) undergoing microsurgical testicular sperm extraction (mTESE), and to explore predictive factors of sperm retrieval and pregnancy.

DESIGN: Retrospective study of prospectively collected data.

MATERIALS AND METHODS: KS patients undergoing mTESE by a high-volume surgeon at Weill Cornell between 1995 and 2019 were reviewed. Men were included if sperm retrieval data was available. Demographic data included male and partner age. Testicular size was documented. History of previous mTESE was recorded. Sperm retrieval and pregnancy were captured dichotomously (yes/no) and fertilization rate per injected oocyte was quantified. Adjusted logistic regression modelling was used to examine predictors of sperm retrieval and pregnancy.

RESULTS: A total of 287 men with KS were included. Median age was 32 (IQR 28-36). Median partner age was 29 (IQR 26-33). Mean FSH values were 34.6 ± 16.0 IU/mL. Mean testis size on the left was 2.8 ± 2.5 cc, and right 2.9 ± 2.6 cc. A total of 15 (5.22%) of men had prior failed sperm retrieval procedure. Sperm was retrieved in 175 men (61.0%). Fertilization rate per injected oocyte was 3.7 ± 4.6. A total of 120 (41.8%) were able to achieve a pregnancy. Of those with prior mTESE, 6 of 15 (40.0%) had sperm retrieved and 2 of 15 (13.3%) were able to achieve a pregnancy. Adjusted logistic regression models (Table 1) indicate that testis size was associated with sperm retrieval (OR 1.52, 95% 1.18-1.98) and pregnancy (OR 1.24, 95%CI 1.08-1.42). Although no age cut-off precluded retrieval, increasing male age was marginally associated with a decreased likelihood of sperm retrieval when examined continuously (OR 0.89, 95%CI 0.85-0.94) and when examined in categories (Table 1). A similar trend was seen for pregnancy (continuous age: OR 0.87, 95% CI 0.79-0.95).

CONCLUSIONS: The sperm retrieval rates in KS patients was 61.0% in our series, with a total of 41.8% able to achieve a clinical pregnancy. Only testis size was associated with both sperm retrieval and pregnancy in our series, and increasing age only portends a slight decreased association with success.

Table 1 – Adjusted models of clinical outcomes

	Sperm Retrieval (OR, 95%CI)	Pregnancy (OR, 95%CI)
Continuous Age		
Male Age (continuous)	**0.89 (0.85-0.94)**	0.87 (0.79-0.95)
Female Age	-	1.09 (0.98-1.21)
Male FSH	1.02 (0.99-1.03)	1.02 (0.99-1.03)
Testis Size	**1.53 (1.18-1.98)**	1.24 (1.08-1.42)
Categorical Age		
Age		
<25.0	*Ref*	*ref*
25.0-29.9	0.72 (0.23-2.19)	0.89 (0.33-2.37)
30.0-34.9	0.55 (0.19-1.54)	0.75 (0.24-2.40)
35.0-39.9	0.15 (0.05-0.43)	0.25 (0.06-1.05)
>40.0	0.17 (0.05-0.59	0.17 (0.03-1.00)
Female Age	-	1.04 (0.95-1.14)
Male FSH	1.01 (0.99-1.03)	1.02 (0.99-1.03)
Testis Size	1.57 (1.19-2.05)	1.23 (1.07-1.42)

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UNDERSTANDING MOLECULAR MECHANISMS ASSOCIATED WITH INFERTILITY IN MEN WITH LOW LEVELS OF SEMINAL REACTIVE OXYGEN SPECIES THROUGH COMPARATIVE PROTEOMICS.

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OBJECTIVE: Approximately 30% to 80% of idiopathic infertile men having increased seminal reactive oxygen species (ROS) levels suffer from a condition known as male oxidative stress infertility (MOSI), which affects about 37 million men with idiopathic infertility around the world. Although low concentrations of ROS are critical for spermatozoa physiological functions and fertilization, increased ROS are harmful to the spermatozoa. Hence, it is important to understand why patients with low ROS levels are still infertile despite the fact that low ROS are involved in physiological function. The current study was planned to identify molecular pathways defective in infertile men with low ROS levels using a comparative proteomic approach.

DESIGN: Semen samples with low ROS levels from fertile (n=5) and infertile men (n=5) were subjected to sperm global proteomic analysis. *In silico* analysis was carried out on differentially expressed proteins (DEPs) detected in spermatozoa of infertile patients with low seminal ROS levels in comparison to fertile men with low ROS levels. Based on the *in silico* analysis, key proteins associated with sperm function and oxidative stress mechanisms were validated using western blot.

MATERIALS AND METHODS: Proteomic profiling of sperm from low-level ROS fertile and infertile men was performed using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Proteins and peptides were identified using search programs MASCOT and SEQUEST. Spermatozoal proteins in fertile men were compared with those in infertile men. DEPs were subjected to bioinformatics analysis using ingenuity pathway analysis (IPA) software.

RESULTS: A total of 132 DEPs were found in sperm of infertile men compared to fertile men with low ROS levels. Among these, 84 proteins were under-expressed and 37 over-expressed in infertile men with low ROS levels. Further, 7 proteins and 4 proteins were unique to fertile men and infertile men, respectively. Bioinformatic analysis revealed that proteins involved in production of nitric oxide and ROS were dysregulated in the infertile group suggesting physiological ROS-mediated signaling is impaired in infertile men. Validation of key proteins by western blot revealed that APOA1, HSP90β, PRKAR1A, SERPINA5 were under-expressed and FASN was over-expressed in infertile men with low ROS levels.

CONCLUSIONS: The current study provides an in-depth understanding about proteins involved in the carbohydrate and lipid metabolism, small molecule biochemistry, cellular compromise and inflammatory response in infertile men with low levels of ROS. Furthermore, it is evident that redox signaling pathways are dysfunctional in sperm of infertile men, which in turn may affect its physiological functions.

REFERENCES: None

SUPPORT: None

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WITHDRAWN

P-651

WITHDRAWN

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OOCYTE ABILITY TO REPAIR SPERM DNA FRAGMENTATION: THE EFFECT OF MATERNAL AGE ON ICSI OUTCOMES. Assumpto Iaconelli, Jr., MD,[1] Daniela Paes de Almeida Ferreira Braga, PhD,[1] Amanda Souza Setti, MSc,[1] Rodrigo Rosa Provenza, Sr., BSc,[2] Joana Noguères Simas, MSc,[3] Edson Borges, Jr., PhD[1] [1]Fertility Medical Group / Sapientiae Institute, Sao Paulo, Brazil; [2]Fertility Medical Group, São Paulo, Brazil; [3]Sapientiae Institute, São Paulo, Brazil.

OBJECTIVE: Sperm DNA integrity is crucial for the adequate transmission of paternal genetic information and has been recognized as a biomarker of male infertility. Previous studies have suggested a negative correlation between sperm DNA fragmentation (SDF) index and pregnancy after ICSI, while others have found no association between SDF and pregnancy, but have suggested an association with pregnancy loss. Spermatozoa have no mechanism to repair SDF, DNA-repairing activity depends on the oocyte machinery once fertilization takes place. The ability of the oocyte to repair SDF depends not only on the level SDF, but also on the quality of the oocyte. Increasing maternal age has a well-established negative effect on fertility and reproductive success. Therefore, the goal for the present study was to evaluate the effect of SDF on clinical outcomes of assisted reproductive technology in women in different age groups.

DESIGN: Retrospective clinical study.

MATERIALS AND METHODS: This study included data from 540 ICSI cycles, performed from June/2017 to December/2019, in a private university-affiliated IVF center. Cycles were split into three groups according to the maternal age: ≤36 years old (n=285), 37-40 years old (n=147), and >40 years old (n=108). Semen samples were evaluated for SDF using the Sperm Chromatin Dispersion method and for each age group, the cycles were divided again according to SDF index: low fragmentation index (≤30% SDF) and high fragmentation index (>30% SDF). Clinical outcomes were compared between groups using generalized linear models with linear distribution followed by Bonferroni post hoc test, with adjustment for potential confounders or Chi-square test.

RESULTS: For younger patients (≤36 years old) and those between 37 and 40 years old, no significant differences were noted in pregnancy (≤36 years old: 40.0% vs. 39.1%, p=0.840 and 37-40 years old: 27.7% vs. 28.6%, p=0.781), implantation (≤36 years old: 42.3% vs. 41.5%, p=0.880 and 37-40 years old: 28.9% vs. 30.6%, p=0.757), or miscarriage rates (≤36 years old: 9.3% vs. 11.1%, p=0.665 and 37-40 years old: 31.2% vs. 22.2%, p=0.875), for cycles with ≤30% SDF or >30% SDF respectively. However, when maternal age was >40 years old, a significant lower pregnancy (20.0% vs. 7.7%, p=0.040), implantation (19.7% vs. 11.9%, p=0.040), and increased miscarriage rate (12.5% vs. 100.0%, p<0.001) was observed for cycles with ≤30% SDF or >30% SDF respectively.

CONCLUSIONS: High SDF index leads to worse clinical outcomes such as lower implantation rates, pregnancy rates and higher miscarriage rates, in cycles with increased maternal age. The same is not observed when maternal age is < 40 years old. This evidence indicates that the age may affect the oocyte DNA-repairing ability, leading to a poor embryo development, when the oocyte is injected with a DNA-damaged spermatozoon.

SUPPORT: None.

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VALIDATION OF LENSHOOKE™ X1 PRO AND COMPUTER-ASSISTED SEMEN ANALYZER COMPARED WITH LABORATORY-BASED MANUAL SEMEN ANALYSIS. Ashok Agarwal, PhD,[1] Manesh Kumar Panner Selvam, PhD,[1] Li-Sheng Chang, PhD,[2] Fang-Zong Wang, MSc,[2] Cheng-Teng Hsu, PhD[2] [1]American Center for Reproductive Medicine, Cleveland Clinic, Cleveland, OH; [2]Bonraybio Co., Ltd, Taichung City, Taiwan.

OBJECTIVE: To compare two automated semen quality analysis systems [LensHooke™ X1 PRO (X1 PRO) and IVOS CASA] for accuracy, precision and agreement with laboratory-based manual semen analysis (MSA).

DESIGN: Semen analysis was conducted using X1 PRO (Bonraybio®), IVOS CASA (Hamilton Throne) and MSA according to WHO 5th Edition (2010) guidelines in andrology laboratory.

MATERIALS AND METHODS: Semen samples (n=31) were obtained from healthy male volunteers with normal semen parameters and infertile men with a minimum abstinence period of 2 to 3 days. After complete liquefaction, a total of 101 seminal aliquots were prepared and tested using X1 PRO, IVOS CASA and MSA. The test results obtained by X1 PRO and IVOS CASA were compared to MSA using Passing-Bablok regression analysis. Additionally, 10 samples were used to evaluate the intra- and inter-rater agreement for X1 PRO and MSA.

RESULTS: The semen analysis results (sperm concentration, total motility, progressive (PR) motility, motile sperm concentration, and progressively motile sperm concentration) showed strong correlation and agreement for both automated semen analyzers (X1 PRO and IVOS CASA) and MSA with Pearson correlation above 0.92 (P<0.0001). X1 PRO and IVOS CASA were able to differentiate oligozoospermic samples with an accuracy of 100% and 93%, respectively. Furthermore, the positive predictive value for X1 PRO (86.5%) was higher than IVOS CASA (71.7%) in differentiating asthenozoospermic samples. Semen parameter (sperm concentration, total motility and PR motility) showed a high degree of inter- and intra-rater agreement evaluated using X1 PRO and MSA (Table 1). X1 PRO showed an intra-rater precision of coefficient variation, CV <15% for sperm concentration, total motility and PR motility, and was comparable with MSA.

CONCLUSIONS: Both automated semen analyzers (X1 PRO and IVOS CASA) showed high level of accuracy and precision, and their performance was comparable with laboratory-based MSA. Furthermore, high-levels of inter-and intra-rater reliability for semen analysis indicates that new device, X1 PRO can be used in a clinical diagnostic laboratory to offer accurate test results.

Table 1. Inter- and intra-rater agreement for semen parameters measured using LensHooke™ X1 PRO and MSA

	Inter-rater agreement*		Intra-rater agreement**	
Semen parameters	MSA (N=10)	X1 PRO (N=10)	MSA (N=10)	X1 PRO (N=10)
Concentration (10^6/mL)	0.94	0.95	0.98	0.99
Total motility (%)	0.94	0.91	0.99	0.94
Progressive motility (%)	0.88	0.93	0.98	0.92

*Three operators were involved. **Three readings were taken.

REFERENCES: None

SUPPORT: None

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THE INFLUENCE OF VARICOCELE AND MICROSURGICAL VARICOCELECTOMY ON SEMEN QUALITY: A UHPLC-QE-MS UNTARGETED METABOLIC ANALYSIS. Xinzong Zhang, MD,[1] Cuncan Deng, MD,[1] Wujiang Liu, MD,[2] Xiaohua Liu, MD,[2] Huang Liu, MD,[3] Yu Zhou, MD,[2] Tao Pang, dr,[4] Qingguo Zhao, MD,[2] Yunge Tang, Master degree[3] [1]Family Planning Special Hospital of Guangdong Province, Guangzhou, China; [2]Family Planning Research Institute of Guangdong Province, Guangdong, China; [3]Family Planning Research Institute of Guangdong Province, Guangzhou, China; [4]Family Planning Research Institute of Guangdong Province, guangzhou, China.

OBJECTIVE: To study whether varicocele affects the metabolism of semen and whether microsurgical varicocelectomy can reverse the metabolism of semen.

DESIGN: A origina article.

MATERIALS AND METHODS: The semen samples from 30 varicocele patients, 30 patients after microsurgical varicocelectomy, and 30 healthy males were selected to conduct non-targeted metabolomics by liquid chromatography-mass spectrometry. Different metabolites between three groups were analyzed and the metabolic pathways were analyzed by KEGG database. Potential biomarkers were determined by t-test and receiver operating characteristic (ROC) curve analysis.

RESULTS: 275 different expressed metabolites involving in 39 pathways were found between varicocele group and normal group. A total of 8 metabolites were selected as varicocele potential biomarkers by HPLC-QE-MS high-throughput untargeted metabolomics analyses [Area under the curve

(AUC)>0.90]. Varicocele influence semen quality through amino acids metabolism, reactive oxygen species and anti-oxidation relative metabolism, phenylalanine, tyrosine and tryptophan biosynthesis pathway and phenylalanine metabolism pathway. Microsurgical varicocelectomy may improve semen quality by rebalancing dipeptide metabolism which has an antioxidant effect, and regulating ceramide and Sphingolipid metabolism, which is associated with ROS production, oxidative stress, mitochondrial respiratory chain, mitophagy and apoptosis.

CONCLUSIONS: These results suggested that varicocele could change the sperm metabolism, and microsurgical varicocelectomy could improve the sperm quality by changing the sperm metabolism. Further study is needed!

Key words: Varicocele, varicocelectomy, metabolomics, 5-L-Glutamyl-taurine, Amino acid metabolism.

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INFERTILITY INSURANCE: WHAT COVERAGE EXISTS FOR RESIDENTS AND FELLOWS?

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OBJECTIVE: We aimed to evaluate infertility insurance coverage provided to physician trainees at institutions that offer advanced infertility training.

DESIGN: A descriptive study examining health insurance documentation regarding coverage for infertility services.

MATERIALS AND METHODS: Health insurance summary plan documents from US institutions with post-graduate physician training in Andrology and/or Reproductive Endocrinology and Infertility (REI) fellowships were obtained either from fellows themselves, the GME office, or the program website. The summary of benefits documents were individually examined for their descriptions of coverage for infertility services by two authors (WM and EJ). Assessment of coverage for diagnosis, treatment and any discussion of shared costs or maximum lifetime coverage were included. We also assessed for descriptive text specifically indicating services for male infertility care as well as coverage for cryopreservation. Statistical analysis using a fisher exact test was used to evaluate whether having an Andrology program was predictive of an institution including male-specific language in its insurance policy.

RESULTS: We reviewed documents from 24 unique institutions, which included 14 out of the 18 US Andrology fellowships and 18 out of the 48 US REI fellowships. There were 15 of 24 (62.5%) institutions reporting coverage for the treatment of infertility, 6 (25%) institutions that covered diagnosis but not treatment, and 3 (12.5%) institutions that excluded diagnostic or treatment coverage completely. Among the 15 institutions that provided coverage for treatment, 13 reported the lifetime maximum amount, which averaged $14,885 (range of $2,500 - $25,000). In total, we identified only 7 out of 24 (29%) policies that included male-specific language. Only 4 out of 24 (16.7%) plans explicitly described a covered male-specific treatment. Having an Andrology program did not significantly increase the likelihood of including male-specific language in institutional insurance policies.

CONCLUSIONS: We found that for physician trainees, infertility insurance coverage is variable and treatment for male factor infertility is commonly omitted or minimally mentioned in insurance coverage documents. With high costs of infertility treatment, residents and fellows may represent a particularly vulnerable population when faced with fertility concerns.

SUPPORT: None

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SPERM RETRIEVAL RATES AND PREGNANCY OUTCOMES IN MEN WITH AZF DELETIONS.

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OBJECTIVE: To report outcomes in men with AZF deletions following microsurgical testicular sperm extraction (mTESE), as well as assess for predictive factors of sperm retrieval and pregnancy.

DESIGN: Retrospective study of prospectively collected data.

MATERIALS AND METHODS: Between 1995 and 2019, all patients undergoing mTESE by a high-volume surgeon at Weill Cornell in New York City were reviewed. Men with known AZF deletions were included if sperm retrieval data was available. All patients had a repeat extended sperm preparation on the morning of planned retrieval. Patient demographic data was recorded and included both male and female partner age. Testicular size was recorded. Sperm retrieval and pregnancy rates were captured as well as number of fertilized eggs. Multivariable regression models were utilized to assess for predictive factors of sperm retrieval and pregnancy including demographic data and testicular size.

RESULTS: A total of 72 men with AZF deletions were included. Of these, a total of 67 men (93.1%) had AZFc deletions. Of the remaining 5 men, 2 had an AZFb deletion (4.1%), 2 had AZFb+c deletion (2.7%) and 1 had a partial AZFb deletion (1.4%). Median male age was 34 (IQR 30-38), and median partner age was 32 (28-36). Mean FSH levels were 19.1 ± 10.5 IU/mL. Mean testicular size was 10.7 ± 4.7cc on the left side and 10.7 ± 4.9cc on the right. Sperm was retrieved in 0 of 5 men (0%) with non-AZFc deletions and was retrieved in 43 men (64.2%), with AZFc deletions. Fertilization rate per injected oocyte was 2.8 ± 4.1. A total of 31 of 73 men (42.5%) were able to achieve a clinical pregnancy. Using multivariable logistic regression (Table 1) FSH was associated with both sperm retrieval and pregnancy (OR 1.07, 95% CI 1.01-1.14).

CONCLUSIONS: Sperm retrieval rates in men with AZF deletions are approximately 60% in keeping with previously documented numbers in the literature. Higher levels of male FSH are slightly associated with increased successful sperm retrieval and pregnancy.

Table 1 – Adjusted Modelling of Clinical Outcomes

	Sperm Retrieval (OR, 95%CI)	Pregnancy (OR, 95%CI
Male Age	1.00 (0.91-1.09)	0.99 (0.84-1.16)
Female Age	-	0.95 (0.81-1.11)
Male FSH	**1.07 (1.01-1.14)**	**1.07 (1.01-1.14)**
Testis Size	1.07 (0.95-1.20)	1.04 (0.92-1.17)

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FRESH MICRODISSECTION TESTICULAR SPERM EXTRACTION RESULTS IN A HIGHER RETRIEVAL RATE OF SPERM ACCEPTABLE FOR ICSI COMPARED TO FROZEN-THAWED MICRODISSECTION TESTICULAR SPERM EXTRACTION.

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OBJECTIVE: Men who do not make it to intracytoplasmic sperm injection (ICSI), due to poor post-thaw results, are not included in studies comparing fresh and frozen microdissection testicular sperm extraction (mTESE). We hypothesized that fresh mTESE results in a higher rate of obtaining sperm acceptable for ICSI compared to FT mTESE.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We retrospectively reviewed all patients with non-obstructive azoospermia who underwent mTESE at a tertiary care institution from April 2007 to April 2020. The primary endpoint was rate of obtaining sperm usable for ICSI, which was defined as motile sperm at the time of fresh mTESE or post-thaw motile sperm after FT mTESE. Fisher's exact test was used to compare fresh and frozen-thawed mTESE results.

RESULTS: One hundred and nine men underwent 128 mTESEs. Table 1 compares sperm retrieval rates for fresh and FT mTESE. In the entire cohort, fresh mTESE yielded significantly higher retrieval rates of motile sperm acceptable for ICSI compared to FT mTESE ($p<0.0001$). The motile sperm retrieval rate in FT mTESE was 31/97 (32.0%), but post-thaw motile sperm was identified in 17 of these 31 FT mTESEs. Of the 31 fresh mTESEs, 4 (12.9%) found no sperm; all 27 fresh mTESEs where motile sperm was found proceeded to ICSI. Fresh mTESE had significantly higher retrieval rate of sperm acceptable for ICSI compared to FT mTESE ($p=0.01$). Seven patients had a FT mTESE followed by a fresh mTESE based on poor post-thaw results as assessed by an embryologist. Of these, 6/7 (85.7%) had motile sperm retrieved, but just 2/7 (28.6%) had post-thaw motility, both with reported very poor samples; all 7 (100%) had motile sperm on fresh mTESE acceptable for ICSI.

CONCLUSIONS: Our data suggests that there is a percentage of men whose decision to undergo FT mTESE precluded their ability to proceed with an ICSI cycle based on the results of that operation. Patients should be adequately counseled on the likelihood that FT mTESE may result in successful sperm retrieval but inability to proceed to ICSI.

Table 1. Sperm Retrieval Rates in Fresh versus Frozen-thawed Microdissection Testicular Sperm Extraction. FT mTESE = Frozen-Thawed microdissection testicular sperm extraction

	FT mTESE (n=97)	Fresh mTESE (n=31)	p-value
Motile Sperm (n=128)			<0.0001
Yes (n, %)	31 (32.0)	27 (87.1)	
No (n, %)	66 (68.0)	4 (12.9)	
	FT mTESE (n=31)	Fresh mTESE (n=31)	
Sperm Acceptable for ICSI (n=62)			0.01
Yes (n, %)	17 (54.8)	27 (87.1)	
No (n, %)	14 (45.2)	4 (12.9)	

SUPPORT: none

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PATIENT DESIRE FOR DISPOSITION OF CRYOPRESERVED SPERM UPON DEATH AS A SURROGATE MARKER FOR LIKELIHOOD OF CONSENT FOR POSTHUMOUS SPERM RETRIEVAL.

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OBJECTIVE: Decision-making regarding posthumous sperm retrieval can be ethically and legally challenging, as most cases do not clearly delineate in writing whether the deceased would consent for sperm retrieval. We sought to collect and analyze data regarding patient preferences for the disposition of their sperm in the possible event of their death to help better inform this process.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: An IRB approved, retrospective chart review was conducted on patients who froze sperm from January, 2016 through October, 2019 at a single fertility center. We reviewed the disposition of cryopreserved sperm should death occur to a patient. Collected data included age, race/ethnicity, occupation, insurance status, marital status and duration of marriage, prior biological children, and cause of fertility. Patients were excluded if they were not trying to get pregnant at present, prior to cancer therapy, prior to starting gender affirming treatments, or not in a committed relationship.

RESULTS: After review of 550 charts, 403 patients met criteria for inclusion. The mean age was 38.2 years +/- 6.7 (SD). Reasons for sperm cryopreservation were female factor (46.2%), male factor (34.7%), or combined factor (8.9%) infertility; a diagnosis was unknown or unspecified in 9.4% of patients. Overall, 84.9% of patients consented to transfer their sperm to their partner in

case of death. Male-factor infertility (OR for transfer 2.14, 95% CI 1.12 – 4.07, p= .02) and having commercial insurance (OR for transfer 2.11, 95% CI 1.07 – 4.15, p= .03) were predictors of electing to transfer sperm; there was no difference in "transfer to partner" rates with age, race/ethnicity, marital status, duration of marriage, having prior children, or occupation.

CONCLUSIONS: 84.9% of patients who cryopreserved sperm consented to transfer their sperm to their partners if death should occur. There does not appear to be a clear factor that would impact this decision, based on demographic information, prior children, or occupation. Since there is rarely written consent to perform posthumous sperm retrieval, this information is valuable in assessing whether most men who are married or in a committed relationship would consider proceeding in this fashion. This data may be useful to guide physician-institution-patient decision making in these complex situations.

SUPPORT: None

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THE RELATIONSHIP BETWEEN MEDICAL TREATMENT MODALITIES FOR MALE HYPOGONADISM AND ICSI OUTCOMES.

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OBJECTIVE: Male hypogonadism is characterized by testosterone deficiency. For men with hypogonadism who desire fertility, it has been reported that medications such as clomiphene citrate can improve luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels without negatively impacting semen parameters (1). However, it is unclear whether medical treatment for male hypogonadism leads to meaningful improvements in reproductive outcomes following intracytoplasmic sperm injection (ICSI). This study sought to determine whether treatment modalities used for male hypogonadism affect fertilization rates or blastulation rates after ICSI.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: This study was performed at a university-affiliated fertility practice. Men were included for analysis if they had a total testosterone level of less than 300 ng/dL and subsequently underwent a first cycle of ICSI. Men were divided into three treatment categories: no treatment, clomiphene citrate, or an alternative regimen which included any medications aside from clomiphene citrate or a combination of medications. Kruskal-Wallis testing and the Wilcoxon Rank-Sum test were utilized to assess the relationship between treatment groups for hypogonadism and rates of fertilization and blastulation.

RESULTS: A total of 171 male patients (mean age 34.7 ± 4.1 years) met the inclusion criteria. Among them, 44 patients (25.7%) received no medical treatment for hypogonadism, 69 patients (40.4%) received clomiphene citrate, and 58 patients (33.9%) received an alternative regimen. There were no statistically significant differences in patient age (p=0.71), initial FSH level (p=0.72) or initial LH level (p=0.09) between the treatment groups. However, patients receiving an alternative treatment regimen were noted to have lower mean serum total testosterone levels than the other groups (255.3 ng/dL for the no treatment group, 230.9 ng/dL for the clomiphene citrate group, and 217.2 ng/dL for the alternative regimen group, p=0.02). Embryology outcomes were assessed for all patients following ICSI. For men who did not receive any treatment for hypogonadism prior to ICSI, fertilization rate was 73.6% and blastulation rate was 44.3%, for the clomiphene citrate group fertilization rate was 79.1% and blastulation rate was 51.9%, and for the alternative regimen group fertilization rate was 71.5% and blastulation rate was 47.5%. There were no statistically significant differences noted for either fertilization rate or blastulation rate between the treatment groups (p=0.14 and p=0.35, respectively).

CONCLUSIONS: While medical therapy for male hypogonadism may alleviate symptoms associated with testosterone deficiency, various treatment regimens do not appear to have a significant impact on embryology outcomes. Specifically, the type of treatment does not affect fertilization rate or blastulation rate in men with testosterone deficiency.

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SUPPORT: None

P-660 4:30 PM Tuesday, October 20, 2020

DOES CONSULTATION BY A REPRODUCTIVE UROLOGIST (RU) VERSUS REPRODUCTIVE ENDOCRINOLOGIST (RE) IMPACT MALE PARTNER FERTILITY QUALITY OF LIFE (QOL)?

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OBJECTIVE: Limited data have shown that male partners of infertile couples may feel ashamed or stigmatized when labeled as "infertile." While most couples start with a RE, men may undergo RU evaluation. We sought to determine if male partners evaluated by a RU reported different motivating factors and fertility QoL (FertiQoL) compared to those seen by a RE.

DESIGN: Cross-sectional survey.

MATERIALS AND METHODS: Anonymous surveys were given to male partners of couples undergoing evaluation, in-person at a RE clinic or electronically after RU consultation. One part assessed demographics, history, and fertility motivating factors. The second was the validated FertiQoL, which assessed psychological effects of infertility. It contained 2 domains: "Core" (psychosocial and interpersonal QoL) and "Treatment" (fertility environment and treatment tolerability QoL). Responses were scaled 0-100; higher scores indicated more favorable QoL. Descriptive statistics, chi-square, and t-tests were used for data analysis.

RESULTS: Forty-eight men participated: 60.4% (n=29) with the RE and 39.6% (n=19) with the RU. Ethnicity, education, history, and motivating factors were similar between groups (p>0.05). Known male factor was more common in men with a RU versus RE (68.4% (n=13) versus 10.3% (n=3)).

Men undergoing RU consultation scored lower in overall Core, Treatment, and total FertiQoL, indicating differences in the global impact of infertility (p<0.05, Table). Scores were lower in every subscale but not significant for Relational, Social, and Tolerability (p>0.05), indicating that RU consultation did not affect these factors. All men undergoing RU consultation reported this was helpful for understanding fertility, and 95% (n=18) said it was helpful to have a "sperm doctor" as an adjunct to their partners' "egg doctor."

CONCLUSIONS: RU-consulted men reported worse QoL than those seen by a RE, experiencing more sadness, disrupted cognitive function, and negative treatment effects on QoL. These men were more likely to have known male infertility, and all found the RU consultation helpful. While impossible to know, the lower QoL may be from having known male infertility, or due to men feeling freer to express their personal experiences to a RU patient advocate.

TABLE. FertiQoL Scores for men seen by a RE versus RU

	RE (n=29) Mean (std dev^)	RU (n=19) Mean (std dev^)
Core*		
Mind/Body*	85.8 (11.7)	70.2 (19.6)
Emotional*	78.0 (17.5)	63.8 (17.2)
Relational	73.2 (14.9)	69.7 (17.2)
Social	80.0 (15.8)	70.2 (17.6)
Treatment*		
Environment*	81.1 (14.1)	62.8 (16.2)
Tolerability	80.2 (14.4)	75 (20.1)
Total*	79.7 (11.4)	68.2 (12.5)

^std dev= standard deviation; *p<0.05

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P-661 4:30 PM Tuesday, October 20, 2020

ACCESS TO CARE FOR INFERTILE MEN: WEBSITE EDUCATIONAL CONTENT AMONG ASSISTED REPRODUCTIVE TECHNOLOGY (ART) CLINICS IN THE UNITED STATES.

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OBJECTIVE: To characterize United States (U.S.) assisted reproductive technology (ART) clinic websites with regards to inclusion of male factor infertility educational content.

DESIGN: Cross-sectional study of ART clinic website content.

MATERIALS AND METHODS: Using the 2017 and 2018 Centers for Disease Control (CDC) Fertility Clinic Success Rates Reports, 537 ART clinics in the United States were identified. Thirty-eight clinics were excluded from this analysis because either the clinic closed or did not have a website.

Each website was evaluated for presence or absence of the following content: 1) any educational content for patients seeking infertility treatment, 2) educational content about male factor infertility specifically, 3) webpage section dedicated to male factor infertility, 4) discussion of the male fertility testing (i.e. semen analysis), 5) discussion of male factor infertility medical and surgical treatment, and 6) presence of urologist on the infertility team. Specific terms evaluated to identify male factor infertility educational content included: male factor infertility, azo-/oligospermia, hypogonadism, varicocele, semen analysis, surgical sperm extraction, and hormone therapy. Differences in variables were evaluated with respect to clinic location (state) and total number of cycles per year, as reported in the 2018 CDC Clinic Success Rates Reports.

RESULTS: Websites of 499 ART clinics were evaluated. Most websites (94.6%, n=472) include educational content in general, with 85.8% (n=405; 81.2% of the total) discussing male factor infertility specifically and 64.3% (n=321) including a webpage section devoted to male factor infertility. Many clinics (17.8%; n=89) include educational content such as blog posts, podcasts, and videos specific to male factor infertility. The majority (75.8%; n=378) of all clinic websites discuss the male fertility testing evaluation. Less than half (44.1%; n=220) mention treatment options for male factor infertility, with 23.0% discussing medical and 40.7% discussing surgical options. Finally, 10% (n=50) of all clinic websites note the presence of a urologist on the infertility team.

Clinics located in the 17 states with fewer than 4 total ART clinics are less likely to note the presence of a urologist on the infertility team. Additionally, clinics with a greater total number of cycles per year are more likely to include male educational content on their websites.

CONCLUSIONS: Our findings corroborate previous studies that showed U.S. ART clinic websites lack important information about male infertility.[1,2] The variability in information available on U.S. ART clinic websites may act as a barrier to access for male infertility care, particularly in states with few ART clinics or clinics with fewer total cycles. U.S. ART clinics should aim to address the evaluation of and treatment options for male factor infertility on their websites in order to overcome barriers to access for male infertility care.

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SUPPORT: The authors received no funding for this research.

P-662 4:30 PM Tuesday, October 20, 2020

SPERM WITH VERY LOW MOTILE DENSITY (MD) MAY BE A CAUSE OF REDUCED CHANCE OF LIVE DELIVERY DESPITE TRANSFER OF NORMAL MORPHOLOGIC EMBRYOS.

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OBJECTIVE: To determine if a male factor, specifically low MD, can reduce the chance of a live baby despite normal fertilization and the production of embryos with good morphology.

DESIGN: Prospective comparison study.

MATERIALS AND METHODS: To eliminate an oocyte factor as a confounding variable, the study selected pairs of patients sharing donor oocytes. The only couples selected were those where the male partners of 1 couple had a MD below $<10x10^6$/mL and the other male partner $\geq 10x10^6$/mL. The low MD group when evaluating outcome was further divided into very low MD of $<5x10^6$/mL and 5-9.9x10^6/mL. Only cycles where both couples had a fresh embryo transfer (ET) on day 3 were included. Intracytoplasmic sperm injection (ICSI) was used for couples where MD was $<10x10^6$/mL unless strict morphology was $\leq 4\%$ when ICSI was used even with normal MD.

RESULTS: There were 242 ETs in low MD groups and 245 in normal MD group.

Comparison of in vitro fertilization (IVF) outcome according to MD in pairs sharing oocytes

Motile Density ($10x10^6$/mL)	<5	5-9.9	≥10
# transfers	143	99	245
% fertilized	72.1%	70.9%	70.9%
% 6-8 cell day 3	57.3%	60.2%	62.4%
% clinical preg./transfer	47.6%	49.5%	56.3%
% miscarriage/clinical preg. live	20.6%	8.2%	16.7%
% delivered	37.8%	45.5%	46.9%
% implantation	26.5%	26.7%	30.9%

Chi-square = NS. Power analysis showed one would need to triple the number of subjects to show that the difference in live delivery rates comparing very low MD vs. normal MD was significant. Evaluating a subset with normal morphology using strict criteria, the live delivered pregnancy rate for very low MD was 36.1% (26/72) vs. 48.3% and miscarriage rate was 29.7% vs. 13.3%. Thus, low strict morphology was not a confounding variable. Since both low MD groups had ICSI performed, and the less severe group did as well as the normal MD group, ICSI did not seem to be a confounding variable. There was an average of 1.8 embryos transferred in the very low MD group vs. 1.9 in the normal MD group.

CONCLUSIONS: Though the differences were not significant, possibly the results could suggest that even using the best quality oocytes, males with very low MD may be responsible for unexplained failure to achieve a live birth even with the transfer of normal quality embryos by morphologic criteria. Since good oocytes can sometimes correct sperm defects, it may be that these differences may be even greater if the oocytes retrieved are of less quality. Thus, in cases of repeated failure to achieve live deliveries in couples where the sperm has very low MD, instead of switching to donor oocytes, one could consider first trying donor sperm. A larger possibly multicenter study is needed to support or refute this suggested cause of unexplained infertility.

SUPPORT: None

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IDENTIFYING THE BEST METHOD OF RETRIEVING SPERMATOZOA WITH THE HIGHEST GENOMIC INTEGRITY. Danielle Rebecca Tavares, B.A., Alessandra Parrella, M.Sc., Philip Xie, B.S., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To determine whether the best way to retrieve spermatozoa with an intact genome is to obtain specimens directly from the testicle or from the ejaculate through a microfluidic device.

DESIGN: During the course of 48 months, men with high DNA fragmentation in their ejaculate and related ART failure were offered testicular biopsy or microfluidic selection in order to identify spermatozoa with the highest genomic integrity. Spermatozoa from these two different origins were used for ICSI while controlling for maternal age. Fertilization, implantation, and pregnancy outcomes according to the sperm source used were recorded and compared.

MATERIALS AND METHODS: A total 111 consenting men had their ejaculated spermatozoa screened for SCF by TUNEL using a commercial kit on a minimum of 500 cells with a normal threshold of £15%. Testicular biopsy was carried out by micro-TESE. Ejaculated spermatozoa were selected by microfluidic processing. Both sources of spermatozoa were used for ICSI.

RESULTS: A total of 111 men (paternal age 36.6±5) with normal semen parameters (concentration of 41.5±25 x 10^6/mL, 42.1±14% motility, and increased SCF (22.4 ± 9%)) underwent 167 ICSI cycles with their female partners (maternal age 33.7±3) without achieving pregnancy. Subsequently, 22 couples underwent testicular biopsy. Those testicular specimens (concentration of 1.8±4 x 10^6/mL (P<0.01) and 5.0±11% motility (P<0.01), and an SCF of 12.6 ± 6% (P<0.0001)) were used in 37 ICSI cycles, yielding a fertilization rate of 61.6% (204/331, P<0.01), a superior implantation rate of 10.6% (9/85, P<0.01), a CPR of 23.5% (8/34, P<0.01), and a delivery rate of 17.6% (6/34, P<0.01). Another 22 couples underwent 28 ICSI cycles with ejaculated spermatozoa processed by a microfluidic device (concentration of 1.5±13 x 10^6/mL (P<0.01), 97.4±5% motility (P<0.01), and an SCF of 1.2 ±1%, lower than both raw and testicular specimens (P<0.0001)), resulting in a fertilization rate of 76% (203/266, P<0.01), an implantation rate of 26% (15/57, P<0.05), and a CPR of 50% (13/26, P<0.01), of which 2 patients delivered and 10 pregnancies are ongoing.

CONCLUSIONS: Our study demonstrates that sperm DNA fragmentation can severely lower the chances of achieving pregnancy by impairing embryonic development with consequent implantation failure. While retrieving spermatozoa directly from the germinal epithelium represents a valuable option, microfluidic sperm selection provides an optimal alternative by reducing surgical risks and costs.

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ASSESSING SPERM RETRIEVAL AND PREGNANCY OUTCOMES IN RE-DO MTESE PROCEDURES AMONG MEN WITH NOA. Nahid Punjani, MD MPH,[1] Ryan Flannigan, MD,[2] Kathleen Hart, BSN RN MA,[1] Peter N. Schlegel, M.D.[1] [1]Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY; [2]University of British Columbia, Vancouver, BC, Canada.

OBJECTIVE: To report the outcomes of redo microsurgical testicular sperm extraction (mTESE) procedures and assess predictors of sperm retrieval and pregnancy outcomes.

DESIGN: Retrospective study of prospectively collected data.

MATERIALS AND METHODS: All patients undergoing mTESE by a high-volume surgeon at Weill Cornell in New York City between 1995 and 2019 were reviewed. Men were included if they had a documented prior mTESE for sperm retrieval either completed either outside or at our institution. Demographic data included both male and partner age. Testicular size was reported and testicular histopathology when possible was reported as a percentage. mTESE outcomes includes sperm retrieval (yes/no), fertilized eggs per injected oocyte (rate), and pregnancy (yes/no). Adjusted logistic regression models were utilized to determine factors predictive of sperm retrieval including male age, male FSH levels and testicular size. Factors assessed which may predict pregnancy included male age, female age, male FSH and testis size.

RESULTS: A total of 144 men with re-do mTESE were included. The average age was 36 (IQR 32-40). Average partner age 33 (IQR 29-37). Mean left testicular size was 7.3 ± 5.2 cc and right testicular size was 7.7 ± 5.5 cc. Mean FSH values were 26.3 ± 16.4 IU/mL. Sperm retrieval occurred in 74 men (51.4%). Mean fertilized eggs were 2.3 ± 3.6. Pregnancy occurred in 26 of 138 men (18.8%). Using multivariable logistic regression (Table 1) testis size was associated with sperm retrieval (OR 1.14, 95% 1.03-1.27), and although not significant trended towards increased pregnancy rates (OR 1.12, 95% 0.99-1.27).

CONCLUSIONS: Re-do mTESE is a feasible option for those interested. Testis size is marginally associated with sperm retrieval in repeat procedures. Although it may be possibly more technically challenging and with limited pre-operative factors predictive of success, it is a reasonable choice for a high volume and skilled reproductive urologist.

Table 1 – Adjusted logistic regression models

	Sperm Retrieval (OR, 95%CI)	Pregnancy (OR, 95%CI)
Male Age	1.05 (0.98-1.13)	0.91 (0.79-1.05)
Female Age	-	1.13 (0.94-1.35)
Male FSH	1.02 (0.99-1.05)	1.02 (0.98-1.06)
Testis Size	**1.14 (1.03-1.27)**	1.12 (0.99-1.27)

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REPRODUCTIVE OUTCOMES OF COUPLES WITH SEVERE MALE FACTOR AND ADVANCED PATERNAL AGE. Krishna Mantravadi, Sr., MBBS, PGDHOM, Masters in clinical embryology,[1] Gayathri Gedela, Master in Clinical Embryology,[1] Vijay Kumar Sharanappa, Sr., MBBS, MD, MCE,[2] Shankhadeep Debnath, MSC Molecular Biology and Biotechnology,[1] Rajesh Mani Raghupathy, MBBS, PGDCE,[1] Durga Gedela Rao, Sr., MRCOG,[1] Sandeep Karunakaran, Sr., MS, PGDHM, PGDMLE[1] [1]Oasis fertility, Hyderabad, India; [2]OASIS FERTILITY, Hyderabad , TELANGANA, India.

OBJECTIVE: To evaluate whether couples with advanced paternal age and severe male factor infertility have altered embryo euploidy rates and analyse the reproductive outcomes with transfer of an euploid embryo

DESIGN: Retrospective Case Control Comparative Study. Private Teaching Fertility Clinic

MATERIALS AND METHODS: Couples with women <37 and severe male factor infertility underwent Pre-Implantation Genetic Testing for Aneuploidy (PGT-A) at our clinic during 2014 January and June 2019 were only evaluated in this study (n = 84). This study group was further sub-classified based on the male partners' age into men (< 39 years) (n = 54) and men (>40 years) (n = 13). Couples with women with advanced maternal age (>37 years) were excluded from this study (n = 70).

All women underwent controlled ovarian stimulation, Transvaginal oocyte retrieval and ICSI for severe male factor infertility as per our clinics standard operating procedures (SOP). Embryos were cultured till blastocyst stage and subjected to Trophectoderm biopsy and a freeze all policy was adopted. Biopsied tissue was sent for genetic evaluation by next generation sequencing (NGS). Couples with at least one Euploid embryo were offered elective single embryo transfer (eSET) in a frozen cycle. Mean euploid embryo rates and reproductive outcomes after eSET in younger and older men group were compared.

Control group underwent FET with two blastocysts (DET) and reproductive outcomes were compared between the two groups.

RESULTS: 307 embryos subjected for PGT-A with mean euploidy in Young and old men was 47.23 % and 36.23 % respectively.

The reproductive outcomes for Young and Older men were as follows:

Clinical Pregnancy Rate: 68.5 % Vs 46.15 % (P=0.1415)

Implantation Rate: 65 % Vs 38 % (P=0.0769)

Miscarriage Rate: 7 % Vs 12 % (P=0.3297)

Live Birth Rate: 61 % Vs 38 % (P=0.1361)

The reproductive outcomes for Older men with PGT-A and eSET and older men without PGT-A with DET were as follows

Clinical Pregnancy Rate: 46.15 % Vs 45.71 % (P=0.9483)

Implantation Rate: 38 % Vs 33.6 % (P=0.7603)

Miscarriage Rate: 12 % Vs 15.71 % (P=0.7333)

Multiple Pregnancy Rate: 0 % Vs 17 % (P=0.1104)

Live Birth Rate: 38 % Vs 27.14 % (P=0.4301)

Data from this study is suggestive that, Younger men with Younger women seem to have better embryo euploidy rates and reproductive outcomes.

Advancing paternal age seems to affect the reproductive outcomes in spite of transferring a euploid embryo. In spite of an euploid embryo older men had vert low IR and LBR.

Couples undergoing ART cycles with severe male factor infertility, advanced paternal age can be a detrimental factor.

Role of PGT-A to optimize reproductive outcomes for older men with severe male factor infertility doesn't seems encouraging in this study. Smaller sample size is the biggest limiting factor of this study, but calls for further research on the advanced paternal age and effects on reproductive outcomes.

CONCLUSIONS: Advanced paternal age can be detrimental factor and alter reproductive outcomes in severe male factory infertility couples.

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OLDER AGE AND LOWER SPERM MOTILITY ARE ASSOCIATED WITH ELEVATED SPERM DNA FRAGMENTATION INDEX. Jordan C. Best, B.S.,[1] Ruben Blachman-Braun, M.D., M.Sc.,[1] Daniel Gonzalez, B.S.,[1] Premal Patel, M.D.,[2] Taylor P. Kohn, MD, MPhil,[3] Ranjith Ramasamy, MD[4] [1]University of Miami Miller School of Medicine, Miami, FL; [2]University of Manitoba, Winnipeg, Mexico; [3]Johns Hopkins University School of Medicine, Baltimore, Mexico; [4]University of Miami, Miami, FL.

OBJECTIVE: To analyze the association of elevated sperm DNA fragmentation index (DFI) with clinical demographics and gross semen parameters.

DESIGN: A retrospective study was performed to evaluate consecutive men that underwent semen analysis in combination with sperm DFI testing between 2009-2018 at a reproductive medical center.

MATERIALS AND METHODS: We included men who underwent semen analysis as well as DFI testing evaluated by Sperm Chromatin Structure Assay (SCSA), regardless of their underlying etiology for infertility evaluation. An adjusted multiple linear regression analysis was performed to determine the relationship of clinical characteristics and gross semen parameters with sperm DFI%. All statistics were performed with SPSS 24.

RESULTS: A total of 441 men were included in this analysis, with overall median DFI of 12.8% [7.6 – 20]. Our multiple regression model predicts 37.9% of DFI variation ($R^2 = 0.392$, adj. $R^2 = 0.379$). The analysis showed that every additional year of life leads to a DFI increase of 0.54% (CI 95%: 0.38 to 0.71; $p < 0.001$), and an observed decrease in total sperm motility of -0.33% (CI 95%: -0.39 to -0.27; $p < 0.001$) for each percent increase in DFI% (Table 1). Due to the association between age and DFI, we evaluated the effect of advance paternal age on DFI comparison between age groups. DFI independently increased with advancing paternal age (20 – 30 years = 11% [6.5 - 15.2], 30.1 – 40 years = 11.1% [7.1 - 17.2], 40.1 – 50 years = 16.6% [10 27.1] , >50 years = 23.5% [14.5 - 35]; $p < 0.001$).

CONCLUSIONS: Older age and lower sperm motility were strongly associated with increased DFI. Men above the age of 40 appeared to have a steep increase in sperm DFI compared to men younger than 40. Further, studies should be performed to assess the clinical implications of assessing DFI in older men and those with isolated low sperm motility.

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SPERM RETRIEVAL RATES BY MICRO-TESE VERSUS CONVENTIONAL TESE IN MEN WITH HISTOPATHOLOGY CONFIRMED NON-OBSTRUCTIVE AZOOSPERMIA: A SYSTEMATIC REVIEW. Sandro C. Esteves, M.D., Ph.D.,[1] Thairo Alves Pereira, MD.[2] [1]ANDROFERT & University of Campinas (UNICAMP), Campinas, Brazil; [2]University of Campinas (UNICAMP), Campinas, Brazil.

OBJECTIVE: Summarize the evidence from a variety of study designs on the effectiveness of sperm retrieval (SR) techniques, microdissection testicular sperm extraction (micro-TESE) and conventional TESE (cTESE), in patients with histopathology-confirmed non-obstructive azoospermia (NOA).

DESIGN: Systematic review.

MATERIALS AND METHODS: We conducted a systematic search using Pubmed to identify all relevant studies published from 1999 to 2019. Articles were only included if they were written in English, provided histopathology confirmation for the NOA diagnosis, and were not review articles or letters. Studies were analysed for inclusion independently by the two authors, any discrepancies were resolved by discussion. A total of 109 articles were identified from the title. This was reduced to sixty-three suitable articles using the full-text, due to the lack of histopathology data. A total of 11,472 patients were included, 5861 and 5611 subjected to micro-TESE and cTESE, respectively.

RESULTS: In non-comparative studies, SR success was higher (p=002) using micro-TESE (49.9%) vs. cTESE (47.4%) (Relative risk [RR]: 1.06; 95% confidence interval [CI]: 1.02-1.10). In this analysis, the number need to treat (NNT) by micro-TESE vs. cTESE to achieve an additional successful SR was 35 (95% CI: 21-101). Among patients with Sertoli cell-only (SCO) or tubular atrophy/hyalinization, SR success by micro-TESE vs. cTESE were 34.7% and 31.2%, respectively (p=0.02; RR: 1.11; 95% CI: 1.01-1.21),

Table 1. Overall clinical and gross semen parameters of the analyzed men. In addition to a multiple linear analysis showing the association between DFI and the clinical characteristics and gross semen parameters.

		Multiple linear analysis			
			95% CI		
	Variables n = 411 (100%)	B	Lower	Upper	p-value
Age in years	37.1 [33.3 - 40.9]	0.54	0.38	0.71	**< 0.001**
Prior fertility					
No (%)	263 (64%)	Ref.			—
Yes (%)	148 (36%)	0.02	-2.10	2.14	0.983
Smoking history					
No (%)	358 (87.1%)	Ref.			—
Yes (%)	53 (12.9%)	-1.54	-4.56	1.47	0.314
Varicocele history					
No (%)	394 (95.9%)	Ref.			—
Yes (%)	17 (4.1%)	3.73	-1.32	8.77	0.147
Sperm concentration (million/cc)	36.4 [15.7 - 67.7]	-0.02	-0.05	0.02	0.326
Semen volume (cc)	2.7 [2 - 3.8]	-0.41	-1.14	0.31	0.261
Sperm morphology (% normal forms)	3 [1 – 6]	-0.02	-.016	0.13	0.825
Total sperm motility (%)	48.3 [35.3 – 63]	-0.33	-0.39	-0.27	**< 0.001**

B = Unstandardized regression coefficient; Ref: Reference value

with a NNT by micro-TESE vs. cTESE of 28.6 (15.5-178). When the analysis was limited to those studies directly comparing both techniques, SR success by micro-TESE vs. cTESE were 49% and 35.8% (p=0,0004; RR: 1.37; 95% CI: 1.14-1.65), with a NNT of 7.5 of 7.5 (95% CI: 4.9-16.6). In this subset analysis, SR success among patients with SCO or tubular atrophy/hyalinization were 36.1% vs. 13.3% (p<0.001; RR: 2.7, 95% CI: 1.72-4.24), with a NNT of 4.4 (95% CI: 3.2-7.1).

CONCLUSIONS: Micro-TESE provides higher SR success than cTESE in men with histopathology confirmed NOA, in particular, SCO and tubular atrophy/hyalinization. The magnitude of effect was remarkably higher in studies directly comparing both techniques, which highlights the heterogeneity of study populations of non-comparative studies. Therefore, pooled analysis of studies directly comparing SR techniques are preferred to guide clinical decision-making.

SUPPORT: None

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REPRODUCTIVE EFFECTS OF DIABETES, DYSLIPIDEMIA AND HYPERTENSION IN TESTICULAR SPERM EXTRACTION (TESE) WITH INTRACYTOPLASMIC SPERM INJECTION (ICSI) FROM VASECTOMIZED MALES.

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OBJECTIVE: TESE-ICSI is common approach for vasectomized males aiming to reverse infertility, yielding shorter time to pregnancy compared with surgical reversion when female infertility factors are present. During vasectomized period, the male may have developed pathologies that can affect the later success of ICSI. We aim to assess if the presence of male comorbidities, as diabetes mellitus (DM), dyslipidemia (DL) and hypertension (HTA), impact the likelihood of achieving a newborn after TESE-ICSI in these couples, both in cycles with their own and donated oocytes.

DESIGN: Retrospective study.

MATERIALS AND METHODS: From data since 1995, study population was screened according to the presence of these pathologies. Main outcomes were live birth rate (LBR) by embryo transfer (ET), by complete donation cycle (CDC) and by couple, using Chi-square to compare proportions and Kaplan Meier curves compared with Breslow tests, to estimate cumulative live birth rates (CLBR), per embryos consecutively replaced until achieving a newborn.

RESULTS: Mean time since vasectomy using their own oocytes (n=390) was 11.7 years (CI95% 11.1-12.3). 3.4% of them showed DM. The LBR were not significantly different when comparing DM *vs* non-DM per ET (55.6% *vs* 33.3%), per CDC (27.8% *vs* 22.8%) and per couple (38.5% *vs* 43.1%), but the DM group had a higher CLBR (p=0.02), needing fewer embryos to obtain the same LBR as the non-DM group. The LBR were not statistically different in males with DL (4.2% of all) and in non-DL: 25.0% *vs* 34.0% per ET, 13.8% *vs* 23.4% per CDC, and 25.0% *vs* 43.8% per couple. Also, the CLBR were comparable between DL and non-DL group: when 2 embryos were transferred was 37.5% and 33.3%, with 4 embryos replaced, rates were 68.7% and 56.6% respectively. Similar live birth rate (p>0.05) were observed in vasectomized men suffering HTA (5.5% of all) and non-HTA ones: 20.7% *vs* 34.6% per ET, 12.2% *vs* 23.7% per CDC and 28.6% *vs* 43.8% per couple. The CLBR was equivalent, 33.6% *vs* 28.2% and 44.9% *vs* 37.2% when 2 and up to 3 embryos were transferred. A total of 123 couples used donated eggs. Mean time since vasectomy was 13.3 years (CI95% 12.0-14.5); a 7.6% had DM, 4.2% DL and a 6.7% HTA. Non-significant differences in LBR between those with DM and non-DM patients: 13.3% *vs* 37.1% per ET and 18.2% *vs* 47.9% per CDC. LBR was statistically significant (p=0.03) when calculated per couple (22.2% *vs* 62.7%). The CLBR was comparable between them (p>0.05). The overall results of DL patients were not statistically different from non-DL men; LBR was 50.0% *vs* 34.9% per ET, 75.0% *vs* 45.0% per CDC and 60.0% *vs* 59.7% per couple. The CLBR was equivalent. HTA group showed no significant differences with respect non-HTA: 30.8% *vs* 35.6% per ET, 50.0% *vs* 45.6% per CDC and 50.0% *vs* 60.4% per couple. The CLBR were up to 52.9% *vs* 57.1% when a total of 4 embryos were transferred consecutively, but it was not statistically significant.

CONCLUSIONS: Diabetes seems to negatively impact oocyte donation treatments in patients undergoing TESE-ICSI after vasectomy, while on the cases with own eggs such effect disappears, deserving deeper exploration. HTA and DL seem irrelevant for success in these cases.

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A NEW METHOD FOR ACCURATE PREDICTION OF SPERMATOGENESIS: FSH/T AND T IN SEMINAL PLASMA.

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OBJECTIVE: To find a new method to predict spermatogenesis.

DESIGN: FSH, LH, T in serum and seminal plasma of spermatozoa and azoospermia were detected. The relationship between these hormones and their ratio and the number of spermatozoa were analyzed to find the best balance ratio which can stimulate spermatogenesis during the interaction of these hormones.

MATERIALS AND METHODS: We randomly selected 140 men for the study using a random number table. They were divided into the spermatozoa group (70 people) and the azoospermia group (70 people) depending on whether any sperm could be found after centrifugation of their ejaculated semen at 3000 g/min. The FSH, LH and T in their seminal plasma and serum were measured by *ELISA*, and the correlations between these indicators and sperm count were determined in order to find a new method to predict spermatogenesis.

RESULTS: There was no difference between the two groups in terms of age, height, weight, *BMI*, days of abstinence, semen volume, semen pH value or semen liquefaction time ($P>0.05$). The levels of *s*-FSH (17.07±4.09) and *s*-LH (37.85±44.08) of the spermatozoa group were higher than those of the azoospermia group (8.64±5.81, 22.26±31.30) (t_1=9.924, p_1=0.000; t_2=2.412, p_2=0.017), but the *b*-FSH (7.17±7.56) and *b*-LH (4.04±2.95) values of the spermatozoa group were lower than those of the azoospermia group (21.05±16.82, 10.03±7.82) (t_1=-6.299, p_1=0.000; t_2=-6.004, p_2=0.000). The level of *s*-T (65.59±24.04) of the spermatozoa group was higher than that of the azoospermia group (47.13±13.99)(t=5.551, p=0.000), but there was no difference in the level of *b*-T (17.33±8.62, 15.35±8.38) between the two groups (t=1.378, p=0.171). After controlling for the interference due to grouping factors, individually, *s*-FSH, *s*-LH, *b*-FSH, *b*-LH, *b*-T and *b*-FSH/T were not correlated with spermatogenesis (r_1=-0.112, r_2=0.111, r_3=-0.055, r_4=-0.018, r_5=-0.039, r_6=-0.049; p_1=0.189, p_2=0.195, p_3=0.519, p_4=0.835, p_5=0.649, p_6=0.569). However, *s*-FSH/T was positively correlated with spermatogenesis (r=0.201, p=0.018), while *s*-T was negatively correlated with spermatogenesis (r=-0.474, p=0.000). The composition analysis showed that among these eight factors, three main components could be extracted: blood gonadotropin (contained *b*-FSH, *b*-LH, and *b*-FSH/T), seminal plasma gonadotropin (contained *s*-FSH, *s*-LH, and *s*-FSH/T) and T (contained *s*-T and *b*-T), among which *s*-FSH/T and *s*-T are the most important factors for spermatogenesis. When *s*-FSH/T was greater than 0.13 (*AUC* 0.735, sensitivity 0.986, specificity 0.486, and prediction probability 0.87) and *s*-T was less than 63.0 (*AUC* 0.723, sensitivity 0.557, specificity 0.929, and prediction probability 0.87), spermatogenesis increased.

CONCLUSIONS: *s*-FSH/T and *s*-T can be used to accurately predict spermatogenesis.

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TRPV1 AS A MODULATOR OF ROS-INDUCED SPERM FUNCTION AND ITS CORRELATION WITH PREGNANCY OUTCOME (NATURAL CONCEPTION AND ART).

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OBJECTIVE: Being both thermo and redox sensitive, the transient receptor potential vanilloid 1 (TRPV1) constituted a group of relevant ion channels influencing sperm function. This study aims to investigate the expression profile of TRPV1 in sperm and its correlation with pregnancy outcome both by natural means and ART. Further, the role TRPV1 in mediating reactive oxygen species (ROS)-induced sperm function was examined.

DESIGN: Perspective case-control study and *in-vitro* experimental study.

MATERIALS AND METHODS: Semen samples were collected from male partners of couples who conceived either by natural means (NC) where fertile donors (NC+, n=10) were compared to partners of recurrent pregnancy loss (RPL; NC-, n=7) or by ART where the spermatozoa of male partners who achieved pregnancy by IVF (IVF+, n=10)/ICSI (ICSI +, n=9) were compared with their respective experimental group with failed pregnancy (IVF-, n= 23/ICSI-, n=10). TRPV1 expression was probed with immunocytochemistry and flow cytometry. Effect of TRPV1 modulators (RTX/ iRTX) +/- H_2O_2 on sperm function and calcium influx was evaluated. A secondary in-silico analysis of TRPV1 was undertaken with candidate fertility proteins to find out the probable pathways involved. Data were analysed by 1-way ANOVA or Kruskal-wallis test depending on normality distribution of data, and $p<0.05$ was considered significant.

RESULTS: Reduced expression of TRPV1 in sperm of IVF+/- and ICSI+/- men with respect to NC+ men imply the relevance of TRPV1 in mediating a successful fertilization in female reproductive tract. Unsuccessful pregnancy outcome with an under expression of TRPV1 in sperm of NC-/IVF-/ICSI- men, as compared to their successful counterparts postulate the role of channel in conception and maintenance of pregnancy. Enhancement of motility and triggering of acrosomal reaction post TRPV1 agonist (RTX) treatment, suggested that disruption of these signalling cascades *in-vivo*, in IVF+/ ICSI+ males would explain their need to undertake assisted techniques for a successful fertilization *in-vitro*. A significant increment in percentage of spermatozoa with reacted acrosome was observed after H_2O_2 treatment +/- RTX, as compared to untreated groups. The effect was attenuated by incubating with TRPV1 antagonist iRTX, implicating the role of TRPV1 in mediating the H_2O_2 response. The augmented Ca^{2+} influx due to channel activation in H_2O_2 +/- RTX, was demonstrated by calcium imaging. Cross-talk between TRPV1 with fertility candidate proteins showed that networks associated with cell death and survival were primarily affected.

CONCLUSIONS: The current study is a novel work, which demonstrated that reduced expression of TRPV1 in spermatozoa of RPL and IVF/ICSI failure patients compromised their fecundity potential. Influence of TRPV1 activation on motility and acrosomal reaction is also established. This is also the first report showing the direct role of TRPV1 in mediating H_2O_2 induced Ca^{2+} influx and acrosomal reaction in spermatozoa. If validated in larger population with different semen parameters, it would have therapeutic significance especially in ART setup.

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AN EVALUATION OF SEMEN PARAMETERS IN MEN WITH CONFIRMED COVID-19 INFECTION.

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OBJECTIVE: Our aim was to evaluate the semen parameters of men with COVID-19 infection.

DESIGN: A prospective study was performed to evaluate the gross semen parameters in men with COVID-19 infection. Samples of saliva and semen were collected and analyzed.

MATERIALS AND METHODS: We included men age 18-70 years old who tested positive for COVID-19. Subjects were contacted about willingness to participate. Packages with sterile specimen containers were mailed to the subject's house with a preaddressed package included to return to our lab. The semen then underwent gross semen analysis for volume, concentration, pH and motility.

RESULTS: A total of 12 men were enrolled in the study with a median age of 35.5 (IQR = 19.5) (Table 1). The median duration of infection was 37 days (IQR = 21) and 2/12 (16.7%) had associated orchitis symptoms during the infective period. For the 11/12 men who returned a semen specimen, median

volume was 1.6cc (IQR = 1.65), median pH was 7.2 (IQR = 0.2), median concentration was 14 million/cc (IQR = 30.25), and median motility of 0% (IQR = 12.5).

CONCLUSIONS: We evaluated 11 men's gross semen parameters after confirmed infection with COVID-19. The median concentration for these men is abnormally low compared to World Health Organization guidelines, and further evaluation is needed to determine the impact that COVID-19 infection can have on the testis and for what duration.

Table 1. The age, duration of infection and gross semen parameters of enrolled men.

Subject	Age	Duration (DAYS) of Infection at time of SA	Volume	pH	Concentration (million/cc)	Motility
1	30	35	1.6	7.2	5	0
2	39	27	3.9	7.2	30	32
3	56	16	1.1	7.2	317	0
4	31	37	1.6	7.2	46	0
5	32	9999	9999	9999	9999	9999
6	20	58	2.6	7.6	22	0
7	66	47	0.7	7.2	0.72	0
8	41	24	2.5	7.6	14	0
9	67	24	0.3	7.2	33	27
10	29	46	1.1	6.8	1	0
11	32	39	2.7	7.6	1.1	0
12	44	52	0.6	7.2	1.4	25

*9999 is substituted for missing data

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IMPACT OF TESTICULAR DELIVERY AND VASAL VEIN LIGATION ON CLINICAL OUTCOMES IN MEN UNDERGOING MICROSURGICAL VARICOCELECTOMY. Gal Wald, BA,[1] Nahid Punjani, MD MPH,[1] Christopher Gaffney, MD,[2] Marc Goldstein, M.D.,[3] James A. Kashanian, MD[4] [1]Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY; [2]Weill Cornell Medical College- New York Presbyterian Hospital, New York, NY; [3]Center for Male Reproductive Medicine and Microsurgery, Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY; [4]Weill Cornell Medicine - New York Presbyterian Hospital, New York, NY.

OBJECTIVE: To assess the impact of microsurgical varicocelectomy technique on clinical outcomes in patients with severe oligospermia.

DESIGN: Retrospective data collection.

MATERIALS AND METHODS: Men diagnosed with varicocele between 2017 and 2020 were reviewed. We included men who underwent microsurgical varicocelectomy at Weill Cornell by two high-volume surgeons who differed slightly in surgical technique in addition to ligating routine dilated veins: Method 1) testicle delivery with gubernacular vein ligation, ligation of dilated vasal veins >2.5mm, and preservation of normal vasal veins and Method 2) no testicle delivery and only ligation of markedly dilated vasal veins in recurrencent cases. Patients were stratified according to their preoperative sperm concentration (SC): >5 M/mL and <5 M/mL with and without azoospermia. Post-operative SC improvement and TUNEL were compared based on technique using the Wilcoxon ranked-sum test (Stata v14).

RESULTS: 313 men patients were included; a 162 with Method 1 and 151 with Method 2. The two cohorts were of similar age (35, IQR 27-42 and 34, IQR 28-39, respectively) and BMI (25.4, SD 4.0 vs 25.9, SD 4.5, respectively). For Method 1, 84 (51.9%) had bilateral surgery, 76 (46.9%) left only, and 2 (1.2%) right only. For Method 2, 63 (41.7%) had bilateral surgery, 84 (55.6%) left only, and 4 (2.6%) right only. Both methods produced a similar improvement in the TUNEL assay (p=0.33). In patients with SC >5 M/mL, there was no observed difference between Method 1 and 2 (p=0.24) post-operatively. Similarly, there was no statistical difference in patients with SC <5M/mL (p=0.48) and after excluding azoospermic men (p=0.55).

CONCLUSIONS: Delivery of the testis and ligation of dilated vasal veins does not influence changes in semen aparameters or TUNEL assay after microsurgical repair. Future studies will assess whether the differences in technique effect the short and long term recurrence rates.

Table 1 – Testicular Delivery and Vasal Vein Ligation Effeect on Clinical Outcomes

	No Delivery	Testicular Delivery	
> 5 M/mL			
Pre-op	20.7 (20.2), n=36	18.8 (19.9), n=51	
Post-op	34.7 (33.2), n=36	26.9 (27.0), n=51	
Difference	14.5 (20.3), n=35	8.1 (19.7), n=51	p=0.24
<5 M/mL (all)			
Pre-op	0.8 (1.1), n=12	0.4 (0.8), n=26	
Post-op	2.7 (5.4), n=12	6.8 (14.4), n=26	
Difference	2.1 (5.3), n=11	6.4 (14.2), n=26	p=0.48
<5 M/mL (no azoospermia)			
Pre-op	1.8 (0.8), n=5	1.25 (0.8), n=9	
Post-op	6.2 (7.3), n=5	14.64 (17.3), n=9	
Difference	4.40 (7.7), n=5	13.39 (17.2), n=9	p=0.55
TUNEL			
Pre-op	25.5 (6.6), n=6	16.1 (6.1), n=16	
Post-op	14.6 (8.2), n=6	8.8 (7.6), n=16	
Difference	10.9 (10.8), n=6	7.2 (8.8), n=16	p=0.33

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PREDICTORS OF DETERIORATION OF SEMEN PARAMETERS IN MEN TREATED WITH CLOMIPHENE CITRATE FOR INFERTILITY. Christopher M. Deibert, MD, MPH,[1] Jacob T. Pfeifer, BS,[2] Thomas Schroeder, BA[2] [1]University of Nebraska, Omaha, NE; [2]University of Nebraska Medical Center, Omaha, NE.

OBJECTIVE: To better understand the correlations associated with decreases in Total Motile Sperm Count (TMSC) after a clomiphene challenge and predict which men would be ideal candidates for clomiphene citrate (Clomid) therapy.

DESIGN: We retrospectively analyzed male patients treated for infertility with clomiphene citrate at the University of Nebraska Medical Center from 2015-2019. We excluded patients with no follow-up semen analysis or hormonal labs, concurrent HCG treatment, and/or prior varicocele surgery. Our final samples size was 45 patients, from this sample we tracked testosterone response and the men's semen analysis parameters.

MATERIALS AND METHODS: 45 patients were categorized into 7 groups based on changes in the semen parameter TMSC: increased >10 million, increased >5 million, increased >2 million, decreased >2 million, decreased >5 million, decreased >10 million, or stayed the same. From these groups we tracked how many men doubled their TMSC and performed statistical analysis to correlate Testosterone response and TMSC response while on Clomiphene citrate.

RESULTS: While using Clomiphene citrate, 57.8% of patients (n=25) showed an increase in total motile sperm production with 48.9% of men doubling their sperm production. However, 24.4% of men (n=11) had no increase in sperm production and 17.8% of men (n=8) paradoxically had a decrease in sperm production. Of the patients who had an increase of >10 million, 89.5% doubled their initial TMSC. Of those men that had a decrease in sperm production, 37.5% had a TMSC that decreased by greater than 10 million (Table 1). Increased testosterone response showed positive correlation with increased TMSC.

CONCLUSIONS: Clomiphene citrate is a well-established option for the treatment of male hypogonadism. However, nearly 1 in 5 men experience a paradoxical effect resulting in decreased TMSC. Though counseling on

therapy has always included that counts may not increase, discussing possible decrease is also necessary.

Table 1. Categories based on TMSC response showing the total % of patients, and the number of patients that doubled their TMSC.

TMSC response	# of patients	% of TOTAL Patients	# of TMSC Doubled	% of patients that Doubled TMSC in Respective TMSC response
Increased >10 million	19	42.2%	17	89.5%
Increased >5 million	3	6.7%	3	100.0%
Increased >2 million	4	8.9%	2	50.0%
Decreased >2 million	4	8.9%	0	0.0%
Decreased >5 million	1	2.2%	0	0.0%
Decreased >10 million	3	6.7%	0	0.0%
Stayed the same	11	24.4%	0	0.0%
TOTAL	45		22	

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ANTIRETROVIRAL THERAPY IN HIV-POSITIVE MEN AND IVF OUTCOMES IN EGG DONATION PLUS SURROGACY PROGRAMS. Diana Obidniak, Dr.,[1] Alexander Gzgzyan, Prof.,[2] Dariko Niauri, Prof.,[2] Igor Kogan, Prof.[3] [1]AVA-Peter, Saint-Petersburg, Russian Federation; [2]Saint Petersburg State University, Saint-Petersburg, Russian Federation; [3]FSBSI "The Research Institute of Obstetrics, Gynecology and Reproductology named after D.O. Ott", Saint-Petersburg, Russian Federation.

OBJECTIVE: The aim of the study was to investigate if antiretroviral therapy (HAART) in HIV-positive men brings significant impact on outcomes of assisted reproductive technology.

DESIGN: Study Design: observational

Size: 38 cycles of embryo transfers

Duration: 24 months

MATERIALS AND METHODS: With the aim to minimize bias associated with female infertility impact on IVF outcomes we have indicated following inclusion criteria: egg donation cycle with preimplantation genetic testig (PGT-A) and surrogacy program in couples with HIV – positive and HIV- negative men. Exclusion criteria: severe male factor, abnormal karyotype, absence of antiretroviral therapy in HIV-positive men. From January 2018 till December 2019 38 cycles satisfying matching were included. The cases were divided into study group - HIV-positive +HAART (N = 19) and control group – HIV- negative (N = 19). In all cases selective embryo transfer was performed with endometrial preparation being carried out according to standartized protocol of hormone replacement therapy with ultrasound monitoring. The primary assessed outcome was clinical pregnancy rate. The secondary assessed outcome was miscarriage rate.

RESULTS: As a primary assessed outcome the clinical pregnancy rate was analysed: there was no difference comparing between groups (13/19 (68.4%), 13/19 (68.4%) X^2=0.0, p>0.05). The secondary assessed outcome was miscarriage rate being 7-fold higher in study group in comparison to control group (7/13 (53.8%) vs 1/13 (7.6%), X^2=6.5, p=0.011).

CONCLUSIONS: These data demonstrate that HAART in HIV-positive men seems may cause significantly (7-fold) elevated risk of pregnancy loss.

There is need for proper investigation of HAART effect on sperm quality and DNA fragmentation as possible reasons for elevated risk of miscarriage.

Given strict matching criteria the number of included cases is highly limited. Further investigation is needed.

SUPPORT: N/A

P-675 4:30 PM Tuesday, October 20, 2020

ASSOCIATION OF AGING AND OBESITY WITH DECREASED INTRATESTICULAR TESTOSTERONE. Thiago Fernandes Negris Lima, MD,[1] Fabio Stefano Frech, BS,[2] Ruben Blachman-Braun, M.D., M.Sc.,[2] Evgeniya Rakitina, MS,[2] Premal Patel, M.D.,[3] Ranjith Ramasamy, MD,[1] [17]ohp[1]University of Miami, Miami, FL; [2]University of Miami Miller School of Medicine, Miami, FL; [3]University of Manitoba, Winnipeg, MB, Canada.

OBJECTIVE: To evaluated the association between BMI and LH, BMI and ITT (using serum 17-hydroxyprogesterone (17-OHP) as a biomarker) in a cross-sectional study. Obesity's negative association with serum testosterone (T) levels can be explained by either decreasing luteinizing hormone (LH) production from the pituitary gland and/or directly impact intratesticular testosterone (ITT) production. We hypothesize that obesity will negatively impact ITT production when compared to non-obese men.

DESIGN: We performed a cross-sectional analysis of men with symptoms of testosterone deficiency and male infertility between July/2018 - April/2020.

MATERIALS AND METHODS: We included men with symptoms of testosterone deficiency and/or infertility and measurements of 17-OHP, serum testosterone, serum estradiol and LH levels. We excluded men receiving agents that alter ITT, exogenous testosterone, CC or hCG during the baseline assessment. Primary outcome was to evaluate the effect of BMI on 17-OHP and LH. Univariable and multiple linear regression analysis were performed using confounding variables to predict 17-OHP and T.

RESULTS: A total of 340 men were selected. Median age was 38 [33 - 44] years, BMI 27.8 [25.4 - 31.1] kg/m^2, T 363 [256.3 - 469.6] ng/dL, 17-OHP 60.5 [39.3 - 85.8]ng/dL, estradiol 22 [16.3 - 30], and LH 4.2 [2.8 - 5.7] mIU/mL. As expected, older and obese men were associated with having a lower T level as compared to younger and non-obese men. Interestingly, increasing age and higher BMI were associated with a lower 17-OHP level. Contrarily, age and BMI weren't associated with LH levels (p=0.478). In the multiple regression model, increasing BMI and older age predicted a decrease in 17-OHP ($p < 0.001$). (Table 1).

CONCLUSIONS: Obesity and aging negatively affected 17-OHP independent of LH. This suggests that obesity-related changes in serum T and 17-OHP (ITT) could be due to direct effect to testicular function, rather than secondary effect from decline in pituitary function.

Table 1. Univariable and multivariable logistic regression analysis for 17-OHP (ng/dL)

	Univariable					Multiple linear regression				
			95% CI					95% CI		
Variable	R^2	B	Lower	Upper	p-value	Adj. R^2	B	Lower	Upper	p-value
Age in years	0.078	-1.15	-1.57	-0.73	**< 0.001**	0.185	-0.84	-1.25	-0.42	**< 0.001**
BMI (kg/m^2)	0.060	-2.01	-2.85	-1.16	**< 0.001**		-1.73	-2.54	-0.92	**< 0.001**
Testicular volume (cc)	0.003	0.61	-0.57	1.79	0.313		0.97	-0.12	2.07	0.082
Diabetes mellitus	0.012	-19.22	-37.99	-0.44	**0.045**		-11.40	-28.90	6.11	0.201
History testosterone abuse	0.014	-12.94	-24.77	-1.11	**0.032**		-2.24	-13.34	8.86	0.692
LH (mIU/mL)	0.072	3.76	2.32	5.20	**< 0.001**		3.94	2.545	5.33	**< 0.001**

B = Unstandardized regression coefficient, R^2 = coefficient of determination, Adj. R^2 = Adjusted coefficient of determination;

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TESTICULAR ULTRASOUND AS A PROGNOSTIC FACTOR FOR IMPROVEMENT IN SEMEN PARAMETERS AFTER VARICOCELECTOMY.

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OBJECTIVE: It is difficult to identify the sub-groups of infertile men who will benefit most from varicocelectomy. We theorize that advanced processing of ultrasound images can predict testicular sperm density as posterior acoustic enhancement could result in increased echogenity and heterogeneity as ultrasound waves pass through larger seminiferous tubules. The objective of our study was to evaluate testicular ultrasound heterogeneity as a predictor for improved semen parameters after varicocelectomy.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Infertile men undergoing varicocelectomy were included if they had a pre-operative testicular ultrasound plus pre- and post-operative semen analysis. Azoospermic men were excluded. Greyscale testicular ultrasound images were assessed with pixel intensity histogram. The standard deviation (SD) of the histogram was theorized to measure heterogeneity and thus representative of testicular sperm density. The average histogram SD of bilateral testicles was taken. Linear regression was performed to assess the correlation between the pre-operative average histogram SD and the change in total motile sperm count (TMSC) following varicocelectomy.

RESULTS: Twenty-two men were included. Median preoperative TMSC was 22.1 million sperm (IQR: 9.0-44.5). Fifteen men experienced an increase in TMSC after varicocelectomy: median increase 16.1 million sperm (IQR: 2.9-24.0) and median pixel SD 10.94 (IQR: 9.53-12.54). The remaining seven men experienced a decline in TMSC: median decrease 27.6 million sperm (IQR: 19.9-29.6) and median pixel SD 8.04 (IQR: 7.69-9.30). A greater pre-operative average histogram SD was associated with a greater improvement in TMSC following varicocelectomy ($p=0.004$, $R^2=0.34$).

CONCLUSIONS: This novel method to evaluate testicular heterogeneity may help predict which men will experience an improvement in semen parameters after varicocelectomy.

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INTRACYTOPLASMIC SPERM INJECTION OUTCOME OF EJACULATED VERSUS TESTICULAR SPERM IN CRYPTOZOOSPERMIC MEN.

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OBJECTIVE: Cryptozoospermic men have very low quality of spermatozoa in their ejaculates, resulting in poor ICSI outcomes. It is widely discussed that spermatozoa may damage when passing through the male reproductive tract by affecting sperm DNA intgrity. In the other hand, potential immaturity of testicular spermatozoa could have a negative impact on ICSI outcomes affecting fertilization and embryo developement. Nowadays, the use of testicular spermatozoa in ICSI when ejaculate sperm is available remain controversial and has not been applied yet to routine.the aim of our study is to evaluate if testicular sperm superior could be superior to ejaculated sperm for intracytoplasmic sperm injection in cryptozoospermia cases?

DESIGN: Prospective cohort study held in a Fertillia ART center in Tunisia from october 2018 to december 2019. A total of 41 couples, who underwent ICSI cycles followed by embryo transfer were included. Our study was conducted on couples with cryptozoospermic partner. Cases with female infertility factor were excluded. Fertilization rate (FR), embryo quality, implantation rate (IR) and pregnancy rate (PR) were reproductive variables considered to be compared among study groups.

MATERIALS AND METHODS: Fourty one patients with cryptozoospermia were randomly allocated to two groups. Groupe 1 (n=21) used ejaculated sperm, and group 2 (n=20) had testicular sperm. There was no differences in age, duration of infertility and type of infertility between the two groups.

RESULTS: The mean female and male age were respectively comparable between group 1 and 2 (32.55 VS 33.2 years ; $p>0.05$) ; (41.6 VS 42.5 years ; $p>0.05$). No differences regarding number of oocytes retrieved or MII oocytes were reported but it was observed, a slight improvement in sperm count and progressive motility in testicular sperm comparing to ejaculated sperm. Fertilization rate was significantly higher in testicular sperm group (Group 1) when compared to ejaculated sperm (57% VS 48% ; $p<0.01$). Furthermore, statistical significance was also achieved when comparing IR (6.5% vs 19%) and PR (11% vs 31%) between respectively group 1 and group 2. Comparing the two groups, no differences were found in the quality and the number of embryos transferred.

CONCLUSIONS: We conclude that the use of testicular sperm should be applied to patients with cryptozoospermia undergoing ICSI

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THE IMPACT OF TESTICULAR DELIVERY AND VASAL VEIN LIGATION ON SERUM TESTOSTERONE IN MEN UNDERGOING MICROSURGICAL VARICOCELECTOMY.

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OBJECTIVE: To determine if microsurgical varicocelectomy technique impacts serum testosterone levels.

DESIGN: Retrospective data collection.

MATERIALS AND METHODS: Men undergoing microsurgical varicocelectomy between 2017 and 2020 for any indication by two high-volume surgeons at Weill Cornell were reviewed. Surgeon 1 (Method 1) used testicle delivery with gubernacular vein ligation as well as ligation of dilated vasal veins >2.5mm. Surgeon 2 (Method 2) did not perform testicle delivery and therefore no ligation of gubernacular veins, and only removed vasal veins in the case of a recurrence. Pre-operative and post-operative serum testosterone levels were compared based on the two methods, for all patients, as well as for unilateral and bilateral cases using the Wilcoxon ranked-sum test (Stata v14).

RESULTS: 313 patients were included. Of these, 162 (51.8%) had microsurgical varicocelectomy using Method 1 and 151 (48.2%) using Method 2. Demographic data was similar between groups. Median age for Method 1 was 35 (IQR 27-42) and 34 (IQR 28-39) for Method 2. Mean BMI was 25.4 ± 4.0 kg/m^2 for Method 1, and 25.9 ± 4.5 kg/m^2 for Method 2. The majority had bilateral surgery for Method 1 (n=84, 51.9%), and 78 (48.1%) had a unilateral procedure. For Method 2, 63 (41.7%) patients had bilateral surgery with the remaining 88 (58.3%) having a unilateral procedure. A statistically significant difference was observed for testosterone levels between groups, with a difference of 145.0 ± 232.7 ng/dl for Method 1 as compared to 37.8 ± 105.0 ng/dl for Method 2 ($p=0.03$). When subdivided as unilateral and bilateral, the difference was 187.4 ± 254.7 for Method 1 examining only unilateral varicocelectomies, versus 55.0 ± 112.1 for Method 2 ($p=0.09$). For bilateral cases the difference was 115.5 ± 215.2 for Method 1 versus 16.3 ± 95.6 for Method 2 ($p=0.11$).

Table 1 – Comparison of pre-operative and post-operative testosterone based on technique

Testosterone	Method 1	Method 2	
All			
Pre-op	362.5 (128.3), n=56	337.4 (116.7), n=27	
Post-op	507.5 (236.6), n=56	375.2 (135.4), n=27	
Difference	145.0 (232.7), n=56	37.8 (105.0), n=27	**p=0.03**
Unilateral			
Pre-op	326.5 (105.6), n=23	288.3 (89.2), n=15	
Post-op	513.9 (248.7), n=23	343.3 (123.5), n=15	
Difference	187.4 (254.7), n=23	55.0 (112.1), n=15	**p=0.09**
Bilateral			
Pre-op	387.5 (138.0), n=33	398.8 (121.2), n=12	
Post-op	503.0 (231.6), n=33	415.1 (144.2), n=12	
Difference	115.5 (215.2), n=33	16.3 (95.6), n=12	**p=0.11**

CONCLUSIONS: Microsurgical varicocelectomy improves serum testosterone levels with both techniques, but improvement appears to be greater with gubernacular and enlarged vasal vein ligation. Future prospective studies investigating this observation are warranted.

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IS TESTICULAR SIZE DISCREPANCY ASSOCIATED WITH SEMEN PARAMETERS IN BOYS WITH VARICOCELES?. Justin M. Dubin, MD,[1] Belen Mora, BA,[1] Nehizena S. Aihie, MD,[1] Laura Angulo-Llanos, MD,[1] Thomas A. Masterson, III, MD,[1] Alireza Alam, MD[2] [1]University of Miami Miller School of Medicine, Miami, FL; [2]Nicklaus Children's Hospital, Miami, FL.

OBJECTIVE: Varicocele is the most common surgically correctable cause of infertility in adult men; however, >80% are asymptomatic. While believed to cause a progressive decline in semen parameters, treating varicoceles in the pediatric population is controversial because of uncertain pathogenesis. Current recommendations are to correct a varicocele when there is a >20% ipsilateral testicular size discrepancy, but associations with semen parameters are not well studied. We hypothesized that boys with varicoceles and >20% testicle size discrepancy will have lower sperm concentration and motility compared to boys with varicoceles and <20% size discrepancy

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: We retrospectively identified boys <18 years old diagnosed with a varicocele from a large regional pediatric urological practice from 2013 to 2020. We included patients with at least one semen analysis and scrotal ultrasound with measurements of the right and left testicles. We then compared semen sperm concentration and motility of boys with >20% testis size discrepancy to those with <20% discrepancy, calculated as (right-left)/(total testis volume). Unpaired t test was used to determine significance.

RESULTS: We identified 819 boys with a diagnosis of varicocele. Of them, 72 had a semen analysis and testicular ultrasound. There were 26 boys with >20% ipsilateral testicular size discrepancy and 46 with <20% ipsilateral testicular size discrepancy. For boys with >20% ipsilateral testicular size discrepancy, the mean semen concentration and motility were 55.7 $\pm$ 65.9 million and 44.8 $\pm$ 23.9% compared to 59.9 $\pm$ 48.7 million (p= 0.76) and 52.1 $\pm$ 20.7% (p= 0.17) for boys with <20% testis size discrepancy, respectively. We also compared semen parameters for those with >20% testicular discrepancy vs those with <10% discrepancy (28 boys), for which there was no significant difference.

CONCLUSIONS: Based on a single institution cohort, it appears that testicular size discrepancy is not associated with semen concentration or motility in boys with varicoceles.

SUPPORT: None

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PRESENCE OF VARICOCELE-ASSOCIATED PAIN DOES NOT PREDICT SEMEN ANALYSIS OUTCOMES FOLLOWING MICROSURGICAL REPAIR. Nahid Punjani, MD MPH,[1] Gal Wald, BA,[1] Christopher Gaffney, MD,[2] Marc Goldstein, M.D.,[3] James A. Kashanian, MD[4] [1]Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY; [2]Weill Cornell Medical College- New York Presbyterian Hospital, New York, NY; [3]Center for Male Reproductive Medicine and Microsurgery, Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY; [4]Weill Cornell Medicine - New York Presbyterian Hospital, New York, NY.

OBJECTIVE: To assess whether varicocele-associated pain predicts semen analysis parameters after microsurgical varicocelectomy.

DESIGN: Retrospective data collection.

MATERIALS AND METHODS: We assessed all men who were diagnosed with a varicocele by two surgeons at Weill Cornell Medicine between 2017 and 2020. Men with varicocele who did not undergo surgical treatment and who did not have both pre-operative and post-operative semen analysis data available were excluded. All included patients had a microsurgical varicocelectomy. Patients were stratified based on the presence of pain at the time of clinical assessment. Contrast between demographics (t-test and chi-square) and semen parameters (Wilcoxon-rank sum) between the two groups were assessed using Stata v14.

RESULTS: A total of 313 men were included, with relatively similar proportions completed by both surgeons (48.2% and 51.8%). A total of 98 (31.3%) had typical varicocele-associated pain at the time of assessment, and the remainder (n=215, 68.7%) did not. The pain group was younger than the no pain group (30.5 vs. 35.0, respectively, p<0.01). Although not statistically different, there was a greater portion of left sided-only varicoceles compared to right sided-only or bilateral varicoceles in the pain group (58.2% vs. 47.9%, respectively, p=0.09). No significant differences were demonstrated between sperm concentration, motility, volume or morphology pre-operatively, or post-operatively in the pain versus no-pain group (Table 1).

CONCLUSIONS: In our series, almost 1/3 of men presented with typical varicocele-associated pain. Pain does not predict response to varicocelectomy, but individuals with pain tend to be younger, and trend toward more left sided varicoceles.

Table 1 – Comparison of demographics and semen parameters for pain vs. no pain

	Pain (N=98)	No Pain (N=215)	p-value
Demographics (mean, n)			
Age (median, IQR)	30.5 (23-41)	35.0 (31-41)	p<0.01
BMI (median, IQR)	24.2 (22.7-26.8)	25.18 (23.0-27.9)	p=0.32
Side	2 (2.0%)	4 (1.9%)	p=0.91
Right	57 (58.2%)	103 (47.9%)	p=0.09
Left	39 (39.8%)	108 (50.2%)	p=0.09
Bilateral			
Semen Parameters (mean, SD)			
Concentration	21.4 (17.9)	15.9 (19.8)	p=0.10
Pre-Op	32.7 (29.6)	15.9 (19.8)	p=0.24
Post-Op	11.3 (21.1)	10.2 (18.8)	p=0.97
Difference			
Volume	3.2 (1.8)	2.8 (1.5)	p=0.57
Pre-Op	2.4 (1.0)	2.7 (1.2)	p=0.44
Post-Op	-0.8 (1.7)	-0.2 (1.5)	p=0.13
Difference			
Morphology	5.9 (7.6)	2.8 (2.5)	p=0.06
Pre-Op	4.6 (2.5)	4.0 (4.0)	p=0.10
Post-Op	-1.4 (6.3)	1.2 (4.4)	p=0.24
Difference			
Motility	47.4 (24.1)	44.5 (17.0)	p=0.06
Pre-Op	55.5 (10.9)	50.3 (14.4)	p=0.10
Post-Op	8.2 (20.0)	5.9 (19.6)	p=0.34
Difference			

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POSTWASH TOTAL MOTILE SPERM COUNT EFFECT ON PREGNANCY OUTCOMES IN INTRAUTERINE INSEMINATION. Melissa A. Mathes, MD, Elizabeth A. Kastrick, MD, Stephanie Gustin, MD The University of Nebraska Medical Center, Omaha, NE.

OBJECTIVE: Intrauterine insemination (IUI) is a frequently used method to treat couples with infertility. There is evidence of decreased pregnancy rates with total motile sperm count (TMSC) less than 5 and 10 million (1,2), yet there has been efficacy of reported IUI success with TMSC under 1 million (2). As such, there remains to be a consensus on semen parameters for which to recommend IUI in the infertile population. Further defining TMSC and associated pregnancy rates allows for more precise patient counseling and may also delineate a clearer threshold for escalation of care to in vitro fertilization. This may decrease the time to pregnancy and the financial burden of offering infertility treatment that is less likely to be effective. The aim of this study was to determine a minimum threshold of TMSC on semen analysis to offer IUI cycles.

DESIGN: A retrospective cohort study of all IUI cycles at a private practice infertility center from June 2014 to May 2018.

MATERIALS AND METHODS: This is a retrospective cohort study of all IUI cycles at a private practice infertility center from June 2014 to May 2018. We obtained female characteristics including age, gravida, parity, BMI,

AMH, AFC, tubal patency, stimulation, number of dominant follicles, and ET. Semen was processed with a gradient centrifugation process and the following semen parameters were collected: post wash TMSC, concentration, motility, and wet mount morphology. Our primary outcome of interest was the presence or absence of clinical pregnancy after each cycle. Clinical pregnancy was defined as fetal cardiac activity on ultrasound.

RESULTS: A total of 999 women underwent 2169 IUI cycles during this four-year period. The average couple underwent 2.17 IUIs. The overall clinical pregnancy rate was 19.8% per cycle while pregnancy rate of only the first IUI per patient was 19.2%. Overall, clinical pregnancy rate per couple was 40.2%. During the first IUI each couple underwent, there was an increase in clinical pregnancy with increasing TMSC, OR 0.44 for TMSC $\leq$1M, 0.56 for TMSC 2-5M, and 0.99 for TMSC 6-10M, compared to TMSC >10M with p-values of 0.27, 0.057 and 0.975 respectively. Using receiver operating characteristic curves, we did not identify a TMSC threshold to offer IUI but rather a linear increase of sensitivity and specificity to predict pregnancy with increased TMSC. The lowest TMSC resulting in pregnancy was 660,000. With TMSC 6-10M, pregnancy outcomes improved with morphology >4% OR 0.84, compared to morphology <4% OR 0.25. There were 39 multifetal gestations, 9.1% of all clinical pregnancies.

CONCLUSIONS: Although no distinct threshold of TMSC was identified to offer IUI versus proceeding with ART, there is a positive correlation between TMSC and IUI success. There appears to be improved outcomes with morphology >4% when TMSC <10. A follow up study, using a larger sample size, is necessary to further characterize the upper limits of efficacy of IUI specimens. Well-defined pregnancy rates based on semen parameters will allow for more direct counseling of infertility patients and also allow for more targeted therapy recommendations based on pregnancy success rates.

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Table 1 – Clinical Outcomes Stratified by Physical Exam Grade

	Right				Left			
	N	Pre-op	Post-op	p-value	N	Pre-op	Post-op	p-value
Grade I								
T	31	19.8 ± 27.6	26.7 ± 34.9	**<0.05**	18	23.8 ± 32.2	28.0 ± 31.0	0.86
TUNEL	9	15.0 ± 8.2	8.3 ± 3.4	0.09	9	21.5 ± 12.2	11.4 ± 10.1	0.16
SC	31	341.2 ± 126.9	453.4 ± 163	<0.01	19	289.3 ± 109.3	485.4 ± 232.0	<0.01
Grade II						34.3 ± 35.4		
T	35	24.8 ± 25.2	36.7 ± 36.9	**<0.01**	57	16.3 ± 8.4	34.7 ± 35.7	0.66
TUNEL	12	13.4 ± 4.5	13.3 ± 8.3	0.94	17	348.8 ± 135.2	12.4 ± 5.4	0.17
SC	33	374.6 ± 151.6	439.6 ± 219.2	0.10	52		448.9 ± 173.7	<0.01
Grade III								
T	5	18.1 ± 16.6	33.0 ± 16.2	**<0.05**	86	24.4 ± 24.6	36.0 ± 30.9	**<0.01**
TUNEL	2	20.6 ± 10.3	12.3 ± 13.1	0.65	31	15.1 ± 5.7	10.7 ± 6.7	<0.01
SC	10	345.4 ± 142.5	313.8 ± 170.7	0.54	91	354.9 ± 152.7	391.5 ± 177.3	<0.05

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SUPPORT: None

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DOES MICROSURGICAL VARICOCELECTOMY IMPROVE CLINICAL OUTCOMES IN ALL VARICOCELE GRADES.

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OBJECTIVE: To assess the impact of varicocele grade on microsurgical varicocelectomy.

DESIGN: Retrospective data collection.

MATERIALS AND METHODS: Men between 2008 and 2020 diagnosed with varicocele were reviewed. We included men who had documented sonographic assessment and underwent microsurgical varicocelectomy (unilateral or bilateral) at Weill Cornell by a single high volume surgeon. Patients were stratified according to varicocele grade based on physical examination. Clinical outcomes (sperm concentration (SC), TUNEL and testosterone (T) levels) were compared among men pre-operatively and post-operatively using the nonparametric Wilcoxon signed-ranked test (Stata v14).

RESULTS: A total of 396 patients were included. Median age was 36 (IQR 31-42) and median BMI was 25.3 (IQR 23.1-27.6). On physical exam, median orchidemeter assessed testis size was 18cc (IQR 15-20) on the right and 15cc (IQR 12-18) on the left. 136 patients underwent varicocelectomy on the left (34.3%), 8 on the right (2.0%), and 252 bilateral (63.6%). Of these men, 389 had documented physical exam grade on the left (Grade III: 55.8%, Grade II: 25.7%, Grade I: 9.3%, None: 9.3%) and on the right (Grade III: 5.1%, Grade II: 21.1%, Grade I: 21.1%, None: 52.7%). For Grade III varicoceles, T, TUNEL and SC has significant improvement on the left ($p<0.05$, $p<0.01$, $p<0.0001$, respectively) and SC on the right ($p<0.05$). For grade II varicoceles, significant differences were seen in T on the left ($p<0.0001$) and SC on the right ($p<0.01$). Patients with grade I had significant improvement in T on the left ($p<0.01$) and both T and SC on the right ($p=0.001$, $p<0.05$, respectively) (Table 1).

CONCLUSIONS: Microsurgical varicocelectomy improves testosterone levels and semen concentration irrespective of clinical grade. Repair of grade III varicocele had statistically significant improvements in all three parameters: SC, T and TUNEL.

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URINE-DERIVED STEM CELLS DERIVED EXOSOMES FACILITATE ENDOGENOUS SPERMATOGENESIS RESTORATION OF BUSULFAN-INDUCED NON-OBSTRUCTIVE AZOOSPERMIA MICE.

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OBJECTIVE: Non-obstructive azoospermia (NOA) is the most severe issue without effective treatments in male infertility. The aim of this study is to investigate whether transplantation of urine-derived stem cells (USCs) or USCs-exosomes (USC-exos) could promote endogenous spermatogenesis restoration in a busulfan-induced NOA mice model.

DESIGN: Animal study was designed.

MATERIALS AND METHODS: USCs were cultured and characterized by flow cytometry. High-density USCs were cultured in hollow fiber bioreactor for exosomes collection. USC-exos were isolated from USCs conditional media and identified by transmission electron microscopy, western blot and Flow NanoAnalyzer. USC-exos exhibited a sphere- or cup- shaped morphology with a mean diameter of 66.5±16.0 nm and expressed CD63 and CD9. USCs and USC-exos were transplanted into interstitial space in testes of NOA mice (40 mg/kg) as following groups: Normal group, groups treated with no injection, PBS or USCs on the 0 days after busulfan administration respectively, and groups treated with no injection, PBS, USCs or USC-exos on the 36 days after busulfan treatment separately.

RESULTS: Thirty days after USCs and USC-exos transplantation, the spermatogenesis was restored by both USCs and USC-exos in NOA mice of 36 days after busulfan-treated confirmed by immunofluorescence staining and hematoxylin and eosin (H&E) staining. Moreover, spermatogenic genes (*Pou5f1*, *Prm1* and *SYCP3*) and spermatogenic protein UCHL1 were significantly increased in both USCs 36 and USC-exos36 group compared to PBS treated group demonstrated by using *qRT-PCR* and western blot analysis. However, transplantation of USCs at day 0 after busulfan treatment didn't improve the spermatogenesis of NOA mice.

CONCLUSIONS: Our study demonstrated that USCs could facilitate endogenous spermatogenesis restoration of busulfan-induced NOA mice through paracrine exosomes, but could not protect the mice testicles at early stage of destruction caused by busulfan. This study provides a novel insight in the treatment of NOA.

SUPPORT: no

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THE IMPACT OF ADVANCED MALE AGE ON ASSISTED REPRODUCTION PROCEDURES' OUTCOMES.

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OBJECTIVE: Male reproductive aging may affect several determinants in ART outcomes. The literature usually considers the age of 40 as the upper limit. After this period, the semen seems to have changes in qualitative factors that may modify fertility and cause adverse events in future generations. Does male age influence assisted reproduction techniques when laboratory and clinical parameters are evaluated?

DESIGN: A retrospective cross-sectional study was conducted using a database from an assisted reproduction clinic, in Brazil, between 2015 and 2018. A total of 2125 procedures met the eligible criteria.

MATERIALS AND METHODS: The sample was divided into two groups according to male age: group 1 (n=1429) ≤40 years and group 2 (n=696) men ≥41 years. ICSI was performed in all cases. Mann-Whitney test, Student's t-test and Chi-square test were applied for statistical analysis. Data were adjusted for "female age" and "vasectomy" by Analysis of Covariance (ANCOVA), when applicable. The null hypothesis was rejected when $p < 0.05$.

RESULTS: A decrease in seminal volume and sperm motility was observed in group 2 (p=0.001), with no changes in seminal concentration (p>0.05). A higher number of cleavage embryos were transferred in group 2, while a higher number of blastocysts were transferred in group 1 (p≤0.001). Apgar index in the first and fifth minutes were lower in group 2 for single and twin pregnancies (p<0.05). The IVF indication due to oligospermia was the highest in group 1, while the highest in group 2, was the vasectomy.

CONCLUSIONS: Advanced male age appears to be a possible influential factor on seminal characteristics, specially sperm volume and motility. Hence, even though previous literature points out female age as the main IVF outcome influencer, male age should not be left aside.

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THE USE OF SERUM INHIBIN B TO ASSESS RECOVERY OF SPERMATOGENESIS IN MALES WITH HISTORY OF RECENT EXOGENOUS ANDROGEN EXPOSURE.

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OBJECTIVE: Predicting adequate recovery of spermatogenesis in post-vasectomy males seeking vasectomy reversal or sperm aspiration in a setting of recent testosterone replacement therapy (TRT) is clinically challenging. The time to recovery of spermatogenesis after cessation of TRT varies from 6 months to 2 years, or never in some cases. FSH levels are not reliably predictive as they are affected by TRT itself and common treatments administered post TRT. Diagnostic aspirations can confirm the presence of spermatogenesis, though they carry inherent procedural risk and cost without producing any usable sperm. Accurate, non-invasive, and predictive screening is needed. This study assesses the value of serum inhibin B levels in accurate prediction of the return of spermatogenesis in this unique population.

DESIGN: An IRB approved retrospective case series of ten consecutive post-vasectomy patients with recent testosterone replacement therapy (TRT) who underwent a vasectomy reversal or sperm aspiration procedure between January 1st, 2016 and March 1st, 2018 performed by a reproductive urologist.

MATERIALS AND METHODS: FSH, testosterone & inhibin B levels were followed after cessation of TRT. A cutoff value of serum inhibin > 130 pg/mL was used to predict the presence of adequate spermatogenesis for timing of surgical intervention with vasectomy reversal or sperm aspiration procedures. Sperm motility and density (number of sperm per high performance field) were assessed in the extracted testicular tubules in all sperm aspiration procedures. For vasectomy reversals, intraoperative vasal/epididymal fluid was assessed for the presence of sperm and/or sperm parts. Post-reversal total sperm counts were measured using standard semen analysis testing by independent laboratories.

RESULTS: Evidence of adequate spermatogenesis was noted in eight patients with inhibin B levels > 130 pg/mL around the time of their procedures (five sperm aspirations, three vasectomy reversals). Decreased spermatogenesis was noted in two patients with inhibin B levels of < 130 pg/mL (both were sperm aspiration procedures). Time to normalization of inhibin B ranged from 1 to 15 months. Shorter times (1 to 6 months) were seen in men who used injectable testosterone and longer times (9 to 15 months) for those with implanted testosterone pellets.

CONCLUSIONS: Serum inhibin B levels provided accurate, non-invasive prediction of the recovery of spermatogenesis in males with recent TRT. If validated in larger studies, serum inhibin B levels could help optimize the timing of vasectomy reversals and sperm aspiration procedures.

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IMPACT OF SPERM DNA FRAGMENTATION ON PRE- AND POST-WASH SEMEN SAMPLES AND PREGNANCY OUTCOME WITH INTRACYTOPLASMIC SPERM INJECTION.

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OBJECTIVE: The spermatozoa nuclear component especially it's DNA integrity is essential for normal fertilization, pregnancy & embryo development. Currently sperm DNA fragmentation (SDF) testing is one advanced sperm function test used along other conventional tests to evaluate male infertility.We aim to assess the impact of SDF on pre- & post-wash semen parameters and to investigate effect of various SDF cut-off values on pregnancy outcome with Intracytoplasmic sperm injection (ICSI).

DESIGN: Retrospective, Chart review.

MATERIALS AND METHODS: The charts of 2277 patients who underwent ICSI were reviewed. 481 infertile men who had SDF testing were included. Patients demographic & laboratory data along with ICSI cycle

outcome were included. Semen samples & SDF were analyzed according to WHO 5thedition guidelines & sperm chromatin dispersion (Halosperm kit, Halotech, Madrid, Spain) respectively. Patients were divided according to SDF cut-offs; <20, 20-30 & >30%. Variables were reported as mean ± SE and compared using Kruskal Wallis Test. P value of <0.05 was considered statistically significant

RESULTS: The mean patient age was 36.88 ± 0.362, while mean SDF was 25.41± 0.72. The pre & post wash semen parameters in patients with SDF cut-offs <20, 20-30 & >30% were compared (Table 1). Significantly worse results were obtained with increasing SDF cut-offs for pre- & post-wash sperm concentration, total motility & post-wash normal morphology.

SDF was significantly inversely correlated with **pre wash parameters** (concentration: r -.140, p=o.oo3; total Motility: r -.282, p<0.001; normal morphology: r -.143, p=0.003) and **post wash parameters** (concentration: r -.156, p=o.oo1; total Motility: r -.218, p<0.00; normal morphology: r -.140, p=0.002)

The clinical pregnancy rate decreased with increasing SDF cut-offs (44.4% with SDF <20%, 31.4% with SDF 20-30% and 24.3% with SDF >30), though the result was not statistically significant

CONCLUSIONS: SDF negatively impacts pre-& post-processing semen parameters for patients undergoing ICSI. This may influence ICSI pregnancy rate, though the impact was not statistically significant in this cohort.

RESULTS: 390 patients performed TESE-ICSI cycles with their own oocytes, with a mean time postvasectomy of 11.7 years (CI95% 11.1-12.3) and a BMI of 26.5 kg/m^2 (CI95% 26.1-27.0). Of all of them, 130 (33.9%) were smokers. No statistical differences were found between groups based on time since vasectomy in LBR per ET (Q1:30.5%, Q2:40.0%, Q3:40.7%, Q4:26.9%) and per COS (Q1:21.3%, Q2:23.3%, Q3:28.1%). However, significantly lower live birth rate per couple (p=0.02) was shown in the group with the highest vasectomy time: Q1:41.4%, Q2:48.3%, Q3:52.3%, Q4:31.2%. No significant differences were found in CLBR depending on the number of embryos transferred comparing post-vasectomy periods. When two embryos were replaced, CLBR were in Q1:34.5% and in Q4:27.7% and reached 52.5%(Q1) and 48.7%(Q4) when four embryos were consumed, increasing the chances of having a newborn by 18% in the first group and 21% in Q4. When up to 7 embryos were replaced, the CLBR was 72.4% in Q1 and 74% in Q4. When considering the BMI, none of the LBR compared were statistically significant. CLBR were higher in the lower BMI quartiles (Q2:46.5 % *vs* Q4:28.6% with two embryos replaced, Q2:55.0% *vs* Q4:59.9% and Q2:63.4% *vs* Q4:67.6% when four and even six embryos were transferred, respectively), without statistically significant differences. The live birth rate of smokers was comparable to those of non-smokers: 33.7% *vs* 33.8% per ET, 22.5% *vs* 23.2% per COS, and 43.8% *vs* 42.50% per couple. Cumulative LBR per embryo was similar in both groups with no statistical difference between them (p>0.05).

Parameters	Total	SDF <20	SDF 20-30	SDF >30	P Value
Pre wash Concentration (M/ml)	38.94 ± 1.69	45.24 ± 2.79	35.82 ± 2.61	30.57 ± 2.87	0.016
Pre wash Total Motility %	38.61 ± 0.9	44.18 ± 1.28	37.82 ± 1.62	29.26 ± 1.68	<0.001
Pre wash Normal Morphology %	12.49 ± 0.61	12.01 ± 0.78	14.53 ± 1.35	11.18 ± 1.27	0.121
Post Wash Concentration (M/ml)	13.93 ± 0.63	15.96 ± 0.95	13.854 ± 1.12	9.95 ± 1.16	<0.001
Post Wash Total Motility %	4.21 ± 0.27	5.24 ± 0.45	3.99 ± 0.43	2.45 ± 0.47	<0.001
Post Wash normal Morphology %	12.31 ± 0.65	12.12 ± 0.89	13.36 ± 1.31	11.53 ± 1.37	0.010

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TIME SINCE VASECTOMY, BUT NEITHER SMOKING NOR BODY MASS INDEX (BMI) INFLUENCE IN VASECTOMIZED MEN REPRODUCTIVE OUTCOMES UNDERGOING TESTICULAR SPERM EXTRACTION WITH INTRACYTOPLASMIC SPERM INJECTION (TESE-ICSI). Nicolas Garrido, PhD,[1] Lorena Valls, M.D,[2] Irene Hervas, MSc,[3] Rocio Rivera-Egea, PhD,[4] Maria Gil Julia, MSc, MRes,[3] Jose Maria Martinez-Jabaloyas, M.D[4] [1]IVI Foundation - IIS La Fe Biomedical Research Institut, Valencia, Spain; [2]Hospital Clínico de Valencia, Valencia, Spain; [3]IVI Foundation - IIS La Fe Biomedical Research Institute, Valencia, Spain; [4]IVIRMA Valencia, Valencia, Spain.

OBJECTIVE: Vasectomy is the most common male contraceptive method, but changes in personal circumstances may result in regret and consideration of a reversal or undergoing an assisted reproduction treatment (ART). Although suspected relevant, little is known about the influence of factors conditioning their reproductive outcomes and data available so far are limited. This information would aid counseling and medical care. The objective of this study is to evaluate if time since the seminal duct was intervened, BMI and smoking habits negatively affect the reproductive success of TESE-ICSI

DESIGN: Retrospective study.

MATERIALS AND METHODS: Data from vasectomized patients who underwent TESE-ICSI were assessed. Quartiles (Q_n) were established to compare time since vasectomy and BMI, and tobacco consumption. Main outcome was live birth rate (LBR) per embryo transfer (ET), per controlled ovarian stimulation (COS) and per couple. Chi-square test were applied to compare proportions and Survival curves using the Kaplan Meier and Breslow's tests were built to compute the cumulative live birth rate (CLBR) considering the number of embryos consecutively transferred until a newborn was achieved.

CONCLUSIONS: The time since the vasectomy renders worse reproductive success rates per patient, while BMI and tobacco consumption seem not to be influencing outcomes in a program of ICSI using own oocytes from vasectomized males.

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THE IMPACT OF HIGH SPERM CHROMATIN FRAGMENTATION ON INTRAUTERINE INSEMINATION OUTCOME. Mounia Haddad, M.D., Derek Keating, B.A., Alessandra Parrella, M.Sc., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To evaluate how the genomic integrity of spermatozoa affects IUI pregnancy outcomes in couples with unexplained infertility.

DESIGN: During the last 4 years, 132 couples with unexplained infertility who were undergoing IUI treatment at our center were included. In these couples, the male partners had normal semen parameters and the female partners had negative infertility workups. To identify an eventual male factor, we screen all men for sperm chromatin fragmentation (SCF) assay. IUI clinical outcome was assessed and compared between couples with normal and abnormal SCF.

MATERIALS AND METHODS: Men with normal semen parameters consented to have their SCF measured by a terminal deoxynucleotidyl dUTP transferase nick-end labeling (TUNEL) assay. At least 500 spermatozoa were assessed per patient, and a threshold of ≤15% was considered normal. Female partners (≤37 years old) with negative infertility workups underwent IUI in a natural or stimulated cycle.

RESULTS: Of 335 IUI cycles, 261 were carried out in 91 couples in which the male partner had normal SCF. The average maternal age was 34.1 ± 3

years, and the average paternal age was 36.3 ± 4 years. The men had the following semen parameters: a volume of 2.3 ± 1 mL, a concentration of 46.2 ± 29 x10^6 per mL, 43.8 ± 3% motility, and an average SCF of 9.5 ± 3%. There were 29 documented clinical pregnancies (29/261, 11.1%), determined by the presence of at least one fetal heartbeat detected by ultrasound; 9 patients have delivered babies, 18 pregnancies are ongoing, and 2 were spontaneous abortions.

A total of 41 couples in which the male partner (36.9 ± 5.9 years) had abnormal SCF underwent 96 IUI cycles (maternal age, 33.5 ± 2.7 years). The men had the following semen parameters: an average SCF of 21.7 ± 6 ($p<0.0001$), a volume of 2.6 ± 1 mL, a significantly lower concentration of 32.1 ± 20 x10^6, and a lower motility of 44.9 ± 4%. These IUI attempts yielded a clinical pregnancy rate of only 4.1% (4/96; $p<0.0001$); 3 pregnancies are ongoing, and 1 patient has delivered.

CONCLUSIONS: In couples with unexplained infertility in which the male partner has normal semen parameters and the female partner has a negative infertility workup and is of young reproductive age (≤37 years old), SCF screening can help identify a stealth male factor. An assessment of the genomic integrity of the male gamete may serve as a useful tool for predicting pregnancy outcome and tailoring reproductive treatments.

REFERENCES: None

SUPPORT: None

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THE IMPACT OF SPERMATOZOA RETRIEVED FROM DIFFERENT REGIONS OF THE EPIDIDYMIS ON REPRODUCTIVE OUTCOMES.

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OBJECTIVE: To determinate the area of the epididymis that yields spermatozoa most capable of supporting embryonic development.

DESIGN: During the last 9 years, 46 men affected by obstructive azoospermia (OA) consented to have spermatozoa surgically retrieved from three areas of the epididymis: caput, corpus, and cauda. Sperm characteristic were analyzed and compared among the retrieval sites that were used for ICSI with their female partners. Clinical outcomes were compared among the different sources of spermatozoa.

MATERIALS AND METHODS: Consenting men underwent epididymal sperm retrieval, with specimens evaluated according to WHO 2010 criteria. A total of 36 specimens retrieved from the caput, 7 from the corpus, and 3 from the cauda were used for ICSI, controlling for maternal age (≤37 years old). Fertilization, implantation, and delivery rates were assessed and compared for all three areas of the epididymis. Unpaired *t* and Fisher's exact tests were used to compare outcomes. A *P* value of <0.05 was considered significant.

RESULTS: A total of 46 men were divided into three groups according to the spermatozoa source used: caput, corpus, and cauda. Paternal age was comparable among the three groups (39.7± 12). Average and standard deviation of spermatozoa concentration was 35.1± 39 in the caput, 40±29 in the corpus, and 30.2± 59 x10^6/ml in the cauda. The mean motility was 15.8±15% in the caput, rising to 40.1±29% in the corpus ($P<0.01$), and decreasing to 7±12% in the cauda ($P<0.05$). The mean numbers of injected oocytes were comparable at 12.7, 11, and 12.5, for the caput, corpus, and cauda, respectively. The fertilization rate with specimens from the caput was 65.8% (303/460), it rose to 77.6% (59/76) with specimens from the corpus ($P<0.05$), and reached the highest level at 88% (44/50, $P<0.05$) with spermatozoa from the cauda. The proportion of high-quality embryos was 73.5% (25/34) from sperm retrieved from the caput, 75% (3/4) from the corpus, and reached 100% (3/3) from the cauda. There was a trend of increasing implantation rates through the regions of the epididymis. With specimens retrieved from the caput, the implantation rate was 34.8% (23/66), it rose to 44.4% (4/9) from the corpus, and increased to 57.1% (4/7) from the cauda. The same trend was observed for delivery rates. In cycles using caput spermatozoa, the delivery rate was 48.4% (16/33) with 5.8% (1/17) pregnancy loss. In cycles using spermatozoa from the corpus, the delivery rate was 75% (3/4) with no pregnancy loss. Ultimately, the cycles with cauda had the highest delivery rate, with 100% (3/3).

CONCLUSIONS: This study supports the current knowledge that while progressing through the epididymal regions, testicular spermatozoa undergo structural and metabolic changes that translate in phenotypic and functional processes. During the epididymal journey, spermatozoa appeared to enhance their ability to support embryonic development and implantation. Although they have poorer kinetic characteristics, we have found that spermatozoa retrieved from the cauda epididymis yield higher fertilization and pregnancy rates. Larger studies are needed to confirm these findings.

SUPPORT: None

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THE ROLE AND MECHANISM OF SPERMATOGONIAL STEM CELLS NECRPTOSIS IN MOUSE MODEL OF HYPOSPERMATOGENESIS.

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OBJECTIVE: To investigate the effects and mechanisms of necroptosis of Spermatogonial Stem Cells(SSCs) on testicular spermatogenesis in a mouse pathological model.

DESIGN: Animal study was designed.

MATERIALS AND METHODS: The C57BL/6 mouse model was induced by two intraperitoneal injections of busulfan with a three-hour interval. The changes of spermatogenesis were observed at at different time points (0, 9, 18, 27, and 36 days). Meanwhile, Western blotting and immunofluorescence were used to test the expression of UCHL1 (a SSCs marker) and the core components of necroptosis, including RIPK3 and pMLKL

RESULTS: The testicular histology was dramatically different on day 18, with frequent disarrangement of spermatogenic cells, the reduced height of the seminiferous epithelium and SSCs depletion and all the germ cells including SSCs were cleared by day 36. Further analysis showed that the appearance of pMLKL in testes accelerated the cell death of SSCs, resulting in the loss of $UCHL1^+$ SSCs and damage to spermatogenesis in mice with busulfan-induced gonadotoxicity.

CONCLUSIONS: Two intraperitoneal injections of busulfan at a dose of 40 mg kg^{-1} with a three-hour interval could establish a safe, stable and efficient mouse model of hypospermatogenesis. The RIPK1/RIPK3/pMLKL pathway mediates SSC necroptosis resulting in the decreased spermatogenic function in mouse testes.

SUPPORT: no

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REPRODUCTIVE OUTCOMES OF ADVANCED PATERNAL AGE MEN USING TESTICULAR SPERMS IN ASSISTED REPRODUCTIVE CYCLES?.

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OBJECTIVE: To evaluate reproductive outcomes of Advanced Paternal Age (APA) men using Surgically Retrieved Testicular Sperm (SRS) in Assisted Reproductive Technology (ART) cycles.

DESIGN: Retrospective Observational Longitudinal Cohort study In Private Teaching ART centre.

MATERIALS AND METHODS: Men over the age of 40 were classified as APA and recruited in this study. Age range of male partners was in between 40-50 years. Couples where women were young (<37yrs age) and male partners underwent SRS in ART cycles were considered for this study during January 2014 to July 2019 (n=103). Couples undergoing self-gamete cycles were considered for the study and couples undergoing PGT-A were excluded from the study.

APA men & Younger women in whom ejaculated sperm was used in ART cycles acted as control group for this study (n=71).

All women underwent controlled ovarian stimulation and Transvaginal oocyte retrieval (OPU). Male partner's underwent either fresh SRS on OPU day or frozen SRS was used for ICSI as per our clinics standard operating procedures (SOP). Embryos were cultured till blastocyst stage and a freeze all policy was adopted. Two Blastocysts were transferred in a Frozen Embryo Replacement Cycle (FET).

Reproductive outcomes were compared between the two groups.

RESULTS: The reproductive outcomes for Study Vs Control group were as follows:

Clinical Pregnancy Rate – 45.71% Vs 56.16% (p value 0.1767)
Implantation Rates -33.6% Vs 42.15% (p value 0.2525)
Miscarriage Rates – 15.71% vs 8.22% (p value 0.1457)
Live Birth Rates – 27.14% vs 53.33% (p value 0.0005)
Multiple Pregnancy rate – 21.42% Vs 5.48% (p value 0.0038)

Data from this study is suggestive that, testicular sperms from APA men could alter reproductive outcomes in ART cycles. APA men undergoing ART cycles with SRS need to be counselled appropriately about the limitations. Role of PGT-A in such group of men to optimize reproductive outcomes needs further research.

CONCLUSIONS: Testicular Sperm of advanced paternal age men seems to have detrimental effects on reproductive outcomes.

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A MORE EFFICIENT METHOD FOR RECIPIENT PREPARATION IN SPERMATOGONIAL STEM CELL TRANSPLANTATION IN MICE INDUCING BY INTRAPERITONEAL INJECTION OF BUSULFAN. Guihua Liu, Ph.D.,[1] Xing Yang, Ph.D.,[1] Tingting Li, Doctor[2] [1]The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; [2]Reproductive Medicine Research Center, Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: To establish an efficient and hypotoxic spermatogonial stem cells (SSCs) recipient preparation method in mice.

DESIGN: Experimental laboratory study.

MATERIALS AND METHODS: A total of 70 twelve-week-old male C57BL/6J mice were performed intraperitoneal injection of busulfan at different doses (20, 30 and 40mg kg^{-1} body weight) and investigated the effects 36 days later. And further analysis the effects at the different time points (0, 9, 18, 27, 36, 45, 63 days) after busulfan-treated at the total of dose of 40 mg kg^{-1} .Survival rate, testicular histology, Western Blot analysis and immunofluorescence of UCHL1, levels of inhibin B in serum and growth factors gene expressions in testes.

RESULTS: The survival rates of the mice after the administration of different doses of busulfan were 100%. Compared to control or that in lower dose of busulfan (20 or 30 mg kg^{-1}), mice treated with 40 mg kg^{-1} busulfan was optimal used to recipient preparation, by depleting substantially all of the germ cells and a friendly niche microenvironment in testes 36 days later after busulfan-treated. In addition, long-term observation at the day 63, there was still hardly germ cell in testes.

CONCLUSIONS: Double intraperitoneal injections of busulfan (40 mg kg^{-1} in total) at an interval of 3 hours to mice was an efficient and hypotoxic method for recipient preparation in SSCs transplantation, which could promote the exploration of the mechanism of azoospermia and the treatment of infertility.

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PCA3 AND TMPRSS:ERG ASSESSMENT IN SEMEN: RESULTS OF A PHASE I STUDY. Nahid Punjani, MD MPH,[1] Russell P. Hayden, M.D.,[2] Peter Y. Cai, MD,[1] John T. Wei, MD,[3] Javed Siddiqui, MS,[3] Vanessa L. Dudley, MSHS,[2] Miriam Feliciano, BSc,[2] Marc Goldstein, M.D.[2] [1]Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY; [2]Center for Male Reproductive Medicine and Microsurgery, Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY; [3]University of Michigan, Ann Arbor, MI.

OBJECTIVE: To assess if quantification of PCA3 and TMPRSS2:ERG levels in semen provides an improved prostate cancer assay to be used in prostate cancer algorithms, commencing with a phase I feasibility study.

DESIGN: Phase I Clinical Trial.

MATERIALS AND METHODS: Research ethics approval was obtained for our phase I feasibility study. Patients with semen volumes greater than 3mL were enrolled to donate discarded semen specimens. Our collaborators at the University of Michigan have developed a unique assay to test PCA3 and T2:ERG in human semen. De-identified samples were processed in two different ways to determine the most effective methods for shipment and minimization of sample degradation to Michigan, but also to determine if the presence of absence of sperm was required for the PCA3/T2:ERG assay.

RESULTS: Data was collected prospectively on a total of 8 patients with semen volumes greater than 3mL. Four patients had no centrifugation of their samples (sperm present) and the other four were centrifuged and separated (sperm absent). PCA3 and T2:ERG levels were assessed in all patients. The T2:ERG levels in the sperm present samples were 383, 1519, 172 and 166 c/mL with an average of 560 c/mL. In the sperm absent samples, T2:ERG levels were 137, 13567, 300, 870 c/mL with an average of 3719 c/mL.

CONCLUSIONS: Our results indicate that our PCA3/T2:ERG semen assay is able to detect T2:ERG in both the presence and absence of sperm. We also demonstrate feasibility of specimen shipment. Phase II studies are underway to validate the assay in prostate cancer patients, define appropriate cut-offs, as well as further optimization including whether digital rectal massage is necessary. This assay may have the potential to be a game-changer for prostate cancer screening, obviating the need for prostate biopsy in a large number of men.

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NEWBORN RATE IS NOT IMPAIRED BY TIME FROM VASECTOMY, SMOKING AND BODY MASS INDEX (BMI) IN COUPLES WITH VASECTOMIZED MALE REQUIRING AN ASSISTED REPRODUCTIVE TECHNIQUE USING OOCYTE DONATION (OD). Irene Hervas, MSc,[1] Lorena Valls, M.D,[2] Nicolas Garrido, PhD,[3] Rocio Rivera-Egea, PhD,[4] Maria Gil Julia, MSc, MRes,[1] Jose Maria Martinez-Jabaloyas, M.D[4] [1]IVI Foundation - IIS La Fe Biomedical Research Institute, Valencia, Spain; [2]Hospital Clínico de Valencia, Valencia, Spain; [3]IVI Foundation - IIS La Fe Biomedical Research Institut, Valencia, Spain; [4]IVIRMA Valencia, Valencia, Spain.

OBJECTIVE: The most employed definitive contraceptive method for men is vasectomy, although a non-negligible percentage of vasectomized men have regrets and express a renewed desire to have a child. In the case a relevant female factor infertility is present, OD has emerged the last years as a valid and widely employed option. In these cases, the main alternative is testis sperm extraction (TESE) together with intracytoplasmic sperm injection (ICSI) technique. To date there is little reports evaluating the clinical outcomes of vasectomized patients requiring the use of OD and the factors that may adversely affect reproductive outcome, such as time since the vasectomy, smoking or high BMI. The aim of this study is to analyze the influence of these male risk factors on TESE-ICSI outcomes from vasectomized men in an OD program.

DESIGN: Retrospective study.

MATERIALS AND METHODS: Data from couples who underwent TESE-ICSI treatment (using donor' oocytes) were assessed, and variables of interest (time since vasectomy, BMI and smoking) were compared using quartiles (Q_n). The live birth rate (LBR) by embryo transfer (ET), by complete donation cycle (CDC) and by couples was analyzed. Proportions were compared with Chi-square tests. Survival curves based on Kaplan Meier and Breslow tests were constructed to calculate the cumulative live birth rate (CLBR) per number of embryos transferred consecutively until the first newborn.

RESULTS: From 123 couples, the average male of BMI was 27.0 kg/m^2 (CI95% 26.3-27.7) and 21.8% consumed tobacco. Mean time since surgery was 13.8 years (CI95% 12.0-14.5). Based on time since vasectomy, no statistical differences were found between groups in LBR per ET (Q1:25.4%, Q2:34.4%, Q3:36.20%, Q4:42.6%), per CDC (Q1:34.1%, Q2:41.2%, Q3:48.60%, Q4:60.6%) and per couple (Q1:50.0%, Q2:58.3%, Q3:68.0%, Q4:62.5%). The CLBR comparing post-vasectomy periods were, when two and four embryos replaced, 39.2% (Q1) and 44.0% (Q3), and 46.0% (Q1) and 69.5% (Q3) respectively, but it was non-significant. None of the LBR compared were statistically significant by BMI groups by ET, by CDC and by couple. The cumulative LBR was not influenced when compared based on the BMI: Q:36.0%, Q2:47.6%, Q3:40.7% and Q4:33.2%, and Q1:64.4%, Q2:66.7%, Q3:78.6% and 65.6% when two and four embryos were replaced accordingly. The smoking groups presented comparable LBR with non-smokers males: 34.1% *vs* 35.7% per ET, 53.6% *vs* 44.1% por CDC, and 57.7% *vs* 60.2% per couple. Cumulative livebirth rate per embryo transferred was no statistically significative among smokers and non-smokers when two embryos replaced (43.8% *vs* 37.7%), three embryos (50.1% *vs* 47.6%) and four embryos (66.7% *vs* 66.3%) were transferred.

CONCLUSIONS: The time since the vasectomy and the male risk factors analyzed, BMI and tobacco consumption, seem not to impair the probability

of achieve a newborn in couples with vasectomized males undergoing an ICSI treatment with donated oocytes.

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EVALUATION OF A NEWLY ENGINEERED DEVICE FOR PENILE VIBRATORY STIMULATION IN MEN WITH SPINAL CORD INJURY. Emad Ibrahim, MD, HCLD(ABB),[1] Christian F. S. Jensen, MD,[2] Ivan Sunara, MD,[3] Kajal Khodamoradi, MS,[1] Teodoro C. Aballa, MS,[1] Stacy Elliott, MD,[4] Jens Sonksen, MD, PhD,[5] Dana A. Ohl, MD,[6] Claes Hultling, MD, PhD,[3] Charles M. Lynne, MD,[1] Stephen W. J. Seager, DVM,[7] Nancy L. Brackett, PhD, HCLD[1] [1]University of Miami Miller School of Medicine, Miami, FL; [2]University of Copenhagen, Herlev, Denmark; [3]Karolinska Institute, Stockholm, Sweden; [4]University of British Columbia, Vancouver, BC, Canada; [5]Herlev & Gentofte Hospital, University of Copenhagen, Herlev, Denmark; [6]University of Michigan, Ann Arbor, MI; [7]National Rehabilitation Hospital, The Plains, VA.

OBJECTIVE: Most men with spinal cord injury are anejaculatory and will require medical assistance to obtain their sperm in order to achieve biologic fatherhood. Penile vibratory stimulation is generally recognized as the first line of treatment for semen retrieval in anejaculatory men with spinal cord injury. The purpose of this study was to evaluate the performance of a newly-engineered device available in October 2019 (Ferticare 2.0) for penile vibratory stimulation in men with spinal cord injury.

DESIGN: Cohort study.

MATERIALS AND METHODS: The Ferticare 2.0 device was applied to 15 men with spinal cord injury in a three-step protocol. Step 1: one device (2.5mm amplitude, 100 Hz) was applied to the glans penis for 2 minutes. Step 2: If no ejaculation occurred, the amplitude was increased to 4.0mm (100 Hz) and the device similarly applied. Step 3: If no ejaculation occurred, two devices, each 2.5mm and 100 Hz were applied to the dorsum and frenulum of the glans penis. Subjects at risk for autonomic dysreflexia were pretreated with sublingual nifedipine (20mg), 15 minutes prior to simulation. Blood pressure and other symptoms of autonomic dysreflexia were monitored. Following stimulation, subjects answered a questionnaire about their experience with the device. The measured distance from zero of a vertical mark on a 10 cm line indicated a rating between 0 and 10. Questionnaires were not requested from subjects who did not respond to PVS.

RESULTS: Thirteen of 15 subjects had antegrade ejaculation with the device. Blood pressure and other symptoms of autonomic dysreflexia were well-managed. No adverse events occurred. The two subjects that were failures to PVS with other devices were also failures to PVS with the Ferticare 2.0. Two of the 15 subjects had retrograde ejaculation (subjects 6 and 8). The remaining 13 subjects had no retrograde ejaculation, including the two PVS failures. All subjects commented they would recommend the device to other men with spinal cord injury.

CONCLUSIONS: A newly engineered device, the Ferticare 2.0, is safe and effective for inducing ejaculation in men with spinal cord injury.

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ASSOCIATION OF THE SERUM METABOLOMIC PROFILE BY NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY WITH SPERM PARAMETERS: A CROSS SECTIONAL STUDY OF 325 MEN. Karema Alrashid, MD,[1] Scott M. Nelson, MD, PhD,[1] Deborah A. Lawlor, PhD,[2] Mary Ann Lumsden, MD,[1] Neil Goulding, PhD[2] [1]University of Glasgow, Glasgow, United Kingdom; [2]MRC Integrative Epidemiology Unit at the University of Bristol, Bristol, United Kingdom.

OBJECTIVE: Are 155 circulating metabolic measures relevant to lifestyle and metabolic health associated with sperm parameters (as measured by concentration, motility and total motile sperm count (TMSC))?

SUMMARY ANSWER: An extensive range of metabolites were not associated with semen parameters, however, several metabolites exhibited differential direction of associations with the odds of a low TMSC and warrant replication.

WHAT IS KNOWN ALREADY: Robust identification of additional modifiable and non-modifiable risk factors for poor semen quality have had limited success. An alternative approach to identify risk factors for an abnormal semen analysis would be to examine circulating metabolites by means of a high throughput cost efficient NMR platform, which may provide insights into downstream factors as well as more upstream exposures.

DESIGN: Cross-sectional study of 325 men prospectively recruited between 1 April 2017 and 31 March 2019.

MATERIALS AND METHODS: Men intending to undergo assisted conception at a University Hospital, had a detailed demographic, lifestyle, fertility and medical history and semen analysis. Non-fasting serum lipids, lipoprotein subclasses, and low-molecular weight metabolites (including amino acids, glycolysis and inflammatory markers) were quantified by NMR spectroscopy. Multivariable linear and logistic regression were used to examine the associations of serum metabolic profiles (exposures), with functional sperm concentration, motility and TMSC (outcomes) with adjustment for confounders.

RESULTS: Participants were mean 37.2 (SD 5.7) years and had a median sperm concentration of 35 million/ml (IQR 15, 69 million/ml) and median motility of 53% (IQR 42,67). 76% of men had a TMSC >15 Million, 10% 5-15 Million and 14% <5 Million. In both univariate and confounder adjusted analyses an extensive range of lipids and lipoproteins, glycolysis related metabolites, amino acids, ketone bodies, creatinine or albumin, did not show strong statistical evidence of associated with sperm concentration, motility, or the odds of having a reduced or low TMSC (all $P_{Bonferroni} > 0.0029$).

LIMITATIONS: Sperm parameters were measured on a single sample, in accordance with recent WHO guidance, and by non-automated techniques which may have introduced random measurement error that could have attenuated to the null.

CONCLUSIONS: This study provides preliminary data on a range of metabolic pathways and their association with semen parameters. The differential direction of associations with sperm motility and potentially of important clinical effect sizes warrant further exploration and replication in a larger prospective study.

Keywords: semen analysis, sperm, metabolomics

P-697 4:30 PM Tuesday, October 20, 2020

LEPTIN SECRETED FROM HUMAN LEYDIG STEM CELLS TARGETS HEDGEHOG SIGNALING TO AUGMENT ENDOGENOUS FUNCTION. Himanshu Arora, PhD,[1] Kajal Khodamoradi, MS,[1] Madhumita Parmar, BS,[1] Rehana Qureshi, PHD,[2] Ranjith Ramasamy, M.D[1] [1]University of Miami Miller School of Medicine, Miami, FL; [2]University of Miami Miller School of Medicine, MIAMI, FL.

OBJECTIVE: Although testosterone deficiency (TD) can be present among 1 in 5 men 40 years or older, the factors responsible for TD remain largely unknown. Leydig cells produce testosterone in the testes under the pulsatile control of luteinizing hormone (LH) from pituitary gland. Leydig stem cells have the potential to differentiate into adult Leydig cells that can lead to increasing testosterone however the factors underlying reasons for differentiation remain unknown. In the present study we evaluated the paracrine factors released from testicular microenvironment (TME), which is comprised of Sertoli and peritubular myoid cells, in modulating differentiation of Leydig stem cells to Adult Leydig cells and production of Testosterone. Additionally, we explored the underlying mechanism of action of these paracrine factors.

DESIGN: A total of 13 men with testicular failure underwent testis biopsies for sperm retrieval were used for the study.

MATERIALS AND METHODS: Using an IRB approved protocol, about 10mg of testicular tissue from each of these men were processed for Leydig stem cell isolation, culture and characterized. Cytokine antibody array was performed to identify the paracrine factors released by Sertoli and Peritubular Myoid cells using unsorted and $CD146^{+ve}$ sorted cells. The cells were treated with hedgehog signaling agonist and antagonist to validate the specificity of paracrine factors identified. Immunostaining was performed to validate the changes at protein levels. Flow cytometry was performed to study the shift in the population of cells post Leptin treatment. GraphPad Prism was used for statistical analysis. All data were presented as the means ± SEM. The statistical significance between two groups was estimated by unpaired two-tailed t test.

RESULTS: The current study revealed that the testicular microenvironment (TME), which is comprised of Sertoli and peritubular myoid cells, plays an instrumental role in Leydig stem cell differentiation and testosterone production under the regulation of the desert hedgehog signaling pathway (DHH). Additionally, identifying the paracrine factors that are released by TME and understanding their impact on Leydig stem cell (LSC) differentiation is key to unraveling and developing new niche-based therapy for TD. In the current study, LSCs were isolated from 13 men undergoing testis biopsies

for sperm retrieval and evaluated the paracrine factors in the presence or absence of TME. TME-secreted leptin induces LSC differentiation and increases T production. These effects of Leptin on LSC differentiation and T production, however, are inversely concentration-dependent: positive at low doses and negative at higher doses. Mechanistically, Leptin acts on LSCs upstream of DHH; Leptin-DHH regulation functions unidirectionally insofar as DHH gain or loss of function has no effects on Leptin levels.

CONCLUSIONS: Taken together these findings identify leptin as a key paracrine factor released by cells within the TME that modulates LSC differentiation and testosterone release from mature Leydig cells, a finding with important clinical implications for TD.

SUPPORT: Supported by the American Urological Association Research Scholar Award to HA and RR

P-698 4:30 PM Tuesday, October 20, 2020

SERUM TESTOSTERONE LEVEL RISES DRASTICALLY AT THE MOMENT OF EJACULATION. Yoshitomo Kobori, MD, PhD, Akiyoshi Osaka, MD, Toshiyuki Iwahata, MD, PhD, Hiroshi Okada, MD, PhD Dokkyo Medical University Saitama Medical Center, Koshigaya, Japan.

OBJECTIVE: Testosterone is the major sex hormone in males and plays an important role in development of the penis and testes, muscle size, bone growth, sex drive, and sperm production. Changes in serum testosterone level at ejaculation are unclear, although sexual function is influenced by testosterone. We measured pre- and post-ejaculatory testosterone levels over time and evaluated changes in these levels. We also measured levels of prolactin and cortisol, which are hormones that also affect sexual function.

DESIGN: Laboratory investigation.

MATERIALS AND METHODS: We enrolled 7 men (age 32–41 years, mean 35.7 years) with normal sexual function, and collected blood samples before, during, and after masturbation. Testosterone, prolactin, and cortisol levels were evaluated before erection, after erection, just before ejaculation, at ejaculation, and 10 min after ejaculation.

RESULTS: Serum testosterone level increased significantly over time from before erection to the moment of ejaculation, and decreased to the pre-erection level 10 min after ejaculation (pre-erection, 5.86±2.45ng/mL; at ejaculation, 7.01±3.61 ng/mL; 10 min after ejaculation, 6.22±2.89 ng/mL; $p < 0.05$). Cortisol increased significantly over time from before erection to after ejaculation (pre-erection, 5.63±3.82μg/dL; at ejaculation, 6.94±4.59 μg/dL; 10 min after ejaculation, 7.70±4.99 μg/dL; $p < 0.05$). And prolactin increased approximately 2-fold over time from before erection to after ejaculation (pre-erection, 12.83±2.36ng/mL; at ejaculation, 17.48±4.51 ng/mL; 10 min after ejaculation, 23.47±6.27 ng/mL; $p < 0.05$).

CONCLUSIONS: All 3 hormones changed drastically with ejaculation. The increase in testosterone level may be due to prostate contraction and testicular secretion. In addition, prolactin and cortisol levels changed before and after ejaculation. Changes in hormone secretion due to ejaculation may affect daily health and sexual function.

	before	erection	climax	ejaculation	after 10 min
Testosterone	5.06±2.45	5.26±2.79	5.44±3.39	5.61±3.61	5.27±2.89
Cortisol	5.63±3.82	5.98±3.71	6.53±4.30	6.94±4.59	7.70±4.99
Prolactin	12.83±2.36	12.51±2.22	14.68±3.59	17.48±4.51	23.47±6.27

REFERENCES: none.

SUPPORT: none.

P-699 4:30 PM Tuesday, October 20, 2020

TREATING HYPERPROLACTINEMIA DOESN'T IMPROVE SEXUAL FUNCTION IN END STAGE RENAL DISEASE PATIENTS. Haitham Elbardisi, MD, Kareim Khalafalla, MD, Mohamed Arafa, MD, Sami Alsaid, MD, Ahmad Majzoub, MD Hamad Medical Corporation, Doha, Qatar.

OBJECTIVE: Chronic kidney disease is associated with gonadal dysfunction. Patient usually present with deceased libido, erectile dysfunction & defective ejaculation. Significant derangements of the hypothalamic pituitary axes is commonly identified in uremic patients with reduced total & free serum testosterone levels and increased LH & FSH levels. Elevated levels of prolactin is usually seen in ESRD & is thought to contribute to the high prevalence of hypogonadism & sexual dysfunction. This study aims to evaluate the effect of treatment of hyperprolactinemia on sexual function in ESRD patients.

DESIGN: Prospective Cohort study.

MATERIALS AND METHODS: All patients attending the clinic with ESRD in Hamad general hospital dialysis service during the study period from 1/3/2017 - 1/7/2017 were screened for eligibility. A total of 102 patients were included. Patients receiving treatment for fertility, erectile dysfunction & other medications that may affect sexual functions e.g. cytotoxic drugs, androgens, estrogens, thiazides were excluded.

Patients were evaluated and were asked to fill the International index of erectile function (IIEF) and Premature ejaculation diagnostic tool (PEDT) to assess their sexual function. Serum hormones were collected. Patients with hyperprolactinemia were then offered treatment with Gabergolin 0.5mg once per week for 3 months. In the follow up visit, patients were reevaluated with hormones and IIEF/PEDT questionnaires.

RESULTS: Patients had a mean age of 52.4 ± 12.1 years & mean BMI of 29.9 ± 9.3. 75 patients (73.5%) were on hemodialysis & 13 (12.7%) on peritoneal dialysis. All patients were diabetic, 35 patients (34.3%) had chronic heart disease, while 99 patients (97.1%) were hypertensive. Premature ejaculation a& moderate to severe ED were reported by 88.2% (N) and 52.9% (N) of patients. Mean basal testosterone levels were 12.95 ± 6.46 while mean basal prolactin levels were 514.22 ± 592.89. 55 patients (53.9%) were diagnosed with hyperprolactinemia. 26 patients (25.5%) agreed to receive cabergoline treatment. No statistically significant improvement in prolactin levels (P= 0.597), testosterone levels (P= 0.1), PEDT score (P= 0.923) and IIEF score (P=0.393) was seen in the treated group in comparison to the non-treated group.

CONCLUSIONS: Correction of hyperprolactinemia in ESRD appears not to affect sexual function.

Table

Parameters	Pre-treatment	Post-treatment	P Value
Prolactin	916.91 ± 985.73	394.55 ± 366.77	0.597
Testosterone	12.43 ±7.95	12.77±6.039	0.10
IIEF Score	11.48 ± 4.79	12.28 ± 4.86	0.393
PEDT Score	14.60 ± 4.40	16.28 ± 4.99	0.923

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A NORTH AMERICAN PROSPECTIVE COHORT STUDY OF ANTHROPOMETRIC FACTORS AND SEMEN QUALITY. Marlon D. Joseph, MPH,[1] Elizabeth E. Hatch, Ph.D.,[1] Michael L. Eisenberg, M.D.,[2] Kenneth J. Rothman, Dr.P.H.,[1] Tanran R. Wang, MPH,[1] Lauren A. Wise, Sc.D.[1] [1]Boston University School of Public Health, Boston, MA; [2]Stanford University, Stanford, CA.

OBJECTIVE: We prospectively evaluated the association between anthropometric variables and selected semen parameters.

DESIGN: A prospective cohort study.

MATERIALS AND METHODS: We analyzed data from 301 men (520 samples) participating in a semen testing substudy of Pregnancy Online Study (PRESTO), a preconception cohort of North American couples. After enrollment, male participants aged ≥21 years were invited to perform semen testing using the Trak™ system. Selected anthropometric variables (weight at age 17 years, current weight, height, and waist circumference) and covariate data were obtained via baseline questionnaire. We estimated the percent difference in mean log-transformed semen parameter values (%D) and 95% confidence intervals (CI) for associations between selected anthropometric variables and semen volume (mL), total sperm count (TSC, million), sperm concentration (million/mL), motility (%) and total motile sperm count (TMSC, million). Models were adjusted for abstinence time, age (years), current or occasional smoker (yes vs. no), hours of work per week, alcohol

intake (drinks/week), sugar-sweetened sodas (drinks/week), average hours of sleep per night, vigorous exercise (hrs/week), education (years), depressive symptoms, anxiety symptoms and use of psychotropic medications.

RESULTS: The distribution of current BMI (kg/m^2) in the cohort at baseline was: 32.2%, 33.2%, 19.6%, and 15.0% for categories of <25, 25-29, 30-34, and ≥35 kg/m^2, respectively. Adjusted %Ds (CIs) comparing current BMI ≥35 vs. <25 kg/m^2 were 6.6 (-8.9, 24.7), -16.4 (-40.4, 17.1), -10.9 (-38.7, 29.5), -4.3 (-26.1, 24.0) and -14.0 (-47.9, 42.0) for semen volume, sperm concentration, TSC, motility, and TMSC, respectively. Adjusted % Ds (CIs) comparing waist circumferences of ≥42 vs. <31 inches were -1.2 (-16.7, 17.2), -19.2 (-45.0, 18.5), -20.2 (-48.3, 23.3), -10.7 (-30.8, 15.1), and -28.4 (-59.6, 27.2) for semen volume, sperm concentration, TSC, motility, and TMSC, respectively. Additionally, few consistent associations between weight change since age 17 and semen parameters were observed.

CONCLUSIONS: Preliminary results indicate slight inverse associations between waist circumference and semen parameters, particularly sperm concentration and motility.

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A RE-EVALUATION OF THE EFFICACY OF TREATING SPERM WITH LOW HYPO-OSMOTIC SWELLING (HOS) TESTS WITH THE PROTEIN DIGESTIVE ENZYME CHYMOTRYPSIN-GALACTOSE (CG). Jerome H. Check, M.D., Ph.D.,[1] Carrie K. Wilson, B.A.,[2] Aniela Bollendorf, M.T.,[2] Donna Summers, M.S.,[2] Diane L. Check, BS, MT[2] [1]Cooper Medical School of Rowan University, Camden, NJ; [2]Cooper Institute for Reproductive Hormonal Disorders, P.C., Mt. Laurel, NJ.

OBJECTIVE: Since 1989 there have been several publications concluding that males whose semen specimens show a low HOS test almost never achieve a live pregnancy following intercourse, intrauterine insemination (IUI) or in vitro fertilization-embryo transfer (IVF-ET) using conventional oocyte insemination. The studies find that sperm with low HOS allow normal fertilization but implantation failure. Yet IVF with intracytoplasmic sperm injection (ICSI) fully corrects the problem and allows normal live delivered pregnancy rates. These findings led to the hypothesis that the sperm with low HOS scores are associated with a toxic factor causing functional impairment of the embryo membrane leading to implantation failure. Some studies suggest that treating the sperm with the protein digestive enzyme CG prior to IUI and avoidance of unprotected intercourse can allow live deliveries. The purpose of this study was to corroborate or refute these previous studies, and determine the confounding effect of motile density, normal morphology and % motility in influencing IUI success with sperm with low HOS scores treated with CG prior to IUI.

DESIGN: Prospective comparison study.

MATERIALS AND METHODS: Males with 2 low HOS test scores <50%, who chose IUI with CG treated sperm over IVF with ICSI, were the test subjects. They were advised to avoid unprotected intercourse during the follicular phase. The pregnancy rates in their first IUI cycle were determined. Only males where the CG treatment increased the HOS score to ≥50% were included.

RESULTS: The pregnancy rates according to certain semen parameters are seen in the table. In males with normal motile density irrespective of strict normal morphology or % motile density had a live delivered pregnancy rate of 10.9%. The confounding effect of other parameters being abnormal cut this success rate to half or less compared to normal motile density. Nevertheless, live deliveries occurred even with these confounding abnormalities.

CONCLUSIONS: The results corroborate that IUI with CG-treated sperm and avoidance of unprotected intercourse allows normal live deliveries with sperm with low HOS scores. The presence of other male factors reduces the success rate in half.

SUPPORT: None

P-702 4:30 PM Tuesday, October 20, 2020

FUTURE FERTILITY AND PRESERVATION BELIEFS: PRACTICES AMONG A COHORT OF KLINEFELTER SYNDROME MEN. Douglas Timmons, MD, MPH,[1] Steven Gay, MD,[2] Alan H. DeCherney, MD[3] [1]University of Miami Miller School of Medicine/Jackson Memorial Hospital; [2]Program in Reproductive Endocrinology and Gynecology, NICHD, NIH, Bethesda, MD; [3]Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD.

OBJECTIVE: Our clinic routinely evaluates patients with sex chromosome disorders and among these is XXY, Klinefelter Syndrome. Klinefelter Syndrome (KS) has a prevalence of 2 in 1000 males, and is most commonly associated with a 47, XXY karyotype.[1] The most common symptoms are: gynecomastia and low sexual drive, psychosocial problems and infertility.[2] The diagnosis of Klinefelter Syndrome is often suspected in patients with infertility, and approximately 90% of patients with KS suffer from non-obstructive azoospermia with advancing age-related hyalinization of testicular tissue driving premature gonadal failure.[3] Historically, patients with KS had no fertility options, but now with advancements in Assisted Reproductive Technologies (ART), specifically microsurgical Testicular Sperm Extraction (TESE), almost half of patients can father their own biological children with early enough evaluation and treatment.[4] Younger age is associated with an increased likelihood to obtain viable sperm via TESE.[5] Our objective was to evaluate men with the diagnosis of Klinefelter Syndrome to specifically look at previous attempts at fertility preservation, and desires for future fertility and preservation.

DESIGN: A retrospective chart review was performed on all patients with the diagnosis of Klinefelter Syndrome who were seen by our Reproductive Endocrinology and Infertility team between January, 2018 and August, 2019.

MATERIALS AND METHODS: Basic demographic data was obtained as well as information on age at diagnosis, hormonal medication use, previous fertility preservation, and attitudes towards future fertility preservation. Descriptive statistics were used, and t-tests with significance set to $p<0.05$.

RESULTS: Twenty one (n=21) patients were ultimately identified and included for review. Mean age at time of visit was 35.2 (SD = 11.5), and the mean age at diagnosis was 17.2 (SD = 10.9). Of these 21, 7 reported a desire for future fertility potential; 3 of these 7 had already undergone TESE, and 2 of these reported retrieval of usable sperm. 1 patient had micro-TESE performed without successful retrieval of sperm and 1 patient was referred for microTESE. All available semen analysis (n=10) documented azoospermia. An additional four patients reported azoospermia at outside clinics. 24% of patients with KS were diagnosed during an infertility evaluation. 38% of patients desire or are unsure if they want fertility preservation. Those who desire or are unsure of future fertility were significantly younger than those who do not desire future fertility (25.6 ± 6.4 vs. 41.2 ± 9.8; $p<0.001$).

CONCLUSIONS: Improvements in ART now provides men with Klinefelter Syndrome fertility options that previously did not exist and a significant proportion of our cohort desired these fertility options. Younger patients have

Pregnancy rates per IUI cycle with CG-treated sperm according to various semen parameters

	MD <10	MD ≥10	Normal morphology strict criteria <5	Normal morphology strict criteria ≥5	Motility <30%	Motility ≥30%
# IUI's	118	55	82	64	44	128
% pregnant	11.0%	16.4%	8.5%	18.8%	6.8%	14.8%
% clinical pregnancy	6.8%	16.4%	6.1%	15.6%	2.3%	12.5%
% miscarriage/clinical preg.	25.0%	33.3%	20.0%	40.0%	0.0%	31.3%
# live delivered	6	6	4	6	1	11
% live delivered	5.1%	10.9%	4.9%	9.4%	2.3%	8.6%
Avg. age female	37.8	39.1	37.4	37.8	37.6	38.4

stronger desires for future fertility, and men with KS who are interested in fertility preservation would benefit from earlier evaluation and sperm extraction.

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P-703 4:30 PM Tuesday, October 20, 2020

DOES TESTICULAR SPERM ALTER REPRODUCTIVE AND PERI-NATAL OUTCOMES IN ART CYCLES? 10 YEARS' EXPERIENCE OF AN INDIAN CLINIC.

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INTRODUCTION:

It is well known that introduction of intracytoplasmic sperm injection (ICSI) is a breakthrough in the treatment of male infertility. The use of epididymal and testicular sperm has been beneficial in the treatment of azoospermic men.

OBJECTIVE: To identify the impact of surgically retrieved sperm (SRS) on reproductive and peri-natal outcomes in Assisted Reproductive Treatment (ART) cycles.

DESIGN: This is a retrospective study design at our private IVF clinic duration is from 2009 to 2019.

MATERIALS AND METHODS: The sample size of this study is a total of 989 subjects underwent SRS under general anaesthesia. Of these only 552 couples were included in this study with female partner's age $\leq$ 37 and had self-gamete cycles. Among them only 342 subjects (till June 2019) had embryo transfer.

Couples with ejaculate sperm (ES) and self-oocytes who had ICSI cycles acted as control group for this study (n=425).

In study group male partners underwent SRS and female partner's underwent controlled ovarian stimulation and trans vaginal oocyte retrieval as per our clinic's standard operating protocols (SOP). Embryos were cultured till blastocysts and a freeze all policy was followed. Frozen Embryo transfer with two good grade blastocysts (grading done as per Istanbul Consensus by Alpha scientists) was done in subsequent cycles.

Primary Outcomes: Live birth rates (LBR) and Peri-Natal outcomes- Obstetric complications (Gestational diabetes (GDM), Pregnancy Induced Hypertension (PIH), Intra-Uterine Growth Restriction (IUGR), and foetal anomalies.

Secondary Outcomes: Reproductive out comes – Fertilization rate (FR); blastocyst rate (BR); Implantation rate (IR); Clinical pregnancy rate (CPR); Miscarriage rate (MR) and Multiple Pregnancy rates (MPR).

RESULTS: Mean Reproductive and Perinatal outcomes of Study Vs Control group are as follows:

FR – 92.6% Vs 92.3% (P=0.8760)
BR – 37.18% Vs 48.4% (P=0.0018)
CPR – 58.18 Vs 62.93% (P=0.1807)
IR – 40.63% Vs 48.97% (P=0.0212)
MR- 7.02% Vs 9.98% (P=0.1477)
MPR – 10.81% Vs 17% (P=0.0148)
LBR – 40.06% Vs 51.4% (P=0.0018)
GDM – 3.8% Vs 1.8% (P=0.0891)
PIH – 2.63% Vs 2.12% (P=0.6431)
IUGR – 0% Vs 0.71%
Lost to Follow up – 10% Vs 0% (P=0.8760)

Congenital Anomalies – One baby with Angleman's Syndrome in study groups Vs one baby with hydrocephalus, one death due to Respiratory distress and 3 deaths in NICU after preterm birth in control group.

Data from this study is suggesting that use of SRS seems to offer beneficial reproductive and perinatal outcomes.

Though Blastocycst rate and LBR is significantly higher in control group, SRS groups still has acceptable outcomes.

CONCLUSIONS:Use of SRS in ART cycles do not seem to alter reproductive and peri-natal outcomes and couples should be reassured and counselled appropriately. However, long term follows up of the health of such off springs is still warranted.

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CLINICAL OUTCOMES IN PATIENTS WITH CONGENITAL BILATERAL ABSENCE OF THE VAS DEFERENS (CBAVD) UNDERGOING TESTICULAR SPERM EXTRACTION-INTRACYTOPLASMIC SPERM INJECTION (TESE-ICSI).

Tomomoto Ishikawa, M.D., Kotaro Kitaya, M.D. Reproduction Clinic Osaka, Osaka, Japan.

OBJECTIVE: Obstructive azoospermia (OA) is caused by congenital including bilateral absence of the vas deferens (obstructed in the long term) or acquired (vasectomy, inguinal hernioplasty in childhood, etc.). It is known that long-term obstruction is related to a defect of spermatogenesis, however, clinical outcomes after ICSI with testicular sperm in the etiology OA, classified as congenital or acquired causes have hardly been investigated.

DESIGN: A retrospective study.

MATERIALS AND METHODS: We performed a retrospective study based on two reproduction centers in Japan and evaluated 206 NOA patinets including 50 cases with CBAVD performed in our clinic between September 2013 and December 2019. In addition, a total of 108 TESE-ICSI cycle with 47 couples for CBAVD and 293 TESE-ICSI cycles with 138 couples for other obstruction were performed. Sperm retrieval rate was 100% and TESE-ICSI was performed with only motile spermatozoa. The diagnosis of CBAVD is based on normal-size testes (>16mL), normal FSH and nonpalpable vas deferens. The diagnosis of OA also required confirmation of normal spermatogenesis by testicular biopsy. TESE-ICSI cycles were evaluated in embryonic development rates and CPR. Additionally, paternal and maternal age, numbers of oocytes retrieved, baseline FSH, LH and E2 levels of women, and FSH, LH and Testosterone of men were compared between the two groups.

RESULTS: The wives age at ICSI was 33.9±4.4 years for CBAVD and 35.9±5.1 years for other obstruction. The sperm retrieval rate with TESE was 100%, in which motile spermatozoa were retrieved and used for ICSI for all patients. Two pronuclei (2PN), blastocysts development, and good-quality blastocysts rates were 57.2%, 44.8%, and 19.6% in CBAVD and 64.0%, 53.3%, and 23.0% in other obstruction, respectively. 2PN and blastocysts development rate in CBAVD was significantly lower than in other obstruction (P<0.001). However, no significant difference was found in good-quality blastocysts rates. Embryo transfer was performed 44 couples with CBAVD patients undergoing TESE-ICSI which were divided into clinical pregnancy positive (n=37) and negative (n=7) groups. There was no difference for paternal and maternal age, numbers of oocytes retrieved, baseline FSH, LH and E2 levels of women, and FSH, LH and Testosterone of men. CPR per ET cycle and per couple were similar in CBAVD (40.2% and 84.1%, respectively) and in other obstructive (41.3% and 79.4%, respectively).

CONCLUSIONS: Long-term obstruction is not related to a sperm retrieval by conventional TESE and clinical pregnancy, however, embryonic development were not similar as the other OAs. In CBAVD couples, the selection of motile sperm from testicular tissue could be a critical key to succeed and rationale for good embryonic development.

REFERENCES: None.

SUPPORT: None.

P-705 4:30 PM Tuesday, October 20, 2020

VARICOCELECTOMY IS ASSOCIATED WITH IMPROVEMENT IN SPERM CAPACITATION AND THE PROBABILITY OF GETTING PREGNANT IN INFERTILE MEN. Christopher Gaffney, MD,[1] Philip Xie, B.S.,[2] Nahid Punjani, MD MPH,[3] Jonathan Fainberg, MD,[3] Aaron Brant, MD,[3] Alessandra Parrella, M.Sc.,[2] Gianpiero D. Palermo, M.D., Ph.D.,[2] James A. Kashanian, MD[4] [1]Weill Cornell Medicine, New York, NY; [2]The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY; [3]Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY; [4]Weill Cornell Medicine - New York Presbyterian Hospital, New York, NY.

OBJECTIVE: Male infertility is associated with poor sperm capacitation function as measured by Cap-Score™. We sought to determine if Cap-Score™ would improve following microsurgical varicocelectomy.

DESIGN: We performed a prospective cohort study comparing the preoperative and post-operative Cap-Scores™ (Androvia LifeSciences) and routine semen analyses parameters in men who presented with infertility, were found to have a unilateral or bilateral varicocele on physical exam, and were treated with unilateral or bilateral microsurgical varicocelectomy.

MATERIALS AND METHODS: Varicoceles were diagnosed and graded by a single urologist in the standing position. Semen analyses were performed on fresh ejaculates according to WHO criteria. We recorded semen volume, concentration, motility, percent normal forms, Cap-Score™ and the probability of getting pregnant (PGP) and compared pre-operative values with post-operative values using Wilcoxon Rank-Sum tests in R Studio®. PGP is a validated calculated metric based on semen volume, concentration, and Cap-Score™ .

RESULTS: We identified 11 men (mean age 37.6 +/- 6.7) who presented with male factor infertility, were diagnosed with unilateral or bilateral varicoceles, and were treated with microsurgical varicocelectomy. Each of these men had a semen analysis and Cap-Score™ preoperatively and 3 months post-operatively. There was no statistical difference between semen volume, concentration, motility, or morphology before and after varicocelectomy, though there was a trend toward improvement in concentration (**Table**). Of the 11 men, 9 (81.8%) demonstrated improved Cap-Score™ and PGP after treatment. On average, Cap-Score™ increased 5.0% (p=0.03) and PGP increased 8.9% (p=0.03) after varicocelectomy **(Table).** The change in Cap-Score™ was not associated with the grade of varicocele or whether the patient had a unilateral or bilateral repair. Thus far, 2 men reported a clinical pregnancy, 1 from an IUI cycle and 1 spontaneous conception.

CONCLUSIONS: It is known that varicocelectomy improves semen parameters and conception. This study confirms that microsurgical varicocelectomy may augment male fertility by improving sperm capacitation ability. In doing so, varicocelectomy improves the probability of getting pregnant.

Table. Semen parameters and Cap-Score™ before and after microsurgical varicocelectomy

	Before Varicocelectomy		After Varicocelectomy		
	Mean	STD	Mean	STD	p-value
Volume (ml)	2.6	1.1	2.1	0.8	0.24
Concentration (million/ml)	24.4	17.4	35.6	27.1	0.19
Motility (%)	41.0	8.0	42.4	5.4	0.22
Morphology (%)	2.7	1.1	2.5	1.1	0.13
CAP Score (%)	26.7	4.5	31.7	5.2	**0.03**
PGP (%)	31.5	7.4	40.4	9.5	**0.03**

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RELATION BETWEEN SPERM MORPHOLOGY AND PREGNANCY RATE AFTER AN INTRAUTERINE INSEMINATION. Mario Alfonso Patron Vazquez, Sr., Ob-Gyn,[1] Julio C. Rosales, M.D.,[2] Genaro Garcia Villafaña, Sr., MD,[1] Karla Mariel Alcalde, MD,[2] Karla Alejandra Cantú, M. Sc.,[2] Marianna Perez Vargas, MD[1] [1]IECH Fertility Center, Monterrey, NL, Mexico; [2]IECH, Monterrey, NL, Mexico.

OBJECTIVE: To determine if sperm morphology after capacitation affects intrauterine insemination outcomes.

DESIGN: Retrospective cohort study between December 2018 and April 2019.

MATERIALS AND METHODS: A total of 166 couples with unexplained infertility and 284 cycles of ovarian stimulation for intrauterine insemination were done at the IECH Fertility Center in Monterrey, Nuevo León, México and were divided between two groups: Group 1 (study group) were patients with teratospermia (sperm morphology <4%) and Group 2 (control group) were patients with normal sperm morphology (>4%). The main variable results were pregnancy rate per cycle. Sperm count, progressive motility, total count and morphology were analyzed in spermogram.

RESULTS: Demographic outcomes were homogeneous among two groups. Male patients between 31-35 years had major proportion of severe teratospermia. No statistical significance pregnancy rate was observed with the two groups (17 vs 23 p=0.2 OR=1.6). Cohort point to predict birth rate in this studied population was 5.5% with a specificity of 81% and sensibility of 30%. Patients with teratospermia had primary infertility with statistical significance comparable with control group (79.79% vs 68.42&, p= 0.0493, OR 1.82).

CONCLUSIONS: Teratospermia can't be count as a parameter to predict pregnancy in this population. Couples with unexplained infertility and sperm morphology greater that 5.5% increases chances of getting pregnant.

P-707 4:30 PM Tuesday, October 20, 2020

REPRODUCTIVE PARAMETERS IN MEN WITH SOLITARY TESTIS. Andrew Hany Rezk, BA,[1] Michael B. Tradewell, MD, MS,[1] Jesse Ory, MD,[2] Emad Ibrahim, MD, HCLD(ABB),[1] Ranjith Ramasamy, M.D[1] [1]University of Miami Miller School of Medicine, Miami, FL; [2]University of Miami, Miami, FL.

OBJECTIVE: Men with solitary testis frequently report difficulties with fertility yet there is limited data available to help guide counseling. Expanding our knowledge about sperm parameters and gonadotropin levels in men with solitary testis is essential. The objective of this study was to evaluate the reproductive parameters in men with solitary testis presenting for male infertility evaluation.

DESIGN: An observational study of semen parameters and hormonal evaluation of infertile men with solitary testis.

MATERIALS AND METHODS: Data was gathered from a male infertility clinic database between January 2016 and March 2020. All men had semen analysis data, serum FSH, LH, and total testosterone (T) collected within +/-90 days. Etiology and timing of testis loss was collected. We excluded data from men with recent testosterone or steroid use.

To further assess spermatogenesis, sperm concentration and sperm motility data from men with solitary testis (case) were paired with matching semen parameters in men with bilateral descended testis (control). Medians and interquartile ranges [25-75] are reported. Statistical analysis including univariate and multivariate analysis using continuous variables (median, IQR, and range) were performed in *R*. P-values <0.05 were deemed statistically significant.

RESULTS: We identified 34 men with solitary testis. The median age was 36.27 [32.31-40.51] years. 19 men had solitary testis due to cancer, 8 due to cryptorchidism, and 7 due to trauma/torsion. Eight men did not have a recorded time of testis loss. In the remaining 26 men, the median time between orchiectomy and clinic visit was 7.75 [3.27-19.58] years and eight had a prepubertal orchiectomy.

A total of 11 / 34 men were azoospermic. In the remaining men with sperm, the median sperm concentration was 8.00 [1.50-17.00] mill/ml. Among all men, the median LH level was 6.6 [3.47-10.81] IU/L and the median T was 400 [303.00 - 499.00] ng/dl. We performed a case-control analysis with 1:1 sperm concentration and motility match between men with solitary testis and bilateral testis was completed. FSH in men with solitary testis was 14.6 [7.70-26.07] IU/L, which was significantly more elevated than men with bilateral testis (FSH: 6.8 [3.57-12.28]), p=0.012. There was no difference in T and LH.

CONCLUSIONS: Infertile men with solitary testis may have underlying sub-fertility compounded by loss of a testicle. One third of men with solitary testis were azoospermic. The elevated FSH levels in men with solitary testis compared to men with bilateral testis and matched semen parameters indicates the compensatory mechanism in these men to continue spermatogenesis and may indicate a higher degree of testicular strain.

P-708 4:30 PM Tuesday, October 20, 2020

EXPRESSION AND SIGNIFICANCE OF C1ORF100 IN TESTIS OF PATIENTS WITH NON-OBSTRUCTIVE AZOOSPERMIA. Wujiang Liu, MD,[1] Xinzong Zhang, MD,[1] Huang Liu, MD,[2] Yu Zhou, MD,[3] Cuncan Deng, MD,[3] Qingguo Zhao, MD,[3] Yunge Tang, Master degree[3] [1]Family Planning Special Hospital of Guangdong Province, Guangzhou, China; [2]Family Planning Research Institute of Guangdong Province, Guangzhou, China; [3]Family Planning Research Institute of Guangdong Province, Guangdong, China.

OBJECTIVE: To investigate the expression and significance of c1orf100 in testis of patients with non obstructive azoospermia.

DESIGN: An original ariticle.

MATERIALS AND METHODS: With informed consent, testis tissue of 20 cases of non obstructive azoospermia with different stage of spermatogenesis block were collected for affymetrix gene-chip test after mTESE surgery. Testis tissue of 20 cases of obstructive azoospermia were used as control after testicular puncture. The stage of spermatogenesis block was confirmed by tissue pathology. RT-PCR, real-time PCR, Western blot and immunohistochemistry were performed to confirm the finding of gene chip.

RESULTS: The expression of c1orf100 in testis of non obstructive azoospermia was significantly decreased compared with obstructive azoospermia, which was related to the stage of spermatogenesis block. RT-PCR, real-time PCR and Western blot confirmed the above rusults from mRNA and protein levels respectively. Immunohistochemistry showed that c1orf100 was mainly expressed in the nucleus and cytoplasm of spermatogenic cells at all stages, and its expression intensity was related to the stage of spermatogenesis block. The expression of c1orf100 was significantly reduced in testis of patients with sertoli cell only syndrome.

CONCLUSIONS: c1orf100 may be a new molecular marker related to spermatogenesis, which is worthy of further study.

REFERENCES: None

SUPPORT: This research was funded by the Project of Medical Science and Technology Research Foundation of Guangdong Province (No. A2019336) and Guangzhou Science and Technology Plan Project (No. 201707010394).

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VARICOCELE INDUCE OXIDATIVE STRESS AND SPERM DNA DAMAGES IN INFERTILES PATIENTS. Mariem ben Khelifa, PhD, Hanen Elloumi, Dr, Sonia Mnallah, Dr, med Habib BEN Aribia, Dr, Mohamed Khrouf, Dr, Fethi Zhioua, Dr, Khaled Terras, Dr, Moncef Benkhalifa, PhD, Khaled Mahmoud, Dr FERTILLIA center, Tunis, QC, Tunisia.

OBJECTIVE: Varicocele is one of the most common andrological pathologies in the general population and particularly common in infertile men. The pathogenesis of varicocele related infertility is not completely defined to explain the correlation of varicocele and infertility. Imbalance between excessive reactive oxygen species production and antioxidant protection causes sperm DNA injuries, thus rendering the spermatozoa less fertile in a subset of varicocele patients.Therefore we studied the relationship between OS levels, DNA integrity and sperm parameters in infertile men with or without varicocele.

DESIGN: This is a prospective comparative study, performed between januray and december 2019, includes patients with primary or secondary infertility (>3 years). Semen samples were obtained from 115 patients. The patients were grouped into 2 groups : 31 patients with a clinically diagnosedof a grade II or III varicocele and a control group (84 men). Exclusion criteria for control group were presence of varicocele, evidence of urogenital infections, and a history of smoking or excessive alcohol.

MATERIALS AND METHODS: In each semen sample, which was collected after sexual abstinence of 2–5 days in addition to conventional sperm parameters the following parameters were measured : (i) Spermatozoa with DNA strand breaks were assessed by TUNEL (cut-off value<30%), (ii) Abnormal chromatin condensation using Aniline Blue assays (cut-off value<20%), (iii) Oxidative stress was measured by MioXSYS Analyzer. Data were analyzed with SPSS and a correlation analysis was performed using non transformed values. Statistical significance was set at p<0,05.

RESULTS: There were no difference in age and duration of infertility the two groups. No difference exist between patients of control group and patients of varicocele groups concerning semen parameters, h: sperm concentration (34.48 vs 31.83 x 10^6 sperm/mL) progressive motility (30% vs 29%), and vitality (61.45% vs 59%). However all parameters showed a tendency towards being lower in the group with varicocele. There is a significative difference between OS and DNA fragmentation and chromatin decondensation between the two groups. The varicocele group showed a positive correlation between OS and DNA fragmentation and also between OS and chromatin decondensation.

CONCLUSIONS: The presence of varicocele may impair sperm DNA integrity and fertility. Given the extant literature, varicocele repair and antioxidant should be considered to reduce DNA damage in sperm.

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EFFECT OF MICROSURGICAL VARICOCELECTOMY ON NONOBSTRUCTIVE AZOOSPERMIA (NOA) AND SEVERELY OLIGOZOOSPERMIA. Tomomoto Ishikawa, M.D., Kotaro Kitaya, M.D. Reproduction Clinic Osaka, Osaka, Japan.

OBJECTIVE: Varicoceles are the most frequent physical abnormality found in infertile men and surgical ligation of spermatic vein is generally accepted as the treatment of choice for this condition. The aim of this study is to assess the treatment outcome and the benefits after microsurgical varicocelectomy in men with nonobstructive azoospermia (NOA) and severely oligozoospermia.

DESIGN: Retrospective clinical analysis.

MATERIALS AND METHODS: The records were retrospectively evaluated for 41 patients with NOA and 259 severely oligozoospermic patients who underwent microsurgical inguinal varicocele ligation. The age was 34.34.3 (meanSD) years. Two hundred sixty-nine (90%) underwent a unilateral left-sided procedure (33 of 41 with NOA, 236 of 259 with severe oligospermia), and 31 (10%) underwent a bilateral procedure. Severely oligozoospermia was defined as $<5x10^6$/ml in all analyses submitted. Our indication of varicocelectomy for NOA patients was more than 12 ml of testicular volume preoperatively and the palpable varicocele. We obtained institutional review board approval as well as individual patient signed consents. Chi-square test was used to compare continuous variables between the groups. In all cases, statistical significance was set at $P < 0.05$. ±

RESULTS: After ligation, induction of spermatogenesis was achieved in six men (14.6%). We could not find the predictive factor retrospectively (e.g. hormone levels or testicular volume). The sperm concentration increased from 2.71.4 to 12.16.5 million/mL ($P<0.001$) with severely oligozoospermic patients. The sperm motility did not change significantly. Twenty seven (10.4%) of the 259 oligospermia men have contributed to unassisted pregnancies. Among 259 patients with severely oligozoospermia, improvement of sperm concentration was seen in 152 patients (responders, 59%). Between responders and non-responders with severely oligozoospermia, no significant differences were seen in FSH level (9.25.5 and 10.44.9 IU/L, respectively), LH level (4.72.2 and 5.13.5 IU/L, respectively), testosterone level (4.32.2 and 4.52.4 ng/mL, respectively), left testicular volume (15.63.3 and 16.13.4 mL, respectively), the percentage of varicocele grade III (52 and 54 %, respectively), and the volume of semen (2.80.7 and 2.91.2 mL, respectively).

CONCLUSIONS: Microsurgical varicocelectomy resulted in the induction or enhancement of spermatogenesis for several men with NOA or severely oligozoospermia. It is reasonable to be considered an option in selective patients with NOA before testicular sperm extraction and severely oligozoospermia.

REFERENCES: None.

SUPPORT: None.

P-711 4:30 PM Tuesday, October 20, 2020

THE CONFOUNDING EFFECT OF ADDITIONAL ABNORMAL SEMEN PARAMETERS ON PREGNANCY OUTCOME FOLLOWING IN VITRO FERTILIZATION-EMBRYO TRANSFER (IVF-ET) USING SPERM FROM MEN WITH ABNORMAL HYPO-OSMOTIC SWELLING (HOS) TESTS. Jerome H. Check, M.D., Ph.D.,[1] Carrie K. Wilson, B.A.,[2] Donna Summers, M.S.,[2] Diane L. Check, BS, MT,[2] Jung Choe, M.D.[1] [1]Cooper Medical School of Rowan University, Camden, NJ; [2]Cooper Institute for Reproductive Hormonal Disorders, P.C., Mt. Laurel, NJ.

OBJECTIVE: In the early days of IVF-ET, before the advent of intracytoplasmic sperm injection (ICSI), a low HOS test was found to be by far the best single semen parameter to predict failure to achieve a live delivery

despite normal fertilization and normal embryo development. Unfortunately, for unknown reasons, this simple inexpensive test is not performed in most fertility centers when evaluating the male's semen analysis. The purpose of the present study was to evaluate whether the association of an additional abnormal semen parameter, i.e., either low motile density, low normal morphology by strict criteria, or low % motility, negatively effected the live delivered pregnancy rate in males with low HOS test scores with IVF with ICSI.

DESIGN: Prospective observational comparative study.

MATERIALS AND METHODS: The male partners of couples seeking help for infertility had semen analyses performed for standard parameters and also for the HOS test. If the HOS test score was <50% the couples were explained that successful live deliveries with this abnormality is extremely rare without treatment. The two treatment options were either IVF with ICSI or performing intrauterine insemination (IUI), but with this toxic protein causing the implantation defect, the sperm would first be treated with the protein digestive enzyme chymotrypsin. The first IVF cycle of those choosing IVF with ICSI was evaluated. The data were sub-analyzed into 3 sets of pairs – low motile density vs. normal ($<10x10^6$/mL vs. $\geq 10x10^6$/mL), subnormal morphology vs. normal by strict criteria ($\leq$4% vs. >5%) and low percent motility vs. normal (<30% vs. $\geq$30%).

RESULTS: The results are seen in the table below.

	MD $<10x10^6$/mL	MD $\geq 10x10^6$	Normal morphology strict criteria <5%	Normal morphology strict criteria ≥5%	% motility <30%	% motility ≥30%
# transfers	106	76	95	74	71	111
Avg. age	38.6	40.6	39.1	40.0	39.1	39.8
% clinical preg./transfer	32.1%	25.0%	37.9%	21.6%	25.4%	31.5%
% delivered	27.4%	15.8%	31.6%	13.5%	22.5%	22.5%

CONCLUSIONS: Having an additional abnormal semen parameter, in addition to a subnormal HOS test score, does not reduce success with IVF with ICSI. The HOS abnormality increases in frequency with advancing age of the male. Older men are more likely to try to conceive with women that are also of mildly advanced reproductive age. One could interpret the data that sperm of males with low HOS test scores have a trend for lower pregnancy rates if other semen parameters are normal. However, the most likely explanation for the trend for lower live delivery rates using sperm with additional semen parameter normal was slightly higher female age in these groups. Though only 1-2 years different, the age for the normal group was at a critical age where pregnancy rates plummet.

SUPPORT: None

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THE EFFECT OF PATERNAL AGE ON ICSI OUTCOME IN UNEXPLAINED INFERTILITY. Mohamed Arafa, MD, Kareim Khalafalla, MD, Ahmad Majzoub, MD, Hasan Burjaq, MSc, Moza Al Badr, MSc, Sami Alsaid, MD, Haitham Elbardisi, MD Hamad Medical Corporation, Doha, Qatar.

OBJECTIVE: Unexplained infertility is reported in 15%-30% of infertile cases. The most effective treatment in such cases is IVF/ICSI. Advanced male age is reported to negatively affect semen parameters, however its effect on ICSI outcome is controversial. This study aims at evaluating the effect of paternal age on ICSI outcome in couples with unexplained infertility.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: Male patients with normal semen parameters undergoing ICSI in the assisted reproduction center using ejaculated sperm during the period from January 1st, 2014 till June 1st, 2019 were screened for inclusion in the study. Couples with female factor (wife age ≥40yrs, AMH level <2.8pmol/L, and/or other gynecologic problems) were excluded.

Patients demographics, clinical and laboratory data were collected. Semen data at time of ICSI was collected; semen analysis results (WHO 5th edition), Oxidation reduction potential (ORP) (MiOXSYS analyzer) and sperm DNA fragmentation (SDF) (Halosperm kit, Ref ≤30%). Female demographics and clinical data as well as ICSI outcome was also collected.

Numbers (percentages) were used to report categorical values while mean ± SE was used to report numerical values. Results were compared using Kruskal Wallis Test and a p value of <0.05 was considered statistically significant. The SPSS version 20 (IBM, Armonk, NY) was used to conduct the statistical analysis.

RESULTS: A total of 117 couples with unexplained infertility were included in the study. The mean age of the male was 35.6±0.4years while that of the female was 33.2 ± 1.3 years. There was no significant correlation for age with most semen parameters except for normal sperm morphology (positively correlated, r -.232, p=0.012) and SDF (negatively correlated, r .276, p=0.010).

The overall clinical pregnancy rate was 29.1%. Patients were divided into 2 groups, clinical pregnancy and No clinical pregnancy (Table 1). The male age was significantly lower in clinical pregnancy group. Semen volume, sperm concentration, total motility, normal morphology, SDF and ORP were better in the Clinical pregnancy group but the difference was not statistically significant.

CONCLUSIONS: In patients with unexplained infertility, younger paternal age favors success of ICSI.

Parameters	Clinical Pregnancy (n=34)	No Clinical Pregnancy (n=83)	P value
Male Age	35.4 ±0.92	37.93 ±0.79	0.04*
Vol (ml)	3.3±0.22	2.9±0.14	0.72
Concentration (millions/ml)	57.2±6.8	53.8±3.5	0.66
Motility (%)	56.3±1.79	55.8±1.05	0.79
Normal Morph (%)	9.8±0.99	10.9±0.78	0.39
DNA Fragmentation (%)	17.8±1.17	20.7±1.23	0.096
ORP (mV/106 sperm/mL)	1.5±0.36	1.3±0.14	0.62

*Significant

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PERINATAL OUTCOMES OF SURGICALLY RETRIEVED SPERMS IN NON OBSTRUCTIVE AZOOSPERMIA, 10 YEARS EXPERIENCE OF AN INDIAN CLINIC. Amaz Areeb N, Jr., Master in Bio Technology,[1] Krishna Mantravadi, Sr., MBBS, PGDHOM, Masters in clinical embryology,[2] Durga Rao Gedela, MBBS, DGO, MRCOG, fellowship in infertility and reproductive endocrinology,[3] Sandeep Karunakaran, Sr., M.B.B.S, MS, PGDHM, PGDMLE,[4] Rajesh Mani Raghupathy, MBBS, PGDCE,[5] Yedluri Rupasree, M.Sc Biotechnology, PhD Biotechnology, PGDCE,[5] Afsha Firdouse, M.Sc Biochemistry, PGDCE[5] [1]Oasis Fertility, Chennai, India; [2]Oasis center for reproductive medicine, Hyderabad, India; [3]oasis fertility, Hyderabad, India; [4]OASIS FERTILITY, Hyderabad , TELANGANA, India; [5]Oasis fertility, Hyderabad, India.

OBJECTIVE: To look at the perinatal outcome of surgically retrieved spermatozoa (SRS) in individuals with Non obstructive Azoospermia (NOA).

DESIGN: This is a Retrospective Study at our Private IVF clinic from 2010 to 2019. 989 patients underwent SRS under general anaesthesia. Of

these 264 patients were indicated for NOA. 155 patients had successful Sperm retrieval and 93 patients finally had successful frozen embryo transfers with two good grade blastocysts and 425 ICSI cycles with Ejaculate sperms (EjS) were in control group.

MATERIALS AND METHODS: In this study couples who had successful SRS from testes and Intra-Cytoplasmic Sperm Injection (ICSI) with self-Oocytes and had blastocysts frozen for transfer were included.

All NOA patients underwent SRS either before the oocyte retrieval (OPU) and frozen for subsequent use or SRS was done at OPU and fresh testicular sperms used for ICSI. SRS was done as per our clinics standard operating protocol (SOP). All women underwent controlled ovarian stimulation, OPU and ICSI with fresh or frozen SRS. Embryos cultured till blastocyst stage and a freeze all policy was followed. Two blastocysts were transferred in a frozen cycle.

PRIMARY OUTCOMES – Live Birth rate (LBR) and Perinatal outcomes

SECONDARY OUTCOMES – Reproductive Outcome Fertilization rate (FR), Blastocyst rate (BR), Implantation Rate (IR), clinical pregnancy rate (CPR), Miscarriage rate (MR), Multiple Pregnancy Rate(MPR) and Lost for follow up (LFU).

RESULTS: Mean outcomes of Study Vs Control group were as follows:

FR - 92.35% Vs 92.30% (P= 1.0000)
BR - 42.59% Vs 48.8% (P=0.2779)
CPR - 64.52% Vs 62.93% (P= 0.7735)
IR - 45.35% Vs 48.97% (P= 0.5273)
MR -7.53% Vs 9.98% (P=0.4667)
LFU is 9.78% Vs 0%
LBR - 46.47% Vs 51.4% (P=0.3895)
MPR -27.27% Vs 17% (P=0.0219)

Maternal complications

Gestational Diabetic Mellitus - 3% Vs 1.8% (P= 0.4562)

Pregnancy Induced Hypertension (PIH) – 0% Vs 2.1% (P=0.1590)

Intra-Uterine Growth Restriction (IUGR) – 0% Vs 0.3% (P= 0.5973)

Perinatal outcomes –

Average BW - 2.52 Kg Vs 3.01 kg

%Normal BW (>2.5kgs)– 59.52% Vs 63% (P= 0.5307)

% Low BW (1.5-2.5kgs)- 30.95% Vs 31% (P=0.9925)

%Very Low BW (<1.5kgs) - 9.52% Vs 6% (P= 0.2170)

pre-term Birth (<37weeks gestation) - 15.5% Vs 12.8% (P= 0.4876)

Congenital Anomalies in Study Group

one baby was diagnosed with Angelman syndrome (AS), one infant diagnosed with Rabdomyoma at 5th month in study group

Congenital Anomalies in Control Group

one baby with hydrocephalus, one ARDS due to meconium aspiration and the baby died after 18 days, 3 babies died in NICU after pre term delivery.

Data from this study doesn't seem to adversely affect Reproductive and Perinatal outcomes with use of Testicular sperms for ICSI in NOA men.

CONCLUSIONS: In NOA use of SRS doesn't seem to alter reproductive and perinatal outcomes. However, long term follow up of these children is still advised.

P-714 4:30 PM Tuesday, October 20, 2020

IDENTIFICATION OF A NOVEL SOMATIC STEM CELL POPULATION IN ADULT MOUSE TESTIS INVOLVED IN TISSUE HOMEOSTASIS AND REGENERATION. Adrienne N. Shami, B.S.,[1] Yu-chi Shen, Ph.D.,[1] Hailey Larose, Ph.D.,[1] Lindsay Moritz, B.S.,[1] Gabriel Manske, B.S.,[1] Qianyi Ma, Ph.D.,[1] Xianing Zheng, B.S.,[1] Meena Sukhwani, Ph.D.,[2] Kyle E. Orwig, Ph.D.,[2] Jun Z. Li, Ph.D.,[1] Sue Hammoud, Ph.D.[1] [1]University of Michigan, Ann Arbor, MI; [2]University of Pittsburgh School of Medicine, Pittsburgh, PA.

OBJECTIVE: The somatic cells of the testes have critical functions in maintaining spermatogenesis and testosterone production. Similar to other tissues, these functions decline with age, but whether adult testis somatic cells maintain the ability to repair or regenerate remains unclear. Here, we test the functional significance of a recently identified adult mouse testis interstitial cell population expressing the transcription factor Tcf21 in testis homeostasis, aging, and injury.

DESIGN: We utilized single-cell RNA-sequencing (scRNAseq), *in vitro* cell differentiation assays, genetic lineage tracing, and targeted ablation methods to characterize the fate and potential of Tcf21$^+$ cells *in vitro* and *in vivo*.

MATERIALS AND METHODS: To determine whether this population has mesenchymal stem cell properties, we enrich for Tcf21$^+$ cells using flow cytometry and perform clonogenic and trilineage differentiation assays. Using knowledge from our scRNAseq data, we direct the differentiation of adult Tcf21$^+$ cells to testosterone producing Leydig cells and smooth muscle cells. We further characterize the molecular mechanism of *in vitro* differentiation using scRNAseq across several timepoints, and compare *in vitro* derived cells to *in vivo* cells. Finally, to examine the fate and potential of the cells *in vivo* during gonadogenesis, homeostasis and aging, we combine genetic lineage tracing with or without genetic and chemical ablation approaches.

RESULTS: Through genetic lineage tracing experiments we show that the Tcf21$^+$ cells in the fetal gonad contribute to all somatic lineages of the fetal testis, as well as the ovary. In the adult testis, Tcf21$^+$ cells serve as a reserve somatic progenitors in response to tissue injury and maintain testis tissue homeostasis during aging. *In vitro*, we demonstrate that the Tcf21$^+$ cells are multipotent mesenchymal progenitors which give rise to multiple somatic lineages, including two terminally differentiated testis somatic cell types: Leydig and myoid. Consistent with this multipotency, we find that the testis Tcf21$^+$ population has high transcriptomic similarity to resident fibroblast populations in other organs.

CONCLUSIONS: In summary, we show that the recently described population of Tcf21$^+$ cells are bipotential somatic progenitors in the fetal gonad, and this population persists in the adult testis where it can replenish somatic cells during aging and following injury. We also show that the testis Tcf21+ population resembles resident fibroblast populations in multiple organs which have been previously implicated in tissue homeostasis and regeneration. Therefore, we believe that the testis, like other organs, maintains a reserve multipotent somatic cell progenitor. Here, we demonstrate methods for enrichment and differentiation of adult Tcf21+ cells *in vitro*, with potential as a platform for further study of testicular pathology and therapeutics. Future translational studies will determine if an analogous cell population exists in humans, as these somatic progenitor cells have enormous potential for the development of novel treatments for hypogonadism and infertility.

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RAISED SPERM DNA FRAGMENTATION – WILL INTERVENTION WITH SURGICAL RETRIEVAL OF TESTICULAR SPERMS OPTIMIZE REPRODUCTIVE AND PERI-NATAL OUTCOMES ?A DECADE'S OBSERVATIONAL STUDY FROM AN INDIAN CLINIC. Krishna Mantravadi, Sr., MBBS, PGDHOM, Masters in clinical embryology,[1] Afsha Firdouse, M.Sc BioChemistry, PGDCE,[1] Rajesh Mani Raghupathy, MBBS, PGDCE,[2] Yedluri Rupasree, M.Sc Biotechnology, PhD Biotechnology, PGDCE,[1] Durga Rao Gedela, MBBS, DGO, MRCOG, fellowship in infertility and reproductive endocrinology,[2] Sandeep Karunakaran, Sr., M.B.B.S, MS, PGDHM, PGDMLE[3] [1]Oasis fertility, Hyderabad, India; [2]oasis fertility, Hyderabad, India; [3]OASIS FERTILITY, Hyderabad , TELANGANA, India.

OBJECTIVE: For Individuals with Raised Sperm DNA Fragmentation (SDF), will intervention with Surgical Retrieval of Sperms (SRS) from testes optimize Reproductive and Peri-Natal outcomes in Assisted Reproductive Techniques (ART) cycles.

DESIGN: This is a retrospective study at our private IVF clinic from 2010 to 2019.

MATERIALS AND METHODS: SAMPLE SIZE: Couples with history of at least one failed IVF cycle were offered testing for SDF by SCSA method. SDF >30% was considered high and such couples were offered SRS from testes and testicular sperms were used for ICSI (n= 342). Couples were counselled about the risks, benefits and experimental nature of this intervention. Written consent was obtained from the couple and taken through an ART cycle with SRS from tests. Women underwent controlled ovarian stimulation and oocyte retrieval as per our clinic's standard operating protocol (SOP). Fertilized oocytes were cultured till blastocyst stage and freeze all policy was adopted. Two blastocysts were transferred in a frozen embryo replacement cycle.

INCLUSION CRITERIA: Individuals who had successful SRS with self-gamete cycles were included in this study.

Exclusion CRITERIA: Donor gamete cycles and individuals who had failed SRS were excluded from this study.

Primary Outcomes: Implantation rate (IR), Live birth rates (LBR) and Perinatal outcomes

(Gestation Diabetes (GDM), Pregnancy Induced Hypertension (PIH), Intra Uterine Growth Restriction (IUGR), mean Pre-Term Birth rate (PTB), Birth weight (BW Normal - >2.5kgs), Low Birth weight (LBW – 1.5-2.5kgs), Very LBW (VLBW - <1.5kgs)

Secondary Outcomes: Fertilization rate (FR); blastocyst rate (BR), Clinical pregnancy rate (CPR); Miscarriage rate (MR) and Multiple Pregnancy rate (MPR)

RESULTS: Mean of the outcomes were as follows:

FR - 93.35%, **BR** - 35%, **IR** - 40.34%, **CPR** - 56.90 %, **MR** was 12.03 %, **MPR** – 17.2% , **LBR** - 35.23, **GDM** – 6.06%, **PIH** – 6.82%, No IUGR reported in the study group. 17.4% had PTB. Mean BW was 2.5 kg. Out of this **Normal BW** was 55.6 %, **LBW** was 36.7 % and **VLBW** was 13.3 %.

Use of SRS in couples with raised SDF seems to offer optimal reproductive and perinatal outcomes. Couples seeking ART with raised SDF, SRS can be offered as an active intervention.

CONCLUSIONS: Testicular sperm for Raised SDF seem to offer beneficial reproductive and perinatal outcomes in ART cycles. TESA can be offered as an active intervention.

POSTER SESSION: PCOS

P-716 4:30 PM Tuesday, October 20, 2020

POLYMORPHISMS AND HAPLOTYPE OF MITOCHONDRIAL DNA CONTROL REGION ARE ASSOCIATED WITH POLYCYSTIC OVARY SYNDROME IN A CHINESE POPULATION. Dongmei Ji, master,[1] Xiaohong Deng, bachelor,[2] Kai Zong, master,[3] Xinyuan Li, bachelor,[2] Yu Cao, bachelor,[2] Yunxia Cao, Doctor[2] [1]reproductive genetics, mitochondrial disease, Hefei, China; [2]The First Affiliated Hospital of Anhui Medical University, Hefei, China; [3]molecular biology, Heifei, China.

OBJECTIVE: To investigate the relationship between mitochondrial DNA (mtDNA) D-loop region mutations, mtDNA haplogroup and polycystic ovary syndrome (PCOS), as well as the correlation of D-loop variants and clinical characteristics of PCOS, in a Chinese population.

DESIGN: Case-control study.

MATERIALS AND METHODS: A total 420 PCOS patients and 390 controls were enrolled in this study.PCOS patients were divided into BMI matched and mismatched groups relative to controls.Biochemical estimation of basal hormone levels, fasting glucose and insulin levels were carried out. The D-Loop region of whole blood samples was amplified and sequenced, and polymorphisms identified by comparison to the Cambridge Reference Sequence. Patient haplogroup was identified from D-Loop single nucleotide polymorphisms (SNPs). Polymorphisms and haplotype was subsequently correlated with disease state and clinical characteristics via regression analysis. For analysis of clinical characteristics, subjects were grouped according to high or normal levels.

RESULTS: Significant differences were detected at 6 loci in comparison of BMI matched patients and controls; T16086C, C16234T, G207A, 16049Gins, 16036GGins and A16051G.The T16086C variant was associated with PCOS while the other 5 SNPs were associated with the control group.In the same groups, A189G was found to be positively associated with hyperandrogenemia, and T489C negatively. Polymorphism T16086C was associated with increased ratio of LH:FSH whereas 16049Gins, 16036GGins, C16234T, A16463G were associated with normal LH:FSH. Polymorphism T152C was associated with normal insulin resistance (IR). In the patient group with high BMI relative to controls, C151T, 249d and A16203G were associated with PCOS, whereas C150T and T16362C where associated with the control group. Polymorphism A16203G showed a further association with hyperandrogenemia group. Polymorphism T16357C was associated with increased LH:FSH, while 16036GGins, 16049Gins, T16093C and C16266T were associated with normal LH:FSH. Polymorphisms A93G, 249d, C16187T and T16203C were associated with high IR, while G207A and 16049Gins were associated with normal IR. Analysis of haplogroups suggested that A15 is negatively associated with PCOS.

CONCLUSIONS: A number of mtDNA D-loop mutations appear to confer susceptibility or resistance to PCOS in Chinese women, whereas haplotype A15 decreases risk. However, BMI influences which D-loop variants confer risk and must be taken into account.

P-717 4:30 PM Tuesday, October 20, 2020

THE IMPACT OF POLYCYSTIC OVARY SYNDROME ON PLACENTAL HISTOPATHOLOGY PATTERNS IN IVF SINGLETON LIVE BIRTHS. Ginevra Mills, MD, FRCSC,[1] Alexander Volodarsky-Perel, M.D.,[1] Michael H. Dahan, M.D.[2] [1]Division of Reproductive Endocrinology and Infertility, McGill University Health Care Centre, Montreal, QC, Canada; [2]McGill University, Montreal, QC, Canada.

OBJECTIVE: The objective of this study was to evaluate placental histopathology patterns in placentas of women with polycystic ovary syndrome (PCOS) who underwent in-vitro fertilization.

DESIGN: This is a retrospective study utilizing full gross and histopathologic assessment of placentas of 100% of women who had IVF and delivered at the Royal Victoria Hospital (RVH) from 2009-2017, regardless of complications or mode of delivery. Women with pre-existing diabetes were excluded from analysis.

MATERIALS AND METHODS: Placentas were examined in one pathology department and pathological reports were revised by one perinatal gynecology pathologist. Pathologic findings were categorized into anatomic, inflammation, villous maturation, and vascular malperfusion features. A multivariate logistic regression model was used to adjust the results for confounding factors potentially associated with significant placental and perinatal characteristics including (but not limited to) age at embryo transfer (ET), embryo stage at ET, embryo quality, BMI, gravidity, hypothyroidism, development of gestational diabetes (GDM), gestational age at delivery, placental delivery method, birth weight, and placental weight,. Adjusted odds ratios (aOR) with 95% confidence intervals (95% CI) were calculated.

RESULTS: Demographic characteristics of women with PCOS (n=47) and ovulatory controls (n=1121) were comparable with respect to age at oocyte retrieval (p=0.12) and embryo transfer (ET) (p=0.11), BMI (p=0.92), smoking history (p=0.69), gravidity (p=0.69), and parity (p=0.11). There was also no difference between the two groups with respect to mode of delivery (p=0.84), gestational age at delivery (p=0.29), or preterm labour rate (p=0.37). Women with PCOS developed GDM more often compared to those without PCOS (38.3% vs. 9.8% p<0.001). Placentas from PCOS women were more likely to have anatomical differences including circumvallate placentas (aOR 8.3, 95% CI 1.9-37.3) and hypercoiled umbilical cord (aOR 6.8 95% CI 1.3-36.8). Villitus of unknown etiology (VUE) occurred more often in placentas from women with PCOS compared to controls (aOR 6.1, 95% CI 1.5-25.6). There was an increased likelihood of chorangiosis (aOR 2.7, 95% CI 1.3-5.8), evidence of fetal vascular malperfusion based on one criteria (aOR 2.7, 95% CI 1.1-7.4), or more than one criteria (aOR 6.4, 95% CI 1.6 – 25.9), more nucleated fetal red blood cells (aOR 5.2, 95% CI 1.1-24.5), and higher likelihood of chorangiomas (aOR 9.4, 95% CI 1.6-55.1) in placentas from PCOS women than in controls.

CONCLUSIONS: Placental histopathological characteristics are significantly impacted by an underlying diagnosis of PCOS at the time of pregnancy initiation. Placentas in women with PCOS are more likely to have important anatomic changes and vascular placental abnormalities. The effect of these features, as well as the underlying mechanism of their development should be evaluated in further studies.

P-718 4:30 PM Tuesday, October 20, 2020

CYTOKINE CONTENT OF FOLLICULAR FLUID IN WOMEN WITH POLYCYSTIC OVARIAN SYNDROME (PCOS). Lauren Rouleau, MD, PhD,[1] Anna K. Knight, PhD,[1] Sabrina A. Gerkowicz, MD,[2] Shang Weirong, PhD,[1] Laurie J. McKenzie, M.D.,[3] Alicia K. Smith, PhD,[1] Heather S. Hipp, MD[1] [1]Emory University School of Medicine, Atlanta, GA; [2]IVFMD, South Florida Institute for Reproductive Medicine, Miami, FL; [3]Baylor College of Medicine, Houston, TX.

OBJECTIVE: Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorders among women and is often associated with infertility. Previous studies have shown that women with PCOS have higher levels of proinflammatory markers (IL-1, IL-6, and TNF-alpha), but they have focused on a limited number of inflammatory biomarkers in peripheral blood only. We investigated differences in cytokine concentration of follicular fluid between women with and without PCOS, hypothesizing that women with PCOS will have significantly higher levels of pro-inflammatory cytokines.

DESIGN: Nested case control study.

MATERIALS AND METHODS: Follicular fluid was obtained at a single time point during oocyte retrieval from women undergoing a cycle of in vitro fertilization. Women with PCOS were identified according to the Rotterdam criteria, while control women were those undergoing oocyte retrieval for planned fertility delay, oocyte donation, male factor infertility, uterine factor infertility, or unexplained infertility. 58 unique samples of follicular fluid were collected at the time of oocyte retrieval. Descriptive statistics for age, body mass index (BMI), parity, and ovarian reserve parameters of the cohort were examined, followed by t-tests to determine any significant differences between the groups. The follicular fluid samples were analyzed using Ray Biotech Quantibody® Human Cytokine Antibody Array 440, which is a multiplexed sandwich enzyme linked immunosorbent assay (ELISA) quantitative array platform. Primary outcome was cytokine concentrations and secondary outcomes were number of oocytes retrieved, embryo quality, miscarriage rates, and live birth rates. The cytokine data was analyzed using quantile regression, while controlling for age and BMI.

RESULTS: There were no significant differences in age, BMI, number of blastocyst stage embryos, or estradiol level on trigger day between women with PCOS and controls in our cohort. Women with PCOS did have higher anti-Müllerian hormone ($p=0.014$) and number of oocytes retrieved ($p=0.021$). After controlling for age and BMI, out of 440 cytokines, 12 had statistically significant differences between patients with PCOS and controls: IL-1 receptor 2, IL-17, MMP9, MMP13, XEDAR, IL-37, decorin, TGFb2, matrilin3, trapin2, thrombopoietin, and AgRP ($p<.05$). Although IL-17, a pro-inflammatory cytokine, was elevated, IL-37, an anti-inflammatory cytokine was also elevated, clouding the overall impact of pro-inflammatory cytokines in follicular fluid of PCOS patients. No cytokines were statistically significant after multiple test correction using FDR <0.05.

CONCLUSIONS: There were few significant differences in cytokine content of follicular fluid in patients with PCOS compared to controls. MMP9, MMP13, decorin, and matrilin3 are all involved in collagen/extracellular matrix rearrangement, raising the possibility of an intrinsic structural difference in the ovaries of these patients on a cellular level. The results suggest inflammatory content of follicular fluid may not be the driving pathology in differences in IVF outcomes in patients with PCOS.

P-719 4:30 PM Tuesday, October 20, 2020

DIFFERENCES IN PCOS PRESENTATION AMONG BLACK WOMEN IN CALIFORNIA AND ALABAMA. Katherine VanHise, MD,[1] Sahar Wertheimer, MD,[1] Roy G. Handelsman, MD,[1] Rae A. Buttle, BA,[1] Jessica L. Chan, MD, MSCE,[1] Erica T. Wang, MD, MAS,[1] Ricardo Azziz, MD, MPH,[2] Margareta D. Pisarska, MD[1] [1]Cedars-Sinai Medical Center, Los Angeles, CA; [2]University of Alabama at Birmingham, Birmingham, AL.

OBJECTIVE: To compare the PCOS phenotype among Black women in California vs. Alabama.

DESIGN: Tertiary-care based cohort study.

MATERIALS AND METHODS: Black women and adolescents (age $\geq$12) from Los Angeles and Birmingham presented for consultation from 1980 to 2010. Demographic data were obtained including age, hyperandrogenism and menstrual cycle history. A modified Ferriman-Gallwey (mFG) was performed to assess clinical hyperandrogenism (defined as mFG$\geq$4). Markers of metabolic dysfunction were measured including body mass index (BMI), waist-to-hip ratio (WHR), glucose and insulin during a 2-hour glucose tolerance test. Categorical variables between the groups were compared using student's t-tests, rank sum or X^2 tests, as appropriate. A logistic regression was performed to adjust comparisons for BMI.

RESULTS: Three hundred twenty-three Black patients were identified, of which 184 were diagnosed with PCOS by Rotterdam criteria. Alabama patients were younger in age and had higher BMI (Table 1). Even after adjusting for BMI, women in Alabama were more likely to be hirsute, adjusted odd ratio (aOR) 3.08 (CI95%: 1.8-5.2, $p<0.001$), and were more likely to have oligo-ovulation (aOR 1.97, CI95%: 1.2-3.2, $p=0.007$). 0 min. and 60 min. glucose, and 60 min. insulin values, were higher in the Alabama cohort.

Table 1

	California	Alabama	Unadjusted p-value
Total Black, n=323	134	189	
PCOS (%)	73 (62.9%)	111 (95.7%)	<0.001
Age (SD), yr	32.2 (8.0)	28.8 (9.1)	0.0007
BMI (SD), kg/m^2	31.4 (8.7)	34.1 (8.4)	0.006
WHR (SD)	0.85 (0.1)	0.84 (0.1)	0.35
Mean mFG score (SD)	5.6 (5.0)	8.1 (5.3)	<0.001
Clinical HA (%)	78 (58.2%)	155 (82.0%)	<0.001
Oligo-ovulatory (%)	75 (56.8%)	138 (74.2%)	0.001
% elevated glucose, 0 min.	2 (5.4%)	14 (19.2%)	0.04
% elevated glucose, 60 min.	0 (0%)	7 (9.6%)	0.048
% elevated glucose, 120 min.	5 (13.2%)	12 (16.4%)	0.44
% elevated insulin, 0 min.	10 (29.4%)	33 (42.3%)	0.20
% elevated insulin, 60 min.	24 (68.6%)	37 (47.4%)	0.037
% elevated insulin, 120 min.	19 (52.8%)	38 (48.7%)	0.69

CONCLUSIONS: In this study, Black women with PCOS in Alabama had a higher prevalence of oligo-ovulation and clinical HA compared with Black women with PCOS in California, even after adjusting for BMI. Some markers of metabolic dysfunction were also higher in Black women with PCOS in Alabama, even after adjusting for BMI. These data suggest that there are geographic differences in PCOS phenotypes, reinforcing the need for more investigation on the environmental determinants of PCOS.

P-720 4:30 PM Tuesday, October 20, 2020

METABOLIC AND REPRODUCTIVE PCOS-LIKE TRAITS FOLLOWING ESR1 KNOCKDOWN IN THE MEDIOBASAL HYPOTHALAMUS OF ADULT FEMALE RHESUS MONKEYS. David H. Abbott, Ph.D,[1] Emily P. Greinwald, BS,[2] Jesi A. Felton, BS,[2] Matthew T. Flowers, PhD,[2] Molly M. Willging, BS,[2] Robert A. Shapiro, PhD,[2] Kim L. Keen, BS,[2] Ei Terasawa, PhD,[2] Daniel J. Uhlrich, PhD,[2] Jon E. Levine, PhD[2] [1]University of Wisconsin, Madison, WI; [2]University of Wisconsin, Madison, WI.

OBJECTIVE: In primates, including humans, the estrogen receptor mediating neural hypothalamic control of metabolic and reproductive function is unknown. This study therefore tests the hypothesis that diminished estradiol (E2) action by neuronal ESR1 in the female nonhuman primate mediobasal hypothalamus (MBH) causes weight gain and hyperandrogenism resembling polycystic ovary syndrome (PCOS) in women.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Eleven, ovary intact, adult female rhesus macaques, pair housed with female peers, received five 12μl MRI-guided MBH infusions into the rostral-to-caudal extent of both right and left ARC. Each infusion comprised gadolinium contrast agent and adeno-associated virus 8 (AAV8) particles containing either a shRNA specific for ESR1 (n=6, ERaKD) or scrambled shRNA (n=5, control). Mid-surgery MRI scans identified targeting accuracy. 1-2.5 years following AAV8 infusion, EIA-determined P4 values were obtained from twice weekly serum samples; samples obtained during the follicular phase of menstrual cycles or anovulatory periods were submitted to liquid chromatography, tandem mass spectrometry (LCMS) for additional steroid hormones.

RESULTS: ERaKD females, while gaining more body weight than controls, did not increase their daily calorie consumption. Both ERaKD and control female groups exhibited comparably regular menstrual cycles. ERaKD females, however, exhibited hyperandrogenism and elevated LH levels.

CONCLUSIONS: Taken together, these results suggest that knockdown of ARC ESR1 disrupts metabolic regulation and LH stimulation of ovarian function, contributing to female monkey hyperandrogenism and weight gain emulating PCOS in women.

SUPPORT: NIH grants P50 HD028934,Â R01 DK121559

P-721 4:30 PM Tuesday, October 20, 2020

INSULIN RESISTANCE INCREASES OBSTRUCTIVE SLEEP APNEA RISK IN NON-OBESE WOMEN WITH POLYCYSTIC OVARY SYNDROME. Xiaojie P. Zhou, MD,[1] Eleni Greenwood Jaswa, MD, MSc,[2] Nikolaus J. Lenhart, BS,[1] Jamie Corley, BA,[1] Marcelle I. Cedars, MD,[1] Heather G. Huddleston, MD[2] [1]University of California San Francisco, San Francisco, CA; [2]University of California, San Francisco School of Medicine, San Francisco, CA.

OBJECTIVE: Reproductive-aged women with polycystic ovary syndrome (PCOS) experience increased rates of obstructive sleep apnea (OSA). Although obesity is a well-known risk factor for OSA, prior studies suggest that obesity does not fully account for the increased OSA risk observed in women with PCOS. The aim of this study was to evaluate the effect of insulin resistance, independent of body mass index (BMI), on OSA risk.

DESIGN: Cross-sectional study

MATERIALS AND METHODS: All patients seen at a university-based clinic between 2017-2020 with a confirmed PCOS diagnosis by the Rotterdam criteria were included. Clinical and laboratory measurements were collected. A body mass index $\geq$ 30 kg/m^2 was considered obese. A homeostatic model assessment of insulin resistance (HOMA-IR) score $\geq$ 2 was considered insulin resistant. Participants completed the validated Berlin questionnaire consisting of 3 categories related to OSA risk. A positive score in 2 or 3 categories is considered high-risk for OSA. Multiple imputation was performed to account for missing data. Multivariate logistic regression was used to assess the association between obesity and OSA risk with adjustment for age, insulin resistance, free testosterone level and depression symptoms as measured by the Patient Health Questionnaire-9. An interaction term between BMI and insulin resistance was included to assess for effect modification.

RESULTS: A total of 182 women with PCOS were included, of which 38.5% screened high-risk for OSA. For all participants, the mean age was 28.2 years (SD 6.2) and the mean BMI was 31.0 kg/m^2 (SD 9.0). Of those who screened high-risk for OSA, 85.7% were obese and 14.3% were non-obese. We found evidence of an interaction between obesity and insulin resistance in that the degree of association between insulin resistance and OSA risk varied according to the presence of obesity (interaction coefficient -2.32, 95% CI -4.70 to -0.10, p=0.041). Participants who were obese without insulin resistance had substantially higher odds of being high-risk for OSA as compared to those who were non-obese (OR 100.9, 95% CI 13.0-784.9). Among the obese women, being insulin resistant did not affect the odds of being high-risk for OSA compared to not being insulin resistant (OR 0.69, 95% CI 0.12 to 4.06). However, among the non-obese women, being insulin resistant led to increased odds of being high-risk for OSA (OR 7.6, 95% CI 1.8-32.6).

CONCLUSIONS: Although obesity is the predominant driver of OSA risk in women with PCOS, features unique to PCOS such as insulin resistance help explain the increased risk of OSA in non-obese women in this population. Given the diverse phenotypes of PCOS, better understanding the particular OSA risk factors experienced by different subgroups will aid in personalizing treatment.

P-722 4:30 PM Tuesday, October 20, 2020

THE EFFECTS OF MELATONIN ON *IN VITRO* CULTURE OF MOUSE EMBRYOS FROM EXPERIMENTAL MODELS OF POLYCYSTIC OVARY SYNDROME. Marcela de Oliveira Pinheiro, Bs,[1] Doris Ferreira Moriyama, M.Med.Sci,[2] Gabrielle Ferrante Alves de Moraes, Ms,[1] Edson G. Lo Turco, PhD[3] [1]São Paulo Federal University, São Paulo, Brazil; [2]Sao Paulo Federal University, School of Medicine, Department of Surgery, Division of Urology, Human Reproduction Section, Sao Paulo, Brazil; [3]IonMedicine - Precision Medicine, Sao Paulo, Brazil.

OBJECTIVE: Analyse the effects of embryo culture media with melatonin supplementation on the development and quality of mouse embryos from experimental models of PCOS and control groups.

DESIGN: Prospective study.

MATERIALS AND METHODS: This work used C57BL/6J mice strain (n = 60) divided into 3 large groups: PCOS (20μL of testosterone cypionate), placebo (20μL of peanut oil), and control. When these mice reached 28 days of age, superovulation was achieved with i.p. injections of 5 IU of pregnant mare's serum gonadotrophin, followed by 5 IU of equine chorionic gonadotrophin 42-48 hours later. A few hours after equine chorionic gonadotrophin administration, females were paired with males and left together overnight. On the following morning (18-24 hours later), the presence of vaginal plug was checked and the positive females were culled by cervical dislocation, 1-cell embryos were then flushed from the oviducts. Collected embryos (n=316) were then divided into each study group and cultured in single step medium with or without melatonin supplementation at 37$\underline{o}$C and 6% CO_2. Once the blastocyst stage was reached it was evaluated: i) cleavage, morula and blastocyst rate; (ii) morphological assessment of the blastocysts; (iii) DNA fragmentation in blastocyst cells by TUNEL test.

RESULTS: We observed that the blastocyst rate (n=316) was lower in the PCOS group when compared to the placebo and control groups. Melatonin supplementation did not have a positive effect on embryonic development on the PCOS group. morphological assessment, a significant difference was found for the variables quality index (PCOSm: 7,3±1,66, PCOS: 7,5±1,50, Placm: 13,2±0,90, Plac: 14,3±1,21, Contrm: 14,2±1,17, Contr: 13,7±1,42), blastocyst expansion (PCOSm: 3,3±0,37, PCOS: 3,4±0,32, Placm: 4,2±0,93, Plac: 4,2±0,10, Contrm: 4,1±0,13, Contr: 4,0±0,12) and trophectoderm (PCOSm: 1,4±0,12, PCOS: 1,2±0,11, Placm: 1,6±0,05, Plac: 1,6±0,06, Contrm: 1,7±0,06, Contr: 1,6±0,08), with the placebo and control groups showing consistently higher scores. In the TUNEL test (n=142), the supplemented PCOS group had a higher mean rate of apoptotic cells/total cells (A/T) when compared to the group without supplementation, indicating a poorer quality of the blastocysts (PCOSm: 16,5±3,61, PCOS: 11,9±2,14).he placebo and control groups supplemented with melatonin showed a lower mean A/T (Placm: 6,6±0,76, Contrm: 6,2±0,78) when compared to the non-supplemented groups, indicating a superior blastocyst quality (Plac: 7,1±0,85, Contr: 8,4±1,33).

CONCLUSIONS: This study concluded that melatonin supplementation in the embryonic culture media did not have a positive effect on the PCOS group consideringhe blastocyst rate, morphological assessment and DNA fragmentation on blastocyst cells. In contrast, the melatonin supplementation on the control group had a positive effect on all variables analysed.

SUPPORT: This study was financed in part by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

P-723 4:30 PM Tuesday, October 20, 2020

TRANSCRIPTOMIC LANDSCAPE OF GRANULOSA CELLS AND PERIPHERAL BLOOD MONONUCLEAR (PBMN) CELLS IN WOMEN WITH PCOS AND POOR OVARIAN RESPONSE (POR). Mauro Cozzolino, MD,[1] Shiny Titus, PhD,[2] Sonia Herraiz, Ph.D.,[3] Antonio Pellicer, MD,[3] Richard Thomas Scott, Jr., MD,[4] Emre Seli, M.D.[1] [1]Yale School of Medicine, New Haven, CT; [2]Foundation for Embryonic Competence, Basking Ridge, NJ; [3]IVIRMA Foundation, Valencia, Spain; [4]IVI RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: To investigate transcriptomic characteristics of follicular and somatic cells in young women with PCOS and poor ovarian response (POR), compared to normo-responder controls.

DESIGN: Prospective experimental study.

MATERIALS AND METHODS: Young reproductive age women (<35 years old) with PCOS (n=5; selected based on Rotterdam criteria); poor ovarian response (n=5; selected based on Poseidon criteria – group 1a with number of oocytes retrieved <4); and normo-responder controls (n=5) undergoing IVF were included in the study. Peripheral blood mononuclear cells (PBMNCs) and granulosa cells (GCs) were collected on the day of retrieval, and total RNA was isolated using RNeasy Micro kit (Qiagen). RNA sequencing libraries were constructed using the Nextera® XT DNA Library Preparation Kit (Illumina, San Diego, CA) and multiplexed using Nextera® XT Index Kit (Illumina, San Diego, CA). Libraries were quantified by Qubit and Tapestation 4200. Differentially expressed genes were determined using false discovery rate (FDR) of p-value $<$ 0.01, fold change $>$ 2. Ingenuity Pathway Analysis (IPA) software was used to perform pathways analyses.

RESULTS: Mean age was similar between the groups (PCOS: 32.5 $\pm$ 0.7; POR: 34.2 $\pm$ 1.4; controls: 31.0 $\pm$ 2.1), while, as expected, women with POR had significantly lower number of oocytes retrieved (PCOS: 16 $\pm$ 4.9; POR: 2 $\pm$ 1.5; controls: 21 $\pm$ 3.6; p<0.05). In PBMNCs, 65 genes were differentially expressed in PCOS (55 increased, 10 decreased; affecting STAT3 and AKT pathways), and 16 were differentially expressed in POR (4 increased, 12 decreased; affecting cytokine signaling pathways), compared to controls. Direct comparison of PCOS to POR revealed 16 genes (9 increased, 7 decreased;) to be differentially expressed. In GCs, 4 genes were differentially expressed in PCOS (all 4 decreased; affecting inositol synthesis pathways), and none in POR, compared to normal controls. Importantly, when GCs

from women with POR were compared to those from PCOS, 58 genes were found to be differentially expressed (13 increased, 45 decreased), affecting pathways related to mitochondrial function and oxidative phosphorylation (down-regulated), and aging/sirtuin (up-regulated).

CONCLUSIONS: Our findings suggest that somatic PBMNCs and GCs from young reproductive age women with PCOS and POR have unique transcriptomic signatures. Specifically, GCs from women with POR demonstrate suppression and activation of pathways, associated with mitochondrial function and aging, respectively. Our findings could be exploited for future mechanistic studies and to develop novel diagnostic approaches.

P-724 4:30 PM Tuesday, October 20, 2020

THE ROLE OF GENETICS IN HYPERANDROGENIC PCOS: WHAT'S THE BIG, HAIRY DEAL? Emma Radley, M.A.,[1] Nepheli I. Raptis, B.A., M.A.,[1] Hanna Mandell, M.A.,[1] Christy Oso, B.A.,[1] Lauren Grimm, M.A.,[1] Jessi Anderson, MPH,[1] Zoran J. Pavlovic, M.D.,[2] Angeline Beltsos, MD,[1] Roohi Jeelani, MD[1] [1]Vios Fertility Institute, Chicago, IL; [2]Rush University Medical Center, Chicago, IL.

OBJECTIVE: To determine if patients with clinically presenting hyperandrogenic Polycystic Ovary Syndrome (PCOS) are at increased risk of producing aneuploid embryos in order to further define the unique characteristics of this sub-classification.

DESIGN: Although hyperandrogenism is one of the three pillars of a PCOS diagnosis, only a portion of patients present with the associated clinical symptoms, such as adult acne and hirsutism. PCOS patients have been shown to have significantly decreased embryo quality, which is hypothesized to be due to hyperandrogenism. Both PCOS patients and those presenting with hyperandrogenism have shown increased miscarriage rates. As studies continue to produce evidence supporting the association between hyperandrogenism and aberrant gene expression, we sought to examine if patients with clinically presenting hyperandrogenic PCOS were more likely to develop aneuploid embryos compared to PCOS patients without hyperandrogenic symptoms. Understanding the pathophysiology of clinically presenting hyperandrogenic PCOS may be key in appropriately treating this specific patient population.

MATERIALS AND METHODS: Retrospective chart review was performed at a private multi-site infertility center. Patients with a serum anti-mullerian hormone level of >5 ng/mL, who underwent in-vitro fertilization, and utilized pre-implantation genetic testing for aneuploidy between April 2017 and September 2019 were included. Patients were then separated into two groups, consisting of those with self-reported hyperandrogenism symptoms (hyperandrogenic PCOS) and those who self-reported an absence of hyperandrogenic symptoms (classical PCOS). The average rate of aneuploid embryos were then calculated for each group. Two sample t-tests and chi square analysis were used to analyze the data (SPSS Inc., Chicago, IL).

RESULTS: A total of 349 embryos biopsied within the hyperandrogenic PCOS group and 256 embryos biopsied within the classical PCOS group were analyzed. Those with hyperandrogenic PCOS had average aneuploidy rate of 54.2%. Those with classical PCOS had an average aneuploidy rate of 45.1%. There was no significant difference in aneuploidy rate between the hyperandrogenic or classical PCOS groups ($p = 0.10$). There was no significant difference in age between the two groups ($p = 0.4$).

CONCLUSIONS: The lack of a significant difference in aneuploidy rates between patients with hyperandrogenic PCOS and classical PCOS continues to improve our understanding of the characteristics and mechanisms underlying pregnancy outcomes. Our data supports that the unique outcomes of hyperandrogenic presenting PCOS patients are not in fact due to increased embryonic genetic abnormalities. These findings emphasize the importance of continuing to analyze the unique characteristics of this sub-classification of PCOS to further understand the mechanisms affecting pregnancy outcomes and create more appropriate treatment protocols.

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SUPPORT: *Vios Fertility Institute, Chicago, IL, United States*

P-725 4:30 PM Tuesday, October 20, 2020

IMPACT OF NEW 2018 INTERNATIONAL DIAGNOSTIC CRITERIA FOR THE DIAGNOSIS OF POLYCYSTIC OVARY SYNDROME. Katherine E. Kostroun, MD,[1] Kathryn M. Goldrick, MD,[1] Jessica N. Mondshine, BS,[1] Randal D. Robinson, MD,[2] Cheria C. Brown, RN,[1] Jennifer F. Knudtson, MD[1] [1]University of Texas Health Science Center San Antonio, San Antonio, TX; [2]University of Texas Health Science Center San Antonio, San Antonio, SC.

OBJECTIVE: Polycystic Ovary Syndrome (PCOS) has been historically diagnosed based on the Rotterdam criteria of 2 of 3 factors: irregular menses, clinical or biochemical evidence of hyperandrogenism, and ≥ 12 ovarian follicles in an ovary or ovarian volume or ≥ 10 mL. The recommendations from the International Evidence-Based Guideline for the Assessment and Management of Polycystic Ovary Syndrome published in 2018 changed the ultrasound criteria from ≥ 12 to ≥ 20 antral follicles in an ovary for the diagnosis of PCOS (1). The purpose of this study was to evaluate whether application of the new guidelines would decrease the rate of diagnosis of PCOS.

DESIGN: Retrospective Chart Review

MATERIALS AND METHODS: This study evaluated women, age 12-65, with the ICD code of 'Polycystic Ovary Syndrome' in 2017 in a university hospital system with a large Hispanic population. Data regarding demographics, as well as clinical, laboratory, and ultrasound criteria for diagnosis of PCOS was collected as available for the patients via electronic health records into REDCap. Analysis was performed with SAS 9.4 (Cary, NC) software with Chi-square tests used to determine significance, and p-value <0.5 was determined to be significant.

RESULTS: Of the 500 women included in the study, 183 had ultrasounds with antral follicle data. Of those, 153 (84%) demonstrated ≥ 12 follicles on a single ovary, whereas only 43 (23.5%) had ≥ 20 follicles on a single ovary ($p<0.001$). Taking into account all available diagnostic information on chart review, 258 (52%) patients met criteria for PCOS based on Rotterdam criteria, whereas only 195 (39%) met criteria based on the new 2018 guidelines ($p<0.0001$).

CONCLUSIONS: There is a significantly decreased rate of diagnosis of PCOS in patients with the application of the 2018 recommendations from the International Evidence-Based Guideline for the Assessment and Management of Polycystic Ovary Syndrome. This study confirms the importance of a detailed, skilled ultrasound exam, that includes antral follicle count, in patients who do not meet diagnostic criteria for PCOS based on hyperandrogenism and oligomenorrhea alone. Because of the high percentage of Hispanic patients in our study, these findings may not apply to other populations.

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SUPPORT: K23 HD097307 (JFK)

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IS VITAMIN D SUPPLEMENTATION RELATED TO SEXUAL DYSFUNCTION (SDY) AND DEPRESSION IN WOMEN WITH PCOS?. Rachel Booth, DO,[1] Rachel Blair Danis, MD,[2] Rose Maxwell, PhD,[3] Marilyn Kindig, DO,[1] Richard S. Legro, M.D.,[4] Frank Stanczyk, PhD,[2] Steven R. Lindheim, M.D.[1] [1]Wright State University, Dayton, OH; [2]University of Southern California, Los Angeles, CA; [3]Wright State University, OB/GYN, Dayton, OH; [4]Penn State College of Medicine, Hershey, PA.

OBJECTIVE: Polycystic ovary syndrome (PCOS) has been reported to be associated with significant health-related quality of life (HR-QOL) morbidities including depression and SDy. Clinical hyperandrogenism, obesity, and Vitamin D (Vit D) have also been associated with HR-QOL issues. Therefore, we conducted a pilot study to determine if dietary Vit D supplementation could reduce depression and SDy in women with PCOS.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: We recruited women of reproductive age (ages 18 to 39 yrs) who were diagnosed with PCOS by Rotterdam Criteria, self-reported SDy without severe depression and who did not desire fertility. Vit D 600IU was consumed daily for 6 months. Serum levels of total Vit D were measured at baseline and at study completion (25(OH) Vitamin D

ELISA kit, Abcam). Patients completed the Beck Depression Inventory (BDI) and the Female Sexual Functioning Index (FSFI), which includes domains for desire, arousal, lubrication, orgasm, satisfaction, and pain, at study initiation and at 6 months. Pearson correlation was used to determine associations between total Vit D levels, BDI, and FSFI scores and paired T-Tests were used to determine change over time.

RESULTS: Forty-seven women were initially evaluated; 5 were excluded with severe depression. Of these, 76% (32) with objective SDy on FSFI (< 26.6), had a mean age: 29.2 ± 6.4 yrs (± SD), Body Mass Index (BMI): 38.0 ± 8.5 kg/m2, Ferriman-Gallwey Score: 12.6 ± 7.9, total FSFI: 18.6 ± 6.9; BDI: 15.2 ± 8.8, and Vit D: 41.0 ± 71.2 ng/mL. At baseline, Vit D levels did not correlate with BDI or total FSFI ($p>0.05$), though it was associated with a healthy sexual desire ($r=0.393$, $p=0.032$). Of those that completed the study, 18 of 20 (90%) subjects had improved FSFI scores. Mean FSFI score at baseline was 20.1±5.43 and improved significantly to 25.25 ± 6.38 ($p<.05$). Of the 17 patients that completed both BDI surveys, baseline means changed from 13.8 ± 7.3 to 5.2 ± 4.1 ($p<.001$), and 11/13 (84.6%) with mild to moderate depression had improvement in their BDI scores. At 6 mo, Vit D levels were unchanged from baseline (29.1 ± 21.2 ng/mL) nor were significantly associated with changes in SDy and BDI.

CONCLUSIONS: SDy and BDI scores improved over a 6-mo period after supplementation with Vit D, however this improvement was not correlated with total Vit D levels at baseline and at 6 mo. Correlations with bio-available Vit D levels, the impact of placebo, and identifying a therapeutic dose of Vit D remain to be elucidated.

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EVALUATING OVARIAN VOLUME AS A SINGLE MARKER FOR POLYCYSTIC OVARY SYNDROME (PCOS) AND METABOLIC DYSFUNCTION.

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OBJECTIVE: To determine if ovarian volume alone is an adequate marker for Polycystic ovary syndrome (PCOS) and metabolic dysfunction.

DESIGN: Tertiary-care based cohort study.

MATERIALS AND METHODS: Patients age >14 presented for consultation to 4 academic institutions from 1980 to 2010. Markers of hyperandrogenism (HA) included the modified Ferriman-Gallwey score (mFG), free testosterone (T), and dehydroepiandrosterone sulfate (DHEAS) values. Markers of metabolic dysfunction included body mass index (BMI), waist circumference (WC), high-density lipoprotein (HDL), triglycerides (TG), hypertension (HTN, defined as ≥ 135/85), and insulin and glucose levels during a 2-hour glucose tolerance test. Women were divided into two groups according to ovarian volume (OV): ≥10 mL (OV≥10) and volume <10 mL (OV<10). Categorical variables were compared using χ^2 tests and continuous variables were compared using Student's t-test or Wilcoxon rank-sum, as appropriate. Spearman's rank correlation was calculated to correlate OV with antral follicle count (AFC).

RESULTS: Seven-hundred eighteen women were included, of which OV≥10 was present in 362 women (50.4%) and OV<10 in 356. There was a positive correlation of OV with AFC (r_s =0.54, $p<0.0001$). The mean ages of women (SD) in OV<10 and OV≥10 women were 30.1(7.3) and 29.1(5.8) years, respectively. ($p=0.03$). PCOS by Rotterdam criteria was found in 89.4% of the OV≥10 group and 68.0% of the OV<10 ($p<0.001$). Higher OV was associated with a higher prevalence of HA overall (73.1% vs 58.1%, $p<0.001$), and with an mFG ≥4 (67.5% vs 54.7%, $p=0.001$) and elevated free T (30.1% vs 19.1%, $p=0.002$) specifically. Metabolic parameters including BMI, WC, and 1-hr insulin levels were significantly higher in the OV≥10 group compared to OV<10 women; HTN, HDL, TG and 2-hr glucose values were similar between the groups.

CONCLUSIONS: Ovarian volume of ≥10 mL, as a single marker, is associated with HA and metabolic dysfunction in PCOS. Given that the measurement of AFC is less precise, particularly in less experienced sites, the use of OV alone decreases the complexity of the evaluation and increases the ability to capture patients with risk for PCOS or metabolic dysfunction.

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DO POLYCYSTIC OVARIAN SYNDROME PATIENTS WITH LOWER HEMOGLOBIN A1C LEVELS HAVE BETTER IVF OUTCOMES?.

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OBJECTIVE: Current data suggests that better blood glucose control contributes to better overall health in women with Polycystic Ovarian Syndrome (PCOS). However, it is unclear whether it directly correlates with better outcomes for *in vitro* fertilization (IVF) in these patients. We hypothesized that Hemoglobin A1C levels, as a measure of long-term blood glucose control, would correlate with IVF outcomes in PCOS patients. The objective was to investigate the relationship between available A1C levels and IVF outcome measures in PCOS patients seen at the NYU Fertility Center.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: PCOS patients who underwent IVF at the NYU Fertility Center from 2012 to 2019 with an available A1C level were identified. Only the first IVF cycle was evaluated for each patient. Outcomes were number of oocytes retrieved, number mature, number fertilized, number blastocysts, number biopsied, and of number euploid, aneuploid, and mosaic embryos. Pearson's correlation was used for analysis, and correlation coefficients with $p<0.05$ were considered significant.

RESULTS: 72 IVF cycles were included for analysis of number of oocytes retrieved, number mature, and number blastocysts. 55 of these patients underwent preimplantation genetic screening (PGS); all of these were analyzed for number of euploid, aneuploid, and mosaic embryos. First, BMI was positively correlated with A1C ($R=0.33$). A1C was negatively correlated with number of oocytes retrieved ($R=-0.26$), number mature ($R=-0.25$), number fertilized ($R=-0.23$), number blastocysts ($R=-0.24$), and percentage blastocysts per mature oocyte ($R=-0.24$).

CONCLUSIONS: Overall, higher A1C level near time of cycle start in PCOS patients is correlated with a lower number of oocytes retrieved, number of mature oocytes, number fertilized, number of blastocysts, and percentage of blastocysts per mature oocyte. Although the correlation between BMI and A1C makes it difficult to dissociate effects of A1C from those of BMI, these results show that overall better metabolic and weight control contribute to better IVF outcomes.

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RACIAL AND ETHNIC DIFFERENCES IN THE PREVALENCE OF DIAGNOSED POLYCYSTIC OVARY SYNDROME IN WOMEN RECEIVING AMBULATORY CARE.

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OBJECTIVE: To assess the prevalence of polycystic ovary syndrome (PCOS), a common endocrine disorder among women of reproductive age, according to race and ethnicity, including Asian sub-groups.

DESIGN: Cross-sectional electronic health record (EHR) study conducted within a retrospective observational cohort study of adults who were health plan members in 2016 of a large integrated northern California healthcare delivery system.

MATERIALS AND METHODS: We used EHR data for 405,580 women age 21-44 who had a body weight measured in 2016 and height (in 2015-2016) to calculate body mass index (BMI, kg/m2). We then identified within this population women with one or more ambulatory diagnoses of PCOS (ICD-9 256.4, ICD-10 E28.2) between 1/1/2015 and 12/31/2016. Race/ethnicity was classified as non-Hispanic White, Black, Hispanic, and Asian, with additional identification of Chinese, Filipino, and South Asian ethnicity. The proportion of women with a diagnosis of PCOS was examined by race/ethnicity.

RESULTS: The prevalence of diagnosed PCOS varied by race/ethnicity and was 1.6% among white women but ranged as high as 3.5% among South

Asian women and as low as 1.1% among Chinese women (Table 1). The prevalence among Hispanic and Black women was 1.9% and 1.7%, respectively. When examined by age strata within race/ethnic group, diagnosed PCOS was more prevalent among women age 21-34 years than women age 35-44 years.

Table 1

Race/Ethnicity (Number of women)	White (161,592)	Hispanic (94,607)	Black (33,909)	Chinese (24,366)	Filipino (27,551)	South Asian (24,410)
Mean BMI (SD)	27.9 (7.2)	30.0 (7.2)	31.6 (8.5)	23.6 (4.3)	27.0 (5.8)	25.8 (4.9)
PCOS diagnosis (%)	1.6 %	1.9 %	1.7 %	1.1 %	1.7 %	3.5 %
Age 21-29 years	1.6 %	2.3 %	2.0 %	1.1 %	1.9 %	5.3 %
Age 30-34 years	2.0 %	2.4 %	2.5 %	1.9 %	2.1 %	4.1 %
Age 35-44 years	1.3 %	1.4 %	1.2 %	0.8 %	1.4 %	2.0 %

CONCLUSIONS: The proportion of Northern California women with a diagnosis of PCOS varied by race/ethnicity and was higher during peak reproductive years. Among women of Asian race, the prevalence of PCOS varied by more than 2-fold and was highest for women of South Asian ethnicity. Our study supports the need to further understand ethnic differences in PCOS and reproductive health.

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DOES CONTROLLED OVARIAN HYPERSTIMULATION RESPONSE VARIES WITH PCOS PHENOTYPES: A PROSPECTIVE COHORT STUDY AT A TERTIARY INFERTILITY CENTRE IN INDIA.

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OBJECTIVE: Polycystic ovarian syndrome(PCOS) is a highly prevalent disorder affecting 15 -25% of infertile women .This disorder has 4 different phenotypes and Controlled ovarian stimulation in these patients represents a task for fertility specialist as response varies from resistance to COH to exaggerated response [1,2]. The present study was undertaken to assess response to controlled ovarian hyperstimulation in various PCOS phenotypes

DESIGN: A prospective cohort study was carried out at a tertiary level infertility centre in India from 1st January 2018 through December 2019. Two hundred and fifty infertile women diagnosed with PCOS according to Rotterdam's criteria were divided into 4 phenotypes. Inclusion criteria were: Age < 40 years, BMI< 30, AMH> 1.5 ng/ml PCOS women undergoing IVF. Other causes of infertility including severe endometriosis, uterine factor, severe male factor, hydrosalpinx were excluded from the study. The primary outcome measured was clinical pregnancy rates. Secondary outcomes measured were doses of gonadotropins used, estradiol levels on the day of trigger and number of oocytes retrieved in different phenotypes.

Four Phenotypes of PCOS are defined as

A. Polycystic Ovaries on USG (PCO) + clinical and/ biochemical hyperandrogenemia (HA) + Oligo/anovulation (OA) (PCOS complete)

B. HA + OA

C. PCO + HA

D. PCO + OA

MATERIALS AND METHODS: The patients underwent controlled ovarian hyperstimulation with recombinant FSH (150 IU-225 IU) from day 2 of cycle with antagonist added from day 6 of stimulation(fixed protocol) and followed up with regular follicular monitoring. Injection ovitrelle 250 mcg was given as trigger routinely except if > 14 follicles of > 11mm size were noted on day of trigger, wherein agonist trigger was given. IVF was done for all patients.

RESULTS: Phenotpye D was the most prevalent phenotype at our sitting (49.60%). Women with phenotype A had significantly higher AMH ($p<0.05$)) and significantly higher estradiol levels on the day of trigger ($p < 0.05$) compared to other 3 groups. Phenotpye B needed highest doses of gonadotropin with respect to all other phenotypes ($p < 0.05$). Phenotype C had significantly higher testosterone levels compared to rest of the phenotypes ($p < 0.05$). Clinical pregnancy rates were significantly higher in phenotype D (50.8%) when compared to other phenotypes (A- 34.48%, B-31.82%, C-30.23%, $p< 0.05$).

CONCLUSIONS: Various PCOS phenotypes show different response to controlled ovarian hyperstimulation. Phenotype A seems to have a highest risk of OHSS and the use of GnRH agonist trigger and freeze all strategy might be beneficial in such cases. Phenotpye B appears to be the most resistant phenotype, hence a higher starting dose of gonadotropin might be needed for optimal response. Phenotype C had highest levels of hyperandrogenism and lowest pregnancy rates. Phenotype D had highest clinical pregnancy rates when compared to other phenotypes, suggesting hyperandrogenism might be responsible for a negative impact on pregnancy rates.

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P-731 4:30 PM Tuesday, October 20, 2020

MESENCHYMAL STEM CELLS SECRETOME REGULATES STEROIDOGENESIS AND DECREASES ANDROGEN PRODUCTION IN PCOS CELL MODEL VIA SECRETING BMP-2.

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OBJECTIVE: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women with characteristics of inflammation,

hyperandrogenism, and polycystic ovaries. Most available therapies for PCOS aim to regulate the steroidogenesis and decrease ovarian androgen production to enhance fertility. Our previous study shows the ability of human bone marrow mesenchymal stem cells conditioned media (MSC-CM) to inhibit androgen production by human theca-like cell model (H295R cells). Previous studies demonstrated the ability of BMP-2 as a modulator of androgen production and alteration in steroidogenesis pathway enzymes in bovine theca cells. BMP-2 is a prominent member of the TGF-beta family and an important mediator of the regenerative and immune-modulating functions of MSCs. In this study, we analyzed the effect of BMP-2 on steroidogenic pathway enzymes and androgen production using a human PCOS *in-vitro* model.

DESIGN: We hypothesize that BMP-2 secreted by human MSCs is a key factor for regulating steroidogenesis and have the ability to suppress androgen production in a human PCOS cell model.

MATERIALS AND METHODS: The human adreno-carcinoma (H295R) cell line was used as an *in-vitro* PCOS model. Cells were cultured at a density of 1.8 x10^5 cells per well in six-well plates and treated for 48 hours with recombinant human BMP-2 with a dose range of 0 to 100 ng/ml with a negative control. After treatment, cells were washed and serum-free media were added for additional 24 hours. After incubation, cells and media were collected for analysis. The mRNA expression for CYP17A1, CYP11A1, DENND1A genes was quantified by real-time PCR. The testosterone level in media by automated chemiluminescence immunoassay system, BMP-2 level in the MSC-CM by ELISA. To confirm the effect of MSC-CM is due to BMP-2; we neutralized Normal MSC-CM with an anti-human BMP-2 antibody as well as knockdown the BMP-2 gene in MSCs. Student t-test was used for statistical analysis.

RESULTS: H295R cells treated with BMP-2 for 48 hours secreted significantly low level of total testosterone in a dose-dependent manner (0ng/ml: 68.60±10.6 ng/dl, 3.125 ng/ml: 40.17±4.11 ng/dl, 6.25 ng/ml: 28.83±8.2 ng/dl, 12.5 ng/ml: 27.73±3.85 ng/dl, 25 ng/ml: 18.8±1.96 ng/dl ($p<0.05$). BMP2 >25ng/ml suppressed testosterone, which was not detected by the system (detection limit: 10ng/dl). CYP17A1 and DENND1A gene expression were significantly downregulated ($P<0.05$) with all the tested concentrations while there was no change in the expression of CYP11A1 gene ($P>0.05$). The concentration of BMP-2 in MSC-CM was 62 pg/ml. H295R cells treated with Normal MSC-CM neutralized with Anti-human BMP-2 antibody or CM from BMP-2 knockdown MSCs shows nullify the effect of both MSC-CM on steroidogenic pathway genes expression.

CONCLUSIONS: BMP-2 significantly suppressed androgen production and expression of androgen-synthesizing genes in human theca-like H295R cells compared to the control. BMP-2 is a key player in mediating the favorable effects of MSC-CM on the human PCOS cell model. MSCs could provide a novel stem cell therapy for patients with intractable PCOS.

SUPPORT: Start-up Fund from The University of Illinois, Chicago, USA.

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COMPARISONS OF GLUCOSE INTOLERANCE TESTING FOR THE DETECTION AND DIAGNOSIS OF PREDIABETES AND TYPE II DIABETES MELLITUS IN REPRODUCTIVE AGE WOMEN WITH POLYCYSTIC OVARY SYNDROME.

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OBJECTIVE: Polycystic Ovary Syndrome (PCOS) is one of the most common metabolic conditions affecting reproductive-age women. Its etiology is not completely understood. PCOS is diagnosed using the 2003 Rotterdam Criteria (ROT), in which patients must meet at least two of the three following criteria: (1) clinical or biochemical evidence of hyperandrogenism, (2) anovulation/oligomenorrhea and (3) polycystic ovarian morphology on ultrasound with the exclusion of other etiologies (e.g., congenital adrenal hyperplasia, androgen-secreting tumors, Cushing's syndrome). Although not included in the Rotterdam criteria, one of the metabolic features of PCOS is glucose intolerance and insulin resistance. PCOS patients have a four to eight-fold increased risk of developing Type II Diabetes Mellitus (DM) making the proper diagnosis imperative in this patient population. Therefore, we sought to determine the most sensitive way to screen for abnormal glucose metabolism in this patient population.

DESIGN: A retrospective chart review (IRB# 19-477) was performed for all women (18-45 years of age) who presented to the Reproductive Endocrinology and Fertility clinic at Southern Illinois University School of Medicine who received glucose testing (2 hour oral glucose tolerance test (OGTT) with a 75gm glucose load, Hemoglobin A1c (Hgb A1c) and insulin levels (fasting and 2-hour post-prandial) at their initial visit as part of their evaluation for PCOS between 07/01/2012 and 07/01/2019.

MATERIALS AND METHODS: Of the 646 charts that were reviewed, 345 women met the eligibility criteria, of which 118 were confirmed to have PCOS based on the 2003 Rotterdam Criteria; however, we removed 17 subjects who were utilizing Metformin/Glucophage at the time of evaluation. Additional criteria such as age, body mass index (BMI), gravity and parity, etc. were also collected. Glucose intolerance was defined by the American Diabetes Association guidelines (fasting glucose: 100-125 mg/dL, normal < 100 mg/dL; 2hr OGTT 140 to 199 mg/dL, normal < 140 mg/dL; Hgb A1C 5.7% to 6.4%, normal < 5.7%.

RESULTS: Of the 101 PCOS subjects, the 2 hour OGTT detected glucose intolerance in 7.5% of the population. Fasting glucose found 14.5% of the subjects to have glucose intolerance and Hgb A1C identified 9.5% of the PCOS patients to have glucose intolerance.

CONCLUSIONS: Based on these preliminary results, fasting glucose tests may be the more sensitive test for women with PCOS. However, these variations in sensitivity prove further investigations are warranted. Furthermore, we aim to determine which characteristics/phenotypes may exacerbate this discordance between diagnostic tests.

SUPPORT: The study was funded by the Department of Obstetrics & Gynecology at Southern Illinois University School of Medicine.

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METFORMIN SHOULD BE RECOMMENDED FOR MORE PATIENTS WITH PCOS BASED ON UPDATED GUIDELINES.

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OBJECTIVE: In 2018, the International Evidence-Based Guidelines for the Assessment and Management of PCOS were released to integrate best practices for the diagnosis and treatment of PCOS. Among these guidelines are updated recommendations for the use of metformin in patients with PCOS. These recommendations advise that patients with PCOS and BMI≥25, impaired glucose tolerance, and/or adolescents age <18 should take metformin to prevent metabolic sequelae of PCOS (1). Previously, metformin use was recommended for patients with PCOS who displayed evidence of glucose intolerance and/or hyperinsulinemia (2,3). The objective of this study was to evaluate patients with PCOS who are and should be taking metformin based on these updated recommendations.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: A retrospective chart review of women ages 12-65 who were seen at a university system in 2017 with an ICD code for PCOS were identified and demographic, clinical, laboratory, and ultrasound data were collected in REDCap database. Forty-two women with a self-reported history of diabetes were eliminated to assess patients who were on metformin for PCOS. Patients with PCOS based on updated guidelines were identified with 2 out of 3 of the following criteria met 1) oligo or amenorrhea, 2) clinical and/or laboratory hyperandrogenism, 3) either ovary displaying ≥20 follicles between 2-9mm and/or volume > 10mL (1). It was determined whether the patients with PCOS based on new guidelines were currently taking metformin, and if they should be taking metformin based on updated recommendations as above. Patients with previously diagnosed PCOS were similarly analyzed, and it was determined if they should be taking metformin based on evidence of glucose intolerance and/or hyperinsulinemia. Statistical analysis was performed with SAS 9.4 (Cary, NC) software using Chi-square, and p-value <0.05 was considered significant.

RESULTS: Significantly more women with PCOS by updated guidelines should be taking metformin than women with PCOS by previous guidelines. Using the old guidelines 12% of patients should be taking metformin which increased to 91% using the new guidelines ($p<0.0001$). Ninety-nine percent of patients who should be taking metformin by new guidelines meet criteria by BMI (Table 1).

CONCLUSIONS: Based on updated guidelines, practitioners should prescribe metformin to more patients with PCOS, particularly those patients who are overweight and obese.

	PCOS, should be taking metformin (n=144)
BMI ≥25	142 (98.6%)
Impaired glucose tolerance (A1c >5.7)	22 (15.3%)
Adolescence (age <18)	17 (11.8%)

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THE IMPACT OF POLYCYSTIC OVARIAN SYNDROME ON EVALUATION OF REPRODUCTIVE POTENTIAL MEASURED BY ANTI-MUELLERIAN AND FOLLICLE STIMULATING HORMONES.

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OBJECTIVE: Our primary objective is to determine the association between BMI and AMH in reproductive age females with and without PCOS that undergo infertility treatment.

DESIGN: Retrospective cohort study in an academic fertility center

MATERIALS AND METHODS: Our study included total of 1937 subjects, 182 with PCOS (9.4%) – PCOS group, and 1755 without PCOS (90.6%) – non-PCOS group. The age, BMI, AMH and FSH levels were analyzed. Multivariable analyses were performed with one way ANOVA and Kruskal-Wallis tests and correlation analyses were performed using Pearson and Spearman tests for normally and lognormally distributed datasets respectively.

RESULTS: As expected, patients with PCOS were significantly younger, with lower FSH levels, higher BMI and AMH than non-PCOS patients (*p<0.001*). There was a mild negative association between BMI and AMH in the non-PCOS group (r=-0.06, p=0.015). FSH was positively associated with age as predicted, and negatively associated with BMI and AMH in the entire cohort, and in the non-PCOS patient population. None of these associations were found in PCOS group (Table).

CONCLUSIONS: Here we demonstrate that the inclusion of PCOS patients in research involving AMH studies results in significant change of AMH levels even in larger samples size and when the PCOS patients make up less than ten percent of the total study subjects.

Based on the results we infer that there is a negative association of AMH and FSH with BMI in infertile patient population in the absence of polycystic ovarian syndrome. The negative correlation of BMI and AMH is no longer found when PCOS subjects are included in the equation, however the correlation of BMI and FSH remains unchanged. This implies that FSH might be a better marker of BMI impact on ovarian reserve when PCOS patient population is included in the studies. Here we demonstrate that the inclusion of PCOS patients in research involving AMH studies results in significant change of AMH levels even in larger samples size and when the PCOS patients make up less than ten percent of the total study subjects.

Correlation Analyses	PCOS group r value	PCOS group P value	Non-PCOS group r value	Non-PCOS group P value	All r value	All P value
AMH vs. BMI	N/A	NS	-0.06	0.015	N/A	NS
AMH vs. FSH	N/A	NS	0.35	< 0.001	0.37	< 0.001
AMH vs. Age	r=0.38	< 0.001	0.36	< 0.001	0.39	< 0.001
FSH vs. Age	N/A	NS	0.23	< 0.001	0.23	< 0.001
FSH vs. BMI	N/A	NS	-0.1	< 0.001	-0.1	< 0.001
Age vs. BMI	0.21	0.004	0.14	< 0.001	0.13	< 0.001

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INCREASED CERVICAL INSUFFICIENCY RISK IN PCOS WOMEN UNDERGONE ART TREATMENT: A RETROSPECTIVE COHORT STUDY.

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OBJECTIVE: To explore the correlation between cervical insufficiency (CI) and polycystic ovary syndrome (PCOS) in Chinese women undergone assisted reproductive technology (ART) treatment. The pregnancy outcomes of PCOS women with CI were further analyzed.

DESIGN: A retrospective cohort study.

MATERIALS AND METHODS: We retrospectively analyzed the CI incidence in women who had an IVF or ICSI treatment at the Six Affiliated Hospital of Sun Yat-sen University between 2010 and 2018.Rotterdam criteria diagnosed PCOS women were randomly matched with non-PCOS cohort based on maternal age, body mass index (BMI), infertility duration and parity history. CI was diagnosed by cervical dilation and/or cervical shortening without contractions or labor, in the absence of other clear causes. The demographic data, clinical characteristics and the prevalence of CI for both groups were analyzed.

RESULTS: In total, 1489 PCOS women and 1489 matched non-PCOS women were included, 34 women were diagnosed with CI (1.14%) overall. Compared with non-PCOS cohort, PCOS women experienced higher prevalence of CI compared with non-PCOS control (1.54% versus 0.74%, P=0.038) , accompanied with a significantly smaller uterus (4.12 ± 0.52cm versus 4.30 ± 0.55cm, P<0.001) and higher serum testosterone (0.59±1.84 nmol/L versus 0.36±0.37 nmol/L, P<0.001). After adjusting for maternal age, BMI, infertility duration, mean uterine diameter, gravidity and parity and basal hormone levels, Logistic regression analysis indicated that PCOS status per se (OR:2.050,95% CI:1.009-4.206), BMI ≥ 25kg/m^2 (OR:3.870,95% CI: 1.833-8.173) and twin pregnancy (OR: 2.401,95%CI: 1.110-5.193) were associated with an increased risk of CI. Among those women diagnosed with CI, PCOS women terminated gestational at 25.35±5.91weeks, which was even earlier than non-PCOS cohort(30.91±6.73 weeks, P= 0.021). The miscarriage rate in PCOS women was 52.17% compared to 18.18% in non-PCOS cohort. PCOS women experienced more undesirable consequences for both maternal and newborn.

CONCLUSIONS: Our study revealed a higher prevalence of CI among PCOS women undergone ART treatment. An even worse maternal and newborn morbidity may incurred.

	PCOS group (n=1489)	Non-PCOS group (n=1489)	P
BMI (kg/m^2, mean ± SD)	22.65±3.01	22.41±2.97	0.652
Testosterone (nmol/L, mean ± SD)	0.59±1.84	0.36±0.37	<0.001*
Mean diameter of the uterus (cm, mean ± SD)	4.12±0.52	4.30±0.55	<0.001*
CI (%)	23 (1.54)	11 (0.74)	0.038 *
Termination gestational age (w) in women with CI	28.55±6.53	25.35±5.91	0.021*
Miscarriage in women with CI	12 (52.17)	2 (18.18)	0.101
Preterm birth in women with CI	8 (34.78)	4 (36.36)	
Term birthin women with CI	3 (13.05)	5 (45.46)	

SUPPORT: NO

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EFFECTS OF VITAMIN D ADMINISTRATION IN THE MOUSE MODEL OF POLYCYSTIC OVARIAN SYNDROME. Huiling Xu, master, Shumin Qiu, bachelor, Peiyang Lin, master, Xiuhua Liao, doctor, Beihong Zheng, bachelor Fujian Maternity and Child Health Hospital, Affiliated Hospital of Fujian Medical University, FuZhou, China.

OBJECTIVE: To investigate effects of vitamin .D(Vit.D) administration in patients with polycystic ovary syndrome(PCOS)

DESIGN: Experimental animal study.

MATERIALS AND METHODS: Forty female pre-pubertal mice were randomly divided into 4 groups: the control, PCOS, PCOS+low dose Vit.D and PCOS+high dose Vit.D groups(N=10 per group). The PCOS mouse model was developed by 6mg/kg/day dehydroepiandrosterone(DHEA) administration with subcutaneously injections and high fat diet feeding. After 30 days, Vit.D was administrated by intraperitoneal injection in the following 40 days, 130ng/100g/week 1,25(OH)2D3 in low dose Vit.D group, and 1300ng/100g/week 1,25(OH)2D3 in high dose Vit.D group. Controls were injected with vehicle alone and fed with normal diet. At the end of the 70 days, blood samples were collected and the ovarian and liver tissues were taken.

RESULTS: All the mice in PCOS+high dose Vit.D group died in two weeks after Vit.D administration. In the other three group, the weight of the PCOS mice was significantly higher than the weight of the controls before Vit.D administration(31.10±2.52, 31.76±2.54 VS 28.82±1.83g, PCOS group, PCOS+low dose Vit.D group VS control group, P=0.022). However, at the end of the study, the weight of the mice in PCOS group was significantly higher than those in control group and PCOS+low dose Vit.D group (41.41±3.90 VS 35.50±2.50, 34.55±2.31 g, P=0.000). The serum 25(OH) D concentration was significantly higher in PCOS+low dose Vit.D group than in control group and PCOS group (99.29±18.31 VS 19.55±4.10,18.04±6.51 ng/ml,P=0.000). The testosterone levels in PCOS group were significantly higher than those of control group and PCOS+low dose Vit.D group (1.27±0.27 VS 0.95±0.15 ,0.90±0.17 ng/ml, P=0.001). Furthermore, total cholesterol levels in control group were lower than in PCOS and PCOS+low dose Vit.D group (3.08±0.44 VS 4.55±0.47, 4.42±0.45mmol/L, P=0.011). Moreover, the ratio of liver weight to body weight was significantly different among the three groups (0.045±0.0046 VS 0.036±0.0043 VS 0.041±0.0031, control group VS PCOS group VS PCOS+low dose Vit.D group, P=0.000).

CONCLUSIONS: Our results indicate that low dose Vit.D has positive effects on the hormonal changes and obesity observed in PCOS, maybe through liver metabolism regulation, and high dose Vit.D administration may be harmful.

SUPPORT: Sponsored by Fujian provincial health technology project (grant no.2019-2-11), and Hospital Project of Fujian Maternity and Child Health Hospital (grant no. YCXQ18-25)

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THE CLINICAL CORRELATION BETWEEN POLYCYSTIC OVARY SYNDROME (PCOS) AND PITUITARY ADENOMA. Sang il Kim, MD St. Vincent's Hospital, The Catholic University of Korea, Suwon, Korea, Republic of (South).

OBJECTIVE: In this study, we investigate the incidence of pituitary adenoma combined with PCOS, cut-off prolactin (PRL) level to detect pituitary adenoma and treatment strategy.

DESIGN: This a retrospective cohort study.

MATERIALS AND METHODS: Medical records from November 2009 to March 2019 were reviewed in our institute, retrospectively. Total of 584 patients was enrolled. According to initial serum PRL level, patients were divided in 5 groups: A (0 ∼25 ng/mL); B (25∼50 ng/mL); C (50∼75 ng/mL); D (75∼100 ng/mL); E (≥ 100 ng/mL). We investigated the frequency of sella MRI and the incidence of pituitary adenomas as each group. Receiver operating characteristic (ROC) curve analysis was performed to determine a cut-off value of serum PRL level that could found pituitary adenoma in hyperprolactinemic PCOS patients.

RESULTS: Of 584 patients diagnosed PCOS, sella MRI was performed in 18 (3.1%, 18/584) patients. Finally, a total of 13 (2.2%, 13/584) patients with pituitary adenoma were identified. The mean value of serum prolactin level of these patients was 73.0 ± 54.5 (range, 20.8 ∼ 211.9) ng/mL. The mean age and follow up period were 26 ± 6.2 (range, 17 ∼38) years and 33.8 ± 27.5 (range, 3∼84) months, respectively. In group A to C, of the 11 patients who underwent sella MRI, 6 had pituitary adenoma (54.5%, 6/11). On the other hand, in Group D to E, of the 7 patients who underwent sella MRI, all of them had pituitary adenoma (100%, 7/7). One patient in group A had observation because PRL level was not as high as 20.8 ng/dL. One patient in group B had a PRL of 26.67 ng/dL and underwent surgery (transsphenoidal approach) because the mass size was 2.9 × 3 × 1.9 cm and there was visual field defect with optic chiasm compression. The remaining patients were treated with bromocriptine or cabergoline and followed-up with OBGY department. Most of all (77%, 10/13) showed a favorable outcome (normalization of PRL level, menstruation and/or success of pregnancy). The results of the ROC curve analysis of the prolactin threshold level for predicting pituitary adenoma in PCOS patients were as follows: The area under the ROC curve (AUC) was 0.831. P-value was 0.001 (95% CI 0.583 to 0.963). Sensitivity and specificity were 69.2 % and 100 %, respectively. The cut-off value was 53.

CONCLUSIONS: PCOS and hyperprolactinemia are common causes of infertility in reproductive women. The PCOS patients with a PRL level of 53 ng/mL or greater may need to consider a sella MRI scan for detecting pituitary adenoma. To expect a favorable clinical course for these patients, a systemic diagnosis, treatment and follow-up plan should be established. Therefore, a multidisciplinary approach between neurosurgery and OBGY is essential.

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PCOS AND UTERİNE ABNORMALITY; POSSIBLE CONNECTION AND RELATIONSHIP WITH MATERNAL SERUM AMH LEVELS. Gürkan Uncu, Prof.,[1] Kiper Aslan, M.D.,[1] Ozge Albayrak, M.D.,[2] Aylin Dayan, M.D.,[2] Isıl Kasapoglu, M.D.[2] [1]Bursa Uludag University Faculty of Medicine, Bursa, Turkey; [2]Uludag University School of Medicine, Gynecology and Obstetric ART Center, Bursa, CT, Turkey.

OBJECTIVE: To determine the incidence of uterine abnormalities in PCOS patients higher than normo-ovulatory patients?

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The study was conducted at a University Hospital, Department of Obstetrics and Gynecology. Total of 103 women, 51 PCOS, and 52 male factor infertility were included into the study. Hysterosalpingography (HSG) images of all patients were numbered. Six different shapes of the intrauterine cavity were figured. All HSG images were evaluated by ten senior reproductive endocrinologists and surgeons. Seniors were blinded to the research and choose the most appropriate figure for each patient's HSG image. The consensus rate was used to determine the normality of the HSG image.

RESULTS: BMI (27.2 + 6.2 vs. 23.9 + 4.5, p:0.03), Antral follicle count (20 (9-20) vs. 12 (9-18) p:0.05), Anti-Mullerian hormone (4.1 ng/ml (2.5-7.2) vs. 2.3 ng/ml (1.6-3.8), p<0.01) and Serum total testosterone levels (0.59 mcg/l + 0.19 vs. 0.4 mcg/l + 0.16, p:0.02) were significantly higher in PCOS group than the Male factor group. The percentage of the normal uterine cavity (Figure-I) was significantly lower in the PCOS group. (45.9 % and 73.1 %, p<0.01) The abnormal cavities were compared; Arcuate Uterus (Figure-II, ESGE - ESHRE Normal / ASRM VI, 22.18% vs 6.6% p<0.05), Partial Septate Uterus (Figure-III, ESGE - ESHRE U2a / ASRM Va, 5.1% vs 0% p<0.05), Complete Septate Uterus (Figure-IV, ESGE - ESHRE U2b / ASRM Vb, 5.47% vs 1.2% p<0.01) and Y-Shaped Uterus (Figure-VI, ESGE - ESHRE U1c) / ASRM Unclassified, 7.47% vs 0 p<0.05) were significantly higher in PCOS patients. T-Shaped Uterus (Figure V, ESGE - ESHRE U1a / ASRM VII - 13.8% vs. 18.9%) was comparable between the groups. There was no correlation between serum AMH levels and the presence of uterine abnormality.

CONCLUSIONS: This study provides that, compared to the healthy population, the uterine abnormality frequency is clearly higher in PCOS patients. The increased ratio of the abnormal uterine cavity may be related to excessive intrauterine exposure to maternal androgens and AMH.

SUPPORT: None.

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INTELLIGENT ALGORITHM COMBINED WITH DEVICE THAT DETECTS LUTEINIZING HORMONE LEVELS CAN IMPROVE THE PREDICTION ACCURACY OF OVULATION DAY. Zheng Yang, PhD, Ning Li, MS, Sylvia M. Kang, MS, MBA. Quanovate Tech Inc., Pleasanton, CA.

OBJECTIVE: Based on daily quantitative luteinizing hormone (LH) measurements, an intelligent algorithm was developed to improve the prediction accuracy of women's ovulation day.

DESIGN: Registry/Database Study. A group of consented Mira products (by Quanovate Tech Inc.) users was asked to provide their menstrual cycle information via the Mira App, and take daily quantitative urine LH measurement by the Mira analyzer and Mira Fertility test wands. The generated data were centralized in a database and analyzed in comparison to the traditional calendar method, which determines the ovulation days as the 14th day before the next menstrual cycle.

MATERIALS AND METHODS: Mira fertility test wands quantitatively detect the LH levels in urine, in conjunction with the Mira analyzer, which reads the immunofluorescent signal generated by the test wand and converts the signal into quantitative concentrations of the LH. Urine samples with LH from Mira users were continuously monitored by the Mira analyzer and Mira Fertility test wands daily for four menstrual cycles. The test data were collected by the Mira app which syncs data from the Mira analyzer via Bluetooth. 327 samples were analyzed.

By analyzing the collected data, we have established an algorithm for the prediction of ovulation day. This system combines the users' hormone test results and cycle information. The ovulation prediction of the users' first cycles was based on the calendar method since no LH tests of a complete cycle were done. As the number of cycles tested and hormone test data increase, it automatically adjusts parameters and learns the users' cycles to improve the accuracy of ovulation day prediction.

The actual ovulation day is obtained by a retrospect analysis of each cycle to find the LH surge day in that given cycle. The deviation between the predicted ovulation day and the actual ovulation day is calculated. If the deviation is within one day, plus or minus, it is defined as an accurate prediction. In the control group where we measured the users' first cycles, the calendar method was used to predict ovulation.

RESULTS: In the control group, the average rate of ovulation prediction accuracy of the users' first cycles using the calendar method is 29%. In the experiment group, the average rate of ovulation prediction accuracy of the users' every later cycle gradually rises. The accuracy rate is 35% for cycle 2, 58% for cycle 3, and 77% for cycle 4.

CONCLUSIONS: Combining the LH hormone measurements, cycle information, and intelligent algorithms, the prediction accuracy of ovulation day can be greatly improved compared with the calendar method. The more cycles a woman tests her LH hormone with this method, the higher accuracy the ovulation day prediction is.

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AMH LEVELS MAY PREDICT FOR MULLERIAN ANOMALIES AND PREGNANCY OUTCOMES PATIENTS WITH PCOS. Kiper Aslan, M.D.,[1] Ozge Albayrak, M.D.,[2] Kubra Ozlem Bilgic, M.D.,[2] Isıl Kasapoglu, M.D.,[2] Berrin Avcı, M.D., PhD,[3] Gürkan Uncu, Prof.[1] [1]Bursa Uludag University Faculty of Medicine, Bursa, Turkey; [2]Uludag University School of Medicine, Gynecology and Obstetric ART Center, Bursa, CT, Turkey; [3]Uludag University School of Medicine, Bursa, Turkey.

OBJECTIVE: To investigate the effect of AMH levels on uterine anomaly and adverse pregnancy outcomes in patients with PCOS.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The electronic database of ART Center of a tertiary university hospital was screened between the years 2012-2020. 143 PCOS patients with 336 cycles underwent IVF/ICSI were enrolled in to the study. Uterine abnormality and pregnancy outcomes were evaluated with anti-mullerian hormone (AMH) level per cycle. HSG and 2D-USG used for detection of uterine abnormalities. Demographic parameters, pregnancy outcomes were analyzed. AMH levels were compared between the cycles with normal or abnormal uterus.

RESULTS: Of the 143 patients with 336 ART cycles mean (standard deviation) age and body mass index were 30.7 (4.25) years and 28.3 (5.8), respectively. The median AMH values 6.5 (3.8-10.5) ng/dl. Of the 19 patients (%13.3) with uterine anomalies, arcuate uterus was found in 4, septum uteri in 8, T-shape uterus in 4, unicornus bicollis in 1, unicollis unicollis in 1 and V-shape uterus in 1. Pregnancy rate was %33.1 and livebirth rate was %15. Preterm delivery occurred in 4 of the singleton pregnancies and two of them were because of preeclampsia. The mean AMH value was 7.5 ng / dl in patients without uterine anomaly, whereas the mean AMH value of patients with uterine anomaly was 11.8 ng / dl ($p = 0.056$).

CONCLUSIONS: These results reveal that AMH levels in PCOS patients with uterine anomaly were higher than without uterine anomaly, but there was no statistically significant difference between two group. If the number of cases increases, statistically significant results can be obtained. Contrary to previous studies, preterm birth rates were not increased.

SUPPORT: None.

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POLYCYSTIC OVARY SYNDROME KNOWLEDGE AMONGST PRIMARY CARE PROVIDERS AND GENERALIST OBSTETRICIAN GYNECOLOGISTS. Micaela J. Stevenson, BS,[1] Yolanda R. Smith, MD,[2] Molly B. Moravek, MD, MPH[2] [1]University of Michigan Medical School, Ann Arbor, MI; [2]University of Michigan, Ann Arbor, MI.

OBJECTIVE: Approximately 6-10% of women in the United States have Polycystic Ovary Syndrome (PCOS). While PCOS is commonly associated with subfertility and infertility, this disorder predisposes patients to several comorbid conditions including metabolic syndrome, hypertension, hyperlipidemia, obstructive sleep apnea, and endometrial cancer. Thus, primary care providers must have an adequate understanding of this diagnosis to manage and screen for these conditions. The objective of this study was to assess primary care provider knowledge of PCOS diagnostic criteria and associated comorbidities.

DESIGN: Cross-sectional survey.

MATERIALS AND METHODS: Adult primary care physicians and general obstetrician gynecologists at an academic institution completed an anonymous, online survey assessing knowledge of PCOS. Response data were processed using R. We fit multilevel logistic regression models to participants' response errors. The models allowed intercepts to vary randomly at the participant and item levels. We report means and standard deviations of error rates, as well as regression coefficients. We also report z-stats and p-values and use an alpha-threshold of 0.001 to infer statistical significance. Our analyses focused on response error rates to different items presented in the questions about diagnostic criteria and comorbidities of PCOS.

RESULTS: Data collection is ongoing. 28 generalist Obstetrician gynecologists (Ob/Gyn), 27 internal medicine physicians, and 20 family medicine physicians participated in this study. For the diagnostic criteria question, the mean error rate across all participants was 25% ($\sigma = 0.43$). Metabolic syndrome was correctly selected as a diagnostic criterion by 77% of respondents. The mean error rate for identification of PCOS associated comorbidities across all participants was 0.15 ($\sigma = 0.36$). 87% of respondents correctly indicated that osteoporosis was not an associated comorbidity of PCOS and 57% of respondents identified hypertension as a comorbidity of PCOS. Overall, Ob/gyn physicians had an error rate of 17%, family medicine physicians had an error rate of 29% and internal medicine physicians had an error rate of 31% all for diagnostic criteria ($p=0.04$). For associated comorbidities, Internal Medicine physicians had error rates of 24%, Ob/gyns had an error rate of 13% and family medicine physicians had an error rate of 7%. ($p= <0.001$)

CONCLUSIONS: Current data suggests that physicians of all primary care specialties incorrectly identified some diagnostic criteria and comorbidities commonly seen with PCOS. Continuing medical education on PCOS diagnostic criteria and associated comorbidities would likely be useful for all of the surveyed specialties.

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CHARACTERISTICS OF WOMEN WITH PCOS WHO UNDERGO ENDOMETRIAL BIOPSIES. Kathryn M. Goldrick, MD, Katherine E. Kostroun, MD, Jessica N. Mondshine, BS, Randal D. Robinson, MD, Erin B. Mankus, MD, Jennifer F. Knudtson, MD University of Texas Health Science Center, San Antonio, TX.

OBJECTIVE: In 2018, the International Evidence-Based Guidelines for the Assessment and Management of PCOS were released to integrate best

practices for the diagnosis and treatment of PCOS. These guidelines do not include recommendations about endometrial biopsies for women with PCOS. Although patients with PCOS are at increased risk of endometrial hyperplasia and carcinoma due to unopposed estrogen and oligomenorrhea, no clear guidelines for endometrial biopsy for women with PCOS exist. The objective of this study is to assess characteristics of patients with PCOS who undergo endometrial biopsies.

DESIGN: Retrospective chart review

MATERIALS AND METHODS: A retrospective chart review of women ages 12-65 who were seen at a university hospital system in 2017 with an ICD code for PCOS were identified and demographic, clinical, laboratory, and ultrasound data were collected in REDCap Database. Patient characteristics were compared for women who did and did not undergo endometrial biopsy, and results of endometrial biopsies were analyzed. Statistical analysis was performed with SAS 9.4 (Cary, NC) software with data analysis performed via t-test and Chi-square test, as appropriate, and a p-value <0.05 was considered significant.

RESULTS: Of the 450 patients with PCOS identified, 51 patients had endometrial biopsies. Factors associated with having an endometrial biopsy performed were older age, diabetes, and irregular menses which were significantly different between the groups. Ethnicity, BMI, PCOS by updated guidelines, previous hormone treatment, and metformin use were not different between groups. Of the endometrial biopsies performed, 76% were benign, 20% had hyperplasia, and 2% had malignancy.

CONCLUSIONS: Having diabetes, irregular menses, or older age increased the chance of endometrial biopsy being performed. As expected, a high percentage (22%) of patients with PCOS had endometrial hyperplasia or cancer on endometrial biopsy. Although most endometrial biopsies performed in our study were benign, future research is needed to establish clear guidelines for performing endometrial biopsies for women with PCOS since this group is at increased risk for endometrial hyperplasia and malignancy.

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SUPPORT: K23 HD097307 (JFK)

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CLINICAL IMPACT OF THE 2017 ASRM EMBRYO TRANSFER GUIDELINES.

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[1]Walter Reed National Military Medical Center, Bethesda, MD; [2]Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD.

OBJECTIVE: To evaluate whether implementation of the new ASRM transfer guidelines in our clinical practice resulted in differences in pregnancy outcomes. The American Society of Reproductive Medicine published updated embryo transfer guidelines in March of 2017 in an attempt to decrease twin and higher-order multiple pregnancies. These updated guidelines recommend strong consideration for single embryo transfer for favorable prognosis patients under 38 years of age.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All women < 38 years old who underwent a second embryo transfer, after a prior failed embryo transfer, in the preceding two years or following the national guideline change were included. The primary outcomes assessed were the number of embryos transferred, and whether a clinical pregnancy, live birth, and/or twin live birth resulted. PGT and donor oocyte cycles were excluded. Published SART data was also compared between 2016 and 2017 to assess for national changes in the twin birth rate in patients <38 years of age. Differences in twin clinical pregnancy and live birth rates were compared by chi square test. Statistical significance was set at $P<0.05$.

RESULTS: 2424 transfer cycles from 2015-2018 were analyzed. 325 of these were second cycle transfers with 224 having a prior failed transfer. After implementation of the new transfer guidelines, the number of double embryo transfers was significantly reduced (21.9% vs 1.3% P<0.001). There was no change in clinical pregnancy rate after adaptation of the new guidelines (68.6% vs 67.9%, $P=0.908$); however, there was a significant reduction in the twin live birth rate (18.0% vs 4.3%, $P=0.033$). There were no higher order multiple gestations. The national SART data also showed a reduction in twin live births when comparing 2016 to 2017. In over 90,000 cumulative retrieval cycles in patients <35 years old, the twin rate decreased from 16.5% to 13.3% ($P<0.001$). In over 50,000 cumulative retrieval cycles in patients 35-37 years old, the twin rate decreased from 15.6% to 12% ($P<0.001$). The SART data was less pronounced in the twin reduction, likely because it was not limited to patients with a prior cycle.

Women age < 38	Before Guideline Change	After Guideline Change	*P* Value
Clinical Pregnancy	68.6%	67.9%	0.908
Total Live Birth	42.4%	44.3%	0.767
Twin Live Birth	18.0%	4.3%	0.033

CONCLUSIONS: Implementation of the 2017 ASRM guidelines decreased the twin live birth rate in favorable prognosis women in our institution and at a national level, without impacting the live birth rate. Even after a previous unsuccessful embryo transfer, women <38 can be offered a single embryo and still achieve similar live birth rates but with significantly lower multiple gestation rates.

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USE OF MEDROXYPROGESTERONE ACETATE (MPA) IN DONOR CYCLES DECREASES MEDICATION COSTS.

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OBJECTIVE: Traditionally IVF stimulation protocols have utilized GnRH agonists or antagonists in order to prevent premature LH surge. As progestins can also inhibit the preovulatory rise in LH, medroxyprogesterone acetate (MPA) has recently been used instead of GnRH antagonists/agonists to prevent premature ovulation during IVF cycles. More data is needed in regards to the reliability of MPA in suppressing LH surge, its effects on IVF outcomes, and associated improvement in cost. The aim of this study is to determine whether using MPA instead of GnRH antagonists is associated with a change in medication cost and IVF outcomes.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Prior to February 1, 2019 oocyte donor cycles at our IVF center utilized a GnRH antagonist protocol. After that date a MPA protocol, which consisted of starting 10 mg MPA on the first day of stimulation was introduced. All donor MPA cycles from February 2019 to October 2019 were compared to the antagonist protocol cycles in the preceding year. Additionally a paired analysis was performed on 15 oocyte donors who first underwent a traditional antagonist cycle followed by a MPA cycle. Medication costs gonadotropins, antagonist (Ganirelix), and MPA were obtained from sourcing pharmacy. Statistical analyses were performed using a student's t-test and chi-square test.

RESULTS: A total of 355 antagonist cycles and 31 MPA cycles were included in this analysis. Mean number of stimulation days and mean number of oocytes retrieved did not significantly differ between the two groups (p=0.83; p=0.338). Average number of days of antagonist use was 4 days. Cost per antagonist cycle of Ganirelix was $420.00. MPA cost per cycle was $15.00. The estimated medication cost savings per cycle with MPA was determined to be $405.00. In the paired analysis there was no significant difference in mean total dose of gonadotropins, mean number of MII oocytes, mean number of useable blastocysts or mean number of euploid blastocysts.

CONCLUSIONS: Utilization of MPA in donor cycles may lessen the financial burden of IVF medication costs and does not appear to significantly alter IVF outcomes compared to traditional antagonist cycles.

	MPA Mean, n (%)	St Dev	ANTAG Mean, n (%)	St Dev	P-value
Stim Days	9	1.1	9	1.2	0.486
Mean total GND Dose (IU)	2943	958	2797	874	0.666
Mean #MII	20	9.8	19	12.3	0.808
%MII	294/355 (82.8%)		291/400 (72.8%)		0.961
Mean #2PN	16	7.9	16	8.6	0.999
%2PN	241/294 (82%)		239/291 (82%)		0.787
Mean useable blasts (UB)	9.8	6.6	9.7	6	0.966
% UB per MII	147/294 (50%)		146/291 (50.1%)		0.332
% UB per 2 PN	147/241 (61%)		146/239 (61%)		0.78
Mean # Euploid	7	4.4	8	4	0.525
% Euploid per UB	97/147 (66%)		105/146 (71.9%)		0.271

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P-745 4:30 PM Tuesday, October 20, 2020

SEPTAL RESECTION IN WOMEN WITH UTERINE SEPTUM SCHEDULED FOR IN-VITRO-FERTILIZATION (IVF); A DECISION ANALYTIC MODEL. Ahmed M. Abdelmagied, MD,[1] Mohammed Khairy Ali, MD,[1] Ali Hassan Hamed, MD, FRANZCOG,[2] Mostafa N. Ibrahim, MD,[1] Amal Y. Zaman, MD,[3] Magdeldin Gaafar Taha, MD,[3] Fawzia Ahmed Habib, MD[3] [1]Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; [2]Department Of Obstetrics and Gynaecology, Ballarat Health Services, Ballarat, Victoria, VIC, Australia; [3]Department of Obstetrics and Gynecology, Faculty of Medicine, Taibah University, Saudi Arabia.

OBJECTIVE: Evidence is lacking to guide treatment decisions for uterine septum incision prior to IVF. The present work aimed to evaluate the cost-effectiveness and live birth (LB) outcomes of septal resection in the setting of IVF women with septate uterus.

DESIGN: A Decision analytic tree (model)

MATERIALS AND METHODS: A decision-analysis model was constructed to compare four strategies for septal resection in women indicated for IVF. Strategy (1: Res-All) adopts resection for all internal fundal depressions (FD) >1cm, depicting the clinical relevance of defining uterine septum as >1cm FD. Strategy (2: Res-Long) resects FD ≥1.5cm coinciding with ASRM-2016 definition of septate uterus. The third strategy (3: Res-After-failure) resects all FD after 2 failed IVF cycles. The fourth strategy is the reference standard that does not provide any resection (4: No-Res). The 4 strategies were analyzed in 2 models. Model (1) assumed improving LB after resection of any FD more than 1 cm. However, in Model (2) only FD ≥1.5 cm would benefit from resection. Calculations were done for a hypothetical cohort of 100 women undergoing 3 consecutive IVF cycles. Input probabilities were derived from the best available evidence in literature. For cost estimates, we utilized Medicare 2019 national fee rates in US dollars. Analyses were done using TreeAge Pro Healthcare 2020.

RESULTS: In base-case analyses of Model (1), Res-All was the most cost-effective, while in model (2) Res-Long was the most cost effective. Both dominated Res-After-failure and No-Res strategies in models (1) and (2) (Table). In Model (1) sensitivity analysis, both Res-All and Res-Long strategies would result in cost savings if the probability of LB in unresected septum is below 18%, with maximum cost savings of 9500 dollars per LB gained. If the probability was between 18-31%, Res-All and Res-Long strategies remained cost-effective (extra-costs with more effects) at $50,000/QALY willingness-to-pay threshold. Savings were generated through subsequent reduction in failed IVF cycles. In Res-Long strategy, increasing prevalence of FD ≥1.5cm would raise the cost per LB in Model (2), and would lower it in Model (1).

Model (1)	Cumulative Cost	Cumulative LBR	Cost per LB
Res-All indentations	2,489,454	74.1%	33619
Res-Long indentations	2,627,205	52.2%	50370
Res-After-failure	3,247,290	42.7%	76114
No-Res	2,847,217	14.8%	192979
Model (2)			
Res-All indentations	2,506,025	73.2%	34251
Res-Long indentations	2,343,600	73.2%	32031
Res-After failure	2,886,208	53.2%	54210
No-Res	2,563,612	35.8%	71684

CONCLUSIONS: While septal resection initially presents extra-costs, it could potentially save money for both the health care system and infertile couples by preventing reproductive failures of IVF cycles.

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P-746 4:30 PM Tuesday, October 20, 2020

EFFICIENCY MARKERS FOR ART CENTERS TO EVALUATE QUALITY AND DELIVERY OF CARE. Bhuchitra Singh, MD, MPH, MS,[1] Mingyu Yan, BBA,[2] Mingqian Wang, MS,[3] Estefania Jordan, BBA,[2] Mindy S. Christianson, MD,[4] Valerie L. Baker, MD,[4] James Segars, MD[1] [1]Johns Hopkins University School of Medicine, Baltimore, MD; [2]Johns Hopkins Carey Business School, Baltimore, MD; [3]Carey Business School, Baltimore, MD; [4]Johns Hopkins Fertility Center, Lutherville, MD.

OBJECTIVE: To identify and develop standardized operational efficiency markers for quality and delivery of care at an ART Center. Efficiency markers combine a quality of care variable, such as patient satisfaction, and the cost required to deliver that degree of satisfaction. They can be used to quantify improvements in healthcare quality.

DESIGN: Quality assessment/improvement study.

MATERIALS AND METHODS: This work was done in two phases; Phase 1 was presented at the ASRM Conference 2018 where we presented a detailed process flow analysis (PFA) of the ART center at Johns Hopkins and identified bottlenecks. Here we report Phase 2, a secondary literature review and development of operational markers for efficiency in quality and delivery of care. The study team developed markers to analyze efficiency of the steps in the flow charts. Markers were reviewed from the other service industries such as hospitality, airlines, and restaurants to align patient-interests of the markers. According to the Donabedian quality of care measurement model, the instruments were categorized into structure, process, and outcome markers.

RESULTS: Our analysis identified 12 major processes from initial intake evaluation, through monitoring, retrieval, and embryo transfer. Within these, there were 42 sub-areas for quality monitoring and improvement efforts at the Hopkins ART center. The study details the instruments developed for comprehensive evaluation of patient-reported measures of satisfaction with care; clinical outcomes such as cumulative live birth rate, complication rates such as OHSS; delivery of general services outcomes like show-up rate, rate of insurance approval; process markers such as number of embryo transfers, average wait time/face time ratio for clinical visits. and structure markers such as IVF nurse/ patient ratio, number of front desk staff/ daily patient visits, number of board-certified certified reproductive endocrinologist. These operational efficiency markers aim to provide metric data to continuously identify the operational efficiency status to serve the reproductive needs of the patients.

CONCLUSIONS: The developed markers measure meaningful patient-centered outcomes, critical structural components, and essential processes that are necessary for continuous monitoring and adaptive changes for an ART center. This comprehensive strategy ultimately can improve the quality and delivery of care while supporting cost-containment at every level by efficient staffing and utilizing existing resources to full capacity.

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P-747 4:30 PM Tuesday, October 20, 2020

COST EFFECTIVENESS ANALYSIS OF UNIVERSAL SCREENING FOR SICKLE-CELL TRAIT PRIOR TO IVF IN STATES WITH AND WITHOUT AN IVF INSURANCE MANDATE. Benjamin S. Harris, MD, MPH,[1] Benjamin J. Peipert, MD,[2] Laura J. Havrilesky, MD, MHSc,[3]

Kelly S. Acharya, MD[1] [1]Division of Reproductive Endocrinology and Infertility, Duke University Medical Center, Durham, NC; [2]Duke University Medical Center, Durham, NC; [3]Division of Gynecologic Oncology, Duke University Medical Center, Durham, NC, NC.

OBJECTIVE: To evaluate the cost-effectiveness of universal screening for sickle-cell trait (SCT) prior to in-vitro fertilization (IVF). Preliminary studies have shown that in couples known to both carry SCT, IVF with preimplantation genetic testing (IVF-PGT) for selection of embryos unaffected by sickle cell disease (SCD) is a cost-effective strategy[1]. However, it is unknown whether universal SCT screening to identify these dual-carrier couples is cost-effective, or if the value of a specific screening strategy is impacted by the greater number of IVF cycles and resulting higher conception rate afforded by IVF insurance mandates.

DESIGN: Cost-effectiveness analysis

MATERIALS AND METHODS: A simple decision model was designed from a societal perspective with a 1 year horizon, to compare SCT screening to no screening. The primary outcome was cost-effectiveness in US dollars per quality-adjusted life year (QALY) gained. QALY totals were assigned to cases of live offspring based on prior published studies (33 QALYs for HbSS offspring and 67 QALYs for unaffected offspring). We assumed that 50% of dual-positive couples (patient and partner with SCT) would choose IVF-PGT. In states with no insurance mandate, we assumed and that an average of 1.3 cycles of IVF-PGT were employed during the time horizon, with a 70% IVF conception rate. In states with an IVF insurance mandate, we assumed an average of 3 cycles of IVF-PGT were employed due to lower cost constraints on patients, with an 85% IVF conception rate. Rates of natural conception, IVF-PGT, early and late pregnancy loss, amniocentesis, therapeutic abortion, SCD lifetime costs and productivity, and prenatal care were derived from the literature, CPT and APC codes, and our experience at a single suburban academic IVF center. Multiple one-way sensitivity analyses were performed to test model assumptions.

RESULTS: In the base case primary analysis, the mean cost of the SCT screening strategy was lower than for no SCT screening ($322,548 vs. $322,580). No screening resulted in 0.00039 more QALYs than SCT screening, and was cost-effective with an ICER of $83,096/QALY. In the case of an IVF insurance mandate, the mean cost of the SCT screening strategy remained $14 lower than for no SCT screening and also resulted in 0.00048 more QALYS, making SCT screening a dominant strategy. In sensitivity analysis of the base case model, when the IVF conception rate exceeds 76%, SCT screening becomes a dominant strategy.

CONCLUSIONS: Universal SCT screening is cost-effective when compared with no screening if the IVF conception rate exceeds 76%. These conditions would be met if every dual-carrier couple with SCT had the financial resources to pursue the recommended follow-up treatment with maximization of pregnancy rates through multiple IVF-PGT cycles. Ultimately, the cost-effectiveness of this intervention is contingent upon disease prevalence and the cumulative IVF conception rate. Therefore, in states where patients have insurance coverage to undergo multiple IVF-PGT cycles, SCT screening could be considered a value-based strategy.

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P-748 4:30 PM Tuesday, October 20, 2020

TOO LITTLE, TOO MUCH, OR JUST RIGHT? HOW PATIENTS FEEL ABOUT THEIR SPENDING ON FAMILY BUILDING. Colin Johnson, MD, Rachel Cusatis, PhD, Kathryn E. Flynn, PhD, Jay I. Sandlow, MD, Judith Myers, MS, Kate D. Schoyer, MD Medical College of Wisconsin, Milwaukee, WI.

OBJECTIVE: To understand how couples and individuals feel about their financial investment in adding a child to their family 6 years after seeking a consultation with a reproductive specialist.

DESIGN: Longitudinal cohort study using prospectively collected patient-reported data and retrospectively collected clinical data.

MATERIALS AND METHODS: 64 couples and 28 individuals seeking initial consultation with a reproductive specialist enrolled in this study. Questionnaires were administered prior to their first consultation, at 1 year, and at 6 years. Participants were asked yes/no questions regarding their thoughts about their financial investment in adding a child to their family (see Table 1). The Decisional Regret Scale was also administered, a 5-item scale assessing regret (0-100), referencing "the decision you made about how to add a child to your family." An additional open-ended question allowed participants to provide detail about their experience. Medical records were used to ascertain whether each participant achieved a live birth using fertility treatments. Chi-squared tests were used for comparisons.

RESULTS: 45 couples and 34 individuals (77 women and 47 men) responded to the 6-year survey. 7% of participants wish they had spent more money and 28% of participants wish they had spent less. There were no gender differences in responses, but there were significant differences between those who had a live birth using fertility treatments and those who did not (Table 1). Additionally, those who expressed moderate or severe regret (score $\geq$25) were more likely to wish they had spent more money on treatments compared to those with no regret or minor regret (p=0.012). Qualitative themes included income limitations, desiring to afford a specific treatment (such as IVF), and the expense of treatments with uncertainty about effectiveness.

CONCLUSIONS: The majority of patients were satisfied with how much money they spent on family-building, though over one-quarter wished they had spent less, and this was more often those who were successful in achieving a live birth through fertility treatments. Additionally, the often onerous financial aspects of fertility treatments in the U.S. may be associated with regret about those treatments over time.

Table 1. Participants who Responded "Yes" to Statements about Money Spent on Family-Building

Statement	Responded "Yes" to Statement		p-value
	Live Birth	No Live Birth	
I wish I had spent more money on trying to add a child to my family	2/69 (3%)	7/55 (13%)	**0.036**
I wish I had spent less money on trying to add a child to my family	26/68 (38%)	9/55 (16%)	**0.008**
I am satisfied with how much money I spent trying to add a child to my family	55/67 (82.1%)	43/55 (78%)	0.589

SUPPORT: Funding came from R21HD071332 from the National Institute of Child Health and Human Development as well as the Department of Obstetrics and Gynecology at the Medical College of Wisconsin

P-749 4:30 PM Tuesday, October 20, 2020

AN ARTIFICIAL INTELLIGENCE PLATFORM TO OPTIMIZE IVF MANAGEMENT DURING OVARIAN STIMULATION: WORKFLOW IMPROVEMENT AND OUTCOME-BASED PREDICTIONS. Gerard Letterie, MD,[1] Andrew MacDonald, MS,[2] Zhan Shi, PhD[3] [1]Seattle Reproductive Medicine, Seattle, WA; [2]Quick Step Analytics, Seattle, WA; [3]University of Washington, Seattle, WA.

OBJECTIVE: to describe and assess the accuracy of an integrated AI platform designed to reduce monitoring during ovarian stimulation to a single day; adjust outcome predictions and enable level loading of oocyte retrievals based on that single day of observations.

DESIGN: descriptive study of a novel AI-based suite of software tools to determine optimal scheduling options and predict outcomes based on clinical profiles at the start of and ongoing data collection during ovarian stimulation and identify options to enable level loading of oocyte retrievals

MATERIALS AND METHODS: Data for the study was in the form of IVF cycles. Our data set included: patient profiles of age, serum concentrations of anti-mullerian hormone, antral follicle counts and BMI; observations during ovarian stimulation to include estradiol (E2) concentrations (in pg/ml);

Table 1. Sensitivity analysis

m-TESE cost ($)	WTP ($)						
	8,000	10,000	12,000	14,000	16,000	18,000	20,000
1,000	**cTESE**	**cTESE**	**cTESE**	**cTESE**	mTESE	mTESE	mTESE
1,200	**cTESE**	**cTESE**	mTESE	mTESE	mTESE	mTESE	mTESE
2,000	mTESE	mTESE	mTESE	mTESE	mTESE	mTESE	mTESE
5,000	mTESE	mTESE	mTESE	mTESE	mTESE	mTESE	mTESE

ultrasound measurements of follicle diameters in 2 dimensions (in mm). Outcomes included number of mature oocytes stratified into 2 groups: 0 to 10 (Group I) and > 10 (Group II)mature oocytes . The database consisted of 2603 total autologous cycles composed of 305,472 clinical data points. There were 1591 complete records encompassing 4731 visits. Eighty percent of the cycles were used for training and validation and 20% for challenge. Predictive algorithms were evaluated and written using Python, NumPy logistic function, Panda and SKLearn. Data was organized using Jupyter Notebook.

RESULTS: The accuracy of the algorithm to predict the single best day for monitoring was 0.95 and identified Day 9 as the single best day. Errors in predicting too early or too late were 0.4 and 0.5 days respectively. Accuracy for prediction for total number of mature oocytes when baseline testing alone or when baseline testing in combination with data during day of observation was 0.76 and 0.80 respectively. In addition, no combination of baseline factors or data observed during stimulation was more influential in the algorithm's predictive power than AMH alone. Sensitivity and positive predictive value for estimating the total number of mature oocytes in Groups I (0 to 10) was 0.78 and 0.79 and for Group II (>10) were 0.73 and 0.72 respectively. After identifying the single day for evaluation, the algorithm identified a range of 3 retrieval days specified by the earliest and the latest day, as options where the number of mature oocytes retrieved was unchanged leaving open the option of a range of 3 days to schedule and level load retrievals.

CONCLUSIONS: We describe a robust suite of integrated management tools encompassing three interrelated nodal points for management, scheduling techniques and decision making during IVF to include reducing monitoring to a single best day during ovarian stimulation; adjustment of outcomes (PR) based on that data and options to level load oocyte retrievals. These tools will enable an improved work flow and reduction in patient care visits without any reduction in the surveillance of response or outcomes during IVF. As such this, algorithm should improve workflow and reduce costs due to reduced need for monitoring and personnel.

SUPPORT: None

P-750 4:30 PM Tuesday, October 20, 2020

FINANCIAL DECISION ANALYSIS FOR SURGICAL SPERM RETRIEVAL APPROACHES. Tracy X. Han, MD, MBA, Ramy Abou Ghayda, MD, MHA, MPH, Brittany D. Berk, MD, John Joseph Ernandez, Jr., BA, Martin Kathrins, MD Brigham and Women's Hospital and Harvard University, Boston, MA.

OBJECTIVE: To determine the most financially optimal surgical approach for testicular sperm retrieval for men with non-obstructive azoospermia (NOA).

DESIGN: A decision tree was created examining five potential surgical approaches for men with NOA pursuing one cycle of ICSI. An expected financial net loss was determined for each surgical option based on couples' willingness to pay (WTP) for one cycle of ICSI resulting in pregnancy. The branch with the lowest expected net loss was defined as the most optimal financial decision (minimizing loss to a couple). Fresh TESE implied TESE was performed in conjunction with programmed ovulation induction. Frozen TESE implied TESE was performed initially, and ovulation induction/ICSI was canceled if sperm retrieval failed. The surgical options included fresh conventional TESE (c-TESE, with and without "back-up" sperm cryopreservation), fresh microsurgical TESE (m-TESE, with and without "back-up" sperm cryopreservation), and frozen m-TESE. Success was defined as pregnancy after one ICSI cycle.

MATERIALS AND METHODS: Probabilities of successful sperm retrieval with c-TESE/m-TESE, post-thaw sperm cellular loss following frozen m-TESE, ovulation induction/ICSI cycle out-of-pocket (OOP) costs, ICSI pregnancy rates for men with NOA, standard c-TESE cost and average WTP for ICSI cycle were gathered from the systematic literature review. Costs were in USD and adjusted to inflation (as of April 2020). Two-way sensitivity analysis was performed on varying couples' WTP for one cycle of ICSI and varying m-TESE OOP costs.

RESULTS: According to our decision tree analysis (assuming minimum m-TESE cost of $1,000 and WTP of $8000), the expected net loss for each branch was as follows: -$17,304 for fresh c-TESE, -$17,282 for fresh m-TESE, -$9,828 for frozen m-TESE, -$17,971 for fresh c-TESE with "backup", and -$18,298 for fresh m-TESE with "backup". Two-way sensitivity analysis with variable WTP values and m-TESE costs confirmed that frozen m-TESE consistently presented the lowest net loss compared to other options. Interestingly, when directly comparing fresh m- and c-TESE with "back-up", scenarios with decreasing WTP and lower m-TESE costs demonstrated c-TESE with "back-up" as more optimal than m-TESE with "back-up" (Table 1).

CONCLUSIONS: Our study suggests that frozen m-TESE is the most financially optimal decision for the surgical management of NOA, regardless of m-TESE cost and couple's WTP.

P-751 4:30 PM Tuesday, October 20, 2020

FROM PEN TO KEYBOARD: TRANSITION TO A SPECIALTY ELECTRONIC MEDICAL RECORD. Baruch Abittan, M.D., Stephanie R. Brownridge, M.D., Randi H. Goldman, M.D., Christine Mullin, M.D. Northwell Health Fertility, North Shore University Hospital/Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: The importance of converting paper medical records to electronic versions has been nationally recognized. There are certain specialties, including Reproductive Endocrinology and Infertility (REI), which have lagged behind the initiative in transitioning to an electronic medical record (EMR). Our objective is to describe the essential steps required for a successful transition to EMR in a large university academic REI clinic, and to report results from an internal survey regarding the perception of transition among multidisciplinary staff members.

DESIGN: Descriptive and Survey study.

MATERIALS AND METHODS: We reviewed the processes executed during our transition from paper to electronic health records. To ensure that the system was designed to match the workflow of the practice, a plan was determined for all fields of the division (andrology, embryology, third party reproduction, clinical services outside of IVF, billing, radiology and laboratory services). The process began with clear goals of implementing an EMR system at 6 ambulatory locations, which was accomplished in a series of 5 rollout periods. Six months following the go live date of EMR implementation, an anonymous survey was administered to staff members regarding the EMR transition and effect of EMR on remote-work during the COVID-19 pandemic.

RESULTS: Patients' safety is of paramount importance, and correct identification of patient, partner, and gametes is a vital objective while transitioning to a paperless system. Challenges recognized during this process were communication, services sharing a single location with differing needs (andrology, embryology, third party reproduction, billing, laboratory, clinical), requirements from multiple regulatory bodies (eg. FDA, CDC, SART), integration of fertility software into existing University health system EMR, complexity of a workflow with multiple providers interacting with patients, and the unique safety procedures involved with fertility care, including witnessing of specimens. Thirty-eight staff members, including physicians, nurses, embryologists, and office staff responded to the survey. Most respondents were between age 31-40y (32%), 21-30y (21%), or 51-60 y (21%). Sixteen percent of respondents did not feel comfortable with EMR use prior to implementation. Almost one third of respondents (29%) had been working in the fertility field for 1-5 y, 27% for 6-10 years, and another 21% for more than 20 years. Seventy percent of staff members felt the education received prior to EMR transition was well organized with attainable goal. Most (90%)

were satisfied with the EMR transition process, 79% identified a positive impact on work patterns since EMR transition, and 87% reported improved communication. Over 90% of staff members believed that the EMR transition prepared them to utilize TeleHealth remotely during the COVID-19 pandemic.

CONCLUSIONS: With proper planning and commitment of administration and staff, a successful transition from paper charts to EMR can be accomplished in a busy REI practice.

P-752 4:30 PM Tuesday, October 20, 2020

PRINCIPLES OF ONLINE DEFAMATION FOR PHYSICIANS. Christopher P. Moutos, MD,[1] Kajal Verma, MD,[2] John Y. Phelps, MD, JD, LLM, MHA[3] [1]University of Texas Medical Branch, Galveston, TX; [2]University of Nevada, Las Vegas, Las Vegas, NV; [3]University of Nevada Las Vegas, Las Vegas, NV.

OBJECTIVE: The goal of this study is to highlight online defamation lawsuits initiated by healthcare providers and discuss situations in which litigation may be an appropriate response to potential claims of online defamation. We also aim to propose solutions for addressing unfavorable online reviews in a way that may avoid the litigation process.

DESIGN: Case law review

MATERIALS AND METHODS: Local county and district court dockets, along with NexisUni, a legal database of appealed court cases, were used to identify relevant lawsuits and legal principles pertaining to online defamation cases. Media coverage was used to further characterize details of specific lawsuits identified. Materials from the American College of Obstetrician and Gynecologists were used to help form recommendations for physicians in handling online interactions.

RESULTS: Successful defamation lawsuits must establish four key elements: (1) presence of a false or defamatory statement; (2) fault, amounting to at a minimum negligence; (3) an unprivileged communication to a third party; (4) harm or damages suffered by the plaintiff due to the statement. The specific lawsuits *Desert Palm Surgical Group v. Petta*, *McKee v. Laurion*, and *Great Wall Medical PC v. Levine* serve as examples of lawsuits that were unsuccessful or have faced significant, ongoing difficulty in the court system due to failure in establishing each of the four principles of a successful defamation case. Successful cases do exist though, as seen in *Austin Eye Clinic v. Hall*. The cases of *Reit v. Yelp Inc* and *Braverman v. Yelp Inc* demonstrate the difficulty in healthcare providers seeking action directly against a website itself, rather than an individual reviewer. Online defamation lawsuits can be resource intensive and harm a practice's reputation due to negative media attention. In addressing patient reviews online, physicians must be mindful to protect patient confidentiality as outlined by the Health Insurance Portability and Accountability Act (HIPAA).

CONCLUSIONS: Physicians considering a lawsuit should weigh the alleged defamatory statement against the four criteria which a defamatory claim must meet. They should also consider the ability to identify the author, the author's ability to pay if damages are awarded, and the opportunity cost of time spent in the legal process. In situations where a physician believes they have sufficient grounds for a case, they should seek professional legal advice. Those choosing to respond online should do so in a professional manner that adheres to HIPAA guidelines. Physicians who are proactive in soliciting evaluations from patients have seen overall positive results. Evidence exists that most online reviews of physicians are positive and having negative reviews is not wholly detrimental to a practice.

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SUPPORT: None

P-753 4:30 PM Tuesday, October 20, 2020

IMPACT OF IMPLEMENTATION OF A NEW EMBRYO CULTURE SYSTEM ON EFFICIENCIES OF CLINICAL OPERATIONS IN A MODERN IVF CLINIC. Natalie Hesketh, MSc, Teija Peura, PhD, Andrew Murray, MSc, Sarah Dalati, PhD, Mark Bowman, MB BS PhD, Steven J. McArthur, BSc Genea, Sydney, NSW, Australia.

OBJECTIVE: Although our clinics achieved significant improvements in embryo developmental outcomes and pregnancy rates after the introduction of continuous culture medium and timelapse system, the downstream impact on operational efficiencies remained unknown. In the face of increasing competition these impacts are becoming increasingly important for the clinics, and hence the objective of this study was to examine if implementation of the new system had positive effects also on IVF clinic operational outcomes.

DESIGN: Alongside the change of culture system in a chain of IVF clinics, operational efficiencies were monitored to assess the possible advantages or disadvantages to clinical operations. Overall procedure times per patient and number of cycles per embryologists were tracked. In addition, patient satisfaction regarding monitoring their embryo videos during their cycle was recorded to assess the effect on competitiveness of the clinics' services. The data was collated from 2017-2019.

MATERIALS AND METHODS: Clinical cycles across eight clinics in 2017 to 2019 were included into the study. Cycle procedure and clinical process timings, each broken into 16 separate steps, were captured from clinical records. Average cycle numbers per full-time equivalent embryologists were likewise captured in 8 clinics. 358 patients were surveyed over 8-month period during their cycle about their experiences of accessing their embryo images and videos using a 5-level Likert scale questionnaire.

RESULTS: Average procedure times decreased from 570 to 555 to 490 minutes per patient in 2017, 2018 and 2019, resulting in average savings of 1h 20 min per patient (14% decrease), with biggest relative time savings achieved in embryo assessments and embryo hatching (in-situ) for PGT. Clinical hours per cycle varied from 6.9 to 7.0 to 6.1 hours in 2017, 2018 and 2019, again with biggest time savings gained for embryo checks. Number of cycles per embryologist increased from 107 to 126 to 160 (50% increase) in 2017, 2018 and 2019. Although more flexibility in staffing due to facilitation of remote embryo assessment was the biggest factor, not all efficiency improving factors were directly related to the new culture system.

84.8% of surveyed patients agreed or strongly agreed that their IVF experience was enhanced by access to their images, citing factors such better inclusion of their partner, provision of greater understanding and feeling of being more connected with their treatment. Subsequent surveys showed that even in cycles not leading to pregnancy, majority of patients still felt better connected to and more satisfied with their treatment when having access to their images.

CONCLUSIONS: Implementation of new embryo culture system led to positive trickle-down effects in efficiencies, costs, staffing and patient satisfaction. Rather than looking at laboratory operations and culture systems in isolation, it is hence important to consider the wider picture to ensure IVF clinics' operational and financial success alongside clinical outcome successes.

POSTER SESSION: PREIMPLANTATION GENETIC TESTING

P-754 4:30 PM Tuesday, October 20, 2020

PREIMPLANTATION GENETIC TESTING (PGT) SUCCESS IN THE UNITED STATES (2014-2017): MULTIPLE OUTCOME MEASURES INDICATE SUPERIORITY OF PGT OVER NO PGT. David H. McCulloh, Ph.D.,[1] James A. Grifo, MD, PhD[2] [1]NYU Langone Fertility Center, New York, NY; [2]NYU Langone Prelude Fertility Center, New York, NY.

OBJECTIVE: Studies have compared outcomes of transferring embryos tested for Preimplantation Genetic Testing (PGT) with untested embryos (No PGT). Most studies using comprehensive chromosome analysis (CCA: qPCR, array based or sequencing) found benefits for PGT in single centers (1,2,3). One multi-center randomized controlled trial showed benefit only for patients >35 years (4). Data spanning the United States (US) are available; but have not been reviewed since results from 2011 & 2012 (5)(mainly day 3 biopsies with a mix of aCGH and FISH). This study evaluates over 420,000 cycles from 2014-2017 comparing outcomes using PGT (mainly blastocysts using CCA) versus no PGT.

DESIGN: Analysis of Data Collected from the SART Registry (www.sart.org).

MATERIALS AND METHODS: Data for non-banking cycles (years: 2014-2017, inclusive) were segregated by use of PGT biopsy or not. Outcomes included: Livebirth (LB) per cycle (up to 1 transfer), miscarriage, multiple pregnancy and preterm deliveries. The mean number of embryos transferred was determined for each group.

Table 1

Outcome	Group	Female Age (years)[1] <35	35-37	38-40	41-42	>42
LB/cycle (# cycles)	PGT	43.5% (37,903)	37.6% (27,440)	28.0% (29,999)	17.0% (15,120)	6.9% (8,222)
	No PGT	41.8% (134,266)	32.5% (62,944)	20.6% (55,618)	10.1% (28,102)	3.3% (21.395)
# embryos	PGT	1.18	1.18	1.15	1.14	1.19
Xfrd	No PGT	1.56	1.73	2.04	2.44	2.57
LB/cycle dx-adjusted	PGT	44.8%	37.9%	28.0%	16.7%	7.4%
	No PGT	43.0%	33.0%	21.1%	10.3%	2.9%
Miscarriage	PGT	11.4%	12.3%	13.6%	15.0%	16.9%
	No PGT	12.3%	16.6%	25.3%	37.6%	54.3%
Multiple Birth	PGT	10.7%	10.0%	8.6%	7.8%	3.7%
	No PGT	21.4%	20.8%	19.2%	14.4%	9.5%
Premature Birth	PGT	15.0%	14.9%	15.0%	14.8%	13.1%
	No PGT	21.7%	21.2%	21.4%	19.6%	18.2%

[1]In each age group, every outcome was significantly different when comparing between PGT and No PGT (2 x 2 Contingency X^2 with $P < 0.05$)

RESULTS: LB per cycle was significantly greater for PGT in all age groups (see table), despite transfer of more embryos (no PGT). The excess live birth rate (PGT) varied among age groups. Miscarriage, multiple pregnancy and preterm delivery rates were significantly greater with no PGT (all ages). After adjusting for significant differences in reasons for ART in each age group, PGT had greater LB rates (all ages).

CONCLUSIONS: Cycles in the US revealed that PGT provided better rates for all ages: Higher LB, lower miscarriage, lower multiple pregnancy (associated with fewer embryos transferred) and lower preterm birth (associated with lower multiple pregnancy rate). LB rates, adjusted for reasons for ART, indicated that reasons for ART do not account for the significant advantage of PGT over no PGT. Confounders include: cases with PGT intent that had no biopsy (included as No PGT) and cases with PGT for other than PGT-A (included as PGT).

References:
1. Yang et al. (2012) Mol. Cytogenet. 5:24
2. Scott et al. (2013) Fertil. Steril. 100: 697-703
3. Forman et al (2013) Fertil. Steril. 100(1): 100-107
4. Munne et al. (2019) Fertil. Steril. 112:1071-1079
5. Kushnir et al. (2016) *Fertil. Steril.* 105(2): 394-400
SUPPORT: none

P-755 4:30 PM Tuesday, October 20, 2020

MULTICENTER PROSPECTIVE NON-SELECTION STUDY OF BLASTOCYST TRANSFER WITH LOW-MEDIUM-GRADE MOSAICISM.

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OBJECTIVE: To investigate the clinical outcome of blastocyst transfer with low-medium-grade mosaicism in a non-selection study

DESIGN: Multicenter prospective non-selection study involving five IVF clinics in Italy. Trophectoderm biopsies showing intermediate chromosome copy number (CN) values consistent with low mosaicism (20-50%) were blindly reported as euploid. The presence of mosaicism did not influence the embryo selection process as unbiased comparison of transfer outcomes between the fully euploid and putative-mosaic groups was performed. Ethical committee approvals were obtained at each site.

MATERIALS AND METHODS: The study involved 783 patients (mean female age 37.50 ± 3.3) undergoing homologous IVF cycles with blastocyst-stage PGT-A and single frozen euploid embryo transfer (SEET) between Sept 2018 and Dec 2019. A total of 845 cycles with at least one embryo available for transfer (euploid or putative mosaic) were included. Main exclusion condition was blastocyst of the worst morphological class. Miscarriage rate and live birth rate (LBR) per transfer were the main outcome measures.

RESULTS: A total of 897 SEET of tested blastocysts were performed in the course of the study, 484 (54%) were euploid, 282 (31,4%) showed low putative-mosaicism (20%-30%), and 131 (14,6%) showed moderate putative-mosaicism (30%-50%). Miscarriage rate was 12% (n=29/241), 11% (n=15/136) and 12.7% (n=8/63) for the three groups respectively; LBR was 43.4% (n=210/484), 42.9% (n=121/282) and 42% (n=55/131), respectively. Logistic regression analysis confirmed the lack of association between the "PGT-A category" and miscarriage risk (P=0.71) and live-birth rate per transfer. Therefore, no differences were observed in the clinical parameters testing across the three categories tested. The only prognostic factor for LBR was blastocyst developmental timing (OR=0.67 for day 6 vs day 5 and OR=0.19 for day 7 vs day 5). Mean mosaicism rate was not increased in biochemical pregnancy losses (BPL) and embryos resulting in miscarriage vs ongoing pregnancies, and in embryos resulting in LB vs embryos failing to implant. Mean number of mosaic chromosomes was also similar between LBR and control. The number of chromosomes with intermediate CN values per embryo was not associated with BPL (OR=1.00; 95%CI:0.85-1.18), miscarriage (OR=1.05; 95%CI=0.89-1.23) or LBR outcome (OR=0.98; 95%CI 0.91-1.07). Our data shows that the exclusion from transfer of all putative mosaics above 20% variability, results in an overall relative reduction in expected cumulative LBR of -36%.

CONCLUSIONS: Intermediate chromosome CN values consistent with low/moderate-grade mosaicism (30-50%) do not provide any clinically useful criteria for defining embryonic reproductive competence and should not be considered for aneuploidy categorization and embryo selection purposes in PGT-A cycles. The previously reported mild association can be explained by a selection bias involving the transfer of putative mosaic embryos to patients that failed previous euploid embryo transfers, thus of lower prognosis.

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CONFIRMATION RATE OF WHOLE CHROMOSOME CALLS ON A TARGETED NEXT-GENERATION SEQUENCING PLATFORM ARE HIGHLY CONSISTENT WITH INITIAL TROPHECTODERM BIOPSY.

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OBJECTIVE: The ability of preimplantation genetic testing for aneuploidy (PGT-A) based on a single trophectoderm biopsy to reflect the reproductive competence of an entire embryo has been a great source of debate. Some studies have even reported live births after transfer of purportedly aneuploid embryos, and concluded that viable embryos are being discarded due to inaccurate PGT-A results. These studies fail to capture the scope of analytic error in the initial PGT-A result. This study seeks to describe the accuracy of an initial clinical call made by PGT-A by targeted Next Generation Sequencing (NGS) in its ability to reflect the whole embryo by analyzing multiple biopsies from the same embryo.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Donated clinical embryos with prior euploid or whole chromosome aneuploid results determined by a targeted NGS platform were rebiopsied into multiple pieces. To obtain clinical-sized biopsies, embryos were biopsied anywhere from 2 to 12 times depending on blastocyst expansion after warming. NGS was then performed on these rebiopsies, and results were compared to the initial trophectoderm biopsy. All rebiopsies for the study were analyzed by the PGTseq-A platform with calls made by a single reviewer who was blinded to the initial clinical calls.

RESULTS: A total of 106 euploid embryos and 97 aneuploid embryos underwent rebiopsy. In embryos with an initial euploid call, 104 of the 106 embryos had confirmation of euploid status in all subsequent rebiopsied pieces (98.1%). Of the 97 embryos initially called aneuploid, 92 (94.8%) of these were confirmed with the same results in all subsequent rebiopsies.

	Embryos with initial call	Embryos with confirmatory rebiopsy results
Euploid Call	106	104 (98.1%)
Aneuploid Call	97	92 (94.8%)

CONCLUSIONS: This analysis finds a euploid or aneuploid clinical call made by targeted PGTseq-A to be almost always reflective of the entire embryo. The high correlation of subsequent biopsies with an initial biopsy provide reassurance that clinical decisions based off an initial trophectoderm biopsy can be made with confidence.

SUPPORT: None

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EFFECTS OF SPERM AGE ON EMBRYO PLOIDY IN PGT-A. Sally A. Rodríguez, ScM, CGC, Sophia Tormasi, BSc, TS(ABB), Catherine Welch, MBA, TS(ABB), Jason Nefalar, BSc, Laura Shin, BSc, Mike M. Moradian, PhD HCLD, Sequence46, Los Angeles, CA.

OBJECTIVE: PGT-A is routinely offered to patients undergoing IVF. Advanced maternal age (AMA), defined as ≥35 years, has a known significant effect on embryo ploidy status. The effects of advanced paternal age (APA), defined as ≥40 years, on ploidy have been studied less. This study assesses euploid and mosaic rates of embryos created with donor sperm (DS), non-APA sperm, and APA sperm, stratified by use of donor egg (DE), non-AMA eggs, and AMA eggs.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: All samples received 5/2018 - 5/2020 were included, except for those sent for PGT-SR or with suspected rearrangements. Samples created with known donor gametes were categorized with their respective age groups. Whole-genome amplification, next generation sequencing, and data analysis was performed using the Ion ReproSeqTM PGS Kit and Ion ReporterTM software (Thermo Fisher Scientific). Results were reported as 1) no abnormal cells detected, 2) abnormal cells detected (with percentages if mosaicism was identified), or 3) did not pass quality control (QC) metrics, leading to embryo categories euploid, aneuploid, mosaic, and QC failure. Results were tallied and chi square analyses were performed to compare euploid and mosaic rates between DS samples and non-APA and APA sperm samples.

RESULTS: A total of 23,239 samples from 4,691 cycles were included. Table 1 displays ploidy rates for each group and corresponding chi square p-values.

CONCLUSIONS: Our data shows that sperm age can have an effect on embryos' ploidy status, as shown by a significantly higher euploid rate in embryos created with DE and DS compared to those created using DE and either non-APA or APA sperm; this effect was noted even with a small sample size. Amongst embryos created with AMA eggs, DS has less of an effect, demonstrating that egg age is still the primary factor affecting embryo ploidy. Clinicians can use this information when counseling patients on the effects of AMA and APA on embryo ploidy.

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UNDERLYING RISK FOR A PARENTAL BALANCED CHROMOSOME REARRANGEMENT IDENTIFIED THROUGH PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY USING SNP MICROARRAY ANALYSIS WITH INFORMATICS. Jessica Adsit, MS, Katherine L. Howard, MS, Carrie Chou, MS, Dalar Ratousi, MS, Nina Wemmer, MS, Katrina Merrion, MS Natera, Inc., San Carlos, CA.

OBJECTIVE: To determine the rate of parental balanced chromosome rearrangements identified following preimplantation genetic testing for aneuploidy (PGT-A) with embryo results suggestive of a parental

Table 1. Euploid & Mosaic Rates by Group

Embryo Categories	% Euploid	χ2 p-value (Euploid)	% Mosaic	χ2 p-value (Mosaic)	Average Egg Age (years)	Average Sperm Age (years)
DE + DS	97/146 66.44%	-	19/146 13.01%	-	25.2	28.2
DE + S<40	1770/3146 56.26%	p = 0.015	581/3146 18.47%	NS	25.8	34.6
DE + S≥40	1478/2593 57.00%	p = 0.025	456/2593 17.59%	NS	26	46
E<35 + DS	265/494 53.64%	-	99/494 20.04%	-	31.6	26.3
E<35 + S<40	2662/4808 55.37%	NS	757/4808 15.74%	p = 0.013	31.8	33.7
E<35 + S≥40	455/829 54.89%	NS	129/829 15.56%	p = 0.037	32.1	46.2
E≥35 + DS	396/1145 34.59%	-	129/1145 11.27%	-	39.4	27.4
E≥35 + S<40	2122/5251 40.41%	p = 0.0003	646/5251 12.30%	NS	37.7	36.3
E≥35 + S≥40	1559/4827 32.30%	NS	458/4827 9.49%	NS	39.4	45.1

DE: donor egg; DS: donor sperm; S<40: non-APA sperm; S≥40: APA sperm; E<35: non-AMA egg; E≥35: AMA egg; NS: not significant

rearrangement and to assess any correlation between the number of embryos with an abnormality involving the same chromosomes and the likelihood of confirming a parental rearrangement.

DESIGN: Retrospective study of all trophectoderm (TE) biopsy samples received between April 2014-February 2020 that were suggestive of a parental rearrangement due to a pattern of deletions/duplications and/or aneuploidy involving the same chromosome(s) and parental origin.

MATERIALS AND METHODS: TE biopsies were performed at in vitro fertilization (IVF) centers and shipped to a single reference laboratory for PGT-A using Illumina CytoSNP-12b microarrays and bioinformatics which determine parental origin of each chromosome. For cases with results suggestive of a parental rearrangement, clinics were contacted, and parental chromosome analysis was suggested.

RESULTS: Fifty-seven flagged cases were identified with a total of 228 TE samples. The average number of TE samples tested per case was 7 (range 2-23). Clinics provided follow up on 49 cases, 44 of which pursued chromosome analysis. A chromosome rearrangement was confirmed in 37 patients (84.1%) including 35 translocations and 2 inversions. For all cases, parental origin was consistent with the prediction based on embryo results (29 paternal and 8 maternal). Broken down by the number of TE results suggestive of a parental rearrangement: 16 cases had 5 or more suggestive results with a parental rearrangement confirmed in 13 (81.3%); 14 cases had 3-4 suggestive results with a parental rearrangement confirmed in 13 (92.9%); 14 cases had 1-2 suggestive results with a parental rearrangement confirmed in 11 (78.6%).

CONCLUSIONS: In this study, 84.1% of patients with PGT-A results suggestive of a parental rearrangement were confirmed to carry a translocation or inversion. While having 3 or more embryos with suggestive results correlated to a very high rate of a confirmed parental translocation or inversion (81.3%-92.9%), high confirmation rates (78.6%) were also seen in cases with only 1 or 2. The ability to determine parental origin of abnormalities on PGT-A can be used to identify possible patterns in embryo results, suggest partner-specific karyotype analysis, and may allow for the option of PGT for structural rearrangements in future IVF cycles.

References: Gardner, R. and Sutherland, G. Chromosome Abnormalities and Genetic Counseling; 3rd ed (Aug 28, 2003): 142.

SUPPORT: Natera, Inc.

P-759 4:30 PM Tuesday, October 20, 2020

GENDER SELECTION, IS IT TIME TO ABANDON THE ALBUMIN SPERM SEPARATION METHOD?

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OBJECTIVE: Prior to the advent of preimplantation genetic testing for aneuploidy screening (PGT-A), gender selection has traditionally relied on the Ericsson albumin sperm separation method in which X chromosome bearing sperm are sorted from Y chromosome bearing sperm based on their difference in density. We wished to validate the benefit of the Ericsson sperm separation method against PGT-A results in couples undergoing sperm sorting with the modified Ericsson albumin separation method followed by IVF with PGT-A for gender selection.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients undergoing IVF in 2018 who stated a desired sex preference (gender selection) were offered modified Ericsson sperm separation prior to ICSI. Patients undergoing IVF in the same time period, who did not state a particular sex preference, served as controls. In the gender selection group, after a standard sperm wash via swim up method, the sperm pellet was layered with 0.5cc of 10% synthetic serum substitute and incubated at 37°C for 45minutes. If male sex was desired, the lower 0.25cc was carefully removed. If female sex was desired, the upper 0.25cc was used (Ref 1). The enhanced layer was re-centrifuged and the sperm pellet was re-suspended and used for standard ICSI. In the control group, a standard sperm swim-up was employed followed by ICSI. Blastocysts were biopsied and PGT-A was performed through next generation sequencing platform.

A sample size of 670 embryos was determined to give a 95% confidence interval to identify a 15% difference between the two groups.

RESULTS: 129 couples were identified in the gender selection group and 221 couples served as controls. The demographics between the two groups were similar in terms of woman's age and number of embryos biopsied. The gender selection group was significantly more likely to have advanced paternal age, previous pregnancy and live birth, and prior ART treatment. Of the 129 couples in the gender selection group, 28% desired female and 72% desired male gender.

A total of 2,229 embryos were biopsied and PGT performed (874 embryos in the gender selection group and 1355 blastocysts in the control group).

The percentage of male embryos in the gender selection group desiring male gender was 45.75% versus 49.48% in the control group (P=0.13), while the percentage of female embryos in the gender selection group desiring female gender was 51.72% versus 50.52% in the control group (P=0.71).

The odds ratio for a particular gender was not different between the modified Ericsson method and standard sperm washing technique. Gender selection via the modified Ericsson method did not reveal a specific advantage towards male or female gender.

CONCLUSIONS: While some limited studies have shown separation of sperm on albumin columns can affect the sex ratio at birth, our study is the first to evaluate the modified Ericsson albumin sperm separation method for gender selection in patients undergoing IVF with PGT. We did not find a significant improvement in the likelihood of one desired gender over another. Patients should be counseled that IVF with PGT-A remains the best treatment option for gender selection.

References: 1. Rawlins et al. Prog. Soc. Gynec. Invest., 35th Annual Meeting, Baltimore, 1988, Abstract No. 156

P-760 4:30 PM Tuesday, October 20, 2020

THE UTILITY OF PGT VS NON-PGT FROZEN EMBRYO TRANSFER BY PATIENT AGE GROUP.

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OBJECTIVE: To examine differences in cycle outcomes between patients undergoing autologous frozen embryo transfer (FET) having received embryos that either were euploid by preimplantation genetic testing for aneuploidy (PGT-A) or were untested.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: 3,994 FET cycles from January 2015 through December 2019 were evaluated following transfer of PGT-A euploid embryos using Next-Generation Sequencing (NGS) or single nucleotide polymorphism (SNP) array, versus untested embryos. A total of 4,605 embryos were transferred. Patients were categorized by age based on SART classification. Outcome measures include average number of embryos transferred, implantation rates (IR), clinical pregnancy rates (CPR) and presence of fetal cardiac activity (FCA). Differences between outcomes were calculated (Delta).

RESULTS: FETs without PGT-A had a decline in IR, CPR and FCA with increasing patient age. FETs with PGT-A, the IR, CPR and FCA had similar rates across all age groups. The Delta in IR for patients utilizing PGT-A tested embryos increased as patient age category increased (<35=12%, 35-37=17%, 38-40=24%, 41-42=36% and >42=50%). Likewise, the Delta in CPR and FCA also increased as patient age category increased (CPR <35=5%, 35-37=13%, 38-40=20%, 41-42=29% and >42=37%, and FCA <35=3%, 35-37=18%, 38-40=20%, 41-42=31% and >42= 38%).

2015-2019 FET

FET w/o PGT-A	<35	35-37	38-40	41-42	>42
Transfer n	1177	590	307	110	53
Avg # Transferred	1.23	1.21	1.22	1.37	1.38
IR/Embryo	52%*	50%*	40%*	26%*	17%*
CPR/Transfer	57%	54%*	44%*	33%*	30%*
FCA/Transfer	53%	48%*	41%*	25%	23%*
FET w/PGT-A					
Transfer n	539	574	438	160	46
Avg # Transferred	1.05	1.04	1.05	1.03	1.04
IR/Embryo	64%*	67%*	64%*	62%*	67%*
CPR/Transfer	62%	67%*	64%*	62%*	67%*
FCA/Transfer	56%	66%*	61%*	56%*	61%*
IR Delta	12%	17%	24%	36%	50%
CPR Delta	5%	13%	20%	29%	37%
FCA Delta	3%	18%	20%	31%	38%

CONCLUSIONS: With increasing patient age, there is a steady increase in IR, CPR and FCA per transfer for PGT-A tested embryos versus untested embryos. However, the nonsignificant difference of 3% in FCA in the <35 age group highlights the limitations of PGT-A in younger women. Outcomes per transfer in this analysis, as opposed to outcomes per cycle start, do not reflect other potential pitfalls of PGT-A including fewer eligible embryos for transfer due to false positives or lack of embryo survival at FET. Additionally, patients who received a fresh embryo transfer without PGT-A and became pregnant is not considered in this dataset. PGT-A demonstrates increasing benefit with advancing female age, but it shows no significant advantage in younger women. Further analyses are needed to clarify these issues. * indicates P<.05 within age group and appropriate parameter comparison.

SUPPORT: None

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RELATIONSHIP BETWEEN PGT-A & CUMULATIVE LIVE BIRTH RATE IN AUTOLOGOUS & DONOR CYCLES: AN ANALYSIS OF 178,511 PATIENTS REPORTED TO SART CORS.

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OBJECTIVE: Cumulative live birth rate (CLBR) outcome prediction models may not account for patient intent at the start of the stimulation cycle, cycle cancellation, or elimination of cycles without transferable embryos. We evaluated & compared the CLBR per cycle start, oocyte retrieval (ER), & embryo transfer (ET) +/- PGT-A across maternal age groups, using autologous or donor oocytes.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Autologous & donor oocyte IVF cycles from 2014-2016 reported to SART CORS were evaluated. Inclusion criteria were the first reported ovarian stimulation cycle per patient, combined with the first fresh ET or frozen-thawed embryo transfer (FET) & all subsequent linked FETs. For the PGT-A group, only day 5 & 6 FETs were included. PGT-A cycles without transferable embryos were included in the 'all cycle starts' group. PGT-A cycles without FET and no reason that could be clearly categorized were excluded. Comparisons were stratified by patient age categorically. The primary outcome measure was CLBR per stimulation cycle start. Secondary outcomes were CLBR per ER & per cumulative ET. Chi-square tests were used to assess the association between CLBR across groups. Two-sided p-values <0.05 were considered statistically significant.

RESULTS: 178,511 stimulation cycle starts were analyzed. Increasing age was associated with decreasing CLBR for all stimulation cycle starts (including planned PGT-A cycles) using autologous oocytes. Similarly, the subgroup of cycles which resulted in ER with intention for fresh ET without PGT-A showed inverse CLBR with increasing age (p <0.001 for both analyses).

A subgroup of patients was analyzed per cumulative ET, not per cycle start. In this subgroup, PGT-A FET had higher CLBR vs. fresh ET stratified by age (71.5% vs. 64.2% age <30; 69.7% vs. 59.6% age 30-34; 66.0% vs. 45.5% age 35-39; 57.5% vs. 16.7% age ≥40). FET without PGT-A also had a higher CLBR vs. fresh ET stratified by age (72.3%, 67.9%, 53.9%, & 23.7% for ages ≤30, 30-34, 35-39, ≥40, respectively) (p<0.001 for all comparisons). PGT-A FET had a higher CLBR vs. FET without PGT-A at age >30 (p<0.05), but not at age <30 (p>0.5).

Donor oocyte cycles had higher CLBR per stimulation cycle start for all age groups compared with autologous oocytes (p<0.001). Donor oocyte PGT-A FET resulted in a higher CLBR vs. fresh ET at age 35-39 (p = 0.04) & vs. FET without PGT-A at age ≥40 (p < 0.001), but not at other ages.

CONCLUSIONS: Increasing age is associated with decreasing CLBR in all cycles. For the subset of patients undergoing ET, PGT-A is beneficial at age >30; this improvement is minimal at ages 30-34 & most pronounced at age ≥40. However, it should not be concluded that PGT-A improves CLBR per cycle overall, but rather just in the subset in which ET is done. Under age 30, PGT-A is superior to fresh ET, but not to FET without PGT-A, suggesting limited utility in this age group. Donor oocytes produced the highest CLBR per cycle start & after ET at all ages, but there is no benefit to PGT-A if the recipient is age <35. Patient counseling regarding use of PGT-A & donor oocytes should be age dependent & individualized.

SUPPORT: None.

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USING UNBALANCED EMBRYOS AS REFERENCES IN DISTINGUISHING CARRIER AND NORMAL EMBRYOS BY SNP ARRAY FOR RECIPROCAL TRANSLOCATIONS.

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OBJECTIVE: To validate the feasibility of using unbalanced embryos as references in the detection of normal euploid embryos by SNP array based preimplantation genetic haplotyping (PGH) in preimplantation genetic testing (PGT) for reciprocal translocations.

DESIGN: The purpose of this study was to compare the consistency of results from using unbalanced embryos as references with family members, thus to evaluate the feasibility of only using unbalanced embryo as a reference to distinguish normal and carrier embryos, for the situation when no family member was available.

MATERIALS AND METHODS: Haplotypes were first established based on SNPs from family members. Blastocysts were biopsied and screened by SNP array based comprehensive chromosome screening (CCS). After CCS, balanced embryos were further tested to identify normal euploidies by haplotyping using either family member as a reference, or unbalanced embryos generated by adjacent-1 or adjacent-2 segregation mode. Karyotypes of transferred embryos were validated by prenatal diagnosis.

RESULTS: A total of 110 couples with reciprocal translocations were analyzed. After CCS, 288 out of 995 embryos were found balanced. Using family members as references, 142 of 288 balanced embryos were tested to be normal, 144 carriers, and the other 2 undetermined. Next, unbalanced embryos were selected as references, and all the results of carrier and normal embryos were consistent with the previous results. A total of 107 embryos were transferred, resulting in 66 clinical pregnancies. Of the 66 clinical pregnancies, 34 received prenatal diagnosis. Karyotypes from prenatal diagnosis were all in accordance with the results of tested embryos.

CONCLUSIONS: PGH based SNP array is a rapid and effective way to identify normal embryos from balanced ones for translocation carriers. In case no family member was available as a reference, unbalanced embryos can be used for distinguishing normal and carrier embryos.

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CUMULATIVE LIVE BIRTH RATE IN WOMEN 37 YEARS OF AGE OR LESS WHO UTILIZE PREIMPLANTATION GENETIC TESTING-ANEUPLOIDY (PGT-A) VERSUS UNTESTED EMBRYOS.

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OBJECTIVE: To determine the effect of PGT-A on the cumulative live birth rate (LBR) in women ≤37 years of age

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: Data were collected from Society for Assisted Reproductive Technology (SART) reporting clinics on all 31,900 patients ≤37 years of age undergoing their first retrieval between Jan 2014 and Dec 2015. Subsequent transfer cycles utilizing embryos from the initial retrieval cycle alone were followed through December 2016. The women were grouped based on age, <35 and 35-37 years of age. Generalized linear mixed models were used to control for clinical and demographic variables found to be in the top model selected for by Bayesian Information Criterion. The primary outcome was cumulative live birth, defined as the occurrence of at least one delivery in the follow-up period. Secondary outcomes included multifetal births, miscarriage, and time to pregnancy. Time to pregnancy resulting in delivery was calculated for cycles resulting in a live birth by adding 10 days (standard amount of time from embryo transfer to the pregnancy test) to the number of days between medication start in the retrieval cycle and the embryo transfer that resulted in the live birth.

RESULTS: There were 29,362 patients using untested embryos (91%) and 2,535 patients using PGT-A embryos (7.9%) included. For patients <35, the crude cumulative live birth rate for PGT-A (70.6%) vs untested (71.1%)

embryos was similar. After adjusting for confounding factors, the adjusted odds ratio (aOR) for the LBR with PGT-A was 0.81 (0.72 - 0.92, p< 0.001). For patients 35-37, there was no significant difference in the LBR for PGT-A (66.6%) vs untested embryos (62.5%), aOR 0.98 (0.86 – 1.11). There was a significant decrease in multifetal births in the PGT-A group compared to the untested group for patients <35 (8.6 % vs 23.2%) aOR 0.32 (0.26 - 0.41, p<0.001) and patients 35-37 (10.5% vs 22.8%) OR 0.42 (0.33 - 0.54, p<0.001). There was no significant difference in miscarriage rate between PGT-A and untested groups in either age group, < 35 aOR 1.12 (0.90 – 1.4), 35-37 aOR 0.84 (0.66 – 1.06). The average time from onset of the IVF cycle to a pregnancy resulting in live birth for patients < 35 was 2.17 months (SD 2.86) for untested transfer cycles and 4.10 months (SD 3.12) for PGT-A transfer cycles. For patients 35-37, the average time to pregnancy utilizing untested embryos was 2.14 months (SD 2.86) and for PGT-A cycles was 4.44 months (SD 3.48). All adjusted odds ratios were adjusted for age, BMI, race, length of follow-up, and total 2PN embryos.

CONCLUSIONS: There was a decreased cumulative LBR in women <35 who utilized PGT-A compared to those who did not use PGT-A and no difference in LBR in women 35-37. A strategy utilizing PGT-A for these age groups does not appear to lead to improved LBR or reduced miscarriage rates compared to transferring untested embryos in this national data. Notably, PGT-A was associated with a marked reduction in multiple births although this strategy required a longer time to pregnancy compared to transfer of untested embryos.

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IMPACT OF SLIGHT VARIATIONS OF EXTRACELLULAR CULTURE MEDIA pH (PHE) ON EMBRYO QUALITY, EUPLOIDY RATES AND MITOCHONDRIAL DNA (mtDNA). Andrea Abdala, M.Sc., Ibrahim Elkhatib, M.Sc., Aşina Bayram, M.Sc., Ana Arnanz, M.Sc., Ahmed El-Damen, M.Sc., Barbara Lawrenz, M.D., Ph.D., Human M. Fatemi, M.D., Ph.D., Neelke De Munck, M.Sc., Ph.D. IVIRMA Middle East Fertility Clinic, Abu Dhabi, United Arab Emirates.

OBJECTIVE: To determine if variations in pHe affect blastocyst quality, euploidy rates and blastocyst mtDNA content.

DESIGN: A retrospective study was performed between July 2018 and October 2019, including 44 patients with at least 4 fresh autologous mature oocytes and non-male factor infertility. After injection, sibling oocytes were cultured under two different pHe.

MATERIALS AND METHODS: A total of 604 sibling mature oocytes were injected and split: 321 under 6.0% CO_2 and 283 under 7.5% CO_2, cultured in continuous Global® Total® LP media in 5% O_2 and 89% or 87.5% N_2, respectively. The working pH (pHe=7.374±0.003 for 6.0% CO_2 and pHe=7.299±0.004 for 7.5% CO_2) was within the range indicated by the manufacturer (7.20-7.40). Trophectoderm (TE) biopsy for preimplantation genetic testing for aneuploidies (PGT-A) with determination of mtDNA content was performed on day 5, 6 or 7 of embryo development. The primary endpoint was to determine if the pHe has an impact on blastocyst quality classified as excellent (AA or BA), good (AB or BB) and poor (AC, BC, CA, CB, CC), using Gardner scoring for inner cell mass (ICM) and TE, respectively. As a secondary endpoint, the effect of pHe on euploidy rates and mtDNA content of biopsied blastocysts was evaluated.

RESULTS: The mean age of women was 33.0±6.6 years old. Total blastulation rate on day 5 was not significantly different between 6.0% and 7.5% CO_2 (67.8% vs 68.4%, p=0.156). Blastocyst quality did not differ between excellent (OR=0.94, 95% CI: 0.46-1.92, p=0.879), good (OR=1.19, 95% CI: 0.74-1.89, p=0.467) and poor quality (OR=0.87, 95% CI: 0.55-1.36, p=0.542) for embryos cultured under 6.0% compared to 7.5% of CO_2. Additionally, blastocyst biopsy rate per normally fertilized oocyte was not significantly different between 6.0% and 7.5% CO_2 (53.3% vs 59.2%, p=0.335). However, euploidy rate was significantly increased in the 6.0% group (55.7% vs 35.7%, p=0.035). From a linear mixed model, considering non-independence of the data, the mean mtDNA content of biopsied blastocysts cultured under 6.0% was significantly lower than 7.5% CO_2 (30.39±9.1 vs 32.91±10.3, p=0.037).

CONCLUSIONS: Slight variations of pHe do not have an impact on blastocyst quality, however, euploidy rates and mean mtDNA content are significantly affected when embryos are cultured in a lower pHe.

SUPPORT: None.

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DOES BODY MASS INDEX INFLUENCE EMBRYO EUPLOIDY RATES? Mohamad Irani, MD,[1] Zev Rosenwaks, M.D.[2] [1]Advanced Fertility Center of Chicago, Chicago, IL; [2]The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: Obesity is associated with increased miscarriage rates after natural conception and assisted reproductive technology. However, the underlying mechanism responsible for this association is poorly understood. Here we aim to determine the effect of body mass index (BMI) on embryo euploidy rates.

DESIGN: This is a retrospective cohort study including in vitro fertilization (IVF) with preimplantation genetic testing for aneuploidy (PGT-A) cycles between 2013 and 2017.

MATERIALS AND METHODS: Cycles were divided into three age groups (<35, 35–40, and >40 years old). Embryo euploidy rates were compared between women with a BMI <30 kg/m^2 and those with a BMI ≥30 kg/m^2 (obese) within each age group. χ^2 and Fisher's exact tests were used for categorical variables. Student's *t* test was used for parametric data. Values were expressed as mean ± standard error of mean.

RESULTS: A total of 2,164 IVF/PGT-A cycles were included. In the youngest age group, women with a BMI ≥30 kg/m^2 had comparable numbers of oocytes harvested (14.4 ± 1.1 vs. 16.4 ± 0.4, P=0.1), numbers of biopsied embryos (6.8 ± 0.6 vs. 7 ± 0.2, P=0.7), and euploidy rates (53.2% vs. 55.4%, P=0.6) with those with a BMI <30 kg/m^2 (Table 1). Similarly, euploidy rates were not significantly different between women with a BMI ≥30 kg/m^2 and those with a BMI <30 kg/m^2 in the 35-40-year-old age group (39.9% vs. 37.5%, respectively, P=0.4) as well as in the >40-year-old age group (14.8% vs. 13.9%, respectively, P=0.7) (Table 1).

CONCLUSIONS: Obesity does not significantly affect embryo euploidy rates.

	BMI <30 kg/m^2	BMI ≥30 kg/m^2	*P* value
Age < 35 years old			
# oocytes harvested	16.4	14.4	0.1
# embryos biopsied	7.0	6.8	0.7
Euploidy rate (%)	55.4	53.2	0.6
Age 35–40 years old			
# oocytes harvested	13.4	13.6	0.8
# embryos biopsied	5.6	5.4	0.7
Euploidy rate (%)	37.5	39.9	0.4
Age >40 years old			
# oocytes harvested	11.9	11.6	0.7
# embryos biopsied	4.3	4.2	0.7
Euploidy rate (%)	13.9	14.8	0.7

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A COMPARISON OF NON-INVASIVE AND TROPHECTODERM BIOPSY PGT-A. FIRST EXPERIENCE IN ARGENTINA. Francisco Antonio Leocata Nieto, PhD,[1] Jeremías Zubrzycki, PhD,[2] Hernán Dopazo, PhD,[2] Ariel Octavio Ahumada, PhD[1] [1]PROCREARTE, Buenos Aires, Argentina; [2]BIOCÓDICES, San Martín, Argentina.

OBJECTIVE: The discovery of cell-free embryonic DNA (cfDNA) present in the medium in which developing embryos are being cultured in vitro led to the use of this spent culture medium (SCM) as a source of DNA in PGT studies. Different non-invasive PGT (niPGT-A) protocols are in validation and standardization stages worldwide. The objective of this work is to validate a NICS protocol (Yikon Genomics) by comparing the results obtained in PGT-A cycles performed with samples obtained by trophectoderm (TE) biopsies, the current gold standard.

DESIGN: This study evaluates the ploidy state concordance between SCM and embryo biopsies, analyzing the media collected from 30 single D5-D6 blastocysts culture droplets, followed by TE biopsy.

MATERIALS AND METHODS: Embryos were grown in Global Total LP (Life Global) microdrops (37° C, 5% O2, and 6% CO2). On D3, embryos were transferred to a new dish with 30 μl media drops until the moment of

performing the TE biopsies on D5-D6. After biopsy, embryo were transferred to an additional dish, until vitrification. The SCM of the original dish was transferred to PCR tubes containing 5 μl of lysis buffer (Yikon Genomics). The samples were stored at -80°C until processing. Whole-genome amplification (WGA) and subsequent library preparation for TE samples were performed following the Veriseq protocol (Illumina, San Diego, CA, USA), while for medium samples, the NICSInst protocol (Yikon Genomics) was used. All samples (from TE and SCM) were sequenced using the Illumina MiSeq platform according to the recommendations detailed in the mentioned protocols. About 1 million reads were obtained per sample, allowing a resolution of ~10 Mpb. For the subsequent analysis, the BlueFuse Multi (Illumina) and ChromGO (Yikon) software were used for the TE and medium samples, respectively.

RESULTS: WGA was 100% effective for all the samples (TE and SCM). A total of 17 true-positives, 9 true-negatives, 0 false-positive, and 4 false-negatives were obtained after comparisons. These values correspond to 87% concordance, 81% sensitivity, 100% specificity, 100% positive predictive values (PPV), and 69% negative predictive values (NPV). False-negative results correspond to two cases of full autosomal aneuploidies, and two cases of low-level mosaicism detected through the TE biopsy. In the four cases, the culture media showed euploid results.

CONCLUSIONS: niPGT-A starting from cfDNA showed excellent results in comparison to the current gold standard method (TE biopsy). Discordances correspond to four false-negatives, where the non-invasive method showed euploid results while TE biopsy showed aneuploidies. If niPGT-A is a more reliable representation of the whole embryo than TE biopsy, this 13% of discordance, is the kind of result that points out that the non-invasive method is a valuable alternative tool for PGT-A.

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LIVE BIRTH RATE FOLLOWING PGT RESULTS IN LOWER LIVE BIRTH RATE COMPARED TO UNTESTED EMBRYOS TRANSFERRED AT DAY 5/6. Kevin J. Doody, M.D., Kathleen M. Doody, MD
CARE Fertility, Bedford, TX.

OBJECTIVE: Embryos progressing through day 5/6 can be transferred fresh or following thaw without biopsy for genetic testing. Alternatively, these embryos may be biopsied, cryopreserved and subsequently thawed and transferred using information obtained from aneuploidy screening. The outcomes of treatments employing these two distinct strategies were compared.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Analysis of publicly available ART outcomes using the 2018 SART National Summary Report was performed. Filters were applied to view the outcomes of the two groups: 1) Autologous IVF cycles without PGT with day 5/6 embryos transferred, and 2) Autologous IVF cycles with PGT. Both groups were compared with respect to their first embryo transfer only.

RESULTS: PGT resulted in a lower chance of live birth in all age groups compared to transfer of day 5/6 embryos without PGT (Table). Although PGT results in higher pregnancy rates following transfer, the majority of PGT procedures done in women over age 38 did not ultimately result in an embryo transfer. Although the rate of miscarriage increased with age in both treatment groups, PGT resulted in a markedly lower risk of pregnancy loss.

CONCLUSIONS: Previous studies have concluded that PGT for aneuploidy improves the success rate for embryo transfers. These studies have generally failed to do appropriately corrected comparisons. Success rates calculated "per transfer" do not reliably approximate "intent to treat". Success rates should be calculated "per PGT cycle". Women in all age groups very frequently will not have euploid embryos available for transfer following biopsy and genetic testing. When the success rate "per PGT cycle" is compared to a similar cohort possessing developing embryos suitable for transfer on day 5/6, the apparent improved success rate obtained by performing PGT is erased. The increased implantation rate following transfer of tested euploid embryos is more than counter-balanced by decreased ET procedures following biopsy and testing. PGT is best viewed as a strategy to decrease the risk of pregnancy loss and does not improve chance of live birth.

SUPPORT: None

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THE EFFECT OF MATERNAL AGE ON CHROMOSOMAL MOSAICISM: AN ANALYSIS BY CHROMOSOME TYPE AND MOSAIC RESULT. Jenna Reich, BS,[1] Jennifer K. Blakemore, MD,[2] Andria G. Besser, MS, CGC,[3] Brooke Hodes-Wertz, MD, MPH,[4] James A. Grifo, MD, PhD[3]
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OBJECTIVE: Previous work by our group (1) showed that the rate of chromosomal mosaicism decreases with maternal age. However, the types of chromosomes involved, as well as the types of chromosomal mosaicism in individual embryos, have not yet been examined. Our objective was to determine whether maternal age was associated with the rate of sex and autosomal chromosome mosaicism and the rates of various types of mosaicism.

DESIGN: Retrospective cohort study of all blastocysts that underwent trophectoderm biopsy for preimplantation genetic testing for aneuploidy (PGT-A) from 1/2015 to 12/2018 at our center.

MATERIALS AND METHODS: All patients with blastocysts that underwent trophectoderm biopsy for PGT-A via Next Generation Sequencing with $\geq$1 chromosome in the mosaic range (20-80%) were included. The primary outcomes were: 1) the rate of sex and autosomal chromosome mosaicism and 2) rates of segmental mosaicism, full chromosome mosaicism and complex ($\geq$3 mosaic chromosomes) stratified by maternal age. Statistical analyses included Kruskal-Wallis (KW) and linear regression (LR) to control for paternal age, with $p<0.05$ considered significant.

RESULTS: 1,670 patients with 10,545 embryos biopsied overall and 3,611 embryos with $\geq$1 mosaic chromosome met inclusion criteria. The number of embryos biopsied decreased with maternal age ($p<0.01$) as expected. 3,366 (93.2%) embryos had only autosomal chromosome mosaics, which was independent of maternal age ($p=0.05$). Alternatively, the percent of embryos with $\geq$1 sex chromosome mosaic (6.8% n=245) was significantly associated with maternal age without clear trend by age group ($p<0.01$). Table 1 shows PGT-A results by type of mosaicism stratified by maternal age. Segmental mosaicism peaked at maternal age 35-37, while complex mosaicism increased

	<35		35-37		38-40		41-42		>42	
Age	No PGT	PGT	No PGT	PGT	No PGT	PGT	No PGT	PGT	No PGT	PGT
# cycles	18801	14715	7104	11106	4272	11159	1514	5113	709	2655
no transfer	—	25.8%	—	37.2%	—	53.1%	—	71.4%	—	87.2%
Mean # ET	1.2	1.1	1.4	1.1	1.7	1.1	1.9	1.1	2.1	1.1
Positive hcg / ET (%)	69.3	75.9	62.1	75.0	57	73.3	43.5	70.4	26.5	63.6
Clinical preg / ET (%)	59	67.1	51.2	65.7	45.6	64.3	32.6	61.7	18.5	54.8
Miscarriage rate (%)	14	10.5	17.5	11.5	23.8	12.7	38.3	13.3	46.6	17.1
Implantation rate (%)	50.1	62.5	40.4	61.5	29.9	58.9	16.7	56.1	8.0	46.0
Live birth rate (%)	49.9	43.9	41.0	35.8	33.2	25.9	19.2	15.0	9.3	5.7
Twins (%)	10.9	6.3	13.6	5.4	15.2	5.1	11.0	3.5	9.1	4.0

Table 1. PGT-A Results by Maternal Age from Total Embryos Biopsied

	<35 (n=483)	35-37 (n=421)	38-40 (n=463)	>41(n=303)	p-value
Total Embryos Biopsied	3715	2770	2705	1355	**KW < 0.001** **LR < 0.001**
Segmental Mosaic Chromosomes (%)	2.9	4.4	3.5	3.2	**KW < 0.04** **LR < 0.008**
Full Chromosome Mosaics (%)	14.5	14.9	15.3	14.8	**KW = 0.123** **LR = 0.617**
Complex Mosaicism (%)	9.5	10.7	12.1	22.9	**KW < 0.001** **LR < 0.001**

*LR used to control for paternal age

with maternal age. Full chromosome mosaicism was similar across age groups.

CONCLUSIONS: Among our embryo cohort, rates of segmental mosaicism varied and complex mosaicism increased with maternal age. These results remained significant when controlling for paternal age. The rate of sex chromosome mosaicism was associated with maternal age but may not be sufficiently powered given the low number of chromosomes. Our results provide further data for counseling patients about mosaic embryo results.

References: 1.Â An Analysis Of The Effect Of Maternal And Paternal Age On Chromosomal Mosaicism, Pacific Coast Reproductive Society Annual Conference – Cancelled by COVID-19

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PRENATAL AND POSTNATAL GENETIC TESTING AFTER PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) FOR A NON-SELECTION CLINICAL TRIAL.

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OBJECTIVE: PGT-A detects whole chromosome aneuploidy before transfer and thus increases live birth rates and decrease early pregnancy failure rates. A prospective and blinded non-selection study using Next Generation Sequencing (NGS) based PGT-A (PGTseq-A) validated the ability of an 'aneuploid' analytical result to predict the failure to deliver. This study was aimed to further validate the accuracy of PGTseq-A. Prenatal genetic testing (through CVS or amniocentesis) or postnatal genetic testing (through newborn buccal DNA) was performed after the non-selected transfer cycles, then karyotypes was compared to the unblinded PGTseq-A results. Products of conception (POC) were tested when the miscarriage happened.

DESIGN: Retrospective

MATERIALS AND METHODS: Fetal tissues (CVS, amniocentesis, or POCs) and newborn buccal swabs were collected for 120 non-selected single embryo transfer cycles. Genomic DNA (gDNA) were isolated using QIAGEN DNA isolation kits. The karyotypes were analyzed by a targeted NGS platform which amplifies~5000 amplicons across the human genome.

RESULTS: Among the 120 transferred embryos, 100 embryos yielded healthy deliveries and 20 embryos resulted in clinical miscarriages. For 5 transferred embryos with deliveries, both prenatal and postnatal samples were tested. PGTseq-A showed that 2 embryos had whole chromosome mosaicism, 2 embryos had segmental mosaicism, and 1 embryo was euploid. The prenatal and postnatal genetic testing showed all the newborns were euploid. For the other 95 transferred embryos with deliveries, only newborn buccal DNA was collected. Based on PGTseq-A, 2 embryos yielded nonconcurrent results, 3 embryos were whole chromosome mosaic, 2 embryos were segmental mosaic, and 88 embryos were euploid. All the newborn gDNA showed normal karyotypes. For the 20 embryos with miscarriages, POCs were collected and tested. PGTseq-A revealed that 1 embryo had nonconcurrent result, 13 embryos were aneuploid, and 6 embryos were euploid. Three POC samples had maternal contamination, and the karyotypes of the remaining 17 POCs were 100% consistent with PGTseq-A results.

CONCLUSIONS: This study demonstrated the accuracy of PGTseq-A. It also showed the reproductive potential of embryos with undetermined safety (whole chromosome mosaicism or segmental mosaicism) based on the limited number of transferred embryos.

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RELIABILITY OF THE NEXT-GENERATION SEQUENCING (NGS) DIAGNOSIS OF MOSAICISM TO PREDICT THE CHROMOSOMAL CONSTITUTION OF THE INNER CELL MASS.

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OBJECTIVE: To investigate the reliability of next-generation sequencing (NGS) for diagnosing mosaicism and the predictive diagnostic value of trophectoderm (TE) biopsy for assessing the genetic status of the inner cell mass (ICM) in mosaicism.

DESIGN: Prospective study.

MATERIALS AND METHODS: Sixty-eight human embryos diagnosed clinically as mosaicism were rebiopsied and dissected into three parts: TE, ICM and the remaining parts of embryos (a combination of TE and ICM). All the samples were examined and compared with original clinical diagnosis. Whole genome amplification using the Malbac DNA amplification system followed by NGS via the ThermoFisher DA8600 platform was performed. Statistical analysis was performed using chi square.

RESULTS: Among the 68 blastocysts, the original mosaicism diagnosis was confirmed in at least one additional biopsy in 14 (20.6%) blastocysts; 12 (17.6%) displayed de novo abnormalities; and 42 (61.8%) showed a euploid profile in all segments. Among 59 rebiopsied ICM specimens, the results for 10 (16.9%) were consistent with the original trophectoderm (TE) biopsy; 6 (10.2%) displayed de novo abnormalities; and 43 (72.9%) were euploid. Stratification analysis showed that the type of mosaicism within the original biopsy diagnosis was associated with the concordance across the embryos. The concordance rate with the ICM results was highest for whole-chromosome mosaicism (41.2%), followed by complex mosaicism (20.0%), while that for segmental and mixed mosaicism was lowest (3.3% and 0%, respectively). However, it was not associated with the gain or loss of chromosomes (P=0.138). Closer examination of the level of mosaicism within the original biopsy diagnoses revealed that the concordance rate increased with increasing levels of mosaicism (P<0.001). In addition, the second TE biopsy for mosaicism showed a sensitivity of 68.8% and specificity of 92.9% for predicting abnormalities in the ICM portions.

CONCLUSIONS: This novel study exposes false-positive errors in NGS-based PGT and the limitations of a single TE biopsy for predicting the cytogenetic constitution of the ICM and whole embryos. It also provides suggestions for the transfer of mosaic embryos, indicating that those with segmental mosaicism and a low rate of aneuploidy should be prioritized and that a second TE biopsy is an option for doctors and patients facing a dilemma.

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VALIDATION OF PREIMPLANTATION GENETIC TESTS FOR ANEUPLOIDY WITH CELL-FREE DNA FROM SPENT CULTURE MEDIA (SCM): CONCORDANCE ASSESSMENT AND IMPLICATION.

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OBJECTIVE: Preclinical validation of cell-free DNA in SCM represents ploidy status of the chromosomal constitution of a blastocyst.

DESIGN: Validation study

MATERIALS AND METHODS: Seventy-five vitrified blastocysts with known karyotypes were donated for research, under informed consent, by patients undergoing IVF for treatment of infertility at Henan Provincial People's Hospital in China. All blastocysts were warmed and cultured individually at 37 °C in an atmosphere of 5% O_2 and 6 –7% CO_2, balanced with N_2. The SCM drops, TE biopsied cells, and the corresponding whole blastocysts samples are stored at -80 °C for library preparation. Multiple annealing and looping-based amplification cycle (MALBAC) techniques are utilized for whole genome amplification to ensure increasing amplification uniformity and less amplification biases. Next generation sequencing (NGS) was performed on the Illumina Hiseq 2500 platform with 2.0 Mb raw reads generated for each sample. All analyses have been incorporated into a pipeline and can be automatically generated.

RESULTS: To conduct a valid comparison of ploidy concordance assessment, we evaluated the full concordance rates between SCM and WB (SCM-to WB), and between TE and WB (TE-to-WB) as well as sensitivity, specificity and overall diagnostic accuracy. In addition, we comparatively adjusted the thresholds aimed at removing DNA amplification noise to more accurately distinguish aneuploid from euploid blastocysts. Interpretable NGS results in the SCM group are 78.67% (59/75) under Threshold 1 and 74.67% (56/75) under Threshold 2, respectively, and are significantly lower than their corresponding TE and WB groups. This manifests intrinsic low quantity/abundance and poor integrity in nature in DNA from SCM. Subsequently, remarkable differences in full concordance rates (including mosaicism, and segmental aneuploidies) are seen: 32.2% (SCM-to-WB, 19/59) and 69.33% (TE-to-WB, 52/75), ($P<0.001$) under threshold 1. Using the same approach, the full concordance rates show a similar trend when threshold 2 is adjusted as an alternative diagnostic threshold. In such a case, full concordance rates were 27.27% (15/55) in SCM-to-WB, and, 76% (57/75) in TE-to-WB ($P<0.001$). Collectively, the NGS data from SCM also translated into lower sensitivities, Positive Predictive Value (PPV), Negative Predictive Value (NPV), and overall diagnostic accuracies and to higher Negative Likelihood Ratio (NLR).

CONCLUSIONS: Cell free DNA is detectable in majority of SCM samples during blastocyst culture, but suboptimal and likely linked to degraded DNA in nature. The full ploidy concordance assessment further demonstrates that TE-to-WB is more accurate representation of the chromosomal constitution of the whole blastocyst in comparison with that of SCM-to-WB. Before PGT-A with the use of DNA from SCM for clinical implementation, new WGA techniques must be custom-tailor designed to overcome the nature of low DNA quantity and quality associated with DNA in SCM.

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PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) AND TIME TO PREGNANCY.

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OBJECTIVE: The utilization of PGT-A as an adjunct to IVF remains controversial. The objective of this study was to evaluate whether PGT-A decreases time to pregnancy for patients undergoing a single oocyte retrieval cycle.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: 18,143 women undergoing autologous IVF with and without PGT-A at an academically-affiliated infertility practice between January 2015-December 2018 were included. Ovarian stimulation protocols were performed per provider preference and both natural and programmed frozen embryo transfer (FET) protocols were utilized. For patients undergoing PGT-A, only those with a FET within three months of oocyte retrieval were included. Outcomes were compared according to age at oocyte retrieval (<38, ≥38 years). The primary outcome was time to pregnancy. This was defined as the time (days) from oocyte retrieval to the first positive serum hCG in a cycle resulting in a live birth. Live birth rates per transfer and cumulative live birth rate per retrieval were also calculated. Outcomes were compared using a chi square test.

RESULTS: 12,740 women underwent oocyte retrieval during the study period, with 16,215 transfers performed. All PGT-A patients underwent cryo-all cycles. 2378 (69.9%) control patients underwent a fresh embryo transfer. 5403 retrievals (42.4%) resulted in a live birth (43.7% in the PGT-A and 41.9% in the control group, $p=0.07$). In women <38 years (7689), a total of 11,217 transfers were performed that resulted in 4173 live births (37.2%). Live birth rates per transfer were significantly different (48.1% in the PGT-A and 34.6% in the control group, $p<0.05$). Live birth rates per retrieval in this group were 54.5% in the PGT-A and 54.2% in the control group ($p=0.84$). In women ≥38 years (5051 retrievals), a total of 4998 transfers were performed that resulted in 1230 live births. Live birth rates per transfer were significantly different (52.3% in the PGT-A and 17.5% in the control group, $p<0.05$). Live birth rates per retrieval were also significantly different (31.5% in the PGT-A and 20.7% in the control group, $p<0.05$).

Of those <38 years who had a live birth, mean time to pregnancy (TTP, mean (SD)) was 71.9 (109.2) days and differed between groups. TTP in the PGT-A group was 104.3 (88.0) and for controls was 62.9 (112.8) ($p<0.05$). In women ≥38 years, mean TTP was 67.1 (103.5), with TTP in the PGT-A group 90.1 (71.4) and in the control group 53.2 (116.7) ($p<0.05$). Excluding fresh transfer cycles from the control cohort, mean TTP was 168.2 (162.6); 165.0 (156.7) for those <38 and 189.5 (196.5) for those ≥38.

CONCLUSIONS: As has been previously reported, PGT-A patients benefit in relation to live birth rates per transfer. However, for those who achieved live birth within this cohort, utilizing PGT-A did not decrease time to pregnancy. This is largely influenced by the use of fresh transfers. PGT-A without a prior indication, in particular for younger patients, may add both time and cost without significant benefit. Clinicians should consider time to pregnancy as a critical factor when providing counseling to patients regarding this method.

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RNA FOR PGT-A AND IDENTIFICATION OF NEW BIOMARKERS OF CLINICAL OUTCOME IN IVF.

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OBJECTIVE: Preimplantation genetic testing for Aneuploidies (PGT-A) has been performed to screen embryos for nearly three decades. For certain patient populations, the selection of genetically fit embryos increases the chances of a healthy pregnancy in IVF. However, euploid embryos do not always lead to successful pregnancies. The discovery of new biomarkers is important to improve IVF success rates. Here we aim to evaluate the dual utility of RNA-Seq from trophectoderm biopsies to report ploidy of the embryos accurately and identify new biomarkers to distinguish unhealthy embryos.

DESIGN: Comparing results from conventional PGT-A to RNA for chromosomal copy number evaluation, and differential expression analysis between euploids and aneuploids.

MATERIALS AND METHODS: PGT-A was previously performed on twenty-four embryos using Illumina® VeriSeq PGS at the Zouves Fertility Center (ZFC). Eight embryos were euploids and sixteen showed diverse aneuploidies. The embryos were donated to research by signed informed consent. For each embryo, a second trophectoderm biopsy was collected, cDNA was generated using Takara SMART-Seq® v4 Ultra Low Input RNA Kit for Sequencing at ZFC, libraries were created using Illumina® Nextera XT and sequenced on a NextSeq 500 at TBUSA. Data were analyzed using custom pipelines. Briefly, copy number alterations were detected using reads count and B-minor allele frequencies. Differential expression analysis was performed using DESeq2.

RESULTS: The RNA-Seq method showed high concordance in reporting chromosomal aneuploidies compared to VeriSeq PGS. The eight euploids samples characterized by VeriSeq PGS showed no chromosomal alteration when using the RNA-Seq method. Perfect karyotype concordance was also observed in fifteen of the sixteen previously identified aneuploid embryos. For the sex chromosomes, the concordance between the RNA-Seq method and VeriSeq PGS was 100% (24/24). Interestingly, we observed that exclusively the male embryos invariably expressed three genes located on chromosome Y: *EIF1AY, RPS4Y1*, *DDX3Y.* Differential expression analysis between the euploid and aneuploid groups was used to identify potential new biomarkers. One candidate is *NMI* (encoding N-myc and STAT interactor), which showed higher expression in aneuploid samples. The expression of *NMI* has also been reported to be dysregulated in cancer cells.

CONCLUSIONS: In this proof-of-concept study, we show that RNA analysis can potentially replace DNA analysis for the purpose of PGT-A, with the added advantage of providing biomarkers of clinical outcome.

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ASSESSMENT OF CELL-FREE DNA FROM EMBRYO SPENT MEDIA AND ITS EFFECT ON NON-INVASIVE PGT-A CONCORDANCE TO CONVENTIONAL PGT-A AND CALCULATED COPY NUMBER NOISE.

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OBJECTIVE: Recent advances in PGT-A have explored the use of embryo spent media as an alternative sample input to trophectoderm (TE) biopsy. Multiple groups have shown that spent media can be used to determine calculated copy number (CCN) for non-invasive PGT-A (niPGT-A). However, several knowledge gaps remain on the state of cfDNA in spent media and its effect on niPGT-A. The objective of this study was to assess the DNA concentration and fragmentation of cfDNA in spent media and evaluate how cfDNA input affects niPGT-A results and CCN noise.

DESIGN: Prospective study. DNA concentration and fragmentation were compared between samples cultured for 24hr vs 48hr and euploid vs aneuploid embryos. Spent media samples were subjected to niPGT-A and analyzed for clinical concordance to PGT-A on TE biopsy. CCN noise was evaluated in niPGT-A results in relation to sample DNA quantity and fragmentation.

MATERIALS AND METHODS: Embryos were group cultured until day 4 when they were transferred into fresh culture media. Embryos were cultured for 24 or 48hr before media extraction and storage at -80°C. Importantly, no zona breach or invasive embryo manipulation was performed prior to media collection. Media samples were tested by the DNA Quantification and Quality Assessment Kit developed in-house to assess DNA concentration and fragmentation. Media samples were also tested by the niPGT-A kit and analyzed on a CNV Analysis Software developed by Takara Bio. In parallel, TE biopsy samples were tested by VeriSeq and analyzed on BlueFuse software. The clinical concordance of the niPGT-A vs PGT-A was analyzed for each sample and compared to DNA concentration and fragmentation, as well as CCN noise in the niPGT-A.

RESULTS: DNA concentration ranged from negligible to 2.53 pg/μL. There was no statistical difference in DNA concentration between media from euploid and aneuploid embryos. There was a trend suggesting 48hr incubation increased DNA concentration compared to 24hr (24hr: 0.449 pg/μL $\pm$ 0.675; 48hr: 1.076 pg/μL $\pm$ 0.648, p-value = 0.056, n=23). DNA fragmentation analysis showed that DNA was not highly fragmented across samples.

niPGT-A was performed on samples ranging in input DNA quantities from 0.49-12.67 pg. All samples successfully amplified. Concordance compared to TE biopsy was 80% for samples with an input above 1 pg, while samples below 1 pg had 0% concordance (n=12). There was no relationship between DNA fragmentation and clinical concordance to TE biopsy. CCN noise also decreased with increasing input DNA quantity ($R^2 = 0.9197$) and decreasing DNA fragmentation ($R^2 = 0.7065$).

CONCLUSIONS: Our results show that spent media cultured with minimal embryo manipulation results in relatively large DNA fragments occurring across a wide range of DNA concentrations. Our data suggest that longer embryo culture periods increases the cfDNA found in the media. We discovered that input DNA quantity is critical for accurate niPGT-A results, with a minimum threshold of 1pg DNA to achieve highly concordant results with TE biopsy. Additionally, higher input DNA samples had reduced CCN noise, allowing higher confidence and resolution in calling abnormalities.

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PRE-IMPLANTATION TESTING WITH COMPREHENSIVE CHROMOSOME SCREENING: WHAT VALUE DOES IT ADD TO IVF SUCCESS? A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED STUDIES.

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OBJECTIVE: Preimplantation genetic testing for aneuploidy (PGT-A) has the capacity to improve selection of competent embryos for transfer in IVF cycles. Previous meta-analyses found lower miscarriage and higher clinical and ongoing pregnancy rates from euploid embryos identified by PGT-A compared to those selected by morphology alone. However, results from randomized control studies (RCTs) have been inconsistent with a recent large study demonstrating benefit in only a select group, thereby calling into question the indications for PGT-A. Hence, the purpose of this meta-analysis is to investigate the age-stratified pregnancy outcomes of embryo selection by PGT-A compared to traditional morphologic grading.

DESIGN: Meta-analysis of RCTs.

MATERIALS AND METHODS: Electronic databases were searched from their inception to December 2019. RCTs comparing pregnancy outcomes in PGT-A and unbiopsied embryo transfer cycles were identified and random effects meta-analysis employed to calculate average odds ratios (OR) for clinical pregnancy rate (CPR), ongoing pregnancy rate (OPR), and spontaneous abortion (SA) rate. Heterogeneity of exposure effects were evaluated using Forest plots and I^2 statistic while publication bias was assessed using Egger's test.

RESULTS: Among 1251 citations identified, 467 articles met eligibility criteria and seven RCTs were included for statistical analysis comparing pregnancy outcomes from PGT-A cycles versus routine IVF based on embryo morphology selection. Among a pooled cohort of 1851 cycles (905 PGT-A, 946 control), no significant difference in CPR (OR 1.16, 95%CI 0.63–2.13; 4 studies, n=624) and OPR (OR 1.40, 95%CI 0.86-2.29; 5 studies, n=1212) was observed. Stratified analysis by maternal age demonstrated similar OPRs among women <35-years-old (OR 1.24, 95%CI 0.56-2.76; 3 studies, n=615) while a small but significant increase was observed in PGT-A cycles among women 35-43 years-old (OR 1.49, 95%CI 1.00-2.22; 3 studies, n=868). SA rates were also significantly lower in PGT-A cycles across all maternal age groups (OR 0.58, 95%CI 0.34-0.97; 4 studies, n=455). There was no evidence of systematic bias in the funnel plots and Egger's test was non-significant for all analyses.

CONCLUSIONS: Our meta-analysis of RCTs found no overall difference in CPR and OPR with PGT-A compared to embryo selection by morphologic grading. However, SA rates were lower in PGT-A cycles and subgroup analyses suggest an increase in pregnancy outcomes in women 35-43 years-old. Significant heterogeneity was observed between studies (I^2=43.5-81.5%), likely owing to differences in patient population, day of biopsy, and sequencing techniques. Hence, the use of PGT-A should be individualized based patient and provider characteristics, while future prospective trials should evaluate the benefit of PGT-A in specific populations (e.g. recurrent implantation failure) and report clinically important outcomes of interest such as cumulative live birth rate, time-to-live birth, cost-effectiveness, and implications of mosaic results.

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PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY CONFERS GREATER BENEFIT TO YOUNG PATIENTS WITH POLYCYSTIC OVARIAN SYNDROME.

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OBJECTIVE: We have previously shown that there is no difference in pregnancy outcomes between patients with and without polycystic ovarian syndrome (PCOS) undergoing their first single frozen euploid blastocyst transfer, despite patients with PCOS having an increased risk of miscarriage. This suggests that aneuploidy contributes to pregnancy failure in patients with PCOS. The aim of this study is to determine whether PGT-A improves pregnancy outcomes among young patients <35 years (y) with and without PCOS.

DESIGN: Retrospective cohort study at an academic medical center.

MATERIALS AND METHODS: Patients with and without PCOS who underwent their first single embryo transfer of a blastocyst with or without PGT-A from 2015-2018 were included. The primary outcome was live birth

rate (LBR) per embryo transfer. Group 1 consisted of patients with PCOS <35y of age and was further sub-divided into Group 1A and 1B based on utilization of PGT-A (yes vs. no, respectively). Group 2 consisted of patients without PCOS <35y and was further sub-divided into Group 2A and 2B, based on utilization of PGT-A. Student's t-tests and chi-square tests were used to compare patient characteristics and clinical outcomes, as appropriate.

RESULTS: Of the 191 patients with PCOS under 35y, 113 patients underwent PGT-A (Group 1A) and 78 did not (Group 1B). The LBR for Group 1A was significantly higher than Group 1B (59.3%, vs. 42.3%; p=0.03), representing an increase in the LBR by 17 percentage points with utilization of PGT-A (Table 1). Of the 773 patients without PCOS <35y (Group 2), 462 patients underwent PGT-A (Group 2A) and 311 patients did not (Group 2B). The LBR for Group 2A was significantly higher than Group 2B (50.8%, vs. 38.5%; p<0.01), representing an increase in the LBR by 12 percentage points with utilization of PGT-A. The miscarriage rate was significantly lower for patients with and without PCOS with utilization of PGT-A (8.0% vs. 19.2% and 7.1% vs. 12.9%, respectively; p<0.05 for both).

Table 1. Clinical Outcomes in Women <35y of Age With and Without PCOS Undergoing a Euploid Embryo Transfer vs. Non-Diagnosed Blastocyst Transfer

	PCOS			Non-PCOS		
	+PGT n=113	-PGT n=78	p value	+PGT n=462	-PGT n=311	p value
Avg. Age	30.5	30.7	0.59	31.6	31.4	0.14
Avg. BMI	25.8	27.8	0.04	24.7	25.1	0.45
Avg. Parity	0.42	0.5	0.72	0.55	0.59	0.47
%Biochemical	7.1	10.2	0.18	9.1	11.3	0.39
%Spontaneous Abortion	8.0	19.2	**0.04**	7.1	12.9	**0.01**
%Live birth	59.3	42.3	**0.03**	51.1	38.9	**<0.01**

CONCLUSIONS: In our population, while PGT-A confers an increase in LBR per transfer for all patients younger than 35y, we demonstrated a greater increase in live birth rate by 17 vs. 12 percentage points for patients with PCOS vs. patients without PCOS. This data may aid in counseling patients with PCOS regarding the utility of genetic testing for aneuploidy.

SUPPORT: None.

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EFFECTS OF DIFFERENT BIOPSY PROTOCOL ON RATE OF MOSAICISM AFTER NEXT-GENERATION SEQUENCING (NGS) IN PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) CYCLES.

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OBJECTIVE: The incidence of mosaicism at blastocyst stage using next generation sequencing (NGS) method is highly variable between clinics, ranging from as low as 2% to as high as 40%. A consistent high incidence of mosaic embryos in some clinics may be indicative of clinical treatment, embryology, analysis approach or in some cases be patient-related factors (Fragouli et al., 2019). However, little is known about the influence of biopsy protocol on the rate of mosaicism in preimplantation genetic testing for aneuploidy (PGT-A) cycles.

DESIGN: This was a retrospective analysis.

MATERIALS AND METHODS: Women undergoing PGT-A at a single fertility center from July 2018 to December 2019 were included. Cycles with abnormal sperm parameters were excluded. Intracytoplasmic sperm injection (ICSI) was applied in all PGT cycles. PGT-A was performed via trophectoderm biopsy on day5 or 6 and analyzed using NGS at a single reference lab. Two different biopsy protocols were used. For method one, a 5-10 μm opening was made by laser before transferring the embryos into extended culture on the afternoon of day 3. This allowed some trophectoderm cells to herniate through the hole before biopsy on day 5 or 6. For method two, the zona pellucida was opened immediately before biopsy on day 5 or 6. Approximately 3–5 trophoblast cells were sucked and removed from biopsied blastocysts. The rates of mosaicism at the blastocyst stage were compared between two protocols.

RESULTS: Fifty seven PGT-A cycles were included for analysis: 37 from method one and 20 from method two, resulting in 143 and 73 biopsied blastocysts. There was no difference in two groups regarding the female age, number of blastocysts biopsied, euploid and aneuploid blastocyst rates. However, the rates of mosaic blastocyst in method one group was 14.69%, significantly higher than that in method two group (5.48%, P=0.045).

CONCLUSIONS: Different biopsy protocols may influence the rate of mosaicism at blastocyst stage. Method two, namely, the zona pellucida was opened immediately before biopsy on day 5 or 6, may be preferable to method one, to minimize the rate of mosaicism in NGS PGT-A cycles.

SUPPORT: no

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INCREASED INCIDENCE OF ECTOPIC PREGNANCY IN IN VITRO (IVF) PREIMPLANTATION GENETIC SCREENED EUPLOID EMBRYOS.

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OBJECTIVE: Determine whether there is an increased rate of sustained ectopic pregnancies following the transfer of PGT-A tested euploid embryos compared to untested embryos.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: An analysis was performed on 27,348 patients who were treated from November 22, 1999 to October 31, 2019. All patients underwent in vitro fertilization with day 5 blastocyst single or double embryo transfers. The study group comprised patients who underwent transfer of PGT-A tested euploid embryos. Control patients were those undergoing transfer of untested embryos. The primary outcome was the rate of sustained ectopic pregnancy which was defined as absence of chorionic villi after D&C, visualization of an adnexal mass consistent with ectopic pregnancy on ultrasound or an ectopic pregnancy that was surgically removed. If the above criteria were not met it was categorized as a pregnancy of undetermined location (PUL) and was not included in this analysis. Chi-square and t-tests were performed on our normally distributed population. Logistic regression was performed to control for confounders.

RESULTS: Patients using PGT-A were older and more likely to have a frozen embryo transfer (Table 1). The rate of sustained ectopic pregnancy was higher in the PGT tested group (0.79% vs 0.44%). After performing logistic regression, sustained ectopic pregnancies were found to be 1.63 more likely to result from a PGT tested embryo.

Table 1

	NO PGT-A	PGT-A	p-value
Number	14,229	13,119	
Age	32.5 (4.6)	34.4 (4.5)	<0.001
Frozen Transfer	7,579 (53.3%)	11,883 (90.6%)	0.000
Ectopic	63 (0.44%)	103 (0.79%)	<0.001
PUL	227 (1.6%)	104 (0.79%)	<0.001

CONCLUSIONS: This data suggests that there is an increased likelihood of persistent ectopic pregnancy in PGT-A tested euploid embryos than in untested embryos. This finding is likely due to euploid embryos being more likely to sustain implantation in both intrauterine and extra-uterine locations. More studies are warranted to determine whether this finding is also seen in other IVF facilities.

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EVALUATION OF THE INHERITANCE OF COPY NUMBER VARIATIONS (CNVS) IN THE EMBRYOS WHEN THE SAME CNV PRESENTS IN MORE THAN ONE EMBRYO AFTER PGT-A FROM IVF CYCLES. Heather Garnsey, BS, MPS,[1] Yiping Zhan, Ph.D,[2] Chaim Jalas, N/A,[1] Vaidehi Jobanputra, PhD,[1] Richard Thomas Scott, Jr., MD,[3] Xin Tao, Ph.D[1] [1]Foundation for Embryonic Competence, Basking Ridge, NJ; [2]The Foundation for Embryonic Competence, Basking Ridge, NJ; [3]IVI RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: CNV involves both duplications and deletions of DNA sequences, which may cause human diseases. Some CNVs can be identified using targeted next generation sequencing-based preimplantation genetic testing for aneuploidy (PGTseqA). When the same patterns of CNVs are observed in multiple embryos, one of the parents may carry the CNV. In this study, we requested follow-up parental testing to confirm whether the same CNVs presenting in more than one embryo are inherited.

DESIGN: Retrospective observational

MATERIALS AND METHODS: PGTseqA amplifies ~5000 amplicons across the human genome and evaluates the copy number of the amplicons. Validations for CNVs were performed using 5-cell samples from cell lines with known CNVs, and trophectoderm (TE) biopsies from embryos with a previously diagnosed parental structural rearrangement. Microarray testing of the couples was requested when multiple embryos from their cohorts showed the same CNV.

RESULTS: Among 6782 PGTseqA cycles, 51 cycles from 42 patients showed the same CNVs in more than one embryo and 43 CNVs were observed. The size of deletions or duplications involved in CNVs ranged from 3.5 kb to 8.6 Mb, and included from 2 to 17 amplicons. Microarray results were received from 36 couples, and 94% (34 out of 36) confirmed that one of parents carried the CNVs, including one couple where one parent carried two CNVs. For the ClinVar pathogenic category, 11 out of 35 CNVs were classified as benign or not reportable, and the euploid embryos carrying the CNVs were available for transfer. Five were likely benign and 15 had uncertain significance. Finally, 2 were possibly pathogenic, 1 was likely pathogenic, and 1 was pathogenic.

CONCLUSIONS: The confirmation of parental CNVs further validated the diagnostic accuracy of deletions or duplications in embryo biopsies. Genetic counseling about the PGTseqA and parental CNV results will help patients to decide whether they will transfer the embryos with parentally-inherited CNVs.

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ENDOMETRIAL RECEPTIVITY ANALYSIS (ERA) FOR PATIENTS WITH PGT-A NORMAL FROZEN EMBRYO TRANSFERS (FET): A RETROSPECTIVE ANALYSIS. Joshua C. Combs, MD,[1] Jeanne E. O'Brien, MD, MSc,[2] Kate Devine, MD,[2] Mae W. Healy, DO,[1] Samad Jahandideh, PhD,[2] Alan H. DeCherney, MD,[3] Micah J. Hill, DO,[1] Nicole Doyle, MD, PhD[2] [1]Walter Reed National Military Medical Center, Bethesda, MD; [2]Shady Grove Fertility Center, Rockville, MD; [3]Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD.

OBJECTIVE: Determine implantation rate (IR) and live birth rate (LBR) for patients undergoing a single PGT-A normal frozen embryo transfer according to standard progesterone timing versus ERA timed transfer.

DESIGN: Retrospective cohort study at a large reproductive center from 2018 and 2019.

MATERIALS AND METHODS: Patients with or without a history of prior unsuccessful FET with PGT-A normal vitrified embryos completed ERA prior to analysis. The outcome of the first FET following ERA was assessed for all patients classified as receptive (FET according to standard protocol) and non-receptive (ERA adjusted FET). Outcomes were compared between PGT-A normal embryo transfer in patients with versus without ERA testing. Exclusion criteria were vaginal progesterone only, uterine factor and PGT-A untested embryos. Descriptive statistics were used to characterize outcomes. Chi square was used to compare dichotomous outcomes.

RESULTS: The clinical outcomes of 307 ERA patients were compared to 1937 control FET cycles. For patients who underwent ERA testing, results were classified as receptive for 194 patients and non-receptive for 113 patients. A single PGT-A normal FET in the receptive group resulted in 67.5% and 43.2% IR and LBR, respectively. In comparison, the IR and LBR in the non-receptive and therefore ERA timed FET group were 74.3% and 46.9%, respectively. This difference was not statistically significant ($p > 0.05$). Patients without ERA testing had an IR and LBR of 62.2% and 50.2% for their last recorded transfer cycle. Compared to the ERA adjusted FET groups this was not statistically significantly different.

CONCLUSIONS: There was no significant difference in IR or LBR for patients who did undergo ERA testing prior to PGT-A normal embryo FET compared to those whose endometrial receptivity status was unknown and therefore included both receptive and non-receptive patients. We recognize that a randomized controlled trial is needed to sufficiently assess the clinical utility of ERA testing.

	Frequency	Percentage
ERA Receptive – FET According To Standard Protocol		
HCG +	131/194	67.50%
HCG -	63/194	32.50%
Live Birth	84/194	43.20%
ERA Non-Receptive – ERA Adjusted FET		
HCG +	84/113	74.30%
HCG -	29/113	25.70%
Live Birth	53/113	46.90%
FET For ERA Untested Patients		
HCG +	1205/1937	62.20%
HCG -	732/1937	37.80%
Live Birth	972/1937	50.20%

*No comparisons between the 3 groups were statistically significant.

SUPPORT: None

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A NOVEL METHOD TO ATTENUATE EMBRYO ANEUPLOIDY DUE TO PATERNAL INHERITANCE. Alessandra Parrella, M.Sc., Danielle Rebecca Tavares, B.A., Mounia Haddad, M.D., June Wang, B.A., Derek Keating, B.A., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To test the efficacy of a sperm-selection method to generate genetically healthy embryos in couples with recurrent embryo aneuploidy.

DESIGN: Consenting men with high sperm DNA fragmentation (SCF) in their spermatozoa who were treated at our center during the last three years were included. Spermatozoa were selected by density gradient centrifugation (DGC) for ICSI cycles, which frequently yielded aneuploid embryos, resulting in no embryo transfer or failed implantation. In subsequent ICSI cycles, their spermatozoa were processed by microfluidics sperm selection (MFSS). SCF, including the assessment of double-stranded DNA breaks (DSBs), was performed before and after each selection method. SCF, embryo aneuploidy, and clinical outcomes were assessed and compared.

MATERIALS AND METHODS: A total of 29 men underwent semen analysis according to WHO 2010 criteria. SCF was carried out by TUNEL on at least 500 spermatozoa with an established threshold of 15%. DSBs were measured by a neutral Comet test using a modified in-house protocol. A threshold of $\leq$3% was considered normal, with at least 200 spermatozoa assessed per patient. Clinical outcomes were compared between ICSI cycles performed with the DGC and MFSS methods. Preimplantation genetic testing for aneuploidy (PGT-A) was carried out on the resulting blastocysts. Euploid embryos were replaced into the uterine cavity, and implantation and clinical pregnancy rates (CPR) were recorded.

RESULTS: A total of 29 men (40±7 years) had the following semen parameters: a concentration of 38.7 ± 39 x10^6/mL, 31 ± 17% motility, and 2.1 ± 1% morphology. After DGC and MFSS, the sperm concentration was 18±29 and 7.3±11 x10^6/mL, with 55.2±30% and 98.3±2% motility, respectively (P<0.0001). The average SCF decreased from 22±9% in the raw samples to 16±3% following DGC, and dropped to 1.8±1% after MFSS processing (P<0.0001). The DSB rate was 3.8±2% in the raw samples, 2.8±1% after DGC, and only 0.3±0.1% after MFSS. These couples (female partner, 37.2±5 years) underwent 42 ICSI cycles with DGC-selected spermatozoa and achieved a fertilization rate of 61.8% (254/411) with 23.8% (26/109) of the embryos identified as euploid. The replacement of

these euploid embryos yielded an implantation rate of only 4.3% (1/23) and a CPR of 8.3% (1/12), with 8.3% (1/12) resulting in a pregnancy loss. When these couples underwent subsequent ICSI cycles with MFSS, a fertilization rate of 80.2% (334/416) ($P<0.00001$) was achieved, with 48.9% (90/184) of the embryos identified as euploid ($P<0.0001$). A total of 29 embryos were replaced, resulting in an implantation rate of 65.5% (19/29; $P<0.0001$) and a CPR of 73% (19/26) ($P<0.001$), resulting in 5.2% (1/19) pregnancy loss and 69.2% (18/26) ongoing pregnancy or deliveries ($P<0.0001$).

CONCLUSIONS: Spermatozoa with DNA damage, particularly double-stranded nicks/breaks, may impair the ability of the oocyte to repair the male genome. Because the male genome contributes to embryo aneuploidy, selecting spermatozoa with the highest motility and chromatin integrity may enhance the chances of obtaining a euploid embryo for transfer and boost embryo implantation.

SUPPORT: None

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THE VALUE OF NONINVASIVE PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY ON HUMAN CELL-FREE DNA FROM BLASTOCOELE FLUID WITH GENOME SEQUENCING: A PROSPECTIVE COHORT STUDY.

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OBJECTIVE: Noninvasive preimplantation genetic testing for aneuploidy (niPGT-A) on cell-free DNA in blastocoele fluid (BF) is a promising but controversial method for selecting euploid embryos in assisted reproductive technologies.

DESIGN: Examine whether niPGT-A of BF can predict clinical outcomes and identify fetal ploidy for clinical use.

MATERIALS AND METHODS: In this prospective cohort study performed in a single IVF center, 182 blastocysts from patients undergoing their first in vitro fertilization and embryo transfer (IVF-ET) cycle in 2017 were analyzed (one blastocyst per patient). There were 33 withdrawals from the study. BF was collected prior to blastocyst vitrification. Clinical pregnancy outcomes were followed up till baby was born and karyotyping. Cell-free DNA from the BF was amplified (WGA) for next generation sequencing (NGS) -based comprehensive chromosome screening (CCS). The results were compared with clinical outcomes from newborn baby karyotyping, Chorionic Villus Sampling (CVS) results from miscarriages, or fetal Noninvasive Prenatal Test (NIPT) results from ongoing pregnancies.

RESULTS: A total of 139 BF samples produced CCS results for analysis (76.37%). Balanced euploidy was observed in 34 samples (24.46%) and aneuploidy in 92 samples (75.54%). A total of 113 patients (76.87%) achieved clinical pregnancy. Of those, 14 (11.38%) miscarried in their first trimester. CVS analysis results revealed a weak correlation between miscarriage tissue DNA samples and BF DNA samples. All 97 live-born babies showed normal phenotype and almost matched their NIPT results from pregnancies, even though some of the results of BF tests indicated abnormal genotypes. When compared all the testing results of BF, NIPT and CVS, there were about 30% consistencies.

CONCLUSIONS: When compared with PGS, niPGT-A is a lower risk method for the preimplantation screening of embryos, but currently can only identify weak correlations between clinical outcomes and BF ploidy analysis results. The future of niPGT-A is promising but the technology is not yet ready for clinical use.

SUPPORT: This work was supported by the China National 973 program (2012CB944902); National Key R&D Program of China (2016YFC1000207); Jiangsu Provincial Science and Technology Project (BL20122009 and BE2011798); and the Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD).

P-783 4:30 PM Tuesday, October 20, 2020

ANALYSIS OF 3,967 EMBRYOS USING A USING A NOVEL NON-INVASIVE PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (NIPGT-A) PLATFORM.

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OBJECTIVE: Preimplantation Genetic Testing for Aneuploidy (PGT-A) has been widely used around the world to identify ploidy status of embryos. The primary modality for obtaining DNA from blastocysts has been trophectoderm (TE) biopsy, which requires removal of embryonic cells. A validated niPGT-A platform, termed Non-Invasive Chromosomal Screening (NICS™, Yikon Genomics, Lewes, DE), has been developed which allows embryonic DNA to be amplified by analysis of embryo culture media only and has been shown to have an approximate 90% positive correlation with TE biopsy PGT-A [1]. The purpose of this study to report the outcome analysis of a large sample of embryos tested using this novel niPGT-A platform.

DESIGN: Retrospective data analysis at a fertility center with university-based affiliation.

MATERIALS AND METHODS: Patients electing to have their embryos undergo PGT-A were offered to utilize the novel non-invasive platform instead of conventional TE biopsy after appropriate informed consent. Spent media was collected on Day 5, 6, or 7 of embryo culture per NICS™ protocol and processed on site using multiple annealing and looping-based amplification cycles followed by next-generation sequencing to obtain ploidy information on all chromosomes. Chi-square test was used to compare the percentage of euploid versus mosaic embryos.

RESULTS: There were 3,967 embryos tested with niPGT-A obtained from 845 patients (mean age = 39.0 ± 5.3) between July 1st, 2019 and May 17th, 2020. 96.2% of embryos had results with the proportion of reported euploid, mosaic, and aneuploid at 27.3%, 18.1%, and 54.6%, respectively. 3.8% (n=150) of all tested embryos had "no result" reported. 114 embryos with "no result" were retested, all of which resulted in usable ploidy data: 39.8% were euploid, 18.6% were mosaic, and 41.6% were aneuploid. Compared to embryos that initially had a reportable result, retested embryos had a significantly higher rate of euploidy (p=0.003), lower rate of aneuploidy (p=0.006), and similar rate of mosaicism (p=0.89). Data was further stratified based on established Society for Assisted Reproductive Technology (SART) age groups. Excluding mosaic results, rate of euploidy decreased with age: 87.5%, 68.8%, 34.7%, 23.0%, and 11.9% in patients under 35, 35-37, 38-40, 41-42, and over 42 years old, respectively ($p<0.001$). The ratio of female to male embryos was 1.03.

CONCLUSIONS: The novel niPGT-A platform, NICS™, can be safely implemented and can effectively distinguish mosaic embryos from aneuploid or euploid ones. Embryos resulting as "no result" initially can be successfully retested and have higher likelihood of being euploid. These data are very helpful in counseling patients desiring niPGT-A, rather than the traditional TE biopsy testing on their embryos. Caution in counseling patients should be taken when generalizing results as certain clinical and embryologic practice parameters could affect DNA capture and successful amplification.

References: 1. Xu, J., et al., *Noninvasive chromosome screening of human embryos by genome sequencing of embryo culture medium for in vitro fertilization.* Proc Natl Acad Sci U S A, 2016. 113(42): p. 11907-11912.

P-784 4:30 PM Tuesday, October 20, 2020

CLINICAL OUTCOME COMPARISON BETWEEN TRANSFER OF EUPLOID AND MOSAIC BLASTOCYSTS IDENTIFIED USING A NOVEL NON-INVASIVE PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (NIPGT-A) PLATFORM.

Meir Olcha, MD,[1] Manar Elzaky, BS, MS,[1] Malgorzata Jaremko, PhD,[1] Zaher Merhi, MD, HCLD,[2] John J. Zhang, MD, PhD[3] [1]New Hope Fertility Center, New York, NY; [2]SUNY Downstate University and New Hope Fertility Center, New York, NY; [3]New Hope Fertility Center, New York City, NY.

OBJECTIVE: The primary modality for obtaining DNA from blastocysts for Preimplantation Genetic Testing for Aneuploidy (PGT-A) has been trophectoderm biopsy, which requires removal of embryonic cells that could potentially damage the embryos. Recently, the advent of a validated niPGT-A platform has been developed which allows embryonic DNA to be amplified by analysis of embryo culture media only and has been shown to have an approximate 90% positive correlation with traditional biopsy based PGT-A [1]. The purpose of this study was to evaluate the clinical outcome after single embryo transfer (SET) of euploid or mosaic embryos identified via niPGT-A.

DESIGN: Retrospective data analysis at a fertility center with university-based affiliation

MATERIALS AND METHODS: Biochemical and clinical (CPR) pregnancy rates were evaluated after SET of 132 euploid and 14 mosaic embryos between November 1st 2019 to April 20th 2020 at a single fertility center. All embryos had assisted hatching prior to media collection. Spent media was collected on Day 5, 6, or 7 of embryo culture per niPGT-A protocol [2]. Ploidy information on all chromosomes was derived on site using the NICS™ (Yikon Genomics, Lewes, DE) niPGT-A platform that utilizes multiple annealing and looping-based amplification cycles followed by next-generation sequencing. Initial ß-hCG levels were analyzed 7 days after SET. Biochemical pregnancy was defined by the absence of identifiable pregnancy on ultrasound despite positive serum ß-hCG. CPR was defined by the presence of a fetal heartbeat at 6-7 weeks of pregnancy. In all cycles, oral estradiol and vaginal progesterone were used for endometrial lining preparation and a minimum thickness of 7 mm was required for all SETs. Embryo transfers performed by physicians in training were excluded from the analysis. Chi-square test was used to calculate pregnancy rates and compare outcome between euploid and mosaic embryos transferred.

RESULTS: 146 patients with a mean age of 36.5 years were included in the study. A total of 91 out of 132 (68.9%) euploid embryos and 5 out of 14 (35.7%) mosaic embryos transferred resulted in a ß-hCG >5 mIU/ml. The CPR was 51.1% for euploid embryos and 28.6% for mosaic ones (p=0.01). The biochemical pregnancy rate was 26.3% for euploid embryos and 24% for mosaic embryos (p=0.7). The ratio of male to female embryos was 0.91 for Euploid and 1.0 for mosaic embryos (p=0.8).

CONCLUSIONS: These novel data show that niPGT-A, performed on the NICS™ platform, can be utilized successfully with comparable pregnancy rates to traditional PGT-A. Whether the use of NICS reduces embryo damage compared to conventional biopsy based PGT-A will be determined in our future studies.

References: 1. Xu, J., et al., *Noninvasive chromosome screening of human embryos by genome sequencing of embryo culture medium for in vitro fertilization.* Proc Natl Acad Sci U S A, 2016. 113(42): p. 11907-11912.

2. Fang, R., et al., *Chromosome screening using culture medium of embryos fertilised in vitro: a pilot clinical study.* J Transl Med, 2019. 17(1): p. 73.

P-785 4:30 PM Tuesday, October 20, 2020

CREB1 INTEGRATES THE METABOLIC AND GROWTH NETWORKS ASSOCIATED WITH THE AGING OF HUMAN GRANULAR CELLS. Kuan-Hao Tsui, M.D; Ph.D, Chia-Jung Li, Ph.D Department of Obstetrics and Gynecology, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan.

OBJECTIVE: This study investigated whether changes in metabolism occur during granulosa cells (GCs) senescence and the mechanisms that regulate these changes.

DESIGN: Experimental laboratory study.

MATERIALS AND METHODS: We used excessive oxidative stress to induce cell senescence and examined the phenotype of aging. Protein and gene expression of different enzymes related to metabolism in senescent granulosa cells were analyzed by qPCR, protein array or immunofluorescence. Further, we applied bioinformatics methods and integrated publicly available resources to study the role of CREB1 gene expression in reproduction.

RESULTS: Here, we show that mitochondrial regulator CREB1 is induced by excessive oxidative stress (OS) in human HGL5 granulosa cells, and at the cellular level, OS-like activation of CREB1 impacts a network that integrates mitochondrial status with metabolism and growth parameters. Proteomics profiling reveals that diverse functions, including biogenesis pathways, growth, structure, and macromolecule homeostasis, are responsive to CREB1. Delayed cellular proliferation, altered cytoskeleton, and attenuated growth signaling through post-transcriptional and post-translational mechanisms were also identified as outcomes of CREB1-directed mitochondrial activation. Furthermore, endogenous CREB1 expression was correlated with this same metabolism and growth network. These data show that small changes in metabolism have broad consequences that arguably would profoundly alter cell function.

CONCLUSIONS: We suggest that this CREB1 sensitive network may be the basis for the association between mitochondrial function and aging where small deficiencies precipitate loss of function across a spectrum of cellular activities.

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IMPACT OF BLASTOCYST RE-BIOPSY AND RE-FREEZE ON PREGNANCY OUTCOMES: A SYSTEMATIC REVIEW AND META-ANALYSIS. Chelsea N. Fortin, MD, Molly B. Moravek, MD, MPH, Min Xu, Ph.D, Nicholas Henderson, PhD, MA University of Michigan, Ann Arbor, MI.

OBJECTIVE: While blastocyst vitrification and biopsy are generally considered safe, it is unclear if multiple biopsies and vitrification-warming procedures negatively impact clinical outcomes. This situation arises when patients request preimplantation genetic testing (PGT) on already cryopreserved embryos. Another scenario necessitating additional vitrification-warming procedures is failure to obtain a result from the initial trophectoderm biopsy, in which case a second biopsy would also be necessary. There is very limited information on the clinical outcomes following transfers of blastocysts twice biopsied and vitrified-warmed. The objective of this study was to compile the available literature on the clinical pregnancy (CP) rates of blastocysts transferred after undergoing multiple vitrification-warming and/or biopsy procedures.

DESIGN: Systematic review and meta-analysis.

MATERIALS AND METHODS: A systematic search of the literature was conducted using the PubMed database. Studies were selected for inclusion if they compared blastocysts 1) biopsied and vitrified-warmed once (1Bx + 1V/W), 2) biopsied once but vitrified-warmed twice (1Bx + 2V/W), and/or 3) biopsied and vitrified-warmed twice (2Bx + 2V/W). A total of six retrospective cohort studies met inclusion criteria. Data involving patient and blastocyst characteristics, PGT results, and clinical outcomes were extracted. Study quality was assessed using the Newcastle Ottawa scale for non-randomized comparative cohort studies. The studies were evaluated independently by two of the authors and any discrepancies were settled by a third author. From the six studies included, a multiple-treatments random-effects meta-analysis comparing the risk difference in CP rate for the three groups identified above was performed.

RESULTS: A total of 9437 single euploid blastocyst transfers were included in the analysis. The pooled CP rate was significantly lower in the 2Bx + 2V/W group compared to the 1Bx + 1V/W group, with an estimated difference of 13%, 95% CI [4.3-21.6%]. No significant differences in CP rate were observed between the 1Bx + 1V/W and 1Bx + 2V/W groups (risk difference, 4.5%; 95% CI [-2.1-11.1%]) or between the 1Bx + 2V/W and 2Bx + 2V/W groups (risk difference, 8.5%; 95% CI [-2.3-19.3%]).

CONCLUSIONS: These findings indicate that CP rates are significantly reduced when blastocysts are biopsied and vitrified-warmed twice compared with blastocysts biopsied and vitrified-warmed once. For patients who receive an inconclusive diagnosis from the initial biopsy, this risk should be weighed against the risk of transferring a possible aneuploid embryo. However, given the retrospective nature of the limited number of studies available, further research is needed to confirm this finding.

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PREIMPLANTATION GENETIC TESTING (PGT) WAS NOT ASSOCIATED TO ADVERSE MATERNAL AND NEONATAL OUTCOMES. Mauro Cozzolino, MD,[1] Juan A. Garcia-Velasco, MD, PhD,[2] Antonio Pellicer, MD[1] [1]IVIRMA Foundation, Valencia, Spain; [2]IVI-RMA Madrid,Universidad Rey Juan Carlos, Madrid, Spain.

OBJECTIVE: To assess whether trophectoderm biopsy for preimplantation genetic testing (PGT) has increased the risk of maternal and neonatal outcomes compared with pregnancies achieved with IVF without PGT.

DESIGN: Retrospective observational cohort study.

MATERIALS AND METHODS: Women receiving fertility care at IVIRMA with PGT-A or without PGT-A were enrolled in study from January 2016 to April 2019. Patients between 18 and 45 year, in whom at least one embryo was transferred after blastocyst stage biopsy were considered. Cases of no embryo survival after vitrification or pregnancies with oocyte donation was excluded. Patients with missed information about maternal and neonatal outcomes were excluded. Primary outcomes was preeclampsia defined by the presence of hypertension (persistent systolic blood pressure (BP) 140 mm Hg or higher and/or diastolic BP 90 mm Hg or higher) after 20 weeks of gestation in a previously normotensive woman with proteinuria. The incidence of gestational diabetes and small for gestational age was considered secondary outcomes.

Neonatal outcomes such as preterm birth (<37 weeks), birth weight, birth defects, Apgar score at 5 minutes, neonatal intensive care unit (NICU) admission, were considered as secondary outcomes. The study was approved by the Ethics Committee of the IVIRMA (identification code #1910-FIVI-096-MC). Statistical analysis was performed using Fisher's Exact Test, $p<0.05$. Statistical analyses were conducted using the R statistical software 3.1.0.

RESULTS: The study included 544 pregnancies with PGT-A and 2051 without PGT-A. There was not a statistically significant increase in the risk of preeclampsia among PGT-A pregnancies compared with pregnancies without PGT-A, with an incidence of 4.4% versus 4.1%, OR 1.03, 95% CI (0.61-1.67) p=0.94. The incidence of preterm birth (<37 weeks) was 15% in patients with PGT-A versus 14.1% in pregnancies without PGT-A, OR 1.08, 95% CI (0.82-1.40), p=0.54. Similar incidence in small for gestational age (SGA) was observed in pregnancies with PGT-A compared to without PGT-A OR 0.99, 95% CI (0.75-1.22), p=1.Conversly, in pregnancies with trophectoderm biopsy the rate of gestational diabetes was increased 10.1 % versus 7.4%, OR 1.40, 95% CI (0.99-1.96), p=0.05. No statistically, difference were observed for neonatal intensive care unit admission, Apgar punctuation and birth defects.

CONCLUSIONS: The pregnancies with PGT-A have not increased the rate of preeclampsia, preterm birth, SGA, while PGT-A increase the risk of gestational diabetes. Trophectoderm biopsy was not associated with adverse neonatal outcomes. Although in pregnancies with PGT-A gestational diabetes was increased, the sample size is a limitation of the study. Thus, larger studies including patients by different infertility centres are needed to add more insight into the safety of PGT.

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IMPACT OF BLASTOCYST BIOPSY TECHNIQUE ON DNA QUALITY AND PGT-A RESULTS. Michael J. Abeyta, BS,[1] Chaochun Lin, BS,[1] David M. Pardo, PhD,[1] William B. Schoolcraft, MD,[2] Jason E. Swain, PhD, HCLD[3] [1]CCRM San Francisco, San Francisco, CA; [2]CCRM Colorado, Lone Tree, CO; [3]CCRM IVF Network, Lone Tree, CO.

OBJECTIVE: Blastocyst biopsy is an invasive procedure with a technical signature. Improper biopsy technique, such as taking too many cells, can impair blastocyst quality. It is thought that biopsy technique may also impact quality of the biopsied cells and resulting genetic content, which may influence results called/reported by the genetics lab. Two blastocyst biopsy techniques were compared to determine the impact on PGT-A results.

DESIGN: Prospective trial

MATERIALS AND METHODS: To control for technician and lab variation, all biopsy procedures were conducted at a single IVF center by a single embryologist over an approximate 1 month period of time. All PGTA testing was performed at a single genetics lab. Only high quality blastocysts (HQB) >=3BB were biopsied. All embryos were breached on Day 3 of culture to create a small opening for subsequent herniation. Resulting HQBs were biopsied by either the "Standard" approach or the "Flick" technique. Standard biopsy entailed gentle suction by a holding and biopsy pipet, with several laser pulses (~3-6) and simultaneous stretching to biopsy trophectoderm cells. The Flick approach used the same biopsy setup and laser settings, but utilized 2 laser pulses at the top and bottom of the herniated cells and then a gentle flick using a finger to tap the side of the biopsy pipet to shear trophectoderm cells from the rest of the blastocyst. 4-6 cells were taken from all blastocysts and subjected to PGT-A testing using an NGS platform. Data were analyzed using Chi Square analysis.

RESULTS: The Standard biopsy technique was utilized on 73 blastocysts while the Flick technique was used on 67. All samples yielded DNA for amplification. A "no result" is given when the genetic material from the biopsied cells is of insufficient quality to make a reliable call. The Standard approach yielded results on 98.6% of samples, which not significantly different than the Flick technique at 94.0%. However, the 6% no result rate using the Flick approach was higher than our established acceptable threshold for internal quality control. Both Standard and Flick biopsy approaches yielded similar blastocyst euploid rates (54.8% vs. 54.2%).

CONCLUSIONS: Prior reports suggest that biopsy technique may significantly impact PGT-A results, likely via impact on the quality of the biopsied genetic material. While the Standard biopsy technique used in this study used more laser pulses, this was done in a controlled fashion. By contrast, the Flick used fewer laser pulses but a less controlled motion to shear the cells via vibration. Though both approach appeared equally effective, this vibration from the Flick technique may have caused further damage to the cells and enclosed DNA resulting in the slight increase in the observed "no result" rate, Future studies with a larger data set will help further assess efficacy of these techniques and determine if one approach appears superior compared to another when biopsying specific stages of blastocysts.

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COMPARISON OF THE STRUCTURE OF CHROMOSOMAL ABNORMALITIES IN THE EMBRYOS OBTAINED AFTER REPRODUCTIVE NUCLEAR TRANSFER VERSUS IVF-ICSI-PGT-A. Dmytro O. Mykytenko, MD, DSc, Kateryna Lavrova, PhD, Tetiana Cherneha, MSc, Pavlo Mazur, MSc, Lada Diachenko, MSc., Valery Zukin, MD, PhD Clinic of Reproductive Medicine "Nadiya", Kyiv, Ukraine.

OBJECTIVE: The safety of reproductive nuclear transfer (or mitochondrial replacement therapy) in cases of IVF in patients with severe forms of infertility or a family history of mitochondrial diseases causes lively debate worldwide. Meanwhile, births of 13 children following this technique have already been announced. However, while the safety of the artificially created mitochondrial heteroplasmy is being discussed, the issue of possible induction of chromosomal abnormalities in the embryos caused by the manipulations with the nuclei at the stage of reconstruction is not addressed. This particular issue is the subject of this study.

DESIGN: The study included a comparison of chromosomal abnormalities in the embryos obtained following reproductive nuclear transfer (259 blastocysts) and IVF-ICSI-PGT-A (3236 blastocysts).

MATERIALS AND METHODS: Obtained TE biopsy samples were 3 times washed in the separate 1xPBS-1%PVP drops followed by WGA procedure (SurePlex DNA Amplification System, Illumina). Samples were analyzed by NSG method for preimplantation genetic testing for aneuploidies (PGT-A). NGS: analysis was performed using VeriSeq PGS Kit, RH-101-1001, Illumina. Interpretation of the chromosomal NGS-patterns was performed in accordance to manufacturer's recommendations. Standard statistical methods were used for analysis.

RESULTS: In the embryos obtained after reproductive nuclear transfer, more frequent involvement of chromosomes 8, 10, 12, 14, 18 and 20 (complete and structural abnormalities) and less frequent involvement of chromosomes 1, 2, 9, 13, 16 were observed.

A significant change in the monosomy/trisomy ratio for chromosomes 1, 2, 3, 4, 6, 7, 8, 17 was also observed.

The distribution of the embryos obtained after reproductive nuclear transfer according to the patient's age at the time of oocyte retrieval showed an abnormally high proportion of the embryos with abnormalities in chromosomes 10 and 11, as well as a shift to more frequent involvement of the chromosomes from groups A, B and C in patients aged $\geq$37 years (164 blastocysts, aneuploidy level 91%). In the younger age group, a more frequent involvement of the chromosomes from groups D, E, F and G was observed (94 blastocysts, aneuploidy level 44%).

CONCLUSIONS: The analysis showed a significant change in the structure of chromosomal abnormalities in the embryos obtained after reproductive nuclear transfer. Further research is required to identify through what mechanisms the reproductive nuclear transfer causes changes in the structure of chromosomal abnormalities and whether this phenomenon may have any prognostic value in the assessment of the effectiveness of manipulations with the cell nuclei or in clinical efficacy.

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THE EFFECT OF GERMLINE MUTATIONS ON THE ABILITY OF SURGICALLY RETRIEVED SPERMATOZOA FROM AZOOSPERMIC MEN TO SUPPORT EMBRYONIC DEVELOPMENT. Stephanie Cheung, B.S., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To identify eventual germline mutations involved in spermatogenesis and the ability of spermatozoa retrieved from azoospermic men to support embryonic development.

DESIGN: For over 20 months, we recruited infertile men undergoing epididymal aspiration for obstructive (OA; n=17) and testicular retrieval for nonobstructive (NOA; n=10) origins. Three men functioned as fertile controls. Gene mutations were compared according to the etiology of the azoospermia and in relation to whether they were able to generate a pregnancy (fertile) or not (infertile).

MATERIALS AND METHODS: Specimens were provided by consenting men, who were being treated at our center for infertility. DNA was extracted and amplified from at least 500 spermatozoa (DNA concentration, 705±562 ng/ul; quality, 1.7±0.1 nm). Following NGS, gene mutations, duplications, and deletions were detected using the CLC Genomic Server 9.0. Genes were considered duplicated or deleted when the read depth was >1.5 or <0.5 times the median read depth in the control. Common gene mutations in the OA and NOA cohorts were assessed according to the couples' clinical outcomes.

RESULTS: Of the 27 couples (paternal age, 41.3±5yrs) included, 17 OA men underwent epididymal sperm retrieval with an average concentration of $1.3\pm3x10^6$/ml and 7±14% motility, while 10 NOA men yielded twitching spermatozoa with a concentration of $0.03\pm0.2x10^6$/ml and 0.5±1% motility. Whole genome karyotype assessment showed an overall sperm aneuploidy rate below only 2%, specifically 1.7% in the OA and 1.9% in the NOA cohort.

In the OA group overall, only 3 housekeeping genes were mutated (ATP4A, SLC17A7, and OR1D4). However, in the NOA cohort, 5 genes involved in RNA transcription (POLR2L), apoptosis (AP5M1), and basic spermiogenic function (AP1S2, AP1G2, and APOE) were deleted.

The OA men and their partners (maternal age, 34.8±3yrs) underwent 17 ICSI cycles, resulting in a pregnancy and delivery rate of 47.1% (8/17). For those able to reproduce (n=8), all shared a mutation in ZNF749, which is mainly responsible for spermatogenesis. Those who remained infertile had a common mutation in PRB1, a gene involved in DNA replication.

When NOA men were treated in 10 ICSI cycles with their partners (maternal age, 38.2±2yrs), the pregnancy rate was 70% (7/10). Of those 7 men, 1 mutation (MPIG6B) related to stem cell lineage differentiation was in common. The remaining 6 who remained childless had mutations in genes associated with spermatogenesis (6 genes), apoptosis (4 genes), acrosomal function (2 genes), and, most importantly, in early embryonic development (MBD5, CCAR1, PMEPA1, POLK, REC9, REPIN1, MAPRE3, and ARL4C).

CONCLUSIONS: Screening infertile men for germline mutations can help characterize spermatogenic function in relation to the etiology of their azoospermia and provide valuable information on their reproductive potential. In men capable of reproducing, gene mutations were limited to those associated with spermatogenic function. For men unable to reproduce, particularly the NOA cohort, the mutated genes were mostly related to multiorgan functions and embryo development.

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ANOTHER CHANCE FOR SUCCESS: THE LIKELIHOOD OF OBTAINING A EUPLOID EMBRYO FOR TRANSFER AFTER AN IVF CYCLE WITH NO EUPLOID EMBRYOS. Nola S. Herlihy, MD,[1] Amber M. Klimczak, MD,[2] Brent M. Hanson, MD,[2] Julia G. Kim, MD, MPH,[2] Ashley W. Tiegs, MD,[2] Emily K. Osman, MD,[2] Emre Seli, MD,[2] Richard Thomas Scott, Jr., MD[2] [1]IVI-RMA New Jersey, Basking Ridge, NJ; [2]IVI RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: Although most patients achieve at least one euploid blastocyst with their first IVF cycle using preimplantation genetic testing for aneuploidy (PGT-A), a minority will not have any suitable embryos for transfer and need to be counseled about the utility of attempting another cycle. The objective of this study was to determine the likelihood that those patients achieve a euploid embryo in their subsequent IVF cycle.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: This was a retrospective review of all patients who underwent IVF with PGT-A using Next Generation Sequencing (NGS) from July 2016 to October 2019 at a University-affiliated clinical practice. Patients were included if their first IVF cycle resulted in no euploid embryos for transfer and they underwent at least one more IVF cycle using PGT-A. Patients using donor eggs and those who did PGT for monogenic diseases or structural rearrangements were excluded.

RESULTS: A total of 438 patients were identified who underwent PGT-A resulting in no euploid embryos. Of those patients, 223 (51%) had at least one euploid embryo for transfer in their second IVF cycle. Results by SART age group and number of blasts tested in the initial cycle are presented in Table 1. Overall, euploidy rates in the second cycle are not diminished compared to expected rates per age group

CONCLUSIONS: Patients undergoing PGT-A who achieve no euploid blastocysts in their first cycle may be reassured that this outcome is not indicative of an inherent defect in embryo quality. They should be offered the opportunity to attempt another IVF cycle and should be counseled that they retain a high likelihood of achieving a euploid blastocyst in their second attempt.

TABLE 1. Likelihood of obtaining a euploid blastocyst in a subsequent IVF cycle according to number of blastocysts initially tested. n : the number of patients in that group; first % number: corresponds to percentage of patients with a euploid blastocyst to transfer in their second cycle; second % number: corresponds to overall euploidy rates in the second cycle.

	Number of tested blastocysts in first cycle			
Patient Age	1	2	3-4	≥5
<35yrs	n=29	n=14	n=8	n=0
	72.4%, 74.2%	66.7%, 64.4%	87.5%, 65.5%	
35-37yrs	n=48	n=18	n=13	n=1
	81.3%, 54.5%	72.2%, 53.4%	92.3%, 53.6%	100%, 85.7%
38-40yrs	n=72	n=39	n=27	n=12
	40.3%, 38.1%	53.8%, 40.8%	74.1%, 37.3%	75.0%, 23.7%
41-42yrs	n=47	n=32	n=20	n=3
	29.8%, 23.4%	18.8%, 9.4%	55.0%, 22.8%	100%, 26.9%
>42yrs	N=31	N=14	N=8	N=1
	6.5%, 5.3%	14.3%, 8.3%	37.5%, 16.0%	0%, 0%

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AGE-RELATED PREGNANCY LOSS IS LARGELY OVERCOME WITH SINGLE EUPLOID EMBRYO TRANSFER. Mandy G. Katz-Jaffe, PhD, Susanna McReynolds, PhD, Lauren Henry, BS, Nathan McCubbin, BS, Rachel S. Mann, BS, MS, Rachel Tucci, BS, Sue McCormick, BS, William B. Schoolcraft, MD Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Oocyte aneuploidy is significantly associated with increasing maternal age and is the primary cause of reproductive failure including pregnancy loss for women of advanced maternal age (AMA; ≥38 years). Preimplantation genetic testing for aneuploidy (PGT-A) has been shown to improve IVF live birth outcomes from embryo transfer for AMA infertility patients. The aim of this study was to evaluate the efficacy of single euploid embryo transfers to reduce the impact of AMA on pregnancy loss.

DESIGN: Retrospective large cohort study

MATERIALS AND METHODS: A total of 3,773 single euploid transfers (SET) from 2010-2019 at a large IVF clinic, which underwent PGT-A at a single Genetics laboratory, were included in this cohort analysis. Donor oocyte and gestational carrier cycles were excluded. Groups were defined based on maternal age at the time of oocyte retrieval: <35 years (n=1,261 SETs), 35-37 years (n=1,074 SETs), 38-40 years (n=950 SETs), 41-42 years (n=397 SETs) and >43 years (n=91 SETs). Outcome measures included clinical pregnancy (visualized gestational sac and fetal pole), miscarriage (visualized fetal heart tone followed by loss) and live birth. Statistical analysis was performed where appropriate with Fisher's exact, Kruskal-Wallis and Benjamini-Hochberg adjustment, significance at $p < 0.05$.

RESULTS: Clinical pregnancy and live birth rates significantly decreased with AMA of ≥38 years (Table 1; *P<0.001). In contrast, miscarriage was not significantly different across the maternal age groups, including for AMA women (≥38 years). Only 2.4% of sustained implantations resulted in monozygotic twinning with monozygotic twinning 2.5x more likely to result in a pregnancy loss ($p < 0.05$).

CONCLUSIONS: This large cohort analysis of SETs has revealed that the age-related increase in pregnancy loss associated with aneuploidy has been largely overcome with PGT-A and the selection of euploid embryos for transfer. A small but significant decrease in live birth outcomes still remains for AMA women undergoing infertility treatment and represents the additional embryonic and maternal factors associated with reproductive success.

SUPPORT: None

	<35 Years	35-37 Years	38-40 Years	41-42 Years	43+ Years
	n=1,261 SETs	n=1,074 SETs	n=950 SETs	n=397 SETs	n=91 SETs
Clinical Pregnancy Rate	68.0%	70.0%	63.3%*	62.0%*	61.0%*
MAB Rate	6.3%	6.6%	4.7%	5.3%	3.6%
Live Birth Rate	63.7%	65.4%	60.3%*	58.7%*	59.3%*

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GENERALIST PHYSICIANS' REFERRAL BEHAVIOR ON PRE-IMPLANTATION GENETIC TESTING (PGT) FOR SINGLE GENE DISORDERS: DO WE NEED TO PLAY CATCH UP? Sarah M. Capelouto, MD,[1] Melanie Evans, MS, MD,[2] Jennifer Shannon, MD,[1] Katelyn Jetelina, PhD, MPH,[3] Orhan Bukulmez, MD,[1] Bruce R. Carr, MD[1] [1]UT Southwestern Medical Center, Dallas, TX; [2]The University of Texas, Southwestern Medical Center, Dallas, TX; [3]University of Texas Health Science Center at Houston, Dallas, TX.

OBJECTIVE: Pre-implantation genetic testing is a growing aspect of fertility treatment. However, prior national analyses reveal that the majority of cycles are for aneuploidy screening, while only about 15% are for monogenic disease, PGT-M [1]. To explore why so few PGT-M cycles are performed, we aimed to study physicians on the front lines of such referrals. Specifically, we evaluated the knowledge, barriers, and referral behaviors regarding PGT-M across generalist groups, comprised of internists, pediatricians and Ob/Gyns, in hopes of advancing PGT-M utilization.

DESIGN: Cross-sectional survey.

MATERIALS AND METHODS: We distributed an anonymous survey on PGT-M among generalists at our academic medical campus from March-May 2020 at grand rounds or online via REDCap. The survey included constructs on demographics, PGT-M knowledge (definition, success rates, who performs, does our institution offer), and referral/practice behavior. Bivariate analyses evaluated associations between physician specialty and demographics with their PGT knowledge and practice behavior.

RESULTS: A total of 145 respondents participated in our survey: 65 Ob/Gyns, 36 internists, and 44 pediatricians. Overall, 88% of physicians believed patients at risk of passing on genetic disorders should be provided PGT-M information. Despite this belief, few reported discussing PGT-M with their patients (24%) or referring for testing (23%). Moreover, most physicians only discussed (54%) or referred (79%) once a year. Objective PGT knowledge had a major effect on practice behavior. Among physicians that got 2 of 4 knowledge questions correct (compared to 1 of 4), the odds of discussing PGT were eight times higher and the odds of placing a referral five times higher ($p < 0.001$). Compared to internists and pediatricians, Ob/Gyns answered significantly more knowledge questions correctly. With this in mind, the odds of referring for PGT-M were eight times higher for Ob/Gyns compared to pediatricians, and ten times higher compared to internists ($p<0.001$). Subjective knowledge of PGT also correlated with practice behavior. Compared to Ob/Gyns, internists and pediatricians had lower odds of feeling they had enough basic PGT knowledge to adequately answer patient questions on the topic. Those odds were significantly lower for internists (OR 0.06, 95% CI 0.01-0.46) but non-significantly lower for pediatricians (OR 0.41, 95% CI 0.16-1.07). Lastly, demographics played a role. Internists, and physicians who graduated medical school before 1980, more likely believed that lack of physician knowledge was a barrier to PGT-M use.

CONCLUSIONS: While the majority of generalists surveyed believed patients at risk of passing on genetic disorders should be provided PGT-M information, less than 1 in 4 discussed PGT with their patients or placed testing referrals. Our study shows there is opportunity to promote a greater understanding of PGT among generalists. Follow-up interventions to advance knowledge could take the form of grand rounds lectures or continuing medical education courses led by fertility specialists, in turn expanding the use of PGT-M for all patients.

References: 1. Chang J, Boulet SL, Jeng G, Flowers L, Kissin DM. Outcomes of in vitro fertilization with preimplantation genetic diagnosis: an analysis of the United States Assisted Reproductive Technology Surveillance Data, 2011-2012. Fertil Steril 2016;105:394-400.

SUPPORT: None

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ADVANCED PATERNAL AGE DOES NOT INFLUENCE BLASTOCYST EUPLOIDY RATES IN DONOR EGG CYCLES. Daniel Skora, M.D., Jennifer A. Rodriguez, B.Sc., Rebecca A. Chilvers, M.D., Satin S. Patel, M.D., Jerald S. Goldstein, M.D., Carlos A. Guerrero, Ph.D. Fertility Specialists of Texas, Frisco, TX.

OBJECTIVE: The average age of parentage has been increasing over the last decades. Research has suggested that advanced paternal age (APA) may play a role in increased risk of several disorders in offspring, including: schizophrenia, musculo-skeletal syndromes, and autism spectrum disorders[1]. The question remains whether there are changes in euploidy rates associated solely with APA. Most studies assessing APA effects are confounded by concomitant advanced maternal age. To avoid this confounder, we looked at euploidy rates in our donor egg population assessed by PGT-A to assess rate of aneuploidy by paternal age.

DESIGN: Retrospective analysis of data collected from January 2017 through January 2020. Donor egg cycles were divided into 4 treatment groups based on paternal age. Clinical end points and laboratory parameters were analyzed using Fisher's exact test and t-test as appropriate.

MATERIALS AND METHODS: A total of 210 donor egg cycles and 1410 blastocyst biopsies were included in this study. Blastocysts were biopsied on Day 5/6 and aneuploidy testing was performed via NextGen Sequencing. Males with epididymal or testicular sperm and oocyte donors >30 years of age were excluded.

RESULTS: Euploidy rates remained within the margin of error for all paternal age groups; around 70% euploid (Table 1). No difference was noted in euploidy rate between groups. Furthermore, there was no difference between treatment groups for semen quality parameters, blastocyst quality, number of oocytes retrieved and egg donor age.

Table 1. Effect of paternal age on blastocyst euploidy rate.

Paternal Age Group	# of Cycles	# of Blastocysts Biopsied	Euploidy Rate (%)
<35	53	353	254/353 (71.9%) [a]
35-40	70	464	326/464 (70.2%) [a]
41-45	47	313	217/313 (69.3%) [a]
>45	40	280	196/280 (70.0%) [a]

[a] Different superscripts within columns indicate significant differences ($P<0.05$)

CONCLUSIONS: These findings suggest that the euploidy rate of blastocysts determined by PGT-A is not associated with paternal age. Other disorders associated with APA are more likely a result of imprinting or epigenetic changes not detected by PGT-A.

References: [1]Nybo Andersen AM, Urhoj SK .Fertil Steril. 2017 Feb;107(2):312-318.

SUPPORT: n/a

P-795 4:30 PM Tuesday, October 20, 2020

OUTCOMES FOLLOWING TRANSFER OF EMBRYOS WHOSE PGT-A RESULTS WERE INDETERMINATE AND THAT WERE NOT RE-BIOPSIED. Tamar Alkon-Meadows, MD,[1] Carlos Hernandez-Nieto, MD,[1] Joseph A. Lee, BA,[1] Rose Marie Roth, MSc, TS(ABB), CLT (NYS),[1] Richard Slifkin, BA, TS(ABB), CLT(NYS),[1] Deborah Cassis-Bendeck, MD,[1] Martha Luna-Rojas, MD,[1] Alan B. Copperman, MD,[2]

Benjamin Sandler, MD[2] [1]Reproductive Medicine Associates of New York, New York, NY; [2]Icahn School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: PGT-A with *NGS* is broadly utilized by reproductive specialists at modern ART treatment centers to improve embryo transfer selection. However, there are technical limitations to PGT which might prevent formal designation of the embryo as euploid or aneuploid. While re-biopsy of the embryo is possible, some studies suggesting that the selection of twice biopsied embryos at time of transfer might compromise overall implantation[1]. Hence, patients have been known to electively select embryos with indeterminate results for transfer. The aim of this study is to evaluate clinical outcomes following transfer of indeterminate embryos compared to re-biopsied euploid embryos.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: The study included patients who underwent a single FET of blastocysts that underwent a trophectoderm biopsy from 2016 to 2020. Cohorts were separated into 2 groups: (Group 1: single biopsy embryos with an indeterminate result; Group 2: initial embryo biopsy with indeterminate result that underwent a secondary biopsy and was diagnosed as euploid). Patients whose PGT-A results were indeterminate had extensive clinical and genetic counseling and signed informed consent prior to re-biopsy and/or ET. Demographic characteristics, embryology parameters and clinical outcomes were compared. Comparative statistics and an adjusted multivariate regression were used for analysis.

RESULTS: 61 FET cases were included in the analysis: indeterminate PGT results embryos (n= 21); double biopsied euploid embryos (n=40). Patients that elected to transfer indeterminate result embryos had higher age at oocyte retrieval (39.0 vs 36.9, p=0.02) and at ET (39.3 vs 37.2, p=0.01) than patients in group 2. All other demographic variables, embryonic quality at ET, implantation, clinical pregnancy (CPR), ongoing pregnancy (OPR) and clinical pregnancy loss (CPL) rates were statistically comparable among groups. After adjusting for BMI, age, AMH, and embryo quality at FET, transfer of an indeterminate embryo was not associated with lower odds of implantation (OR 1.03 CI95% 0.2-4.3, p=0.96), CPR (OR 1.02 CI95% 0.2-3.8, p=0.40), OPR (OR 1.4 CI95% 0.3-4.9, p=0.60) when compared with double biopsied embryos. Also, there was no association with higher CPL rates (OR 0.4 CI95% 0.3-5.2, p=0.50).

CONCLUSIONS: This is the first study to describe outcomes when embryos biopsied for PGT-A were indeterminate and selected for transfer without re-biopsy. Our study suggests that implantation and ongoing pregnancy rates are lower when indeterminate embryos are selected for transfer compared to the selection of embryos that underwent a second biopsy and were found to be euploid, albeit the differences were not statistically significant. We recommend re-biopsy of embryos upon an initial indeterminate result to allow for enhanced transfer selection and greatest reproductive potential. However, for patients that have frozen indeterminate embryos and are unable to undergo another IVF cycle, comparable reproductive outcomes are achievable, especially in younger patients who have a higher prevalence of embryonic euploidy.

References: 1. Cimadomo D, Rienzi L, Romanelli V, Alviggi E, Levi-Setti PE, Albani E, et al. Inconclusive chromosomal assessment after blastocyst biopsy: prevalence, causative factors and outcomes after rebiopsy and re-vitrification. A multicenter experience. Hum Reprod. 2018;33(10):1839–46

SUPPORT: None

P-796 4:30 PM Tuesday, October 20, 2020

OBSTETRIC AND NEONATAL OUTCOMES OF PREGNANCIES RESULTING FROM PREIMPLANTATION GENETIC TESTING: A SYSTEMATIC REVIEW AND META-ANALYSIS. Wei Zheng, MD, Yichun Guan, MD, PhD, Chen Yang, MD, Shuheng Yang, MD, Simin Sun, MD, Mingkun Mu, MD, Ruowen Zu, MD, Junfang Yan, MD, Bingnan Ren, MD The Third Affiliated Hospital of Zhengzhou University, Zhengzhou, China.

OBJECTIVE: This study aims to investigate whether preimplantation genetic testing (PGT) pregnancies increase the risks of adverse obstetric and neonatal outcomes compared to IVF/ICSI pregnancies or spontaneous conceptions (SC).

DESIGN: a systematic review and meta-analysis.

MATERIALS AND METHODS: PubMed, EMBASE, Web of Science and Cochrane Library from January 1990 to November 2019 were searched. Published studies were included if they reported data on obstetric and neonatal outcomes for PGT and IVF/ICSI or SC. The primary outcomes were low birth weight (LBW) and congenital malformations (CMs), whereas secondary outcomes were preterm delivery (PTD), birth weight (BW), very low birth weight (VLBW), very preterm delivery (VPTD), Neonatal Intensive Care Unit (NICU) admission, placenta previa (PP), gestational age, preterm premature rupture of membranes, gestational diabetes and pre-eclampsia. Besides, we pooled results of PGT singleton pregnancies, and subgroup analyses included preimplantation genetic diagnosis (PGD) and preimplantation genetic screening (PGS) singleton pregnancies.

RESULTS: Thirteen studies were included in this meta-analysis. The relative risks of having LBW (RR = 4.08, 95% CI: 2.83–5.89), CMs (RR = 2.24, 95% CI: 1.48–3.37) and PTD (RR = 3.30, 95% CI: 2.37–4.58) were significantly higher in PGT pregnancies, when compared with SC; and the BW significantly reduced in PGT pregnancies (RR = –91.66, 95% CI: –161.09 to –22.23). Furthermore, The risks of LBW [relative risk (RR) = 0.90, 95% confidence interval (CI) : 0.80–1.00], VPTD (RR = 0.61, 95% CI: 0.41–0.93) and VLBW (RR = 0.70, 95% CI: 0.50–0.98) were significantly lower when PGT pregnancies compared with IVF/ICSI pregnancies (both single and multiple pregnancies), but the risk of PP (RR = 2.97, 95% CI: 1.37–6.42) was significantly higher in PGT pregnancies than IVF/ICSI pregnancies. We further found that PGT singleton pregnancies significantly decreased the risks of LBW (RR = 0.68, 95% CI: 0.49–0.94), VPTD (RR = 0.51, 95% CI: 0.25–1.00) and VLBW (RR = 0.52, 95% CI: 0.28–0.97) compared with IVF/ICSI singleton pregnancies. The subgroup analysis indicated there was a significantly lower risk of LBW (RR = 0.66, 95% CI: 0.48–0.92) in PGD singleton pregnancies compared with IVF/ICSI singleton pregnancies, but the results of PGS singleton pregnancies were comparable with those of IVF/ICSI singleton pregnancies. No statistical differences were noted in the remaining outcomes.

CONCLUSIONS: This systematic review and meta-analysis revealed that PGT pregnancies might increase the risks of adverse neonatal outcomes when PGT pregnancies compared with SC. However, the other factor, like infertility background may have a greater impact on neonatal outcomes because PGT pregnancies reduced the risk of adverse neonatal outcomes when compared with IVF/ICSI pregnancies. The overall obstetric outcomes are reassuring, but embryo biopsy of PGT, especially trophectoderm biopsy, may affect the development of placental and increases the risk of PP.

References: None

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OBESITY AND MITOSCORE: DETERMINANT OF ART SUCCESS? Maria Bustillo, M.D,[1] Ineabelle Collazo, BS,[2] Katherine L. Palmerola, BS, MD,[2] Sabrina A. Gerkowicz, MD,[2] Juergen Eisermann, M.D,[1] Nicholas Hendon, BS,[2] Himanshu Arora, PhD[3] [1]IVFMD, South Florida Institute for Reproductive Medicine, MIAMI, FL; [2]IVFMD, South Florida Institute for Reproductive Medicine, Miami, FL; [3]University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: Mitochondrial gene copy number (mtDNA or "MitoScore") may reflect embryo stress and energy supply, which may impact implantation. In assisted reproductive technology (ART), multiple factors affect outcome, with emerging evidence suggesting that patient body mass index (BMI) and body fat are critical players. However, little is known regarding the impact of BMI or percent body fat on an embryo's MitoScore.. In the present study we compared MitoScore, BMI and percent body fat in ART outcomes, as this information may be important to maximizing the success rate of single embryo transfer in ART

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: Data from 166 women (2016-2017), who underwent ART with pre-implantation genetic testing for aneuploidy (PGT-A) was analysed. PGT-A and MitoScore testing on euploid embryos were performed by Igenomix. Body fat was measured with Tanita body composition analyser (Model TBF-410). MitoScore, BMI and percent body fat were compared between pregnant and nonpregnant cohorts following ART. Additionally, Mitoscore, BMI, and percent body fat were compared in subgroups of the pregnant cohort (live birth, biochemical, spontaneous abortion). GraphPad Prism (GraphPad Software) was used for statistical analysis. All data are presented as the means ± SEM. The statistical significance between two groups was estimated by unpaired one-tailed t test. In all cases, $p < 0.05$ was considered statistically significant.

RESULTS: Data from 166 women was analysed, including 130 with positive beta human chorionic gonadotropin (bhCG): 104 live births, 15

biochemical pregnancies, and 11 spontaneous abortions. MitoScore, BMI and percent body fat were significantly lower in pregnant compared to non-pregnant women (MitoScore- p=0.04, BMI- p=0.05, percent body fat- p=0.03). Correlation studies between MitoScore, BMI and percent body fat in subgroups of the pregnant cohort showed that MitoScore was positively correlated with BMI in patients with biochemical pregnancies (p=0.04) and not correlated in patients with live births (p=0.63) or with spontaneous abortions (p=0.48). MitoScore was not correlated with percent body fat in any of the pregnant subgroups.

CONCLUSIONS: Our findings suggest that MitoScore, BMI and percent body fat could act as critical parameters in determining the success of ART in regards pregnant or non-pregnant outcomes. Many factors need to be considered to reliably establish and clarify this correlation. Further analyses of other determinants such as age and infertility diagnosis and inflammatory markers are underway to establish the significance of MitoScore.

SUPPORT: This work was supported in part by the *IVFMD, South Florida Institute for Reproductive Medicine*

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EFFICACY OF PGT-A WITH A SINGLE BLASTOCYST. Alexis Gadson, MD,[1] Wendy Kuohung, MD,[1] Denny Sakkas, PhD[2] [1]Boston University School of Medicine, Boston, MA; [2]Boston IVF, Waltham, MA.

OBJECTIVE: Pre-implantation genetic testing for aneuploidy (PGT-A) has been used to allow the transfer of a euploid embryo to achieve a higher chance of pregnancy. Currently, PGT-A is offered to IVF patients on a self-pay basis, even in states with a legislative mandate to cover infertility treatment. It is unclear if PGT-A improves clinical pregnancy rates if the cycle yields only one blastocyst of sufficient quality to biopsy and cryopreserve. The objective of this study was to determine if there is any difference in clinical pregnancy rates between patients with a single freezable blastocyst who undergo PGT-A compared to those who undergo transfer of a single untested blastocyst.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: We reviewed deidentified cycles of women undergoing a frozen embryo transfer cycle between January 1, 2014 and March 31, 2020, and whose prior IVF cycle yielded a single high-quality blastocyst for transfer at Boston IVF. Criteria for PGT-A cycle was the presence of only one blastocyst available for biopsy and cryopreservation. Non PGT-A patients included the cycle being a frozen embryo transfer cycle with transfer of a single thawed blastocyst. Exclusion criteria included cycles utilizing donated eggs. Patient data including age at cycle start, pre-implantation testing type, cycle data (cycle number, trophectoderm and inner cell mass grade, dates of treatment), and outcomes (presence of fetal heart rate in a clinical pregnancy) were collected for each cycle. Chi square analysis was used to determine differences between the single blastocyst patients utilizing PGT-A and the group that did not (control).

RESULTS: A total of 13,293 charts were included in the initial analysis. Patients who had a single blastocyst and underwent PGT-A were extracted from the database and analyzed separately. Clinical pregnancy rates in patients who had a single embryo transfer and did not undergo PGT-A were 50.4% in patients less than 35 years old, 47.5% in patients 35-37 years old, 37.7% in patients 38-40 years old, and 26.2% in patients over 40 years old. In patients with a single blastocyst who elected to undergo PGT-A, the clinical pregnancy rate was found to be 60.4% in patients under 35 years old (p=0.15), 61.0 % in patients age 35-37 (p=0.02), 62.3% in patients age 38-40 (p<0.0001), and 55.6% in patients older than 40 (p <0.001). The rate of aneuploidy amongst patients with a single blastocyst undergoing PGT-A was 54.7%; those patients did not undergo embryo transfer and thus were not included in this analysis.

CONCLUSIONS: Use of PGT-A for a single blastocyst was associated with a statistically significant increase in clinical pregnancy rate in women over age 35 who elected to undergo PGT-A prior to frozen single embryo transfer. Despite the retained risk of an aneuploid diagnosis, PGT-A still allows these older than 35 patients to achieve improved pregnancy rates with frozen embryo transfer. Although out-of-pocket costs may be higher and patients should be aware of the high likelihood of embryo aneuploidy, patients with only one blastocyst available still benefit from PGT-A.

SUPPORT: Internally funded.

P-799 4:30 PM Tuesday, October 20, 2020

THE IMPACT OF USING ARTIFICIAL INTELLIGENCE IN REPORTING HIGH RESOLUTION NGS RESULTS UPON PRIORITIZATION OF EMBRYOS SELECTED FOR TRANSFER. Nawal Mohamed Saad, Sr., BSc, Nada Elmegharbel, Ashrakat Abdeltawab, Mona Ashraf, Hanaa Alkhader, Hosam Zaki. Elfostat new city, Cairo, Egypt.

OBJECTIVE: There are many factors that influence the interpretation of the plots of high resolution NGS (hr-NGS) in PGT A examination of the embryos, such as the Genetist experience, cut-off points, and the chromosomal number. The PGT A results differentiate between euploidy embryos that are given first priority for embryo transfer (ET), second priority for low mosaic, and aneuploidy or high level mosaic those who are not transferred . This study compares between manual calling of the results versus using artificial intelligence platform.

DESIGN: This is a prospective ongoing study.

MATERIALS AND METHODS: A total of 720 biopsied sample from 280 patients processed according to Miseq Illumina protocol. Results are manually called subjective methodology (SM) using Bluefuse software and also uploaded up to **PGTai^{SM}** platform Coopersurgical.

RESULTS: The mean age of the female partners is 34 years. There was a difference in 138 results out of 720 (19%) comparing between the "SM" and **PGTai^{SM}** platform interpretation. The following table shows the differences between four categories in both SM and PGTai results:

	SM	PGTai^{SM}
categories	No. of embryos	
Euploid	31	14 low level mosaic 11 high level mosaic 5 aneuploid 1 QA fail
Aneuploid	27	1 low level mosaic 15 high level mosaic 1 euploid 10 QA fail
High level mosaic	29	2 low level mosaic 14 euploid 12 aneuploid 1 QA fail
Low level mosaic	46	12 high level mosaic 28 euploid 5 aneuploid 1 QA fail

The PGTai platform changes some of the results in all reported categories. That would change the prioritization of embryos for transfer. There were 16 embryos that were reported euploidy by SM, while they are deemed "untransferable" by PGTai, being 5 aneuploidy and 11 being of high level mosaic. Again, in the same group 14 embryos were of low mosaic level which would have been given a second priority. In the aneuploidy group only 2 embryos (1 euploid and 1 low level mosaic) would have been possibly transferred according to PGTai.

In the high level mosaic group 16 embryos would have been given priority for embryo transfer as 14 were found euploidy while 2 were of low mosaic level. In the low level mosaic group 28 embryos would have been given first priority as found to be euploid, while 17 embryos would have must been considered to be as 12 of high level mosaic and 5 were aneuploidy.

CONCLUSIONS: PGTai is thought to be more valid than manual subjective calling of results as based upon true data set of live births and sustained pregnancy outcomes. This study shows a strong difference of 19% in results that changes how embryos are prioritized for ET. Moreover, same embryos would have been not transferred as being aneuploidy as of high mosaic level. Further studies are needed to evaluate if using PGTai would improve live birth rate and decrease miscarriage by better selection of embryos.

References: D.S. Cram, D. Leigh, A. Handyside, L. Rechitsky, K. Xu, G. Harton, J. Grifo, C. Rubio, E. Fragouli, S. Kahraman, E. Forman, M. Katz-Jaffe, H. Tempest, A. Thornhill, C. Strom, T. Escudero, J. Qiao, S. Munne, J.L. Simpson, A. Kuliev, PGDIS Position Statement on the Transfer of Mosaic Embryos 2019, Reproductive BioMedicine Online, Volume 39, Supplement 1, 2019

P-800 4:30 PM Tuesday, October 20, 2020

BATCHING OF BLASTOCYSTS TOGETHER WITH PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) IS A HIGHLY SUCCESSFUL STRATEGY FOR ADVANCED MATERNAL AGE AND YOUNGER WOMEN WITH DIMINISHED OVARIAN RESERVE. Lilach Marom Haham, MD,[1] Michal Dviri, MD,[2] Adi Kuperman, M.D, MHA,[1] Anjila Roumia, MD,[3] Svetlana Madjunkova, MD, PhD,[1] Clifford Lawrence Librach, MD[1] [1]CReATe Fertility Centre, Toronto, ON, Canada; [2]University of Toronto, Toronto, ON, Canada; [3]CReATe fertility centre, Toronto, ON, Canada.

OBJECTIVE: In the recent years the number of women at the advanced maternal age (AMA, ≥ 38 years) undergoing fertility treatments is growing, owing to many women delaying childbearing. The increased rate of chromosomal aneuploidy in the AMA population, as well as the low oocyte and embryo yield in women with decreased ovarian reserve (DOR), are leading factors contributing to poor in vitro fertilization (IVF) treatment outcomes. A strategy of accumulating embryos throughout several stimulation cycles, often called batching, increases the number of embryos available for PGT-A, reduces the cost of multiple testing runs, and increases the likelihood of having normal embryos for transfer now and for future pregnancies. However, data regarding the outcomes of this strategy are lacking. The aim of our study was to evaluate the outcomes of batching for PGT-A.

DESIGN: A retrospective cohort study.

MATERIALS AND METHODS: The study had institutional REB approval. Infertile women performing consecutive IVF cycles for accumulation of blastocysts for PGT-A at the CReATe Fertility Centre (Toronto, Canada) between 2017-2019 were included. Patients were divided to three main groups according to age and ovarian reserve: [1] AMA [2] AMA and DOR [3] DOR. DOR was defined according to POSEIDON groups 3 and 4 or retrieving ≤ 4 oocytes with conventional stimulation protocol. Patients using donor oocytes were excluded. The primary outcomes were number of euploid embryos accumulated per patient, clinical pregnancy rate (CPR), and the number of euploid and mosaic embryos for future usage. T-test and ANOVA were used to compare continuous and dependent variables between the groups. P <0.05 was statistically significant.

RESULTS: A total of 61 patients performed embryo pooling for PGT-A in this cohort. The mean age was 38.9±3.2. The mean number of cycles per patient was 3.4±1.2 (range 2-7). The mean number of total blastocysts, euploid and mosaic embryos accumulated per patient was 6±3 (range 1-17), 2.1±1.7 (range 0-7) and 0.4±0.6 (range 0-2) respectively. 43 of these patients (70.5%) used their embryos and underwent FET cycles yielding a clinical pregnancy rate of 58.9% and a miscarriage rate of only 3.4%. The mean time to pregnancy was 5.8±3 months. The mean number of remaining euploid and mosaic embryos for future usage was 1.5±1.5 (range 0-6) and 0.5±0.7 (range 0-2), respectively. When comparing the three main study groups: 1. AMA (n=21), 2. AMA and DOR (n=20) and 3. DOR (n=13), no significant difference in CPR was observed (48.6%, 64.7%, 50%, respectively; p=0.6), the mean number of remaining euploid (1.6, 1, 1.3, respectively; p=0.3) and mosaic embryos (0.6, 0.3, 0.3, respectively; p=0.2) for future usage.

CONCLUSIONS: To our knowledge, this is the largest series to date of blastocysts batching for PGT-A. This strategy increases the likelihood of having a normal embryo for transfer and may optimize treatment outcomes by exploiting the short "window of opportunity" to preserve normal embryos for future use, for both older women with, or without, DOR, as well as younger women with DOR.

P-801 4:30 PM Tuesday, October 20, 2020

THE ASSOCIATION BETWEEN THE GENDER OF PATIENTS WITH ROBERTSONIAN TRANSLOCATION AND EUPLOID RATE. Jing Wang, M.D,[1] Baomin Lubachela.[2] [1]medical genetic, guangzhou, China; [2]medical examination, guangzhou, China.

OBJECTIVE: To give a better counseling on the chances of available embryos to the robertsonian translocation carriers.

DESIGN: A single center, retrospective, observational study.

MATERIALS AND METHODS: Patients who were robertsonian translocation carriers without other gene or chromosomal diseases were chosen for the study. On the day of occyte retrieval, the semen sample will be tested routinely. Biopsy was performed when the trothectoderm was suitable for the manipulation either on day5 or day6. Six to eight cells were taken routinely for NGS analysis. The patients were divided into two groups based on the gender of robertsonian translocation carries, the male patients group and the female patients group. Moreover, the embryos were divided into euploid group and aneuploidy group according to the NGS results.

RESULTS: A total of 1253 embryos from 156 PGT cycles of 146 couples were enrolled in the study, during July 2017 to September 2019. The male and female patients were 87 and 69, respectively. There were 53 male patients with the known robertsonian translocation suffering poor semen parameters, the abnormal rate was 60.92% compared with 21.74% in the companions of the female patients. Out of 1253 analysed embryos, 1242 had a chromosomal result, indicating that the detection rate was 99.12%. The euploid rate was statistically higher in the male patients group which was 49.26% than the female patients group that was 28.65%(P<0.05). Logistic regression analysis adjusted for male and female ages suggested that the gender of patients had a positive impact on the euploid rate(OR=2.497, 95% CI 1.965-3.173, P<0.001).

CONCLUSIONS: Although the robertsonian translocation has an negative influence on the semen quality which may lead to male infertility, the euploid rate is still acceptable if the patients undergo PGT. This study shows that the male patients have a more bright future when considering the euploid rate, however, the mechanism is still uncertain. We need more fundamental researches to tackle this problem.

P-802 4:30 PM Tuesday, October 20, 2020

ASSOCIATION BETWEEN STANDARD MORPHOLOGY ASSESSMENT AND CHROMOSOME CONSTITUTION AFTER NGS ANALYSIS. Pamela Villanueva, MD, PhD,[1] Huayhua Julio, BSc,[2] Luis Noriega-Hoces, MD,[1] Javier Noriega, MD,[1] Luis Guzman, PhD.[1] [1]Laboratorios de Reproduccion Asistida PRANOR, Lima, Peru; [2]ADN Diagnostico, Lima, Peru.

OBJECTIVE: To determine the correlation between standard morphology assessment and chromosome constitution in blastocyst analyzed by NGS.

DESIGN: Retrospective observational study

Table 1. Association between chromosome constitution and embryo morphology

	Good	Fair	Poor
Euploid	1092 (53.06%)	880 (42.76%)	86 (4.18%)
OR	1	0.74 (0.65-0.84)**	0.70 (0.52-0.94)*
Aneuploid	301 (44.93%)	331 (49.40%)	38 (5.67%)
OR	1	0.99 (0.82-1.19)	0.94 (0.64-1.39)
Mosaic	290 (43.81%)	339 (51.21%)	33 (4.98%)
OR	1	1.25 (1.03-1.51)*	1.25 (0.82-1.89)
Double Aneuploid	86 (39.09%)	109 (49.55%)	25 (11.36%)
OR	1	1.04 (0.75-1.44)	1.94 (1.15-3.26)*
Complex Mix	79 (31.60%)	147 (58.80%)	24 (9.60%)
OR	1	1.54 (1.13-2.10)**	2.03 (1.24-3.33)**

OR (IC 95%): Odds Ratio (Confident Interval 95%),* p<0.05, ** p<0.001.

MATERIALS AND METHODS: Data was collected retrospectively from June 2016 to October 2019. In 1221 IVF cycles, 4719 blastocysts were biopsied and analyzed by NGS. DNA from trophectoderm cells were amplified by using Sureplex, hr-NGS was performed with VeriSeq PGS assay, (MiSeq-Ilumina). NGS data was analyzed with Bluefuse sofware (Ilumina). Chromosome constitution was classified according to the genetic results as: euploid, single aneuploid, double aneuploid, complex aneuploidy (>3 chromosomes are aneuploid), (single, double and complex) mosaic, complex mix and mix (aneuploid and mosaic). Embryo morphology was classified as good, fair, or poor based on SART. Descriptive statistics and multilevel model for logistic regression considering a patient as second level and blastocyst as first level were used to evaluate the association between chromosome constitution and embryo morphology which was adjusted by levels of trophectoderm and inner cell mass, maternal age, fertilization technique and day of embryo biopsy. $p<0.05$ as significant level. All analyses were performed by Stata.

RESULTS: For all blastocyst analyzed the frequency was euploid (43.6%), single aneuploid (14.2%), double aneuploid (4.7%), complex aneuploid (2.4%), single mosaic (14%), double mosaic (4.9%), complex mosaic (7.3%), mix (2.9%) and complex mix (5.3%). Most of the embryos biopsied have a good (46.8%) and fair (47.9%) quality and 5.3% were poor quality.

Euploidy embryos were associated to have good morphology as is shown in table 1. Interestingly, poor embryo quality have a significantly increased frequency of double aneuploidy ($p=0.013$). On the contrary, any associations were found for double mosaic, complex aneuploid and mix.

CONCLUSIONS: NGS results confirmed the association between embryonic morphology and euploidy. Mosaicism was reported more frequently in fair embryos, while double aneuploidy and mixed complex are more associated with embryos with low embryo quality.

P-803 4:30 PM Tuesday, October 20, 2020

BIPARENTAL INHERITANCE OF MITOCHONDRIAL DNA IN RHESUS MACAQUES. Hong Ma, PhD,[1] Hayley Darby, MS,[1] Crystal Van Dyken, BS,[1] Aleksei Mikhalchenko, PhD,[1] Nuria Marti-Gutierrez, PhD,[1] Amy Koski, BA,[1] Dan Liang, PhD,[1] Ying Li, MS,[1] Yeonmi Lee, PhD,[2] Eunju Kang, PhD,[2] Paula Amato, MD,[1] Shoukhrat Mitalipov, PhD[1] [1]Oregon Health & Science University, Portland, OR; [2]ASAN Medical Center, Seoul, Korea, Republic of (South).

OBJECTIVE: It is generally believed that the mitochondrial genome (mtDNA) is inherited exclusively through the maternal lineage from oocytes. We investigated fate of paternal mtDNA in rhesus macaque (*Macaca mulatta*) offspring generated by natural breeding or Assisted Reproductive Technologies (ART).

DESIGN: Live offspring were produced by ART employing intracytoplasmic sperm injection of oocytes with sperm from geographically isolated subpopulations of *Macaca mulatta*. In addition, offspring were generated by natural breeding.

MATERIALS AND METHODS: DNA samples from 28 organs/tissues were collected from monkeys post necropsy and high-depth whole mtDNA sequencing (MiSeq) was used to evaluate contribution of maternal and paternal mtDNA.

RESULTS: Sequencing analyses showed no detectable paternal mtDNA contribution in five of the six tested monkeys. However, mtDNA variants of one monkey produced by natural mating matched to both maternal and paternal mtDNA haplotypes in twenty organs/tissues, with paternal mtDNA heteroplasmy levels ranging from 5% to 33%. Interestingly, paternal mtDNA was absent in eight other organs of this animal, suggesting tissue specific segregation of paternal mtDNA. Analyses of blood samples from additional 10 offspring fathered by this male revealed that one monkey carried variants matched to the paternal mtDNA at 31% heteroplasmy.

CONCLUSIONS: Our results demonstrate paternal mtDNA contribution from one particular male.

P-804 4:30 PM Tuesday, October 20, 2020

TROPHECTODERM BIOPSY PRIOR TO AUTOLOGOUS FROZEN BLASTOCYST TRANSFER IS NOT ASSOCIATED WITH ADVERSE OBSTETRICAL OUTCOMES. Michael S. Awadalla, MD, Kristen E. Park, BA, Kyle R. Latack, BA, Lynda K. McGinnis, PhD, Ali Ahmady, PhD, Richard J. Paulson, MD, MS Keck School of Medicine, University of Southern California, Los Angeles, CA.

OBJECTIVE: To determine if trophectoderm biopsy prior to autologous frozen blastocyst transfer is associated with gestational age at delivery, birth weight, or cesarean rate in ongoing singleton gestations.

DESIGN: retrospective cohort study

MATERIALS AND METHODS: We identified all patients at a university-affiliated center that had viable singleton gestations after autologous frozen blastocyst transfers from January 2016 through December 2018. Obstetrical outcomes of 67 viable singleton pregnancies after blastocyst trophectoderm biopsy for preimplantation genetic testing (PGT) with next generation sequencing were compared to 78 viable singleton pregnancies from unbiopsied frozen blastocysts. All transfers occurred in programmed frozen transfer cycles. Cycles that utilized a gestational carrier, donor oocytes, or frozen oocytes were excluded. Primary outcomes included gestational age at delivery, birth weight, and cesarean rate. The study had 80% power at a significance level of 0.05 to detect a 4-day difference in median gestational age at delivery, 300-gram difference in median birth weight, and 20% difference in cesarean rate. Secondary outcomes included preterm delivery, low birth weight, and birth weight over 4000 grams.

RESULTS: There were no significant differences between the two groups in terms of maternal age, BMI, or ethnicity. There were no differences in the PGT cohort compared to the reference cohort for median gestational age at delivery, median birth weight, cesarean rate, preterm delivery rate, rate of low birth weight, or rate of birth weight over 4000 grams (Table). There were no differences in the primary outcomes for subgroup analysis based on fetal sex, single embryo transfer, nulligravid, and no history of prior term birth.

CONCLUSIONS: Trophectoderm biopsy prior to frozen blastocyst transfer is not associated with adverse obstetrical outcomes related to gestational age at delivery, birth weight, or cesarean rate.

	No PGT (ref) n = 78	PGT n = 67	RR (95% CI)	P value
Demographics and baseline characteristics				
Maternal age (SD)	35.6 (4.3)	35.8 (3.7)		0.77
Maternal BMI kg/m^2 (SD)	24.5 (5.4)	24.0 (5.2)		0.59
Number of embryos transferred	1.6 (0.6)	1.2 (0.4)		< 0.01
Prior preterm birth	4 (5%)	2 (3%)		0.69
Outcomes				
Cesarean delivery	34 (44%)	34 (51%)	1.16 (0.82-1.64)	0.41
Birth weight in grams	3430 [3033, 3714]	3420 [3050, 3799]		0.97
Birth weight >4000g	6 (8%)	9 (13%)	1.75 (0.66-4.65)	0.29
Low birth weight, <2500g	7 (9%)	8 (12%)	1.33 (0.51-3.48)	0.59
Gestational age in weeks	39.4 [39.0, 40.4]	39.4 [39.0, 40.3]		0.80
Delivery prior to 37 weeks	6 (8%)	8 (12%)	1.55 (0.57-4.25)	0.41
Delivery prior to 34 weeks	1 (1%)	1 (1%)	1.16 (0.07-18.3)	1.00

Data are reported as mean (SD), median [IQR] or n (%).

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MUTATION ANALYSIS AND CHARACTERIZATION OF COL7A1 C.4531_4564-42DEL FROM TROPHECTODERM (TE) BIOPSIES USING NEXT GENERATION SEQUENCING (NGS) SIMULTANEOUSLY WITH PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A). Xin Tao, Ph.D,[1] Li Ma, BS,[1] Yiping Zhan, Ph.D,[2] Heather Garnsey, BS, MPS,[1] Richard Thomas Scott, Jr., MD,[3] Chaim Jalas, N/A[1] [1]Foundation for Embryonic Competence, Basking Ridge, NJ; [2]The Foundation for Embryonic Competence, Basking Ridge, NJ; [3]IVI RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: The COL7A1 gene encodes a protein called pro-α1(VII) chain that is used to assemble a larger protein called type VII collagen. Type VII collagen plays an essential role in strengthening and stabilizing the skin. Mutations in *COL7A1* can cause Dystrophic epidermolysis bullosa (DEB). Each of the couple undergoing IVF carries a recessive mutation in COL7A1. The patient carries a point mutation (c.266+2T>C), which can be detected by mutation direct Taqman qPCR genotyping assay. The partner carries an 87 base pair (bp) deletion (c.4531_4564-42del), which can't be detected by Taqman genotyping assay, or informative SNPs within the deletion region. No partner's parental DNA is available to set up linkage analysis. In this study, we developed an NGS assay to detect the 87bp deletion from TE biopsies. The PGT-A by NGS was performed simultaneously.

DESIGN: Experimental study.

MATERIALS AND METHODS: A primer pair amplifying 214bp amplicon which covered the 87bp deletion was designed and added to the primer pool for PGT-A and c.266+2T>C point mutation. c.266+2T>C point mutation was detected by Taqman assay. Sequencing was performed on Illumina NextSeq 550 using single 150bp reads. Reads were aligned to a human referenc genome (GRCh37/hg19) with the Burrows-Wheeler Aligner (BWA). PGT-A was analyzed using an in-house clinical established bioinformatics workflow. c.4531_4564-42del was evaluated using Integrative Genomics Viewer (IGV) 2.3.

RESULTS: The workflow was validated on parental DNA and 5-cell samples. Eight TEs from usable blastocysts were tested for PGT-A and COL7A1 PGT-M. All the embryos were euploid. One embryo inherited maternal c.266+2T>C point mutation, three embryos had paternal c.4531_4564-42del variant, and one embryo showed compound heterozygous, which would not be suitable for transferring. The remining three embryos were negative for both mutations. There were four carrier embryos and three wild type embryos available for transfer.

CONCLUSIONS: This study provided a new strategy to access the microdeletion for PGT-M when there is no linkage analysis available.

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HOW EFFECTIVE IS TARGET SEQUENCE ENRICHMENT DURING WHOLE GENOME AMPLIFICATION ON THE IMPROVEMENT OF PGT-M RESULTS? Evrim Unsal, Assoc Prof,[1] Leyla Ozer, MD, PhD,[2] Merve Polat, PhD,[2] Suleyman Aktuna, PhD,[2] Volkan Baltaci, MD, PhD[3] [1]cinnah caddesi 47/1, ankara, Turkey; [2]Yuksek Ihtisas University, Ankara, Turkey; [3]Yozgat Bozok University, Yozgat, Turkey.

OBJECTIVE: PGT-M has been applied for many years for any genetic disease that can be diagnosed. Development of Whole Genome Amplification (WGA) technologies enabled simultaneous monogenic disease testing and euploid embryo selection (combined PGT). As a result of widespread use of whole exome/genome sequencing technologies, variety of single gene diseases referred for PGT-M has started to increase thus leading to a considerable elevation in the number of setup studies conducted for rare diseases.

DESIGN: In this context, a steady test setup and uniform WGA unaffected by the Alel Drop Out (ADO) trap, has become a necessity. For this purpose, here we demonstrate that ADO ratio is reduced for a wide range of PGT-M conditions using target sequence enrichment (TSE), which also allows sequential aneuploidy screening.

MATERIALS AND METHODS: 739 biopsy samples from 118 PGT-M patients were classified in three groups: PGT-M only (group 1; 389 biopsy samples/56 patients), combined PGT (group 2; 108 biopsy samples/23 patients), combined PGT with TSE (group 3; 242 biopsy samples/39 patients). Doplify Kit (PerkinElmer) and in house designed target sequence specific primers were used for WGA. Initially, routine STR based PGT-M protocol using biopsies directly (group 1), WGA products without TSE (group 2) or with TSE (group 3) was followed. After the selection of eligible embryos, WGA samples were further processed using PG-Seq Kit (PerkinElmer), with (10 samples) or without further mutation specific enrichment for direct mutation analysis and aneuploidy screening.

RESULTS: According to our findings, ADO ratio was 2% and 7.1% for group 1 and 2 respectively. On the other hand, ADO ratio for group 3 was 3% showing that TSE protocol dramatically reduces ADO ratio compared to similar patient gropus without TSE. Eventhough blastomere use for WGA is contradictory, blastomere biopsies were included in this study. ADO ratio was unquestionably high for blastomere; 8.1% in group 1 and 13.3% in group 2. Only 7 blastomere biopsies from 2 patients were included in group 3 and ADO was not observed. In order to prove this result, additional data for blastomere cell type are needed. Moreover, we further processed 30 WGA products obtained from group 3 for both mutation confirmation and aneuplody screening. This methodology allows us to detect mutation regions with high read depth (500X-4000X) together with aneuploidy screening for 24 chromosomes.

CONCLUSIONS: In combined PGT applications, WGA is the most critical stage and TSE increases the accuracy of the test. Eventhough a potential saturation in STR markers is expected , the number of new designs for novel conditions is still increasing annually. Most patients referred to our center carries a rare disease thus STR markers are designed almost solely for that patient. This creates an extensive STR bank which is seldomly used for a couple of cases due to this high variability in PGT demand. TSE method is valuable especially for such laboratorie,since it allows combination of PGT-M and PGT-A by using existing STR markers and primers thus enables efficient use for primers for rare disorders.

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COMPARISON OF ETHICAL PERSPECTIVES OF INDIVIDUALS CONSIDERING PREIMPLANTATION EMBRYO GENETIC TESTING FOR ANEUPLOIDY (PGT-A) VS. MONOGENIC DISORDERS (PGT-M). Jiahui Zhang, BA,[1] Lisa M. Pastore, PhD,[2] Lisa R. Rubin, PhD[3] [1]Renaissance School of Medicine at Stony Brook University, Stony Brook, NY; [2]Stony Brook Medicine, Stony Brook, NY; [3]The New School, New York, NY.

OBJECTIVE: To identify and compare patient perspectives toward the ethics of preimplantation genetic testing among patients considering using PGT to screen for aneuploidy (PGT-A) and monogenic disorders (PGT-M).

DESIGN: A cross-sectional study of patient perspectives using an online questionnaire.

MATERIALS AND METHODS: A 17-item questionnaire was created to assess various ethical concerns regarding the use of PGT, including clinical indications for PGT, the greater implications of PGT for society, and unused embryo disposition. A total of n=152 patients from 31 US states who recently considered using PGT-A (n=80) or PGT-M (n=72) completed the questionnaire. Chi-square and Fishers' exact tests were run in STATA with α=0.05.

RESULTS: The majority of respondents in both PGT-A and PGT-M groups were female (92%), married (91%), white non-Hispanic (80%), and educated at or beyond a college level (89%). The majority of both PGT-A and PGT-M considerers supported using PGT to screen for diseases fatal in childhood (86-89%), those causing lifelong disabilities (76-79%), and those arising in adulthood and have no treatment (60-67%). Similar proportions of PGT-A and PGT-M considerers opposed using PGT to screen for physical (80-87%) or intellectual traits (74-86.0%). More PGT-M than PGT-A considerers opposed the implantation of genetically abnormal embryos when requested by parents (29% PGT-A vs. 56% PGT-M, $p = 0.007$). Respondents in both groups agreed that PGT aids in parental decision-making, although some expressed concern over its potential to further socioeconomic inequalities or lead to unforeseen consequences. Regarding the disposition of embryos without known genetic defects, more PGT-A considerers favored freezing (95% PGTA vs. 82% PGT-M, $p = 0.018$) or donating to research (73% PGT-A vs. 57% PGT-M, $p = 0.044$) than PGT-M considerers. For embryos with known genetic abnormalities, more PGT-M considerers supported donating to research than PGT-A considerers (56% PGT-A vs. 81% PGT-M, $p = 0.001$).

CONCLUSIONS: PGT-A and PGT-M considerers agreed on the clinical indications for PGT by supporting its use in screening for disease conditions and opposing its use in trait selection. PGT-A and PGT-M considerers also agreed that PGT aids in parental decision-making. More PGT-M considerers opposed the implantation of a genetically abnormal embryo when requested

by parents. More PGT-A considerers supported freezing embryos without known genetic defects or donating them to research, while more PGT-M considerers supported donating embryos with known genetic defects to research.

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PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDIES (PGT-A) IS NOT ASSOCIATED WITH IMPROVED LIVE BIRTH RATES IN PATIENTS UNDER 35 YEARS OLD. Elnur Babayev, MD, MSc,[1] John X. Zhang, PhD,[2] Marymllen Pavone, MD[1] [1]Northwestern University, Chicago, IL; [2]Northwestern Medicine, chicago, IL.

OBJECTIVE: Preimplantation genetic testing for aneuploidies (PGT-A) is being widely used in ART practice. Although the rate of aneuploidy is significantly lower in younger patients, the availability of PGT-A has led to significant utilization of this technology in this group. The goal of this study was to analyze the association of PGT-A with live birth rates (LBR) in patients under 35 years old.

DESIGN: This was a retrospective observational study

MATERIALS AND METHODS: We analyzed single blastocyst transfer outcomes in patients <35yo in our institution from Jan/1/2015 to Jun/1/2018. Only the first embryo transfers in each group were evaluated. Outcomes of first fresh blastocyst transfer was compared to first frozen blastocyst transfer with or without PGT-A. Live birth rates were compared using Odds Ratio. Chi-Square test was used for statistical analysis. $p < 0.05$ was considered statistically significant. We also compared clinical pregnancy rate (CPR), miscarriage, biochemical and ectopic pregnancy rates among groups.

RESULTS: 264 fresh single blastocyst and 228 frozen single blastocyst transfers were performed, which included 158 untested (FET) and 70 euploid embryos (FET-euploid). 65% of all biopsied embryos were euploid. Overall, live birth rate was 52.5%. LBR following fresh ET was 48.5%. Euploid transfers had 58.6% LBR, and for untested FETs this number was 56.3%. FET alone or FET with euploid blastocysts was not associated with increased live birth rates when compared to fresh transfers in patients <35yo, OR 1.39 (95% CI 0.93-2.07) and 1.5 (95% CI 0.88-2.55), respectively. This analysis showed a non-significant trend of increased LBR in FET and FET-euploid groups compared to fresh transfers. However, LBR was not different between FET and FET with euploid groups, OR 1.08 (95% CI 0.61-1.91). CPR showed a similar trend, but was not significantly different between fresh, FET and FET-euploid groups. Miscarriage rates were also not significantly different; 16%, 14%, and 13% for fresh, FET and FET-euploid cycles, respectively. We had 4 ectopic pregnancies in fresh transfer group and one in FET group. Biochemical pregnancy rate was significantly lower in FET group 0.25 (CI 95% 0.11-0.58) compared to fresh transfers, but not significantly different between FET and FET-euploid groups.

CONCLUSIONS: PGT-A is not associated with improved live birth rates in patients <35yo. The trend of increased LBR observed in this age group with FET cycles, both untested and FET-euploid, is likely secondary to cryopreservation and subsequent embryo transfer in frozen cycle, which points to the role of endometrial factors. Prospective studies examining the role of PGT-A in younger patients should compare euploid embryo transfers to frozen untested embryo transfers, instead of fresh transfers, given potential benefit of cryopreservation in this age group. Decreased biochemical pregnancy rate in FET cycles at least partially explains the trend of increased LBR compared to fresh cycles in our study.

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PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY: IS IT REALLY COST EFFECTIVE? Michael Saad-Naguib, MD, Douglas Timmons, MD, MPH, George R. Attia, MD, MBA University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: Preimplantation genetic testing for aneuploidy (PGT-A) is increasingly used in patients undergoing in vitro fertilization (IVF).[1] However, this is not without debate.[2] Physicians must also factor in additional costs for aneuploidy testing. Neal et al. created a decision analytic model showing IVF with PGT-A can reduce costs when compared to IVF alone in patients with more than 1 embryo.[1] However, the multi-center STAR trial by Munne et al. concluded PGT-A did not improve overall pregnancy outcomes in all women.[2] With this new finding, we question the cost efficacy of PGT-A. To our knowledge, no cost efficacy studies have been done with the findings of the STAR trial. We plan to demonstrate a theoretical model using the new findings from the STAR trial in which we will determine if PGT-A is cost effective.

DESIGN: An IRB exempt hypothetical cost-analysis study.

MATERIALS AND METHODS: In this hypothetical study, we created a comparison model with 100 patients undergoing single frozen embryo transfer in a PGT-A group and 100 control IVF patients. We performed an analysis between patients less than 35 years old and a subsequent analysis looking at patients 35-40 years old. Procedural costs were based on those used in our clinic. All costs up to the point of embryo biopsy were assumed to be equal. Pregnancy and live birth rates in the non-PGT group were based on SART data. The percentage of euploid embryos in the PGT-A group were obtained from the STAR trial. Each group of patients was then taken thru 2 frozen embryo transfer cycles. After this, the cost per live birth in each cycle and the average cost per live birth over two cycles was determined.

RESULTS: In patients less than 35 years old undergoing IVF without PGT, the cost per live birth in the 1st cycle was $12,500, while the cost per live birth after the second cycle was $26,785. In women under 35 undergoing IVF with PGT-A, the cost per live birth after one cycle was $21,250, and the cost after two cycles was $31,250. In patients 35-40 years old using IVF without PGT-A, the cost per live birth was $18,518 after one cycle and $42,800 after the second cycle. In the 35-40 year old PGT-A group, the cost per live birth after one cycle was $26,176. After two cycles, the cost was $36,176. The average cost per live birth over 2 cycles in patients under 35 with and without PGT-A was $24,583 and $17,417, respectively. The average cost per live birth over 2 cycles in patients 35-40 years old with and without PGT-A was $29,637 and $27,190, respectively.

CONCLUSIONS: This data further demonstrates PGT-A is not cost effective in patients under 35 years old. In light of the new data from the STAR trial, in patients 35-40 years old, PGT-A is cost neutral if a patient requires two cycles of frozen embryo transfer.

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SUPPORT: No financial support

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THE INCIDENCE AND PARENTAL ORIGIN OF WHOLE AND SEGMENTAL ANEUPLOIDIES IN HUMAN IMPLANTATION EMBRYOS. Jing Wang, M.D,[1] Baomin Lu bachela.[2] [1]Medical genetic, Guangzhou, China; [2]medical examination, guangzhou, China.

OBJECTIVE: To investigate the incidence and parental origin of whole and segmental aneuploidies in human early embryos and identify the relationship between the aneuploidies and parental origin and age.

DESIGN: This is a retrospective observational study. A total of 2232 trophectoderm biopsies from 235 couples who underwent 278 PGT-M cycles from 2015 to February 2020 were identified.

MATERIALS AND METHODS: The average age of the female was 31.76±4.075 years, while that of the male was 34.26±5.137 years. All couples had normal karyotypes, due to monogenetic disease to perform with preimplantation genetic testing. Aneuploidy screening was performed by quantitative analysis by SNP array. Meanwhile, haplotypes were constructed using the genotypes of the parent and the reference. Then, the parental origin of aneuploidy was determined by the haplotype results of the embryo.

RESULTS: In 2232 biopsy samples, the incidence of chromosomal aneuploidy (both whole and segment) was 27.2% (608/2232). Only one chromosomal aneuploidy was detected in 462(76.0%) of the TE samples, of which 437 involved autosomal chromosomes. 73.7% (322/437) were the whole chromosome aneuploidies, and 26.3% (115/437) were segmental aneuploidies. The trisomy accounted for 39.8%, and the monosomy accounted for 60.2%. The whole chromosome abnormally was mainly caused by the maternal chromosome abnormality. On the contrary, the segmental aneuploidy was mainly caused by the paternal chromosome abnormality. The incidence of whole chromosome aneuploidy from maternal chromosome errors was higher in the group of women over the age of 35 years, comparing with the group of women under the age of 35 years (trisomy, 9.0% *vs* 3.2%, *p=0.000*; monosomy, 12.5% *vs* 5.3%, *p=0.000*). There was no significant difference in segmental aneuploidy between mother and father ages.

CONCLUSIONS: Only single autosomal abnormalities were analyzed. The whole chromosome abnormally was mostly caused by the abnormality of maternal origin, and the haplotype analysis of trisomy showed that it was mostly caused by the error of MI. The incidence of trisomy and monosomy was increased with the increase in maternal age. For segmental aneuploidy, especially the loss, it seems that paternal abnormalities were more common. Neither paternal segment loss nor maternal segment loss was associated with age.

P-811 4:30 PM Tuesday, October 20, 2020

PGT-A DOESN'T SEEM TO BENEFIT RECURRENT IMPLANTATION FAILURE COUPLES TO OPTIMIZE LIVE BIRTHS. Krishna Mantravadi, Sr., MBBS, PGDHOM, Masters in clinical embryology, Shankhadeep Debnath, MSC Molecular Biology and Biotechnology, Nandita Relekar Sanjay Relekar, Master in Clinical embryology, Durga Gedela Rao, Sr., MRCOG Oasis fertility, Hyderabad, India.

OBJECTIVE: To assess the role of Pre-Implantation Genetic Testing for Aneuploidy (PGT-A) in couples with Recurrent Implantation failure (RIF) to optimize Live Birth Rates (LBR).

DESIGN: This is retrospective data of couples at our private fertility teaching clinic, with RIF and undergoing PGT-A (n=54) during January 2014 to July 2019. Women with RIF and no PGT-A acted as control (n=189) for this study. Women with at least two fresh/frozen embryos transfers with minimum 4 blastocysts transferred in total and never conceived were considered as RIF and offered PGT-A.Only women with one euploid embryo, who underwent frozen embryo transfers (FET) were recruited in this study.Women of all age groups who had Blastocysts available for transfer were included in the study.Only self-gamete cycles were considered in this study.

MATERIALS AND METHODS: All the women with RIF underwent controlled ovarian stimulation and oocyte retrieval as per our clinic's standard operating protocol (SOP). ICSI was the choice of insemination considering history of failed implantation, fertilized oocytes were cultured till blastocysts and freeze all policy was adopted. Blastocysts were biopsied and trophectoderm tissue was subjected to genetic testing through Next-Generation Sequencing (NGS). Study group women underwent elective Single Euploid Blastocyst transfer (eSET) and control group women underwent transfer with un-screened double Blastocyst Transfer (DET) in a frozen cycle. Primary Outcome was LBR and secondary outcomes – Miscarriage Rates (MR), Multiple Pregnancy Rates (MPR), Implantation Rates (IR) and Time To Pregnancy (TTP) (from Oocyte retrieval to clinically viable pregnancy)

RESULTS: Mean of Reproductive outcomes in Study Vs Control Group were as follows:

IR - 47.50 % vs. 41.50% (p value 0.45)
MR - 9.25% vs. 17.89% (p value 0.18)
MPR- 0% Vs 17% (p value 0.0012)
LBR - 46.8% vs 45 % (p value 0.82)
TTP was 6.5 months vs. 9.5 month.

Outcomes in Study and Control Group are comparable in this study. eSET of Euploid embryo and Un-Screened DET seem to be offering similar pregnancy outcomes in RIF patients, except for higher MPR in control group.

Data from this study is questioning the role of PGT-A in RIF patients to improve LBR. Transferring a Euploid eSET only seems to offer lower MPR and shorter TTP in RIF couples.

CONCLUSIONS: PGT-A for RIF couples doesn't seem to improve take home baby rates. Couples need to be counselled appropriately while offering PGT-A for RIF.

P-812 4:30 PM Tuesday, October 20, 2020

DOES POOR BLASTOCYST MORPHOLOGY IMLPY LOWER EUPLOIDY RATE IN PATIENTS UNDERGOING PGT-A? Shujing He, MM,[1] Lei Jia, Master,[2] Wenlong Su, MS,[3] Cong Fang, PHD, MD[4] [1]The Sixth Affiliated hospital of Sun Yat-Sen University, Guangzhou, China; [2]Reproductive Medicine Research Center, Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; [3]Sixth Affiliated hospital of Sun Yat-Sen University, Guangzhou, China; [4]The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: The aim of this study is to figure out whether poor blastocyst morphology implies lower euploidy rate and whether blastocysts of low morphological scores deserve to be performed trophectoderm (TE) biopsy.

DESIGN: This is a single center retrospective observational study performed between June 2018 and April 2020.

MATERIALS AND METHODS: The study included the data analysis of 798 blastocysts from 197 couples undergoing preimplantation genetic testing for aneuploidies (PGT-A) via next generation sequencing. According to the patients' chromosome karyotype, blastocysts were divided into two groups: preimplantation genetic screening (PGS, patients with normal chromosome karyotype) and preimplantation genetic diagnosis (PGD, patients with chromosomal rearrangements). According to the Gardner grading system, the morphological score of good quality blastocyst was $\geq$3BB, and that of poor quality blastocyst was <3BB (including 3BC, 3AC, 4BC, 4CB, 4CA and 4AC). We also analyzed the impact of maternal age by dividing female into young group (age<35) and old group (age$\geq$35). Chi-square test was used to assess differences. All statistical analysis was performed using SPSS 22.0. P <0.05 were considered to be statistically significant.

RESULTS: Euploidy rate in total PGT-A was 41.2% (259/628) and 28.2% (48/170) in good and poor quality blastocyst groups, respectively (P<0.01). In PGD group, euploidy rate was 37.1% (159/429) and 18.9% (18/95) in good and poor quality blastocyst groups (P<0.01), which indicated that blastocyst morphology was significantly associated with genetic condition (euploidy or aneuploidy). Whereas, there was no statistical differences in PGS group. For patients undergoing PGS, euploidy rate was 50.3% (100/199) and 40.0% (30/75) in good and poor quality blastocyst groups, respectively (P>0.05). When considering maternal age, in young group, there was strong association between blastocyst morphology and euploidy rate. Euploidy rate was 42.5% (211/497) and 29.8% (39/131) in good and poor quality blastocyst groups, respectively in young group (P<0.01). But in old group, euploidy rate was36.6% (48/131) and 23.1% (9/39) in good and poor quality blastocyst groups (P>0.05).

CONCLUSIONS: Poor blastocyst morphology implied lower euploidy rate in patients undergoing PGD. For patients undergoing PGS, it is worthy to perform trophectoderm (TE) biopsy of blastocysts of low morphological scores. And TE biopsy of poor quality blastocysts may benefit the patients with advanced maternal age.

SUPPORT: Found Program: Medical Scientific Technology Research Foundation of Guangdong Province of China (A2020226); National Natural Science Foundation of China (81801449)

P-813 4:30 PM Tuesday, October 20, 2020

NON-INVASIVE CHROMOSOME SCREENING AND ITS CORRELATION AGAINST RANKING PREDICTION MADE BY ERICA, A DEEP-LEARNING EMBRYO RANKING ALGORITHM. Alejandro Chavez-Badiola, MD,[1] John J. Zhang, MD, PhD,[2] Adolfo Flores-Saiffe Farias, Sr., MSc, PhD,[1] Gerardo mendizabal-Ruiz, PhD,[3] Meir Olcha, MD,[4] Andrew J. Drakeley, MD FRCOG,[5] IVF 2.0[1]IVF 2.0 LTD, Maghull, United Kingdom; [2]New Hope Fertility Center, New York City, NY; [3]Universidad de Guadalajara, Guadalajara, Mexico; [4]New Hope Fertility Center, New York, NY; [5]Liverpool Women's Hospital, Liverpool, United Kingdom.

OBJECTIVE: to compare euploidy predictions made by ERICA, a deep-learning embryo-ranking tool, against the results of a non-invasive chromosomal screening (NICS)

DESIGN: prospective, comparative study at a single New Hope Fertility Center

MATERIALS AND METHODS: blastocyst images aimed for NICS were collected through the erica.embryoranking.com platform over six consecutive months (September 2019 to March 2020). Inclusion criteria were i) NICS performed on all the embryos at blastocyst stage in the given cycle; ii) woman's age <45 years old. Exclusion criteria included: i) Genetics' report of mosaics; ii) insufficient DNA report or mosaicism; iii) unclassifiable embryos due to low quality images. ERICA's generated prognoses were retrieved from the platform, and compared against the NICS report using confusion matrix analysis. True euploid proportion Z test was performed between the good/bad prognosis groups in relation to ERICA's predictions.

RESULTS: a total of 595 embryo images (218 cycles), were considered for this study. After applying inclusion and exclusion criteria, only 109 embryo images were included for analysis (29 euploid). 46 images were excluded due to age constraints; 410 due to poor quality in the image; 5 due to insufficient DNA; and 34 due to a report of mosaics. ERICA had a 0.75 specificity and an overall accuracy of 0.66 against NICS report. Euploid proportion of poor prognosis embryos according to ERICA (score < 0.5) was 17/77 (22%); euploid proportion of good prognosis embryos (ERICA score >0.5) was

12/32 (37.5%). We computed the Z-score for two population proportions and obtained Z= -1.66, for a p-value of 0.0485.

CONCLUSIONS: on the one hand, predicting ploidy has proven challenging even for well stablished although controversial tests (i.e. T-biopsy PGT-A). On the other hand, ERICA has previously shown a good correlation against PGT-A. Since both NICS, and ERICA are non-invasive studies aimed at classifying embryos in accordance to their ploidy status, we wondered if the previous correlation shown against PGT-A were to be maintained in this feasability study. Results suggest ERICA was better than chance at predicting ploidy, although it didn't achieve the previously reported accuracy against PGT-A, we expect further training, and a larger testing sample might improve ERICA's predicting capabilities. NICS still has to prove its value as a replacement for the classic PGT-A, which lends an opportunity to test, in a future study, the outcome of the combination of both technologies as a comprehensive non-invasive embryo assessment. Although reporting on DNA amplification during NICS is beyond the reach and objective of this study, we found the low rate of tested embryos with failed DNA amplification noteworthy (<1%). Further studies testing ERICA against NICS should increase the sample size.

P-814 4:30 PM Tuesday, October 20, 2020

DOES PRE-IMPLANTATION GENETIC TESTING FOR ANEUPLOIDY OPTIMISE THE REPRODUCTIVE OUTCOMES INWOMEN WITH IDIOPATHIC RECURRENT PREGNANCY LOSS? Krishna Mantravadi, Sr., MBBS, PGDHOM, Masters in clinical embryology,[1] Sherin Mathew, MSc,[1] Shivanand Soorve, Sr., BSc,[1] Durga Gedela Rao, Sr., MRCOG,[1] Sandeep Karunakaran, Sr., M.B.B.S, MS, PGDHM, PGDMLE[2] [1]Oasis fertility, Hyderabad, India; [2]oasis fertility, Hyderabad, India.

OBJECTIVE: To evaluate the role of Pre-Implantation Genetic Testing for Aneuploidy (PGT-A) for improving live birth and reducing miscarriage in patients with Idiopathic Recurrent Pregnancy Loss (RPL).

DESIGN: This is a retrospective study where patients with previous two or more pregnancy loss (idiopathic) who underwent IVF cycles in the period of January 2014 to June 2019 were considered. A total of 112 patients were analysed for the study. Out of which 82 patients underwent PGT-A (n=82) and 30 patients did not underwent PGT-A (n=30), but had history of RPL considered as the control group.

MATERIALS AND METHODS: All the women underwent controlled ovarian stimulation and oocyte retrieval as per our clinic's standard operating protocol (SOP). ICSI was the choice of insemination considering history of multiple pregnancy loss, fertilized oocytes were cultured till blastocysts. Day 5, day 6 biopsy was done in study group and freeze all policy was adopted. Trophectoderm biopsy and Next-Generation Sequencing (NGS) were used for PGT-A. Study group underwent elective Euploid Single Embryo Transfer (eSET) in a Frozen Embryo Replacement cycle (FET). Control group underwent transfer of two blastocysts (DET) in FET cycle. Live Birth Rate (LBR), Multiple Pregnancy Rates (MPR) and Miscarriage Rate (MR) were considered as primary outcomes. Aneuploidy rates were evaluated in the study group.

RESULTS: Mean reproductive outcomes in Study Vs Control group were as follows: MR - 9.68% vs 23.33% (p value 0.0610) MPR – 0% Vs 10% (p value 0.0039) LBR- 32.32% vs 30.00% (p value 0.8160) Aneuploidy in Study group - 55.74% No difference in LBR was observed when PGT-A was introduced in RPL patients. However a marked reduction in MR was observed with PGT-A in RPL patients. In Idiopathic RPL women, though the incidence of miscarriage comes down with transfer of an Euploid embryo, take home baby rates doesn't seem to improve. Role of PGT-A for RPL women needs further research through well designed randomized control trials.

CONCLUSIONS: PGT-A as an intervention for Idiopathic RPL women doesn't seem to improve Live Birth.

P-815 4:30 PM Tuesday, October 20, 2020

IS IT POSSIBLE TO DETECT ALL SEGMENTAL CHROMOSOMAL IMBALANCES WITH NGS USING CUSTOM ANALYSIS ALGORITHMS? Merve Polat, PhD,[1] Volkan Baltaci, MD, PhD,[2] Leyla Ozer, MD, PhD,[1] Evrim Unsal, Assoc Prof,[3] Suleyman Aktuna, PhD[1] [1]Yuksek Ihtisas University, Ankara, Turkey; [2]Yozgat Bozok University, Yozgat, Turkey; [3]cinnah caddesi 47/1, ankara, Turkey.

OBJECTIVE: Next Generation Sequencing (NGS) has been used for PGT of chromosome rearrangements with a resolution of ≥ 5-20 Mb, which is declared detection limit of available commercial kits. However, many patients carry a chromosome rearrangement below these detection limit values thus a customized analysis approach enables effective use of this method for a broad range of chromosomal imbalances.

DESIGN: In this study we aimed to detect small unbalanced chromosome segments (≥1 MB) below manufacturer's recommended resolution limits.

MATERIALS AND METHODS: NGS library of genomic DNA from 4 patients with unbalanced segmental imbalances were prepared using PG-Seq Kit 2.0 (PerkinElmer), 48 samples were sequenced with MiSeq (Illumina) and analysed with PG-Find Analysis Software. Six small unbalanced chromosome segments previously detected with Microarray were evaluated with the sizes of 0.5 MB to 4.5 MB. Three of patients included in the study had products of familial subtelomeric translocations and one of them had a product of familial paracentric inversion. Reanalysis was performed for samples, where standard analysis fails to detect target rearrangements with specific analysis algorithm to focus on target regions by altering filtering paramateres. Each sample was assessed for the size of the segmental gain/loss (Mb), copy number for each segment, concordance with Microarray results and was compared in terms of different algorithms we used.

RESULTS: NGS was capable of detecting 7/8 (87.5%) unbalanced segments previously identified using Microarray. 6/8 (75%) of variants were ≤4.5 Mb. The rest of variants were 8.6 MB and 17.9 MB respectively (Table 1). One of the variants was very small (0.5MB) that we couldn't detect by NGS. According to assessment of individual data quality, optimum number of reads was 500000 per sample to detect segmental gains/losses ≥1 MB.

CONCLUSIONS: This study has shown that analysis with different filtering algorithms makes NGS qualified to detect unbalanced chromosome rearrangements ≥1 Mb. Further studies can be designed with lower sample size (24) in order to increase read/sample, which may enable detection of chromosomal imbalances bellow 1 MB. Further studies with PGT samples should be required to define the detection limit of NGS method.

Table 1. True positive detection of CNV's with customized analysis algorithm is presented.

CNV Size	Standard Algorithm	Customized Algorithm
1,4 MB	NO	YES
17,9 MB	YES	YES
2,6 MB	NO	YES
1,15 MB	NO	YES
1,2 MB	NO	YES
4,5 MB	NO	YES
8,6 MB	YES	YES
0,5 MB	NO	NO

POSTER SESSION: REGENERATIVE MEDICINE AND STEM CELLS

P-816 4:30 PM Tuesday, October 20, 2020

EXOSOMES DERIVED FROM MENSTRUAL BLOOD-DERIVED STROMAL CELLS RESTORED OVARIAN FUNCTION IN RAT MODEL OF PREMATURE OVARIAN INSUFFICIENCY. Siwen Zhang, Master, Jichun Tan, PhD, Pingping Li, PhD Shengjing Hospital of China Medical University, shenyang, China.

OBJECTIVE: Premature ovarian insufficiency (POI) is one of the major causes of infertility. We previously demonstrated that transplantation of menstrual blood-derived stromal cells (MenSCs) effectively improved ovarian function in POI murine model. Recent studies indicated that MSC-derived exosomes were important components in tissue repair and enhanced oocyte activity in vitro. In this study, we investigated the therapeutic effects of exosomes derived from MenSCs (MenSCs-Exos) in POI model and its mechanism in restoring ovulation.

DESIGN: MenSCs-Exos was prepared from serum-free culture media of MenSCs by ultra-centrifugating. Rat POI models were established and we

evaluated the therapeutic effect of MenSCs-Exos on ovarian restoration *in vivo* and its mechanism.

MATERIALS AND METHODS: Rat POI models were established by intraperitoneally injection of VCD. 48 POI model rats were randomly assigned to four groups received different treatment: PBS, MenSCs, MenSCs-Exos and exosome-free MenSCs culture supernatant. Estrous cycle, ovarian morphology, follicular composition, serum hormones, fertility and molecular changes were investigated.

RESULTS: MenSCs-Exos significantly promoted the proliferation and development of primordial and primary follicles. MenSCs and MenSCs-Exos were stromal tropism in POI ovaries. Both MenSCs and MenSCs-Exos application effectively restored the estrous cycle, regulated the serum level of E2 and AMH and FSH, markedly improved the live birth outcome in POI rats. MenSCs and MenSCs-Exos treatment regulated the compositions of follicular extracellular matrix and up-regulated the expressions of Dazl and Foxl2 in ovary cortex.

CONCLUSIONS: Overall, MenSCs-Exos markedly improved ovarian reserve and promoted fertility in POI rats, suggesting an ovarian restorative effect. The therapeutic effect of repeated application of MenSCs-Exos was sustainable, which was consistent with that of MenSCs transplantation. Our results indicated MenSCs-Exos is a promising cell-free bioresource in the treatment of POI.

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LONG-TERM ENGRAFTMENT AND SAFETY OF HUMAN BONE MARROW DERIVED CD133+ CELLS IN A RAT MODEL OF ASHERMAN'S SYNDROME. Xavier Santamaria, MD, PhD,[1] Nanda Kumar, PhD,[2] Carlos Simon, MD, PhD[3] [1]Asherman Therapy, Paterna, Spain; [2]Universitat de Valencia, Paterna, Spain; [3]Igenomix Foundation, INCLIVA, Valencia, Spain, Department of Obstetrics and Gynecology, Valencia University, valencia, Spain, Department of Obstetrics and Gynecology, BIDMC, Harvard University, Boston, MA- USA Boston, U.S.A., Valencia, Spain.

OBJECTIVE: Asherman Syndrome (AS) is defined by presence of intrauterine adhesions, due to the loss of endometrial stem cells. CD133+ bone marrow-derived stem cells (BMDSCs) contribute to human endometrium regeneration and represent an advanced cell therapy to treat this disease. Our aim is to describe the short-term and long term engraftment as well as safety and Mechanisms of Action (MoA) of pure and stable population of human CD133+ cells in a model of AS with athymic rats.

DESIGN: Prospective randomized controlled trial in AS athymic rats conducted in Good Laboratory Practice (GLP) and Good Manufacturing Practices (GMP) conditions.Human cells were obtained from voluntary donors from the study PreENTIRE (NCT03665649)

MATERIALS AND METHODS: CD133+ BMDSCs were mobilized after injecting Granulocyte Colony Stimulating Factor in three healthy donors with a mean age of 34,4 years-old (range 22-43), and isolated with CliniMACS. Potency, stability and viability was assessed as well as FACS analysis for peripheral blood markers (CD56, CD66b, CD14,CD19, CD3, CD45 and CD34) and endothelial markers (CD31, VE-Cadherin, VEGFR-2, CXCR4 and CD133).In vitro exosome secretion and trasdifferentiation was confirmed. A total of 2mL with a mean of 1,72x106 cells/mL (range 1,26-2,36 x106 cells/mL) CD133+ BMDSCs were intra-arterially injected into athymic female nude rats (n=33) distributed into two experimental groups: group A treated with vehicle and group B with CD133+ cells throughout a catheter implanted in the carotid artery towards the heart. AS was previously induced in the left uterine horn 2 weeks prior to administration and each of these groups were assessed 24 hours, 14 days and 6 months after instillation. Uterine cell engraftment was assessed by Immunohystochemistry of both horns (damaged and non damaged) of the mice with the specific human nuclear protein Ku80. Additional markers such as human specific CD133 were assessed. Finally, safety assessment relied on mortality, local and systemic clinical signs, body weight and food consumption recorded throughout the study period, in addition to clinical pathology determinations and histopathological evaluation of 21 tissues performed at sacrifice.

RESULTS: The results of this experimental study showed that human CD133+ BMDSCs remain in the endometrial tissue up to six month after stem cell instillation.However, engrafted cells express Cd133 marker 48h hours after instillation but this maker progressively disappeared at 14 days and 6 months. Moreover, a higher engraftment was observed in damaged horns and human cells seem to be aggregated in a clonal manner, specially in the group of 6 months after stem delivery.Regarding safety, the administration of these cells didn't display significant side effects representing a long-term safe treatment in this animal model.Hystopathologically, not pathological findings were associated with this treatment in none of the 21 different tissues assessed.

CONCLUSIONS: CD133+BMDSCs represent a safe therapy with engraftment potential up to six months after stem cell therapy. CD133 expression decreases in engrafted cells after 6 months.

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P-818 4:30 PM Tuesday, October 20, 2020

miRNA-144 INCREASES ESTROGEN-PRODUCING GENES EXPRESSION AND SUPPRESS APOPTOSIS IN HUMAN GRANULOSA CELL LINE. Sahar Esfandyari, DVM The University of Illinois College of Medicine, Chicago, IL.

OBJECTIVE: Primary ovarian insufficiency (POI) — also called premature ovarian failure — occurs when the ovaries stop functioning normally before age 40 and often leads to infertility. POI is frequently caused by chemotherapy in cancer patients. Chemotherapy reagents are Gonadotoxic and destruction granulosa cells, which are vital for oocyte maturation and follicular development. The incidence of POF is growing and the underlying molecular mechanisms are not still clear. However, women with POF exhibited downregulation of miRNA-144 in their plasma compared with normal women. miRNA-144-5p also has been shown to be downregulated in the POF tissues of animal models compared with that in normal ovarian tissues. Recently published reports have described that intraovarian transplantation of human mesenchymal stem cells (hMSCs) can restore fertility in a chemotherapy-induced POI mouse model. A previous study demonstrated that various growth factors, cytokines, and miRNAs (including miRNA-144), both free and in exosomes are secreted by Bone marrow mesenchymal stem cells. In this study, we evaluated the effects of miRNA-144 mimic on estrogen synthesis such as CYP19A1, StAR and also apoptosis genes expression and secreted estrogen level using human non-luteinized granulosa cell line (HGrC1).

DESIGN: We hypothesize that HGrC1 cells transfected with miRNA-144 mimic will exhibit an increase in the estrogen synthesize gene expression and estrogen level.

MATERIALS AND METHODS: HGrC1 were seeded on 6-well plates at a density of 3×10^5 cells per well and cultured for 24 hours. Cells were transfected with different concentrations 25 and 50 pM of mirVana has-miR-144-5p mimic or negative control-1 mimic using manufacturer protocol. After 24 hours of transfection the medium changed with regular media and after 24 h HGrC1 cells and conditioned media were collected for analysis. The mRNA and protein expression of CYP19A1, StAR, AKT-I, Bax and Caspase3 were quantified by RT-PCR and Western blot, while estrogen level in media was measured by Automated chemilumenescence immunoassay system.

RESULTS: Human HGrC1 cells transfected with 50pM of miRNA-144-5p mimic secreted significantly higher level of estrogen (9.28 $\pm$ 0.5 pg/ml) compared to control C (7.335 $\pm$ 0.1 pg/ml) ($P<0.05$). the expression level of estrogen synthesizing genes CYP19A1 and StAR was significantly increased ($p<0.05$). The expression of anti-apoptosis gene AKTI increased significantly at mRNA and protein level ($p<0.05$) while the expression of apoptotic genes Bax and caspase3 was significantly decreased ($p<0.01$) at RNA level.

CONCLUSIONS: The miR-144-5p mimic induced a significant upregulation in estrogen-producing pathway genes and decrease apoptosis in human non-luteinized granulosa cell line (HGrC1). Mesenchymal stem cell therapy may be a viable novel treatment option for POI patients.

P-819 4:30 PM Tuesday, October 20, 2020

THE USE OF SEMIPERMEABLE SPHERES ENGULFED WITH MOUSE EMBRYONIC STEM CELLS TO GENERATE MALE GERM CELLS. Sherina Lawrence, B.S., Mounia Haddad, M.D., Philip Xie, B.S., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To test the efficiency of direct spherification in supporting differentiation of mouse embryonic stem cells (mESCs) into meiotic male germ cells.

DESIGN: Biological 3D scaffolding was utilized to culture and differentiate mESCs. Two main methods were investigated: 1) mESCs were injected into pre-formed spheres (IN), and 2) a suspension of mESCs was directly encapsulated (DE) into spheres. To coax differentiation, spheres were bathed in a growth factor cocktail. After mechanical breaching of the spheres, serial isolation at different time intervals was carried out. These isolated cells were analyzed with germ cell stage–specific markers.

MATERIALS AND METHODS: MESCs were initially cultured on a 6-well dish, trypsinized, and resuspended in stem cell medium. For the IN method, the suspension was injected by using a 1 mL syringe into pre-formed spheres. For the DE method, spheres were formed by suspending mESCs in a base spherification solution and encapsulated by exposure to sodium alginate. Four spheres were bathed in EpiLC differentiating medium containing Activin A, bFGF, and KSR for 3 days, and then submerged in spermatogonial stem cell (SSC) medium composed of DMEM, GDNF, FGF2, 2-mercaptoethanol, L-glutamine, B27 supplement, and 1 μM retinoic acid (RA) for 7 days. Each sphere measured at a diameter of 8 to 10 mm, containing approximately $6.3x10^5$ cells per sphere. Cells were isolated and analyzed after 3 days for OCT4 and Nanog, and DAZL and VASA at day 10.

RESULTS: Both IN and DE proved successful in supporting the growth of mESCs. However, optic visualization through the membrane of the IN sphere showed a lower concentration compared to the DE approach. Embryoid body formation was first observed in the DE group at day 4, indicating greater efficiency with this approach. Confident with the sustainability and efficiency of DE, we attempted differentiation solely by this method, by bathing the spheres in EpiLC medium. After 3 days of culture, two spheres were breached and their cellular content was analyzed, showing OCT4 expression in about 85% of cells and a more conspicuous decrease in Nanog expression (<40%), indicating successful progression to EpiLCs. The remaining two spheres cultured in SSC medium with RA from day 4 to 10 showed an increase in embryoid body size that even extruded through the sphere wall. At day 10, the spheres were mechanically breached, and isolated cells showed positivity for VASA (~5%) and DAZL (~5%), confirming meiotic differentiation into germ cells.

CONCLUSIONS: Successful sustenance and propagation of mESCs using direct spherification indicates the feasibility of this 3D culture system to promote differentiation towards the male germ line. The ability to support differentiation to post-meiotic stages confirmed by biological proof would render this culture method sustainable for *in vitro* neogametogenesis.

P-820 4:30 PM Tuesday, October 20, 2020

SENSITIVE TOXICITY TESTING OF ART DISPOSABLES USING HUMAN PLURIPOTENT STEM CELLS. Ye Yuan, PhD,[1] Courtney Grimm, MS,[1] Rachel C. West, PhD,[1] William B. Schoolcraft, MD,[1] Rebecca L. Krisher, PhD[2] [1]Colorado Center for Reproductive Medicine, Lone Tree, CO; [2]CCRM Colorado, Lone Tree, CO.

OBJECTIVE: To develop a novel assay to sensitively detect toxicity using human pluripotent stem cells (hPSC) for human IVF clinic quality control (QC) testing.

DESIGN: Prospective research study

MATERIALS AND METHODS: To determine the sensitivity of hPSC culture to Triton X100 (TX100), cells were cultured for 48 h in StemFlex medium containing various dilutions of TX100 (10^{-5}, 5×10^{-6},10^{-6}, 10^{-7}) and compared with non-treated control cells. To compare the hPSC QC assay with known MEA results, StemFlex medium was exposed to previously tested plastics for 12 h at 37ºC prior to hPSC culture. Medium incubated at 37 ºC for 12 h without plastic exposure was used as the control. Media was refreshed daily for each treatment group. Colonies were digested with TrypLE and the resulting single cell suspensions were stained with Trypan blue to count the number of live cells.

RESULTS: After 48h, TX100 at higher concentrations (10^{-5}, 5×10^{-6}) triggered complete hPSC death. The number of viable hPSC was significantly decreased when exposed to TX100 at 10^{-6} ($1.1 \pm 0.2 \times10^5$ cell/well vs. $5.2 \pm 0.2\times10^5$ cell/well in control, n=3, p=0.002) and 10^{-7} ($1.9 \pm 0.2 \times10^5$ cell/well vs. $5.2 \pm 0.2\times10^5$ cell/well in control, n=3, p=0.003). Medium exposed to plasticware that had passed the MEA yielded a similar number of viable cells compared to control ($5.7 \pm 0.7 \times10^5$ cell/well vs. $5.2 \pm 0.2\times10^5$ cell/well in control, n=3, p=0.7). However, culture in medium exposed to plastics that had failed the IVM MEA resulted in fewer viable cells compared to the control ($2.9 \pm 0.4 \times10^5$, $1.5 \pm 0.4 \times10^5$, and $4.5 \pm 0.02 \times10^5$ cell/well for three independent plasticware vs. $5.2 \pm 0.2\times10^5$ cell/well in control. n=3, P=0.05, 0.01, and 0.08, respectively).

CONCLUSIONS: Our hPSC culture system was able to detect the known contaminant, TX100, at a lower concentration than the IVM MEA, and demonstrated the ability to replicate known MEA results for QC testing for commonly used plasticware. We are currently working on simplifying the procedures and performing the assay in a high throughput capacity. This QC assay has the potential to provide a sensitive, consistent, cost-effective, and less time-consuming platform for human ART QC.

SUPPORT: None

POSTER SESSION: REPRODUCTIVE ENDOCRINOLOGY

P-821 4:30 PM Tuesday, October 20, 2020

INSULIN RESISTANCE & INFERTILITY: ASSESSING THE SIGNIFICANCE OF INSULIN RESISTANCE AMONG WOMEN SEEKING FERTILITY CARE. Rachel Ruderman, MD, MPH, Lydia Hughes, MD, Sedona Speedy, MD, Christina E. Boots, MD, MSCI Northwestern University, Chicago, IL.

OBJECTIVE: To assess prevalence and significance of insulin resistance (IR) among women seeking fertility care

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: A database query was performed on patients aged 18 to 47 of the Reproductive Endocrinology and Infertility division from 2014 to 2020 who had a hemoglobin A1c (A1c) value. All women

	Normal (A1c < 5.7)	Insulin Resistance (A1c 5.7-6.4)	Diabetes (A1c 6.5+)	*p-value*
Age	34.33 (+/- 4.40)	34.86 (+/- 5.11)	35.16 (+/- 5.51)	0.02
BMI	26.18(+/- 6.18)	32.39(+/- 8.12)	34.32(+/- 9.77)	<0.001
Normal (18.5-24.9)	1238 (90.6%)	117(8.6%)	12(0.9%)	
Overweight (25-29.9)	662(82.9%)	116(14.5%)	21(2.6%)	
Obese (30+)	514 (58.2%)	319(36.1%)	50(5.7%)	
Race				0.00
White	1488(85.9%)	214(12.4%)	30(1.7%)	
Non-White	629(66.7%)	265(28.1%)	49(5.2%)	
AMH	4.00(+/- 4.28)	3.89(+/- 3.88)	2.90(+/- 2.74)	NS
TSH	1.88(+/- 1.20)	2.09(+/- 3.55)	2.25(+/- 2.01)	0.02
Total Gonadotropins	2661.92(+/- 1279.42)	2898.40(+/- 1337.10)	3359.09(+/- 1446.60)	0.02
Total Oocytes	14.91(+/- 9.57)	14.65(+/- 9.66)	13.60(+/- 7.91)	NS
Frozen Blasts	4.21(+/- 3.44)	4.01(+/- 3.18)	3.20(+/- 2.78)	NS

NS = non-significant

who present to this office are screened with a A1c if their BMI is >25kg/m2. Data was correlated to in vitro fertilization (IVF) data. Insulin resistance was defined per the American Diabetes Association. Statistical analysis was performed using student's T test, ANOVA, or chi square. Linear and logistic regression were used to adjust for confounding variables.

RESULTS: 3170 women were included in the study. The prevalence of IR was 17.9% and diabetes was 2.7%. Mean A1c value was 5.4 +/- 0.58. After adjusting for age, a higher body mass index (BMI) (OR 1.12, 95% CI 1.11-1.14, $P<.001$) and a non-white race (OR 2.38 95% CI 1.97-2.89, $P<.001$) were predictive of an elevated A1c. IR was significantly associated with increased total gonadotropin dose ($P = 0.02$), but was not associated with worse IVF outcomes, such as number of oocytes retrieved, pregnancy or live birth rate after adjusting for age and anti-Mullerian hormone (AMH). IR was not associated with any particular diagnosis of infertility. Of the 464 women with IR who conceived and received care in our hospital system, 18% (102) developed gestational diabetes (GDM), compared to 6.9% (173/2345) of women without IR.

CONCLUSIONS: Insulin resistance is a common finding among women seeking fertility treatment, especially when BMI is >30kg/m2, and should be considered during preconception evaluation. While IR was not associated with worse IVF outcomes, patients with IR may require higher doses of gonadotropins and have a higher risk of GDM. Preconception evaluation and lifestyle counseling provide a unique and motivational opportunity to improve pregnancy and long term health outcomes.

SUPPORT: Northwestern University Department of Obstetrics & Gynecology

P-822 4:30 PM Tuesday, October 20, 2020

OOCYTE SECRETED FACTORS REGULATE *FSHR* AND *AMH* mRNA LEVELS IN CUMULUS CELLS.

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OBJECTIVE: Considering that (1) FSH activity decreases cumulus-oocyte communication via retraction of transzonal processes (TZP), (2) AMH inhibits FSH signalling by decreasing *FSHR* expression and adenylyl cyclase activation, and (3) the oocyte is an active player in the cumulus-oocyte complex (COC) regulating cumulus cell metabolism and gene expression via oocyte-secreted factors (OSF), we tested the hypothesis that the oocyte decreases mRNA abundance of *FSHR* while increasing that of *AMH* in cumulus cells through OSF, as part of an effort to preserve its communication with cumulus cells thus safeguarding its developmental competence.

DESIGN: The relative mRNA abundance of *FSHR and AMH* in cumulus cell was compared among 3 treatment-groups: (1) Intact COC subjected to *in vitro* maturation (IVM); (2) oocytectomized COC (OOX) subjected to IVM and (3) OOX subjected to IVM with the addition of denuded oocytes (OOX+DO; 1 DO/μL). Four culture replicates including all three treatment-groups were performed.

MATERIALS AND METHODS: COC were aspirated from 3-8mm follicles of bovine ovaries. Oocytectomy was achieved by aspiration of the ooplasm with a micromanipulator while preserving the structure of the COC. COC and OOX underwent IVM in pools of 20 for 22 hours. IVM was performed in 100 μL of TCM199 with Earl's salts supplemented with 1μg/mL FSH, 0.4% BSA, 22 μg/mL sodium pyruvate, 75 μg/mL of amikacin at 38,5°C and 5.5% CO_2 in humid atmosphere. Abundance of mRNA encoding *FSHR* and *AMH* in cumulus cells was assessed by real-time RT-PCR using Power SybrGreen (LifeTech®) and *RPL15* (ribosomal protein 15) as the reference gene. Effects of treatments were tested by ANOVA and groups were compared with the Tukey test. Statistically significant differences were those with $p<0.05$, while p values >0.05 and <0.1 were considered as tendency of difference.

RESULTS: Oocytectomy decreased *AMH* mRNA levels ($p=0.005$) while tended to increase *FSHR* mRNA abundance ($p=0.077$) in cumulus cells. The addition of denuded oocytes (DO) reversed the effects of oocytectomy on both genes. Relative *AMH* mRNA levels (*AMH/RPL15* mRNA abundance, mean ± EPM) were 0.875 ± 0.1, 0.3675 ± 0.02 and 0.7825 ± 0.1 for COC, OOX and OOX+DO, respectively. For *FSHR*, the respective values (*FSHR/RPL15* mRNA abundance) were 1.495 ± 0.54, 2.575 ± 0.52 and 0.875 ± 0.29.

CONCLUSIONS: Oocyte secreted factors seem to reduce *FSHR expression* while enhancing *AMH* expression in cumulus cells. We speculate that this is part of an effort of the oocyte to restrain FSH activity in the COC in order to preserve its communication with cumulus cells thus favouring developmental competence.

P-823 4:30 PM Tuesday, October 20, 2020

CONTRASTING TOXICITY OF D-GALACTOSE ON OOCYTES AND EMBRYOS.

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OBJECTIVE: A rare mutation in galactose-1-phosphate uridyltransferase, an enzyme in the Leloir pathway of galactose metabolism, causes classic galactosemia (CG), a metabolic disorder characterized by harmful accumulation of D-galactose and its metabolites galactose 1-phosphate (gal 1-P) and galactitol in physiological systems. One especially susceptible system is the female reproductive tract, specifically the ovaries, which often leads to primary ovarian insufficiency (POI) even with careful monitoring of diet. However, some number of pregnancies in CG patients has been reported even though the general perception is that they are infertile. Previous studies have delineated a mechanism of D-galactose toxicity in oocytes associated with apoptosis and excessive reactive oxygen species, but considering the incidence of pregnancy in CG patients, embryos could be less affected by D-galactose toxicity. Therefore, the aim of this study is to explicate the effects of D-galactose and its metabolites on embryos and subsequent development.

DESIGN: This was an experimental case-control design.

MATERIALS AND METHODS: D-galactose (2 mM), galactitol (11 mM) and gal 1-P (0.1 mM), with concentrations corresponding to those typically found in plasma of CG patients under dietary restrictions, were used to treat one-cell mouse embryos (n = 31) for 4 h. After exposure, the embryos were then incubated in culture for 120 h. Similar procedures were used to treat metaphase II mouse oocytes (n = 120), which were then fertilized *in vitro*, and then cultured for 120 h. Cells were analyzed for development at 24, 48, and 96 h. Cleavage stage embryos were assessed for nuclear fragments, morphology, and blastomere count. Blastocyte stage embryos were assessed for blastocoel expansion, trophectoderm morphology, and inner cell mass quality.

RESULTS: No differences were found between directly treated embryos and untreated controls. Conversely, there was significant decline in cleavage and blastocyst development in embryos derived from treated, fertilized oocytes compared to untreated controls.

CONCLUSIONS: Considering the relatively high pregnancy rate observed in women with CG-associated POI compared to all women with POI, D-galactose exposure does not appear to be embryotoxic. Thus, oocytes that avoid the harmful effects of D-galactose or its metabolites have the potential for a normal developmental course even if they are then later exposed to D-galactose or its metabolites. These results should encourage women with CG to maintain optimism for childbearing and childbirth.

P-824 4:30 PM Tuesday, October 20, 2020

NOVEL ANTI-MÜLLERIAN HORMONE RECEPTOR 2 BINDING PEPTIDE (AMHR2BP) STALLS GRANULOSA CELLS PROLIFERATION.

Laura Detti, MD,[1] Ghassan M. Saed, PhD[2] [1]Cleveland Clinic, Cleveland, OH; [2]Wayne State University School of Medicine, Detroit, MI.

OBJECTIVE: Anti-Müllerian hormone decreases hormone production, and cellular proliferation/apoptosis, in in both, *in vitro* and *in vivo*, ovarian cortex [1-3], and in luteinized granulosa cells (GCs) [4]. We sought to investigate whether a novel AMHR2BP could perform similarly to native AMH in a primary luteinized GC culture.

DESIGN: Experimental study

MATERIALS AND METHODS: A primary culture of GCs isolated from follicular fluid was used. Cells were seeded in well cell culture plates at a density of 100,000 cells/well in medium. Following an overnight incubation (37°C, 5% CO2), cells were treated with AMHR2BP 10 ng/ml (AMHR2BP group), or Phosphate-buffered saline (PBS, control group), for an additional 24 hours. After incubation, real-time RT-PCR was performed to quantify GCs expression of AMH, AMH-R2, FSH-R, Inhibin B, cell proliferation (Ki67) and apoptosis (Caspase 3).

RESULTS: Cellular expression of AMH, AMH-R2, FSH-R and Inhibin B, were significantly reduced by AMHR2BP-treated cells compared to a Negative peptide and control groups ($p \leq 0.005$ for all). In addition, AMHR2BP-

Variable Groups	AMH pg/μg RNA	AMH-R2 pg/μg RNA	FSH-R pg/μg RNA	Inhibin B pg/μg RNA	Ki67 pg/μg RNA	Caspase3 pg/μg RNA
Control	3.05±0.1	9.88±0.3	4.43±0.3	101.8±5.9	425.1±16.6	1101.6±91.4
Negative BP	2.91±0.2	9.95±0.1	4.42±0.4	94.0±2.7	428.3±6.8	1140.4±16.8
AMHR2BP	1.60±0.1	4.17±0.2	1.65±0.1	46.9±1.1	229.5±6.7	207.3±4.7
p-value	0.005	<0.001	<0.001	0.001	<0.001	<0.001

treated cells showed decreased cell proliferation, as well as decreased apoptosis by greater than 50%. The Table shows the cellular mRNA expression of (A) AMH, its receptor AMH-R2, FSH-R, and inhibin B, and (B) Ki67 and Caspase3, in granulosa cells cultured for 24 hours in plain medium (control), 10 mcg novel AMHR2BP (AMHR2BP), and a negative peptide.

CONCLUSIONS: Binding to AMHR2, the novel AMHR2BP reproduced native AMH's effects [5], with inhibition of cell proliferation and apoptosis in luteinized GCs. AMHR2BP also downregulated cellular expression of the major regulatory hormones and receptors. AMHR2BP could be used in place of AMH in AMH-regulated functions.

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P-825 4:30 PM Tuesday, October 20, 2020

THE INCIDENCE OF UNDETECTABLE AMH LEVELS IN WOMEN SEEKING PROACTIVE FERTILITY HORMONE TESTING. Sharon Briggs, PhD, Avner Hershlag, MD Modern Fertility, San Francisco, CA.

OBJECTIVE: To determine the frequency of undetectable anti-mullerian hormone (AMH) among women not currently seeking fertility treatment.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: Our cohort consists of over 11,000 participants who represent a subset of people who used an at-home fertility hormone test between May 2018 and March 20th, 2020. To be included, participants must have consented to research and not reported a previous diagnosis of polycystic ovary syndrome or primary ovarian insufficiency (POI). Participants were subset by age and whether they were currently using contraceptives.

RESULTS: Undetectable levels of AMH were found in 0.9% of our cohort, representing 102 women. In our age-restricted analysis, the frequency ranged from 0.2% in women under 35, 1.98% in women 35-39, and 6.85% in women 40 and older. 63 women (0.74%) in this cohort meet the definition of primary ovarian insufficiency: under the age of 40 with undetectable AMH levels.

Results were similar when restricting the analysis to women who were not using contraceptives at the time of testing (Table 1).

CONCLUSIONS: AMH has become the most common test used in reproductive medicine to evaluate ovarian reserve. While it is hotly debated in the literature whether AMH can be used to predict fecundity in general, undetectable AMH clearly represents a decrease in the number of eggs available to create a viable pregnancy either naturally or with assistance.

Undetectable AMH was found with notable frequency in our cohort — nearly 2% of women between ages 35 and 39 had undiagnosed POI. Given the association with various health conditions and a decreased chance of natural pregnancy, identification of undiagnosed POI should prompt followup with a physician and fertility specialist.

It is important to note that this is a cohort of women seeking proactive fertility hormone information; they are unlikely to be seeing a fertility specialist. Without fertility testing and identification of undetectable AMH levels, these women may have tried to achieve pregnancy at home for months, potentially years, before seeking help. Measuring AMH at-home can help women identify an issue and see a fertility center or physician. This can give them valuable time and opportunity to optimize their chances for a child.

Table 1. Frequency of undetectable AMH by age and contraceptive status.

Cohort	Age	% Undetectable (<0.08 ng/ml)
All customers (n=11277)	All ages	0.9%
Mean (SD) Age: 31.8 (4.3)	<35 (n=8481)	0.22%
	35-39 (n=2226)	1.98%
	40+ (n=569)	6.85%
Customers not on contraceptives (n=7387)	All ages	1.03%
	<35 (n=5114)	0.2%
Mean (SD) Age: 32.5 (4.5)	35-39 (n=1762)	1.76%
	40+ (n=511)	6.85%

P-826 4:30 PM Tuesday, October 20, 2020

SLEEP DURATION AND TIMING ARE NOT ASSOCIATED WITH ANTIMULLERIAN HORMONE LEVELS. Caitlin Elizabeth Martin, MD, MS,[1] Allison P. Schelble, MD,[2] Ashley Eskew, MD, MSCI,[3] Joan Riley, PhD, HCLD,[2] Emily S. Jungheim, MD, MSCI[4] [1]Washington University School of Medicine, St. Louis, MO; [2]Washinton University School of Medicine, St. Louis, MO; [3]Atrium Health, Charlotte, NC; [4]Northwestern Feinberg School of Medicine, Chicago, IL.

OBJECTIVE: Many women who consider future family building seek advice regarding modifiable behaviors and reproductive health. To determine if sleep duration and timing are associated with AMH levels in a reproductive aged, Midwestern cohort of women.

DESIGN: Cross sectional study.

MATERIALS AND METHODS: 200 women aged 18-44 years with regular menstrual cycles were enrolled into the LORE study, a cross-sectional cohort study designed to investigate associations between lifestyle factors and ovarian reserve. Women who were currently pregnant or who had history of major chronic illness, infertility or ovarian surgery were excluded. Fasting blood was drawn and stored at -80 degrees for batched analysis. Samples were run on the Roche Elecsys analyzer for AMH levels. Participants also completed a survey that included questions regarding typical bedtime and wake time on work and non-work days. Sleep measures included duration of sleep, midsleep point (defined as the midpoint time between bedtime and wake time, also known as chronotype), and social jetlag (the difference in midsleep point on workdays and non-work days of >1 hour). Standard bivariate statistics were run to determine associations between sleep duration, timing of sleep and AMH levels. SPSS v.25 was used for analysis.

RESULTS: Participants had an average age of 30.9 ± 6.7 years and an average body mass index of 28.3 ±7.1. The majority of the participants were white (n=136, 68%); thirty percent were black (n=60). The average AMH level was 2.9 ±2.0 ng/mL. Average duration of sleep was 7.2 hours (Range 4.0 to 11.0 hours). Average mid sleep point on work nights was 2:51 AM and on non-work nights was 3:54 AM. Average social jet lag was 1:31 hours (range 0 to 14:30 hours). None of these measures were associated with AMH.

CONCLUSIONS: This data suggests that for healthy, reproductive aged women in the Midwest, modifying sleep duration and timing is unlikely to improve or adversely affect AMH.

SUPPORT: Financial Support: UL1TR000448.

COMPARISON OF CONTROLLED OVARY STIMULATION PROTOCOLS FOR *IN VITRO* FERTILISATION: A META-ANALYSIS.

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OBJECTIVE: The purpose present of meta-analysis is to compare the effectiveness of different types of GnRH agonist (GnRH-a) protocols (long-acting follicular, long-acting luteal and short-acting luteal protocols) and GnRH antagonist (GnRH-ant) protocol for IVF.

DESIGN: Meta-analysis.

MATERIALS AND METHODS: In this meta-analysis, a literature search was performed in both English and Chinese databases (PubMed, Embase, Cochrane, CNKI and Wanfang) using pre-defined search strings till 1st March 2019. The methodology adhered to Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines and registered in PROSPERO (CRD42019139396). RCTs and observational studies that compared GnRH-a protocols (long-acting follicular, long-acting luteal and short-acting luteal) and GnRH-ant protocols were included. The primary outcome was live birth rate (LBR); the secondary outcomes were clinical pregnancy rate (CPR), implantation rate (IR) and safety in terms of miscarriage rate (MR) and ovarian hyperstimulation syndrome (OHSS) rates. 'R software' was used for statistical analysis. Outcomes were reported in terms of relative risk (RR) and 95% confidence interval (CI) with P value <0.05 considered statistically significant.

RESULTS: Literature search retrieved 5331 studies of which 111 were included. Long-acting follicular agonist protocol (13 studies) consisted of 1878 and 2342 women in agonist and antagonist arms respectively. No significant difference was observed in LBR (RR=1.38, 95%CI: 0.79-2.39, *P*=0.2542) and MR (RR=0.97, 95%CI: 0.63-1.49, *P*=0.8833). CPR (RR=1.48, 95%CI: 1.37-1.59, *P*<.0001) and IR (RR=1.39, 95%CI: 1.10-1.76, *P*=0.0062) were significantly higher in agonist group whereas OHSS was significantly lower in GnRH-ant group (RR=1.35, 95%CI: 1.06-1.72, *P*=0.015).The long-acting luteal agonist protocol included 24 studies: 6579 and 2900 women in agonist and antagonist arms, respectively. There was no significant difference in LBR (RR=1.02, 95%CI: 0.91-1.14, *P*=0.75), CPR (RR=1.48, 95%CI 0.80-2.76, *P*=0.21) and MR (RR=0.90, 95%CI: 0.64-1.26, *P*=0.536). CPR/transfer (RR=1.07, 95%CI: 1.01-1.14, *P*=0.0194) and IR (RR=1.17, 95%CI: 1.03-1.32, *P*=0.0161) were significantly higher in agonist group but OHSS was significantly lower in GnRH-ant group (RR=1.29, 95% CI 1.02-1.63, *P*=0.0311).The short-acting luteal agonist protocol included 74 studies:7385 and 11881 women in agonist and antagonist arms, respectively. LBR (RR=1.34, 95% CI 1.22-1.48, *P*<.0001) was significantly higher in the short-acting luteal agonist group. There was no significant difference in CPR (RR=1.01, 95%CI 0.93-1.09, *P*<.834), CPR/cycle (RR=1.05, 95%CI 0.93-1.18, *P*=0.415), CPR/transfer (RR=1.06, 95%CI 0.88-1.27, *P*=0.548), IR (RR=1.02, 95%CI 0.95-1.10, *P*=.563) and MR (RR=0.92, 95%CI 0.74-1.15, *P*=0.473). However, a significantly lower OHSS rate was observed in GnRH-ant group (RR=1.61, 95% CI 1.33-1.94, *P*<0.0001).

CONCLUSIONS: GnRH-a long protocols were found to have potential benefit over the GnRH-ant protocol in terms of live birth rate, clinical pregnancy rate and implantation rate.

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P-828 4:30 PM Tuesday, October 20, 2020

HIF1-ALPHA INDUCED ADRENOMEDULLIN EXPRESSION SUPPORTS ANGIOGENESIS IN 3D LEIOMYOMA XENOGRAFTS. Joy L. Britten, MD,[1] Minnie Malik, Ph.D.,[2] Anthony DeAngelis, MD, PhD,[2] William Catherino, M.D., Ph.D.[1] [1]Uniformed Services University for the Health Sciences, Bethesda, MD; [2]Uniformed Services University of the Health Sciences, Bethesda, MD.

OBJECTIVE: Cellular responses to hypoxia are critical to homeostasis. In eukaryotes, the primary regulator of angiogenesis is the transcription factor hypoxia inducible factor-1 alpha (HIF-1α). Hormonally-stimulated human leiomyoma 3D xenografts express HIF1-α protein and undergo *in vivo* neovascularization. Our objective was to characterize hypoxia regulated genes and HIF-1α regulated angiogenesis in our human leiomyoma cell lines and xenograft model.

DESIGN: Laboratory study

MATERIALS AND METHODS: Leiomyoma and myometrial cells exposed to normal O_2 (21%) and low O_2 (1%) levels and chemically induced hypoxia with cobalt chloride ($CoCl_2$) for 6 and 24 hours; leiomyoma and myometrial cell protein; 3D leiomyoma and myometrial xenograft tissue from placebo-, estrogen- and progesterone-treated groups; Immunohistochemistry and Western blot analyses

RESULTS: Quantitative WB analysis of myometrial cells exposed to hypoxia demonstrate a greater than 3-fold increase (3.35$\pm$0.01-fold **p<0.05) in HIF-1α expression at 24 hours in myometrial cells under hypoxic conditions. Conversely, leiomyoma cells show up regulation of HIF-1α expression (1.16$\pm$0.004-fold **p<0.01) at 6 hours and 24 hours (1.44$\pm$0.05-fold *p=0.05) under normoxic conditions. Adrenomedullin (ADM), a pro-angiogenic protein under HIF-1α transcriptional control, was upregulated in hypoxic myometrial cells at 6 (1.76+/-0.5-fold) and 24 hours (1.28+/- 0.3-fold), compared to normoxic myometrium. Leiomyoma cells show an almost 1.5-fold increased ADM expression under both normoxia and hypoxic conditions at the 6 hour time point. Exposure of myometrial cells to $CoCl_2$ for 24 hours demonstrate a >1.5-fold increase in ADM and a >2-fold increase in the stress inducible protein, sestrin 2. After 24 hours of exposure to $CoCl_2$, leiomyoma cells show a similar increase in ADM expression to that of myometrium at 6 hours, and a >7-fold increase in sestrin 2. IHC results for ADM expression in 3D xenografts show that the estrogen-, estrogen+progesterone and progesterone-treated groups demonstrate intense cytoplasmic/matrix staining for ADM compared to placebo treated groups, particularly under the growth-stimulatory influence of gonadal hormones.

CONCLUSIONS: Angiogenesis is supported by hypoxia induced, HIF-1α facilitated ADM expression in 3D leiomyoma xenografts.

P-829 4:30 PM Tuesday, October 20, 2020

DETERIORATION IN BASELINE REPRODUCTIVE HORMONE PROFILE IS ASSOCIATED WITH INCREASE IN REPRODUCTIVE ENDOCRINE DISORDERS: DATA EVALUATION IN INDIAN WOMEN OVER A 15-YEAR DURATION. Bindu N. Chimote, M.Sc., M.Phil, Ph.D.(Biochemistry); M.Sc. Clinical Embryology (Leeds-UK),[1] Natchandra Manoharrao Chimote, M.Sc., Ph.D[2] [1]Consultant Clinical Embryologist, Nagpur, India; [2]Scientific Director, Vaunshdhara Fertility Centre, Nagpur, India.

OBJECTIVE: To validate if deterioration in reproductive hormone profile of women reporting for fertility treatment may be responsible for increased endocrine anomalies and stagnant success rates post-IVF despite clinical, embryological and technical advances.

DESIGN: Retrospective analysis of anthropometric parameters and baseline hormones in reproductive age (21-44 years) women reporting for fertility consultation over a 15-year duration, phased out into Group A: 2005-2009 (n=814), Group B: 2010-2014 (n=1264), Group C: 2015-2019 (n=1222).

MATERIALS AND METHODS: Baseline reproductive hormones Oestradiol E2, LH, FSH, TSH, Testosterone, Prolactin, Insulin, DHEAS, AMH were estimated by RIA/ELISA using diagnostic kits in women on day2/3 of menstrual cycle. Study population comprised of all women including eumenorrhic normal (non-PCOS), PCOS and POI/F women. We designated women as PCOS (AFC >20, AMH >4ng/ml, LH >FSH, Testosterone >60ng/dL) and POF/POI (AFC <4, AMH <0.43ng/ml, FSH>25mIU/ml, LH= 20-25mIU/ml, Testosterone <20ng/dl) as per standards established in Indian women by our endocrine laboratory. Statistical analysis was done using Graph-pad prism VI software.

RESULTS: A significant rise in age (29.93$\pm$0.17 vs. 31.41$\pm$0.17 vs. 32.19$\pm$0.15 years; p<0.0001), ovarian age (15.83$\pm$0.23 vs. 17.46$\pm$0.20 vs. 17.68$\pm$0.18years;p<0.0001), BMI (23.65$\pm$0.19 vs. 24.39$\pm$0.20 vs. 24.66$\pm$0.15;p=0.0002) and WHR (0.87 vs. 0.89 vs. 0.91;p=0.04) of women reporting for fertility treatment was observed among the study groups A, B, C respectively. The steroid hormones Estradiol (71.03$\pm$1.96 vs. 83.98$\pm$1.23 vs. 96.42$\pm$1.98 pg/ml; p<0.0001) and Testosterone (62$\pm$1.5 vs. 79$\pm$1.4 vs. 105$\pm$2.1; p<0.0001) were significantly higher, displaying correlation of raised androgen with concurrently raised peripheral estrogen levels. Insulin (7.9$\pm$0.3 vs. 8.2$\pm$0.17 vs. 8.5$\pm$0.18μM/L; p<0.0001) and TSH (2.96$\pm$0.18 vs. 3.34$\pm$0.08 vs. 4.01$\pm$0.5mIU/L;p<0.0001) levels also depicted a significant rise whereas Prolactin levels did not differ significantly. Disconcertingly, results showed an increased tendency towards two extremes of Polycystic Ovarian Syndrome (PCOS) (19 vs. 25 vs. 33%; p<0.0001) and Premature Ovarian Insufficiency/failure (POI/F) (11 vs. 13 vs. 15%;p<0.0001) while rates of 'normal' eumenorrhic non-PCOS females declined (69 vs. 62 vs. 52%;p<0.0001) over the years between the 3 study groups respectively. Among PCOS, there was a rise in incidence of obese (BMI >30 kg/m^2) PCOS (9.37 vs. 12.61 vs. 14.37%; p=0.0004) whereas rates of lean-thin (BMI<19 kg/m^2) PCOS declined (16.61 vs. 13.53 vs. 11.49%; p<0.0001) between the three study groups respectively. DHEAS levels were high in young PCOS whereas low in elderly PCOS and women with POI/F condition. AMH levels also displayed increasing tendency towards significant extremes based on PCOS and POI/F status.

CONCLUSIONS: A progressive decadence in baseline reproductive endocrine profile of women reporting for fertility treatment warrants re-establishing ethnicity based normal control values, redefining endocrine anomalies and redesigning of protocols for enhanced IVF outcomes.

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P-830 4:30 PM Tuesday, October 20, 2020

NOMOGRAM TO PREDICT CERVICAL INSUFFICIENCY INCIDENCE IN PATIENTS UNDERGOING IVF/ICSI TREATMENT. Xing Yang, Ph.D., Yao-qiu Wu, M.M The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: This study aimed to identify the risk factors for Cervical insufficiency (CI) occurrence after in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) treatment, and set up a predictive model providing personalized and clinically specific information related to CI incident.

DESIGN: A retrospective observational cohort study.

MATERIALS AND METHODS: This retrospective study included 4710 women pregnant after IVF/ICSI treatment from Jan 2011 to Dec 2018 at The Six Affiliated Hospital of Sun Yat-sen University. CI was first diagnosed during pregnancy based on cervical dilation and/or cervical shortening. Univariate and multivariate logistic regression were used to analysis the correlation of pre-pregnancy clinical covariates with CI occurrence. Nomogram model for CI incidence rate prediction was built from a training cohort of 3108 patients and tested on an independent validation cohort of 1602 patients. A bootstrapping technique was used for external validation.

RESULTS: A total of 109 patients (2.31%) were diagnosed with CI among all the enrolled patients. In multivariable analysis of the training cohort, CI occurrence was significantly related to serum Testosterone (odds ratio [OR], 7.103; 95% confidence interval [CI], 3.451 - 8.987; p <0.001), BMI (OR, 2.382; 95% CI, 1.186 - 5.786; p = 0.009) , uterine length (OR, 0.261; 95% CI, 0.132 - 0.525; p = 0.005) and gravidity (P = 0.031). Testosterone over 0.7ng/ml, uterine shorter than 45mm, increased BMI and gravidity were highly risky for CI occurrence . The nomogram model was built based on BMI, serum T, gravidity and uterine length, the area under the curve (AUC) was 0.839 (95% CI: 0.763 - 0.900) for the training cohort, the AUC for the validation cohort was 0.708 (95% CI: 0.685 - 0.832). The model showed a satisfactory goodness-of-fit and discrimination ability. No significant difference was detected between the predicted probability obtained from the bootstrap correction and the actual probabilities of CI occurrence (P = 0.261), which means the model is well calibrated.

CONCLUSIONS: The user-friendly nomogram graphically presented with pre-pregnancy predicted tool for CI incidence in patients undergoing IVF/ICSI treatment. It is of great importance to monitor highly risk women have polycystic ovary syndrome and take preventive measures prior to IVF/ICSI treatment and subsequent pregnancy as well.

SUPPORT: No

P-831 4:30 PM Tuesday, October 20, 2020

HMG DIMINISH THE AVAILABLE OOCYTES UTILIZATION IN FRESH CYCLES. Peiyang Lin, master, Beihong Zheng, bcahelor, Rongshan Li, bachelor, Huiling Xu, master, Suqin Zhu, master Fujian Maternity and Child Health HospitalAffiliated Hospital of Fujian Medical University, FuZhou, China.

OBJECTIVE: During assisted reproductive therapy, both controlled ovarian stimulation(COS) and embryo culture have important effects on the development and maturation of oocytes. We aim to figure out how to evaluate the effect of ovulation promotion on oocyte development and the final embryonic development outcome.

DESIGN: Univariate analysis, multivariate analysis and case-control matching were used in this retrospective research.

MATERIALS AND METHODS: In this article, we introduced the concept of available oocytes utilization(AOU) to evaluate the effect of COS on oocyte development. A total of 460 fresh cycles with AOU lower than 50% were enrolled in our present study between January 2015 to December 2019, including 106 pregnancy cycles and 354 non-pregnancy cycles.

RESULTS: Univariate analysis and multivariate analysis revealed that basal E2(OR=0.98, p=0.04), endometrial thickness on HCG day (OR=1.25, p<0.01), number of follicular punctured(OR=1.58, p<0.01), number of oocytes retrieved(OR=0.80, p=0.04), number of available oocytes(OR=0.48, p=0.04) and AOU(OR=1.18, p<0.01) were contributed to clinical pregnancy. ROC analysis for fertilization rates showed a possible cutoff for AOU(AUC=0.788, cutoff=34.13%). Based on the ROC results, all 103 cycles with AOU less than 34% were included in the case group, and 103 cycles were selected as the control group according to the 1: 1 case control matching. The dosage of HMG was significantly different between the case group and control group(1064.00±1042.01U VS 675.00±691.67U , respectively,p=0.006). The duration of HMG usage were 7.88±4.73day and 5.79±3.59day in case group and control group(p=0.014).

CONCLUSIONS: Our results indicated that in the low AOU assisted pregnancy cycle, larger dose of HMG will reduce the proportion of available oocytes, which ultimately affects pregnancy outcomes.

SUPPORT: This study was supported by grants from Provincial Natural Science Foundation of Fujian, China (2019J01052054); Fujian Provincial Health Technology Project (2019-1-57); Startup Fund for scientific research, Fujian Medical University (Grant number: 2019QH1134).

P-832 4:30 PM Tuesday, October 20, 2020

SERUM FOLIC ACID, VITAMIN B12 AND VITAMIN D3 LEVELS ARE NOT ASSOCIATED WITH ANTIMULLERIAN HORMONE LEVELS. Caitlin Elizabeth Martin, MD, MS,[1] Joan Riley, PhD, HCLD,[2] Emily S. Jungheim, MD, MSCI[3] [1]Washington University School of Medicine, St. Louis, MO; [2]Washinton University School of Medicine, St. Louis, MO; [3]Northwestern Feinberg School of Medicine, Chicago, IL.

OBJECTIVE: Reproductive aged women often seek advice regarding modifiable behaviors that may improve their future reproductive health. We aimed to determine if serum levels of vitamin B12, vitamin D3 or folic acid were associated with antimullerian hormones (AMH) levels in a reproductive aged, Midwestern cohort of women.

DESIGN: Cross-sectional cohort study.

MATERIALS AND METHODS: There were 200 women aged 18-44 years with regular menstrual cycles who were enrolled into the LORE study, which was designed to investigate associations between lifestyle factors and ovarian reserve. Women who were currently pregnant or who had history of major chronic illness, infertility or ovarian surgery were excluded. Fasting blood was drawn and stored at -80 degrees for batched analysis. Samples were run on the Roche Elecsys analyzer for AMH, vitamin B12, vitamin D3 and folic acid levels. Standard bivariate statistics were run to determine associations between vitamin B12, vitamin D3 and folic acid with AMH levels. SPSS v25 was used for analysis.

RESULTS: Participants had an average age of 30.9 ± 6.7 years and body mass index of 28.3 ±7.1 kg/m^2. About two thirds of the participants were white (n=136, 68%) and one third were black (n=60, 30%). The average AMH level was 2.9 ±2.0 ng/mL. The average vitamin B12 level was 604.2 pg/mL (Range 230.6-2000.0 pg/ML), vitamin D3 level was 22.3 ng/mL(range 6.8-94.9 ng/mL) and folic acid level was 14.9 ng/mL (range 2.2 - 20.0 ng/mL). None of these serum analytes were associated with AMH levels.

CONCLUSIONS: This data suggests that for healthy, reproductive aged women from the Midwest, modifying levels of vitamin B12, folic acid, or vitamin D through supplementation is unlikely to improve or adversely affect AMH.

SUPPORT: Financial Support: UL1TR000448.

P-833 4:30 PM Tuesday, October 20, 2020

ATYPICAL CORE BODY TEMPERATURE PATTERNS AND THE WIDER IMPLICATIONS FOR CONDITIONS RELATED TO PREGNANCY, INFERTILITY, AND MISCARRIAGE RISK. Bradley S. Hurst, MD Atrium Health Carolinas Medical Center, Charlotte, NC.

OBJECTIVE: To determine if pregnancy complications, ovulatory abnormalities and miscarriage risk were associated with atypical Patterns of vaginal core body temperature (CBT) measurements from the OvuSense (OS) system.

DESIGN: Retrospective, longitudinal, comparative, observational study.

MATERIALS AND METHODS: Participants used OS vaginally at night to monitor CBT when not menstruating. Three atypical CBT Patterns published previously, confirmed in updated Total Study Population (TSP) 20,067 ovulatory cycles from 8,177 OS users recorded March 2016 to March 2020: (A) "Crash To Baseline" = first nightly averaged CBT falls by >0.2 degrees Celsius (oC) to lowest cycle CBT point (baseline), (B) "False Start" = rise of >0.1oC did not result in ovulation but instead a return to baseline CBT followed by ovulation two or more days later in the cycle, (C) "Crash After Ovulation" = final CBT >0.2oC lower than the post ovulatory peak CBT.

A detailed medical questionnaire was then issued to study participants and the answers from 382 respondents accounting for 1,534 of the TSP cycles was used for further assessment. TSP used to confirm prevalence of cycle Patterns (A)-(C); and questionnaire assessed per respondent for each following historic 'Diagnosis':

1. Any infertility related diagnosis
2. PCOS
3. PCOS and regular cycles
4. Previous miscarriage = gravida >0, number miscarriages >0.
5. Gestational Diabetes in any previous pregnancy
6. Gestational Hypertension in any previous pregnancy

Diagnostic Odds Ratio (OR) calculated as (w/x)/(y/z) for each Pattern + Diagnosis combination together with their Lower (LCI) and Upper (UCI) 95% Confidence Interval: w. Positive Diagnosis (+D), Pattern >1 cycle for respondent (+P); x. -D+P; y. +D-P; z. -D-P.

RESULTS: Prevalence of Patterns: (A) 61.0%: 282 cycles in 172 respondents; (B) 66.3%: 205 cycles in 136 respondents; (C) 59.8%: 229 cycles in 137 respondents

Pattern	A			B			C		
Diagnosis	*LCI*	*OR*	*UCI*	*LCI*	*OR*	*UCI*	*LCI*	*OR*	*UCI*
Any infertility diagnosis	0.96	**1.43**	2.15	1.48	**1.72**	2.65	0.88	**1.09**	1.67
PCOS	1.19	**1.79**	2.69	1.83	**2.80**	4.29	1.03	**1.57**	2.39
PCOS + Regular Cycles	1.00	**1.76**	3.11	0.79	**1.14**	2.51	0.85	**1.51**	2.69
Previous Miscarriage	3.52	**5.94**	10.03	3.82	**6.84**	12.25	3.80	**6.88**	12.46
Gestational Diabetes	0.69	**2.15**	6.68	0.26	**0.85**	2.81	0.07	**0.34**	1.54
Gestational Hypertension	0.57	**1.50**	3.97	0.18	**0.58**	1.81	0.11	**0.39**	1.39

CONCLUSIONS: Results confirm previous research [1] that atypical CBT Patterns may aid infertility diagnosis, and elevated risk of miscarriage. Pattern A. may also provide a warning for elevated risk of pregnancy issues. It should be noted that the absence of an existing Diagnosis does not necessarily render the results with positive Patterns "false", and the existence of a Pattern could anyway indicate investigation for ovulatory abnormalities.

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SUPPORT: This study was financially supported by Fertility Focus Ltd. and Inc.

P-834 4:30 PM Tuesday, October 20, 2020

ERYTHROPOIETIN-PRODUCING HEPATOCELLULAR A7 RESTRAINS ESTROGEN-NEGATIVE FEEDBACK OF LUTEINIZING HORMONE VIA EPHRIN A5 IN THE HYPOTHALAMUS OF FEMALE RATS. Shang Li, M.D.,[1] Junyu Zhai, M.D. Ph.D.,[2] Yanzhi Du, M.D. Ph.D.[1] [1]Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China; [2]University of California, San Francisco, San Francisco, CA.

OBJECTIVE: We have previously shown that systemic injection of exogenous erythropoietin-producing hepatocellular (EPH) A7-Fc raises serum luteinizing hormone (LH) levels before ovulation in female rats, indicating the induction of EPHA7 in ovulation. In this study, we aimed to identify the mechanism and hypothalamus–pituitary–ovary (HPO) axis level underlying the promotion of LH secretion by EPHA7.

DESIGN: A study based on various rat models.

MATERIALS AND METHODS: Using an ovariectomized (OVX) rat model, in conjunction with low-dose estradiol (E_2) treatment, we investigated the association between EPHA7–ephrin (EFN) A5 signaling and E_2-negative feedback. Various rat models (OVX, E_2-treated OVX, and abarelix-treated) were injected with the recombinant EPHA7-Fc protein through the caudal vein to investigate the molecular mechanism underlying the promotion of LH secretion by EPHA7.

RESULTS: *Efna5* was observed strongly expressed in the arcuate nucleus of the female rat using RNAscope in situ hybridization. Our results indicated that E_2, combined with estrogen receptor (ER) α, but not ERβ, inhibited *Efna5* and *gonadotrophin-releasing hormone 1* (*Gnrh1*) expression in the hypothalamus. In addition, the systemic administration of EPHA7-Fc restrained the inhibition of *Efna5* and *Gnrh1* by E_2, resulting in increased *Efna5* and *Gnrh1* expression in the hypothalamus, as well as increased serum LH levels.

CONCLUSIONS: Our findings demonstrated the involvement of EPHA7–EFNA5 signaling in the regulation of LH and the E_2-negative feedback pathway in the hypothalamus, highlighting the functional role of EPHA7 in female reproduction.

SUPPORT: This work was supported by grants from the National Key Research and Development Program of China (No. 2018YFC1003202 and 2017YFC1001002), the National Natural Science Foundation (No. 81971343, 81671413, 81671414, and 81901549), and Shanghai Commission of Science and Technology (No. 19410760300 and 17DZ2271100).

P-835 4:30 PM Tuesday, October 20, 2020

EFFECT OF GROWTH HORMONE ON BLASTOCYST FORMATION AND IMPLANTATION RATES IN WOMEN UNDERGOING IN VITRO FERTILIZATION. Larissa Matsumoto, MD,[1] Ekaterini koutsantonis Pires, MD,[1] Michelle Nagai, MD,[1] Fernanda Imperial Granjo, MD,[1] Carolina Rebello Costa, MD,[1] Edson G. Lo Turco, PhD,[2] Lucas Yamakami, MD,[3] Renato Tomioka, MD,[3] Orcar Duarte, MD[4] [1]MD, São Paulo, Brazil; [2]IonMedicine - Precision Medicine, Sao Paulo, Brazil; [3]Clinical Chief, São Paulo, Brazil; [4]Clinical Chief in Lab For Life Laboratory, São Paulo, Brazil.

OBJECTIVE: Evaluate the adjuvant effect of human growth hormone (hGH) on blastulation, implantation, and pregnancy rates in women undergoing IVF cycles.

DESIGN: Retrospective chart review at a private infertility center

MATERIALS AND METHODS: This analysis uses data from a total of 293 IVF treatments from jan/2015 to april/2020. Patients with the poor ovarian response or who did not obtain blastocysts in previous cycles were selected and were split into two groups IVF with 2,66mg/day of hGH starting at the beginning of the stimulation until the trigger and without hGH protocol. The data analysis we have performed the T-test to assess the comparisons between groups, with a confidence interval of 95% and a statistical significance of p< 0,05.

RESULTS: A total of 293 cases, with 100 IVF stimulation cycles without hGH, classified as Controls (CG), and 193 with hGH protocol, classified as Study group (SG), didn't show the average age, (38,67+- 3,46 (CG) and 38,67 +- 3,00 (SG), p= 0,322). No differences between groups with AMH, basal FSH, and basal LH were observed. The number of oocyte retrieved showed no statistical difference, but we observed better results, with a blastulation rate (46% +- 0,37) into the SG when compared with, controls (29% +- 0,31), p= 0,001. The SG shows a better implantation rate (42,6% +- 0,5) and controls was (28,1% +- 044), p= 0,029. The OR for pregnancy rate with GH is 3,098 (IC 1,324-7,247, 95%).

CONCLUSIONS: Different strategies were used to attempt to improve oocyte and embryo quality in IVF cycles, particularly in older, POR, and women with diminished ovarian reserve. In our findings, the use of hGH was related to improvement in embryo quality, implantation rate, and pregnancy rate, as shown in prior studies. Consequently, the use of hGH as adjuvant therapy should be considered to optimize the results of IVF cycles. Large-scale randomized controlled trials are needed to determine the adequate dose and duration of the treatment, as well as to establish which populations would benefit most.

References: no references

SUPPORT: non

POSTER SESSION: MENTAL HEALTH

P-836 3:30 PM Wednesday, October 21, 2020

EXAMINING THE ASSOCIATION BETWEEN INFERTILITY, PREGNANCY INTENTION, AND POSTPARTUM DEPRESSION. Gabriela A. Barber, M.S., Julia R. Steinberg, Ph.D. University of Maryland, College Park, MD.

OBJECTIVE: To examine whether symptoms of postpartum depression differ between women who conceived naturally and intentionally, women who used fertility treatments, and women who had unintended pregnancies.

DESIGN: Cross-Sectional Survey

MATERIALS AND METHODS: Using data from the Pregnancy Risk Assessment Monitoring System (from 2009-2015; 36 states and NYC), we examined whether postpartum depressive symptoms differed between three pregnancy groups: women who reported conceiving naturally and intentionally (n = 91,064), women who reported conceiving naturally and unintentionally (n = 96,284), and women who reported conceiving with fertility treatments (n=5,535). We created two postpartum depressive symptom measures: 1) a continuous standardized measure of postpartum depressive symptoms, and 2) a dichotomous measure (called elevated postpartum depressive symptoms) that differentiated those who were at least one standard deviation above from those who were less than one standard deviation from the mean of postpartum depressive symptoms. We examined unadjusted and adjusted means of the continuous measure and predicted probabilities of the dichotomous measure. We adjusted for sociodemographics, relationship context, birth context, psychological health, and general health.

RESULTS: Women who conceived unintentionally (unadjusted M = 0.07, 95% CI: 0.06 – 0.08; adjusted M = 0.14, 95% CI: 0.09 – 0.20) had more postpartum depressive symptoms than women who conceived naturally and intentionally (unadjusted M = -0.17, 95% CI: -0.18 - -0.16; adjusted M = -0.0004, 95% CI: -0.05 – 0.05) and than women who used fertility treatments (unadjusted M = -0.14, 95% CI: -0.17 - -0.11; adjusted M = 0.01, 95% CI: -0.05 – 0.07), p-values <0.0005. The unadjusted and adjusted predicted probability of having elevated postpartum depressive symptoms was higher for the unintended pregnancy group (unadjusted predicted probability = 20.5%, 95% CI: 20.2% – 20.9%; adjusted predicted probability = 12.9%, 95% CI: 11.9% – 13.9%) compared to those who conceived naturally and intentionally (unadjusted predicted probability = 12.4%, 95% CI: 12.1%-12.7%; adjusted predicted probability = 9.9%, 95% CI: 9.1%-10.6%) and those who conceived using fertility treatments (unadjusted predicted probability = 11.2%, 95% CI: 10.0%-12.3%; adjusted predicted probability = 9.5%, 95% CI: 8.3%-10.8%), p-values < .0005.

CONCLUSIONS: Results suggest that the utilization of fertility treatments in order to conceive does not place women at a differential risk for PPD, whereas having an unintended pregnancy does. These results add to the small existing body of literature that has sought to characterize and examine postpartum mental health outcomes for women that have conceived through the use of fertility treatments. While undergoing fertility treatments may be a stressful experience, our

data do not provide evidence that undergoing such treatments increases women's risk of experiencing PPD relative to women who conceived naturally and intentionally. Instead, having an unintended birth increases risk of experiencing more postpartum depressive symptoms.

P-837 3:30 PM Wednesday, October 21, 2020

ASSOCIATION OF PSYCHOSOCIAL STRESS WITH OVARIAN FUNCTION IN YOUNG CANCER SURVIVORS. Jayeon Kim, MD, MPH,[1] Brian W. Whitcomb, PhD,[2] Brian Kwan, PhDc,[3] Sally A. D. Romero, PhD, MPH,[3] H. Irene Su, M.D., M.S.C.E.[3] [1]CHA Fertility Center Seoul Station, Obstetrics and Gynecology, Seoul, Korea, Republic of (South); [2]University of Massachusetts, Amherst, Amherst, MA; [3]University of California San Diego, La Jolla, CA.

OBJECTIVE: To investigate the association between psychosocial stress and ovarian function in adolescent and young adult cancer survivors (AYA survivors)

DESIGN: A cross-sectional study was conducted estimating the association between perceived stress, measured by self-report and saliva cortisol, and ovarian function, measured by bleeding pattern, dried blood spot (DBS) FSH and LH and saliva estradiol. We included 377 AYA survivor participants.

MATERIALS AND METHODS: AYA survivor participants were ages 15-35 at cancer diagnosis and ages 18 to 40 at study enrollment, had completed primary cancer treatment, had a uterus and at least one ovary, did not have uncontrolled endocrinopathy, and were not on hormone therapy. Recruited from cancer registries, physician referrals and cancer advocacy groups, participants provided self-reported information on psychosocial stress (Perceived Stress Scale-10) and on cancer, reproductive (fertility, contraception, menstrual pattern) characteristics. DBS samples were collected timed to the early follicular phase (cycle days 3-7) for menstruating individuals and on a random day for amenorrheic individuals; saliva samples were collected 3 time points within one day. FSH and LH were measured by ELISA's, cortisol and estradiol were measured by LC/MS.

RESULTS: The median age of participants was 34.0 years (range 19-41) at a median of 6.0 years since cancer diagnosis. The most common cancer was breast (32.1%). Median PSS-10 score was 15 (range 0-36), with 5.3% scoring $\geq$ 26, the cut point suggestive of severe stress. Cortisol levels followed a diurnal pattern and cortisol area under the curve (AUC) was negatively correlated with PSS-10 scores ($P = 0.03$). Neither PSS-10 scores nor cortisol AUC were associated with FSH, LH, estradiol levels or menstrual pattern. Waking cortisol and the cortisol awakening response also were not related to ovarian function measures.

CONCLUSIONS: We observed no association between self-reported and biomarkers of psychosocial stress and ovarian function measures in AYA survivors. The lack of association between psychosocial stress and a variety of ovarian function measures in female AYA cancer survivors suggests that psychosocial stress does not have a significant impact on the reproductive axis of AYA survivors. This finding is important in counseling this population on their menstrual pattern and family building plans.

P-838 3:30 PM Wednesday, October 21, 2020

ASSOCIATIONS BETWEEN QUALITY OF LIFE, SOCIODEMOGRAPHICS AND MILITARY CHARACTERISTICS IN A US VETERAN POPULATION WITH INFERTILITY. Mary K. Skalitzky, BA,[1] Michelle A. Mengeling, MS, PhD,[2] Andrea Holcombe, MS, PhD,[2] Amy M. J. O'Shea, PhD,[2] Karen M. Summers, MPH CHES,[3] Ginny L. Ryan, MD, MA[4] [1]University of Iowa Carver College of Medicine, Iowa City, IA; [2]Iowa City VA Health Care System, Iowa City, IA; [3]University of Iowa, Iowa City, IA; [4]University of Iowa Hospitals and Clinics, Iowa City, IA.

OBJECTIVE: To identify sociodemographic and military characteristics associated with quality of life for male and female US Veterans with infertility.

DESIGN: A cross-sectional survey of a national sample of military Veterans aged 20-45.

MATERIALS AND METHODS: Data were collected using a computer assisted telephone interview which included socio-demographics, reproductive health, and military exposures. Participants completed the Fertility Quality of Life (FertiQoL) tool if the Veteran and/or a current or previous partner had been diagnosed with infertility. The FertiQol tool is a validated instrument providing a summative Core FertiQoL score made up of 4 subscales (Emotional, Mind-Body, Relational, and Social) specific to patients with infertility. Higher subscale and resulting Core scores indicate higher quality of life. PTSD was measured in two ways: Veterans could self-report a past diagnosis or screen positive during the interview via the PCL-5 checklist. Bivariate analyses were completed to evaluate factors associated with the FertiQol scores.

RESULTS: 303 participants completed the FertiQoL: 166 females and 137 males. There were no statistically significant differences between male and female Veterans with regards to marital status, age, education level, household income, history of biological parenting, or PTSD diagnosis or screening. Female Veterans were more likely to report a history of any parenting, including parenting beyond the biological such as adoption (77.7% vs. 67.9%, p=0.05). Male Veterans reported significantly longer deployments, with 57.0% of men vs. 32.7% of women deployed more than 12 months (p=0.0001), and greater exposure to combat arms (53.3% vs. 15.1%, p=0.0001) and experience under enemy fire if deployed (81.3% vs. 59.3%; p=0.0008). Male Veterans also tended to have higher rank (p=0.003).

The mean Core FertiQol score for all 303 Veterans was 68.9 (SD=17.6). Higher total Core FertiQoL scores in male compared to female Veterans (mean 73.4 vs. 65.2, p<0.0001) resulted from higher Emotional, Mind-Body, and Social but not Relational subscale scores. Core FertiQol scores were positively associated with a history of biological parenting (mean = 70.8 vs. 65.2, p= 0.01) and age (p=0.006). Veterans with PTSD were found to have significantly lower Core FertiQoL scores compared to Veterans without PTSD (mean=65.3 vs. 74.0, p<0.0001). There were no differences in scores by marital status, race, income, education, or combat exposure.

CONCLUSIONS: This is the first known study of infertility-related quality of life in the Veteran population using the FertiQoL. Our study demonstrates that among Veterans with infertility, those with PTSD have poorer quality of life as measured by the FertiQol. Results show higher FertiQol Core and certain subscale scores in male Veterans, consistent with prior studies suggesting men experience less distress following an infertility diagnosis. Our findings support prior work showing age and biological parenthood, though not other parenting, mitigate the negative quality of life effects of infertility.

SUPPORT: The research reported here was supported by the Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development (HSR&D) Service grantÂ IIR 13-294. The content is solely the responsibility of the authors and does not necessarily represent the views of the Department of Veterans Affairs.

P-839 3:30 PM Wednesday, October 21, 2020

HEALING ENVIRONMENT IN THE FERTILITY CLINIC. Hoa T. Nguyen, MD, Emily A. Evans-Hoeker, MD Carilion Clinic, Roanoke, VA.

OBJECTIVE: The purpose of our study was to determine if alterations in the ambient environment have an impact on the anxiety level and/or satisfaction of patients undergoing fertility evaluation and treatment.

DESIGN: Cross-sectional survey study administered pre and post implementation of a "healing environment" in the fertility clinic.

MATERIALS AND METHODS: The healing environment intervention included: a cooperative coloring activity in the waiting room, lowering and warming lights in exam and waiting rooms, maintaining a low noise level and using sound machines in exam rooms, utilizing a mild calming natural aroma, and maintaining a comfortable temperature for equipment. The primary outcome was psychological well-being as measured by the validated State-Trait Anxiety Inventory (STAI) 6-Y survey which was self-administered at the time of the patient visit. A lower composite score in the STAI survey indicates a lower current level of anxiety. The STAI 6-Y survey was also made available to staff. The secondary outcome of patient satisfaction was evaluated using the Press-Ganey Survey in follow up to the patient visit as per institutional protocol, with a higher score indicating higher satisfaction. T-test and fisher exact tests were used for statistical analyses. Power analysis demonstrated a need for 35 surveys from each phase of the study to achieve 80% power to detect an effect size of .40 in STAI scores.

RESULTS: A total of 37 and 48 STAI surveys were conducted pre and post intervention, respectfully. The average scores during the pre and post "healing environment" intervention were 35 and 32, respectively (p = .26). Assessing individual components of the STAI, only the component assessing "feeling upset" demonstrated a statistically significant difference between the groups (p = .0396). In the pre intervention group, 21.62% reported feeling "somewhat upset" as compared to 6.25% in the post intervention group. Whereas, 0% reported feeling "moderately upset" in the pre intervention group compared to 6.25% in the post intervention group. Although not

powered, the staff STAI composite score was 38 (medium anxiety state) versus 27.5 (low anxiety state) pre and post intervention respectfully. The Press-Ganey surveys have been completed and are requested.

CONCLUSIONS: Though there was no significant difference in overall STAI scores pre and post intervention, patients rated feeling upset significantly more after implementation of the healing environment. The reason for this is currently unclear. Differences in patient satisfaction scores are yet to be determined.

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SUPPORT: none

P-840 3:30 PM Wednesday, October 21, 2020

EMOTIONAL WELL-BEING DURING FERTILITY TREATMENT: A RANDOMIZED CONTROLLED TRIAL TO EVALUATE THE USE OF AN ONLINE LEARNING PLATFORM AS A RESOURCE.

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OBJECTIVE: Infertility and associated therapies have been characterized as anxiety-provoking. As emotional states can be triggered by stimuli, we assessed the impact of a visual multimedia electronic (e)-learning and e-consent platform on patients' anxiety states prior, during, and upon completion of infertility treatment cycles.

DESIGN: Prospective randomized controlled trial

MATERIALS AND METHODS: Patients aged 18-43 years undergoing their first intrauterine insemination (IUI) or in-vitro fertilization (IVF) cycle were randomized to two groups receiving either: 1) standard fertility counseling with their physician and nurse team (conventional group); or 2) standard counseling plus access to an interactive multimedia e-learning platform (EngagedMD) before and during their treatment cycle (EMD group). Patients completed surveys including a modified 19-question State-Trait Anxiety Inventory (STAI) at three time points to quantitively assess their treatment experience: T1 (prior to treatment), T2 (after the MD/RN teaching session at the start of their cycle), and T3 (after cycle completion). Each STAI item is given a weighted score of 1 to 4, the instrument has a possible score from 19 to 76, and the 50th percentile for an anxious state in women aged 19-39 is 34. Student's t-test and Chi-squared test were used as appropriate.

RESULTS: To date, a total of 77 patients (IUI=35 and IVF=42) with a mean age of 35.2 +/- 4.4 years have been enrolled with no differences in baseline demographics (age, duration of infertility, infertility diagnosis, and education level) for both IUI and IVF and conventional and EMD groups. Overall, STAI scores at T1, T2, and T3 were 37.8 +/- 11.3, 37.0 +/- 10.6, and 37.0 +/- 11.6 respectively, with no difference in IUI and IVF patients at T1 (p=0.51). However, IVF patients scored significantly higher at T2 (40.3 +/- 9.3 vs. 33.7 +/- 11.1, p=0.03) and T3 (41.3 +/- 12.1. vs. 32.7 +/- 9.5, p=0.01) compared to IUI patients at the same timepoints. IUI patients had a significant decrease in their anxiety from T1 to T2 (mean delta -3.1; p=0.05) and T1 to T3 (mean delta -3.9 p=0.01), while patients undergoing IVF treatments had no significant change in their anxiety scores throughout. With respect to conventional and EMD groups, there were no differences in STAI scores in IUI and IVF cycles from T1 to T3. Of the patients undergoing IUI, there was a significant decrease in patients' anxiety levels from T1 to T2 in the EMD group (35.8 +/- 9.3 vs. 31.6 +/- 10.2; p=0.02), while this difference was not seen in the conventional group (37.4 +/- 11.5 vs. 35.5 +/- 12.0; p=0.46).

CONCLUSIONS: Anxiety levels were significantly elevated in first-time IVF patients during and after treatments compared to those undergoing IUI. The addition of an e-learning platform did not alter the level of anxiety compared to traditional teaching methods in IVF patients. In contrast to standard counseling, patients undergoing IUI experienced a decrease in their immediate anxiety level after exposure to EngagedMD. Overall, anxiety levels in this cohort of patients were high, indicating that added psychological resources may be beneficial to this population.

References: none

SUPPORT: none

P-841 3:30 PM Wednesday, October 21, 2020

PERINATAL EXPOSURE TO HIGH DIETARY AGES DELAYS PUBERTY ONSET AND DISRUPTS FOLLICULOGENESIS IN FEMALE OFFSPRING. Zaher Merhi, MD, HCLD,[1] Xiu-Quan Du, N/A,[2] Maureen Charron, Ph.D.[2] [1]SUNY Downstate University and New Hope Fertility Center, New York, NY; [2]Albert Einstein College of Medicine, Bronx, NY.

OBJECTIVE: Nutrition is an important source of exogenous advanced glycation end-products (AGEs) where thermally processed foods present in western-style diets contain large amounts of these pro-inflammatory molecules. Maternal nutrition and the intrauterine environment are important in determining susceptibility to reproductive and metabolic disturbances. The objective of this study was to determine whether perinatal exposure to high amounts of dietary AGEs affect metabolic and the reproductive parameters in female mice offspring.

DESIGN: Animal experiments in a university setting.

MATERIALS AND METHODS: 7 week old female CD1 mice were placed on either a diet low (L-AGE) or high (H-AGE) in AGEs for 2 weeks before mating and then for additional 6 weeks throughout pregnancy and lactation. Offspring from L-AGE dams (n=10) and H-AGE dams (n=13) were all weaned onto the L-AGE diet and studied through 16 weeks of age. Offspring were counted and weighed at birth then weekly. Body weight, growth curve, pubertal onset (age at vaginal opening), estrus cyclicity (vaginal smear), serum levels of anti-Mullerian hormone (AMH), leptin and adiponectin as well as insulin tolerance test (ITT) and glucose tolerance test (GTT) were performed. Ovaries were harvested for follicular count and gene expression by RT-PCR. Data were reported as mean ± SEM. For GTT and ITT, the total area under the curve (AUC) for 120 minutes for glucose concentrations in mg/dL was calculated. Mann-Whitney U test and repeated measures ANOVA were performed as appropriate.

RESULTS: Pups exposed to perinatal H-AGE diet had significantly lower body weight at birth compared to pups exposed to perinatal L-AGE diet (1.38 ± 0.1 vs. 1.58 ± 0.16 grams, $p<0.05$; respectively). Adult offspring exposed to perinatal H-AGE diet exhibited delayed growth and lower serum levels of leptin and AMH ($p<0.05$ for all). There was no significant difference in AUC for GTT ($p=0.7$) or ITT ($p=0.2$) between both groups. Perinatal exposure to H-AGE diet affected the reproductive potential in the adult female offspring by exhibiting delayed vaginal opening and irregular estrus cycles by spending less time in the proestrus phase and more time in the metestrus phase ($p=0.04$). Adult offspring exposed to perinatal H-AGE diet had significantly fewer corpora lutea (CL) in their ovarian sections, exhibited arrested folliculogenesis with most follicles in the secondary follicle stage, and had significantly lower ovarian mRNA expression levels of *Amh* ($p=0.005$), *Amhr2* ($p=0.02$), and *Cyp19a1* ($p=0.03$) compared to adult offspring exposed to perinatal L-AGE diet.

CONCLUSIONS: These results indicate that perinatal exposure to a diet elevated in AGEs causes deficits in perinatal growth, pubertal onset, and reproductive organ development in female mice. Whether these findings translate to humans remains to be determined in future studies.

SUPPORT: This research was supported by a grant from the American Society for Reproductive Medicine and a grant from the Society for Reproductive Investigation.

P-842 3:30 PM Wednesday, October 21, 2020

GETTING STRAIGHT TO THE POINT: DOES INDIVIDUALIZED PRE- AND POST-EMBRYO TRANSFER ACUPUNCTURE INCREASE PREGNANCY RATES? Lauren Grimm, M.A., Kate Phillippi, L. Ac, Lamya Kamel L.Ac, Dipl. OM, DAOM, Roohi Jeelani, MD Vios Fertility Institute, Chicago, IL.

OBJECTIVE: To examine the pregnancy and clinical pregnancy rates of those patients undergoing elective individualized pre- and post-embryo transfer acupuncture compared to receiving no acupuncture on day of frozen embryo transfer (FET).

DESIGN: Retrospective chart review at a private fertility center.

MATERIALS AND METHODS: All patients undergoing FET between the months of May 2018 – April 2020 were included. All patients meeting internal clinic standards for having a frozen embryo transfer can elect to have individualized pre- and post-embryo transfer acupuncture performed on-site 30 minutes before and immediately after embryo transfer. Patients were divided into two groups: those that received acupuncture therapy pre- and post- FET, and those that did not. Patients' past medical and cycle history were reviewed, and pregnancy outcomes recorded. Pregnancy was defined as having received a serum bHCG >5mIUmL, while clinical pregnancy was defined as receiving confirmation of gestational sac on transvaginal ultrasound 14 days following transfer. Two sample t-tests and chi square analysis were used to analyze the data using SPSS (SPSS Inc., Chicago, IL, USA).

RESULTS: A total of 654 cycles were analyzed. Baseline characteristics, including age and BMI, were similar between the two groups ($p>0.05$). There was a statistically significant difference in pregnancy rates between the Acupuncture FET and non-Acupuncture FET groups of 66.8% and 56.65% respectively ($p=0.003$). Similarly, the clinical pregnancy rate between the two groups was also statistically significant, with the acupuncture group having a clinical pregnancy rate of 60.6% compared to 46.95% in the control group ($p=0.017$). Additionally, of the patients that underwent PGT and transferred known euploid embryos, those that received acupuncture had a significantly higher pregnancy rate of 73.93% compared to 63.29% for those that did not ($p=0.042$). For those patients that did not undergo PGT, both pregnancy rates and clinical pregnancy rates were similar, with the acupuncture group having a pregnancy rate of 56.41% and clinical pregnancy rate of 52.56%, compared to 52.63% ($p=0.55$)and 41.4% ($p=0.11$) respectively for the non-acupuncture group. Although not statistically significant it is clinically relevant.

CONCLUSIONS: Previous studies have shown that acupuncture promotes blood flow and regulates the nervous system; therefore, it is thought to be helpful on the day of embryo transfer to promote relaxation and decrease stress while encouraging blood flow to the uterus. Inherent to Chinese Medicine is creating individualized treatments and although the standard diagnostics were not utilized, the past medical and cycle history were used to draw diagnostic conclusions and inform the unique treatments. Overall, individualized acupuncture performed on the day of embryo transfer was associated with statistically significantly higher pregnancy and clinical pregnancy rates. Follow-up research will investigate the difference in live birth rates and the cost-effectiveness of adding an acupuncture regimen to FET treatment protocols.

SUPPORT: None

P-843 3:30 PM Wednesday, October 21, 2020

IMPACT OF ACUPUNCTURE AND TRADITIONAL CHINESE MEDICINE (TCM) ON FROZEN EMBRYO TRANSFERS (FET) OF AUTOLOGOUS EMBRYOS WITH COMPREHENSIVE CHROMOSOMAL SCREENING (CCS): A RETROSPECTIVE COHORT STUDY. Lee Hullender Rubin, DAOM,[1] Carmelo S. Sgarlata, M.D.,[2] Morgan Hogue, MAcOM,[2] Lisa Pate, MAcOM,[2] Elizabeth Richards, MAcOM,[2] Lisa K. Tongel, MAcOM,[2] Hong Jin, DAOM, MD(PRC)[3] [1]Osher Center for Integrative Medicine University of California San Francisco, San Francisco, CA; [2]ORM Fertility, Portland, OR; [3]Oregon College of Oriental Medicine, Portland, OR.

OBJECTIVE: We aimed to assess birth outcomes from Frozen Embryo Transfer (FET) cycles of autologous embryos with Complete Chromosomal Screening (CCS) between patients with no known additional therapies compared with the addition of two distinct acupuncture approaches varying in dose (2 sessions or ≥3 sessions) and treatment (standardized or individualized).

DESIGN: Retrospective cohort study of patient charts from a single, private clinic matched with charts from affiliated acupuncturists' clinics.

MATERIALS AND METHODS: The fertility clinic contracted with six acupuncture associates to perform day of embryo transfer acupuncture (ET Acu) onsite. Charts were reviewed of women who completed an FET cycle with chromosomally screened, euploid, autologous embryos with or without ET Acu between July 2016 and December 2018. The acupuncturists also extracted data from charts from their community clinics of shared fertility clinic patients who added acupuncture therapy prior to embryo transfer (ET). Data was matched by name and ET date then merged with the fertility clinic database for analysis. Cycles with gestational carriers, donor eggs, no transfer, or embryos without chromosomal screening were excluded. Patient groups were categorized as 1) usual care for women who completed FET alone (UC group); 2) UC and ET Acu of two standardized acupuncture sessions before and after ET (ET Acu group); and 3) UC, ET Acu and acupuncture therapy received in the community prior to ET that included Traditional Chinese Medicine (TCM group) therapies such as diet and lifestyle modifications, warming therapy, or if appropriate, Chinese herbal therapy. Comparability between groups was assessed by age and number of embryos transferred. Differences in means were assessed using

one-way analysis of variance and proportions by Chi-square analysis. Main outcome measure was live birth.

RESULTS: We identified 1,035 FET-CCS cycles, of which 526 were UC, 150 were ET Acu, and 359 were TCM. The mean age of women in ET Acu (36.5 ± 3.8) and TCM (36.5 ± 3.7) groups was older than the UC group (35.9 ± 4.3, *p=0.05*) and not comparable. The mean number of embryos transferred in the ET Acu (1.29 ± 0.5) and TCM (1.25 ± 0.4) groups was also more than UC (1.20 ± 0.4), but not significantly (*p=0.095*). There was no difference in live births between UC (67.7%) and TCM (64.6%, *p=0.35*), but both groups were associated with significantly more live births over ET Acu (55.3%, *p=0.005* and *0.05*, respectively). The rate of miscarriage was also similar between UC (6.6%) and TCM (8.9%, *p=0.20*), but again, both were associated with significantly less than ET Acu (15.3%, *p=0.001* and *0.03*, respectively).

CONCLUSIONS: In autologous FET-CCS cycles, individualized acupuncture therapy with three or more visits and FET alone were associated with significantly more live births and fewer miscarriages when compared with ET Acu. In this observational study, patients who chose ET Acu and TCM differed on important variables that may predict birth outcomes thereby limiting interpretation. Future study should determine the ideal acupuncture dose and approach to support FET cycles with screened embryos.

SUPPORT: No financial support to disclose.

P-844 3:30 PM Wednesday, October 21, 2020

SUNNY SIDE UP? THE ROLE OF VITAMIN D IN FOLLICULAR DEVELOPMENT IN WOMEN OF ADVANCED MATERNAL AGE UNDERGOING INTRAUTERINE INSEMINATION.

Christy Oso, B.A.,[1] Nepheli Raptis, B.A., M.A.,[1] Emma Radley, M.A.,[1] Hanna Mandell, M.A.,[1] Lauren Grimm, M.A.,[1] Jessi Anderson, MPH,[1] Zoran J. Pavlovic, M.D.,[2] Angeline Beltsos, MD,[1] Roohi Jeelani, MD[1] [1]Vios Fertility Institute, Chicago, IL; [2]Rush University Medical Center, Chicago, IL.

OBJECTIVE: This study sought to determine whether vitamin D levels influenced follicular development in women of advanced maternal age undergoing intrauterine insemination (IUI).

DESIGN: Retrospective chart review at a private, multi-site fertility clinic.

MATERIALS AND METHODS: All patients over the age of 35 who underwent IUI between January 2017 - August 2019 were included. All patients received a basic fertility work up, including serum vitamin D and estradiol levels, as well as ultrasound evaluations. Sufficient serum vitamin D levels were defined as > 20 ng/mL at baseline while deficient patients were defined as <20 ng/mL. Maximum estradiol and follicle size as determined by ultrasound were used to measure follicular development. T-tests and chi square analysis were used to analyze the data using SPSS (SPSS Inc., Chicago, IL, USA).

RESULTS: A total of 163 patients were analyzed. Baseline characteristics between the two groups, including age and BMI were insignificant. The average baseline vitamin D level for deficient patients was 15.53 ng/mL while the average for sufficient patients was 35.83 ng/nL. For both vitamin D deficient and sufficient patients, no statistically significant relationship between vitamin D and dominant follicle size was found (p=0.249 and p=0.932, respectively). There was also no significant relationship found between vitamin D and maximum estradiol levels (p=0.910 and p=0.234, respectively).

CONCLUSIONS: Much attention has recently been given to the potential role of vitamin D in fertility treatments as its replenishment has been shown to improve IVF success rates. Vitamin D, believed to play an integral role in human reproduction, has receptors located throughout the endometrium and on the granulosa cells of growing follicles. Some in vitro studies demonstrated that treatment of follicles with vitamin D enhanced granulosa cell proliferation, and others found that vitamin D may counteract the inhibitory actions of AMH on the recruitment of primordial follicles, allowing for follicular maturation.The results of previous studies investigating the relationship between vitamin D and fertility treatment have been conflicting. While some studies have shown vitamin D to play a role in IUI success as measured by pregnancy outcomes, others have shown the opposite. The results of this study demonstrate that vitamin D may not play a role in follicular development. Future research is needed to determine whether vitamin D should be replenished for patients pursuing IUI.

References: Irani, M., et al. Role of vitamin D in ovarian physiology and its implication in reproduction: a systematic review. Fertility and Sterility, 2014. 102.2: p. 460-468.

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P-845 3:30 PM Wednesday, October 21, 2020

EFFECTS OF DAIRY INTAKE TO PREGNANCY OUTCOME AMONG WOMEN IN THE UNITED STATES.

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OBJECTIVE: Dairy intake has been considered as a source of calcium and protein to keep bones and muscles functioning properly. Recent studies suggested that dairy intake has also related to reproductive health due to its influence on hormone level. However, no past studies have examined the association between the dairy intake and pregnancy outcome. This study investigated this association in women of reproductive age in the U.S.

DESIGN: The retrospective study utilized the National Health and Nutrition Examination Surveys (NHANES) 2015-2016 public data, including data from biospecimen collection and health questionnaires on diet and pregnancy.

MATERIALS AND METHODS: The sample was consisted of 1366 women between 18-44 years extracted from this data. Simple Logistic regression was used first to examine the bivariate association between dairy intake and pregnancy outcome alone. After that, multiple logistic regression models were fitted to examine the same association, with the presence of confounding factors such as dairy intake, age, estradiol level, education and race.

RESULTS: A majority of women became pregnant trying within a year was 1055 (89.94%), and those who tried a year to become pregnant but still failed were 118 (10.06%). The population who regularly intake dairy (dairy use 5 time per week) was close to non-regularly dairy intake group (27.50% vs. 28.87%). Dairy intake was found not significantly associated with pregnancy with an odds ratio of 0.980 [95%CI = (0.585, 1.641)]. The Multiple logistic regression model showed that age was significantly associated with pregnancy with a p-value at 0.0044, and an odds ratio of 1.061 [95%CI = (1.019, 1.105)]. The odds of pregnancy failure in Mexican American women significantly higher than White women with a p-value at 0.0306, and the odds ratio was 2.542 [95%CI = (1.091, 5.921)].

CONCLUSIONS: This retrospective analysis showed that dairy intake frequency was not associated with pregnancy outcome among women in the United States during 2015-2016. The association did not differ when considering dairy intake alone as an individual factor or taking multiple factors into account including age, estradiol, race or education level.

P-846 3:30 PM Wednesday, October 21, 2020

VITAMIN D SUPPLEMENTATION PROTOCOLS AND BASELINE CHARACTERISTICS IN WOMEN SEEKING FERTILITY CARE.

Alex Finlinson, MD,■ Oluwafunmilayo Ogunremi, MD,[2] Andrea Goldstein, BS,[2] Brittany N. Carson, BS,[2] Sadeq Quraishi, MD,[3] Albert L. Hsu, MD[4] [1]University of Missouri, Columbia, MO; [2]Tufts Medical Center, Boston, MA; [3]Department of Reproductive Endocrinology and Infertility; University of Missouri, Columbia, MO; [4]■ ■ ■.

OBJECTIVE: In women of reproductive age, low serum 25-hydroxyvitamin D (25OHD) levels are associated with lower pregnancy rates. However, guidance on optimal vitamin D supplementation regimens during preconception are sparse. Our goal was to assess the efficacy of two vitamin D supplementation protocols in a cohort of women presenting for preconception or infertility.

DESIGN: We performed a retrospective analysis of 185 patients who presented for preconception or infertility at the University of Missouri between 2017 to 2018. Women who had 25OHD levels ≤20 ng/ml received 50,000 IU of oral vitamin D weekly for 8 weeks, while women with 25OHD 21-29 ng/ml received 50,000 IU of oral vitamin D weekly for 4 weeks. All women were also encouraged to take an extra 1000 IU of oral vitamin D daily, per Endocrine Society recommendations; 25OHD levels were re-assessed after the supplementation period.

MATERIALS AND METHODS: Pregnancy status was assessed as of 12/31/19 for all patients. Means were compared with two-sample t-tests. SAS version 9.4 (SAS Institute, Cary, NC) was used for all analyses.

RESULTS: In an initial comparison of the three groups (normal, insufficient, and deficient vitamin D levels), there was a statistically-significant difference in median BMI. There were differences in pregnancy rates between the three groups (31.7% in deficient group, 56.9% in insufficient group, 44.2% in normal vitamin D group) that will require further analysis. This comparison did not account for differences in fertility diagnoses or treatments. Intriguingly, while also likely not statistically significant, the mean number of days to pregnancy was quite different: 159 days in the deficient group, 234 days in the insufficient group, and 426 days in the normal vitamin D group.

Variable	Group 1 = deficient	Group 2 = insufficient	p-value	Group 3 = normal
# of women	63	68		53
Age (median, range)	31.1 (21-43 y/o)	30.0 (17-43 y/o)	0.254	33 (21-45 y/o)
Calculated age	31.6 (21.4-43.4)	31.4 (18.0-43.2)		33.1 (21.1-45.3)
BMI	**36.6 (17-65)**	**31.0 (17-52)**	**0.01**	26 (18-57)
AMH	6.1 (0.2-23)	3.12 (0.5-16)		2.3 (0.1-37)
FSH	7.9 (2-53.3)	5.95 (2.7-15.5)		7.0 (0.4-16.2)
Initial Vit D level	14.9 (4-20)	26.0 (21-29)	< 0.0001	36 (30-84)
Repeat vit D level	36.2 (11-86)	43.0 (21.9-87)	0.0252	n/a
Pregnant	= 13	= 33		= 19
Not pregnant	= 28	= 25		= 24
%	= 13/41 = 31.7%	= 33/58 = 56.9%		= 19/43 = 44.2%
Days to achieve pregnancy	159 (43-511 days)	234 (35-606 days)		426 (98-537 days)

CONCLUSIONS: Both vitamin D supplementation strategies were successful in improving median vitamin D levels. There are intriguing differences in baseline characteristics (BMI, AMH levels) and pregnancy results (percent pregnant, time to pregnancy), which need to be explored further in subsequent studies.

References: n/a

SUPPORT: n/a

POSTER SESSION: OVARIAN RESERVE

P-847 3:30 PM Wednesday, October 21, 2020

DIFFERENCES IN FOLLICULAR FLUID CYTOKINE PROFILE IN WOMEN WITH DIMINISHED OVARIAN RESERVE. Sina Abhari, MD,[1] Heather S. Hipp, MD,[1] Sabrina A. Gerkowicz, MD,[2] Quinton S. Katler, MD,[1] Laurie J. McKenzie, M.D.,[3] Shang Weirong, PhD,[1] Alicia K. Smith, PhD,[1] Anna K. Knight, PhD[1] [1]Emory University School of Medicine, Atlanta, GA; [2]IVFMD, South Florida Institute for Reproductive Medicine, Miami, FL; [3]Baylor College of Medicine, Houston, TX.

OBJECTIVE: To investigate the expression of cytokines in follicular fluid (FF) of women with diminished ovarian reserve (DOR) undergoing in vitro fertilization (IVF) and explore correlated functional pathways.

DESIGN: Nested case-control study

MATERIALS AND METHODS: Women undergoing ovarian stimulation and planned oocyte retrieval were recruited from the Emory Reproductive Center. We included 51 women with DOR and 30 controls, defined as women undergoing IVF for male factor, tubal factor due to tubal ligation, or oocyte cryopreservation for planned fertility delay (non-oncologic). Follicular fluid samples were collected from each participant at the time of oocyte retrieval and stored for later use. The follicular fluid samples were then assessed using multiplexed sandwich ELISA-based quantitative array platform (RayBiotech). Quantile regression was used to assess the association of DOR diagnosis and cytokine concentrations. The false detection rate was controlled at 5%.

RESULTS: A total of 357 cytokines were investigated in both women with DOR and controls. Expression of 26 cytokines was found to be significantly different in the follicular fluid between the DOR and the control group (*FDR<0.05),* following adjustment for age and BMI. Differentially expressed cytokines belong to diverse functional groups involved in follicular development and maturation including growth factor and related proteins, receptor signaling, apoptosis and inflammation. Among the most significant differentially expressed cytokines were sonic hedgehog ligand (SHH) and Amphiregulin (AR), both of which were lower in women with DOR. SHH is involved in granulosa and theca cell communication and promotes cellular proliferation in mouse ovary. AR has a significant role in oocyte maturation. We also detected a lower level of soluble Fas in women with DOR comparted to controls. The soluble form of Fas has anti-apoptotic activity, and our finding suggests down regulation of this pathway in women with DOR,

CONCLUSIONS: We found 26 cytokines differentially expressed between women with DOR and controls with normal ovarian reserve. Our data suggest feasibility of identifying biomarkers that illuminate how the ovarian follicle microenvironment is altered in the DOR population and identification of pathways playing a role in pathophysiology of DOR.

P-848 3:30 PM Wednesday, October 21, 2020

TUMOR NECROSIS FACTOR-ALPHA (TNFA) INHIBITORS DO NOT IMPACT OVARIAN RESERVE. Pamela B. Parker, M.D., M.P.H., Sacha A. Krieg, M.D., Ph.D., David Lee, MD, Thomas O'Leary, PhD, Diana Wu, MD, Bharti Garg, MBBS, MPH, Paula Amato, MD Oregon Health & Science University, Portland, OR.

OBJECTIVE: Increasing numbers of women are prescribed immunosuppressive and biologic medications for rheumatologic disorders and inflammatory bowel disease. TNFa is a potent cytokine with proinflammatory, cytotoxic, angiogenic, and growth modulatory effects of various target cells. While evidence on the safety of certain biologic medications has led to recommendations for use in pregnancy, few studies have assessed the impact of this immunotherapy on fertility in the preconception period. The purpose of this study is to analyze the impact of anti-tumor necrosis factor-alpha (TNFa) inhibitors on markers of ovarian reserve specifically, anti-mullerian hormone (AMH) level and antral follicle count (AFC).

DESIGN: IRB-approved retrospective cohort study

MATERIALS AND METHODS: We analyzed data from infertility patients seen at a single tertiary academic institution from 2008-2019 who reported taking any of the following anti-TNFa medications: infliximab, adalimumab, golimumab, certolizumab, etanercept, anakinra. AMH levels and AFC were compared to those of age-matched controls undergoing in-vitro-fertilization (IVF) during the same time period. Comparisons were done using two-sample t-tests (continuous variables) and Fisher Exact tests (categorical variables). In addition, we assessed ovarian response and IVF outcomes in a subset of patients taking TNFa-inhibitors who underwent IVF.

RESULTS: A total of 54 subjects were included (18 in study group; 36 controls). There were no differences in baseline characteristics such as age or parity. The most common indications for use of TNFa inhibitors were rheumatoid arthritis (38.9%), ulcerative colitis (22.2%), and Crohn's disease (22.2%). The most common TNFa inhibitors taken were infliximab (44.4%), etanercept (27.8%), and adalimumab (22.2%). There was no statistically significant difference in AMH level (2.07 vs 2.82 ng/mL, p = 0.29) nor AFC (17.95 vs 18.86, p=0.17) between the study group and controls, respectively. Analysis of IVF outcomes revealed no differences between groups in etiology of infertility, gonadotropin dose, duration of ovarian stimulation, cycle cancellation rates, number of oocytes retrieved, fertilization rate, number of embryos, number of embryos transferred, day of embryo transfer, or clinical pregnancy rate.

CONCLUSIONS: We conclude that anti-TNFa medications do not have a significant impact on ovarian reserve or ovarian response to stimulation. The information from this study can assist providers when counseling infertility patients regarding the impact of immunomodulators on fertility. Larger studies are needed to further assess the impact of immunomodulators on ovarian reserve and pregnancy outcomes in the general population.

P-849 3:30 PM Wednesday, October 21, 2020

OVARIAN AUTOLOGOUS PLATELET-RICH PLASMA (PRP) TREATMENT IMPROVES OOCYTE AND EMBRYO QUALITY IN WOMEN WITH POOR OVARIAN RESPONSE. Dimitar Parvanov, PhD,[1] Rumiana Ganeva, MSc,[1] Nina Vidolova, MSc,[1] Kristina Nikolova, MSc,[1] Magdalena Vasileva, MSc,[1] Ivaylo Stoykov, MSc,[1] Fabio Scarpellini, MD,[2] Georgi Stamenov, MD/PhD[1] [1]Nadezhda Women's Health Hospital, Sofia, Bulgaria; [2]Centre for Endocrinology and Reproductive Medicine, Rome, Italy.

OBJECTIVE: The application of platelet rich plasma (PRP) as a non-operative treatment is an innovative approach, introduced only recently in reproductive medicine. A few case studies have shown that intraovarian injection of PRP in women with poor ovarian reserve resulted in an increased number of MII oocytes and cleavage-stage embryos. However, little is known about the effect of autologous ovarian PRP treatment on oocyte and embryo quality. The objective of the present study was to evaluate the role of ovarian PRP treatment on the number and quality of oocytes and embryos in women with poor ovarian response undergoing IVF cycles.

DESIGN: Prospective cohort study

MATERIALS AND METHODS: A total of 132 women with a history of poor ovarian response (according to the Bologna criteria) in the previous cycle(s) were included in this prospective study between June 2019 and February 2020. They were treated with ovarian autologous PRP injection in two subsequent menstrual cycles. Approximately 21 ml autologous blood obtained from peripheral vein was obtained and used to prepare PRP following standard protocols. PRP injection was performed using a 21Gx11.8 inch needle under transvaginal ultrasound guidance. Antral follicle counts (AFC) and FSH levels were determined at baseline. Biomarkers of ovarian reserve (AFC and FSH) and IVF outcome variables (fertilization rate, number and quality of MII oocytes, and the number and quality of blastocysts) were recorded and compared between the cycle before and after PRP treatment. All collected oocytes and obtained Day 5 embryos were graded morphologically (Grades 1–3; Grade 1 being highest relative quality and Grade 3 being the lowest quality of the three grades) based on the standard methods. The results were analysed using Student's paired t-test. $P<0.05$ was considered statistically significant.

RESULTS: Ovarian PRP treatment resulted in insignificantly lower FSH (12.6±1.46 vs. 13.8±1.55, P=0.37) and slightly higher number of mature follicles (3.4±1.8 vs. 2.8±1.5, P=0.56). There were also insignificant increases in the number of retrieved oocytes (4.71±2.6 vs. 4.63±2.8, P=0.34, respectively), fertilization rate (81 vs. 79, P = 0.81) and, consequently the total number of Day 5 embryos (3.93±0.43 vs. 3.29±0.39, P=0.23). However, the percentage of high-quality MII oocytes (67.2% vs. 40.7%, P=0.03) and the percentage of grade-I blastocysts (65.56% vs. 45.89%, P=0.05) were significantly higher after PRP treatment in comparison to the pretreatment period. In addition, the mean MII oocyte quality (1.76±0.61 vs. 2.03±0.73, P=0.05) and blastocyst quality (1.49±0.57 vs. 2.11±0.92, P=0.03) were significantly improved in the post-treatment period.

CONCLUSIONS: The applied autologous ovarian PRP treatment is an effective approach in improving oocyte and embryo quality in poor responders. This approach may contribute to increased pregnancy rates.

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BIOAVAILABLE INHIBIN B (INHB) MAY BE A BETTER MARKER OF OOCYTE YIELD THAN CURRENTLY USED MARKERS OF OVARIAN RESERVE.

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OBJECTIVE: InhB is a dimeric protein secreted by granulosa cells. Its concentration rises at two points in the follicular phase, corresponding to preantral follicular growth and rising follicle-stimulation hormone (FSH). Despite its relationship with folliculogenesis, inhB has shown inter-cycle variability and cross-reactivity with other proteins, making it an inaccurate marker of ovarian reserve or predictor of oocyte yield. However, a new ELISA that specifically measures the β_B and α units detects the true biologically active, or bioavailable, inhB (bio-inhB). We hypothesized that selective measurement of bio-inhB may predict oocyte yield in controlled ovarian stimulation (COS).

DESIGN: Prospective cohort study

MATERIALS AND METHODS: Serum from women undergoing COS was obtained at the: 1) start, 2) middle ("mid"), and 3) end ("final") of COS. A new ELISA (Ansh Labs, Webster, TX) measured bio-inhB in these samples. The trend of bio-inhB ("delta") was calculated. Spearman tests evaluated correlations between bio-inhB and other ovarian reserve markers, such as age, antral follicle count (AFC), FSH, anti-Müllerian hormone (AMH), and oocyte yield. Participants were then stratified by diminished ovarian reserve (DOR) parameters.

RESULTS: Participants (n=64) had an average age of 34.5 years. 45.3% of women had an AMH <2ng/mL, but only 10.5% of women had an FSH >10mIU/mL and 8.2% had an AFC <7. Consistent with prior studies, bio-inhB at the start did not correlate with other ovarian reserve markers. However, mid, final, and delta bio-inhB were positively associated with AFC and AMH and negatively associated with age and FSH, reflecting DOR status (Table).

TABLE. Bio-inhB correlations with other ovarian reserve markers and oocyte yield

	Age	FSH	AFC	AMH	Total oocytes
Bio-inhB, baseline	-0.10	0.24	0.08	0.04	0.12
Bio-inhB, mid	-0.57*	-0.22	0.64*	0.60*	0.71*
Bio-inhB, final	-0.52*	-0.36*	0.89*	0.81*	0.88*
Bio-inhB, delta	-0.51*	-0.38*	0.88*	0.80*	0.87*
Total oocytes	-0.55*	-0.37*	0.86*	0.82*	

*p-value <0.05, Spearman tests used

When examining COS outcome, final and delta bio-inhB correlated strongly with oocyte yield (r= 0.87-0.88, p<0.05, Table). These correlations were stronger than those for age, FSH, and AMH, and similar to that of AFC. Correlations between bio-inhB and oocyte yield strengthened when stratified by age >35 years, AMH <2 ng/mL, and FSH >10mIU/mL.

CONCLUSIONS: When using this specific assay, bio-inhB values reflected ovarian activity in COS and correlated with other ovarian reserve markers. Correlations between bio-inhB and oocyte yield were stronger than those between most markers of ovarian reserve and oocyte yield. In contrast to prior data, bio-inhB may be a valuable tool in predicting oocyte yield, particularly in women with DOR.

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SUPPORT: None

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EFFECT OF NIGHT SHIFT WORK ON ANTI-MULLERIAN HORMONE (AMH) LEVELS IN REPRODUCTIVE-AGED AFRICAN AMERICAN WOMEN (AAW).

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OBJECTIVE: Circadian disruption, as commonly occurs in night shift workers, has been associated with adverse reproductive outcomes. Very few studies have examined the association between night shift work and ovarian reserve, and no prior studies have investigated this association in African American women (AAW). The objective of this study was to determine whether levels of AMH, a widely used serum biomarker of ovarian reserve, are associated with working night shift in a cohort of reproductive-aged AAW.

DESIGN: Cross-sectional study

MATERIALS AND METHODS: This study utilized an established cohort of AAW from Detroit, MI aged 25 to 35 years old, who had been recruited as a part of the NIEHS Study of the Environment, Lifestyle and Fibroids. Anthropometric measurements, self-reported medical history, and serum AMH levels (picoAMH assay, Ansh Labs, Webster, TX) were analyzed. Multivariable linear regression models were used to estimate the impact of night shift work on AMH levels (SAS 9.4- Cary, NC). Models were adjusted for age, age^2, body mass index, recent or current hormonal contraception use, and irregular menses (>35 days). AMH was log transformed for inclusion in the linear regression model.

RESULTS: A total of 1,646 women were included in this analysis with an average age of 29.2±3.4 years old and a median AMH of 4.1 ng/mL (IQR

2.3-6.7). Of these women, 236 (14%) reported working night shifts, with an average of 113±97 night shifts worked per year, and a median AMH value of 3.74 (IQR 1.90-5.91). Adjusted models demonstrated that working night shift was significantly associated with lower AMH levels (-13.5%, 95% CI -23.9% to -1.7%, p=0.02).

CONCLUSIONS: These findings suggest that ovarian reserve, as measured by serum AMH levels, is lower in reproductive-aged AAW who work night shifts than in those who do not work night shifts. Further research is needed to establish the mechanistic link between disruptions in circadian rhythm and decreased ovarian reserve. Providers should have an understanding of the factors that impact ovarian reserve in a diverse cross-section of women, as this will improve our ability to provide personalized recommendations and empowers all patients to make informed reproductive choices.

SUPPORT: This study was supported by NIH grant R01HD088638, the Evergreen Invitational Women's Health Grants Initiative and by the Intramural Research Program of the NIH, National Institute of Environmental Health Sciences.

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REPEATED APPLICATION OF LUTEAL PHASE ESTRADIOL / GnRH ANTAGONIST PRIMING INCREASES IVF SUCCESS FOR POOR OVARION RESERVE PATIENTS.

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OBJECTIVE: The aim of this study is to compare the results of repeated luteal phase estradiol patch / GnRH antagonist protocol (LPP) in patients with poor ovarian response (POR) with other protocols.

DESIGN: 226 patients and 293 cycles were applied to POR patients who underwent luteal estradiol patch / GnRH antagonists priming protocol (LPP), microdose flare up protocol or antagonist protocol in the Gulhane training and research hospital between January 2013 and March 2019.

MATERIALS AND METHODS: Among these, 38 patients underwent LPP protocol in the first cycle and LPP protocol in the second cycle. In 29 patients, LPP protocol was applied in second cycle after microdose flare up or antagonist protocol. 128 patients who underwent LPP only once and 31 patients who received only microdose flare up were also evaluated.

RESULTS: The clinical pregnancy rate was higher in the group that had repeated LPP protocol compared to the group applied with LPP after different protocol (p: 0.035). In this group, b hcg positivity and clinical pregnancy rate per embryo were also significantly higher (p: 0.000, p: 0.001).

CONCLUSIONS: Recurrent LPP protocol seems to be a suitable option in POR patients

POSTER SESSION: OVARIAN STIMULATION

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PROGNOSTIC VALUE OF LOW ANTI-MULLERIAN HORMONE LEVEL DURING IVF AMONG YOUNG WOMEN: A SART CORS STUDY.

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OBJECTIVE: Diminished ovarian reserve (DOR) describes women of reproductive age whose response to ovarian stimulation or fecundity is reduced as compared to women of similar age group. Lower anti-mullerian hormone (AMH) level has been associated with, but not necessarily predict, poor responses to ovarian stimulation, poor embryo quality, an poor pregnancy outcome in IVF. However, there are no useful threshold for critical clinical decision making. Studies have shown that lower AMH in combination with advanced maternal age indicates poor IVF outcome. However little is known about the prognostic value of lower AMH in young IVF population. The goal of the study was to determine association between low AMH level and IVF pregnancy outcomes among women who are < 35 years old.

DESIGN: Retrospective analysis of Society of Assisted Reproductive Technology Clinic Outcome Reporting System Database (SART CORS) from 2012-2016.

MATERIALS AND METHODS: All fresh autologous IVF cycles in women <35 years old were included (n=113,643). Based on AMH level, cycles were stratified into 4 groups; Normal (≥1.05 ng/mL), Low (0.4-<1.05 ng/mL), Very low (0.16-<0.4 ng/mL) and Ultra-low (<0.16 ng/mL). Multivariable logistic regression was used to estimate adjusted odds ratios (aOR) and 95% confidence intervals (CI) representing the association between AMH and each pregnancy outcome. Models were adjusted for patient's age, body mass index (BMI), gravidity, infertility diagnosis, FSH dose used for stimulation, stimulation protocol used, total 2 pronuclei zygote (2PN), and embryo grade.

RESULTS: A total of 83,556 cycles had embryo transfer and were included in the analysis. Live birth rates (LBR) were 48.4%, 40.2%, 35.9% and 32.8% per transfer in women with normal, low, very low and ultra-low AMH level, respectively. After adjusting for potential confounders, compared to women with normal AMH, women with low, very low and ultra-low AMH have a significantly lower risk of live birth (aOR: 0.95, 95% CI: 0.91-0.99; aOR: 0.91, 95% CI: 0.83-0.99; aOR: 0.81, 95% CI: 0.66-0.99, respectively). Maternal BMI, embryo grade and of total 2PN were independently associated with live birth. Overweight and obese women less likely to have a livebirth compared to normal BMI patients (aOR: 0.91, 95% CI: 0.88-0.94; aOR: 0.76, 95% CI: 0.73-0.79). For every 10 unit increase in the total number of 2 PN, we observed a 1.38 increase in the odds of live birth (95% CI: 1.34-1.43). Embryos graded as "fair" and "poor" embryos were less likely to lead to live birth as compared to "good".

CONCLUSIONS: Serum AMH level is an independent predictor of live birth in women who are < 35 years old and seeking IVF treatment for infertility.

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RESVERATROL FOR PREVENTING OVARIAN HYPERSTIMULATION SYNDROME IN WOMEN AT RISK UNDERGOING EGG DONATION: A RANDOMIZED CONTROLLED STUDY.

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OBJECTIVE: Ovarian Hyperstimulation Syndrome (OHSS) is the most serious and potentially life-threatening iatrogenic complication associated with ovarian stimulation protocols, being partially mediated by vascular endothelial growth factor A (VEGF). Previously, our group has reported that resveratrol, a natural polyphenol with anti-proliferative and anti-oxidant properties, exerts anti-angiogenic actions mediated by decreased VEGF in rat granulosa cells *in vitro*. The present study evaluated the role of resveratrol as a potential preventive strategy of OHSS in egg donors at high risk undergoing ovarian stimulation protocols.

DESIGN: A randomized controlled study.

MATERIALS AND METHODS: Fifty-six egg donors at risk to develop OHSS (21 follicles greater than 12 mm and/or estradiol levels ≥ 3000 pg/ml on the day of oocyte maturation trigger) undergoing ovarian stimulation were included. The study group (n=29) received a daily dose of 2 g of resveratrol orally for nine days from the day of GnRH administration as the trigger of oocyte maturation, whereas the control group (n=27) received a daily dose of 2 g of placebo. All participants were monitored every three days with vaginal ultrasound scans and blood tests, evaluating the amount of ascitic fluid, VEGF levels, estradiol concentration and hemoconcentration. The reduction of VEGF concentration was the primary outcome.

RESULTS: Baseline characteristics were comparable between both groups. Resveratrol treatment did not significantly reduce VEGF concentration compared to placebo at any time point (281.72 ± 133.57 vs 224.73 ± 107.28 on Day 9, P=0.08). Similarly, resveratrol did not affect either estradiol concentration (56.41 ± 29.99 vs 53.16 ± 28.44, P>0.05), hemoconcentration (40.03 ± 2.92 vs 40.48 ±2.57, P>0.05) or the amount of ascitic fluid (11.29 ± 7.3 vs 8.61 ± 6.07, P>0.05) in the pouch of Douglas.

CONCLUSIONS: Prophylactic treatment with resveratrol did not reduce either the incidence of OHSS or the VEGF concentration in egg donors at high risk undergoing ovarian stimulation protocols. Higher doses and/or longer exposure periods may be needed to elucidate whether resveratrol can reduce the risk of OHSS as suggested by in in vitro studies.

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IMPACT OF BODY HABITUS ON INCIDENCE OF COMPLICATIONS IN PATIENTS HOSPITALIZED WITH OVARIAN HYPERSTIMULATION SYNDROME. Liat Bainvoll, BS,[1] Rachel S. Mandelbaum, MD,[2] Meghan B. Smith, MD,[2] Caroline Violette, MD,[2] Shinya Matsuzaki, MD, PhD,[2] Jacqueline Ho, MD MS,[2] Kristen Bendikson, MD,[2] Richard J. Paulson, MD, MS,[2] Koji Matsuo, MD, PhD[2] [1]Keck School of Medicine at USC, Los Angeles, CA; [2]University of Southern California, Los Angeles, CA.

OBJECTIVE: The impact of body habitus on risk of complications resulting from ovarian hyperstimulation syndrome (OHSS) has not been well-elucidated. This study aimed to evaluate the association between body habitus and complications resulting from OHSS in hospitalized patients.

DESIGN: A retrospective analysis of the National inpatient Sample, a U.S. population-based database, between 2012-2015

MATERIALS AND METHODS: Women <50 years of age with a diagnosis of OHSS were identified and classified as normal weight, class I-II obesity, or class III obesity. ICD-9 codes were used to evaluate the incidence of OHSS-related complications. Multinomial logistic regression was used to identify factors associated with obese body habitus, and binary logistic regression was used to evaluate independent risk factors for incidence of *i)* any or *ii)* multiple complication(s) that occurred during hospitalization.

RESULTS: Of 2,745 women hospitalized with OHSS during the study period, 2,440 (88.9%) were of normal weight, 155 (5.6%) had class I-II obesity, and 150 (5.5%) had class III obesity. There were a total of 270 (9.8%) pregnant women, 20 (7.4%) of which were obese. Obese women (either class I-II or III) had a higher degree of comorbidity, had lower incomes, and were less likely to have private insurance than non-obese women (all, $P<0.001$). Non-obese women had higher rates of OHSS-related complications than women with class I-II obesity or class III obesity (any complication: non-obese 65.2%, class I-II obesity 54.8%, and class III obesity 46.7%, $P<0.001$; and multiple complications: non-obese 38.5%, class I-II obesity 32.3%, and class III obesity 20.0%, $P<0.001$). In the multivariable model, obesity remained independently associated with lower risk of complications (class I-II odds ratio [OR] 0.57, 95% confidence interval [CI] 0.39-0.83, $P=0.003$; class III OR 0.30, 95%CI 0.20-0.44, $P<0.001$). Obese women were also less likely to require paracentesis (non-obese 32.8%, class I-II obesity 9.7%, and class III obesity 13.3%, $P<0.001$).

CONCLUSIONS: Larger body habitus is associated with decreased OHSS-related complication rates in hospitalized patients. Body habitus may therefore be used in risk stratification of patients to identify those at risk of major complications from OHSS.

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RELUGOLIX, A NOVEL ORALLY ACTIVE GnRH ANTAGONIST IS EFFECTIVE IN IVF PROTOCOL. Hideki Igarashi, M.D., Ph.D.,[1] Jin Kumagai, M.D., Ph.D.,[2] Mayumi Toya, M.D., Ph.D.,[1] Tomoko Hashimoto, M.D., Ph.D.,[3] Yuya Takeshige, Ph.D.,[3] Nobuya Aono, Ph.D.,[1] Yukiko Nakajo, AS,[2] Hiromitsu Hattori, Ph.D.,[1] Tomomi Tosa, MT,[1] Koichi Kyono, M.D., Ph.D.[3] [1]Kyono ART Clinic Sendai, Sendai, Miyagi, Japan; [2]Kyono ART Clinic Morioka, Morioka, Iwate, Japan; [3]Kyono ART Clinic Takanawa, Tokyo, Japan.

OBJECTIVE: The aim of this study was to clarify the effectiveness of relugolix, a novel orally active GnRH (GnRH) antagonist in in vitro fertilization (IVF) protocol.

DESIGN: This study was prospective, without randomization study which was conducted at Kyono ART clinic Sendai, Morioka, and Takanawa in Japan from December 2019 to March 2020. This study was approved by the Ladies Clinic Kyono Ethics Committee.

MATERIALS AND METHODS: This study includes a total of 113 controlled ovarian hyperstimulation (COH) cycles with GnRH antagonist protocol in IVF. 63 cycles were in daily injection of ganirelix (0.25mg) or cetrorelix (0.25mg) group (Ga/Ce group), and 70 cycles were in every 36 hours oral administration of relugolix (40mg) group (Rel group). GnRH antagonist (ANT) was administrated by fixed day 6 protocol or flexible protocol. Hormonal profiling (LH, FSH, E2 and P4) was assessed in the previous or the day of GnRH antagonist administration (ANT start day), and the decision day of oocyte pick-up (Trigger day). Number of retrieved oocyte and MII oocyte, fertilization rate, Day3 good embryo rate and good blastocyst rate were compared between each group. The statistical analyses were done by Welch T test and Chi square test. $P<0.05$ was considered statistically significant.

RESULTS: Patient characteristics including age, BMI and AMH level in each group were similarly. There were no significant differences in hormonal profiling in the ANT start day (Ga/Ce group vs. Rel group: LH; 4.2±5.6 vs. 4.2±5.6, E2; 720.8±544.4 vs. 795.8±443.8, P4; 0.3±0.3 vs. 0.3±0.3, respectively) and the Trigger day (Ga/Ce group vs. Rel group: LH; 3.0±3.9 vs. 2.8±1.7, E2; 1659.3±1044.4 vs. 1606.4±872.8, P4; 0.5±0.7 vs. 0.5±0.3, respectively) between each group. A total number of GnRH antagonist administration in Rel group was significantly fewer than that of Ga/Ce group (2.4±0.7 vs. 3.7±0.9, $p<0.01$). A total dose of HMG/FSH administration was considerably higher in Rel group, though the difference was not statistically significant (2346.3±748.8 vs. 2136.1±634.2, $p=0.08$). Despite no significant difference in average number of retrieved oocyte (Ga/Ce group vs. Rel group: 9.9±5.8 vs. 9.7±5.5) and MII oocyte (Ga/Ce group vs. Rel group: 7.8±4.5 vs. 7.2±4.0), maturation rate in Rel group was significantly lower than that in Ga/Ce group (73.7% vs. 81.7%, $p<0.05$). There were no significant differences in fertilization rate (79.1% vs. 80.0%), good day3 embryo rate (22.6% vs. 24.9%), blastocyst rate (47.0% vs. 49.9%) and good blastocyst rate (26.2% vs. 29.7%) between Ga/Ce group and Rel group. Premature LH surge was observed in one patient in Ga/Ce group, but not in Rel group.

CONCLUSIONS: Our results suggested that relugolix, a novel orally active GnRH antagonist was effective in COH with GnRH antagonist protocol in IVF. As clinical effectiveness of relugolix is expected by less expensive and few times administration compared with ganirelix and cetrorelix, relugolix is useful for patients in cost-benefit.

SUPPORT: None

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TYPE OF FOLLITROPIN ALFA FOR OVARIAN STIMULATION WITH MEDROXYPROGESTERONE ACETATE DOES NOT AFFECT CLINICAL OUTCOMES IN A DONOR-RECIPIENT PROGRAM. María Cruz, PhD,[1] Vanessa Vergara, MD,[2] Antonio Requena, PhD, MD[2] [1]IVIRMA Global Headquarters, Madrid, Spain; [2]Reproductive Medicine Specialist, Madrid, Spain.

OBJECTIVE: To assess stimulation and clinical outcomes using different follitropin alfa preparations, in order to provide important educational and clinical insights on recently introduced stimulation agents in new emerging protocols.

DESIGN: Multicenter (n=11), retrospective, analysis to determine the efficacy of different follitropin alfa preparations with MPA during 2019.

MATERIALS AND METHODS: The study population included women accepted as oocyte donors and undergoing ovarian stimulation (OS) with 3

	Bemfola (n=2810)	Gonal (n=389)	Ovaleap (n=1558)	p-value
Days of stimulation	10.2 ± 0.7	9.6 ± 0.5	10.0 ± 0.1	0.003
Estradiol_hCG (pg/ml)	3026 ± 125	3754 ± 515	3218 ± 155	0.021
Doses FSH (IU)	1909 ± 20	1993 ± 50	1887 ± 25	0.002
Oocytes retrieved	23.3 ± 0.5	26.0 ± 1.2	23.7 ± 0.6	<0.001
Oocytes metaphase II	19.1 ± 0.6	21.1 ± 0.9	18.6 ± 1.5	0.325
Fertilization rate (%)	77.4%	78.6%	78.7%	0.789
Implantation rate (%)	62.1%	60.8%	63.8%	0.223
Pregnancy rate (%)	60.8%	58.8%	62.1%	0.363
Miscarriage rate (%)	6.3%	5.9%	6.9%	0.210
Ongoing pregnancy rate (%)	53.1%	53.7%	55.7%	0.451

different follitropin alfa preparations Ovaleap n=1558; Bemfola n=2810; or Gonal-F n=389. Ovaleap and Bemfola are both biosimilars to the originally approved biological product, Gonal-F. All donors underwent OS in a MPA protocol. On day cycle 2 or 3, donors started to administer daily 150-225 IU of one of the 3 different follitropin alfa preparations. On the first FSH stimulation day, 10 mg MPA was administered daily and then continued until GnRH agonist trigger. Finally, a single dose of 0.1 mg GnRH agonist was administered to trigger final oocyte maturation.

RESULTS: There were some age related significant differences in stimulation characteristics, which were higher in the Gonal-F-stimulated donor group, however, regarding clinical variables analysed, there were no significant differences found between the three study groups (Table 1).

This was further confirmed on applying a linear regression model, which used the clinical pregnancy rate as the explanatory variable. Neither age, the number of oocytes retrieved or the type of follitropin alfa administered significantly affected the chances of achieving a clinical pregnancy The results were as follows: age 1.001 (0-987-1.014, p=0.930); retrieved oocytes 0.998 (0.992-1.003, p=0.414); and type of follitropin alfa 1.034 (0.967-1.107, p=0.327)

CONCLUSIONS: MPA as a substitute for GnRH analogues with OS in a donor-recipient program is effective. Minor differences in FSH isoforms present in follitropin alfa biosimilars versus the originator FSH molecule used for OS with MPA, had no impact on clinical outcomes or stimulation characteristics. Therapeutic equivalence has been established.

SUPPORT: Not apply

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BASELINE PROGESTERONE ELEVATION AT THE ONSET OF OVARIAN STIMULATION IS NEITHER CORRELATED WITH EMBRYO QUALITY NOR EUPLOIDY RATE.

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OBJECTIVE: Elevation of progesterone (P) during day 3 of a menstrual cycle is an uncommon phenomenon during ovarian stimulation cycles. Incomplete luteolysis, endogenous P production by the adrenals and ovarian aging have been described as potential causes of baseline progesterone elevation (BPE). Some authors have postulated that BPE predicts decreased implantation in fresh IVF cycles [1] However, to date, there is no published evidence clarifying a correlation with embryonic morphological appearance and genomic competence. The objective of this study is to asses the association of BPE on ovarian stimulation outcomes and embryonic quality of IVF/PGT cycles.

DESIGN: Retrospective cohort analysis.

MATERIALS AND METHODS: The study included infertile couples who underwent IVF with GnRH antagonist stimulation from 2016-2020. PGT-A with NGS were performed in all cases. Cohorts were segregated in two groups: Group 1: cycles with normal P levels (P $<$1.5 ng/mL) on day 3 of the cycle; Group 2: cycles with BPE (P $\geq$1.5 ng/mL). Patients with OCP pre-treatment, an active follicle on day 3, or oocyte recipients were excluded. Demographics, COH parameters, blastulation, and euploidy rates were evaluated. Comparative statistics and an adjusted mixed model with a GEE framework was utilized for analysis. A sample size of 163 blasts per group was calculated to have an 80% power to detect a 15% difference on euploidy rates (α=0.05).

RESULTS: 16892 blastocysts from 3527 cycles with normal P were compared to 202 blasts from 46 cycles with BPE. A BPE prevalence of 1.2% was found. On an unadjusted analysis, significant differences were found in AMH, baseline estradiol, day of ovulation trigger and estradiol on triggerday between cohorts. No significant differences were found in mean number of oocytes retrieved, maturity, fertilization, blastulation, and utilizable blastocyst rates among cohorts. The average of good, moderate and fair grading blastocysts were comparable among groups. Aneuploidy rates differed between groups (Group 1= 44.2%, BPE= 32.9%;p=0.02), however euploidy and inconclusive embryo rates were comparable between groups. After adjusting for age, BMI, AMH, days of stimulation and number of fertilized oocytes per cycle, no association was found between BPE and blastulation rates (OR 0.98, CI95% 0.5-1.7, p=0.97); euploidy rates (OR 1.05, CI95% 0.6-1.8, p=0.84), or aneuploidy rates (OR 0.86, CI95% 0.5-1.4, p=0.58).

CONCLUSIONS: For patients who undergo ART treatment, BPE at the beginning of the menstrual cycle during does not appear to compromise embryonic quality in freeze all/PGT cycles. Our study demonstrated that BPE is not associated with impaired number of oocytes retrieved, oocyte maturity rates, embryonic quality or euploidy rates when compared with cycles with normal P on day 3. The clinical significance of BPE and success rates following an embryo transfer has yet to be established. Further research, including detailed endocrine monitoring, is necessary to better understand if BPE represents a normal variation within menstrual cycles or if it embodies a measurable consequence derived from a subtle ovarian dysfunction.

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SUPPORT: None

P-859 3:30 PM Wednesday, October 21, 2020

COMPARISON OF PROGESTIN-PRIMED OVARIAN STIMULATION AND GNRH ANTAGONIST PROTOCOL IN CLINICAL OUTCOME FOR PCOS PATIENTS.

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OBJECTIVE: To investigate whether progestin-primed ovarian stimulation (PPOS) can be an alternative as gonadotrophin-releasing hormone antagonist (GnRH-ant) protocol for infertile women with polycystic ovary syndrome (PCOS) during IVF/ICSI.

DESIGN: A retrospective cohort study.

MATERIALS AND METHODS: This retrospective cohort study included 260 PCOS patients who underwent their first IVF/ICSI procedure with PPOS (n=65) or GnRH-ant protocol (n=195) followed by cryopreservation of all embryos from January 2016 to July 2019. Baseline characteristics of the two groups were balanced with propensity score matching using the nearest neighbor random matching algorithm in a ratio of 1:3. The primary outcome measure was the number of oocytes retrieved. The embryological and clinical outcomes were measured and only the first embryo transfer cycle was followed-up.

RESULTS: Basic characteristics such as infertility duration, age, and body mass index (BMI) were comparable in both groups. No significant difference was found in the number (mean $\pm$ SE) oocytes retrieved (20.2 $\pm$ 1.4 for PPOS vs 20.7 $\pm$ 0.6 for GnRH-ant protocol) or high quality embryos (7.5 $\pm$ 0.8 for PPOS vs 7.6 $\pm$ 0.4 for GnRH-ant protocol) between the groups. The FSH dosage, ovarian stimulation duration, ovarian hyperstimulation syndrome incidence were comparable between the groups. There was no significant difference in the clinical pregnancy rate (57.1% for PPOS vs 60.7% for GnRH-ant protocol) or live birth rate (42.9% for PPOS vs 46.4% for GnRH-ant protocol) of the first embryos transfer cycle between the two groups. In the cost-effectiveness analysis, the PPOS protocol was strongly dominant over the antagonist protocol.

CONCLUSIONS: Our results showed that the application of PPOS protocol in PCOS patients could achieve comparable oocyte retrieval and pregnancy outcomes to GnRH-ant protocol, but the medico-economic analysis was in favor of PPOS protocol.

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THE ASSOCIATION OF AMH WITH ENDOMETRIAL THICKNESS IN GONADOTROPIN STIMULATION/INTRAUTERINE INSEMINATION CYCLES.

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OBJECTIVE: The role of *anti-Müllerian hormone* (AMH) and its receptor (AMH-R) on endometrial function and development is not well known. However, endometrial production of AMH has been reported, and endometrial expression of both AMH and AMH-R has shown cyclic variation with unclear significance. Our objective was to evaluate the association, if any, between AMH and pre-ovulatory endometrial thickness (ET) in gonadotropin induction (Gn)/intrauterine insemination (IUI) cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All Gn/IUI cycles (n=11,383) taking place at a large academic fertility center between 11/2007 and 12/2019, were retrospectively reviewed. 1,856 Gn/IUI cycles (from 912 patients) with a recorded pre-treatment serum AMH level and information available on endometrial thickness (ET) (measured by transvaginal ultrasound on either the day of or the day prior to HCG-trigger) were identified and included in the current analysis. Uterine factor infertility patients were excluded.

Statistical analysis: Parametric and non-parametric tests were used as appropriate. Linear regression models, adjusted for potential confounders,

were used to evaluate the effect of AMH on ET (b_{AMH} stands for the regression coefficient of AMH). $P < 0.05$ was considered significant.

RESULTS: Mean (SD) age, BMI, and AMH were: 35.9 (4.0) years, 25.1 (5.1) kg/m^2, and 3.5 (4.2) ng/ml, respectively. Idiopathic infertility was the most common diagnosis (32.0%), and PCOS accounted for 8.7% of the population. Mean (SD) and median (IQR) ET (mm) were: 9.1 (2.3) and 9.0 (7.5, 10.4), respectively, when measured on HCG-trigger day, and 8.4 (2.3) and 8.0 (7.0, 10.0), respectively, when measured the day prior to it.

Unadjusted regression models, showed a positive, albeit weak, correlation between AMH and ET (as measured on both HCG-trigger day and day prior to it) [r: 0.1, b_{AMH} (95%CI): 0.03 (-0.003, 0.06), p: 0.08, and r: 0.1, b_{AMH} (95%CI): 0.04 (0.01, 0.08), p: 0.02, respectively]. When models were adjusted for BMI, prior parity, and peak estradiol (E_2) levels, the positive correlation between AMH and ET became stronger, [r: 0.2, b_{AMH} (95%CI): 0.04 (0.03, 0.11), p: 0.009; r: 0.3, b_{AMH} (95%CI): 0.07 (0.03, 0.11), p<0.001, for HCG-trigger day and day prior to HCG, respectively]. When models were further adjusted for PCOs diagnosis, the results remained significant [r: 0.2, b_{AMH} (95%CI): 0.04 (0.001, 0.08), p: 0.045; r: 0.3, b_{AMH} (95%CI): 0.05 (0.01, 0.10), p:0.03; for HCG-trigger day and day prior to HCG, respectively].

CONCLUSIONS: Pre-treatment, circulating serum AMH levels correlated positively with endometrial thickness in the pre-ovulatory phase of Gn/IUI cycles. Our data suggests a possible independent effect of AMH on endometrial development among patients undergoing Gn/IUI treatments.

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REDUCTION IN OHSS INCIDENCE IN JAPANESE IVF/ICSI PATIENTS WHEN APPLYING INDIVIDUALIZED DOSING WITH FOLLITROPIN DELTA. Osamu Ishihara, MD, PhD,[1] Joan-Carles Arce, MD, PhD[2] [1]Saitama Medical University, Saitama, Japan; [2]Ferring Pharmaceuticals, Copenhagen, Denmark.

OBJECTIVE: To compare the impact of the individualized follitropin delta dosing regimen based on AMH and body weight with regard to OHSS incidence and severity compared to conventional standard dosing regimen in Japanese IVF/ICSI patients.

DESIGN: Randomized, assessor-blind, controlled trial conducted in 347 Japanese women undergoing their first IVF/ICSI cycle (NCT03228680).

MATERIALS AND METHODS: Patients were randomized to controlled ovarian stimulation with follitropin delta (Rekovelle, Ferring Pharmaceuticals) or follitropin beta (Follistim / Puregon, Merck). The dose of follitropin delta was individualized based on serum AMH and body weight, and was fixed throughout stimulation – AMH <15 pmol/L [<2.1 ng/mL]: daily dose of 12 μg, AMH ≥15 pmol/L [≥2.1 ng/mL]: daily dose decreasing from 0.19 to 0.10 μg/kg body weight by increasing AMH (min-max 6-12 μg). Elecsys® AMH, Roche Diagnostics was used. The follitropin beta dose was 150 IU/day for the first five days and could thereafter be adjusted as per the investigator's discretion. A GnRH antagonist protocol was applied. OHSS was classified using Golan's system. Early OHSS was defined as onset ≤9 days after triggering of final follicular maturation, and late OHSS as onset >9 days after triggering. Pre-defined preventive interventions for early OHSS included cycle cancellation due to excessive ovarian response, triggering with GnRH agonist and administration of dopamine agonist. Clinical pregnancy was assessed 5-6 weeks after single blastocyst transfer.

RESULTS: The frequency of early OHSS was significantly (p<0.05) reduced from 18.6% in the follitropin beta group with conventional dosing to 10.0% in the follitropin delta group with individualized dosing. A similar observation was made for moderate/severe early OHSS which was significantly (p<0.05) reduced from 13.0% with follitropin beta to 6.5% with follitropin delta. Preventive interventions for early OHSS occurred for 3.4% and 1.2% for patients in the follitropin beta and delta groups, respectively. Late OHSS occurred at a low and similar frequency of 1.1-1.2% in the two groups. Overall, the frequency of OHSS was significantly (p<0.05) reduced from an incidence of 19.8% with conventional follitropin beta dosing to 11.2% with individualized follitropin delta dosing for OHSS of any grade, and from 14.1% with follitropin beta to 7.1% with follitropin delta for moderate/severe OHSS. The proportion of patients with at least one blastocyst on day 5 was not significantly different between groups with 89.3% for follitropin beta and 82.9% for follitropin delta. The clinical pregnancy rate for all patients who started stimulation was 23.7% for follitropin beta and 25.3% for follitropin delta.

CONCLUSIONS: The individualized follitropin delta dosing regimen based on AMH and body weight resulted in a statistically significant and clinically relevant reduction in OHSS frequency in Japanese IVF/ICSI patients when compared to follitropin beta in a conventional dosing regimen using a 150 IU/day starting dose. This improvement in patient safety with follitropin delta does not compromise efficacy outcomes.

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SUPPORT: Ferring Pharmaceuticals

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ORAL VERSUS INJECTABLE OVARIAN STIMULATION AGENTS FOR INTRAUTERINE INSEMINATION (IUI) IN WOMEN ≥38 YEARS OF AGE WITH DECREASED OVARIAN RESERVE. Russell Frank, M.D.,[1] Naama Steiner, M.D.,[1] Maryam Al-Shatti, M.D.,[1] Jacob Ruiter-Ligeti, M.D,[1] Michael H. Dahan, M.D.[2] [1]McGill University Health Centre, Montreal, QC, Canada; [2]McGill University, Montreal, QC, Canada.

OBJECTIVE: To compare effectiveness of oral versus injectable stimulation agents in women ≥38 years of age with decreased ovarian reserve undergoing IUI

DESIGN: Retrospective cohort study from a university health center

MATERIALS AND METHODS: A database was created of all women aged 38-42 years old who underwent IUI with stimulation at the McGill University Reproductive Centre between 2009-2018. The database contains 1597 IUIs from 944 women. A comparison of outcomes of oral (clomiphene citrate or letrozole) versus injectable (gonadotropins) agents was performed for those with antral follicle count (AFC) ≤6. ANOVA, chi square tests, and stepwise multivariate logistic regression were performed. The primary outcome was clinical pregnancy rate per cycle (intrauterine sac with fetal pole and heartbeat), and secondary outcomes were rate of multiple gestation. Data presented are mean ±SD. Power analysis required 196 cycles for an effect size of 0.2, alpha 0.05 and power 0.80.

RESULTS: 335 IUI cycles in 210 patients met inclusion criteria. Stimulation was with clomiphene citrate in 38 (11.3%), letrozole in 33 (9.8%), and gonadotropins in 264 (78.8%) of cycles. Most common co-etiologies of infertility (excluding age and decreased ovarian reserve as factors) were male factor (34.3%) and tubal factor (8.4%). Among the three stimulation agent groups, there was no significant difference in mean: age of females (p=0.41) or of males (p=0.28), gravidity (p=0.11), parity (p=0.55), or AFC (p=0.98) (see table). Number of stimulated follicles (p=0.21) and follicles (≥14mm) (p=0.10) at trigger also did not differ. The clinical pregnancy rates per cycle were similar (p=0.86), but highest in the letrozole group (see table). A clinical pregnancy was observed in 7.5% of all IUI cycles. There was one multiple gestation total, obtained with gonadotrophins. Analysis controlling for demographic confounders (p≤0.20) (including FSH, estradiol, prolactin, TSH, and total motile sperm count) demonstrated no differences in clinical pregnancy rates (p=0.84).

	Age (females)	Gravidity	Parity	AFC	Clinical pregnancy rate
Clomiphene citrate	40.2 ±1.5	0.9 ±1.0	0.4 ±0.6	4.0 ±1.8	5.3%
Letrozole	40.5 ±1.7	1.5 ±1.8	0.5 ±0.6	4.0 ±1.5	9.1%
Gonadotropins	40.6 ±1.6	1.1 ±1.3	0.4 ±0.7	4.1 ±1.6	7.6%
Total combined	40.5 ±1.6	1.1 ±1.4	0.4 ±0.7	4.0 ±1.6	7.5%

CONCLUSIONS: Letrozole may be the medication of choice for ovarian stimulation in IUI in older women with decreased ovarian reserve, demonstrating the highest pregnancy rate (although not statically so). The overall clinical pregnancy rate of 7.5% remains notable in this typically poor-prognosis population. Gonadotropins offered no benefits over oral medications in this study and likely come with increased associated costs.

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PROGNOSTIC FACTORS OF OVARIAN RESPONSE AFTER FOLLICULAR PROTOCOL WITH MPA TRIGGER WITH GnRH AGONIST. Juan Giles, M.D., Ph.D.,[1] María Cruz, PhD,[2] Pilar Alamá, MD PhD,[1] Laura Caracena, MSc,[1] Carmen Vidal, MD PhD,[1] Ernesto Bosch, MD, PhD[3] [1]IVI-RMA Valencia, Valencia, Spain; [2]IVIRMA Global Headquarters, Madrid, Spain; [3]IVI-RMA, Valencia, Spain.

OBJECTIVE: Oocyte donors present frequently a profile related to suboptimal responses to the ovulation induction with GnRH agonist due to hypothalamic suppression. Previous studies analyzed prognostic factors of GnRH antagonist protocol trigger with GnRH agonist (GnRHa). However, no data are available related to cycle outcomes with progestins (PPOS). Our objective is to evaluate predictors of ovarian response in oocyte donation (OD) cycles conducted in follicular phase with medroxyprogesterone acetate (MPA) and rFSH without rLH supplementation and agonist trigger.

DESIGN: Non inferiority prospective RCT study. EudraCT number 2017-002341-30 and ClinicalTrials.gov registration number is 2017-002341-30

MATERIALS AND METHODS: University-affiliated infertility clinic. Period included from October 2017 to June 2019, to evaluate ovarian response in terms of number of oocytes and determine prognostic factors related to suboptimal response to GnRHa trigger in PPOS. We randomized 318 donors in two groups in a 1:1 ratio. In MPA group 161 participants received intervention (10 mg daily administered orally during OS) and 156 were treated with GnRH antagonist (started once the leading follicle had reached 13 mm). Some donors were pre-treated with oral contraceptives.

Transvaginal ultrasound for follicular growth monitoring and serum extractions for analysis of estradiol (E2), LH, and progesterone (P) were performed on days of starting ovarian stimulation, 5, 7, 9 of stimulation and on the day of triptorelin administration.

RESULTS: No significant differences were observed in donor demographic characteristics. For basal levels, we did not observe statistical differences for any of the hormones evaluated, regardless of contraceptive intake.

On trigger day estradiol levels were significantly higher in the group treated with MPA (3363 pg/ml vs. 1330 pg/ml, p=0.011) in donors who were not taking oral contraceptives. LH levels were significantly higher in the MPA group, both in presence (1.5 IU vs. 1.0 IU, p<0.001) and in absence (1.8 IU vs. 1.2 IU, p<0.001) of oral contraceptives. Percentage of donors who developed early luteinization was similar between groups, regardless donors were taking contraceptives or not.

Basal progesterone level (p=0.031) and LH triggering (p=0.027) determination were negatively correlated with the number of oocytes retrieved during retrieval, while estradiol (<0.001) and progesterone (p=0.026) heights the day of ovulation induction were positively associated with the same main outcome. Oral contraceptive administration and age did not significantly affect ovarian response

CONCLUSIONS: Our findings support determination of basal P and E2, P and LH on trigger day in OD cycles stimulated with rFSH, MPA as co-treatment and trigger with GNRHa in order to identify women with a lower response in terms of number of oocytes.

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SUPPORT: None

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OVARIAN RESERVE PARAMETERS AND IVF OUTCOMES IN 510 WOMEN WITH POOR OVARIAN RESPONSE (POR) TREATED WITH INTRAOVARIAN INJECTION OF AUTOLOGOUS PLATELET RICH PLASMA (PRP).

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OBJECTIVE: Poor ovarian response (POR) accounts for 15% of all assisted reproductive technologies (ART) cycles performed in 2017 and 2018 in the United States, and is associated with increased rate of cycle cancellation, lower number of embryos available for transfer, and overall lower pregnancy rates. Platelet-rich plasma (PRP) is rich in growth factors and cytokines and has been used as an agent that induces tissue regeneration. PRP also promotes follicle development in vitro and has been utilized in small case series as a potential treatment for women with POR. The aim of the current study was to characterize ovarian reserve parameters and IVF outcomes in patients with POR treated with intraovarian injection of autologous PRP.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Reproductive age women (N=510; age range 30-46) diagnosed with POR based on Poseidon criteria ((i) Group 3: Patients <35 years with poor ovarian reserve prestimulation parameters (AFC<5, AMH<1.2 ng/ml) (ii) Group 4: Patients ≥35 years with poor ovarian reserve prestimulation parameters (AFC<5, AMH<1.2 ng/ml)) were included in the study. Autologous PRP was prepared from peripheral blood by centrifugation, and injected transvaginally under ultrasound guidance into at least one ovary using a 35 cm 17 G single lumen needle. Starting on the 2-4th days of the second menstrual cycle after the PRP procedure, AFC and serum AMH and FSH levels were re-assessed, and followed for up to 4 consecutive cycles. Women who were found to have at least one antral follicle were started on ovarian stimulation for IVF-ICSI. Markers of ovarian reserve (AFC, FSH, AMH) and IVF outcome parameters were followed.

RESULTS: A total of 510 patients (mean age 40.3 ± 4.0) with the diagnosis of POR were included in the study. PRP treatment resulted in higher AFC (4.2 ± 2.4 vs 2.6 ± 1.3; p<0.01) and serum AMH (0.52 ± 0.35 vs 0.33 ± 0.26; p<0.01), and lower serum FSH (16.4 ± 14.5 vs 20.9 ± 19.1; p<0.01) levels. After the PRP injection, 20 women (3.9%) conceived spontaneously, and 477 (93.5%) attempted IVF. Among the women who attempted IVF, 50 (9.8% of total) could not undergo oocyte retrieval due to stimulation failure or premature ovulation, 112 (21.9% of total) did not develop embryos due to lack of oocytes or mature oocytes at retrieval, or failed fertilization/cleavage, while 315 (61.8% of total) generated cleavage stage embryos. Among the women who generated embryos, 215 (42.2% of total) preferred to bank embryos for later use, while 100 (19.6% of total) underwent fresh or frozen embryo transfer, resulting in 23 pregnancies (23% per transfer), 18 of which (18% per transfer) resulted in sustained implantation (> 8 weeks) or livebirth.

CONCLUSIONS: Our findings suggest that Intraovarian injection of autologous PRP might be considered in women with poor ovarian response to stimulation. For wider clinical application, its clinical efficacy will need to be demonstrated in prospective randomized clinical trials.

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THE EFFECT OF GROWTH HORMONE ON IVF OUTCOMES DURING OVARIAN STIMULATION: A MATCHED COHORT STUDY.

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OBJECTIVE: While growth hormone (GH) is commonly used as an adjuvant treatment to controlled ovarian stimulation (COS) for IVF cycles, the data regarding its efficacy is inconsistent.

DESIGN: A retrospective matched cohort study of poor responder patients who underwent COS without the use of GH (COS-GH) subsequently followed by COS cycles that included adjuvant GH (COS+GH) treatment.

MATERIALS AND METHODS: A list of all patients having filled a prescription for GH from January 2018 – March 2020 who were undergoing IVF with a single provider was obtained. GH was administered daily at 3mg (9IU) starting on the first day of stimulation and ending on the day of trigger. Only women who had documentation of a previous cycle without the use of GH were included in the study. Several different outcomes were compared including total dose of gonadotropins used, duration of stimulation, number of follicles, number of mature oocytes, endometrial thickness, maximum estradiol (max E2) level, maximum progesterone (max P4) level, number of oocytes retrieved, number of mature oocytes, number of blastocyst embryos (blasts), number of usable blasts and percentage of usable blasts. Usable blasts were defined as those embryos that were transferred to the uterus or frozen. Paired t-tests were used by an independent statistician to analyze the data, and statistical significance was set at $p<0.05$.

RESULTS: 182 cycles (91 patients) were included in the study, and COS-GH cycles were compared to COS+GH cycles. The total dose of gonadotropins used (4252 vs 5757 mIU, p=0.002), duration of stimulation (10.1 vs 10.4 days, p=-.045), max E2 (1932 vs 2411 pg/ml, p=0.010), endometrial thickness (10.6 vs 11.2 mm, p=0.010), number of oocytes retrieved (11.8 vs 14.2, p=0.001), number of mature oocytes (9.7 vs 11.1, p=0.028), number of blasts (2.56 vs 3.98, p=<0.001) and number of usable blasts (1.6 vs 2.5, p=<0.001) were all significantly greater in the GH group.

CONCLUSIONS: Adding growth hormone to the COS protocol in poor responder patients may lead to improvements in the number of oocytes retrieved, mature oocytes, endometrial thickness, number of blastocysts, and the number of usable blastocysts.

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RECOMBINANT LUTEINIZING HORMONE ASSOCIATED WITH RECOMBINANT FOLLICLE STIMULATING HORMONE FOR OVARIAN STIMULATION: DECREASED INCIDENCE OF IMMATURE OOCYTES AND BETTER CLINICAL OUTCOMES. Edson Borges, Jr., PhD, Daniela Paes de Almeida Ferreira Braga, PhD, Amanda Souza Setti, MSc, Assumpto Iaconelli, Jr., MD Fertility Medical Group / Sapientiae Institute, Sao Paulo, Brazil.

OBJECTIVE: It has been demonstrated that the use of GnRH analogues decreases the concentration of LH available to developing follicles, nevertheless, both gonadotrophins, LH and FSH, are crucial to normal follicular development. Luteinizing hormone also plays an important role in oocyte maturation during natural cycles. However, whether patients undergoing COS may benefit from co-administration of r-LH and r-FSH, when either a GnRH-antagonist or a GnRH-agonist protocol is used is to be elucidated. The goal for the present study was to evaluate the effect of the combination of recombinant LH (rLH) with recombinant FSH (rFSH) on ICSI clinical outcomes.

DESIGN: Cohort study.

MATERIALS AND METHODS: Data were obtained via chart review of 6,565 patients undergoing ICSI cycles, with fresh embryo transfer, performed on day five of development, between 2016 and 2019. Ovarian stimulation was achieved by daily doses of r-FSH (FSH-only-protocol); or r-FSH associated with r-LH (FSH-plus-LH-protocol) beginning on day three of the cycle. Pituitary suppression was performed by GnRH-antagonist beginning when at least one follicle $\geq$14mm was visualized, or GnRH-agonist, from day 21 of the previous cycle. The influence of the COS protocol and pituitary blockage on the immature oocytes rate, implantation and pregnancy rates was evaluated by generalized linear models.

RESULTS: The co-administration of r-LH and r-FSH resulted in a significant increase in the mature oocytes rate, either when pituitary blockage was achieved by GnRH-antagonist (85.7% vs 77.2% for FSH-plus-LH-protocol and FSH-only-protocol, respectively, $p<0.001$) or GnRH-agonist (80.1% vs 73.2% for FSH-plus-LH-protocol and FSH-only-protocol, respectively, $p<0.001$). Likewise, the rates of immature oocytes were decreased by the association of r-LH with r-FSH, regardless of the pituitary blockage protocol: for prophase-I (PI) oocytes rate in GnRH-antagonist protocol (2.5% vs 6.5% for FSH-plus-LH-protocol and FSH-only-protocol respectively, $p<0.001$) and in the GnRH-agonist protocol (6.0% vs 8.3% for FSH-plus-LH-protocol and FSH-only-protocol respectively) and for metaphase-I (MI) oocytes rate in GnRH-antagonist protocol (5.5% vs 7.1% for FSH-plus-LH-protocol and FSH-only-protocol respectively, $p<0.001$) and in the GnRH-agonist protocol (6.5% vs 10.1% for FSH-plus-LH-protocol and FSH-only-protocol respectively, $p<0.001$). Additionally, the clinical outcomes were influenced by the COS protocol. The implantation rate was positively influenced by the FSH-plus-LH-protocol, independently on the pituitary blockage type: for GnRH-antagonist (28.2% vs 24.4%, $p<0.001$) and GnRH-agonist (26.0 % vs 21.45%, $p<0.001$). The association of r-LH and r-FSH also led to a significant increase in the pregnancy rate, when pituitary blockage was performed by GnRH-antagonist (38.0% vs 33.0%, p=0.012) but not when it was performed by GnRH-agonist.

CONCLUSIONS: Decreased incidence of immature oocyte and better clinical outcomes are achieved by the use of r-LH associated with r-FSH for COS.

SUPPORT: None.

P-867 3:30 PM Wednesday, October 21, 2020

TO CANCEL OR NOT TO CANCEL? USING AN ARTIFICIAL NEURAL NETWORK (ANN) TO PREDICT UTILITY OF OOCYTE RETRIEVAL VS. CYCLE CANCELLATION IN EXTREMELY POOR RESPONDERS. Baruch Abittan, M.D.,[1] Jill Karten, M.D.,[2] Alixandra Domney, M.D., M.P.H.,[2] Jesse Stewart, B.A.,[3] Oren Segal, PhD.,[3] Randi H. Goldman, M.D.[1] [1]Northwell Health Fertility, North Shore University Hospital/Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY; [2]Department of OBGYN, North Shore University Hospital/Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY; [3]Hofstra University, Hempstead, NY.

OBJECTIVE: Patients with fewer than three follicles on transvaginal ultrasound following ovarian stimulation are often cancelled, as the risks of undergoing oocyte retrieval may outweigh the benefits of yielding fewer than three mature oocytes (MII). However, sometimes patients with greater than three visible follicles still yield fewer than three MII oocytes. We set out to determine if an artificial neural network (ANN) could be used to predict the likelihood of extremely low MII yield despite ultrasound findings of >3 follicles >14mm.

DESIGN: This was a model-prediction study based on a retrospective cohort of patients who underwent first fresh autologous in vitro fertilization cycles resulting in oocyte retrieval between the years 2016-2019. Patients were included if anti-Müllerian hormone (AMH) and follicle stimulating hormone (FSH) were recorded within one year of stimulation and excluded if an aromatase inhibitor was used during the ovarian stimulation.

MATERIALS AND METHODS: One-thousand eleven cycles were initially analyzed and 999 remained in the final model after excluding 12 cycles for extreme outliers (>28 MIIs retrieved). Exclusion of these cycles preserved the model's accuracy within a confidence of 99%. Cycles were categorized into two groups based on number of MIIs retrieved: 1) MII<3 (n=57) and 2) MII$\geq$3 (n=942). Synthetic minority oversampling technique (SMOTE) was used to oversample group 1 (MII<3) during model training (from n=57 to n=942) given the significant cohort-size imbalance between groups, causing a strong bias toward group 2 (MII$\geq$3), and leading to misclassification of low MII-yielding cycles. Of the various machine-learning models tested, an Extra Trees Classifier (ETC) performed best, with a sensitivity of 42% and specificity of 95%.

RESULTS: Patient- and cycle-specific variables utilized in our final prediction model were patient age, AMH, body mass index, peak estradiol on day of trigger shot, number of visible follicles > 14mm on day of trigger, and total injectable FSH dosage.

The ETC performed exceptionally well at predicting cycles that result in at least three mature oocytes at the time of retrieval (group 2; MII$\geq$3). However, the model correctly predicted that a cycle will result in fewer than 3 MIIs only 42% of the time. Cycles were most likely to be misclassified if a patient had between 3-6 follicles >14mm on the day of trigger.

CONCLUSIONS: The goal of this model is to help guide both physicians and patients when deciding whether or not to proceed with an oocyte retrieval for poor responders. Our model is inherently limited by the small sample size of patients with few follicles, requiring an oversampling technique that limits the generalizability of the results. This tool will be prospectively validated,

additional data will be added, and the prediction model will be modified and strengthened.

P-868 3:30 PM Wednesday, October 21, 2020

FRIENDLY PROTOCOL FOR OOCYTE DONORS: FERTILITY OPTIMIZATION IN TIMES OF SOCIAL ISOLATION DUE TO COVID-19?

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OBJECTIVE: Compare the number of oocytes retrieved from oocyte donors subjected to vitro fertilization (IVF) in two different protocols: friendly (corifollitropin alfa + clomiphene citrate (CC) + dydrogesterone) and conventional (daily rFSH + GnRH antagonist). Secondly, to evaluate the frequency of ovarian hyperstimulation syndrome (OHSS), number of visits to the clinic and the clinical pregnancy rates.

DESIGN: Retrospective study

MATERIALS AND METHODS: One hundred and eighteen infertile women aged 21 to 35 years old were divided into two groups: 1) Friendly: corifollitropin alfa (Elonva®), CC (Indux®) and dydrogesterone (Duphaston®); 2) Conventional: follitropin alfa (Gonal®), menotropin (Merional®) and ganirelix (Orgalutran®). All participated in the egg donation program and had ≥ 20 antral follicles before stimulation for IVF. The presence of hereditary or genetic diseases, infectious diseases, endometrial diseases, chronic diseases, adenomyosis, endometriosis were excluded. The variables analyzed were age, time and cause of infertility, number of days of induction and visits to the clinic (until trigger), number of follicles ≥14mm (trigger day), frequency of early ovulation (visualization of an image suggestive of follicular rupture before ovarian puncture), number of mature oocytes, frozen embryos, clinical pregnancy rate and OHSS (mild: pain (use of scopalamine + paracetamol) and/or nausea and/or vomiting; moderate: increased abdominal volume with evidence of clinical ascites without the need for hospitalization and moderate pain (use of codein); severe: hospitalization due to severe symptoms).

RESULTS: Please, see table below. Ovulatory factor, the number of visits to the clinic and the tubal factor were not predictors of obtaining mature oocytes (only antral follycle number was independent predictor).

Variable	Friendly protocol (n=52)	Conventional protocol (n=66)
Age(years)	30±3,8	29,1±4,9
Infertility time(years)	4,4±3,4	4,5 ± 3,2
Cause of infertility:	49,2	50,8
Male(%)	**37,5**	**62,5**
Ovulatory(%)**	**63,6**	**36,4**
Tubal factor(%)**	2,8	3,1
Other(%)		
Induction days	10,4± 1,1	10,5±1,2
Number of visits to the clinic**	**2,8±0,5**	**4,9±2,3**
Follicles≥14 mm(hCG day)	14,7±5,5	12,7±6,2
Early ovulation	1,9	1,5
Number of mature eggs	18,5±10,1	17,2±9,2
Number of frozen embryos	7±4,7	5,3±2,2
Clinical pregnancy rate[n(%)]	20(40)	27(40,9)
OHSS	43,9	56,1
Mild(%)	5,7	6,1
Moderate(%)	1,9	1,5
Severe(%)		

**p<0,05

CONCLUSIONS: Friendly protocol for IVF seems to be safe (same risk of OHSS) and effective (oocyte mature and clinical pregnancy rate) in comparison to the conventional protocol in oocyte donors. The smaller number of visits to the clinic with the friendly protocol can be a great ally in times of social isolation due to the pandemic by COVID-19.

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SUPPORT: Nothing to disclose.

P-869 3:30 PM Wednesday, October 21, 2020

CHANGES IN ENDOCRINE PROFILES POST-TRIGGER FOR OOCYTE MATURATION YIELD HIGHER-QUALITY OOCYTES.

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OBJECTIVE: During the use of assisted reproductive technologies for conception or oocyte cryopreservation, each patient is monitored with serial ultrasounds and serum hormone concentrations: particularly estradiol, progesterone, and the gonadotropins follicle stimulating hormone (FSH) and luteinizing hormone (LH). Several studies have evaluated these levels at the time of trigger for oocyte maturation in comparison with live birth rates. However, very few studies have evaluated the change in endocrine levels on the day after trigger in correlation with oocyte maturation and pregnancy outcomes. Thus, the objective of this study was to determine if the change in endocrine hormone levels on the day after trigger with human chorionic gonadotropin with or without a gonadotropin-releasing hormone agonist affects the number of good quality oocytes during controlled oocyte stimulation cycles.

DESIGN: Retrospective cohort study at an academic-affiliated private practice.

MATERIALS AND METHODS: All patients undergoing controlled oocyte stimulation cycles with the use of gonadotropins for in-vitro fertilization (IVF) or oocyte cryopreservation from September 2018 through December 2019 were assessed for inclusion. The charts of patients with successful oocyte retrieval were systematically examined and all necessary data collected, including serum concentrations of estradiol, progesterone, FSH, and LH throughout each cycle. The primary outcome was the number of mature oocytes (identified as oocytes in metaphase II at the time of oocyte retrieval) in each stimulation cycle. Statistical analysis was performed using student t-test, one-way ANOVA, and Spearman's correlation where applicable. Data are expressed as mean $\pm$ standard deviation. This study was IRB approved.

RESULTS: Of the 372 patients who underwent controlled ovarian stimulation with gonadotropins during the study period, the 360 that were included for analysis had a mean maternal age of 37.3 $\pm$ 4.2 years and BMI of 27.6 $\pm$ 7.8. Most patients underwent antagonist cycles (n=295) compared with those who underwent agonist stimulation cycles (n=65). In all cycles, the percent change in progesterone levels from the day of trigger to the levels one day after trigger was statistically significant with an increasing number of mature oocytes ($R=0.522$; $p<0.0001$). Interestingly, the change in FSH levels before and after trigger were significantly different between antagonist and agonist cycles ($p<0.001$). Antagonist cycles resulted in increased FSH levels post-trigger (17.05% $\pm$ 67.3%), while there was an overall decrease in FSH levels post-trigger in agonist cycles (-11.37% $\pm$ 20.83%).

CONCLUSIONS: The change in serum hormone endocrine levels, particularly progesterone, before and after trigger for oocyte maturation can affect the number of mature oocytes yielded. The greater the change of progesterone levels post-trigger results in a higher number of mature oocytes. The percent change in progesterone levels can be used as a predictor of higher-quality oocyte yield in controlled ovarian stimulation cycles.

P-870 3:30 PM Wednesday, October 21, 2020

PREDICTORS OF VARIABILITY IN OOCYTE YIELD AFTER SUCCESSIVE CONTROLLED OVARIAN STIMULATION CYCLES.

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OBJECTIVE: To determine predictors of variability in oocyte yield observed within patients undergoing successive controlled ovarian stimulation cycles (COS) utilizing the same protocol.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A retrospective chart review identified patients who completed more than one controlled ovarian stimulation cycle, within a 12-month period, at the University of California, Center for Reproductive Health, between January 2018 and December 2019. Descriptive statistics were performed. A mixed generalized linear model (GLM) was used to determine variables associated with variability in oocyte yield. Subgroup analyses were performed to investigate the variability in oocyte yield by treatment protocol.

RESULTS: There were 520 patients included in the analytic sample. Most patients were 40 years old or younger (71.9%) with a primary diagnosis of diminished ovarian reserve (33.6%). The protocols utilized among patients

included were GnRH antagonist (74.6%), Clomid-Flare (13.6%), and Demi--Halt (11.7%). Mean oocyte yield in the sample was 12.4 oocytes (SD 8.6 oocytes). In univariate analyses, predictors of increased variability in oocyte yield included treatment protocol with GnRH antagonist with least squares mean (LSM) of 3.4 and Demi-Halt (LSM 3.6) compared to Clomid-Flare based protocol (LSM 1.6; p<0.001), age less than 35 (LSM 4.2; p<0.001), and ovulatory dysfunction as the primary diagnosis (LSM 5.3; p<0.001). In the multivariate analysis, predictors of increased variability in oocyte yield included treatment with a GnRH antagonist or Demi-Halt protocol and a diagnosis of ovulatory dysfunction. Patients with a diagnosis of diminished ovarian reserve or undergoing stimulation using a Clomid-Flare based protocol exhibited the least variability between cycles. Age was no longer a predictor of variability in oocyte yield after controlling for covariates. In subgroup analyses restricted by treatment protocol, diagnosis remained as a significant predictor of variability in oocyte yield among those who utilized a GnRH antagonist protocol. Conversely, significant residual variability in oocyte yield was observed among those who utilized a Demi-Halt protocol that was not explained by any of the postulated predictors.

CONCLUSIONS: Variability in oocyte yield exists despite the use of the same protocol within the same year in patients undergoing successive COS cycles. Predictors of variability seen in oocyte yield includes characteristics intrinsic to the patient, such as infertility diagnosis and those related to the stimulation including the chosen protocol. However, there remains variability between cycles that is not accounted for which creates a challenge when counseling patients of expected outcomes of a successive cycles. Further prospective studies are needed to understand how adjustments in COS protocols can be utilized to minimize variability yet maximize oocyte yield in patients undergoing successive cycles.

SUPPORT: Not applicable

P-871 3:30 PM Wednesday, October 21, 2020

EMBRYOLOGICAL OUTCOME AND HORMONAL PROFILE AFTER DOUBLE STIMULATION IN PATIENTS WITH POOR PROGNOSIS: INTRA-PATIENT PAIRED STUDY. Bella Martazanova, PhD, Nona Mishieva, PhD, Khava Bogatyreva, PhD, Anna Korolkova, MD, Aydar Abubakirov, PhD Reproductive endocrinology, Moscow, Russian Federation.

OBJECTIVE: Stimulation in both phases of the menstrual cycle became a new approach in poor responder patient's management. Previous studies showed that this approach could be a good opportunity for poor-responder patients because it results in more oocytes and embryos. However, stimulation in the follicular phase makes endocrine and paracrine changes especially in the hormonal profile, which is associated with the corpus luteum function and could lead to changes in the follicle environment during luteal stimulation. Therefore, there is still need for more data about embryological outcomes and hormonal changes after DuoStim, comparing follicular versus luteal phase stimulations in the same ovarian cycle.

DESIGN: A total of 76 patients with a reduced ovarian reserve was included in the intra-patient paired study. Inclusion criteria: age <43 years; AMH <1.2 ng/ml; AFC <6; basal FSH≥11 IU/ml. Exclusion criteria: uterine fibroids≥4 cm, deep endometriosis, cancer, BMI ≥29 kg/m2, smoking, severe male infertility. Group 1 (n=76) received stimulation on the day 2 follicular phase (FP). Group 2 (n=76) received the stimulation in the luteal phase (LP) on the 4th day after the first oocyte pick up (OPU) day in the same menstrual cycle.

MATERIALS AND METHODS: Plasma samples were obtained on stimulation starter day, 6 days after, on triggering and OPU day. Statistical analysis – the Mann-Whitney test, t-test, the chi-squared test; p<0.05 was considered to be statistically significant.

RESULTS: The mean age was 36.7± 3.8 years and anti-mullerian hormone concentration was 0.94± 0.3 ng/ml in the patient's cohort. On the stimulation starting day, the estradiol (E2) and progesterone (P) concentrations were significantly higher in group II LP stimulation patients than in a group I (Table), but then decreased and were similar in both groups on the ovulation triggering day. However, no significant differences in the embryological outcomes were found between the groups (Table).

CONCLUSIONS: The cohorts of oocytes obtained after the luteal phase are similar to their paired follicular phase derived cohorts, and demonstrate an equal number of the blastocyst and Top-quality blastocysts. High estradiol and progesterone levels on the stimulation starting day did not affect the embryological outcome.

	1 group FP (n=76)	2 group LP (n=76)	*P*
Estradiol on stimulation start day (pmol/L)	87,8±18,1	384,27±334,44	*p*<0.001
Estradiol trig. day (pmol/L)	3670,97±2896,0	3697,73±2231,34	NS
Progesterone on stimulation start day (nmol/L)	0,88±0,4	16,7±13,3	*p*<0.001
Progesterone trig. day (nmol/L)	3,8±4,9	5,6±4,6	NS
Retrieved oocytes (n)	3.9±2.6	5.2±3.0	NS
MII oocytes (n)	3.8±2.2	4.3±2.6	NS
Blastocysts (n)	1.7±1.2	2.1±2.2	NS
TOP-blastocysts (n)	1.0±0.6	1.6±0.6	NS

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SUPPORT: None

P-872 3:30 PM Wednesday, October 21, 2020

CUMULATIVE LIVE BIRTH RATES BETWEEN GnRH-AGONIST AND GnRH-ANTAGONIST PROTOCOL IN ONE ART CYCLE WHEN ALL EMBRYOS TRANSFERRED : REAL-WORD DATA STUDY INCLUDING 17842 WOMEN FROM CHINA. Jingwei Yang, M.D.

OBJECTIVE: To compare the cumulative live birth rate (CLBR) of the first ART cycle including all subsequent frozen-thaw cycles in different ovarian stimulation protocol GnRH-agonist long protocol or GnRH antagonist protocol and find the clinical implication for agent choice.

DESIGN: Real-world observational data, such as electronic medical records(EMRs) contain large amounts of clinical information about heterogeneous patients and their response to treatments. The retrospective real-world data from the EMRs of a reproductive institute (2016-2019) to evaluated patients who commencing their first IVF cycle including fresh and subsequent frozen-thaw cycles from first oocyte retrieval and with no left embryos. A total of 17 842 patients and 29 065 cycles were analyzed which included 16 028 patients treated with GnRH-a long protocol and 1814 patients treated with GnRH-ant protocol.

MATERIALS AND METHODS: A total of 17842 women started their first IVF cycle including fresh and subsequent frozen-thaw cycles. Live birth was defined as delivery of any neonate at ≥28 weeks' gestation. CLBR was defined as once a live birth occurs, patients were considered to get a outcome regardless of subsequent cycles. A proportional hazards model was used to evaluate the relative prognostic significance of GnRH-a protocol and GnRH-ant protocol, female age, BMI, the number of retrieved oocytes, AMH, FSH, and the aviable embryos in relation to the CLBR.

RESULTS: Baseline characteristics were significantly different between the GnRH-a and GnRH-ant groups. Patients The mean age of women commencing IVF treatment was 30.83±4.04 years in GnRH-agonist and 34.11±5.77 years in GnRH-antagonist, and the mean number of oocytes retrieved was 13.15±6.24 in GnRH-a and 9.71±7.27 in GnRH-ant(All P value<0.05). When all embryos transferred derived from the cycle, the CLBR was 10586/16028(66.05%) in the GnRH-a group and 886/1814(48.84%) in

the GnRH-ant(OR: 2.03; 95% CI: 1.85-2.25; $P<0.001$). Mean time to the first live birth was 22.86 months in the GnRH-a group compared to 25.54 months in the GnRH-ant group ($P<0.01$). But when stratified analysis was employed to explore the optimal population selection in terms of oocyte numbers, the significant difference was found in the cumulative incidence of first live birth between treatment groups in sub-optimal group[retrieval oocytes(4-9)], the CLBR of GnRH-ant group is lower than GnRH-a ($P<0.000$, HR=0.56, 95%CI:0.39-0.81; Test of PH assumption: $P>0.05$). No significant difference of CLBR was observed in other subgroups between different treatments.

CONCLUSIONS: This study is the real-word data study comparing CLBR in GnRH-antagonist protocol with long GnRH-agonist protocol. After one complete cycle, despite significantly higher CLBR in the long agonist protocol for sub-optimal ovarian response patients, no significant difference between these two treatments in other patients. It's crucial to optimize the utilization of treatments in different ovarian response patients and consider the field of application of GnRH-antagonist protocols in China.

SUPPORT: no

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FREQUENCY AND SEVERITY OF OVARIAN HYPERSTIMULATION SYNDROME (OHSS) AMONG OOCYTE DONORS ACCORDING TO TRIGGER TYPE AND NUMBER OF OOCYTES RETRIEVED.

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OBJECTIVE: To better understand the frequency and severity of OHSS in a population of paid oocyte donors

DESIGN: Survey

MATERIALS AND METHODS: US egg donors (n=289) undergoing 801 oocyte donation cycles a few months to 27 years earlier (=4.8 years, median 2, interquartile range 1-6) were surveyed regarding egg number per retrieval, trigger type (hCG, Lupron, or combined (Dual)), and severity of OHSS. ANOVA or Kendall's test for significant association were used as appropriate.

RESULTS: Lupron triggers (n=337) had milder OHSS (23.7% moderate, 2.7% severe, no critical) compared to hCG (n=253, 29.6% moderate, 9.9% severe, 0.8% critical, p=0.022) or Dual (n=211, 37.4% moderate, 7.1% severe, 0.9% critical, $p<0.0001$) triggers. Fewer eggs (=24) were retrieved with hCG trigger vs Lupron or Dual triggers (=28 for both, p=0.0004). Adjusting for smaller hCG trigger cohort size (Table), severe OHSS was most common after hCG trigger (10-12% w/10-39 eggs, 19% w/40+ eggs) and lower following dual trigger (5-7% w/10-49 eggs, 14% w/+40+ eggs). OHSS was much milder with Lupron trigger, with more than two-thirds of retrievals of fewer than 50 eggs reporting only mild or no OHSS, and severe OHSS ranging from 1% with 10-29 eggs to 4-9% with 30+ eggs.

CONCLUSIONS: Among high-responding egg donors at risk of OHSS, Lupron trigger results in much milder cases of OHSS compared to triggers that include hCG, but does not completely eliminate risk for the condition. Risk for moderate to severe OHSS appears to increase according to number of eggs produced. There were no reports of severe OHSS on cycles in which donors reported producing 10 eggs or fewer.

SUPPORT: This study was supported by the University of California, San Francisco, Institute for Health and Aging; UCSF Individual Investigator Grant (#7501159); and funding from the National Science Foundation (#1828783).

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WHICH IS MORE PREDICTIVE OVARIAN RESERVE MARKER WHEN THERE IS DISCORDANCE BETWEEN ANTI - MULLERIAN HORMONE AND ANTRAL FOLLICLE COUNT IN PATIENTS WITH DIMINISHED OVARIAN RESERVE, AMH OR AFC?.

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OBJECTIVE: To determine the most predictive ovarian reserve parameter in patients with diminished ovarian reserve

DESIGN: Retrospective Cohort Study

MATERIALS AND METHODS: The study was conducted at Bursa Uludag University Hospital, ART Center. Patients who underwent ICSI because of diminished ovarian reserve, age < 40, without chronic systemic disease and without suspicion of malignancy, were screened from electronic database, retrospectively. Patients were subdivided into three groups. The first group (Group A) was consisted of patients with low anti-mullerian hormone (AMH) (<1.1 ng/dl) and low antral follicle count (AFC) (n < 7). The second Group (Group B) was consisted of patients with low AMH (<1.1 ng/dl) and normal AFC (n≥7). The third group (Group C) was consisted of patients with normal AMH (≥1.1 ng/dl) and low AFC (n<7). Demographic values, FORT score (follicle output rate: pre-ovulatory follicle count/antral follicle count x 100) and FOI score (follicle to oocyte index: oocyte number/AFC x 100) of the groups were compared.

RESULTS: Totally 662 cycles were enrolled in to the study. There were 418 cycles in Group A, 167 cycles in Group B and 77 cycles in Group C. Demographic values were comparable, except age. Mean age was lower in group B. (Respectively; 34.7 ± 3.7, 33.1 ± 4.1, 34.7 ± 3.6, p<0.01) As primary result; FORT and FOI score was higher in Group C than the other two groups. (Median FORT Score with quartiles: Group A: 100 (66-150), Group B: 71 (57-100), Group C: 136 (96-200), p<0.01 – Median FOI Score with quartiles: Group A: 83 (50-140), Group B: 71 (40-100), Group C: 108 (66-200), p<0.01) FORT and FOI score had no correlation with age. Thus, the difference of age in the groups does not affect the primary result. (Table-1)

CONCLUSIONS: In this study, we showed that anti-mullerian hormone has more predictive value for stimulation success. Increased AMH level results with increased FORT and FOI score. If there is discordance between AMH and AFC in patients with diminished ovarian reserve, AMH is the more predictive one for stimulation success.

SUPPORT: None.

hCG Trigger	Cohort size	Eggs < 10 (n=8)	Eggs 10-19 (n=90)	Eggs 20-29 (n=83)	Eggs 30-39 (n=51)	Eggs 40-49 (n=13)	Eggs 50+ (n=8)
	Mild OHSS	50.0%	35.6%	37.3%	31.4%	15.4%	37.5%
	Moderate OHSS	12.5%	22.2%	31.3%	35.3%	53.8%	37.5%
	Severe OHSS	0.0%	10.0%	9.6%	11.8%	23.1%	12.5%
Dual Trigger	Cohort size	Eggs < 10 (n=4)	Eggs 10-19 (n=55)	Eggs 20-29 (n=72)	Eggs 30-39 (n=41)	Eggs 40-49 (n=20)	Eggs 50+ (n=19)
	Mild OHSS	75.0%	56.4%	40.3%	29.3%	25.0%	31.6%
	Moderate OHSS	25.0%	27.3%	40.3%	43.9%	50%	31.6%
	Severe OHSS	0.0%	7.3%	5.6%	7.3%	5.0%	26.3%
Lupron Trigger	Cohort size	Eggs < 10 (n=10)	Eggs 10-19 (n=83)	Eggs 20-29 (n=110)	Eggs 30-39 (n=75)	Eggs 40-49 (n=35)	Eggs 50+ (n=24)
	Mild OHSS	70.0%	54.2%	51.8%	45.3%	62.9%	41.7%
	Moderate OHSS	10.0%	15.7%	26.3%	24.0%	22.9%	45.8%
	Severe OHSS	0.0%	1.2%	0.9%	4.0%	8.6%	4.2%

Table 1. Study Results

	Group A Low AMH Low AFC	Group B Low AMH Normal AFC	Group C Normal AMH Low AFC	p
Age	34.7 ± 3.7	**33.1 ± 4.1**	34.7± 3.6	**< 0.01**
BMI	25.8 ± 5	25.1 ± 5	25.7 ± 5	0.18
AMH (ng/dl)	**0.47 (0.22-0.76)**	**0.69 (0.45-0.88)**	**1.2 (1.15-1.71)**	**< 0.01**
AFC	4 (3-5)	**8 (7-10)**	4 (3-6)	**< 0.01**
Pre-ovulatory Follicle (>11 mm)	4 (2-5)	**7 (5-9)**	6 (4-8)	**< 0.01**
Stimulation Protocol	75.4% Antagonist 24.6% Microdose	75.4% Antagonist 24.6% Microdose	71.4% Antagonist 28.6% Microdose	0.75
Oocyte No.	**3 (2-5)**	5 (3-8)	5 (3-7)	**< 0.01**
FORT	**100 (66-150)**	**71 (57-100)**	**136 (96-200)**	**< 0.01**
FOI	**83 (50-140)**	**71 (40-100)**	**108 (66-200)**	**< 0.01**

*Statically significant values are written in bold.

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FINE TUNING OF RECOMBINANT HUMAN FOLLICLE-STIMULATING HORMONE (R-HFSH) DOSE TO INDIVIDUALIZE TREATMENT: REAL-WORLD DATABASE ANALYSIS OF OVULATION INDUCTION CYCLES FOR TIMED INTERCOURSE OR INTRAUTERINE INSEMINATION. Anne E. Martini, DO,[1] Stephanie Beall, MD, PhD,[2] Gilbert L. Mottla, MD,[3] G. David Ball, PhD,[4] Brooke Hayward, SM, MBA,[5] Mary C. Mahony, PhD, HCLD,[5] Allison B. Catherino, PhD[5] [1]National Institute of Child Health and Human Development, NIH, Bethesda, MD; [2]Shady Grove Fertility Center, Towson, MD; [3]Shady Grove Fertility Center, Annapolis, MD; [4]Seattle Reproductive Medicine Center, Seattle, WA; [5]EMD Serono, Inc. (a business of Merck KGaA, Darmstadt, Germany), Rockland, MA.

OBJECTIVE: To describe the real-world incidence and magnitude of individualized gonadotropin dose adjustments (increases and/or decreases) made during ovulation induction (OI) cycles, and to assess the relationship between patient characteristics and dosing changes.

DESIGN: Non-randomized, observational, retrospective cohort.

MATERIALS AND METHODS: Analysis of electronic medical records from a large US database of fertility centers (IntegraMed America, Inc.). Data from r-hFSH–treated OI cycles for patients who had undergone a first OI cycle in 2015–2016, with or without intrauterine insemination, were included. r-hFSH dose could be adjusted in 12.5-IU increments when administered subcutaneously with the follitropin alfa injection device, with or without oral medications for OI (clomiphene citrate or letrozole).

RESULTS: Of the 2832 OI cycles involving r-hFSH administration, 74.6% also included combination treatment with orals whereas 25.4% used r-hFSH only. Patients in the r-hFSH with orals group, compared with those in the r-hFSH–only group, had a lower mean (standard deviation [SD]) age (34.8 [4.85] vs 35.9 [5.04] years) and were more likely to have a normal antral follicle count (≥12; 37.7% vs 28.5%). A greater proportion of patients in the r-hFSH with orals group had normal (1.5–4.0 ng/mL; 28.1% vs 16.3%) or high anti-Müllerian hormone levels (>4.0 ng/mL; 25.9% vs 17.5%), and fewer had a primary diagnosis of diminished ovarian reserve (11.7% vs 26.0%). As expected, the starting dose of r-hFSH was lower for cycles that used r-hFSH with orals than r-hFSH–only cycles (mean [SD]: 74.2 [39.31] vs 139.3 [115.10] IU). Overall, dose changes occurred in 13.7% of r-hFSH with orals vs 43.9% of r-hFSH–only cycles. In those cycles with dose adjustments, dose increases were most common and occurred in 58.8% of r-hFSH with orals and 68.7% of r-hFSH–only cycles; dose decreases occurred in 58.1% and 54.1% of cycles, and both increases and decreases were used in 17.0% and 22.8% of cycles, respectively. Dose adjustments ranged from 12.5 IU to 450 IU. The smallest increments (12.5 IU and 25 IU) were used frequently, more often for upward dose titrations in r-hFSH–only (64.5%) vs r-hFSH with orals (53.5%) cycles than for dose decreases in r-hFSH–only (46.8%) and r-hFSH with orals (35.7%) cycles.

CONCLUSIONS: r-hFSH dose adjustments are common in OI cycles treated with r-hFSH. In OI cycles that also included orals, r-hFSH starting doses were lower and r-hFSH dose changes were fewer than with r-hFSH only. Use of smaller dose-adjustment increments facilitates more individualized treatment, particularly for patients with a good prognosis undergoing a 'low and slow' step-up protocol, to help mitigate risks associated with ovarian hyperstimulation syndrome and multifollicular response leading to multiple pregnancies.

SUPPORT: Study sponsored byÂ EMD Serono, Inc., Rockland, MA, USA (aÂ business of Merck KGaA, Darmstadt, Germany).

POSTER SESSION: PATIENT EDUCATION AND SUPPORT

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IMPACT OF THE INFERTILITY TREATMENT JOURNEY ON THE MENTAL HEALTH AND RELATIONSHIPS OF INFERTILE PATIENTS AND THEIR PARTNERS. Jacky Boivin, PhD,[1] Alice D. Domar, Ph.D.,[2] Rita Vassena, DVM, PhD,[3] Barbara Lynn Collura, MA[4] [1]Cardiff University, Cardiff, United Kingdom; [2]Boston IVF, Waltham, MA; [3]Clinica EUGIN, Barcelona, Spain; [4]RESOLVE: The National Infertility Association, McLean, VA.

OBJECTIVE: To investigate the psychological impact of fertility treatment and its effects on infertile patients and their partners.

DESIGN: An online, international, 30-minute quantitative survey.

MATERIALS AND METHODS: Data were collected from 1,944 respondents across nine countries, between March and May 2019. The survey was developed in English and translated to local languages with translations validated by national linguists. Participants were at different stages of the treatment journey and either infertile patients (n=1,037) or partners to infertile patients (n=907; but not necessarily partners of the patient sample).

RESULTS: Average age was 35.8 (SD=9.66) years, 56% of respondents (n=1,095) were female, 67% (n=1,119) were married and 91% (n=1,773) were heterosexual. The majority of patients were female (n=884; 66%) and the majority of partners were male (n=499; 55%). At infertility diagnosis, the emotion most often experienced for overall respondents was "sadness" (reported by 53%). A diagnosis of anxiety was reported by 43% of infertile patients and 30% of their partners. When undergoing treatment, "anxiety" was experienced by the most respondents (35%).

The infertility treatment journey reportedly had an impact on the mental health of 60% of respondents, but only 44% of respondents sought mental health support. The highest proportion of respondents seeking support was 71% in China, with the lowest in Italy (29%). A greater proportion of patients reported detrimental impacts on mental health (70%) than partners to infertile patients (49%).

One in three respondents indicated their relationship suffered as a result of infertility diagnosis. Overall, 33% of respondents ranked emotional strain within the top two most significant effects on their relationship. Respondents from the United States reported this as the most significant effect.

Patients were more likely than partners to report a detrimental impact on activities of daily living. An "effect on work-life balance" was most commonly experienced, considered to be within the top two most significant activity-associated effects by 31% of patients and 24% of partners.

CONCLUSIONS: Respondents reported a significant impact of their infertility journey on mental health and wellbeing, which in turn negatively

impacted relationships with partners. The disparity between the number of respondents who experienced mental health issues and the number of those who sought support indicates a need for better awareness and accessibility for support services.

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LIVE BIRTH RATES ARE HIGHER IN NULLIPAROUS WOMEN WHO ARE REFERRED TO A SPECIALTY FERTILITY CENTER BY A HEALTHCARE PROVIDER THAN IN WOMEN WHO ARE SELF-REFERRED. Audrey J. Panko, BS, Lara Lemon, PhD, PharmD, Marie Menke, MD, MPH Magee Womens Hospital at UPMC, Pittsburgh, PA.

OBJECTIVE: To evaluate differences in fertility outcomes between provider-referred and self-referred nulliparous patients.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: This study examined nulliparous women ages 18-43 years old who presented for a new patient consultation between January 2015 and December 2018 at a fertility clinic. Women who presented for fertility preservation services or did not present for fertility concerns were excluded. Data regarding referring provider, diagnosis of infertility, evaluation, and treatment prior to and after the first visit with the fertility clinic were collected. Rates of and time from the first consultation to pregnancy and live birth, as identified by episode documentation in the electronic medical record, were also obtained. Chi-squared test was performed for categorical variables and unpaired t-test for continuous variables.

RESULTS: A total of 6378 women presented for new patient consultation between 2015 and 2018; 4118 women (64%) met eligibility criteria. Among these, 1582 (38%) were provider-referred (PR) and 2536 (62%) were self-referred (SR). There were no significant differences between the groups in age, body-mass index, race, ethnicity, type of health insurance, and median income or area deprivation index of the patient's area of residence. Prior to their first new patient consultation with the fertility clinic, provider-referred patients were more likely to have a history of an infertility diagnosis (45% PR versus 34% SR, $p<0.0001$), evaluation of ovarian reserve with either FSH or AMH (50% PR vs 38% SR, $p<0.0001$), anatomic evaluation with HSG (21% PR versus 18% SR, $p=0.012$), and treatment with clomiphene citrate (9% PR versus 4% SR, $p<0.001$). With regards to treatment after their new patient consultation, there were no significant differences between the two groups in treatment with insemination (24% PR versus 23% SR, $p=0.249$) or use of assisted reproductive technology (15% PR versus 16% SR, $p=0.713$). However, live birth rates were significantly higher among provider-referred versus self-referred patients (30% PR vs 26% SR, $p=0.006$). There was no significant difference in the time from the new patient consultation to delivery (482 ± 416 days PR versus 460+373 days SR, $p=0.3107$) between the two groups.

CONCLUSIONS: Our results suggest that provider-referral to an infertility specialist is associated with an increased rate of infertility diagnoses and an increased live birth rate as compared to self-referral. This analysis has important interdisciplinary implications for optimizing access to care, referral patterns, and outcomes for women undergoing fertility evaluation.

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DOES A SMARTPHONE-BASED SEMEN ANALYSIS KIT PREDICT AZOOSPERMIA AFTER VASECTOMY? Josip Vukina, MD,[1] Hanna Pulaski, PhD[2] [1]UPMC Department of Urology, Pittsburgh, PA; [2]Magee Women's Hospital, Pittsburgh, PA.

OBJECTIVE: We sought to determine if a smartphone-based home semen analysis kit could reliably predict azoospermia after vasectomy.

DESIGN: In our practice, patients are normally instructed to provide a semen sample three months after vasectomy to document sterility. After obtaining Institutional Review Board approval, the study was discussed initially with patients during the vasectomy procedure and then consent was obtained at the time of semen analysis. After traditional semen analysis was performed, a portion of the unused semen sample was used to perform smartphone-based semen analysis using the Seem application.

MATERIALS AND METHODS: The Seem smartphone application by Recruit Lifestyle is available for both iOS and Android platforms and can be purchased online. The kit contains a small collapsible container for semen collection, a slide which is placed over the forward-facing camera of the smartphone, and a dropper to load the semen onto the slide. The application utilizes the high-resolution camera that is now ubiquitous in most smart phones to capture video which is then analyzed by proprietary software to determine sperm concentration and motility. After performance of traditional semen analysis, a small portion of the remainder of the sample (which would otherwise be discarded) was used to perform smartphone-based analysis and the results were then compared.

RESULTS: Patients in the study underwent semen analysis an average of 158 days after vasectomy. Except for one patient (who was instructed to repeat semen analysis in 4 weeks and continue contraception), all patients met American Urologic Association guidelines for successful vasectomy allowing for cessation of contraception. Only two patients met this criteria based on smartphone application concentration. For the remainder of the patients, smartphone-application derived concentrations were shown to be significantly higher and inaccurate compared to traditional semen analysis.

Patient	Smartphone Concentration	Smartphone Motility	SA Concentration	SA Motility	Days Since Vasectomy
1	7.4x10^6	0	2 sperm	0%	103
2	27.2x10^6	90.9	3 sperm	NA	181
3	0.0x 10^6	0	0	0%	119
4	9.9x106^6	25	0	NA	108
5	7.4x10^6	66.7	2 sperm	0%	124
6	5.0x10^6	0	0	NA	120
7	0.0x 10^6	0	17 sperm	0%	unknown
8	57.0x10^60	0	0	NA	486
9	79.2x10^6	0	0	NA	139
10	9.9x10^6	0	1 sperm	0%	234
11	5.0x10^6	0	0	NA	133
12	14.9x10^6	0	1 sperm	0%	90
13	5.0x10^6	0	0	NA	178
14	9.9x10^6	0	282 sperm	54%	78
15	14.9x10^6	0	0	NA	78
16	5.0 x 10^6	0	0	NA	193

CONCLUSIONS: While home semen analysis kits similar in appearance to a pregnancy test do exist, to our knowledge, this is the first study to use smartphone-based technology to evaluate post-vasectomy semen analysis. Unfortunately, this tool does not reliably predict azoospermia after vasectomy.

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DOES A WEB-BASED APP DECREASE MEDICATION WASTE, MEDICATION ERRORS AND CLINIC MESSAGES DURING IN VITRO FERTILIZATION CYCLES? Caitlin Elizabeth Martin, MD, MS,[1] Michael Lanham, MD,[2] Courtney A. Marsh, MD, MPH,[3] Kenan Omurtag, MD[1] [1]Washington University School of Medicine, St. Louis, MO; [2]University of Michigan, Ann Arbor, MI; [3]University of Kansas, Overland Park, KS.

OBJECTIVE: To assess whether using a web-based app that assists in medication management during In Vitro Fertilization (IVF) decreases medication waste, errors and patient-initiated messaging, while improving patient satisfaction.

DESIGN: A multicentered, randomized controlled trial.

MATERIALS AND METHODS: There were 104 women recruited prior to starting IVF. Subjects were recruited to assess quality of life during IVF, and then were randomized to use an app, "OnTrack," to assist with medication management vs. no app with conventional medication management. Women in the app arm were also informed of medication changes per clinic protocol. Surveys were e-mailed prior to starting IVF, on day 6 of stimulation, prior to and post egg retrieval. Quantity of medication errors and messages initiated by the patient were recorded. In the final survey, patients listed leftover medication. The approximate cost of medications was obtained from published data[1]. Patient satisfaction was assessed using a Likert scale. University of Michigan Redcap was used for data collection. SPSS v.25 was used for statistical analysis. Independent sample T-tests, Mann-Whitney tests and Fisher's exact tests were used where appropriate.

RESULTS: The median number of portal messages sent by the patient was 3 (range 0-13) in the control arm and 3 (0-18) in the app arm ($p=0.9$); the

median number of calls made by the patient was 0 (0-3) in the control arm and 0 (0-2) in the app arm (p=0.2). Seven patients (7/42, 16.7%) made medication errors in the control arm and 5 (5/46, 10.9%) in the case arm (p=0.5). Patients in the control arm had an average of 492±425 units of rFSH left compared to 455±395 units in the app arm (p=0.7), 5.3±3.9 vials of HMG left in the control arm and 4.4±4 in the app arm (p=0.3), and 1.7±2.3 syringes of GnRH antagonist left in the control arm and 1.8±2.5 syringes in the app arm (p=0.8). The estimated cost of medication waste was $3059±2075 in the control arm and $2766±1798 in the app arm (p=0.5). On a scale of 1-7 (1=completely dissatisfied, 7=completely satisfied), the average patient satisfaction score was 5.85±1.8 in the control and 6.17±1.1 in the case arm (p=0.939).

CONCLUSIONS: A web-based application did not decrease medication errors, waste or patient-initiated messages. The amount of medication ordered may vary per clinic protocols and could depend on insurance coverage, which was not captured by the study. Assessment of medication errors was limited by the medical record. Patient initiated communication was lower than expected; clinics may already excel at giving medication instructions. Patient satisfaction was equal in both groups. The app was a successful adjunct to clinical care. Future directions include studying similar tools alone for medication management and daily decisions as a method to improve clinic efficiency.

References: [1]Lexicomp Online, April 2020

SUPPORT: Michigan Translational Research and Commercialization Program (MTRAC)

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AN ANALYSIS OF FERTILITY PODCASTS: WHAT ARE PATIENTS LISTENING TO OUTSIDE OF THE CLINIC? Virginia-Arlene Acosta Go, MD, Karin Wollschlaeger, MD, Cathlyn Sullivan, DO Saint Joseph Hospital, Denver, CO.

OBJECTIVE: To identify and summarize available podcasts pertaining to fertility, infertility and IVF (in vitro fertilization) in order to provide a better understanding of information accessible to patients outside of the clinical setting.

DESIGN: Cross-sectional analysis

MATERIALS AND METHODS: Apple and Google Podcast Player applications were searched using the key words: *fertility, infertility and IVF* in November 2019. Included podcast results were published in English and had over 50% of episodes relevant to the searched topics. Podcasts were excluded if they were not accessible on both Apple and Google Podcast Player applications. Podcasts were assessed for: author credentials, content, dates of air, ratings and length of episodes.

RESULTS: The query produced 310 podcast results, of which 117 were unique podcasts and met inclusion criteria. The dates of initial episode ranged from 2007 to 2019 with only 9% of podcasts dated prior to 2016. The number of fertility podcasts released in 2019 increased 5-fold since 2016. The majority of podcasts had episodes less than one hour in duration and only 29% had any episodes greater than one hour. Thirty-two percent of podcasts were categorized as *Health and Fitness*, 23% as *Alternative Health* and most others fell into categories including *Nutrition, Mental Health, Christianity, Medicine, Sexuality, Society and Culture*. Twenty-two percent of podcasts were published by authors who identified as prior or current patients, 9% by medical physicians and 8% by authors who identified as "coaches" (life, fertility, health). The majority of podcasts targeted patients rather than providers and offered support rather than medical advice. Many podcasts included interviews with patients, health care providers and other experts in the field. The top three most popular podcasts had over 400 reviews, whereas the average number of reviews per podcast was 49. In general, fertility podcasts were well received and had an average rating of 4.8 out of 5 stars.

CONCLUSIONS: With increasing popularity and accessibility of podcasts, it is important to have a sense of what exists in the realm of fertility podcasts. Medical physicians currently author only a fraction of these podcasts thus there is significant opportunity for growth in this platform for education and patient support. Fertility podcasts may be created and utilized by healthcare providers to supplement information outside of the clinical setting in order to better guide patient care.

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THE EFFECTS OF FEMALE GENITAL MUTILATION ON THE FEMALE SEXUAL FUNCTION: A CROSS-SECTIONAL STUDY. Ahmed M. Abbas, MD,[1] Mennatallah Mohamed Samir, MBBCh,[2] Reham Maher Abdel-Gaber, MD,[2] Emad Eldien Kamal Ali, MD[2] [1]Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; [2]Department of Dermatology, Venereology and Andrology, Faculty of Medicine, Assiut University, Assiut, Egypt.

OBJECTIVE: The existing literature on female genital mutilation (FGM) and sexuality is conflicting regarding its effects on sexual functions. ***The aim of the present study is to e***valuate the effects of FGM on the female sexual function.

DESIGN: A cross sectional study

MATERIALS AND METHODS: The study was carried out between April 2018 and January 2019. We included married women, aged 18 – 45 years old, and sexually active during the last six months. All women were asked to complete the Arabic Female Sexual Function Index (ArFSFI) independently. The cut-off score to define sexual dysfunction on the total FSFI score is 28.1. Then, the gynecologist conducted a thorough clinical examination and a detailed assessment of the type and extent of FGM. Continuous data was expressed in the form of mean ± SD while nominal data was expressed in the form of frequency and percentage.

RESULTS: The study included 200 women divided into two groups; group (I) FGM, n=127 women and group (II) no FGM, n=73 women. There was no statistically significant difference in sexual function between both groups [91 women (71.7%) in group I vs. 53 women (72.6%) in group II, p=0.511]. The mean total ArFSFI score in group I was 25.8±3.05 vs 25.4±3.64 in group II (p=0.598). Additionally, There was no statistically significant difference in the sexual function between women with type I and type II FGM (p=0.555). The mean total ArFSFI score in women with type I was 26.6±2.61 vs 25.4±3.64 in women with type II FGM (p=0.071).

CONCLUSIONS: FGM is not associated with reduced scores of ArFSFI either in all domain scores or the total score. Moreover, no difference in the scores of the ArFSFI between women with type I or type II FGM.

SUPPORT: None

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A PRECONCEPTION LIFESTYLE INTERVENTION IMPROVES SOME GESTATIONAL OUTCOMES AND NEONATAL MARKERS OF ADIPOSITY IN WOMEN WITH OBESITY AND INFERTILITY. Mehdi Rouissi, PhD,[1] Farrah Jean-Denis, MSc,[2] Matea Belan, MSc,[1] Jean-Patrice Baillargeon, Pr[1] [1]Université de Sherbrooke, Sherbrooke, QC, Canada; [2]Research Center of the Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, QC, Canada.

OBJECTIVE: Obesity during pregnancy is associated with a high risk of many pregnancy and neonatal complications. Our aim was therefore to determine whether a lifestyle program targeting women with obesity and infertility and maintained during pregnancy improves maternal and neonatal outcomes, as well as newborn cord blood markers.

DESIGN: Randomized controlled trial

MATERIALS AND METHODS: We report on 46 women who became pregnant and had available outcome data during pregnancy and at birth, among 127 women with infertility and obesity (BMI $\geq$30 kg/m^2), or overweight with PCOS (BMI $\geq$27 kg/m^2), who were enrolled in a lifestyle randomized-controlled trial. Participants were randomized to the control group (CG, n=20), who received standard of care, or the lifestyle group (LSG, n=26), who followed a lifestyle program alone for 6 months, and then in combination with usual fertility care. Follow-up was for 18 months or until the end of pregnancy. In 24 participants (LSG, N=13; CG, N=11), a sample of umbilical cord blood was obtained after delivery, with measurement of non-esterified fatty acids (NEFA), triglycerides (TG), leptin, adiponectin, IL-6, TNF-alpha, CRP, PAI-1 and oxidized LDL.

RESULTS: Baseline results showed no significant differences between groups for age (29.3 vs 31.0 years), BMI (38.7 vs 38.4 kg/m^2) and waist circumference (113.7 vs 112.7 cm). Preconception weight loss was significantly higher in the LSG compared to the CG (-4.86 kg vs -1.21 kg,

p=0.013), but gestational weight gain was similar. During pregnancy, groups did not differ for the rates of most clinical outcomes (such as preeclampsia, gestational diabetes, etc.), but significantly less women in the LSG required insulin for treatment of their gestational diabetes (12.5% vs 42.1%, p=0.027) as well as urgent cesarean section due to failure of vaginal delivery (0.0% vs 21.1%, p=0.021). Regarding neonatal outcomes, there was no significant difference between groups for gestational age and weight at birth, as well as rates of prematurity, L/SGA, etc. However, babies from the LSG displayed significantly lower tricipital skinfolds at birth (4.73 vs 5.72 mm, p=0.031), and trends for lower sum of four skinfolds (16.6 vs 19.1 mm, p=0.056) and increased length (50.8 vs 49.6 cm, p=0.053). In addition, cord blood levels of TG and IL-6 tended to be lower in babies born from women of the LSG vs CG (medians = 0.20 vs 0.39 mmol/L, p=0.06 and 7.2 vs 21.8 pg/mL, p=0.06), with a higher adiponectin/leptin ratio (3.76 vs 2.95, p=0.14).

CONCLUSIONS: In women with obesity and infertility, a lifestyle program initiated prior to fertility treatments and maintained throughout pregnancy improved their weight and was associated with a reduction of some clinically relevant pregnancy and neonatal complications, as well as markers of adiposity (skinfolds) and dysmetabolic (TG, adiponectin/leptin ratio) and pro-inflammatory (IL-6) states. If these results are replicated in a larger sample, it would strongly suggest that women with obesity should be supported to adopt a healthy lifestyle prior conception in order to increase their likelihood of giving birth to a healthy baby.

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LANGUAGE BARRIERS ON FERTILITY CLINIC WEBSITES IN THE WESTERN REGION. Kajal Verma, MD,[1] Christopher de Haydu, MD,[2] Angela H. Liu, MD,[1] Melody A. Rasouli, MD, MBA,[1] Janelle M. Jackman, MBBS,[3] Sriram Eleswarapu, MD, PhD,[4] Cindy M. Duke, MD, PhD[5] [1]University of Nevada, Las Vegas, Las Vegas, NV; [2]University of Miami, Miami, FL; [3]New Hope Fertility Center, New York, NY; [4]University of California, Los Angeles, Los Angeles, CA; [5]University of Nevada, Las Vegas and Nevada Fertility Institute, Las Vegas, Las Vegas, NV.

OBJECTIVE: Fertility clinic websites are an important tool used by patients in selecting a medical practice for obtaining reproductive endocrinology and infertility (REI) services. Patient accessibility to clinic websites can differ for a variety of reasons, including language barriers. The goal of this study is to examine accessibility of fertility services to non-English speaking patients, specifically looking at website translation links and fertility specialists speaking more than one language, as listed on the websites. The availability of this patient facing information on websites was analyzed using county-level demographics within the Western Region of the US (WRUS).

DESIGN: Cross-sectional analysis.

MATERIALS AND METHODS: A survey was developed and two independent investigators at different institutions assessed clinic websites that contributed to the most recent complete (2017) Society for Assisted Reproductive Technology (SART) database in the WRUS (as defined by US Census Bureau). Websites were assessed for content that was partially or fully translated into another language besides English. REI physicians who speak more than one language, as noted by the website, were also identified. The responses were ordered by county level data obtained from the US Census (most recent complete data sets, 2010-2018) for demographic information including language spoken at home and education. Descriptive statistical analyses performed included Chi-square and t-tests.

RESULTS: 100 SART-reporting fertility clinics are located in WRUS. 42% of clinic websites were partially or fully translatable to a language other than English. 30% of websites reported physicians as speaking more than one language. 67% of these bi- or multilingual physicians reported Spanish as an additional language. Compared to the lower 3 quartiles for language, there was a positive association between website translation links and the highest quartile of language, other than English, spoken at home ($p = 0.02$). There was also a significant association between physicians who were bi- or multilingual and the highest quartile of language, other than English, spoken at home ($p = 0.01$). Regarding education, the quartile of counties with the lowest percentage of persons with a high school graduate degree or higher was also positively associated with websites providing translation services ($p = 0.04$).

CONCLUSIONS: Less than half of SART registered fertility clinics in the WRUS include at least part of their websites translated into a language other than English, and predictive factors of website translation services include clinic location in a region with a higher proportion of people speaking a language other than English at home and lower education level. Fertility clinics can overcome language barriers by offering translation services on their websites, thereby increasing accessibility to non-English speaking patients. Further studies to evaluate whether website translation services or the presence of bi- or multilingual physicians are factors in patient decision-making in regards to choosing a fertility clinic are ongoing.

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IS FERTILITY STATUS ASSOCIATED TO SEXUAL DYSFUNCTION? A COMPARATIVE STUDY IN A MEXICAN FERTILITY CENTER. Edelmiro Garza-Padilla, M.D., Julio C. Rosales, M.D., Pablo Diaz-Spindola, M.D., Karla Alejandra Cantú, M. Sc., Irving Olaf Morales, M.D., IECH Monterrey, NL, Mexico.

OBJECTIVE: To determine if the infertility diagnosis correlates with lower scores in the Female Sexual Function Index (FSFI).

DESIGN: Prospective analytical and comparative study.

MATERIALS AND METHODS: The Female Sexual Function Index (FSFI) is a 19-item, self-report scale of female sexual function[1]. Women attending a Mexican fertility clinic from January 2019 to April 2020 were reached via e-mail and requested to fill an online form that included the FSFI questionnaire (Chilean Spanish validated version[2]) and general demographic information, after informed consent. Likewise, a smaller group of non-infertile patients from a general gynaecological practice filled the same forms. Answers were stored in a database for further analysis. Prevalence of sexual disfunction was calculated as a percentage of patients not achieving an overall FSFI score of 26.55[1].

RESULTS: Out of 1,345 participants, 18% responded the online form. Furthermore, 34 patients were excluded to avoid bias favoring sexual dysfunction after selecting, at least one time, the absence of sexual activity in the past 4 weeks in the FSFI questionnaire. The remaining patients were classified in two groups: 142 (69%) self-identified as infertile and 65 (31%) without that diagnosis. Patients from the first group where older (35.15±5.69 vs. 29.5±5.52 years, $p<0.001$) and with higher body mass index (27.76 ±6.45 vs. 23.91 ±5.58 kg/m^2, $p<0.001$). There were no differences in marital status, academic level or gynecological pathologies.

The prevalence of female sexual dysfunction in the infertility group was 68.3%, in contrast to 61.5% for the control group. A tendency for lower scores in the infertile group was seen in each domain and the overall scores of the FSFI, but it only was statistically significant in the arousal domain ($p<0.05$, OR 1.4). After adjusting for age and other variables, this difference gap persisted.

CONCLUSIONS: The present study demonstrated a very high prevalence of sexual dysfunction in our patients, with and without infertility, almost twice as reported in other groups[3,4]. Furthermore, there was no association between the fertility status and the prevalence of female sexual dysfunction (except for arousal) using the FSFI compared to controls. Further studies are warranted to determine if this pattern repeats with larger data set.

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"ADD-ONS" IN ART: DO PATIENTS RECEIVE HONEST INFORMATION THROUGH FERTILITY CLINICS' WEBSITES?. Valentina Galiano, MD,[1] Raoul Orvieto, MD,[2] Ronit Machtinger, MD, PhD,[2] Ravit Nahum, MD,[2] Emanuele Garzia, MD, PhD,[1] Patrizia Sulpizio, MD,[1] Anna Maria Marconi, MD,[1] Daniel S. Seidman, MD[2] [1]San Paolo University Hospital, Milano, Italy; [2]Sheba Medical Center, Ramat Gan, Israel.

OBJECTIVE: "Add-on"procedures are actively promoted by some fertility clinics as proven means to improve IVF success rates, especially in couples with repeated implantation failure.The aim of this study was to assess the accuracy of information about "add-ons" on the internet, considering the conflicting evidence on their effectiveness.

DESIGN: A systematic evaluation of fertility clinics websites. We developed a 10-criteria structured questionnaire to evaluate the quality of information on endometrial scratching, assisted hatching, intralipids infusion and PGT-A, available through the internet.

MATERIALS AND METHODS: The search and review were performed in January-February 2020 by a single investigator. We included English language websites that presented in the Google.com search engine after typing the following key words: "endometrial scratching" (ES), "intralipid infusions" (ILI), "assisted hatching" (AHA), "PGT-A" or "PGS". As the previously used term "PGS" is often still used instead of PGT-A, we searched for both words.

RESULTS: 260 unique websites were evaluated. For the procedures listed, almost all the websites belonged to private clinics. Only for AHA (3 clinics), and PGT-A (2 clinics), we also found public institutions that provided information. An accurate description of the "add-on" procedures was provided in most cases (78.8%). However, only a minority (12%) of these websites reported on the inconclusive effectiveness of these procedures. The use of PGT-A was most often encouraged (52.8%), compared to ES (23.6%) and AHA (16%). The additional cost of the "add-on" procedure was rarely presented (6.9%). Literature references were never provided for ILI and only rarely, 12.7%, for ES, 4.0% for AHA and 5.6% for PGT-A. Date of entry of the information was frequently not reported. None of the websites reported the clinic's pregnancy rates following of the "add-on" procedures.

CONCLUSIONS: The information about "add-ons" available to the public from IVF clinics' websites is often inaccurate. This could perpetuate false myths among patients about the effectiveness of these add-on procedures and raises concern regarding possible commercial bias. It is imperative that IVF clinics' websites better communicate the associated risks and uncertainties of "add-on" procedures to prospective patients.

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MALE REPRODUCTIVE ONCOFERTILITY SPECIALISTS AT NCI DESIGNATED CANCER CENTERS: ASSOCIATION OF WEB SITE CONTENT WITH INSTITUTIONAL RANKING AND LOCATION SOCIODEMOGRAPHICS. Kassandra E. Zaila, B.A.,[1] Sriram Eleswarapu, M.D., Ph.D.,[1] Cindy Duke, M.D., Ph.D.,[2] Christopher de Haydu, M.D.[3] [1]University of California, Los Angeles, Los Angeles, CA; [2]University of Nevada Las Vegas, Nevada Fertility Institute, Las Vegas, NV; [3]University of Miami, Miami, FL.

OBJECTIVE: We previously demonstrated that the availability and quality of patient directed information regarding male fertility preservation on the web sites of National Cancer Institute (NCI) designated cancer centers was lacking. The aim of this study was to investigate whether there are institutional ranking or sociodemographic factors that influence whether male reproductive oncofertility-focused urologists and cancer survivorship are featured on NCI cancer center web sites.

DESIGN: All NCI designated cancer center web sites were queried in a systematic fashion for patient directed information on male reproductive oncofertility. Cancer survivorship information and male reproductive urologist consultation information were assessed.

MATERIALS AND METHODS: Patient directed information available on the web site of each NCI designated cancer center was evaluated for its male reproductive oncofertility content, with a specific focus on cancer survivorship information and information regarding names and links to urology providers who have specific interests in male infertility and microsurgery. These data were then compared with respect to US News & World Report institutional ranking along with sociodemographic data. Sociodemographic factors evaluated included level of educational attainment for the surrounding county and gender disparities within the surrounding county. Descriptive statistical analysis and chi-squared testing were performed.

RESULTS: All 62 web sites of NCI designated cancer centers were evaluated; 92% were affiliated with academic institutions. Among all cancer centers, 50% made mention of male-specific oncofertility risks. The risk of cancer treatment on fertility (not gender specific) was mentioned by 56% of centers. There was a statistically significant association with a greater proportion of women in a state or county with the presence of increased discussion of male oncofertility cancer survivorship on the web sites (p=0.04). Cities with lower percentages of poverty were more likely to have NCI cancer centers list infertility specialists on their webpages without referring them to university department websites (p=0.04). Higher educational attainment in the NCI designated cancer center's region was associated with greater number of infertility/microsurgery male reproductive urologists featured on web sites (p=0.01).

CONCLUSIONS: Web-based access to provider information and fertility options available to patients is an important component of shared decision making. We found a positive association between the percentage of women in a state or county, as well as level of educational attainment, and access to male infertility specialists and survivorship information. These associations raise important questions regarding possible socioeconomic or educational factors influencing information on NCI cancer centers.

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IMPACT OF AN EARLY PREGNANCY EDUCATION PACKET ON PATIENT QUESTION VOLUME. Adina Tanen, BS, Ambika Nohria, BA, Youjin Jenny Jang, BA, Paula C. Brady, MD Columbia University Fertility Center, New York, NY.

OBJECTIVE: To determine whether providing an evidence-based early pregnancy education packet (EPEP) to newly pregnant patients with a prior diagnosis of infertility impacts the volume of patients' pregnancy-related questions.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: The 76 page EPEP - compiled by clinical staff directly from the American College of OB/GYN, the American Society for Reproductive Medicine, the Centers for Disease Control and Prevention and the National Institutes of Health websites - addressed travel, diet, exercise, intercourse, prescription and nonprescription drugs, and pregnancy symptoms. The EPEP was emailed to patients after the first positive serum hCG result. During routine pregnancy scans performed weekly from 6-8 weeks gestation, medical assistants recorded the number and category of patients' pregnancy-related questions, without any identifying information. Data were collected 2 months before and after packet introduction, including demographics of each group (not tied to responses). Univariate comparisons between cases and controls were performed using the Fisher's exact test; a p-value of $\leq .05$ was considered statistically significant. Analyses were performed using online calculators available at http://astatsa.com.

RESULTS: Data were collected during 84 pregnancy scans pre-EPEP and 106 scans post-EPEP. Of note, 40% of patients pre-EPEP had prior deliveries versus only 19% post-EPEP (p=0.001). There was a similar distribution of ART (IVF and IUI) and spontaneous pregnancies (24% pre- and 31% post-EPEP) between the groups. The mean number of questions per visit was 2 pre-EPEP and 1.7 post-EPEP. Pre-EPEP, 73% of patients asked at least one question versus 84% post-EPEP (p>0.05).

CONCLUSIONS: Pregnancy after infertility may be a time of greater stress and lower self-esteem as compared to pregnancies without prior infertility (1-3). In this study, introducing the EPEP was not correlated with a significant change in the volume or distribution of patients' pregnancy-related questions. The study was limited by sample size, and results may be confounded by the higher parity (and thereby, pregnancy experience) of the pre-EPEP group. Methods of educating patients regarding reproductive health and easing the transition of care from reproductive endocrinologist to obstetrician warrant further investigation, particularly as this patient population is potentially more vulnerable to anxiety in pregnancy. Future directions could include utilization of different media and presentation formats, or approaches other than large-volume information-sharing, which some patients may find overwhelming.

Keywords: early pregnancy, patient education, pregnancy-related questions, patient discharge

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ARE THE ONLINE RESOURCES FOR PATIENTS OF NCI CANCER CENTERS ASSOCIATED WITH THE PRESENCE AND VOLUME OF LOCAL FERTILITY CENTERS?

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OBJECTIVE: Patient access to online resources is important for informed decision making. Prior research showed inconsistent web-based patient information on NCI designated cancer centers' (NCICC) websites related to demographic and geographic factors. We investigated the association between volume and presence of fertility centers in the catchment area of NCICCs as they relate to patient oncofertility information on NCICC websites.

DESIGN: Cross-sectional observational study.

MATERIALS AND METHODS: Two independent investigators used previously validated rubric and methods to assess websites of NCICCs for fertility preservation content. A third reviewer from a different institution assessed discordant evaluations. Specific questions included 1) Does the website discuss the effects of cancer and cancer treatment on fertility? 2) Are options of FP for all patients discussed? 3) Is there a standalone page dedicated to FP content? Local and regional data was used to order and compare NCICCs. Factors included publicly available CDC 2017 National Summary and Clinic Datasets for Assisted Reproductive Technology and US Census (2010-2014) data. Chi-square analyses were performed to assess any statistically significant association (P-value < 0.05).

RESULTS: There was an association between the discussion of cancer treatments risks on fertility and fertility preservation on NCICC websites with the number of fertility centers in the state (p-values 0.0056 and 0.0413, respectively). Presence of a stand-alone page on fertility preservation is associated with the number of fertility centers at the state (p-value 0.0308) and county levels (p-value 0.0085), as well as the number of fertility treatment cycles in the state (p-value 0.0309), county (p-value 0.0193), and city (p-value 0.0193) surrounding the NCICC. Discussion of risks of cancer treatments on male fertility was correlated with the number of fertility centers in the state (p-value 0.041), county (p-value 0.0046), and the number of fertility treatment cycles in the state (p-value 0.0414), county (p-value 0.0046), and city (p-value 0.0046). Web-based information on cancer treatments and female fertility was associated with the number of fertility treatment cycles in the city where NCICC is located (p-value 0.0414). Availability of web-based FP resources for male cancer patients was correlated with population density (p-value 0.0192) and income per capita (p-value 0.0309) at the county level. No associations were noted between web-based oncofertility content and percent population below the poverty line, percent population without insurance coverage, percent population with college degree, and percent foreign language spoken at home.

CONCLUSIONS: Understanding barriers for patient access to oncofertility information is important for improving quality of care at NCICC. Analyses suggest that the gap in access to web-based information on fertility preservation at each NCICC may be more related to regional differences in presence of fertility centers and volume of fertility treatments than socioeconomic disparity.

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WHAT DETERMINES HOW PATIENTS ARE COUNSELED REGARDING STIMULATION WITH AUTOLOGOUS OOCYTES?

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OBJECTIVE: To determine factors associated with a patient being declined from pursuing a cycle of in vitro fertilization with autologous oocytes (IVF-AO).

DESIGN: Cross-sectional study

MATERIALS AND METHODS: Female respondents, aged 35 or over, who visited a U.S fertility clinic from January 2015 to March 2020 responded to an online questionnaire via FertilityIQ questionnaire (www.fertilityiq.com). All respondents were asked if they had been declined from pursuing a cycle of IVF-AO by a fertility clinic and if so, which clinic. Examined demographic and clinical predictors included age, race, education, income, clinic type (private vs. academic), care received in a mandated vs. non mandated state, insurance coverage and self-reported infertility diagnosis. Logistic regression was used to calculate adjusted odds ratios for factors associated with being declined from pursuing IVF-AO.

RESULTS: Of the 8,660 women included, 418 (4.8%) reported being declined a cycle of IVF-AO. In the multivariate analysis, predictors of being declined included increasing age (OR: 1.71, $p<0.001$), higher education (OR: 1.36, $p=0.001$), diagnoses of diminished ovarian reserve (DOR) (OR: 3.39, $p<0.001$) and poor oocyte quality (OR: 1.41, $p=0.015$). Predictors of not being declined a cycle of IVF-AO included a higher level of education attained (OR: 0.82, $p=0.013$), and diagnoses of unexplained infertility (OR: 0.61, $p=0.003$) or tubal blockage (OR: 0.42, $p=0.006$). Notably, none of the following were predictive of patients being declined from pursuing IVF-AO: race, clinic type (private vs. academic), care received in a mandated vs. non mandated state, or insurance coverage.

CONCLUSIONS: Nearly 5% of patients who pursued IVF reported being declined from doing a cycle of IVF with autologous oocytes. Patients who were older, of lower income, more educated, or had diagnoses of DOR or poor oocyte quality were more likely to be declined. While some of the clinical predictors, such as age and diagnoses, are expected, others such as income, are concerning. Further studies are needed to confirm these findings and explore how to mitigate these potential biases in the patients who are allowed to pursue IVF-AO.

References: None

SUPPORT: None

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DOES THE US NEWS REPORT SCORE OF NCI-DESIGNATED CANCER CENTERS REFLECT ACCESS TO FERTILITY PRESERVATION TREATMENT INFORMATION?

Angela H. Liu, MD,[1] Christopher de Haydu, MD,[2] Melody A. Rasouli, MD, MBA,[1] Janelle M. Jackman, MBBS,[3] Kajal Verma, MD,[1] Sriram Eleswarapu, MD, PhD,[4] Cindy M. Duke, MD, PhD[5] [1]University of Nevada, Las Vegas, Las Vegas, NV; [2]University of Miami, Miami, FL; [3]New Hope Fertility Center, New York, NY; [4]University of California, Los Angeles, Los Angeles, CA; [5]University of Nevada, Las Vegas and Nevada Fertility Institute, Las Vegas, Las Vegas, NV.

OBJECTIVE: US News Report provides peer-reviewed ranking that informs patient choice of NCI-designated cancer centers for cancer treatments. Counseling for fertility preservation is recommended as a standard of care for patients with new cancer diagnoses. This study aims to compare the US News Report scores of various subspecialty programs at NCI-designated cancer centers and the quality of the centers' web-based oncofertility resources to assess if patient access to information on fertility preservation treatments will be affected when choosing NCICC based on the US News Report scores.

DESIGN: Cross-sectional observational study

MATERIALS AND METHODS: Patient-directed content on the websites of NCI-designated cancer centers (NCICC) was evaluated for information on fertility preservation and oncofertility by independent reviewers from two institutions. The NCICC websites were systematically queried to assess the following - 1) Does the website discuss the effects of cancer and cancer treatment on fertility? 2) Are options of FP for all patients discussed? 3) Is there a standalone page dedicated to FP content? 4) Was parenting-related cancer survivorship addressed? Affiliation with a fertility center was also examined. Scores of each NCICC in the subspecialties of general oncology, pediatric oncology, gynecology, and urology were obtained from the US News Report. Descriptive analyses were performed using Chi-square statistics. P-value $<$ 0.05 defines statistical significance.

RESULTS: The US News Report scores for adult oncology is associated with available discussion of cancer treatment risks on fertility on the NCICC websites (p-value 0.0260). Higher scores in pediatric oncology is associated with web-based information on parenting after surviving cancer treatments (p-value 0.0066). US News Report scores of gynecology programs at NCICC are not associated with any oncofertility website metric. Correlation between US News Report scores for urology programs and web-based content of cancer treatment risks on male fertility was borderline statistically significant (p-value 0.0645). Affiliation with a fertility center is not correlated with availability of FP resources on NCICC websites.

CONCLUSIONS: US News Report scoring of subspecialty programs may not reflect access to consistent quality web-based oncofertility resources for patients receiving treatments at NCICC. Content is tailored for fertility treatments among cancer survivors for pediatric oncology programs ranked by US News Report. Gender-specific fertility preservation information is not correlated with US News Report scores of gynecology or urology programs, suggesting provision of oncofertility resources may not factor into current US News Report scores of these subspecialties at NCI cancer centers.

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COMPLEMENTARY AND ALTERNATIVE MEDICINE CONTENT ON FERTILITY CLINIC WEBSITES IN THE WESTERN REGION. Kajal Verma, MD,[1] Christopher de Haydu, MD,[2] Janelle M. Jackman, MBBS,[3] Angela H. Liu, MD,[1] Melody A. Rasouli, MD, MBA,[1] Sriram Eleswarapu, MD, PhD,[4] Cindy M. Duke, MD, PhD[5] [1]University of Nevada, Las Vegas, Las Vegas, NV; [2]University of Miami, Miami, FL; [3]New Hope Fertility Center, New York, NY; [4]University of California, Los Angeles, Los Angeles, CA; [5]University of Nevada, Las Vegas and Nevada Fertility Institute, Las Vegas, Las Vegas, NV.

OBJECTIVE: Information available to patients on fertility clinic websites is a critical component of the shared decision-making process between patients and physicians. Complementary and integrative medicine (CAM) is an emerging offering within fertility medicine. Examples of CAM therapies include acupuncture, yoga, herbal supplements, and homeopathy. The goal of this study is to assess the prevalence of content specific to CAM on fertility clinic websites. The availability of this patient facing information on websites was analyzed using county-level demographics within the Western Region of the US (WRUS).

DESIGN: Cross-sectional analysis.

MATERIALS AND METHODS: Websites of clinics reporting data to the Society for Assisted Reproductive Technology (SART) from the most recent complete year (2017) were queried for the US Census Bureau-designated Western region. Each clinic website was examined for content related to alternative therapies or complementary medicine, as defined by the American Society for Reproductive Medicine. This was correlated to publicly available data by the US Census Bureau (2014-2018) using county as a geographic proxy to estimate demographic variables within the population. Descriptive statistical analyses performed included Chi-square and t-tests.

RESULTS: 100 SART-reporting fertility clinics are located in WRUS. 33% of clinic websites had discussed content referring to CAM services. From the websites that featured this content, 88% of them discussed acupuncture services, either offered in conjunction with the clinic or providing patients with a list of resources on the website. There was a significant and positive association between CAM services being offered on fertility clinic websites and the ratio of non-Hispanic or Latino white persons in the population, in relation to four quartiles of the population distribution. Education level, income level, and health insurance coverage in a given clinic region were not found to be statistically significant in relation to the presence of CAM services offered.

CONCLUSIONS: Approximately one-third of SART registered fertility clinics in the WRUS currently provide CAM content on their websites. The quality of this content is mixed and varies from extensive details about services such as acupuncture and yoga to vague mention of the term CAM. With ASRM's recognition of CAM as an adjunct in fertility therapy, more standardized information on its role in fertility medicine is needed. Currently, many patients assume that CAM is frowned upon by fertility centers and instead of talking to the clinics, patients are turning to unreliable sources for this information which may ultimately even compromise their own fertility treatment protocols in the process. Our study demonstrates that in order to better integrate CAM within our field, it is incumbent upon fertility centers to provide more concise and accurate information and guidance to their patients regarding safe and recommended CAM, including the best timing for CAM. Further study to expand this analysis across all US demographic regions is ongoing.

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CHALLENGES OF LACTATION AND BREASTFEEDING AMONG MOTHERS CONCEIVED THROUGH ART - A QUESTIONNAIRE BASED SURVEY. Rajani Chelladurai, MS, DNB, FMAS, DMAS, P. P. Gopinath, MD, DGO, FMMC, FICS, FICOG, MBA, Gayathri Devi S S, IV, MD, FRM, Hema Vaithianathan, MD, MRCOG SIMS hospital, Chennai, India.

OBJECTIVE: BREASTFEEDING AFTER ART - EVERY MOTHER'S NIGHTMARE ? The objective was to study the challenges of lactation and breastfeeding among mothers conceived through ART in our centre @ SIMS hospital, Chennai, India.

DESIGN: A questionnaire based survey conducted among mothers delivered after an ART pregnancy.

MATERIALS AND METHODS: This study was conducted between Jan 2018- Dec 2019. A total of 196 postnatal mothers conceived through ART were given questionnaire on challenges faced with lactation and breastfeeding at 3 months postpartum. Data analysis was done using multivariate logistic regression analysis.

RESULTS: It was found that majority of the mothers experienced some difficulty in breastfeeding in the form of either failure to lactate or latching difficulties. A small group had opted for expressed breastfeeding. It was noted that these difficulties were more pronounced among preterm deliveries and multiple pregnancies. Other factors like Caesarean section , coexisting depression and psychological instability were also attributed towards difficulty with lactation. Around 15% mothers had given up on breastfeeding and chose formula feeds at 3 months postpartum.

CONCLUSIONS: Breastfeeding is difficult at the best of times, but following ART it's even harder. When the importance of breastfeeding is being reiterated all across the globe, this subsect of ART pregnancies have been ignored. It is also noteworthy that breastfeeding and postpartum blues following ART is a vicious cycle with one upsetting the other and vice versa . Psychological support from family, counselling on lactation, forming peer groups among such mothers to encourage each other and lactation helplines can help them to understand that breastfeeding following ART is no longer a nightmare.

POSTER SESSION: REPRODUCTIVE SURGERY

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UTERINE DOPPLER BLOOD FLOW EVALUATION OF THE EFFECT OF MISOPROSTOL ADMINISTERED PRIOR TO ABDOMINAL MYOMECTOMY: A RANDOMIZED CONTROLLED TRIAL. Mohamed Khalaf, MD, Ahmed M. Abbas, MD, Asmaa M. Hussein, MBBCh, Hazem Saad El-Dein, MD Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt.

OBJECTIVE: To observe the changes in the vascularity and perfusion of fibroids following administration of sublingual versus rectal misoprostol prior to abdominal myomectomy

DESIGN: A randomized, single-blind, clinical trial

MATERIALS AND METHODS: The study included women with documented uterine fibroids on pelvic imaging scheduled for abdominal myomectomy, aged 18-50 years, pre-operative hemoglobin >8 g/dl, with five or less symptomatic subserous or intramural fibroids and the uterine size less than 24 weeks pregnancy. Sample size was calculated based on a recent study stated that the Resistance index (RI) at 20 min after rectal misoprostol intake was 0.87 ± 0.16. We supposed that sublingual misoprostol will decrease the blood flow to the uterus with increase in RI to 0.97 ± 0.16. Using two sided chi-square test with alpha error of 0.05, a total sample size of at least 82 patients (41 in each arm) had 80% power to detect the difference in mean RI with sublingual misoprostol intake. Women were randomized to (group A) received 400 mcg misoprostol (two tablets) rectally one hour before the operation, and group (B) received 400 mcg misoprostol sublingual at the same time. The fibroid vascularization and that of the surrounding myometrium was visualized using the colour Doppler technique. Blood flow velocity waveforms were obtained by placing the Doppler gate over the maximum colour areas and activating the pulsed Doppler function at that marked site. The vessel was measured after confirming the depth and the angle correction prior to and after insertion. RI and pulsatility index (PI) of the vessel was measured three times (before and 20 min, 40 min after misoprostol intake). The primary outcome was the mean value of intramyometrial blood vessels RI after 20 min misoprostol intake. chi-square test was used to compare the nominal data of the study groups while student t-test was used to compare the quantitative data of the groups.

RESULTS: The study enrolled 82 women (41 in each arm). No statistical significant differences between both groups regarding the baseline or clinical data. No statistical differences regarding RI, PI and systolic/diastolic ratio (S/

D), at different times of assessment between both groups. RI after 20 min was 0.85 ± 0.11 in the rectal group vs. 0.78 ± 0.11 in the sublingual group (p=0.15). similarly, RI after 40 min was 0.90 ±0.11 in the rectal group vs. 0.85 ± 0.19 in the sublingual group (p=0.07). In both groups there were significant increase in RI, PI and S/D ratio after 20 and 40 min in comparison to the pre-operative data (p<0.01).

CONCLUSIONS: Misoprostol significantly decrease the vascularity and perfusion of uterine fibroids weather administered rectal or sublingual one hour prior to abdominal myomectomy.

SUPPORT: none

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NEONATAL OUTCOMES AFTER UTERUS TRANSPLANT- DUETS (DALLAS UTERUS TRANSPLANT STUDY). Liza Johannesson, MD, PhD, Jackie York, MD, Giuliano Testa, MD Baylor University Medical Center, Dallas, TX.

OBJECTIVE: Uterus transplantation is restoring fertility in women absolute uterine-factor infertility and allows them to experience gestation and childbirth. Limited data are available on the outcome of infants born after uterus transplantation. Our aim was to describe the hospital course and laboratory findings of the first 6 infants born in the Dallas UtErus Transplant Study (DUETS).

DESIGN: Prospective review.

MATERIALS AND METHODS: Twenty women received a uterus transplant at Baylor University Medical Center in Dallas (a tertiary referral center) from 2016 to 2019 (NCT02656550). Based on the trial protocol, information about the first 6 infants delivered was collected in a prospective fashion, including infant demographics, hospital course, and laboratory values.

RESULTS: Six infants were delivered, all by cesarean section, from mothers who had undergone uterus transplantation. All mothers had an immunosuppressive regimen and none experienced an episode of rejection during pregnancy. The infants had a median gestational age of 36.3 weeks (range 30.6–37.2 weeks) and median birthweight of 2890 g (range 1771–3140 g). APGAR scores were at least 7 at 1 minute and at least 8 at 5 minutes. All were appropriate size for gestational age. Two infants had complete blood counts with bandemia but negative blood cultures. Blood urea nitrogen and creatinine levels were within expected range.

CONCLUSIONS: The 6 infants born from mothers with uterus transplants had a neonatal course that reflected the gestational age at delivery. No baby was born with an identified deformation or malformation attributed to the transplantation or immunosuppression. Despite exposure to a calcineurin inhibitor throughout pregnancy, there were no adverse effects on renal function. Longer follow-up and a larger number of infants are needed to confirm these observations.

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ORAL KETOPROFEN ONE HOUR PRE-PROCEDURE IS EFFECTIVE FOR PAIN RELIEF DURING HYSTEROSALPINGOGRAPHY: A RANDOMIZED CONTROLLED STUDY. Ahmed M. Abbas, MD,[1] Marwa Samy, MD,[2] Sara M. Hassanein, MD,[2] Mohammed Khairy Ali, MD,[1] Ahmed M. Abdelmagied, MD,[1] Mohamed Khalaf, MD,[1] Osama S. Abdalmageed, MD[1] [1]Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; [2]Department of Radiology, Faculty of Medicine, Assiut University, Egypt.

OBJECTIVE: Hysterosalpingography (HSG) is considered the initial diagnostic tool for assessment of tubal patency. Our objective is to examine the analgesic effect of oral ketoprofen in relieving pain during HSG.

DESIGN: A randomized, double-blind, placebo-controlled study (NCT02905045, clinicaltrials.gov).

MATERIALS AND METHODS: Reproductive-aged infertile women scheduled for HSG were considered for enrollment. Eligible women were recruited and randomized (1:1) to ketoprofen or placebo group All women received oral 150 mg ketoprofen or placebo tablet one hour before the procedure. The study outcomes was the participant's self-rated pain perception utilizing a 10-cm Visual Analogue Scale (VAS) during injection of the dye, 5 minutes and 30 minutes post-procedure. A 2 cm difference in VAS score between both arms was considered a clinically significant difference. Secondary outcomes included the women's satisfaction score and the number of women who asked for additional analgesics.

RESULTS: One hundred women were enrolled and randomized to ketoprofen arm (n=50) or placebo (n=50). Both arms were comparable in baseline clinical and socio-demographic criteria. Oral ketoprofen reduce the median VAS pain scores during injection of the dye (2.5 vs. 4.75, p=0.001) and 30 minutes post-procedure (1.25 vs. 3, p=0.003). The mean satisfaction scores were 8.54±0.33 and 8.11±0.24 in the ketoprofen and placebo groups respectively (p=0.83). Additionally, four women asked for additional analgesics in the placebo group versus two women in the study group (p=0.17).

CONCLUSIONS: The use of oral ketoprofen one hour prior to HSG is effective in relieving the induced pain during and 30 minutes after the HSG procedure

SUPPORT: none

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IN VITRO FERTILIZATION AND PREGNANCY OUTCOMES AFTER UTERUS TRANSPLANTATION: DUETS (DALLAS UTERUS TRANSPLANT STUDY). J. Michael Putman, M.D.,[1] Lilly Zhang, PhD,[2] Giuliano Testa, MD,[3] Anthony Gregg, MD,[3] Robert T. Gunby, MD,[3] Liza Johannesson, MD, PhD[3] [1]Fertility Center of Dallas, Dallas, TX; [2]Fertility Center Dallas, Dallas, TX; [3]Baylor University Medical Center, Dallas, TX.

OBJECTIVE: To review in vitro fertilization and pregnancy outcomes after uterus transplantation.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: Women with absolute uterine factor infertility who were selected to undergo uterus transplantation (UTx) from September 2016 through August 2019. In vitro fertilization was performed before subjects underwent transplant, and good-quality expanded blastocyst stage euploid embryos were obtained and frozen for post successful uterus transplant single embryo transfer. The main outcome measures were healthy live birth, time from successful UTx to embryo transfer, time from successful UTx to live birth.

RESULTS: Twenty subjects underwent UTx and 14 had successful transplants. Fourteen underwent single embryo transfer of a warmed, good-quality, expanded, euploid blastocyst. In 10 of 14 (71.4%) patients, the first embryo transfer resulted in implantation. Ten subjects had a live birth by cesarean section and 3 pregnancies are ongoing. One recipient had 2 live births before removal of her uterus. Time from successful UTx to embryo transfer averaged 154 days (range, 106-235 days). Time from successful Utx to live birth averaged 16.4 months in the first ten recipients.

CONCLUSIONS: Subjects with absolute uterine factor infertility who have successful UTx can achieve excellent ongoing pregnancy and live birth rates utilizing good-quality, expanded blastocyst stage, euploid embryos.

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INTRAPERITONEAL TRIAMCINOLONE MAY REDUCE ADHESION FORMATION THRHOUGH ALTERATION OF MITOCHONDRIAL FUNCTION. Ahmad Arabi, MD,[1] Neeraja Purandare, PhD,[1] Paige Minchella, BS,[1] Siddhesh Aras, MBBS, PhD,[1] Katherine J. Kramer, MD,[2] Maurice-Andre Recanati, MD-MS[1] [1]Wayne State University School of Medicine, Detroit, MI; [2]St. Vincents Catholic Med Ctrs, New York, NY.

OBJECTIVE: To investigate the use of intraperitoneal triamcinolone acetonide in reducing adhesion formation after abdominal myomectomy and determine the molecular mechanism of action in an in vitro model.

DESIGN: Under IRB approval, patients who had previously undergone abdominal myomectomy with uterus >20 weeks) and presented for repeat abdominal surgery (serving as a second look) were enrolled in the study. Patients with a history of intraperitoneal/pelvic infections or intervening surgeries were excluded. The treatment group consisted of patients who had received, during initial surgery, triamcinolone intraperitoneally as documented in the medical record (n=31). Control patients (n=21) received no documented adhesion prevention methods. Human fibroblast cell culture was used as an in vitro model.

MATERIALS AND METHODS: Treatment group received 200mg triamcinolone acetonide in 500 mL dextran at closing of peritoneum. Adhesion number, grade and severity were scored using Leach adhesion score from one individual blinded surgeon with concurrence of the assistant. Age,

race, uterine size, blood loss, operative time, number, aggregate weight and position of fibroids at initial surgery and presenting symptoms were obtained from chart review. Human fibroblasts were incubated at 20%, 2% and 1% hypoxia, cellular ROS measurements were performed with CM-H2DCFDA and ROS-Glo, TGF-b1 was quantified by ELISA, HIF-1a was assessed by western blot and Seahorse Bioanalyzer was used for measurement of intact cellular oxygen consumption. Clinically, Welch's t-test was performed to compare groups assuming unequal variance (F-test) and two tails. Pearson Chi-squared test was performed on categorical data with $p<0.05$ considered significant. Pearson correlation was performed, with p-value analysis. For in vitro experiments, two-sided Wilcoxon rank-sum test was applied to determine statistical significance with $p<0.05$ considered statistically significant.

RESULTS: About 32% of patients (n=10) were found to have adhesions in the treatment group compared to 71% (n=15) in the control group ($p<.01$). Compared to controls, adhesions were significantly less in number (0.71 vs 2.09, $p<0.005$), severity (0.54 vs 1.38, $p<0.004$), and extent (0.34 vs 1.28, $p<0.003$). In vitro studies showed triamcinolone directly prevents the surge of reactive oxygen species (ROS) triggered by 2% hypoxia and prevents the increase in TGF-b1 at 2% hypoxia which leads to the irreversible conversion of fibroblasts to adhesion phenotype. Triamcinolone prevents the increase in ROS in a HIF-1a independent manner, through alteration of mitochondrial function.

CONCLUSIONS: Administration of intraperitoneal triamcinolone significantly reduced adhesion formation by altering mitochondrial function and ROS mediated TGF-b1 release in fibroblasts. Controlling mitochondrial function may allow for adhesion free surgery and reduce postoperative complications and infertility. This is especially relevant when surgeries, such as myomectomies, are indicated for infertility.

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PREDICTIVE VALUE OF DOPPLER ANALYSIS IN UTERINE TRANSPLANTATION. Akshaya Jain, MD,[1] Liza Johannesson, MD, PhD,[1] Giuliano Testa, MD,[1] Elizabeth A. Eagle, DO,[1] Tsung-wei Ma, PhD,[2] Anthony Gregg, MD[1] [1]Baylor University Medical Center, Dallas, TX; [2]Baylor University Medical Center at Dallas, Dallas, TX.

OBJECTIVE: Successful pregnancy with uterine transplantation is contingent on numerous factors. Our study of uterus donors prior to transplant and uterus recipients after transplant explored whether uterine artery Doppler blood flow indices (UAQI) could predict successful implantation.

DESIGN: Retrospective review

MATERIALS AND METHODS: During the years 2016-2019 there were 20 uterus transplantations performed with both living (n=18) and deceased donors (n=2) at Baylor University Medical Center in Dallas. The indication for uterus transplantation was absolute uterine factor infertility in all recipients. In this study we compare the UAQI in living uterus donors with their corresponding uterus recipients (n=11). We also evaluate the UAQI two months prior to and three months after embryo transfer. Successful implantation is defined as viable pregnancy at 12 weeks gestation. UAQI include peak systolic velocity, diastolic velocity and resistance index (RI) which were measured in the bilateral uterine arteries (UA). UAQI from the left and right UA were then analyzed separately and pooled for analysis.

RESULTS: The pooled peak systolic velocity of the UA in the donor is positively correlated to the values in the recipient UA pooled peak systolic velocity at 2 months post-transplantation ($r=0.83$, $p<0.05$). There were a total of 11 embryo transfers in the uterus recipient cohort. We noted 7 successful implantations which resulted in 6 live births and 1 miscarriage at 16 weeks. We noted 4 failed implantations (failed embryo transfer (n=3) and missed abortion at less than 12 weeks gestation (n=1)). When the left UA diastolic velocity was compared across the five month time period, the recipients with live births demonstrated a statistically significant percent increase compared to the recipients with failed implantations ($p<0.02$). This translated to a statistically significant decrease in the left UA RI ($p<0.03$). The pooled peak systolic velocity was higher in the recipients with live births, however, the difference was not statistically significant ($p<0.18$). The pooled UA RI was lower in the live birth cohort and this difference was statistically significant ($p<0.04$).

CONCLUSIONS: Uterus transplant does not appear to adversely impact UA peak systolic velocity when measured two months after transplant. Although more data is needed, the RI holds promise to predict successful implantation in uterus transplant recipients. Additional studies are needed to further elucidate the predictive value of UAQI on pregnancy outcomes.

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HYSTERO-EMBRYOSCOPY A TOOL FOR DIAGNOSIS IN EARLY PREGNANCY LOSS. Ander M. Morales Vicente, Sr., DOCTOR, Leisy Rodriguez, DOCTOR, Norman R. Gomez Diaz, MD, Sara Fortuño Salais, DOCTOR, Juana Crespo Simó, DOCTOR JUANA CRESPO MEDICAL TEAM, VALENCIA, Spain.

OBJECTIVE: Approximatelly 15 % of all recognized pregnancies are spontaneously aborted in the first trimester. Most common cause of miscarriage is aneuploidies, 60-70 % of abortions are due to chromosome abnormalities. Genetic causes lead to developmental arrest and miscarriage and a majority of embryos present with morphological defects.

Although the incidence of early losses is high, embryonic material is difficult to obtain and often poorly described from a morphological perspective. Currently Hystero – embryoscopy (HE) is the only method that allows direct visualization of uterine cavity, implantation area of the gestational sac and anatomical description of the embryo.

In the present study we describe the results of HE performed over 3 years, trying to identify the value of diagnostic HE in detection of morphologic embryo abnormalities, cytogenetic findings and the intra-uterine pathology in early miscarriage patients.

DESIGN: Retrospective

MATERIALS AND METHODS: This study is a review of 101 infertility patients between 1-1-2017 and 12-31-2019 with a diagnosis of early missed abortion and scheduled for HE and posterior curettage.

RESULTS: The women mean age was 38,6 years (23 - 49 y). They had previous pregnancy losses with no previous live birth.

Successful visualization of the uterine cavity was achieved for all cases. An embryo was visualized by HE in mostly all cases and subjected to an anatomic examination. Some embryos showed abnormal development with microcephaly, embryonic neural tube defects or retarded limb development.

Cytogenetic diagnosis from embryo or chorionic villi was obtained in 90.1% of the cases (n:91). An abnormal cytogenetic result was found in 64 % of the embryos (n:65) comprising: trisomy (84.6%), tetraploidy and triploidy (7.7%), unknown genetic material (3.1%), uniparental dysomia (3.1%) and 1 case of chromosomic deletion.

A total of 26 of the aborted embryos had normal karyotype (25.7%) in our study. All patients with normal karyotype embryos had associated factors as possible causes of abortion: uterine malformations or defects (n:26), hematologic disease (n:9) and endocrine disorder (n:1). Cytogenetic diagnosis turned without result in 10 patients (9.9%).

CONCLUSIONS: In our series of 101 missed abortions, we found that the use of HE to direct evaluation of uterine cavity, embryo morphology and direct HE biopsies were more accurate than the standard curettage technique for diagnosis of first trimester miscarriage.

HE is an easy, safe and elective tool for diagnosis of the site of implantation of the sac and the presence of intrauterine abnormalities which play a role in the aetiology of miscarriages. Using HE we diagnosed some embryos with abnormal development and morphological defects. In our study HE enabled precise sampling with reduced maternal cell contamination compared with curettage. We obtained cytogenetic diagnosis in 90.1% cases. An abnormal cytogenetic result was found in 64 % of the embryos determining the cause of miscarriage. This valuable information is important for diagnosis of miscarriages and genetic counselling and itś in support of previous studies published.

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SUPPORT: None

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WOMEN WITH A HISTORY OF PRIMARY INFERTILITY HAVE INCREASED RISK OF FUTURE HYSTERECTOMY AND OOPHORECTOMY.

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OBJECTIVE: To evaluate the incidence of future hysterectomy and oophorectomy for women with a history of primary infertility compared to age-matched referent women from the same community.

DESIGN: A population-based retrospective cohort study.

MATERIALS AND METHODS: A random sample of 300 women first diagnosed with primary infertility between 1980 and 1999 while a resident of Olmsted County, Minnesota, were identified through the Rochester Epidemiology Project (REP) records-linkage system (https://rochesterproject.org/). Records were manually reviewed to confirm the date (index date) and diagnosis of primary infertility. Each woman was 1:1 age-matched (±1 y) to a referent woman residing in the county at the time of the index date who had not been diagnosed with primary infertility or had a prior hysterectomy. The occurrence of hysterectomy and/or oophorectomy both prior to and after index date was collected by manual chart review. Cox proportional hazards models were fit to estimate the hazard ratio (HR) and 95% confidence interval to compare the long-term risk of hysterectomy and oophorectomy, respectively, between infertility cases and referents.

RESULTS: The mean (SD) age at the index date was 29.9 (4.6) and 30.0 (4.6) for 300 infertility cases and 300 referents, respectively. At the time of the index date, 1 infertility case and 1 referent each had a prior bilateral salpingo-oophorectomy (BSO) and 4 infertility cases and 4 referents had a prior unilateral oophorectomy. The median duration of follow-up after the index date was 21.5 years (interquartile range (IQR), 13.0-25.5) and 20.9 years (IQR, 4.9-24.9) for the infertility cases and referents, respectively. Among those without a prior BSO at the index date, risk of subsequent oophorectomy was 2-fold higher in infertility cases compared to referent women (HR 2.06, 95% CI 1.20-3.53) (43 infertility cases and 19 referents). Infertility cases also had a significantly increased risk of hysterectomy (HR 1.56, 95% CI 1.06-2.29) (69 infertility cases and 41 referents). The three most common indications for hysterectomy among both groups (infertility cases vs. referents) were similar: fibroids (25% vs 29%), heavy menstrual bleeding (23% vs. 27%), and endometriosis (17% vs. 15%). Ten of 69 (14%) infertility cases had a hysterectomy for a gynecologic malignancy compared to 3 of 41 (7%) referents.

CONCLUSIONS: Women with primary infertility are at increased risk of subsequent hysterectomy and oophorectomy compared to age-matched referents. Although indication for hysterectomy was similar among groups, more women with a history of primary infertility underwent hysterectomy for treatment of gynecologic malignancy. These findings are significant, as oophorectomy and hysterectomy have been previously demonstrated to negatively impact long-term health.

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FALLOPIAN TUBE ENDOMETRIOSIS IN WOMEN UNDERGOING OPERATIVE VIDEO LAPAROSCOPY AND ITS CLINICAL IMPLICATIONS.

Bailey Gill McGuinness, MD,[1] Farr R. Nezhat, MD,[2] Lauren Ursillo, MD,[1] Meredith Akerman, MS,[1] William Vintzileos, MD,[1] Michael White, MD, PhD[1] [1]NYU Winthrop Hospital, Mineola, NY; [2]Nezhat Surgery for Gynecology/Oncology, Valley Stream, NY.

OBJECTIVE: To determine the incidence of macroscopic and microscopic fallopian tube endometriosis in patients undergoing laparoscopic surgery with a pre-operative diagnosis of endometriosis, pelvic pain, infertility and/or cystic adnexal mass.

DESIGN: This was a retrospective cross-sectional study. Inclusion criteria were all patients who underwent surgery July 2015 to June 2018 at a single gynecological oncology practice specializing in endometriosis. Exclusion criteria were age ≥ 55 years, diagnosis of cancer, laparotomy, prior bilateral salpingectomy, and pre-operative diagnosis other than endometriosis, pelvic pain, infertility or cystic adnexal mass.

MATERIALS AND METHODS: Subjects were divided by those who did and who did not have a salpingectomy at the time of surgery. Diagnosis of tubal endometriosis was based on macroscopic evidence of endometrial implants on the fallopian tube(s) noted within the operative report and microscopic evidence of endometriosis noted within the pathology report. The Monte Carlo estimate for the Fisher's exact test was used to compare groups for endometriosis stage. Results with a $p<0.05$ were considered significant.

RESULTS: 444 surgeries were performed with 185 patients meeting study criteria. 97 patients had a salpingectomy at the time of surgery and 88 patients did not. 153 patients (82.7%) had histologically diagnosed endometriosis within the abdominopelvic cavity. Amongst patients with endometriosis, the incidence of tubal endometriosis was 11-12% macroscopically and 42.5% microscopically after salpingectomy. Patients with tubal endometriosis were more likely to have severe disease ($p=0.0196$). Pre-operative diagnoses between the salpingectomy and no-salpingectomy groups were compared and no significant difference was found. Although pre-operative diagnosis of fibroids and abnormal uterine bleeding were not defined as inclusion or exclusion criteria for this study, approximately 1 in 5 patients with a pre-operative diagnosis of endometriosis, pelvic pain, adnexal mass or infertility also had fibroids and/or abnormal uterine bleeding. Parity, gravity, and medical management of endometriosis had no impact on presence or absence of fallopian tube endometriosis.

CONCLUSIONS: Amongst patients with endometriosis, the incidence of microscopic tubal endometriosis is significantly greater than that of macroscopic disease. This is the first study to evaluate the incidence of both macroscopic and microscopic tubal endometriosis with the use of a control group. There is a need for development of new minimally-invasive diagnostic techniques for early detection of fallopian tube endometriosis, which could guide gynecologists in management of patients with infertility and endometriosis.

P-902 3:30 PM Wednesday, October 21, 2020

SUCCESSFUL USE OF INTRAUTERINE AMINOGRAFT FOR ASHERMAN SYNDROME: AN EXPANDED CASE SERIES. Channing Burks, MD,[1] Kathryn D. Coyne, MD,[1] James H. Liu, M.D.[2] [1]University Hospitals Fertility Center/Case Western Reserve University, Beachwood, OH; [2]UH MacDonald Women's Hospital, Cleveland, OH.

OBJECTIVE: To evaluate pregnancy outcomes after the use of intrauterine aminograft in infertile women with Asherman Syndrome.

DESIGN: Case series

MATERIALS AND METHODS: Women who presented to our center between the years of 2011-2019 with a diagnosis of moderate or severe Asherman Syndrome, a thin endometrial stripe and a desire for future fertility were offered treatment with an amniotic membrane graft. All were informed that the amniotic membrane, Ambios®, a desiccated biologic ophthalamic graft, is an experimental and novel technique for intrauterine use. The amniograft is reputed to have anti-inflammatory and antimicrobial properties in addition to containing keratocyte growth factor. After informed consent was obtained, women underwent an operative hysteroscopy, lysis of intrauterine adhesions and curettage under general anesthesia. A 3.5x3.5 cm graft was rehydrated with normal saline, wrapped around a Cook intrauterine balloon and inserted into the uterus under ultrasound guidance. The balloon was inflated with 5-7 ml of saline. The stent was maintained for a goal of 2 weeks, during which time patients received oral antibiotic prophylaxis (doxycycline 100 mg bid). Post-operatively, women were prescribed 4 weeks of high dose estrogen therapy (estradiol 2 mg tid) along with progestin (medroxyprogesterone acetate 10 mg daily) for the last 12 days of estrogen therapy. An ultrasound was performed post-operatively to assess the growth of the endometrial lining.

RESULTS: Twenty-two women with Asherman Syndrome were included and received the aminograft between the years of 2011 and 2019. Women ranged from 30 to 48 years old. Nine of the twenty-two (41%) women had amenorrhea prior to surgery and all of the women achieved menses post-operatively. The vast majority of women (20/22, 91%) were parous, only two women (2/22, 9%) had never previously conceived. The average increase in pre- versus post-operative endometrial thickness was 3.02 mm, the range was 1-8.2 mm. Twelve out of the twenty-two women (55%) were able to conceive postoperatively and nine out of twenty-two women (41%) had a live birth.

CONCLUSIONS: This case-series demonstrates positive results in regard to improving endometrial thickness, the ability to conceive and have a live birth with the use of the novel aminograft for women with Asherman Syndrome, many of whom previously failed treatment. Our finding deserves further study with a randomized controlled trial comparing women who undergo hysteroscopic lysis of adhesions with aminograft placement to women who undergo hysteroscopic lysis of adhesions only.

P-903 3:30 PM Wednesday, October 21, 2020

THE PREVALENCE OF SUBTLE DISTAL FALLOPIAN TUBE ABNORMALITIES AND THE RELATIONSHIP WITH ENDOMETRIOSIS IN INFERTILITY PATIENTS:A PROSPECTIVE COHORT STUDY. Xingbang Zheng, MD,[1] Xiaoming Yu, MD,[1] Togas Tulandi, M.D., M.H.C.M.,[2] Yaron Gil, MD,[2] He Cai, MD,[3] Hongjing Han, MD,[1] Jing Guan, MD[1] [1]Peking University People's Hospital, Beijing, China; [2]McGill University Health Centre, Montreal, QC, Canada; [3]Northwest Women's and Children's Hospital Affiliated to Xian Jiaotong University, Xian, China.

OBJECTIVE: Clarify the prevalence of subtle distal fallopian tube abnormalities in the infertile population and its relationship with endometriosis.

DESIGN: prospective cohort study

MATERIALS AND METHODS: It is a prospective cohort study conducted in a single fertility referral center between January 2017 and December 2018 which includes all the infertile patients who underwent a laparoscopy examination. We prospectively examined the abdominal cavity including the condition of the fallopian tubes and the presence of endometriosis. Subtle distal fallopian tube abnormalities include fimbrial agglutination, tubal diverticula, accessory ostium and fimbrial phimosis.

RESULTS: A total of 876 patients consented and enrolled in the study, of those, 251 cases were diagnosed with subtle abnormalities, which accounted for 28.65%. 62 cases presented with more than one type of subtle abnormalities. Tubal fimbrial agglutination composed the largest group with 62% (n=156), followed by tubal diverticula with 26%, (n=66) and fimbrial phimosis with 25% (n=64). Tubal accessory ostium was the least common abnormity with 15% (n=39). In sub – analysis we found that 70.91% (178/251) of the study group had endometriosis. The prevalence of subtle tubal abnormalities in the stage I-II patients was significantly higher than found in the stage III-IV group (57.31% (149/260) VS 20.86% (29/139) (P =0.000).

CONCLUSIONS: The prevalence of subtle distal fallopian tube abnormalities is high in the infertile group. This group of diseases is found in high prevalence and probably connected to endometriosis, especially to the peritoneal disease.

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SUPPORT: no financial support

P-904 3:30 PM Wednesday, October 21, 2020

SURGICAL METHODS FOR ENDOMETRIAL POLYPECTOMY AND ASSOCIATED ENDOMETRIAL INJURY. Emily Evans-Hoeker, MD, Adrienne Uphoff, MD, James Casey, MD Carilion Clinic, Roanoke, VA.

OBJECTIVE: Intrauterine procedures have the potential for endometrial injury, possibly leading to formation of intrauterine adhesions and infertility. Methods for removal of endometrial abnormalities, such as endometrial polyps, have traditionally been performed with sharp curettage or hysteroscopic scissors, however, the use of hysteroscopic morcellators has become more common in recent years. It is unclear which method, if any, is associated with lower frequency of endometrial injury. Therefore the purpose of our study was to determine if the frequency of endometrial injury differs between methods for removal of endometrial polyps.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: All pathology samples from polypectomy procedures performed between 2014 and 2019 on women ages 18-50 were included in the study. Because the myometrium is deep to the endometrium and is not itself a target of these procedures, the presence and proportion of myometrium on surgical pathology samples were used to indicate endometrial injury. Pathology samples were re-evaluated by a single, blinded pathologist to measure the primary outcome of presence and proportion of myometrium. Secondary outcomes included operative complications and mention of myometrium on the initial pathology report. Data were evaluated using chi square analysis.

RESULTS: Interim analysis of 195 of the 473 (41%) pathology samples demonstrated increased reporting of myometrial tissue on initial surgical pathology with morcellator use (46% of morcellator pathology reports), in comparison to traditional D&C (8%), and hysteroscopic scissors (3%) ($p < 0.01$). However, blinded pathology review demonstrated no differences in the overall presence of myometrium, presence of isolated myometrium or the proportion of myometrial tissue noted. There was no difference noted in surgical complications between the various methods of polypectomy.

CONCLUSIONS: Interim analysis demonstrated increased reporting of myometrial tissue on initial surgical pathology with hysteroscopic morcellator use, however, no difference was found in the presence or quantity of myometrium upon blinded re-evaluation of samples.

SUPPORT: N/A

P-905 3:30 PM Wednesday, October 21, 2020

DO REPRODUCTIVE AND OBSTETRIC OUTCOMES AFTER HYSTEROSCOPIC SURGERY FOR DYSMORPHIC UTERUS DIFFER FROM THOSE OF PATIENTS WITH NORMAL UTERINE CAVITY? Umut Göktürk, md,[1] Semra Kahraman, Prof. MD,[2] Hacer Uyanikoglu, ass.prof[3] [1]Istanbul Memorial Sisli Hospital, ISTANBUL, Turkey; [2]Istanbul Memorial Sisli Hospital, Istanbul, Turkey; [3]Harran Üniversitesi, Şanlıurfa, Turkey.

OBJECTIVE: The aim of this study was to evaluate reproductive and obstetric outcomes of women who have undergone hysteroscopic metroplasty for dysmorphic uterus.

DESIGN: This retrospective study was conducted at Istanbul Memorial Hospital ART and Genetics Center between 2011 and 2019. A total of 126 patients diagnosed as having dysmorphic uterus with 3D-USG, hysterosalphingogram and hysteroscopy were evaluated. The diagnosis of dysmorphic uterus (Class U1) was made according to the ESHRE/ESGE concensus on the classification of female genital tract congenital anomalies. Patients with normal uterine cavity undergoing diagnostic hysteroscopy were the control group.

MATERIALS AND METHODS: Patients between 25-42 years old with good and top quality blastocysts were included in the study. In frozen-thawed embryo transfer cycle, the endometrium was prepared with either modified natural or artificial cycles. Preimplantation genetic diagnosis (PGT) was performed in women >36 years old. A total of 253 patients were evaluated. 126 patients underwent hysteroscopy to confirm the diagnosis of dysmorphic uterus (Group 1). Diagnostic hysteroscopy was performed in 127 patients with normal uterine cavity (Group 2). Hysteroscopy was performed at midfollicular phase with a bipolar electrode (Versapoint, Johnson & Johnson, Belgium). Lateral, anterior and posterior walls and fundus were expanded until tubal ostiums could be seen from the internal cervical os.

RESULTS: There was no significant difference in age, AMH level, BMI, infertility duration and endometrial thickness between the groups. The mean ages were 33.9 and 32.9 years old in the study and control group, respectively. Single frozen-thawed blastocysts were transferred to 126 patients in 177 cycles in Group 1 and to 127 patients in 201 cycles in Group 2. Clinical pregnancy rates were 64.9%(n=115) and 59.2%(n=119), clinical micarriage rates were 22.6% (n=26) and 16.8% (n=20), ongoing pregnancy rates were 50.2% and 49.2% and live birth rates were 48.5% (n=86) and 48.2% (n=97) respectively. Preterm delivery, before 37 weeks of pregnancy, was 18.1% (n=16) and 14.1% (n=14) in Group 1 and Group 2, respectively. Although clinical abortion rate and preterm birth were higher in Group 1, there was no statistically significant difference between the groups in any reproductive and obstetric outcomes.

CONCLUSIONS: After hysteroscopic metroplasty, patients with dysmorphic uterus have reproductive and obstetric outcomes which are similar to those of patients with normal uterine cavity.

P-906 3:30 PM Wednesday, October 21, 2020

CERVICAL CERCLAGE FOR PREVENTION OF PRETERM DELIVERY IN WOMEN WITH CONGENITAL UTERINE ANOMALIES: A CASE SERIES. Jenna S. Hynes, MD, Amanda Rae Schwartz, MD, Sarah K. Dotters-Katz, MD, MMHPE Duke University Medical Center, Durham, NC.

OBJECTIVE: To characterize a population of women with congenital uterine anomalies (CUA) and cervical cerclage placement, and to evaluate the subsequent incidence of preterm delivery (PTD).

DESIGN: Case Series

MATERIALS AND METHODS: Subjects were identified from an existing database including women with CUAs and a singleton, non-anomalous gestation with delivery from 2013-2018 at a single tertiary care center. Inclusion criteria included women with a CUA (arcuate, septate, unicornuate, bicornuate, or uterine didelphys) and placement of cervical cerclage for any indication. Women with multiple gestations and fetal anomalies were excluded.

RESULTS: Out of 100 women in the database, seven met inclusion criteria; four bicornuate, one unicornuate, one septate, and one didelphys. Five underwent history indicated cerclage placement, one ultrasound indicated, and one exam indicated (Table). Cerclage was placed at a median gestational age of 14w0d (range: 12w0d to 19w2d). Three women experienced a previable delivery with stillbirth or neonatal demise at a median gestational age of 21w1d. Among those delivering beyond viability, the median gestational age at delivery was 32w4d. Of women with history indicated cerclage, 3 of 5 delivered viable infants, as did the patient with the ultrasound indicated cerclage. Delivery complications included chorioamnionitis (n=1) and placental abruption (n=1). No cases of postpartum hemorrhage, endometritis, or need for maternal admission to the intensive care unit were noted. The median birth weight of the four living infants was 1888g (range: 1320 to 2385g) with a median hospital length of stay of 26 days (range: 2-56). One infant suffered from retinopathy of prematurity, while no neonates had intraventricular hemorrhage, neonatal sepsis, or necrotizing enterocolitis.

CONCLUSIONS: There is limited data available regarding the utility of cerclage placement in women with CUAs to prevent PTD. However, in this small case series, more than half of women experienced birth of a viable neonate who survived to hospital discharge following cerclage placement. Further research is needed to support the benefit of cerclage in women with CUAs.

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LAPAROENDOSCOPIC SINGLE-SITE SURGERY VERSUS CONVENTIONAL MULTI-PORT LAPAROSCOPY IN OVARIAN DRILLING: A RANDOMIZED CONTROLLED TRIAL. Ahmed Mohamed Bahaaeldin Mohamed, M.D,[1] Haitham Fathy Gad, M.D,[1] Maya Mahmoud Abdelrazek, Msc[2] [1]Assistant Professor, Cairo, Egypt; [2]Assistant Lecturer, Cairo, Egypt.

OBJECTIVE: To compare the efficacy and safety of Laparoendoscopic single site surgery (LESS) to conventional multiport laparoscopy (CML) for laparoscopic ovarian drilling (LOD) in polycystic ovary syndrome patients (PCOS).

DESIGN: A randomized controlled trial.

MATERIALS AND METHODS: This study was approved by the Faculty of Medicine, Ain Shams University, Research Ethics Committee in August 2017 (protocol no. MD 224/2017). The trial was designed and reported according to the revised recommendations of ClinicalTrials.gov (ClinicalTrial.gov NCT03206892 registered on Jul 2017).

Participants were recruited from the outpatient clinic between August 2017 and June 2019.

The primary outcome of the study was successful procedure without the need of an additional port or conversion to laparotomy. The secondary outcomes measured were: operative time, intraoperative blood loss (using equation: waste irrigation fluid volume X Hb conc in irrigation fluid/ preop

	CUA Type	Cerclage Indication	GA at Prior PTD	GA at Cerclage	Short Cervix	GA at Delivery	Birth Weight (g)	Neonatal Outcome
#1	Bicornuate	History	24w0d	18w0d	No	22w5d	400	Neonatal Demise
#2	Bicornuate	History	18w3d	14w0d	No	29w3d	1320	Living
#3	Bicornuate	History	24w0d	12w0d	No	37w1d	2385	Living
#4	Bicornuate	Exam-indicated	N/A	18w0d	Yes	19w4d	260	Stillbirth
#5	Unicornuate	History	22w5d	12w2d	No	34w3d	2375	Living
#6	Septate	History	16w1d	13w2d	Yes	20w0d	Unknown	Stillbirth
#7	Didelphys	Ultrasound	25w0d	19w2d	Yes	30w5d	1400	Living

Hb) (14), and drop in Hb 24 hours after the procedure, intraoperative complications (extraperitoneal insufflation, blood transfusion, bowel, bladder, or vascular injuries), post operative pain using Visual Analogue Scale (VAS 0-10) at 6, 12, and 24 hours postoperatively, postoperative hospital stay, postoperative complications (hematoma, ileus, wound infection), and cosmetic outcome using Patient and Observer Scar Assessment Scale (POSAS) on day 1 and 7.

Interventions: 70 women with PCOS scheduled for LOD were randomly assigned to either LESS or CML group (35 in each group) underwent LOD using straight laparoscopic instruments. Successful procedure was evaluated by the need of an additional port.

RESULTS: There was no significance difference in demographic characteristics between the groups. In addition, there were no differences in perioperative outcomes regarding operative time, estimated blood loss, postoperative pain, and length of hospital stay, between the two groups. LOD was successful in 94.3% of patients (33/35) in LESS group without the need of an additional port. Port insertion related morbidity were all reported in the CML group in the form of bowel injury by Veress needle (2.9%), extraperitoneal insufflation (5.7%), and wound hematoma (2.9%). While, surgical site infection was reported in the LESS group (5.7%). The median score of the Patient and Observer Scar Assessment Scale (POSAS) was non significant at day 1 (P= .124), while significance on day 7 in favor of LESS group (12 vs. 14, P= .001).

CONCLUSIONS: LESS is feasible, safe, and equally effective to CML with a better cosmetic satisfaction, and less port insertion related morbidity. However, it has a higher risk of superficial wound infection.

SUPPORT: This study was supported by Ain Shams University Maternity Hospital but it did not involve in the analysis or interpretation of data.

P-908 3:30 PM Wednesday, October 21, 2020

THE EFFECT OF BILATERAL TUBAL LIGATION AND BILATERAL SALPINGECTOMY ON FUTURE OVARIAN RESPONSE DURING IVF CYCLES.

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OBJECTIVE: To determine if prior history of bilateral tubal ligation and bilateral salpingectomy will alter the ability of the ovary to respond to gonadotropins during stimulation for IVF cycles and cause total doses of gonadotropins and days of gonadotropin stimulation to be increased.

DESIGN: Retrospective Cohort Study

MATERIALS AND METHODS: This was a retrospective cohort study looking at patients from the Boston IVF Arizona office who completed IVF cycles between 1/1/2015 and 6/1/2019 and who had the diagnosis of tubal factor infertility. The study group consisted of patients with a known history of a bilateral tubal ligation or bilateral salpingectomy procedure prior to the start of their IVF stimulation. The control group consisted of patients with a history of bilateral tubal occlusion by HSG and did not have a history of tubal surgery (unilateral or bilateral). The primary outcome was the total doses of FSH in IUs and total days of stimulation required during stimulation prior to vaginal oocyte retrieval procedures (VORs). Patients with PCOS, ages <28 and >40 years, were excluded from the study..

RESULTS: After exclusions, 19 cycles were included in the study group with a history of bilateral tubal ligation or bilateral salpingectomy, and 20 patients were included in the control group with a history of bilateral tubal blockage of a non-surgical means. The mean age in the control group was 34.8 vs. 35.6 in the study group. The AMH levels were equivalent at 2.49 in both groups. The mean total FSH dose in the control group was 3099 IU's vs. 3475 IU's in the study group, a 10.8% increase in the study group with a P value of 0.25. The mean total days of stimulation in the control group were not different between groups (9.2 days vs. 9.8 days, P value of 0.09)

CONCLUSIONS: In this study, increased doses of FSH and days of stimulation are required to achieve adequate stimulation during IVF cycles in patients with a history of bilateral tubal ligations or bilateral salpingectomies compared to those with non-surgical tubal factor infertility. At this time, these outcomes are not statistically significant and the number of patients enrolled in the study will need to be increased to prove a statistically relationship in the future.

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SUPPORT: None

P-909 3:30 PM Wednesday, October 21, 2020

DETERMINANTS OF SUCCESSFUL PREGNANCY OUTCOME IN ASYMPTOMATIC COMPARED WITH EMERGENT PRESENTATION IN PATIENTS WITH CORNUAL HETEROTOPIC PREGNANCY.

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OBJECTIVE: To compare the pregnancy outcome of patients with incidental and emergent diagnosis of heterotopic cornual and interstitial pregnancy.

DESIGN: Retrospective cohort study of published case reports.

MATERIALS AND METHODS: A computerized MEDLINE search was performed on published case reports of cornual heterotopic pregnancy in English language from 1960 to 2013 using the key words; heterotopic, cornual, interstitial and angular ectopic pregnancy. Reference lists were searched manually for additional relevant studies. Analyses were performed with SPSS version 26.

RESULTS: In eighty-seven (83.7%) of 104 published cases, it was possible to determine that 35 (40.2%) were asymptomatic while 52(59.8%) were symptomatic at the time of presentation (Table 1). The status of the remaining 17 (16.3%) could not be determined as to whether they were asymptomatic or symptomatic.

CONCLUSIONS: Multiple intrauterine pregnancy, cornual rupture, cesarean delivery were significantly more common in patients that were symptomatic compared with those that were asymptomatic at presentation with a trend to being delivered earlier. Asymptomatic patients were more likely to undergo medical treatment for their cornual pregnancy.

Table 1

	Asymptomatic	Symptomatic	p-value
Age*	31, 29.8±3.7	48, 31.5±4.2	0.08
Parity **	20, 0 [0-2]	48, 0[0-6]	0.09
Gestation at Diagnosis**	30, 6.2 [5.7-39.0]	50, 9.0 [5-30]	0.001
Mode of Pregnancy			
Spontaneous n = 12	3 (25%)	9 (75%)	0.35
Assisted Conception n=74	31 (41.9%)	43 (58.1%)	
Side of Cornual Pregnancy			
Left, n = 20	5 (25%)	15 (75%)	0.74
Right, n = 41	8 (19.5%)	33 (80.5%)	
Cornual Rupture, n = 30	1 /35 (3%)	29/52 (97%)	<0.0001
Viable Intrauterine Pregnancy at Diagnosis, n = 84	26/33 (45.6%)	31/51 (54.4%)	0.10
Number of Intrauterine Pregnancy			
Singleton, n = 66	32 (48.5%)	34 (51.5%)	0.02
Twins, n = 20	3 (15%)	17 (85%)	
Triplets, n=1	0 (0%)	1 (100%)	
Type of Initial Surgery			
No Surgery, n = 37	30 (81.1%)	7 (18.9%)	
Laparoscopy, n = 9	2 (22.2%)	7 (77.8%)	
Laparoscopy, then Laparotomy, n = 2	0 (0%)	2 (100%)	
Laparotomy, n = 39	3 (7.7%)	36 (92.3%)	
Medical Treatment at Diagnosis, n = 28	20 (71.4%)	8 (28.6%)	<0.0001
Gestation at Delivery** (weeks)	11, 39 [35-39]	29, 37 [27-39]	0.06
Mode of Delivery			
Vaginal, n = 11	8 (72.8%)	3 (27.2%)	0.01
Cesarean, n = 36	10 (27.8%)	26 (72.2%)	
Hysterectomy, n = 3	0 (0%)	3 (100%)	

*(n=number, mean±SD years) **[n=number, median(range)]

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MANAGEMENT OF CESAREAN SCAR ECTOPIC PREGNANCIES. A COHORT STUDY. Rahana Harjee, MD,[1] Natasha K. Simula, M.D.,[1] Mohamed Ali Bedaiwy, M.D., Ph.D.,[2] Nicole J. Todd, MD[1] [1]University of British Columbia, Department of Obstetrics and Gynaecology, Vancouver, BC, Canada; [2]University of British Columbia, Vancouver, BC, Canada.

OBJECTIVE: Cesarean section scar pregnancies (CSP) are a rare form of ectopic pregnancy occurring in approximately 6% of patients with history of an ectopic pregnancy and cesarean scar. Overall, the prevalence is estimated at 1:1800 to 1:2200 pregnancies. CSPs develop outside the endometrial cavity in the caesarean scar and can be classified as type 1 (growth towards uterine cavity) or type 2 (pregnancy growth toward uterine serosa and abdomen). Primary treatments described include systemic single or multi-dose methotrexate (+/- intra-gestational KCl injection); dilation and curettage (D&C); adjunctive uterine artery embolization; hysteroscopic, transvaginal, laparoscopic or open resection; and hysterectomy. There is no current consensus on CSP management and treatment is currently based on provider preference. Data on fertility outcomes after CSP treatment is sparse.

Our aim was to examine treatment methods and outcomes in CSP patients to provide guidance for a future protocol. Possible risk factors and future pregnancy outcomes would also be examined.

DESIGN: Cohort study at a tertiary centre in Vancouver, British Columbia, Canada.

MATERIALS AND METHODS: A chart review was completed for patients labelled with the International Statistical Classification of Diseases codes associated with ectopic pregnancies between January 2010 and December 2018 at a tertiary care centre (n=404). Patients with CSPs were identified and charts reviewed.

RESULTS: 11 patients had a CSP in the study period. Patients ranged from 25-42 years of age (mean = 36.4); 3 patients had 2 prior cesarean sections, while 8 had only 1 prior cesarean section. 4 patients presented with vaginal bleeding, 1 with bleeding and abdominal pain, and 7 were asymptomatic. Of note, 4 patients were diagnosed on assessment prior to pregnancy termination. On imaging review, 6 patients were found to have type 1 CSPs, while the remaining 5 had type 2 CSPs. A fetal heart rate was detected in 7 patients prior to treatment.

No patients had expectant or primary surgical management. 6 patients were treated with multi-dose methotrexate protocols (4 patients received intra-gestational KCl), and 5 had single dose methotrexate with 1 patient requiring adjunct uterine artery embolization. Of patients managed with multi-dose methotrexate, 2 required additional methotrexate and 1 had hysteroscopic resection (under laparoscopic guidance) for a persistent gestational sac (day 17). In patients with single dose methotrexate, 3 required additional methotrexate and 2 patients had D&Cs for retained products of conception. No patients required a blood transfusion or hysterectomy.

CONCLUSIONS: This study highlights the necessity for a CSP management protocol. Primary medical management, rather than surgical management, appears safe if appropriate follow-up is arranged.

SUPPORT: None

P-911 3:30 PM Wednesday, October 21, 2020

THE SAFETY AND EFFICACY OF AMNIOTIC MEMBRANE GRAFT USE IN PATIENTS WITH INFERTILITY: A PILOT STUDY. Elnur Babayev, MD, MSc, Maryellen Pavone, MD, Magdy P. Milad, M.D., MS Northwestern University, Chicago, IL.

OBJECTIVE: Amniotic membrane graft regulates wound healing by promoting epithelization and suppressing stromal inflammation and scarring. It is being used in ophthalmology, for skin grafting and nerve repair. Promising early studies from China, Egypt and one case series from United States (n=10) suggested therapeutic benefit when placed at hysteroscopy. The aim of this study was to evaluate the safety and efficacy of amniotic membrane graft as an adjuvant to operative hysteroscopy to prevent formation and recurrence of intrauterine adhesions in infertile patients.

DESIGN: Retrospective observational study

MATERIALS AND METHODS: Consecutive infertility patients underwent amniotic membrane graft placement at the time of initial complex operative hysteroscopy at our institution between April/1/2019 and Feb/29/2020. At the end of the procedure, allogeneic, frozen and hydration maintained, commercially available amniotic membrane graft was placed over a Foley balloon and positioned under ultrasound guidance. Patients used oral estrogen for 2-4 weeks followed by a progesterone withdrawal bleed. The Foley

balloon was kept in place for a week. Second look hysteroscopies were performed 5-14 weeks later.

RESULTS: In total, 12 patients with an average age of 37 years (25-46) underwent amniotic membrane graft placement. The initial diagnosis ranged from intrauterine septum (n=5), moderate adhesions (n=2), severe adhesions (n=3) and fibroids (n=2). Among patients undergoing septoplasty, mild intrauterine adhesions were not uncommon at the time of second look (n=2). Interestingly, an additional 2 patients had multiple endometrial polyps on second look hysteroscopy and for one patient "globally thickened endometrium" was described. All patients undergoing initial lysis of adhesions had normal uterine cavity (n=3) or mild adhesions (n=2) at the time of second hysteroscopy. Long term follow-up for 3 patients is pending, however, 2 patients showed recurrence of moderate/severe adhesions 4 months later and they proceeded to use gestational carriers. Of the two patients that underwent amniotic membrane graft placement at the time of hysteroscopic myomectomy, one had a normal endometrial cavity at second look and the other had global endometrial fibrosis and multiple endometrial polyps.

CONCLUSIONS: Our pilot study shows high rate of *de novo* endometrial polyp formation (3/7) following amniotic membrane graft use in patients without prior intrauterine adhesions. This may be secondary to growth promoting effects of amniotic membrane and raises concerns regarding its utility for patients who do not have intrauterine adhesions during initial surgery. For patients with Asherman's syndrome, amniotic membrane graft appears to initially reduce the amount of intrauterine adhesions but may not be efficacious long-term.

P-912 3:30 PM Wednesday, October 21, 2020

COMPARISON OF SURGICAL OUTCOMES BETWEEN REDUCED-PORT ROBOTIC SURGERY, SINGLE PORT LAPAROSCOPY AND CONVENTIONAL LAPAROSCOPY FOR MYOMECTOMY. Hye Jeong Hue, MD,[1] Yeon Hee Hong, MD.,[1] Jung Ryeol Lee, MD, PhD,[1] Chang Suk Suh, MD, PhD,[2] Seok Hyun Kim, MD. PhD.[3] [1]Seoul National University Bundang Hospital, Seongnam, Korea, Republic of (South); [2]professor, United Arab Emirates; [3]Seoul National University College of Medicine, Seoul, Korea, Republic of (South).

OBJECTIVE: To date, few studies have compared the benefits of different surgical modalities for myomectomy. The purpose of this study was to compare the surgical outcomes and postoperative pain scores of reduced-port robotic myomectomy (RPRM) with those of single-port laparoscopic myomectomy (SPLM) and conventional laparoscopic myomectomy (CLM).

DESIGN: Retrospective study

MATERIALS AND METHODS: Data were obtained from medical records of patients who underwent RPRM (n=99) between September 2017 and September 2019. The cases were compared with patients who underwent SPLM (n=74) between December 2013 and September 2017 and who underwent CLM (n=80) between July 2017 and August 2019. The same surgeon performed SPRM and RPRM, and different oncologists performed CLM according to preference. RPRM might have been selected for convenience if the patient had many or large myomas after RPRM had started. Therefore, different periods of data were used for RPRM and SPLM to reduce selection bias. Robotic myomectomy usually requires 4 ports. However, for cosmetic benefits, 3 ports were used, which are called "reduced-port". Patients rated pain for 1, 6, and 24 hours after surgery on the 11-point NRS (0 = no pain, 10 = worst pain). Operative time of RPRM included setup and docking time. Patient basal characteristics and surgical outcomes between the 3 groups were analyzed using Welch, Kruskal-Wallis, Bonferroni, and Pearson chi-square statistically.

RESULTS: There were no differences in basal characteristics (i.e., parity, history of previous abdominal surgery, number, size and location of the largest myoma, and weight of myomas) between the 3 groups. The largest myoma's mean size was 7.3 cm for SPLM, 7.8 cm for CLM, and 8.1cm for RPRM. The mean number of myomas was 1.8 for SPLM, 2.0 for CLM, and 2.3 for RPRM. The total number of myomas ranged from 1 to 5 in all groups. The surgical outcomes (i.e., estimated blood loss, postoperative hemoglobin drop, conversion to multi-port surgery or laparotomy, and complication) were not different significantly between the 3 groups. There was bladder dilatation in 3 patients (1 in SPLM, 2 in RPRM). Wound dehiscence occurred in 8 patients (4 in SPLM, 4 in RPRM). CLM had 3 major complications including wound infection, ileus, or hematoma. This required long-term and re-hospitalization. Operative time was significantly longer in the RPRM than CLM (121.3±48.7 vs. 100.9±38.2 min; p=0.002). SPLM's postoperative hospital stay was significantly shorter than RPRM and CLM (1.97±0.2 vs. 2.07±0.3 vs. 2.24±0.9 days; p=0.003). But, there was no period difference between the RPRM and CLM. Pain scores were significantly lower in the RPRM and CLM compared with SPLM at 1, 6 and 24 hours after surgery (3.3±1.4 vs. 3.3±1.4 vs. 4.5±1.6 at 1hr; p<0.001, 3.3±0.7 vs. 3.1±0.4 vs. 3.8±1.0 at 6hr; p<0.001, 3.1±0.8 vs. 2.9±0.5 vs. 3.1±0.7 at 24hr; p=0.014).

CONCLUSIONS: Most operative outcomes were similar among the three surgical modalities except operative time. The postoperative pain score was significantly lower in the RPRM and CLM than SPLM. RPRM is a safe and feasible option for removing myomas with outcomes similar to SPLM and CLM.

References: NA

SUPPORT: None

P-913 3:30 PM Wednesday, October 21, 2020

PREOPERATIVE UNDERSTANDING OF POSTOPERATIVE MILESTONES AMONG PATIENTS UNDERGOING REPRODUCTIVE SURGERY. Alexander Kotlyar, MD,[1] Pinar H. Kodaman, MD/PhD[2] [1]Yale School of Medicine, Oange, CT; [2]Yale School of Medicine, New Haven, CT.

OBJECTIVE: We sought to determine patient outlooks and expectations on their post-operative course following hysteroscopic and laparoscopic surgery and to identify the most common areas needed for clarification as far as post-operative milestones.

DESIGN: Single-institution, prospective survey

MATERIALS AND METHODS: Patients undergoing surgery within the section of reproductive endocrinology and infertility were provided with a survey at their pre-operative visit. The survey asked patients about their age, ethnicity, and level of education as well as 10 questions about their understanding of the type of surgery they were having, expectations for postoperative pain levels, and- timing of post-operative milestones, such as when to shower and have intercourse. Statistical analysis involved two-tailed t-tests for numerical variables, Fisher's exact test for categorical variables, independence of variables was assessed using generalized linear modeling with a p-value of <0.05 considered to be statistically significant.

RESULTS: Patients who underwent hysteroscopy were overall older than patients who underwent laparoscopy (37.5 y/o (28.0-47.0) vs. 32.7 y/o (19.0-46.0), p<0.05). There was no difference in ethnic distribution and education levels between the two surgical groups. 12.5% of patients presented to their pre-operative appointment without a clear understanding of what kind of surgery they were undergoing. Hysteroscopy patients anticipated experiencing a greater level of pain (7-10/10) following their surgery compared to laparoscopy patients (3-5/10) (p<0.01). Furthermore, hysteroscopy patients were more likely to be unsure of what their post-operative diet should be (p<0.001). The deficits in overall patient knowledge involved when to expect to have a bowel movement with only 18.7% of patients anticipating a bowel movement within 48 hours of surgery. Patients were also uncertain about when to initiate intercourse postoperatively with over 48% of patients being unsure and only 20% understanding that intercourse is be avoided for two weeks or more. Each of the survey responses was independent of age, ethnicity, and education.

CONCLUSIONS: The preoperative visit represents an important opportunity to educate patients about the surgical plan and to clarify postoperative expectations. Areas for improving and reinforcing counseling include postoperative expectations for patients with respect to expected levels of pain, optimal post-operative diet, anticipation of bowel function, and when to resume intercourse.

P-914 3:30 PM Wednesday, October 21, 2020

LAPAROSCOPIC GRAVID HYSTERECTOMY FOR MORBIDLY ADHERENT PLACENTA. Jessica A. Reid, MD,[1] Lisa L. Bayer, MD MPH,[1] Amanda M. Ecker, MD,[1] Joanna Hatfield, MD,[1] Alyssa Covelli Colwill, MD MCR,[1] Leo Han, MD MPH,[1] Melissa Moffitt, MD[2] [1]Oregon Health & Science University, Portland, OR; [2]Roswell Park Comprehensive Cancer Center, Buffalo, NY.

OBJECTIVE: Definitive treatment of previable pregnancy with morbidly adherent placenta is typically gravid hysterectomy via laparotomy. We describe minimally invasive surgical techniques to these complicated cases utilizing laparoscopy.

DESIGN: Retrospective case series from a single academic institution.

	Pregnancy	Prior # of Cesarean Surgeries	Surgical Team	Pathologic Diagnosis	Estimated Blood Loss (mL)	Operative Time (hh:mm)	Complications	Discharged Home
Case 1	IUP @ 20w5d with fetal anomalies	0*	Gyn-Onc, FP	Accreta	1000	03:15	None	POD#1
Case 2	IUP @ 20w5d with vaginal bleeding	3	Gyn-Onc, FP, MFM	Percreta	1500	03:22	Blood transfusion	POD#2
Case 3	Fetal demise measuring 15w2d with fetal anomalies	5	MIGS, FP	Implantation at cesarean scar	2000	04:21	Blood transfusion	POD#2
Case 4	IUP @ 19w2d with fetal anomalies	1	Gyn-Onc, GYN, FP	Increta	3500	02:52	Blood transfusion	POD#1

* History of Asherman Syndrome
IUP=Intrauterine pregnancy; w=weeks; d=days; Gyn-Onc=gynecologic oncologist; FP=family planning; MFM=maternal fetal medicine; MIGS=minimally invasive gynecologic surgeon; GYN=gynecologic surgeon; mL=milliliter; hh:mm=hours:minutes; POD=postoperative day

MATERIALS AND METHODS: After obtaining IRB approval, we searched our electronic medical record for ICD-10-CM diagnosis codes descriptive of morbidly adherent placenta in the first or second trimester (O43.211-232) from 2008 to 2020. Data was extracted and a descriptive summary reported.

RESULTS: We identified four cases of planned laparoscopic gravid hysterectomy performed from 2017 to 2019 (see Table). All cases were within the second trimester (range 15 to 20 weeks) and the majority (n=3) had pathologic evidence of placental invasion. Median estimated blood loss was 1750mL (range 1000 to 3500mL). Median operative time was 3.3 hours. Three patients required blood transfusion. Surgical technique was consistent with a standard laparoscopic total hysterectomy with the following adjustments: pregnancy tissue was evacuated from the uterus after occlusion of the uterine blood supply to allow for vaginal extraction of the uterus. In two cases, standard dilation and evacuation technique was used prior to colpotomy through cervical dilation (n=1) or cervical transection (n=1). In two cases, pregnancy tissue was evacuated within a specimen retrieval bag after colpotomy via hysterotomy (n=1) or cervical transection (n=1).

CONCLUSIONS: Laparoscopic gravid hysterectomy is feasible in the setting of second trimester abnormal placentation. This approach appears to be safe, with the major complication in our series being need for blood transfusion. This option is recommended only with appropriate surgical expertise and careful surgical planning utilizing a multi-disciplinary team.

P-915 3:30 PM Wednesday, October 21, 2020

EFFECTIVENESS OF A NEW, LOWER-COST MANUAL HYSTEROSCOPIC TISSUE REMOVAL DEVICE (POLYGON) IN AN OFFICE SETTING. Jeremy Michael Groll, MD SpringCreek Fertility, Centerville, OH.

OBJECTIVE: This retrospective single site case series was carried out to evaluate the effectiveness of a new, lower-cost manual hysteroscopic tissue removal device (Polygon) in an office setting.

DESIGN: Retrospective single site in an office setting

MATERIALS AND METHODS: Six consecutive premenopausal women previously diagnosed by sonohystogram with presumed endometrial polyps underwent hysteroscopic polypectomy by two different surgeons using a new manual hysteroscopic tissue removal device (Polygon) through a 6.25 mm 0 degree hysteroscope (Myosure, Hologic Inc). Hysteroscope insertion and removal times, device insertion and removal times, fluid used and number of polyps removed were recorded.

RESULTS: In all six patients, the pathology was completely removed. The average total case time was 7.3 minute (range 5-10) although the average time the device was inserted to remove the pathology was only 4 minutes (range 2-6). The average fluid used was 900 cc (range 500-1350). Three women had 1 polyp removed, two women had 2 polyps removed and 1 woman had 5 polyps removed.

CONCLUSIONS: A new, lower cost manual hysteroscopic tissue removal device (Polygon) is effective in quickly removing endometrial polyps in an office setting and merits further evaluations to compare it with other current technologies.

POSTER SESSION: WEIGHT AS A FACTOR

P-916

REASSIGNED

P-917 3:30 PM Wednesday, October 21, 2020

RELATIONSHIP BETWEEN MATERNAL BODY MASS INDEX AND MATERNAL ORIGIN OF ANEUPLOIDY. Dana B. McQueen, MD, MAS,[1] Lydia Hughes, MD,[1] Katrina Merrion, MS,[2] Emily S. Jungheim, MD, MSCI,[1] Christina E. Boots, MD, MSCI[1] [1]Northwestern Feinberg School of Medicine, Chicago, IL; [2]Natera, Inc., CA.

OBJECTIVE: To evaluate the relationship between maternal body mass index (BMI) and embryonic aneuploidy of maternal origin.

DESIGN: Retrospective Cohort Study

MATERIALS AND METHODS: Institutional Review Board approval was obtained. All in vitro fertilization (IVF) cycles utilizing preimplantation genetic testing for aneuploidy via SNP microarrays with bioinformatics between 1/2015 and 1/2020 were reviewed. BMI prior to egg retrieval was collected. Comparison groups included underweight (< 18.5 kg/m^2), normal weight (18.5 -25), overweight (25 -30) and obese (>30). Overall embryonic aneuploidy and maternal aneuploidy (MA) rates were compared. The MA rate was the number of embryos with either MA or mixed (maternal and paternal aneuploidy) divided by the total number of embryos tested. Continuous variables were compared with a student's t-test or ANOVA and categorical variables with a Chi-square. A generalized estimated equation was performed to account for potential confounders. To detect a 10% difference between groups with 80% power and alpha of 0.05, 1368 embryos in the non-obese group and 228 embryos in the obese group were needed.

RESULTS: A total of 1245 IVF cycles and 4699 embryos were included. Parental origin of aneuploidy was available for 453 cycles and 1717 embryos. Baseline characteristics were compared between groups (Table). Female age, as well as several IVF characteristics, were significantly different across groups and were included in the adjusted model. Both the overall embryonic aneuploidy rate and the MA rate increased with increasing maternal BMI (Table). After controlling for significant confounders, BMI did not significantly predict the rate of MA.

CONCLUSIONS: While embryonic aneuploidy and MA rates were significantly higher among obese women compared to normal weight women, this association was no longer significant after adjusting for confounders.

P-918 3:30 PM Wednesday, October 21, 2020

OBESITY AND ENDOMETRIUM: PROTEOMICS IN A WELL-PHENOTYPED COHORT. Emma Giuliani, MD,[1] Maya Millette, BS,[1] Courtney Julia Burns, BSE,[1] Yolanda R. Smith, MD,[1] Carol Elias, PhD,[1] Henriette A. Remmer, PhD,[1] Lisa M. Neff, MD,[2] Erica E. Marsh, MD, MSCI, FACOG[1] [1]University of Michigan, Ann Arbor, MI; [2]Northwestern University, Chicago, IL.

OBJECTIVE: Obesity, a significant public health issue in the US where more than 66.5% of women are overweight or obese, has been associated with infertility, abnormal uterine bleeding, and miscarriage. The impact of obesity on the physiology of human endometrium is largely understudied. We hypothesized that obesity-driven endometrial differences exist between obese (OW; BMI ≥30 kg/m^2) and normal weight women (NWW; BMI 18.5-24.9 kg/m^2).

DESIGN: Case-control study.

MATERIALS AND METHODS: Healthy, 18-40yo, normally cycling, women who were either normal BMI or obese were eligible to apply. Screening saline infusion sonograms and blood testing were done to confirm normal endometrial cavity and endocrine/ovarian reserve profiles (FSH, estrogen, progesterone, testosterone, TSH, and HgbA1C). If the participant screened in, demographic and anthropometric characteristics were collected. Blood samples, ultrasounds, and follicular phase endometrial biopsies were obtained. Endometrial samples were flash frozen for proteomic analysis by 1D-gel electrophoresis, liquid chromatography and mass spectrometry. Differentially expressed proteins were validated by Western Blot (WB) and chosen for functional and pathway analyses (Ingenuity Pathway Analysis and Panther Gene Ontology - Qiagen GmbH, Hilden, Germany).

RESULTS: A total of 221 women expressed interest in the study, 91 met eligibility criteria, 24 completed the screening visit (cycle day 2-5), and 13 completed the study visit (cycle day 7-10). Age, parity, cycle length, follicular phase estrogen, progesterone, and endometrial thickness did not differ between the two groups. Average BMI, %body fat, and visceral fat score measured by bioimpedance analysis were higher in OW than NWW

Mean (SD)	Underweight (N=33 cycles, 137 embryos)	Normal Weight (N=745 cycles, 2968 embryos)	Overweight (N= 291 cycles, 1040 embryos)	Obese (N= 174 cycles, 554 embryos)	P-value
Age, yr	35.9 (4.0)	36.1 (3.8)	37.4 (3.6)	37.8 (3.5)	<0.01
AMH, ng/mL	4.0 (2.3)	3.1 (2.7)	2.7 (2.4)	2.8 (2.4)	0.017
Peak E2, pg/ml	2744.4 (1596.2)	2593.4 (1563.7)	2155.7 (1160.3)	1988.3 (971.4)	<0.01
Oocytes Retrieved	17.3 (9.3)	16.3 (9.7)	14.9 (8.0)	14.7 (7.6)	0.045
Mature Oocytes	11.7 (7.0)	11.1 (7.8)	10.2 (6.3)	9.6 (5.9)	0.029
Fertilized Oocytes	9.6 (5.7)	9.5 (6.5)	8.4 (5.4)	7.9 (4.8)	0.003
Blastocysts Biopsied	4.2 (3.1)	4.0 (3.0)	3.6 (2.9)	3.2 (2.0)	<0.01
Aneuploidy Rate per Embryo Tested (N)	46.7% (64/137)	48.7% (1445/2968)	53.3% (554/1040)	56.9% (315/554)	<0.01
Maternal Aneuploidy Rate per Embryo Tested (N)	32.3% (21/65)	37.6% (370/983)	44.5% (193/434)	51.5% (121/235)	<0.01

(37.8±5.5 vs. 22.1±2.2Kg/m^2, 42.7% vs. 23.6%, 9.7 vs. 2.2; p<0.05). Histological examination of endometrial samples revealed concordant cycle phase and absence of gross abnormalities. A total of 2,930 unique endometrial proteins were identified with a 2,137±55 average protein per sample. 30 proteins were significantly upregulated (>2-fold) and 291 were downregulated (<0.5-fold) in OW vs. NWW (p<0.05). Array findings were validated by WB. Pathway analysis showed significant enrichment of folate/nucleic acid metabolism (p=0.011), RNA degradation (p=0.017) and immune processes (p<0.05) in OW vs. NWW.

CONCLUSIONS: In this well phenotyped population, obesity is associated with significant changes of the proliferative phase endometrial proteome of healthy women by disrupting specific molecular and cellular pathways. This could lead to menstrual bleeding abnormalities and create an altered environment for luteinization. Further studies are needed to investigate obesity-induced proteome alterations during the different phases of the menstrual cycle and the mechanistic pathways of endometrial dysregulation.

P-919 3:30 PM Wednesday, October 21, 2020

ASSOCIATION OF LEPTIN WITH TOTAL AND FREE TESTOSTERONE: RESULTS FROM THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEYS. Thiago Fernandes Negris Lima, MD,[1] Evgeniya Rakitina, MS,[2] Sirpi Nackeeran, BA,[2] Gustavo Fernandes Negris Lima, MEng,[3] Himanshu Arora, PhD,[2] Atil Yilmaz Kargi, MD,[1] Ranjith Ramasamy, MD[1] [1]University of Miami, Miami, FL; [2]University of Miami Miller School of Medicine, Miami, FL; [3]Federal University of Espirito Santo, Vitoria, Brazil.

OBJECTIVE: Leptin is produced in the white adipose tissue and its concentration is positively associated with the amount of body fat. Obese men can have low testosterone (T) but the etiology is unknown. Our objective was to evaluate the effects of leptin on T and calculated free testosterone (cFT). We hypothesized that increased serum leptin can be independently associated with low T.

DESIGN: Cross-sectional analysis.

MATERIALS AND METHODS: We analyzed male participants (ages 20-90) of the NHANES III survey from 1988-1991. We included males who had data on serum leptin, cFT and T levels. Our primary outcome was to evaluate the effect of leptin on T and cFT. The Shapiro–Wilk test was used to determine the normality of variable distributions. Simple linear regression was performed with leptin, age, waist circumference, hypertension, and diabetes as independent variables predicting cFT and T levels. Multiple linear regression was used to determine the best predictors for cFT and T controlling for all confounding variables that were significant in the univariate analysis. All statistical tests were adjusted for NHANES complex survey design.

RESULTS: A total of 1193 men were analyzed. As expected, older and obese men were associated with lower testosterone levels. Interestingly, increasing serum leptin levels was an independent predictor of decreasing serum total and free testosterone levels on multivariable linear regression. An increase of 1ng/mL in leptin levels resulted in a decrease of 5.13 ng/dL and 0.11 ng/dL of T and cFT, respectively (p < 0.05). Also, every additional year of life led to a T and cFT reduction of 2.87 ng/dL and 0.13 ng/dL, respectively, and an increase of 1 cm in the waist circumference corresponded to decrease of 4 ng/dL in T levels (p < 0.05). (Table 1)

CONCLUSIONS: Increasing serum leptin, age and BMI are associated with both decreasing total and free testosterone levels. Leptin could potentially explain the underlying association between obesity and testosterone deficiency.

SUPPORT: no

P-920 3:30 PM Wednesday, October 21, 2020

REPRODUCTIVE AND OBSTETRIC OUTCOMES IN MILDLY AND SIGNIFICANTLY UNDERWEIGHT WOMEN UNDERGOING IN VITRO FERTILIZATION. Phillip A. Romanski, MD,[1] Pietro Bortoletto, MD,[1] Alice Chung, BA,[2] Brady I. Magaoay, BA,[2] Steven Spandorfer, MD[1] [1]The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY; [2]Weill Medical College of Cornell University, New York, NY.

OBJECTIVE: To determine the effect of low body mass index (BMI, kg/m^2) on clinical pregnancy and live birth outcomes in infertile women treated with oocyte retrieval and fresh embryo transfer.

DESIGN: We conducted a retrospective cohort study performed in an academic hospital setting. Patients who underwent their first oocyte retrieval with planned autologous fresh embryo transfer in our IVF clinic between 01/01/2012 and 12/31/2018 were included. Patients were stratified by BMI (kg/m^2): <17.5 (n=76), 17.5-18.49 (n=231), and 18.5-24.99 (n=4,922). Donor oocyte and gestational carrier cycles, as well as cycles missing vital data, were excluded.

MATERIALS AND METHODS: Demographic outcomes were collected. The primary outcomes were pregnancy and live birth rates; secondary outcomes included oocyte quality and embryo morphology. Logistic regression adjusted *a priori* for patient age and number of embryos transferred was used to estimate the odds ratio with a 95% confidence interval (CI) among the BMI study groups for pregnancy outcomes.

RESULTS: A total of 5,229 retrievals resulting in 4,798 embryo transfers met inclusion criteria. A diagnosis of anovulatory infertility was observed in 9.2% of women with a BMI <17.5, 10.0% of women with a BMI of 17.5-18.49, and 6.1% in normal-weight women. After adjusting for patient age and the number of embryos transferred, there were no significant differences in the pregnancy rates for women with a BMI <17.5 (50.0%, OR 0.97; 95% CI 0.60-1.56) and a BMI of 17.5-18.49 (48.5%, OR 0.91; 95% CI 0.69-1.19) compared to normal-weight women (48.7%). In women who achieved pregnancy, there were no significant differences in pregnancy outcomes. Among pregnant patients, the live birth rate was 67.7% in the normal-weight group, which was statistically similar compared to the BMI <17.5 group (57.9%, OR 0.67; 95% CI 0.40-1.13) and the BMI 17.5-18.49 group (72.3%, OR 0.99; 95% CI 0.73-1.33). The miscarriage rate among pregnant patients was 12.6% in the normal-weight group, which was statistically similar compared to the BMI <17.5 group (13.2%, OR 1.14; 95% CI 0.46-2.86) and the BMI 17.5-18.49 group (17.0%, OR 1.41; 95% CI 0.87-2.30). Additionally, there were no significant differences in preterm delivery rate (<37 weeks gestation), low neonatal birth weight (<2500 grams), or cesarean section rates in singleton deliveries for either underweight patient groups when compared to normal-weight patients.

CONCLUSIONS: Overall, underweight patients treated with IVF have similar pregnancy and live birth outcomes compared to normal-weight women. However, there may be a clinically important decreased live birth rate in women with a BMI <17.5. This should be investigated further in future studies. In addition, underweight patients do not have an increased

Table 1. Multiple linear regression model predicting total testosterone (ng/dL) and calculated free testosterone (ng/dL).

	Total Testosterone					Calculated Free Testosterone				
			95% CI					95% CI		
Variable	B	SE	Lower	Upper	p-value	B	SE	Lower	Upper	p-value
Leptin (ng/mL)	-5.13*	2.20	-9.68	-0.59	.0285	-0.11*	0.03	-0.17	-0.06	.0004
Estradiol (pg/mL)	5.38*	1.58	2.12	8.64	.0024	0.12*	0.03	0.05	0.20	.0014
Age (years)	-2.87*	0.43	-5.61	-2.39	<.0001	-0.13*	0.01	-0.15	-0.11	<.0001
Waist Circumference (cm)	-4.00*	0.78	-5.61	-2.39	<.0001	-0.02	0.01	-0.05	0.00	.0963
Diabetes (Yes vs No)	-8.40	22.59	-55.13	38.32	.7133	0.01	0.41	-0.83	0.85	.9794
Hypertension (Yes vs No)	10.62	21.86	-34.59	55.83	.6316	-0.13	0.43	-1.02	0.76	.7659

*p < 0.05; R-square T = 0.38. R-square cFT= 0.47.

likelihood of preterm delivery, low birth weight infant at delivery, or cesarean section. Importantly, there may be nutritional deficiencies present that contribute to other adverse obstetric or neonatal outcomes, which were not able to be assessed in this study. Prior to infertility treatment, underweight patients should receive nutritional consultation.

SUPPORT: None

P-921 3:30 PM Wednesday, October 21, 2020

EFFECT OF ABDOMINAL FAT ON INTRACYTOPLASMIC SPERM INJECTION CYCLES: PRELIMINARY RESULTS. Alaa A. Makhlouf, Msc, Mohammed Khairy Ali, MD, Ahmed M. Abdelmagied, MD, Dina M. Habib, MD, Esraa Badran, MD, Ihab M. El-Nashar, MD, Tarek K. Al-Hussaini, MD, FRCOG, Hosam Salem, MD Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt.

OBJECTIVE: This study aimed at evaluating whether subcutaneous and pre-peritoneal abdominal fat as well as follicular fluid leptin (FFL) predict intracytoplasmic sperm injection (ICSI) outcomes in women without polycystic ovary syndrome (PCOS).

DESIGN: Prospective cohort study (NCT03778684) in an University-affiliated Assisted Conception Center. University IRB approved the study.

MATERIALS AND METHODS: Infertile non-PCOS women indicated for ICSI were considered for enrollment after consent. Included women were grouped based on their waist circumference (WC) into women with central obesity (WC $\geq$ 80 cm; COB group) and without (WC$<$ 80 cm; Non-COB group). At baseline evaluation, women underwent assessment of obesity using different measures and assessment of homeostasis-model for insulin resistance (HOMA-IR). Obesity measures included body mass index (BMI), visceral adiposity index (VAI), and the novel body fat index (BFI). BFI was calculated by multiplying pre-peritoneal and subcutaneous fat (in mm) and divided by height (in cm). FFL was measured from pooled follicular fluid of $\geq$ 17 mm follicles, containing cumulus oocyte complex. Our primary endpoint was ongoing pregnancy rate (OPR). Comparisons between groups were evaluated utilizing the independent t , Wilcoxon rank sum, and chi-square tests as appropriate. Logistic regression model, receiver operating characteristic (ROC) curve and correlation coefficient (r) were also utilized. We planned a sample size of 168 women. Recruitment was temporarily suspended due to COVID-19 pandemic. Recruitment will continue, once IVF procedures are resumed based on our governmental policy

RESULTS: Of 340 women screened, 72 eligible women were included in this preliminary analysis; 40 in COB group and 32 in Non-COB group. Both groups were comparable in age, AMH, duration of infertility, IVF indication, HOMA-IR, cycle characteristics and FFL concentrations. Women in COB group were more likely to have higher BMI (mean$\pm$SD;30.5$\pm$3.9vs25.3$\pm$2.8 $p < 0.005$), BFI (median(IQR),1.8(1.8) vs0.73(0.2), $p<0.005$), and VAI (median(IQR),1.9 (1.06) vs 1.2 (0.65), $p<0.001$). Both groups showed comparable maturation index (73.8%vs77.9%), fertilization rate (71.2%vs72.1%), and OPR (37.5% vs 43.8%). In the correlation analysis, central obesity was more likely to be due to subcutaneous ($r=0.8$, $p<0.001$) rather than pre-peritoneal fat ($r=0.4$, $p<0.001$). None of the obesity measures were correlated with either FFL or OPR. No significant correlation was found between FFL levels and number of oocytes retrieved, maturation and fertilization indices, or rate of good-quality embryos. In ROC analysis, comparable trend was observed among BMI, BFI, VAI, and FFL for predictability of ongoing pregnancy (AUC: 0.48, 0.53, 0.50, and 0.48, respectively). None of these variables was predictor for OPR in the multivariable logistic regression. The only predictors were peak estradiol (OR:1.2,CI:1.1-1.3, $p< 0.05$) and number of mature retrieved oocytes (OR:0.08,CI:0.67-0.92,$p<0.004$).

CONCLUSIONS: Based on this analysis, we could not find evidence that FFL and abdominal fat thickness affect ICSI outcomes.

References: Body fat index: A novel alternative to body mass index for prediction of gestational diabetes and hypertensive disorders in pregnancy. European Journal of Obstetrics & Gynecology and Reproductive Biology, 228, 243-248.

P-922 3:30 PM Wednesday, October 21, 2020

OBESE PATIENTS ARE LESS LIKELY TO PURSUE FERTILITY TREATMENT AND TAKE A LONGER TIME TO DO SO, AFTER INITIAL INFERTILITY CONSULTATION. Anne E. Martini, DO,[1] Jaclyn Kwal, MD,[2] Samad Jahandideh, PhD,[3] Kate Devine, MD,[3] Alan H. DeCherney,

	All	Under-weight (<18.5)	Normal (18.5-24.9)	Over-weight (25.0-29.9)	Class I (30.0-34.5)	Class II (35.0-39.9)	Class III ($\geq$ 40.0)			P-value		
							All	40-43.9	$\geq$44	Class I vs Normal	Class II vs Normal	Class III vs Normal
Patients (n)	2061	28	844	525	278	204	157	79	78			
BMI (kg/m^2)	28.2 $\pm$ 7.3	17.7 $\pm$ 0.8	22.3 $\pm$ 1.7	27.3 $\pm$ 1.4	32.0 $\pm$ 1.3	37.3 $\pm$ 1.5	45.4 $\pm$ 5.1	41.8 $\pm$ 1.3	49.0 $\pm$ 4.9			
Age (y)	33.7 $\pm$ 5.3	32.1 $\pm$ 4.0	33.6 $\pm$ 5.2	34.0 $\pm$ 5.2	33.8 $\pm$ 5.7	33.1 $\pm$ 5.3	34.3 $\pm$ 5.6	34.2 $\pm$ 6.0	34.4 $\pm$ 5.1	NS	NS	NS
Drop-out rate (%)	39.6	25.0	32.7	36.0	42.4	51.0	67.5	55.7	79.5	0.004	<0.001	<0.001
Time to treatment (if pursued) (d)	171.69 $\pm$ 215.4	214.7 $\pm$ 343.2	157.8 $\pm$ 193.7	166.6 $\pm$ 204.1	186.1 $\pm$ 227.4	208.8 $\pm$ 269.5	219.8 $\pm$ 269.4	180.5 $\pm$ 205.1	315.1 $\pm$ 376.5	0.044	<0.001	<0.001
CPR for first treatment (if pursued) (%)	14.6	25.0	16.4	15.2	14.4	11.8	5.1	2.5	7.7	NS	NS	<0.001

Mean $\pm$ SD unless otherwise stated

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OBJECTIVE: In considering impacts of obesity on maternal and fetal health, evidence-based body mass index (BMI) thresholds for fertility treatment are being more commonly implemented. Our goal was to evaluate drop-out rates and time to first treatment by BMI in patients presenting for infertility care.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Charts of patients presenting for infertility care in the first 3 months of 2016 were reviewed to allow 4 years of follow up. Age and BMI at initial consult, time to first treatment (if pursued), infertility diagnosis, treatment type, and cycle outcome were collected. Patients with BMIs recorded >1 month from their initial consult were excluded. Descriptive statistics were applied and stratified by BMI (kg/m^2) and obesity classification. Obesity class III was further subdivided into BMI 40-43.9 and ≥44 based on BMI treatment policies at our center. ANOVA and chi-square were used to compare continuous and categorical variables in obese groups to those with normal BMI.

RESULTS: 2,061 patients met study inclusion criteria, 60.4% of which initiated treatment after initial consult. Mean age and BMI were 33.7 years and 28.2 kg/m^2, respectively. Infertility diagnosis was listed as an-/oligo-ovulation for ≥18% of obese vs ≤12.8% for non-obese women. Drop-out rate and time to treatment increased linearly with BMI, however underweight patients also had longer time to treatment. When obese subgroups were independently compared to normal BMI, drop-out and time to treatment were significantly higher for all obesity classes (P<0.05). If a treatment cycle was pursued, rates of clinical pregnancy decreased as BMI increased.

CONCLUSIONS: Obese patients are less likely to initiate fertility treatment and take longer to do so. Further understanding of weight loss strategies and trends in patients who begin treatment may help to provide better access to and sustainment of effective fertility care in this population.

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DOES BODY MASS INDEX IMPACT EMBRYO MORPHOKINETICS? Luce A. Kassi, MD,[1] Dana B. McQueen, M.D., M.A.S.,[2] Rafael Confino, BS,[3] John Zhang, PhD,[4] Anne P. Hutchinson, M.D.,[4] Mary Ellen Pavone, MD, MSCI,[4] Dana Kimelman, MD[4] [1]Northwestern University Feinberg School of Medicine, Chicago, IL; [2]Northwestern University, Chicago, IL; [3]Northwestern Feinberg School of Medicine, Chicago, IL; [4]Northwestern University Feinberg School of Medicine, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Chicago, IL.

OBJECTIVE: To assess the relationship between maternal body mass index (BMI) and embryo morphokinetics on time lapse microscopy (TLM).

DESIGN: Retrospective Cohort Study

MATERIALS AND METHODS: Institutional Review Board approval was obtained. All IVF cycles between June 2015 and April 2017 were reviewed. Female BMI prior to egg retrieval was collected through chart review. Comparison groups included underweight (< 18.5 kg/m^2), normal weight (18.5-25 kg/m^2), overweight (>25-30 kg/m^2) and obese (>30 kg/m^2). Embryo morphokinetic parameters were assessed with TLM and included time to syngamy (TPNf), time to 2 cells, time to 3 cells, time to 4 cells and time to 8 cells. A generalized linear mixed model was used to control for potential confounders and multiple embryos resulting from a single IVF cycle.

RESULTS: 589 IVF cycles were included in the analysis. There were no significant differences in the median maternal age, AMH, days of stimulation, total gonadotropin used, number of oocytes retrieved, number of mature oocytes or number fertilized oocytes between groups (Table). There was a trend toward less intracytoplasmic sperm injection (ICSI) in the underweight group and this was adjusted for in the final model. There was a total of 2,185 embryos assessed by TLM: 56 in the underweight group, 1273 in the normal weight group, 510 in the overweight group and 345 the obese group. After adjusting for race and ICSI, the mean time to the 8 cell stage in the underweight group was 4.3 (95% CI: -8.31, -0.21) hours less than in the normal weight group (P= 0.025) and 4.6 (95% CI: -8.8, -0.21) hours less than in the obese group (P=0.022).

CONCLUSIONS: Embryo morphokinetic parameters were significantly different between BMI groups, with embryos from underweight women having a faster time to the 8 cell stage than normal weight or obese women. This study demonstrates that weight can be an independent factor contributing to embryo development as observed on TLM.

P-924 3:30 PM Wednesday, October 21, 2020

LIVE BIRTH OUTCOMES IN INFERTILE PATIENTS WITH CLASS III AND CLASS IV OBESITY FOLLOWING CONTROLLED OVARIAN HYPERSTIMULATION. Phillip A. Romanski, MD,[1] Pietro Bortoletto, MD,[1] Brady I. Magaoay, BA,[2] Alice Chung, BA,[2] Steven Spandorfer, MD[1] [1]The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY; [2]Weill Medical College of Cornell University, New York, NY.

OBJECTIVE: To assess the effect of class III (body mass index [BMI, kg/m2] 40-49.9) and class IV obesity (≥50) on clinical pregnancy and live birth outcomes in infertile women treated with oocyte retrieval and fresh embryo transfer.

DESIGN: We conducted a retrospective cohort study performed in an academic hospital setting. Patients who underwent their first oocyte retrieval with planned autologous fresh embryo transfer in our IVF clinic between 01/01/2012 and 12/31/2018 were included. Patients were stratified by BMI (kg/m^2): 18.5-24.9 (n=4,922), 25-29.9 (1,571) 30-34.9 (563), 35-39.9 (218), and ≥40 (115).

MATERIALS AND METHODS: The primary outcomes were pregnancy and live birth rates; secondary outcomes included oocyte quality and embryo morphology. Logistic regression adjusted *a priori* for patient age and number of embryos transferred was used to estimate the odds ratio with a 95% confidence interval (CI) among the BMI study groups for pregnancy outcomes.

RESULTS: A total of 7,389 retrievals resulting in 6,740 embryo transfers met inclusion criteria. Compared to the normal-weight cohort (BMI: 18.5-24.9), women with a BMI ≥40 had a significantly higher rate of cancelled fresh transfer after retrieval (8.3% versus 19.1%, OR 2.59; 95% CI 1.61-4.17 (p-value, test for linear trend with increasing BMI group = 0.003). In patients who had an embryo transfer, there were no differences in pregnancy rates across all BMI groups (BMI 18.5-24.9: 53.1% versus ≥40: 48.4%, OR 0.87; 95% CI 0.57-1.33 (p-value, test for linear trend with increasing BMI group = 0.86)). Among pregnant patients, as the BMI increased, a significant

	Underweight (N=17)	Normal Weight (N= 326)	Overweight (N= 149	Obese (N= 96)	p-value
Age (yr)	35.0 (32.7, 38.4)	35.2 (33.2, 38.6)	36.5 (33.6, 38.5)	36.0 (34.6, 40.5)	0.431
AMH (ng/ml)	2.3 (1.1, 4.3)	2.83 (1.4, 3.9)	3.24 (1.6, 3.8)	2.55 (1.4, 4.3)	0.929
Days Stimulation	10.0 (9.0, 11.0)	10.0 (9.0, 11.0)	10.5 (9.5, 11.5)	10.0 (9.0, 11.0)	0.179
Total IU Gonadotropin	3300 (2400, 4500)	2700 (2025, 3750)	2887.5 (2325, 4500)	3000 (2700, 4537.5)	0.296
Number of Oocytes	14.0 (10.0, 20.0)	14.0 (10.0, 22.0)	12.0 (9.0, 21.0)	12.0 (7.0, 17.5)	0.767
Number of Mature Oocytes	11.0 (7.0, 16.0)	12.0 (8.0, 16.0)	9.0 (7.0, 16.0)	9.0 (6.0, 17.0)	0.781
Number Fertilized Oocytes	8.0 (6.0, 12.0)	9.0 (6.0, 13.0)	7.0 (5.0, 14.0)	8.0 (5.0, 13.0)	0.749
% ICSI	87.5% (14)	97.2% (314)	97.9% (142)	95.8% (92.0)	0.061

Data presented as Median(Q1-Q3) or % (N)

trend of an increased miscarriage rate was observed (BMI 18.5-24.9: 12.6% versus ≥40: 22.2%, OR 1.67; 95% CI 0.85-4.25 (p-value, test for linear trend with increasing BMI group <0.001)). Additionally, among pregnant patients, as the BMI increased, a significant trend of a decreased live birth rate was observed (BMI 18.5-24.9: 67.7% versus ≥40: 53.3%, OR 0.65; 95% CI 0.40-1.05 (p-value, test for linear trend with increasing BMI group = 0.004)). Among singleton deliveries, a significant trend of an increased c-section rate was identified as the BMI increased (BMI 18.5-24.9: 39.0% versus ≥40: 61.5%, OR 2.04; 95% CI 0.65-6.34 (p-value, test for linear trend with increasing BMI group <0.001)).

CONCLUSIONS: Overall, patients with a BMI ≥40 have worse IVF treatment outcomes compared to normal-weight patients. After embryo transfer, the pregnancy rate is comparable to normal-weight women; however, the rate of miscarriage is increased, leading to an overall lower live birth rate for pregnant women in this population. Patients with a BMI ≥40 have a c-section rate that is 50% higher than normal-weight patients. These results are useful for counseling infertile patients with class III and class IV obesity about their expected outcomes with IVF treatment. Prior to infertility treatment, obese patients should be counseled about the general health and infertility-related benefits of weight loss.

SUPPORT: None

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DOES EXTRA WEIGHT SLOW AN EMBRYO DOWN? THE EFFECT OF MATERNAL BMI ON EMBRYO DIVISION TIMINGS IN WOMEN UNDERGOING IN VITRO FERTILIZATION. Theresa Piquette, MD, Amy Pan, PhD, Jayme Bosler, MD, Robert Rydze, MD, Kate D. Schoyer, MD Medical College of Wisconsin, Milwaukee, WI.

OBJECTIVE: Obesity affects multiple endocrine pathways and has been associated with lower fecundity and fertility even in normoovulatory patients. These effects can also influence outcomes for couples undergoing IVF, whose embryos tend to have lower cleavage rates and progression to blastocyst. However, the mechanism(s) whereby maternal body habitus affects the developing embryo are not well understood. The purpose of this study is to elucidate what role maternal BMI has on the morphokinetics of embryo development as monitored by a time-lapse system.

DESIGN: Retrospective chart review

MATERIALS AND METHODS: A review of EmbryoScope time-lapse data and patient medical records from women undergoing their first cycle of IVF between September 2016 to January 2019 was performed. Excluded from analysis were patients with factors known to negatively impact embryo quality, such as diminished ovarian reserve, age>37 years, and cigarette smoking. To detect a difference of 0.125 standard deviations at the T2 time point with 80% power (α=0.05), assuming 9 embryos per patient, 188 normal weight patients (1692 embryos) and 94 obese patients (846 embryos) were needed. A multilevel mixed effects model was performed to investigate the relationships between BMI categories and embryo division timings. Log or square transformation are used to improve fit.

RESULTS: 366 patients met inclusion criteria, yielding 4,475 embryos: 1948 embryos from 162 normal weight women (were no differences between BMI groups in age, AMH level, number of oocytes retrieved, or number of blastocysts available. When comparing embryo division timings based on BMI, there were significant differences between T2 (time to division to 2 cell embryo) where patients with obese BMI had the shortest division timings when compared with patients with normal weight (P=0.018), overweight (P=0.043), and morbidly obese BMI (P=0 .032). This effect persisted for T3, T4, and T5 where embryos from obese patients had the most rapid division timings compared to other weight categories (p<0.05). When analyzing BMI as a continuous variable, there was no significant relationship between BMI and embryo division timing (p=0.35).

BMI categories	Mean T2 (hours)	95% CI
Normal Weight	26.36	26.00, 26.74
Overweight	26.33	25.85, 26.81
Obese	25.63	25.16, 26.11
Morbidly Obese	27.04	25.85, 28.30

CONCLUSIONS: Maternal BMI does not appear to influence embryo morphokinetics in a dose-dependent manner. Future studies are warranted to evaluate other potential factors influenced by obesity, such as oocyte mitochondrial function or embryonic metabolic gene expression that could be contributing to the reduced embryo quality and fecundability seen in obese women

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THE EFFECTS OF OOCYTE DONOR AND RECIPIENT BODY MASS INDEX ON LIVE BIRTH RATES AND PREGNANCY OUTCOMES FOLLOWING ASSISTED REPRODUCTION. Jiaxin Xu, MPH,[1] Heather S. Hipp, MD,[2] Sarah M. Capelouto, MD,[3] Zsolt Peter Nagy, MD, PhD,[4] Daniel B. Shapiro, MD,[4] Jessica B. Spencer, MD, MSc,[5] Audrey J. Gaskins, ScD[1] [1]Emory University, Rollins School of Public Health, Atlanta, GA; [2]Emory University School of Medicine, Atlanta, GA; [3]University of Texas Southwestern Medical Center, Dallas, TX; [4]Reproductive Biology Associates, Atlanta, GA; [5]Emory University School of Medicine, Division of Reproductive Endocrinology and Infertility, Atlanta, GA.

OBJECTIVE: Excess body weight is a risk factor for impaired fertility in women conceiving both with and without medical assistance. However, whether excess body weight negatively influences female fertility on the level of the oocyte and/or uterine environment remains unclear. To expand on the existing literature in autologous and fresh oocyte donation cycles, we used information from a large cohort of vitrified donor oocytes to investigate the influence of donor and recipient body mass index (BMI) on assisted reproductive technology (ART) outcomes.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Between 2008 and 2015**,** 338 oocyte donors and 932 recipients underwent 1651 embryo transfer cycles at a private fertility center in Georgia. We evaluated the associations between donor and recipient BMI and probability of positive pregnancy test (PPT) and live birth using log binomial regression with cluster weighted generalized estimating equations adjusting for donor and recipient age, race, retrieval year, and recipient diagnoses of uterine factor infertility and polycystic ovarian syndrome. Secondary outcomes included the % of oocytes that survived warm, fertilized, and developed into usable embryos. Infant birthweight and gestational age were also examined among live born singletons. All models accounted for the correlation between oocytes from the same donor and correlation between cycles/live births from the same recipient.

RESULTS: The mean (standard deviation) BMI of donors and recipients was 22.3 kg/m^2 (2.3 kg/m^2) and 24.5 kg/m^2 (4.7 kg/m^2), respectively. Approximately 25% of the donors and recipients were racial minorities. The percentage of oocytes that survived warming, successfully fertilized, and developed into usable embryos did not differ across categories of donor BMI. There were also no associations between donor BMI and probability of PPT or live birth. In contrast, there was a statistically significant positive association between recipient BMI and risk of PPT (adjusted risk ratio (aRR) 1.01 per 2 kg/m^2, 95% CI 1.00, 1.02) and live birth (aRR 1.02 per 2 kg/m^2, 95% CI 1.00, 1.03). Recipients with a BMI≥35 kg/m^2 had a higher probability of PPT (RR 1.13, 95% CI 1.02, 1.25) and live birth (RR 1.26, 95% CI 1.07, 1.49) compared to normal weight recipients. Among singleton births, recipients with a BMI<18.5 kg/m^2 had a lower risk of delivery (HR 0.64 95% CI 0.43, 0.95), while women with a BMI ≥35 kg/m^2 had a higher risk of delivery in an earlier gestational week (HR 1.45 95% CI 0.96, 2.20) compared to normal weight women. Recipients with a BMI ≥35 kg/m^2 also had a higher risk of having a low birth weight infant (RR 1.76 95% CI 1.02, 3.02) compared to normal weight women. Donor BMI was not associated with birthweight or gestational length.

CONCLUSIONS: In the setting of vitrified donor oocyte ART, recipient BMI was positively associated with probability of live birth but negatively associated with gestational length and birthweight. Our results suggest that impaired oocyte quality rather than endometrial receptivity may be the overriding factor influencing ART success in obese women using autologous oocytes.

SUPPORT: Dr. Gaskins is supported by a career development grant, R00ES026648, from the National Institute of Environmental Health Sciences (NIEHS). REDCap support was provided by UL1 TR000424 at Emory University.

Table 1. Mitochondrial Score and Aneuploidy Rates

	Underweight (n=5)	Normal weight (n=148)	Overweight (n=57)	Obesity I (n=24)	Obesity II (n=12)	Obesity III (n=9)	p-value
Average Mitochondiral Score	22.52 ± 8.67	24.95 ± 6.68	24.80 ± 6.75	24.59 ± 5.40	23.12±5.23	25.70 ± 3.74	0.89
Aneuploidy rate	0.45 ± 0.18	0.42 ± 0.28	0.39 ± 0.24	0.39 ± 0.28	0.38 ± 0.30	0.52 ± 0.28	0.75

Data are presented as mean ± sd.

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OBESITY DOES NOT IMPACT ANEUPLOIDY RATES OR MITOCHONDRIAL DNA COPY NUMBER IN PATIENTS UNDERGOING PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY. Wes Urian, MD,[1] Molly Siegel, MD,[1] Pamela B. Parker, M.D., M.P.H.,[2] Bharti Garg, MBBS, MPH,[2] Paula Amato, MD,[2] Diana Wu, MD,[2] David Lee, MD,[2] Thomas O'Leary, PhD,[2] Sacha A. Krieg, M.D., Ph.D.[2] [1]Oregon Health and Science University, Portland, OR; [2]Oregon Health & Science University, Portland, OR.

OBJECTIVE: To investigate the impact of body mass index (BMI) on aneuploidy rate and mitochondrial DNA copy number, a known marker of embryo quality, in embryos obtained during in vitro fertilization (IVF) cycles utilizing preimplantation genetic testing for aneuploidy (PGT-A).

DESIGN: This is a retrospective IRB-approved cohort study performed at a single academic institution involving 409 IVF-PGT-A cycles performed during January 2016 to June 2018.

MATERIALS AND METHODS: BMI for all patients was calculated in each respective IVF-PGT-A cycle and classified according to the World Health Organization criteria. Aneuploidy rate was defined as the total number of aneuploidy blastocysts divided by the total number blastocysts from an IVF cycle. Mitochondrial DNA copy number (Mitoscore, iGenomix) was derived for each euploid embryo and averaged across each IVF cycle. Data were analyzed using chi-square tests/Fisher Exact test for categorical variables and one-way analysis of variance (ANOVA) for continuous variables. After excluding donor egg cycles, those utilizing preimplantation genetic testing for mutations or structural rearrangements, cycles with no euploid embryos available for biopsy, and those without a reported Mitoscore, we analyzed a total of 255 IVF cycles.

RESULTS: There were no differences in baseline characteristics such as age, parity, primary infertility diagnosis, or smoking status. We found no significant differences in our primary outcomes of average Mitoscore, euploidy, or aneuploidy rates across the BMI groups. There is a nonsignificant trend towards increased average Mitoscore with increasing BMI (22.52 for underweight vs 25.70 for class III obesity). There were no differences in our secondary outcomes of clinical pregnancy rates, live birth rates, or miscarriages.

CONCLUSIONS: Our study demonstrates that increasing BMI is not associated with changes in mitochondrial score or aneuploidy rates. This suggests that other factors impact IVF success rates in women with obesity, such as inflammatory and endometrial factors.

P-928 3:30 PM Wednesday, October 21, 2020

EFFECT OF BODY MASS INDEX (BMI) ON PREGNANCY OUTCOMES IN FROZEN-THAWED BLASTOCYST TRANSFER (FET) CYCLES. Adrienne R. Schmidt, MD,[1] Prachi N. Godiwala, MD,[2] Reeva B. Makhijani, MD,[2] Chantal Bartels, MD,[2] John Nulsen, MD,[2] Claudio A. Benadiva, MD,[2] Daniel R. Grow, MD,[2] Lawrence Engmann, MD[2] [1]University of Connecticut School of Medicine, Farmington, CT; [2]Center for Advanced Reproductive Services, University of Connecticut School of Medicine, Farmington, CT.

OBJECTIVE: There is limited and conflicting data from either small or non-US cohorts on the effect of body mass index on pregnancy outcomes in FET cycles. We aimed to investigate the effect of BMI on ongoing pregnancy rate (OPR) in FET cycles in a larger US cohort.

DESIGN: Single academic center retrospective cohort study

MATERIALS AND METHODS: 2310 FET cycles (natural, letrozole, or programmed) in patients £42 years using embryos created from autologous oocytes from 2015-2020 were included. Groups were divided by BMI: underweight (BMI <18.5 kg/m^2), normal weight (BMI 18.5-24.9 kg/m^2), overweight (BMI 25-29.9 kg/m^2), and obese (BMI ≥ 30 kg/m^2).The primary outcome was OPR. Secondary outcomes included pregnancy rate (PR), implantation rate (IR), clinical pregnancy rate (CPR), and clinical loss rate (CLR). Chi-square test for categorical data and one-way ANOVA with post hoc Tukey test for continuous data was used. Multiple logistic regression analysis was performed adjusting for age, anovulation diagnosis, number of embryos transferred, FET protocol used, and use of preimplantation genetic testing for aneuploidy (PGT-A). A two-sided p-value of <0.05 was considered statistically significant.

RESULTS: A higher proportion of obese patients carried a diagnosis of ovulation and used a programmed or letrozole FET protocol compared to other BMI groups. Obese and underweight women were less likely to use PGT-A. There was no significant difference in OPR among BMI groups, which persisted after controlling for confounding variables. PR, IR, CPR, and CLR were similar among BMI groups.

CONCLUSIONS: In this large US cohort, BMI did not impact OPR in FET cycles. Large prospective randomized trials are needed to determine the optimal method of in vitro fertilization in obese patients.

References: 1. Insogna, Iris G., et al. "Neutral effect of body mass index on implantation rate after frozen-thawed blastocyst transfer."Â *Fertility and sterilityÂ* 5 (2017): 770-776.

Table 1. FET pregnancy outcomes and patient characteristics by BMI group

Outcome	Underweight (n = 31)	Normal weight (n = 1095)	Overweight (n = 617)	Obese (n = 567)	p value
Patient Age (y, mean ± SD)	33.0 ± 3.3	34.5 ± 3.7	34.5 ± 3.8	34.6 ± 4.0	0.14
Number of Embryos Transferred (n, mean ± SD)	1.19 ± 0.4	1.25 ± 0.5	1.31 ± 0.5	1.32 ± 0.5	0.02
PR (%, n)	74.2 (23/31)	78.4 (859/1095)	77.8 (480/617)	81.0 (459/567)	0.49
IR (%, n)	52.8 (19/36)	61.6 (837/1359)	62.8 (514/819)	62.8 (474/755)	0.62
CPR (%, n)	61.3 (19/31)	67.7 (741/1095)	68.6 (423/617)	71.1 (403/567)	0.42
OPR (%, n)	48.4 (15/31)	59.1 (647/1095)	58.7 (362/617)	58.2 (330/567)	0.68
CLR (%, n)	21.1 (4/19)	12.6 (94/746)	14.3 (61/428)	17.7 (71/401)	0.10

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P-929 3:30 PM Wednesday, October 21, 2020

TIPPING THE SCALE: BODY MASS INDEX AS A PREDICTOR OF EMBRYONIC MITOCHONDRIAL DNA CONTENT.

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OBJECTIVE: This study sought to determine whether or not there is a correlation between Body Mass Index (BMI) and the quantification of mitochondrial DNA (mtDNA) in euploid embryos.

DESIGN: Retrospective chart review at a private, multi-site fertility clinic.

MATERIALS AND METHODS: All euploid embryos from patients who underwent in-vitro fertilization (IVF) with PGT-A from January to February 2020 utilizing a PGT lab that reports mtDNA (MitoScore; Igenomix) were included. Baseline characteristics were measured and IVF cycle statistics recorded. Patients were then divided into groups based on BMI: <18.5, 18.5-24.9, 25-29.9, 30-39.9, >40. T-tests, linear regression and chi-square analysis were used to analyze the data using SPSS (SPSS Inc., Chicago, IL, USA).

RESULTS: A total of 657 embryos were analyzed. The BMI of patients ranged from 17.2 to 47.6, with the average BMI being 34.9. Linear regression analysis showed there was no statistically significant correlation between BMI and mtDNA quantity, with an r-squared value of 0.00. When divided into groups based on BMI, there was no statistically significant difference in the average mtDNA quantity, where average scores were 21.3, 22.7, 23.3, 23.4, and 22.9, respectively ($p>0.05$). Pregnancy rates between all the groups were similar.

CONCLUSIONS: For women undergoing IVF, there are a limited number of ways to appropriately assess oocyte/embryo quality for optimal success. Yet, the quantification of mtDNA may offer a promising new parameter in assisted reproductive technologies (ART). Increased mtDNA have been linked to decreased pregnancy rates and is thought to be indicative of poor embryo quality due to oxidative stress; while lower mtDNA scores have been associated with improved outcomes. Yet, in order to better understand the mtDNA score, investigation into the underlying biological causes associated with elevated levels is warranted. It is well established that excess weight in women attempting pregnancy has a strong correlation to subfertility. Evidence suggests that increased weight directly impairs oocyte quality, fertilization, and embryo development. This is thought to be a result of oxidative stress due to increased lipid peroxidation and circulating reactive oxygen species (ROS), leading to mitochondrial damage and poor oocyte quality, among other things. Our results indicate that while patients with increased weight may experience reduced oocyte quality due to higher levels of oxidative stress, this does not seem to implicate reduced embryonic development, competence, or metabolic health. Further investigation into the clinical utility of Mitoscore is warranted.

SUPPORT: None

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AUTHOR AND SPOUSE/PARTNER DISCLOSURES INDEX: ORAL AND POSTER SESSIONS

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Liu, J. H.	AbbVie[8] *(Clinical Trial paid to institution)*; Allergan[6,8] *(Clinical Trial paid to institution)*; AMAG[6]; Bayer[8] *(Chair of Data Adjudication Committee)*; Dare'[6]; Femasys[8] *(Clinical trial paid to institution)*; Ferring[6]; Mitsubshi-Tanabe[6]; Therapeutics MD[6]
Liu, X.	UCSF CRS[3]
Lo, J. C.	Gilead[4]; IRhythm[4]; Novartis[4]
Loeb, A.	Coloplast[6]
Longobardi, S.	Merck KGaA[3]
López-Yañez, L.	ProcreaTec[3]
Loumaye, E.	OBSEVA SA[1,2,3]
Lukes, A. S.	Abbvie[4,7,8] *(Principal Investigator)*; Bayer[4,8] *(Principal Investigator)*; Merck[4,8] *(Principal Investigator)*; Myovant[4,6,8] *(Principal Investigator)*; Obseva[4,8] *(Principal Investigator)*; Scynexis[4,8] *(Principal Investigator)*
Luyten, J.	Merck[6]
Lyell, D. J.	Bloomlife[6]; Zen Flow[2]
Lynen, R.	Bayer Healthcare[2,3]
Lysenko-Brockman, A.	VCRM[3]
MA, J.	Ipsen[3]
Ma, L.	Foundation for Embryonic Competence[3]
Maalouf, W.	Vitrolife[6]
MacDonald, A.	Quick Step Analytics[2]
Maheshwari, A.	Cooks[5]; Ferring[5]
Mahony, M. C.	EMD Serono, Inc.[8] *(Retired Employee)*
Maisenbacher, M. K.	Natera[2,3]
Malik, M.	SCIEX[3]
Marsh, E. E.	Myovant Sciences[6]
Maslow, B. L.	Ferring Pharmaceuticals[5]; Ferring Pharmaceutical[5]
Masterson, T. A.	Aytu Biosciences[8] *(Add Board)*; Salveo Health[6]

Mathur, V.	Equillium[6]; Myovant[6]; Rigel[6]; Trevi[6,8] *(DSMB)*; Tricida[6,8] *(stock options)*
McArthur, S. J.	Merck[5]
McCaffrey, P.	VastBiome[1]
McCulloh, D. H.	Biogenetics Corporation[1,3,8] *(Part Time Employee)*; Buffalo Infertility and IVF Associates[6]; GranataBio[6,8] *(Advisory Board Member)*; ReproART: Georgian American Center for Reproductive Medicine[1,3,6]; Society for Assisted Reproductive Technology[1,8] *(Chair of Registry Committe/ Recipient of Travel Funds)*; Sperm and Embryo Bank of New York[1,3,8] *(Part Time Employee)*; American Association of BioAnalysts[5]; Ferring Pharmaceutical Company[5]; Southwest Embryology Summit[5]
McKain, L.	Myovant Sciences[2,3]
Medrano, M.	IVIRMA[3]
Merrion, K.	Natera, Inc.[2,3]
Meseguer, M.	Merck[8] *(Speaker Fee Honoraria)*; Vitrolife[8] *(Speaker Fee Honoraria)*
Meyers, J.	Takara Bio USA[3]
Milano, S. P.	FERRING[6]
Miller, K. A.	Igenomix[8] *(Scientific Board)*; MedTech For Solutions[1]
Mir Pardo, P.	Igenomix[3]
Missmer, S. A.	AbbVie[4,6,8] *(Advisory Board member)*; Roche[5]
Mitchell, A. D.	Invitae[2,3]
Mitsuhata, S.	Kurashiki Medical Center[3]
Miyagi, E.	AstraZeneca K.K.[5]; CHUGAI PHARMACEUTICAL CO., LTD.[5]; MSD K. K.[5]
Mol, B.	Guerbet[4,5,6]; Merck[4,6]
Mollan, S. G.	Evofem[6]
Monleón, J.	Hologic[7]
Mor, A.	ACIS LLC[1]
Moradian, M. M.	Sequence46[6]
Moravek, M. B.	Arthrex[6]; Probility Physical Therapy[6]; Team Rehab Physical Therapy[6]
Morbeck, D. E.	ART Compass[8] *(Scientific Advisory Board)*; Fertility Associates[2,3]; The World Egg Bank[8] *(Scientific Advisory Board)*
Moreno, I.	Igenomix R&D[8] *(Part-time employee)*
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Mottla, G. L.	EMD Serono[6]
Munné, S.	Cooper Surgical[6]; OVERTURE LIFE[1,2]; Previvo[8] *(Scientific BOA)*
Murphy, J.	Boston Consulting Group[6]
Murphy, J. D.	Boston Consulting Group[6]
Nadal, A.	Previvo, Inc[3]
Nagai, Y.	Varinos Inc.[1]
Nagy, Z. P.	Inception/Prelude[2]
Nahas, S.	Medtronic[6]
Najmabadi, S.	Previvo genetics[2,6,8] *(Principal investigator)*
Nakajima, S. T.	Previvo Genetics, Inc.[6,8] *(Scientific Advisory Board)*
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Navarrete, F.	Ohana Biosciences[3]
Navarro-Sánchez, L.	Igenomix[3]
Nefalar, J.	Sequence46[3]
Neff, L. M.	Amryt[4]; Novo Nordisk[8] *(Research Investigator)*
Neitzel, D.	Invitae[2,3]
Nelson, L. M.	Predictive Laboratories[1,2]
Nelson, S. M.	Access Fertility[6]; Delivery I[2]; Ferring[4,6,7]; Merck[6,7]; Roche Diagnostics[6,7]
Nguyen, T. V.	Presagen[3]
Nikitos, E.	Institute of Life[3]
Nusblat, D.	CooperSurgical[2,3]
Nussbaum, R. L.	Genome Medical[6]; Invitae[1,2]; Maze Therapeutics[2,6]; Pfizer[6]
O'Brien, J. E.	Ohana[5]
Olariu, A. I.	Medicines360[3]
Omurtag, K.	Medical Electronic Systems[6]
Pal, L.	FLOHEALTH[6]; GLG[6]
Panadero, J.	Igenomix[3]
Panitsa, G.	Business Insight Corporation ltd[3]
Park, J. K.	Ferring Pharmaceuticals[7]
Pasquale, P.	Fertilesafe[8] *(Co-Founder and medical advisory)*
Pastore, L. M.	Gilead[2]
Pastuszak, A. W.	Allotrope Medical[2,8] *(Advisor)*; Bayer AG[7]; Endo Pharmaceuticals[4,6,7]; Inherent Biosciences[2,8] *(Advisor)*; Vault Health[1,2]; Woven Health[1,2]
Patassini, C.	Igenomix Italia srl[3]
Patel, P.	Boston Scientific[6]; Nestle Health[6]; Paladin Pharmaceuticals[5]
Patel, S. S.	Galen[6]; Hologic[6,7]
Patrick, J. L.	Revolution Genetics[1]
Patrizio, P.	FertileSafe[8] *(co-founder and consultant)*
Paulson, R. J.	Ferring Pharmaceuticals[6]
Peigné, M.	Gedeon Richter[7,8] *(congress financial support)*; Merck[7,8] *(congress financial support)*
Peipert, J. F.	Bayer Healthcare[4,6,8] *(Advisory Board member & research support)*; CooperSurgical[4,6,8] *(Advisory Board member & research support)*; Merck[4,8] *(Research support)*
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Pellicer, A.	Dibimed[2]; IVIRMA Global[2]
Penrose, L. L.	Reproductive Solutions Inc.[1,2,4]
Pépin, D.	Bluebird bio[3]
Perrot, V.	Ipsen[3]
Perugini, D.	Life Whisperer[1,2,3]; Presagen[1,2,3]
Perugini, M.	Life Whisperer[1,2,3]; Presagen[1,2,3]
Petersen, S. H.	NTNU[8] *(Student)*
Peterson, C.	Clinical Innovations, Inc[8] *(Royalties)*; TheraTarget, Inc[1,2,4]
Peura, T.	Genea[2,3]
Pisarska, M. D.	Ferring[4,5]; Natera[5]
Pohl, O.	ObsEva[3]
Poindexter, A.	Abbvie[4]; Bayer[4]; Ferring[4]; Myovant[4]; Pfizer[4]; Sebella[4]
Polat, M.	Mikrogen Genetic Diagnosis Center[3]
Poli, M.	Igenomix[6]
Polotsky, A. J.	Prima-Temp[8] *(Prima-Temp consultant)*
Pomeroy, K. O.	Fuji Film Irvine Scientific[7]; The World Egg Bank[3]

Potter, D. A.	Jinxin Fertility[2]
Prien, S. D.	Reproductive Solutions Inc[1,2,4]
Prokopakis, T.	Institute of Life[2]
Prusinski Fernung, L.	DePuy Synthes[8] *(Contractor)*
Psarris, A.	Pharmaten[3]
Psathas, P.	Institute of Life[2]
Puscheck, E. E.	AbbVie[4]; Femasys[8] *(Clinical Events Committee member)*; Ferring Pharmaceuticals[4]; ObsEva[4]
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Quake, S. R.	Mirvie[2,6,8] *(Board member)*
Quinn, G. P.	FLO Health[5]
Quraishi, S.	Abbott Nutrition[5,6]; Alcresta Pharmaceuticals[5,6]
Raghupathy, R. M.	Oasis Fertility[3]
Rahman, F.	origyn fertility & ivf center[3]
Raine-Bennett, T. R.	Bayer AG[4]
Ramasamy, R.	Acerus Pharmaceuticals[6]; Aytu Biosciences[4,6]; Boston Scientific[4,6]; Coloplast[4,6]; Direx[4]; Endo Pharmaceuticals[4,6]; Nestle Health[6]; Acerus Pharma[4,6]
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Reinheimer, T. M.	Ferring Pharmaceuticals A/S[3]
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Rienzi, L. F.	Genera Health Care[5]
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Rios, J. S.	Abbvie[7]
Ritchey, M. E.	Bayer[8] *(Employee of RTI Health Solutions, a non-profit consulting company which conducts research under contract with pharmaceutical companies.)*
Robbins, W. A.	California Walnut Commission[4]
Roberts, D. J.	Cambridge University Press[8] *(Author)*; UpToDate[8] *(author)*
Rodríguez, S. A.	Sequence46[3]
Rodriguez, U. V.	NIUVIDA[1,2]
Roman, H.	ETHICON[5]; Gedeon Richter[5]; Nordic Pharma[5]; Olympus[5]; PlasmaSurgical Ltd[5]
Rossi, B.	Perinatal Resources (Obgyn Board Review Course)[5]
Rubio, C.	Igenomix[3]
Saadat, P.	reproductive fertility center[8] *(clinic which I own and work in)*
Sakkas, D.	EMD Serono[7]; Legacy[8] *(Advisor)*; Ohana[8] *(Advisory Board)*
Sakuraba, Y.	Varinos Inc.[1,2]
Saltus, C. W.	Bayer[8] *(I am an employee of RTI Health Solutions, which received funding from Bayer to conduct this work.)*
Santi, C. M.	NIH[4]
Santoro, N.	Ansh Labs[6]; Astellas/Ogeda[8] *(Scientific Advisory Board)*; Menogenix, Inc[8] *(Scientific Advisory Board, stock options)*
Santos-Ribeiro, S.	Besins[7]; Ferring[5,7]; MSD[4,5,7]; Roche[4]
Sarris, I.	CooperSurgical[5]; Ferring[5]; Merck[5]
Saunders, H.	Gedeon Richter/PregLem SA[3]
Schadt, E.	Sema4[1,2,3]
Schickedanz, A.	Wi Inc. Medical Device Development[3]
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Seifer, D. B.	Rutger's Medical School[8] *(Receive royalties from licensing agreement between Rutger's Medical School and MGH with Beckman-Coulter for the use of AMH to determine ovarian reserve.)*
Seli, E.	ACIS, LLC[2]; Foundation for Embryonic Competence[4,6]
Seth-Smith, M. L.	Overture Life[3]
Seyb, K.	Biogen[3]; Ohana Biosciences[3]
Sfontouris, I. A.	Business Insight Corporation[8] *(Unpaid Scientific Consultant)*; ESHRE[8] *(Coordinator SIG Embryology)*; Eugonia IVF Unit[6]; University of Nottingham[8] *(Honorary Assistant Professor)*
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Sharma, P.	Lilia[6,8] *(Chair of medical advisory board)*
Sharma, R.	Origyn fertility and ivf[3]
Shi, J. M.	Bayer AG[8] *(I am an employee of Kaiser Permanente Southern California, who received funding from Bayer AG for the conduct of this study.)*
Shin, D.	Antares Pharm[7]
Shin, L.	Sequence46[3]
Shin, P.	Promescent[2]
Shipley, S. K.	Shady Grove Fertility Center[3]
Shirazi, T.	Modern Fertility[6]
Sierra, J.	BMS[2]; GSK[3]
Sifuentes, C. J.	Takara Bio USA[3]
Silverberg, K.	Abbvie[5,7]; Baxter Healthcare[5,6]; eMD Serono[6]; Ovation Fertility[2,8] *(Director)*; Quest Diagnostics[5]; Seikagaku[6]
Simon, C.	Igenomix SL[8] *(Head of Scientific Advisory Board)*; MSD[5,8] *(Invited Speaker)*; Ferring[6]; Igenomix[8] *(Head of the Scientific Advisory Board,Head of Scientific Advisory Board)*; Merck[6,8] *(Invited Speaker)*; TEVA[6]; American Society for Reproductive Medicine[8] *(Editorial Editor Fertility and Sterility)*; Instituto de Salud Carlos III; Spanish Government[6]; Theramex[5,8] *(Invited Speaker)*
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Skora, D.	Fertility Pharmacy of America[2]

Skytte, A.	cryos international[3]
Slayden, O. D.	Bayer AG[4]
Smith, C. M.	AbbVie[3]
SMITH, J. F.	Fellow Health inc.[8] *(stock options)*
Smith, Y. R.	UpToDate[8] *(Receive royalty as peer reviewer)*
Snabes, M. C.	AbbVie[3]
Soares, S. R.	Ferring Farmaceuticals[7]; Gedeon Richter[7]
Solignac, C.	Gedeon Richter[3]
Sonksen, J.	Multicept A/S[2]
Spencer, J. B.	JScreen[8] *(Advisor)*
Spinosa, D.	Invitae[2,3]
Sriprasert, I.	TherapeuticsMD[8] *(unrestricted research grant)*
Stachecki, J.	Innovative Cryo Enterprises[8] *(owner)*
Stein, D. E.	RMA of New York[2]
Steiner, A. Z.	Prima-Temp[6]; Seikagaku Corporation[6]
Stewart, E. A.	Bayer[6]; Myovant[8] *(Steering Committe Member with renumeration)*; Peer View[5]; UpTo Date[5]
Sung, H.	Yonsei University[8] *(Professor)*
Sunkara, S.	Ferring[5]; Merck KGaA[5]
Takhar, H. S.	Kaiser Permanente - Southern California[8] *(I am an employee of Kaiser Permanente Southern California, who received funding from Bayer AG for the conduct of this study.)*
Tal, R.	Celmatix[4]
Tanaka, S. E.	Varinos Inc.[3]
Tanrikut, C.	New England Cryogenic Center[8] *(Medical Director)*; Swimmers[8] *(Advisory Board)*
Tao, X.	Foundation for Embryonic Competence[3]
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Terrill, P.	Cytel Inc[3]
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Theodoratos, S.	Astrazeneca[1]; Business Insight Corporation ltd[1]
Thomas, M. A.	Medicines 360[4]
Tian, M.	Pacific centre for Reproductive Medicine[3]
Ting, A.	21st Century Medicine, Inc.[3]; Oregon National Primate Research Center[8] *(Adjunct position)*
Tipping, A. D.	Pfizer[8] *(Received salary support from a study funded by Pfizer)*
Tober, D.	University of California, San Francisco[4]
Todd, N. J.	Bayer Inc[5]
Tolani, A. T.	Gauss Surgical, Inc.[1,2,3]
Tormasi, S.	Sequence46[3]
Torres, R.	Myriad Genetics[3]
Tournaye, H.	Merck[6]; Preglem[6,7]; Theramex[6]
Trawick, E. C.	Xylyx Bio[2]
Trussell, J. C.	Theralogix[2]
Tsai, H.	Bonraybio Co., Ltd.[3]
Tulandi, T.	Ad-hoc consultant for AbbVie[6]
Ubaldi, F. M.	Genera Health Care[5]
Unsal, E.	Mikrogen Genetic Diagnosis Center[3]
Vala, A.	VastBiome[1]
Valbuena, D.	Igenomix[3]
Varela, E.	IVIRMA Madrid[3]
Vasilopoulos, Y.	Institute of Life[2]
Vaughan, D. A.	Granata Bio[6]
Venetis, C.	Beisins[5]; Ferring[8] *(Travel Grant)*; Merck[4,5]; Merck, Sharpe & Dohme[5]
Venier, W.	TMRW[2]
Vergara, C. A.	Niuvida[1,2]
VerMilyea, M. D.	irvine scientific[6]
Villarroel, C.	myovant[6]
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von Stockum, S.	Bayer AG[8] *(independent contractor)*; Myovant[8] *(independent contractor)*
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Walker, J.	Business Insight Corporation Ltd[8] *(Unpaid commercial consultant)*
Walters-Sen, L.	Invitae[2,3]
Wang, F.	Bonraybio Co., Ltd.[3]
Ward, K.	Juneau Biosciences[1,2,3]
Warsi, Q.	Myovant Sciences, Inc[3]
Wassman, E. R.	Predictive Laboratories[2,3]
Weghofer, A.	Abbott[5]
Welch, C.	Sequence46[1]
Wells, D.	Juno Genetics[3]
Welt, C. K.	Medtronic[6]
Wemmer, N.	Natera[2,3]
Will, M.	Fertility Pharmacy of America[2]
Williams, Z.	Abbvie[6,7]
Wirka, K. A.	EMD Serono[3]
Wise, L. A.	AbbVie[6]
Won, J.	RMA of NY[8] *(Intern)*
Wright, J. D.	Clovis Oncollogy[5]; Merck[4]
Xiang, W.	Takarabio USA[3]
Xie, F.	Bayer AG[8] *(I'm an employee of Kaiser Permanente Southern California)*
Yang, Z.	Quanovate Tech Inc.[1,2,3]
Yarnall, S.	EngagedMD[3]
Yeh, J.	TruthMD[2]
Yin, X.	EMD Serono[3]
Yong, P.	Ipsen[8] *(Clinical trial)*
Yong, P. J.	Ipsen[8] *(Clinical trial)*
Young, S. L.	Abbvie Phramaceuticals[6]; Ferring Pharmaceuticals[4,6]
Yu, O.	Bayer AG[4]
Yumura, Y.	Astellas Pharma Inc.[7]; Merk Japan CO., LTD[5]; TOKIBO CO.,LTD[5]
Zandvliet, A. S.	Certara[6]
Zdunich, D.	Predictive Laboratories[3]
Zhan, Y.	Foundation for Embryonic Competence[3]
Zhang, J. J.	Darwin Life and New Hope Fertility[1]
Zhang, L.	Center for Human Reproduction[3]
Zhang, Y.	In Vitrotech Labs, Inc[3]
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VIDEO ABSTRACT SESSION 1

V-01 10:00 AM Saturday, October 17, 2020

NON-INVASIVE SELECTION OF SINGLE SPERM WITH HIGH DNA INTEGRITY FOR ICSI. Zhuoran Zhang, PhD,[1] Changsheng Dai, MASc,[1] Guanqiao Shan, MASc,[1] Khaled Abdalla, MASc,[2] Iryna Kuznyetsova, PhD,[2] Clifford Lawrence Librach, MD,[2] Keith Jarvi, MD,[3] Yu Sun, PhD[1] [1]University of Toronto, Toronto, ON, Canada; [2]CReATe Fertility Centre, Toronto, ON, Canada; [3]University of Toronto, School of Medicine, Toronto, ON, Canada.

OBJECTIVE: To develop a quantitative and non-invasive technique for selecting single sperm with high DNA integrity for ICSI.

METHODOLOGY: In ICSI, embryologists qualitatively select sperm by subjectively observing sperm motility and morphology. The DNA quality of the selected individual sperm is not known. We first tested the DNA quality of the sperm selected by embryologists following the WHO qualitative criteria. Three embryologists selected sperm from the same sample and the DNA integrity of the selected sperm was measured with comet assay on individual sperm. Indeed, the selected sperm had low DNA fragmentation ($p<0.01$ compared to sample population). However, manual selection is highly subjective, and the results varied significantly among embryologists ($p<0.01$). In order to eliminate subjectivity, we have developed a software that automatically selects sperm using quantitative criteria.

To establish the quantitative selection criteria, we first developed computer vision algorithms to measure each individual sperm's 9 motility (velocity, linearity etc.) and 9 morphology (head size etc.) parameters. The measurement is on live sperm without invasive staining. Then the same sperm was transferred for DNA measurement using the comet assay. We have collected a dataset of 440 individual sperm. For each sperm, its motility, morphology and DNA fragmentation data were recorded. With the collected data, we then established our quantitative criteria. Our criteria were based on the WHO quantitative criteria, but we modified the morphology criteria using our data on live sperm without staining. For motility, considering that WHO criterion ($VSL \geq 25$ μm/s) was defined for semen analysis instead of for ICSI where PVP was used to slow down sperm motion, we scaled the motility criterion by measuring sperm velocity change from semen to PVP. We transferred 30 individual sperm from raw semen to ICSI medium supplemented with PVP, and the velocity of individual sperm decreased to almost the same ratio (~0.5). The new motility criterion was determined ($VSL \geq 13.5$ μm/s). The quantitative criteria were first tested on our collected dataset and reduced the DNA fragmentation by 50%.

The quantitative criteria were built into our automated sperm selection software, and compared to manual qualitative sperm selection. From each new sample, both the software and three embryologists selected good sperm. The software outperformed all three embryologists. Compared to the best embryologist, the software further reduced the DNA fragmentation by 30%. The software also showed smaller standard deviation and provided more consistent selection results. Evaluation of ICSI outcomes using sperm selected by the software is underway.

CONCLUSIONS: The developed automation technique is able to non-invasively and quantitatively select single sperm with high DNA integrity without disturbing ICSI flow. Computer vision and quantitative selection improve the DNA quality of the selected sperm, and eliminate the subjectivity in manual qualitative selection.

V-02 10:08 AM Saturday, October 17, 2020

NEW ERA OF MALE INFERTILITY MICROSURGERY: 4K3D ORBEYE VIDEO OPERATING MICROSCOPY. Huixing Chen, M.D. Ph.D., Russell P. Hayden, M.D., Omar Al Hussein Alawamlh, M.D., Peter N. Schlegel, M.D., Marc Goldstein, M.D., Philip S. Li, M.D. Center for Male Reproductive Medicine and Microsurgery, Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY.

OBJECTIVE: Early adaptations of the 2-Dimensional (2D) video operating microscope (VOM) have shown to have better ergonomics, flexibility, and versatility compared to the standard operating microscope (SOM) in male infertility microsurgery (MIM). However, the low resolution, 2D view, and depth of field were significant limitations. Therefore, the emergence of the 4K3D ORBEYE VOM has the potential to revolutionize MIM. In this video, we aimed to demonstrate a comparison of various visual parameters between the ORBEYE VOM and the SOM. We also conducted an animal study to evaluate the surgical experience and efficacy of the VOM.

METHODOLOGY: The depth of field, working distance, and operative field were compared between the 4K3D OBYEYE VOM (Olympus/Sony) and the SOM. Four vasovasostomies (VVs) and four vasoepididymostomies (VEs) were performed on Wistar male adult rats using the 4K3D ORBEYE VOM. Data on operating time to anastomotic completion and patency rates were collected.

CONCLUSIONS: The 4K3D ORBEYE VOM provides high-end on-screen visualization, coupled with enhanced ergonomics and overall surgical experience. The ORBEYE VOM has a depth of field three times greater than seen with the SOM at magnifications of x15 and lower, due to its higher image and video quality with quick zoom-in, auto-focus, and zero on-screen latency capabilities. A larger operative field and a more comprehensive working distance (200-550mm vs. 250mm) were also seen on the VOM. The ORBEYE VOM proved to be non-inferior to the SOM in fine anastomoses, characteristic of MIM. The average operating time to complete an anastomosis for VVs and VEs was 37 and 33 minutes, respectively, with superior patency rates for all procedures. This VOM possesses the potential to improve surgical safety and efficiency by reducing postural fatigue and eye strain, which surgeons experience with the SOM. In addition, it can significantly facilitate teamwork and teaching through its high-resolution screens and zero-latency images.

V-03 10:16 AM Saturday, October 17, 2020

FERTILITY-PRESERVING, SURGICAL MANAGEMENT OF A CESAREAN SCAR ECTOPIC PREGNANCY. Christine Hur, MD, Miguel Luna Russo, MD, Cara R. King, DO, MS. Cleveland Clinic, Cleveland, OH.

OBJECTIVE: The objective of this video is to highlight a fertility-preserving surgical technique for the management of cesarean scar ectopic pregnancy.

METHODOLOGY: A video description of the surgical technique used to manage the cesarean scar ectopic pregnancy of a 28-year-old G6P4014 with desires future fertility preservation.

CONCLUSIONS: This video highlights a surgical technique which allows for the laparoscopic removal of a cesarean scar ectopic pregnancy with the concurrent repair of the uterine defect. It reviews strategies to restore normal anatomy, minimize blood loss and allow for healing in order to allow for future fertility.

V-04 10:24 AM Saturday, October 17, 2020

RESOLUTION OF ABDOMINAL PAIN AFTER COIL EMBOLIZATION OF VARICOCELE WITH ROBOTIC RESECTION OF GONADAL VEIN. Johnathan Doolittle, MD, Viraj Maniar, MD, Peter N. Dietrich, MD, Jay I. Sandlow, MD, Scott Johnson, MD, Jagan K. Kansal, MD, MBA. Medical College of Wisconsin, Milwaukee, WI.

OBJECTIVE: Chronic pain in the region of varicocele embolization is not well described and can be a challenging symptom for a urologist to manage. Metallic coils from embolization are unable to be removed, leaving limited options for treatment after failing conservative measures. It is important to counsel patients of this potential complication when determining the best option for varicocele repair. To our knowledge, there are no reported cases of gonadal vein excision for chronic abdominal pain after coil embolization.

METHODOLOGY: A 63-year-old male presented nine months after coil embolization. His testicular pain resolved but he reported new left sided abdominal pain following coil embolization for a large left varicocele. After failing conservative measures including non-steroidal anti-inflammatory drugs, antibiotics and prednisone, he was referred to urology for further workup and to discuss treatment options. On presentation, the patient reported pain on the left side of his abdomen consistent with the location to gonadal vein. After extensive counseling that surgical removal may not alleviate his pain, robotic gonadal vein excision was offered, and the patient elected to proceed. The video illustrates the robotic excision of the left gonadal vein. Coils were easily visualized through the wall of the vessel. While mild edema of the surrounding tissue in the retroperitoneum was noted, extensive

inflammation was not present, leading to an uncomplicated dissection. The coil-containing gonadal vein was able to be excised in its entirety. The patient was discharged on post-operative day one with only non-steroidal pain medications. Six weeks post operatively, the patient reported no complications, and almost complete resolution of his preoperative pain.

CONCLUSIONS: To our knowledge, this is the first case report demonstrating the surgical removal of the gonadal vein for treatment of chronic abdominal pain after varicocele embolization. After failing conservative measures, this may present another viable treatment option to address this difficult complication in a select group of patients.

SUPPORT: None

V-05 10:31 AM Saturday, October 17, 2020

A NOVEL ROBOTIC ENDOSCOPIC DEVICE USED FOR OPERATIVE HYSTEROSCOPY: ASHERMAN'S SYNDROME. Lara Harvey, MD MPH,[■] Richard Hendrick, PhD,[2] Neal P. Dillon, PhD,[■] Evan Blum, BS,[3] Lauren Branscombe, MS,[3] Scott J. Webster, PhD,[3] Ted L. Anderson, MD PhD.[4] [1]Virtuoso Surgical, Nashville; [2]Virtuoso Surgical, Inc., Nashville, TN; [3]Virtuoso Surgical, Nashville, TN; [4]■ ■ ■.

OBJECTIVE: To trial the use of a novel robotic endoscope prototype for the application of Asherman's syndrome in a uterine tissue model.

METHODOLOGY: The robotic endoscope prototype consists of two arms made of concentric tubes that fit through a standard 23Fr endoscopic sheath. This allows a surgeon to have two-handed capabilities with a variety of endoscopic instruments as well as improved ergonomics. Previous pilot studies have examined the use of this device for hysteroscopic polypectomy and removal of retained intrauterine device.

CONCLUSIONS: The endoscopic robot was successful in lysing simulated intrauterine adhesions in a porcine tissue model in a fluid environment. The device allows two handed surgical technique for hysteroscopic applications. Further study on the utility of this device for gynecologic applications is needed.

SUPPORT: This study was funded by Virtuoso Surgical

V-06 10:38 AM Saturday, October 17, 2020

PELVIC ENDOMETRIOSIS CAUSING HYDRONEPHROSIS. Karine Matevossian, DO,[1] Rachel Yoon, MD,[1] Kirsten Sasaki, M.D.,[2] Charles E. Miller, M.D.[3] [1]Advocate Lutheran General Hospital, Park Ridge, IL; [2]Advocate Lutheran General Hospital, Naperville, IL; [3]The Advanced Gynecologic Surgery Institute/The Advanced IVF Institute, Charles E. Miller, MD & Associates, Naperville, IL.

OBJECTIVE: Step by step narrated demonstration of ureterolysis.

METHODOLOGY: 51 year old female who presents with left sided pelvic pain and hydronephrosis/hydroureter. The patient was positioned in the dorsal lithotomy position in adjustable Allen stirrups. A three port laparoscopic approach was used. The patient underwent a laparoscopic excision of endometriosis with bilateral ureterolysis.

CONCLUSIONS: Laparoscopic excision of endometriosis can be technically challenging and time consuming. A conservative approach with ureterolysis generally resolves the patient's pain. The imaging of choice in diagnosing ureteral complications of endometriosis is MRI. Cystoscopy post surgery can help assess ureteral function but does not guarantee that thermal injury has not occurred.

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SUPPORT: none

V-07 10:44 AM Saturday, October 17, 2020

SURGICAL REPAIR OF A CESAREAN SCAR DEFECT USING A VAGINAL APPROACH. Abigail C. Mancuso, MD,[1] Erin Maetzold, MD,[1] Joseph T. Kowalski, MD,[1] Bradley J. Van Voorhis, MD.[2] [1]University of Iowa Hospitals and Clinics, Iowa City, IA; [2]University of Iowa, Iowa City, IA.

OBJECTIVE: To discuss the signs and symptoms of a cesarean scar defect and describe the techniques for the repair of a cesarean scar defect using a vaginal approach.

METHODOLOGY: We demonstrate a case of a 32-year-old patient with a symptomatic cesarean scar defect desiring surgical repair. Repair of the cesarean scar defect was successfully completed using a vaginal approach.

CONCLUSIONS: There are several surgical approaches used for the repair of cesarean scar defect including hysteroscopic and laparoscopic repair. We have found the vaginal approach to be an expeditious and excellent way to access these defects that often occur low at the level of the cervix. It is important to carefully dissect off the bladder to avoid bladder injury and perform cystoscopy at the conclusion of the case to ensure bladder injury did not occur. The vaginal approach avoids the need for abdominal incisions leading to quick postoperative healing and high patient satisfaction.

References: Erikson SS, Van Voorhis BJ. Intermenstrual bleeding secondary to cesarean scar diverticuli: Report of three cases. *Obstet Gynecol* 1999. 93(5):802-805.

VIDEO ABSTRACT SESSION 2

V-08 10:00 AM Sunday, October 18, 2020

SURGICAL MANAGEMENT OF UNDESCENDED LEFT OVARY AND RUDIMENTARY UTERINE HORN. Lauren Elizabeth Verrilli, MD,[1] Addison William Alley, MD,[2] Joseph M. Letourneau, MD.[1] [1]University of Utah, Salt Lake City, UT; [2]University of Arizona College of Medicine - Phoenix, Phoenix, AZ.

OBJECTIVE: To describe a rare Mullerian anomaly and review important embryologic origins of the female reproductive tract as well as surgical management of a maldescended ovary and rudimentary uterine horn.

METHODOLOGY: This is the case of a 26-year-old G0 with chronic pelvic pain and three years of conservative management who ultimately underwent a laparoscopic resection of a maldescended left ovary and uterine horn.

CONCLUSIONS: While conservative management remains the standard of care for managing cyclical pelvic pain secondary to Mullerian anomalies, surgery remains an option for patients refractory to this treatment. We present surgical planning and technique for performing a laparoscopic unilateral salpingoophorectomy and resection of rudimentary uterine horn and maldescended left ovary.

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SUPPORT: N/A

V-09 10:06 AM Sunday, October 18, 2020

A NEW PIEZO DRILL FOR HUMAN ICSI. Changsheng Dai, MASc,[1] Alexander Lagunov, MSc,[2] Zhuoran Zhang, PhD,[1] Guanqiao Shan, MASc,[1] Jason E. Swain, PhD, HCLD,[3] William B. Schoolcraft, MD,[4] Tom Hannam, MD,[5] Yu Sun, PhD.[1] [1]University of Toronto, Toronto, ON, Canada; [2]CCRM Toronto, Toronto, ON, Canada; [3]CCRM Fertility Network, Lone Tree, CO; [4]Colorado Center for Reproductive Medicine, Lone Tree, CO; [5]Hannam Fertility Centre, Toronto, ON, Canada.

OBJECTIVE: To develop a new piezo-ICSI device that is compatible with standard ICSI setup and capable of reducing oocyte deformation and preventing cytoplasm aspiration during ICSI.

METHODOLOGY: In standard ICSI, oocytes often suffer large deformation before penetration, which may damage the spindle and other cellular organelles. Furthermore, cytoplasm is aspirated into the micropipette to break the oolemma, which disrupts the local cytoskeleton of the oocyte. To facilitate oocyte penetration, piezo drills were developed by using piezoelectric actuators to generate micropipette vibration. However, existing piezo drills use a flat-tipped micropipette (vs. standard sharp ICSI micropipette); additionally, to reduce micropipette's lateral vibration, which is perpendicular to the oocyte penetration direction, damping fluid such as mercury is required in the operation of existing piezo drills, which raises biosafety concerns. The new piezo drill we developed uses a standard sharp-tipped ICSI micropipette and requires no damping fluid. It is readily mounted on a standard micropipette holder within 10 seconds and easily operated by pressing a footswitch. To reduce undesired lateral vibration, flexure beams were designed in the piezo drill to guide and constrain the motion of micropipette only along the oocyte penetration direction. The driving signals were optimized by removing resonant frequencies with a bandpass filter. Experiments were performed on hamster and human oocytes by penetration with and without the piezo drill. For hamster oocytes, evaluation metrics included oocyte deformation and survival rate of penetrated oocytes after 12 hours' incubation. For human oocytes, oocyte deformation and aspirated cytoplasm volume were quantitatively evaluated.

CONCLUSIONS: The developed new piezo drill decreased hamster oocyte deformation from over 50 μm to around 5 μm, and increased the survival rate of the hamster oocytes after penetration to 92.5% (vs. 77.5% without piezo drill and 95% for the control group). Tests on human oocytes revealed that the piezo drill reduced human oocyte deformation by 10 times and broke oolemma without aspirating any cytoplasm (vs. >2,000 μm^3 aspirated cytoplasm without piezo drill), with 100% success rate in oocyte penetration. The use of the new piezo drill in ICSI can potentially reduce oocyte damage by reducing oocyte deformation (thus stress) and minimizing disturbance to the cytoplasm in the oocyte. Clinical trials are ongoing to quantify its benefit in improving fertilization rate, blastocyst rate and embryo quality.

V-10 10:10 AM Sunday, October 18, 2020

CREATION OF A NOVEL INFLATABLE VAGINAL STENT FOR MCINDOE VAGINOPLASTY. Phillip A. Romanski, MD, Pietro Bortoletto, MD, Samantha Pfeifer, M.D. Weill Medical College of Cornell University, New York, NY.

OBJECTIVE: To develop a novel inflatable vaginal stent for use in McIndoe vaginoplasty that can be constructed using standard operating room (OR) supplies.

METHODOLOGY: A McIndoe vaginoplasty is a surgical procedure that is performed to create a neovagina in patients with complete or segmental vaginal agenesis. A cavity is dissected to form the neovagina, and a tissue graft is placed. A stent is then delicately inserted into the cavity to keep the graft in place and promote graft adherence to the dissected space.

Traditionally, a vaginal stent may be created in the OR by placing surgical sponges inside a condom. However, many ORs have restrictions on equipment that can be brought into the OR, as well as restrictions against leaving non-radio-opaque equipment "in" the patient. This device fills the need for a stent that is compliant with OR procedures and is radio-opaque, functional, and can be used for patients with and without a functional uterus. The device is modelled after an effective inflatable vaginal stent that was previously commercially available, but is no longer produced.

An inflatable vaginal stent has multiple advantages compared to a rigid dilator in that it 1) is deflatable so that it does not cause trauma to the delicate tissue graft during insertion, removal, or repositioning; 2) is firm enough to press the tissue graft against the dissected vaginal space, but is soft enough to decrease the risk of pressure necrosis or urethral damage; and 3) has a drainage port to prevent the build-up of fluid that could interfere with tissue healing.

We have developed an inflatable vaginal stent that incorporates all of these unique properties and can be easily constructed using sterile OR supplies. The construction of this device requires: a silicone Foley catheter, sterile foam sponges from a vaginal prep kit, a sterile radio-opaque sponge, a sterile vaginal ultrasound probe cover, a 60cc catheter tip syringe, a long Kelly, a ruler, scissors, 0-vicryl suture, and sterile gloves.

Once inserted, the stent can be left in place for 5-7 days post-operatively, during the critical time of graft adherence. It can then be deflated and gently removed to prevent disruption or trauma to the tissue graft. For those with segmental vaginal agenesis, the Foley may be advanced into the uterus and balloon inflated to further stabilize the utero-vaginal anastomosis.

CONCLUSIONS: Our novel inflatable vaginal stent is useful to surgeons performing a McIndoe vaginoplasty for vaginal agenesis with or without a uterus because it is compliant with OR procedures, as it is constructed from supplies that are accessible in most OR settings. Moreover, it is radio-opaque, adjustable in size, and effective in applying circumferential pressure for graft adherence. We prefer this inflatable vaginal stent to a rigid dilator in the first week of tissue healing to allow for easy insertion and removal of the stent without disrupting the tissue graft, to help prevent tissue necrosis, and to provide a fluid drainage port during graft adherence. We recommend this device as an ideal option for surgeons to consider when performing a McIndoe vaginoplasty.

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Chan JL, Levin PJ, Ford BP, Stanton DC, Pfeifer SM. Vaginoplasty with autologous buccal mucosa fenestrated graft in two patients with vaginal agenesis: a multidisciplinary approach and literature review. J Minim Invasive Gynecol 2017;24(4):670–6.

SUPPORT: None

V-11 10:17 AM Sunday, October 18, 2020

OHVIRA: FERTILITY SPARING SINGLE-STAGE SURGICAL MANAGEMENT. Abigail L. Bernard, MD,[1] Vaishnavi Purusothaman, MD, MA,[2] Linnea R. Goodman, MD.[1] [1]University of North Carolina, Raleigh, NC; [2]University of North Carolina, Chapel Hill, NC.

OBJECTIVE: Obstructed hemivagina and ipsilateral renal anomaly, or OHVIRA, is a rare, obstructive Mullerian duct anomaly comprised classically of the triad of an obstructed hemivagina, ipsilateral renal agenesis, and uterine didelphys. This video is a review of the background, diagnostic imaging, and surgical management of this condition, as well as video footage of the fertility sparing, single-stage technique performed at a university hospital.

METHODOLOGY: Single-stage vaginoplasty was started with a physical exam displaying a fluctuant vaginal mass arising from the right side wall of the vagina. Next, a syringe was used to aspirate the contents of this mass to confirm that this was in fact the hematocolpos as suspected. Once confirmed, electrocautery was used to incise the mass to create an opening large enough to drain the hematometra and then electrocautery was used to extend the incision caudally. Digital palpation was done to assess the extent of the longitudinal vaginal septum and the position of the right cervix. Next, septum transection with the LigaSure™ device was achieved. As resection continued, the cervix on the right was able to be visualized. The use of bipolar cautery allowed the surgeons to excise the vaginal septum with everted edges to minimize the risk of re-adhesion or fusion. The eversion was accomplished without requiring any additional sutures, which improved the ease of the procedure and decreased operative time.

CONCLUSIONS: The OHVIRA diagnosis requires a high index of suspicion by the clinician. Single-stage surgical vaginoplasty should be employed when technically feasible, but a two-stage procedure can be done when infection or anatomic challenges are present. Hemi-hysterectomy should be avoided when possible, as ipsilateral fertility can recover once the obstruction is removed.

References:

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V-12 10:24 AM Sunday, October 18, 2020

VAGINAL ULTRASOUND PROBE FOR ABDOMINAL OOCYTE RETRIEVAL: DEMONSTRATION OF A NOVEL APPROACH.

Jacquelyn Shaw, MD,[1] Frederick L. Licciardi, M.D.[2] [1]NYU Langone Prelude Fertility Center, New York, NY; [2]NYU Langone Health, New York, NY.

OBJECTIVE: The efficacy and safety of use of the transvaginal ultrasound probe for percutaneous abdominal oocyte retrieval in patients with limited vaginal access has been established in prior studies,[1-2] but the technique has not been demonstrated widely.

METHODOLOGY: This video uses a patient case to explain and demonstrate the technique of percutaneous transabdominal oocyte retrieval with the transvaginal ultrasound probe in a patient without vaginal access to her ovaries. Patient consent was obtained prior to creation of the video.

CONCLUSIONS: Abdominal oocyte aspiration using a high frequency transvaginal ultrasound probe should be considered in patients with ovaries inaccessible vaginally. It is safe, effective and an easily skill to acquire.

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SUPPORT: There was no financial support for creation of this video.

V-13 10:30 AM Sunday, October 18, 2020

SURGICAL MANAGEMENT OF ADENOMYOSIS: LAPAROSCOPIC ADENOMYOSIS RESECTION.

Kaia Schwartz, MD,[1] Elliott G. Richards, MD,[2] Tommaso Falcone, M.D.[3] [1]Clevleand Clinic Foundation, CLEVELAND, OH; [2]Cleveland Clinic, Cleveland, OH; [3]Cleveland Clinic, cleveland, OH.

OBJECTIVE: To demonstrate the steps required for surgical removal of diffuse adenomyosis. in a symptomatic woman desiring future fertility.

METHODOLOGY: De-identified video footage was obtained and edited to reflect key components of the procedure. Preoperative imaging is a critical in determining the surgical approach and for setting expectations for the surgical outcome. In this case preoperative imaging revealed diffuse adenomyosis of the posterior wall extending from endometrium to serosa. This case was performed by laparoscopic assisted technique. Five mm trocars were placed in the typical fashion. A suprapubic gel-point access platform was used to extract lesions and to aid in suturing areas that required extensive re-approximation.

At surgery no pseudo-capsule exists so tissue planes are arbitrary. Typically, a sub-serosal dissection is the upper border and continued laterally until somewhat normal myometrium is identified. This border is not well defined. The dissection is directed towards the endometrium which entry is unavoidable. Lesions are often excised is pieces as there is typically no cohesive tissue. Entry into the endometrial cavity identifies the lower border of excision. Closure without tension requires multiple layers.

CONCLUSIONS: Surgery for adenomyosis requires careful preoperative planning. Excision of diffuse adenomyosis often results in entry into the endometrial cavity. Closure of extensive defects is required.

References:

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V-14 10:37 AM Sunday, October 18, 2020

DO'S AND DON'TS FOR SURGICAL MANAGEMENT OF TYPE 2 UTERINE FIBROIDS IN THE ART PATIENT.

Salomeh M. Salari, MD MS,[1] Rhea Chattopadhyay, MD,[2] Rebecca Flyckt, MD.[2] [1]University Hospitals Cleveland Medical Center, Cleveland, OH; [2]University Hospitals Fertility Center/Case Western Reserve University, Beachwood, OH.

OBJECTIVE: Fibroids may impact fertility via multiple proposed mechanisms. Submucosal fibroids in particular may contribute to infertility, recurrent pregnancy loss, and lower implantation rates with embryo transfer. The surgical approach to managing submucosal myomas is guided by FIGO staging. Although hysteroscopic myomectomy may be an appealing option, incomplete resection is a risk with type 2 myomas. The objective of this video is to describe the effectiveness of laparoscopic myomectomy for complete surgical resection of type 2 fibroids in assisted reproductive technology (ART) patients.

METHODOLOGY: We present here a case-based review of an infertility patient seen for second opinion. This patient had undergone treatment with oral fertility medications combined with intrauterine insemination followed by multiple IVF treatments. During the course of her prior IVF cycles, she underwent hysteroscopic myomectomy x 2, with a hysteroscopic resection procedure for a single fibroid prior to each embryo transfer. She was diagnosed with recurrent implantation failure and subsequently underwent prenatal genetic testing for aneuploidy (PGTA), with an endometrial receptivity assay (ERA) as the planned next step. Our evaluation demonstrated residual type 2 myoma with $< 20\%$ endometrial cavity involvement and laparoscopic treatment of this myoma resulted in spontaneous pregnancy.

In this video, we discuss the FIGO classifications of fibroids which were developed based on location and cavity involvement. We review laparoscopic versus hysteroscopic surgical approaches. Though hysteroscopy is desirable due to lack of invasiveness, cost, shorter operating times and faster return to attempting to conceive, in the case of type 2 fibroids, a laparoscopic approach is often the most appropriate. There is no evidence to support shaving "the tip of the iceberg" hysteroscopically, as the intramural component will continue to encroach into the endometrial cavity until it is completely removed.

CONCLUSIONS: Submucosal fibroids can both distort and invade into the endometrial cavity, thus contributing to infertility and failed embryo transfer with assisted reproductive technologies (ART). When type 2 fibroids are incompletely removed, embryo transfer may not be successful. By fully removing type 2 fibroids laparoscopically, the endometrial cavity is optimized for successful pregnancy implantation either by spontaneous conception or ART.

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SUPPORT: none

V-15 10:44 AM Sunday, October 18, 2020

SURGICAL MANAGEMENT OF PROXIMAL TUBAL OCCLUSION: A VIDEO GUIDE FOR CORNUAL CANNULATION.

Kathryn D. Coyne, MD,[1] Channing Burks, MD,[2] Rebecca Flyckt, MD,[3] James H. Liu, M.D.[4] [1]University Hospitals Cleveland Medical Center, OH; [2]University Hospitals Fertility Center/Case Western Reserve University, Beachwood, OH; [3]UH Fertility Center, REI Division; [4]UH MacDonald Women's Hospital, Cleveland, OH.

OBJECTIVE: The aim of this instructional video is to help further educate Reproductive Endocrinology and Infertility (REI) physicians on how to assemble cornual cannulation equipment and as well as how to perform cornual re-cannulation surgery for tubal factor infertility patients with proximal tubal occlusion.

METHODOLOGY: The video includes a step by step instruction for the assembly of a hysteroscopic catheterization system for cornual cannulation. This is followed by a demonstration of how to perform a cornual tubal re-cannulation using this cannulation system and includes both hysteroscopic and laparoscopic views.

CONCLUSIONS: Due to the fact that fertility coverage is not mandated in the majority of states across the United States, we feel it is important to provide surgical alternatives to infertility patients affected by tubal factor when applicable, such as patients with proximal tubal occlusion. The goal of this video is to educate REI physicians on how to surgically manage proximal tubal occlusion with cornual cannulation.

VIDEO AUTHOR INDEX

VIDEO AUTHOR AND SPOUSE/PARTNER DISCLOSURES INDEX

All oral and poster presenters at the ASRM 2020 Virtual Scientific Congress & Expo were required to complete a disclosure form. Each abstract or video author is listed below along with any relationships their partners/spouses disclosed.

[1]Company Officer	[2]Direct Stockholder	[3]Full-Time Company Employee	[4]Grant Recipient	[5]Honoraria
[6]Paid Consultant	[7]Speaker's Bureau	[8]Other	[a]Partner/Spouse	[b]Both

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Licciardi, F. L.	Prelude[2]
Liu, J. H.	AbbVie[8] *(Clinical Trial paid to institution)*; Allergan[6,8] *(Clinical Trial paid to institution)*; AMAG[6]; Bayer[8] *(Chair of Data Adjudication Committee)*; Dare'[6]; Femasys[8] *(Clinical trial paid to institution)*; Ferring[6]; Mitsubshi-Tanabe[6]; Therapeutics MD[6]
Miller, C. E.	AbbVie[6,7,8] *(Research Study)*; Allergen[8] *(Research Study)*; Boston Scientific[6]; Espiner Medical[6,8] *(Research Study / Royalties)*; Gynesonics[2,6]; Halt Medical[2]; Hologic[6]; Karl Storz[4]; Medtronic[6]; Temple Therapeutics B.V.[2,6]
Pfeifer, S.	Roman Health[6]; Theralogix[6]
Sasaki, K.	Myovant Sciences[8] *(Advisory Board)*
Schlegel, P. N.	Abbvie[6]; Lilly[6]; Merck[6]; Theralogix[6]
Webster, S. J.	Virtuoso Surgical, Inc.[1,2]

O-265 9:40 AM Wednesday, October 21, 2020

ACTIVE TREATMENT OR NO TREATMENT (ACTOR-NOT) FOR PERSISTING PREGNANCY OF UNKNOWN LOCATION; A RANDOMIZED CLINICAL TRIAL. Kurt T. Barnhart, MD, MSCE,[1] Karl R. Hansen, MD PhD,[2] Mary D. Stephenson, M.D., M.Sc.,[3] Anne Z. Steiner, MD, MPH,[4] Emily S. Jungheim, MD, MSCI,[5] Kathleen Hoeger, M.D.,[6] Stephen A. Krawetz, PhD,[7] Suneeta Senapati, MD, MSCE,[8] Marcelle I. Cedars, MD,[9] Hao Huang, md, MPH,[10] Esther Eisenberg, MD MPH,[11] Nanette Santoro, MD,[12] Heping Zhang, PhD,[10] and ASRM Authors group [1]University of Pennsylvania, Perelman School Of Medicine, Philadelphia, PA; [2]University of Oklahoma College of Medicine, Oklahoma City, OK; [3]University of Illinois at Chicago, Chicago, IL; [4]Duke University, Durham, NC; [5]Northwestern Feinberg School of Medicine, Chicago, IL; [6]University of Rochester, Rochester, NY; [7]Wayne State University School of Medicine, Detroit, MI; [8]Department of Obstetrics and Gynecology, University of Pennsylvania, Philadelphia, PA; [9]University of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA; [10]Yale University School of Public Health, New Haven, CT; [11]NIH, Bethesda, MD; [12]University of Colorado School of Medicine, Aurora, CO.

OBJECTIVE: Women in early gestation without a pregnancy visualized on ultrasound (pregnancy of unknown location, (PUL)) and serial hCG values consistent with a nonviable gestation are at high risk for ectopic pregnancy. There is no consensus regarding optimal management of PUL among the possibilities of expectant management, uterine evacuation, or administration of methotrexate. The goal of this trial was to determine if active management options are superior to expectant management, and to determine if the two active management strategies are non-inferior.

DESIGN: Multi-center randomized clinical trial conducted by the Reproductive Medicine Network (RMN)

MATERIALS AND METHODS: Women with a persistent PUL were randomized 1:2 between expectant management and active management, and 1:1 between two active management strategies; a) uterine evacuation followed by methotrexate if needed or b) empiric methotrexate. The primary outcome of the trial was successful resolution of the gestation without change from initial treatment strategy. Secondary outcomes included: number and type of unscheduled interventions, time until resolution, adverse events, patient acceptability, and preference.

RESULTS: Of 255 randomized women 253 competed the trial. Women treated with active management had a significantly higher percentage of successful resolution (Rate Ratio [RR] 1.43 (95% CI: 1.04 – 1.96) intention to treat (ITT), RR 1.64 (1.39 – 1.94) per treatment (PT)) and 1.99 (1.35 to 2.92) Instrumental variable adjustment for potential bias due to cross over. There was a lower rate of unscheduled surgery RR 0.43 (0.25 – 0.74) ITT and RR 0.21 (0.11 – 0.55) PT). The two active treatment strategies were non-inferior (difference 6.6%, [-6.0% to 19.2%] ITT and 2.9%, [-4.4% to 10.2% PT]. Time to resolution was 8.1 days shorter with uterine evacuation compared to methotrexate in the per protocol population. All strategies were safe and were rated with high acceptability and satisfaction. One women was diagnosed with a viable gestation after randomization to expectant management. Women expressed a stronger preference for expectant management.

CONCLUSIONS: A greater percentage of women presenting with a persistent PUL achieved uneventful resolution with active management compared to expectant management. Active management resulted in at least a 50% reduction in unscheduled interventions. Active management strategies were similar with the exception that uterine evacuation resulted in a shorter time to resolution. Acceptability and safety of treatment were high for all strategies, but subjects expressed preference for expectant management.

SUPPORT: This work was supported by National Institutes of Health (NIH)/*Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) Grants U10 HD27049 (to C.C.), U10 HD38992 (to R.S.L.), U10HD055925 (to H.Z.), U10 HD39005 (to M.P.D.), U10HD077680 (to KRH); U10 HD077844 (to A.Z.S),Â MO1RR10732 a C06 RR016499 (to Pennsylvania State University),Â UL1 TR001863 (to Yale University) and HD 076279 (to KB)

O-266 9:55 AM Wednesday, October 21, 2020

SINGLE CELL TIPSEQ, A NEW METHOD TO MAP LINE-1 INSERTIONS, PROVIDES INFORMATION ABOUT SUB CHROMOSOMAL GENETIC VARIATION IN HUMAN EMBRYOS. Fabiana B. Kohlrausch, PhD,[1] Fang Wang, PhD,[2] Wilson McKerrow, PhD,[3] David Fenyo, Ph.D.,[3] Jef D. Boeke, PhD,[3] David L. Keefe, MD[4] [1]Fluminense Federal University, Niterói, Brazil; [2]NYU Langone Health, New York, NY; [3]New York University, New York, NY; [4]NYU Grossman School of Medicine, New York, NY.

OBJECTIVE: One third of euploid embryo transfers fail, implicating subchromosomal genetic variation. Retrotransposons play important roles during early development, when they are transiently de repressed during epigenetic re programming. Long interspersed element-1 (L-1), the only autonomous retrotransposon in humans, comprises 17% of the human genome. L-1's repetitive nature limits the utility of conventional assays-positional information is necessary to establish the novelty of L-1 insertions. Recently we developed Single Cell Transposon Insertion Profiling by Sequencing (scTIPseq) to characterize L-1 insertions in individual cells (McKerrow et al, Phil Trans R Soc Lond Bio, 2020). To map L-1 insertions during early human development, we applied scTIPseq to characterize L-1 insertions in human embryos.

DESIGN: Observational study.

MATERIALS AND METHODS: scTIPseq mapped L-1 insertions in 16 human blastocyst stage embryos (6 euploid, 5 trisomic, 5 monosomic) obtained from consenting couples undergoing IVF at NYU Fertility Center. scTIPseq data analysis used TIPseqHunter custom bioinformatics program. This study was reviewed and approved by the NYU IRB.

RESULTS: 18 new and unique insertions were observed in normal (7), trisomic (7), and monosomic (4) embryos. No insertions were located in exons or immediately upstream of genes. Most new and unique insertions were intergenic. Insertions were located in introns of *HS6ST3*, *USH2A, PLEKHG1*, *CD226*, *MET*, *TTLL5*, *MED28*, *SCFD2*, and *EYE*. Just three embryos did not exhibit new and unique insertions. The location or number of novel insertions did not differ by ploidy status.

CONCLUSIONS: Novel L-1 insertions can be detected in human embryos by scTIPseq. The insertions did not differ between euploid and aneuploid embryos, suggesting they are not merely a marker of aneuploidy. Rather, scTIPseq provides novel information about sub-chromosomal structural variation in human embryos. Several studies have measured L-1 expression at different stages of development in mice, but this study for the first time reports new and unique L-1 insertions in human embryos. The intronic L1 insertions do not specifically disrupt genes, as has been reported in some de novo monogenic diseases, but we cannot rule out the possibility that they may affect splicing and/or gene expression during early embryo development.

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SUPPORT: CNPq Brazil, Kaplan Fund, Dept Ob/Gyn NYU Langone.

O-267 10:10 AM Wednesday, October 21, 2020

HIGHER RISK OF PERSISTENT METABOLIC SYNDROME (METSYN) IN BLACK WOMEN WITH POLYCYSTIC OVARY SYNDROME (PCOS): A LONGITUDINAL STUDY. IRIS TIENLYNN Lee, MD, Julia M. Vresilovic, MRA, BS, Maryam Irfan, BS, Robert Gallop, PhD, Anuja Dokras, MD PhD UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM, PHILADELPHIA, PA.

OBJECTIVE: To evaluate the impact of race on the longitudinal risk of MetSyn among women with PCOS

DESIGN: Prospective cohort study

MATERIALS AND METHODS: Women with PCOS based on Rotterdam criteria with $\geq$2 visits over at least one year seen between 2008- 2019 were included. MetSyn was defined as at least three of the five criteria shown in Table. Presence or absence of MetSyn was determined at each visit. Data were collected on demographics, PCOS work-up, medical history, use of PCOS-specific medications (oral contraceptives, metformin, spironolactone). Two-tailed *t*-tests or rank sum tests were used for continuous variables and chi-square tests for categorical variables. Mixed-effects models were

used for longitudinal data to accommodate repeated measures per person, the varying of amount of data and spacing between assessments per person and examine the impact of race and medication.

RESULTS: 269 women with well-defined PCOS (94.8% with hyperandrogenic phenotype) were followed for a mean 5.8±2.7 visits over 5.4±2.6 years with 1.3±0.7 years between visits. During the study period, the overall prevalence of MetSyn was 31.8% in White women (n=188) and 49.4% in Black women (n=81, $p < 0.01$) and increased with time. This difference in MetSyn remained significant when including only women < 30 years (23.0% in White, 48.5% in Blacks, $p < 0.01$). Use of medications did not significantly interact with race: prevalence of MetSyn was 33.1% in White women compared to 51.2% in Black women not taking medications for PCOS ($p < 0.01$). Among women taking medications, 29.4% of White women and 43.2% of Black women had MetSyn ($p = 0.01$). Absence of Metsyn at a prior visit was associated with a higher prevalence of MetSyn at the next visit in Black woman when compared to White women (31.6% versus 13.5%, $p < 0.01$), even when restricting to women <30years (30.5% versus 11.6%, $p < 0.01$). In contrast, both Black and White women with MetSyn at the prior visit had a similar rate of persistent MetSyn at the next visit (72.5% versus 69.8%, $p = 0.62$).

CONCLUSIONS: This is the first longitudinal study in prospectively identified women with PCOS demonstrating a higher persistent risk of MetSyn in Black women compared to White women, regardless of age or medication use. Our study highlights the importance of frequent follow-up visits, starting at a young age, in this high risk population to allow for early identification of modifiable cardiovascular disease risk factors.

Data at first visit

	White n=188	Black n=81	p value
Age (Years±SD)	27.0 (6.58)	27.2(6.1.6)	0.73
Criteria			
BMI ≥30	48.3%	79.2%	<0.001
BP≥130/85mmHg or hypertension	41.0%	52.6%	0.09
Triglycerides ≥150mg/dl	22.6%	6.3%	0.0016
HDL≤50mg/dl	38.9%	58.2%	0.0041
Glucose≥100mg/dl or diabetes	19.5%	40.8%	0.0005
Prevalence of Metsyn	30.9%	44.4%	0.03

References: none
SUPPORT: none

O-268 10:25 AM Wednesday, October 21, 2020

COST EFFECTIVE PROTOCOL WITH LETROZOLE AND 3 DOSES OF GONADOTROPIN COMBINATION AS AN ALTERNATIVE TO CONTINUOUS GONADOTROPIN FOR OVULATION INDUCTION FOR IUI IN CLOMIPHENE CITRATE RESISTANT PCOS PATIENTS - A RCT.

Suvasmita Saha, MD (G&O), Hasibul Hasan Shirazee, MD(G&O) Post Doc Fellow Reproductive Medicine, Fellow in Reproductive medicine, Kolkata, India.

OBJECTIVE: Clomiphene citrate (CC) is the primary drug of choice for ovulation induction in PCOS but resistance to ovarian stimulation or stunted follicular growth is a frequent observation with CC. Inappropriate pregnancy rate & inadequate pregnancy outcomes are also observed with CC. The next approach of ovulation induction in CC resistance cases is using continuous Gonadotropin but it has many disadvantages such as high treatment cost, multi follicular development leading to multiple pregnancy, OHSS and frequent shifting of cycle to IVF-ET treatment. Letrozole induces folliculogenesis by releasing H-P axis from tonic inhibitory effect of estrogen & by augmenting gonadotropin secretion. It helps in follicular development without any adverse effect on the peripheral estrogen sensitive tissues. Adding few ampoules of gonadotropin at interval along with letrozole increases FSH at follicular receptor level & produces good quality oocyte. The purpose of the study was:

-To evaluate the efficacy of combined Letrozole & 3 doses of gonadotropin in CC resistant IUI cases.

-To compare the efficacy and cost effectivity of this protocol with continuous gonadotropin therapy.

DESIGN: This RCT was conducted in a tertiary infertility care centre from July 2017 to January 2019.

MATERIALS AND METHODS: Total 108 anovulatory PCO women in the age group 20 to 36 years who had previous ≥3 failed treatment cycles with CC were randomly divided into Group A (Letrozole plus 3 doses gonadotropin group) & Group B (Continuous gonadotropin group) comprising 54 patients in each group. 2 blood samples from all the patients on Day_2 of cycle and on the Day of hCG triggering were analyzed for endocrine profile. Patients in gr A were studied for total 96 cycles (n = 96) who received tab Letrozole 5 mg daily from D_2 to D_6 and injection U-FSH- HP (75 IU) on D_2, D_5 and D_8 of cycle. Patients in gr B were studied for total 84 cycles (n = 84) & received continuous gonadotropin (U-FSH- HP, 75 IU) starting from D_2 of cycle. Folliculometry was started from D_9 of cycle & ovulation triggering was done by hCG when dominant follicle reached ≥ 18 mm. Single IUI was performed with documented ovulation. Both groups were evaluated in respect of terminal endocrinological profile, number of follicles, ovulation rate, pregnancy rate & outcome, adverse effects & cost effectivity.

RESULTS: Demographic & baseline endocrine profile was comparable. In Gr A & B, mean no of follicles and average terminal estradiol level were 1.8 ±0.6 Vs 4.2 ± 0.8 (p< 0.05) and 266 ± 46 Vs 756 ± 84 pg (p< 0.001) respectively. Ovulation rate and pregnancy rate in both groups were 83.3% Vs 90.5% (p = 0.157) and 18.8% Vs 20.2% (p = 0.774) in Gr A & B respectively. In Gr B, 3 patients (3.6%) developed OHSS and 4 patients (4.8%) needed shifting of cycle to IVF-ET whereas no such incidents happened in Gr A. The average cost per cycle was significantly less in Gr A than Gr B.

CONCLUSIONS: The combined therapy with Letrozole and 3 doses of gonadotropin is a cost effective treatment protocol in CC resistant PCOS patient before proceeding to costly continuous gonadotropin therapy without any significant difference in ovulation and pregnancy rate.

O-269 10:40 AM Wednesday, October 21, 2020

NOVEL ANTI-MULLERIAN HORMONE RECEPTOR 2 BINDING PEPTIDE (AMHR2BP) STALLS OVARIAN FOLLICLE DEVELOPMENT IN A MOUSE MODEL.

Laura Detti, MD,[1] Ghassan M. Saed, PhD[2] [1]Cleveland Clinic, Cleveland, OH; [2]Wayne State University School of Medicine, Detroit, MI.

OBJECTIVE: Anti-Müllerian hormone (AMH) inhibits hormone production, and ovarian cortex follicle development in *in vitro,* and *in vivo*, ovarian cortex, and in luteinized granulosa cells (GCs) [1-3]. We showed a novel binding peptide to AMH receptor 2 (AMHR2BP) to inhibit GCs replication and function [4]. We sought to investigate whether AMHR2BP can inhibit follicular development in vivo.

DESIGN: Translational

MATERIALS AND METHODS: 24 18-weeks old C57BL female mice were assigned to four treatments: Baseline (euthanized just prior to the experiment), AMHR2BP (AMHR2-BP, 50 μg /day), rAMH (recombinant AMH, 1.8 μg /day), and placebo group (normal saline), via intraperitoneal pumps. Mice were euthanized 3 weeks after pump placement and the ovaries were explanted for histological analysis. Primordial (PDF), primary (PRF), secondary (SEF), and tertiary follicles (TEF) were esteemed. In addition, PCR expression of Ki67 (cell proliferation), Caspase3 (apoptosis) and Inhibin B were measured. We used Kruskall-Wallis's test for comparison of medians between groups (SPSS; p<0.05).

RESULTS: AMHR2BP performed similarly to rAMH. Compared with the Baseline (18 weeks' age), the AMHR2BP group showed increased SEFs, and decreased PRFs while PDFs and TEFs were unchanged. Compared with Placebo (21 weeks' age), the AMHR2BP group showed increased PDFs, while PRFs, and TEFs were significantly decreased, and SEFs were unchanged. AMHR2BP also caused a similar Ki67 and Caspase3 expression, and reduced Inhibin B. The table reports the individual groups' data.

CONCLUSIONS: Similarly to rAMH, AMHR2BP treatment for 3 weeks (equivalent to 3 menstrual cycles in the BLC67 mouse) minimized progression of follicular development, thus preserving the ovarian follicle number. In addition, it decreased hormone production, cell replication and apoptosis at cellular level. AMHR2BP could be used to inhibit age-linked loss of ovarian follicle reserve.

Table: Ovarian cortex concentration of PDF, PRF, SEF, TRF, AMH, Ki67, and Caspase3, in the four groups.

Variable	Baseline Median (Q1, Q3)	Placebo Group Median (Q1, Q3)	rAMH Group Median (Q1, Q3)	AMHR2BP Group Median (Q1, Q3)	p-value
PDF/mm^3	1195 (1191, 1248)	614 (538, 705)	1182 (1095, 1248)	1012 (916, 1134)	0.011
PRF/mm^3	788 (670, 817)	1165 (1152, 1176)	514 (497, 548)	383 (306, 533)	0.016
SEF/mm^3	970 (968, 1061)	1613 (1528, 1664)	1144 (1119, 1300)	1371 (852, 1662)	ns
TEF/mm^3	583 (579, 606)	1082 (1076, 1119)	871 (808, 890)	587 (519, 707)	0.045
Inhibin B (pg/μg RNA)	34.53 (34.53, 34.54)	48.41 (47.36, 49.47)	4.07 (3.86, 4.27)	2.22 (1.83, 2.60)	0.001
Ki67 (pg/μg RNA)	22.84 (20.49, 25.21)	69.26 (67.40, 71.12)	8.05 (7.20, 8.89)	5.90 (5.77, 6.02)	0.005
Caspase3 (pg/μg RNA)	1.31 (1.27, 1.36)	3.10 (3.00, 3.20)	0.46 (0.43, 0.50)	0.32 (0.31, 0.33)	0.004

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SUPPORT: University of Tennessee Health Science Center

O-270 10:55 AM Wednesday, October 21, 2020

HUMAN PRE-IMPLANTATION EMBRYOS ARE PERMISSIVE TO SARS-COV-2 ENTRY.

Manuel Viotti, PhD,[1] Mauricio Montano, BA,[2] Andrea Victor, MS,[3] Darren K. Griffin, DSc,[4] Tommy Duong, BS,[5] Nathalie Bolduc, PhD,[5] Andrew Farmer, PhD,[5] Isabel Gonzalez, PhD,[3] Frank Barnes, PhD,[3] Christo Zouves, MD,[3] Warner C. Greene, MD, PhD[2] [1]Zouves Foundation for Reproductive Medicine, Foster City, CA; [2]Gladstone Institutes, University of California San Francisco, San Francisco, CA; [3]Zouves Fertility Center, Foster City, CA; [4]University of Kent, Cabterbury, United Kingdom,; [5]Takara Bio USA, Mountain View, CA.

OBJECTIVE: To determine whether human pre-implantation embryos have the potential to be infected by SARS-CoV-2, the virus responsible for COVID-19.

DESIGN: Assessment of expression levels of SARS-CoV-2 entry mediators in human embryo biopsies by RNAseq analysis, and infection of cultured embryos with SARS-CoV-2 Spike glycoprotein pseudotyped reporter virions expressing green fluorescent protein (GFP).

MATERIALS AND METHODS: Trophectoderm biopsies from blastocyst-stage embryos (n=24) were processed for RNAseq using a commercial kit and sequenced; results were analyzed for expression of factors implicated in SARS-CoV-2 cellular entry. For viral infection experiments, blastocyst-stage embryos (n=94) were hatched from zonas mechanically, and infected by spinoculation with GFP-reporter virions pseudotyped with the SARS-CoV-2 Spike glycoprotein (required for SARS-CoV-2 entry). Embryos were subsequently monitored for fluorescence at 24-48 hours post-infection. Various control conditions were used as specified in the 'results' section. A mixed population of euploid, aneuploid, and untested embryos used in the study were from IVF treatment, donated to research by signed informed consent. The project was approved by an Institutional Review Board.

RESULTS: Cells collected from blastocyst-stage embryos robustly expressed the canonical SARS-CoV-2 entry receptor *ACE2* and the putative activator protease *TMPRSS2*, in addition to other reported entry factors. Embryos exposed to reporter virions pseudotyped with SARS-CoV-2 Spike glycoprotein displayed robust GFP signal, often in numerous cells with cytoplasmic localization. Specificity was confirmed by the absences of fluorescence in embryos treated with virions lacking the Spike glycoprotein ("bald" virus), or when embryos were spinoculated with media alone in the absence of virus. Embryos exposed to Spike glycoprotein-positive reporter virus in the presence of neutralizing anti Spike- or anti-ACE2-blocking antibodies exhibited negligible GFP signal, while control monoclonal IgG antibody-treated embryos maintained GFP expression. These results implicated the canonical Spike-ACE2 axis in the viral entry. Lastly, embryos exposed to reporter virions pseudotyped with Spike glycoprotein of SARS-CoV-1 (which also enters cells via ACE2) displayed GFP fluorescence, while embryos exposed to reporter viruses pseudotyped with Spike glycoprotein of MERS (which utilizes Dipeptidyl Peptidase IV (DPP4) instead of ACE2) resulted in no fluorescence.

CONCLUSIONS: Our results indicate that cells present in pre-implantation embryos are permissive to the canonical Spike-ACE2 viral entry mechanism utilized by SARS-CoV-2. These results encourage further investigation into the potential of SARS-CoV-2 infection in human embryos and may have wider implications in natural conception and ART practice.

P-930 3:30 PM Wednesday, October 21, 2020

EFFICACY AND SAFETY OF LINZAGOLIX (LGX) FOR THE TREATMENT OF HEAVY MENSTRUAL BLEEDING (HMB) DUE TO UTERINE FIBROIDS (UF): RESULTS FROM TWO PHASE 3 RANDOMIZED CLINICAL TRIALS. Elizabeth A. Stewart, MD,[1] Hugh S. Taylor, MD,[2] Robert N. Taylor, MD, PhD,[3] Jacques Donnez, PhD, MD,[4] Elke Bestel, MD,[5] Jean-Pierre Gotteland, PhD,[5] Andrew Humberstone, PhD,[5] Elizabeth Garner, MD, MPH.[6] [1]Mayo Clinic Department of OB/GYN Reproductive Endocrinology and Infertility, Rochester, MN; [2]Yale University School of Medicine, New Haven, CT; [3]University of Utah Health, Salt Lake City, UT; [4]Polyclinique Urbain V (ELSAN Group), Brussels, Belgium; [5]ObsEva SA, Plan-les-Ouates, Switzerland; [6]ObsEva Inc, Boston, MA.

OBJECTIVE: To assess the efficacy and safety of LGX, an oral GnRH receptor antagonist, administered with and without hormonal add-back therapy (ABT: 1 mg estradiol/0.5 mg norethindrone acetate), for the treatment of HMB and other symptoms of UF.

DESIGN: PRIMROSE 1 (USA, n=526) and PRIMROSE 2 (Europe and USA, n=511) are randomized, double-blind, placebo-controlled Phase 3 trials, with essentially identical design, investigating the efficacy and safety of LGX ± ABT once daily for 52 weeks. We report results up to 24-weeks for PRIMROSE 1 and up to 52-weeks for PRIMROSE 2.

MATERIALS AND METHODS: Participants had HMB (> 80 mL menstrual blood loss [MBL]/cycle) due to UF and excluded if they had significant risk of osteoporosis. Subjects were randomized to 1 of 5 treatments: placebo, LGX 100 mg, LGX 100 mg + ABT, LGX 200 mg, LGX 200 mg + ABT. PRIMROSE 2 subjects randomized to placebo or LGX 200 mg were crossed-over to 200 mg LGX + ABT after 24 weeks.

The primary efficacy endpoint was reduction in alkaline-hematin documented HMB to ≤ 80 mL MBL and a reduction of ≥ 50% at 24 weeks. Secondary endpoints included amenorrhea, time to reduced MBL/amenorrhea, days of uterine bleeding, hemoglobin, pain, uterine and fibroid volume and quality of life. Safety endpoints included bone mineral density (BMD) assessed centrally using Dual Energy X-ray Absorptiometry and adverse events (AE). Calcium/vitamin D were not provided nor recommended in the trials.

Individual active vs placebo efficacy comparisons were conducted using a 0.0125 significance level to account for multiplicity.

RESULTS: PRIMROSE 1 subjects had a mean age of 42 years and 63% were Black. The mean baseline MBL was 199 mL. HMB at week 24 was significantly ($p \leq 0.003$) reduced in all active treatment groups compared to placebo. Responder rates were 35, 56, 67, 71 and 75% in the placebo, 100 mg, 100 mg + ABT, 200 mg and 200 mg + ABT groups, respectively.

PRIMROSE 2 subjects had a mean age of 43 years and 5% were Black. The mean baseline MBL was 218 mL. HMB at week 24 was significantly ($p<0.001$) reduced in all active treatment groups compared to placebo. Responder rates were 29, 57, 77, 78 and 94% in the respective groups, and were maintained at 52 weeks.

In both trials, significant improvements compared to placebo were observed for key secondary endpoints, including pain and QoL, at week 24. Mean % loss in BMD ranged from 0–2% after 24 weeks in all active treatment groups except 200 mg LGX without ABT (3–4%). The rate of BMD loss slowed between weeks 24 and 52. The most common AE, hot flushes, were reported in 32–35% of subjects in the LGX 200 mg without ABT group and less than 15% in the other active treatment groups at week 24.

CONCLUSIONS: Once daily LGX 100 and 200 mg, both with or without ABT significantly improved HMB and other symptoms of uterine fibroids at 24 weeks and these improvements were maintained at 52 weeks. An effective GnRH antagonist treatment without hormonal ABT could be important for up to 50% of patients who may have contraindications to hormonal ABT. Limited BMD loss in the LGX 200 mg with ABT and LGX 100 mg without ABT arms suggests these dosing regimens could be suitable for longer-term treatment.

SUPPORT: The work was funded by ObsEva SA.

P-931 3:30 PM Wednesday, October 21, 2020

LINZAGOLIX MAY ADDRESS THE LONG-TERM TREATMENT NEEDS OF WOMEN WITH UTERINE FIBROIDS (UF) WHO HAVE CONTRAINDICATIONS TO HORMONAL ADD-BACK THERAPY (ABT): RESULTS FROM TWO PHASE 3 RANDOMIZED CLINICAL TRIALS. Linda D. Bradley, MD,[1] Erica E. Marsh, MD, MSCI, FACOG,[2] Elizabeth Garner, MD, MPH.[3] [1]Cleveland Clinic Cleveland, OH; [2]University of Michigan, Ann Arbor, MI; [3]ObsEva Inc, Boston, MA.

OBJECTIVE: GnRH antagonists comprise a new class of orally active medications that dose-dependently reduce estradiol (E2) levels, allowing partial suppression for symptom relief of estrogen-driven conditions without the bone (BMD) loss seen with full suppression. A GnRH antagonist developed using a full suppression dose that requires use of hormonal ABT was recently approved for the treatment of UF. Its labeling lists obesity, hypertension, and dyslipidemia as ABT contraindications associated with higher risks of thrombotic, stroke and cardiac events, which disproportionately affect black women. Given the propensity of black women to develop severe UF, availability of a GnRH antagonist that can be used long-term without ABT is important.

Linzagolix (LGX) is a GnRH antagonist being developed for UF treatment. In addition to a high dose (200 mg) with ABT (1 mg E2/0.5 mg NETA), a low dose (100 mg) without (w/o) ABT is being assessed as a potential long-term treatment option for women with ABT contraindications.

DESIGN: PRIMROSE 1 (P1; US, n=526) and PRIMROSE 2 (P2; Europe/US, n=511) are randomized, double-blind, placebo-controlled Phase 3 trials investigating the efficacy and safety of LGX 100 mg and 200 mg once daily, with and w/o ABT. Here we present results from 24 weeks (wks) (P1 and P2) and 52 wks of treatment (P2) with the 100 mg dose w/o ABT.

MATERIALS AND METHODS: Inclusion criteria included having UF and Heavy Menstrual Bleeding (HMB) (> 80 mL menstrual blood loss [MBL]/cycle). The primary endpoint was HMB reduction defined as ≤ 80 mL MBL (by alkaline hematin method) and ≥ 50% reduction at wk 24. Secondary endpoints included amenorrhea, hemoglobin (Hb), pain, and quality of life (QoL). Safety endpoints included BMD and adverse events (AEs). Calcium/vitamin D were not provided.

RESULTS: The 100 mg w/o ABT dose was studied in 191 women, 64% (P1) and 4% (P2) of whom were black; results were similar across the studies. P1 and P2 responder rates (RRs) were statistically significantly better than pbo, at 56.4% (p=0.003) and 56.7% ($p \leq 0.001$), respectively, with an RR of 53.2% in P2 at wk 52. Amenorrhea rates were 34.0% ($p<0.001$) and 38.3% (p=0.009), respectively, and in P2 at 52 wks, 39.2%. MBL reduction was rapid, with ~60% mean % change from baseline within the first 4 wks of treatment. Statistically significant improvements in pain, Hb levels and QoL were also observed.

Week 24 mean % BMD changes were -2.0% [95% CI: -3.3, -0.8] and -2.1% [95% CI: -2.6, -1.5] for P1 and P2, respectively, with additional -0.3% mean change at wk 52 in P2. AEs occurring in > 5% of women were hot flushes (6.0%/14.1%; pbo: 6.7%/3.8%), headache (8.0%/4.0%; pbo 5.8%/5.7%), and anemia (1.0%/19.2%; pbo: 3.8%/10.5%) in P1 and P2, respectively. In the 100 mg w/o ABT arm, one drug-related serious AE (hypertension) (HTN) was observed.

CONCLUSIONS: LGX 100 mg w/o ABT significantly improved HMB and other UF symptoms, with low AE rates and minimal associated BMD loss that showed evidence of plateauing after 24 wks. This regimen has the unique potential to address the needs of black women with UF, many of whom have ABT contraindications.

P-932 3:30 PM Wednesday, October 21, 2020

IS COVID-19 A SEXUALLY TRANSMITTED DISEASE? A SYSTEMATIC REVIEW. Tomer Tur-Kaspa, Grace Hildebrand, BA, David Cohen, MD, Ilan Tur-Kaspa, MD. Institute for Human Reproduction (IHR) Chicago, IL.

OBJECTIVE: SARS-CoV-2 has led to a rapidly spreading COVID-19 global pandemic. From a public health perspective, it is crucial to determine if SARS-CoV-2 is sexually transmitted and its possible effects on human reproduction.

DESIGN: A systematic review of English publications to July 15, 2020, was conducted according to PRISMA guidelines. A search in PubMed, NIH iCite COVID-19 portfolio, Cochrane Library, and Google Scholar

databases was conducted for SARS-CoV-2 and COVID-19 with fertility, reproduction, testes, seminal, prostatic and vaginal fluids, and in cervical smears. The focus of this review is sexual transmission by vaginal intercourse. Fecal-oral transmission has been discussed by others.

MATERIALS AND METHODS: The search revealed 1,107 publications after removal of duplicates, which were reviewed for eligibility by examining titles and abstracts. 141 full-text articles were reviewed and evaluated by two independent reviewers. 57 studies were included in this review based on relevance, including 14 studies which tested the male and female reproductive tracts for SARS-CoV-2 RNA.

RESULTS: COVID-19 may have detrimental effects on male reproduction by inducing orchitis and decreased testosterone levels, sperm count, and motility. No study investigated its effects on female fertility. No epidemiological investigation to date has suggested COVID-19 is a sexually transmitted disease (STD). The lack of co-expression of ACE2 receptors and the TMPRSS2 modulatory protein, needed for SARS-CoV-2 cell entry, in testicular cells, sperm, and oocytes, supports rejection of the hypothesis that gametes transmit SARS-CoV-2. 14 molecular detection studies of SARS-CoV-2 RNA in the male reproductive tract (in testicular biopsies, seminal and prostatic fluids), and the lower female reproductive tract (in vaginal fluids and cervical smears) were published. Only 1 out of 7 studies found positive SARS-CoV-2 RNA tests in seminal fluid (6 out of 143 total men). Interestingly, all seminal fluids of 7 men that demonstrated orchitis-like symptoms, identified in 2 other studies, tested negative. All 28 prostatic fluids tested negative. Only 1 out of 11 postmortem testicular biopsies tested positive, but electron microscopy found no viral particles in the testes. In women, all 35 cervical smears tested negative and only 1 case report described a positive SARS-CoV-2 RNA result in vaginal fluid (1 out of 58 total women). All together, sexual transmission of SARS-CoV-2 has not been confirmed.

CONCLUSIONS: Based on the current world published information, COVID-19 is not an STD. This information is important for clinicians, guidelines for public health, FDA guidelines for gamete and tissue donor eligibility, and for fertility treatments. Universal precautions, practiced in clinical settings and in IVF laboratories to prevent transmission of known or unknown viral infections, are adequate and sufficient at this time. We suggest that recovered patients of COVID-19, especially those with infertility, should be evaluated for their ovarian and testicular function. Prospective longitudinal follow up studies are warranted.

SUPPORT: Supported in part by the Institute for Human Reproduction (IHR), Chicago, IL.

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TRENDS IN FERTILITY PRACTICE DURING THE COVID-19 PANDEMIC: A GLOBAL SURVEY OF 299 CLINICS REPRESENTING 228,500 IVF CYCLES.

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OBJECTIVE: The COVID-19 pandemic is an unprecedented health crisis that has affected IVF practices globally and recommendations by local health authorities and reproductive medicine societies vary widely. Hence, the purpose of this study was to compare regional responses to the COVID-19 pandemic among infertility clinics and gain insight into the extent of practice modifications.

DESIGN: Self-administered online survey.

MATERIALS AND METHODS: Between March–June 2020, a multiple-choice 11-question survey was distributed through the IVF-worldwide online network (https://ivf-worldwide.com/survey/infertility-treatment-during-covid-19-pandemic.html). Responses were screened for completeness and duplicate clinics.

RESULTS: Responses from 299 clinics representing 228,500 IVF cycles were received, with respondents distributed across all 5 continents (34.8% Europe, 25.1% Asia, 18.1% South America, 15.4% North America, 5.3% Africa, and 1.3% Australia/New Zealand).

86.6% of respondents reported that their reproductive medicine society released pandemic-specific recommendations for a complete (53.8%) or partial shutdown (23.7%), which was higher than limits imposed by health authorities (32.5 and 19.7%, respectively). With respect to changes in IVF case volume, 76.6% and 80% of clinics reported a ≥75% reduction in fresh and frozen cycles, respectively, while 73.6% reported a ≥75% IUI case reduction. 3.7% of clinics reported no reduction in case volume.

Among clinics that stopped or reduced services, 69.5% cited government-mandate as a reason for closing, 31.1% due to employer concern for the health and safety of staff, 35.4% due to patient concerns, and 34% due to concerns regarding possible effects of COVID-19 on pregnancy. Lack of PPE was only acknowledged by 5.3% as a reason for closure. The most cited provisions planned prior to re-opening include increased hand sanitization (87%), spacing between appointments (86%), COVID symptom screening (84.3%), and temperature checks (71.6%). Among clinics that continued operations, the most cited provisions that were implemented included hand sanitizing (63%), symptom screening (60.4%), spacing between appointments (56.9%), and temperature checks (52.7%). Interestingly, 37% of clinics that stayed open did not report additional hand sanitization measures and 39.6% did not screen patients and staff for COVID symptoms.

Finally, 93.6% of respondents supported additional provisions for patient counselling including risk of cycle cancellation if a patient or provider tests positive for COVID-19 (85.6%) and possible risks of COVID-19 on adverse pregnancy outcomes (69.9%), miscarriage (67.2%), and fetal anomalies (58.9%).

CONCLUSIONS: COVID-19 resulted in a substantial reduction in IVF cycles, despite significant implications for such a delay on the probability of having a child. Data suggests that there remains room for improvement among clinics that remained open to decrease transmission using accepted procedures. Interestingly, clinics that stayed open were less aggressive at implementing protective provisions than clinics that closed.

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PREDICTING CUMULATIVE LIVE BIRTH BEFORE THE FIRST AND SECOND COMPLETE CYCLE OF IVF: A POPULATION-BASED STUDY OF LINKED CYCLE DATA FROM 79,512 WOMEN.

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OBJECTIVE: To develop prediction models that can estimate the cumulative probability of live birth over three complete cycles of IVF.

DESIGN: A retrospective cohort study.

MATERIALS AND METHODS: Linked fresh and frozen cycle data from women who underwent IVF (including intracytoplasmic sperm injection) in 2014-2016 were extracted from the Society for Assisted Reproductive Technology Clinic Outcome Reporting System database. Discrete time logistic regression was used to develop two models to predict cumulative live birth over three complete cycles of IVF. A complete cycle was defined as all fresh and frozen-thawed embryo transfers originating from one episode of ovarian stimulation. The pre-treatment model estimates the chance of live birth before starting treatment using couple characteristics, while the post-treatment model revises predictions using updated information before the second complete cycle. Potential predictors were female age, body mass index (BMI), serum anti-Mullerian hormone (AMH), previous full-term birth, male infertility, tubal factor, diminished ovarian reserve, polycystic ovaries, endometriosis, uterine factor and unexplained infertility. The post-treatment model also included number of eggs. Age, BMI and AMH were modelled as restricted cubic splines due to their non-linear relationship with probability of live birth. To assess optimism in model discrimination and calibration, internal validation using 300 bootstrap samples was done.

RESULTS: Of 79,512 women who underwent 103,270 complete cycles, 36,850 (46.3%) had a live birth from the first complete cycle, and cumulatively, 44,172 (55.6%) had a live birth over three complete cycles. Factors that were predictive of live birth in the pre-treatment model included female age (35 vs 25 years, adjusted odds ratio 0.62, 95% confidence interval 0.59 to 0.66), BMI (35 vs 25, 0.81, 0.77 to 0.84), previous full-term birth (1.13, 1.09 to 1.17), male infertility (1.21, 1.18 to 1.25), uterine factor infertility (0.85, 0.80 to 0.91), unexplained infertility (1.20, 1.15 to 1.25) and serum AMH (5 vs 2.4ng/mL, 1.23, 1.18 to 1.27). The post-treatment model included these factors as well as egg number (15 vs 9, 1.34, 1.25 to 1.44). The C-statistic for all models was between 0.70 and 0.72. Internal validation showed no over-optimism in discrimination or calibration performance. In a 36-year-old

woman with unexplained infertility, no previous live births, BMI of 25 and AMH of 2ng/L, our pre-treatment model predicts a 51% chance of live birth over her first complete cycle (82% over three complete cycles). If the first treatment is unsuccessful and the same woman starts a second cycle at 38 years old with AMH = 1.5ng/mL, our post treatment model estimates her chance of live birth at 21% after the second complete cycle and 40% over the second and third complete cycles.

CONCLUSIONS: These novel prediction models show accurate performance and are available to patients and clinics free of charge at sart.org. We anticipate that by providing individualised chances of success at two critical stages of IVF, they will help couples prepare emotionally and financially for IVF.

SUPPORT: This study was funded by the Society for Assisted Reproductive Technology.

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ENDOMETRIOSIS AND ADVERSE PREGNANCY OUTCOMES: A POPULATION-BASED COHORT STUDY. Maria P. Velez, MD, PhD, Leah Bahta, BSc, Jessica Pudwell, MSc, MPH, Rebecca J. Griffiths, BSc, Susan Brogly, PhD, MSc, Olga Bougie, MD, MPH. Queen's University, Kingston, ON, Canada.

OBJECTIVE: To assess the risk of adverse pregnancy outcomes in women with endometriosis.

DESIGN: Population-based retrospective cohort study using universal health care databases from Ontario, Canada.

MATERIALS AND METHODS: All singleton pregnancies with an estimated date of confinement between October 2006 and February 2014 were eligible for inclusion. Endometriosis was determined based on a surgical and/or medical diagnosis (defined as an in-hospital surgery with a diagnosis code of ICD9-617 or ICD10-N80 and/or two medical consults billed as ICD9-617). Log-binomial models were used to calculate risk ratios between endometriosis exposure and pregnancy outcomes. Models were adjusted for age, parity, BMI, smoking, income, rurality, medical history, history of infertility and use of Assisted Reproductive Technology (ART- IVF/ICSI).

RESULTS: A total of 19,099 women with and 768,350 women without a history of endometriosis were identified in the cohort. The mean age of endometriosis diagnosis was 26.6 years (± 5.8) with a mean time until pregnancy of 5.6 years (± 4.3). Compared to women without endometriosis, women with endometriosis were older at delivery [33.0 (± 4.9) vs. 30.0 (SD 5.6)], had a higher rate of infertility diagnosis (57% vs. 16%), history of fibroids (9% vs 2%), and use of ART (8% vs. 0.9%), all p-values <0.001. A higher proportion of women with endometriosis received antenatal care by an Obstetrician (79% vs 73%), with a greater mean number of visits coded as a high-risk prenatal assessment (1.1% vs. 0.08%), all p-values <0.001. In the adjusted models, endometriosis was associated with a greater risk of preterm birth, caesarean delivery, placenta previa, and other placental disorders and a reduced risk for induction and a small for gestational age baby (Table).

CONCLUSIONS: Endometriosis is associated with adverse pregnancy outcomes. Future studies should consider care plans and interventions to decrease the risk of adverse pregnancy outcomes in women with endometriosis.

TABLE. Pregnancy outcomes in women with history of endometriosis compared to women with no endometriosis

Outcome	Adjusted RR (95% CI)	p-value
Hypertensive Disorders of Pregnancy	0.98 (0.91 - 1.05)	0.55
Stillbirth	1.25 (0.98 - 1.58)	0.08
Small for Gestational Age (<10%)	0.92 (0.87 - 0.98)	0.01
Preterm Birth (< 37 weeks)	1.14 (1.07 - 1.21)	<0.001
Induction	0.97 (0.95 - 0.99)	0.01
C-Section	1.11 (1.08 - 1.14)	<0.001
Placenta Previa	1.82 (1.58 - 2.10)	<0.001
Placenta Abruption	1.23 (0.99 - 1.53)	0.06
Other Placental Disorders	1.94 (1.37 - 2.74)	<0.001
Postpartum Hemorrhage	1.03 (0.90 - 1.19)	0.64
Uterine Atony	0.86 (0.64 - 1.15)	0.30

SUPPORT: Canadian Institutes of Health Research (CIHR)

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DOES ENDOMETRIAL SCRATCH INJURY HELPS IN IMPROVING REPRODUCTIVE OUTCOMES OF INTRA-UTERINE INSEMINATION TREATMENT? A RANDOMISED CONTROLLED TRIAL. Navdeep Kaur Ghuman, MBBS, M.S. (Obstetrics and Gynaecology), DNB Obstetrics and Gynaecology), FMAS, Pratibha Singh, MBBS, MS(O&G), Sunil Raikar, MBBS, MS(O&G), Priya Singhmor, MBBS. All India institute of Medical Sciences, Jodhpur, Jodhpur, India.

OBJECTIVE: Current evidence suggests that endometrial injury improves clinical pregnancy rate while having no effect on miscarriages in women undergoing IVF/ICSI. However, there is no substantial evidence to advocate the use of endometrial injury to benefit the outcomes of IUI treatment. Additionally, there is no clear consensus about the ideal timing, underlying mechanism and optimum intensity of endometrial injury required. The study examines the effect of intentional endometrial injury/scratch in the early proliferative phase of stimulated cycle on reproductive outcomes (clinical and ongoing pregnancy rates and miscarriage occurrence) of intra-uterine insemination treatment (IUI).

DESIGN: This prospective, randomized control interventional study was conducted in a tertiary level teaching institution from April 2018 to February 2020.

TRIAL REGISTRATION NUMBER: CTRI/2018/04/013501

MATERIALS AND METHODS: 150 eligible couples requiring IUI treatment who agreed to participate were randomly allocated on 1:1 basis to either control or intervention group. The trial participants received up to 3 cycles ovulation induction with clomiphene citrate and intra-uterine insemination. In addition, women in intervention group were subjected to endometrial scratch injury on day 6-7 of their stimulated cycle. 154 cycles in control arm and 128 cycles in intervention group were analyzed for clinical pregnancy, miscarriages and pain experienced by the women during endometrial scratch injury using the statistical package SPSS (version 21).

RESULTS: Similar cumulative clinical pregnancy rates (12.5% Vs 13.6%, RR 1.21, 95% CI 0.44-3.37, p=0.713), biochemical pregnancy rates (17.1% vs 22.9%, RR 1.43, CI 0.59-3.47, p=0.421) and ongoing pregnancy rates (10.93% Vs 11.47%, RR 1.05, CI 0.35-3.21, p=924) were observed in control and intervention arms. Likewise, the relative risk of miscarriage occurrence in the intervention arm was 1.32 (95% CI 0.39-4.32, p=1.000) which was not statistically different from control group. Mean pain score of 6.93 on numerical pain rating scale was experienced by women whilst having endometrial scratch injury.

CONCLUSIONS: There is insufficient evidence to defend the use of endometrial scratch injury in intra-uterine insemination treatment, as it is moderately painful and have uncertain beneficial influence on reproductive outcomes.

SUPPORT: The study received funds from the institution as per institutional norms to procure consumables. No funding was received from any individual or external funding agency.The authors do not have any conflicts of interest to declare.

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INFLAMMATION IN RESPONSE TO SATURATED FAT INGESTION IN NORMAL WEIGHT WOMEN WITH POLYCYSTIC OVARY SYNDROME (PCOS) DOES NOT DEPEND ON THE PRESENCE OF ABDOMINAL ADIPOSITY (AA). Frank González, M.D.,[1] Robert V. Considine, Ph.D.,[2] Ola A. Abdelhadi, M.D., Ph.D.,[3] Anthony J. Acton, Jr., B.S.[2] [1]University of Illinois at Chicago College of Medicine, Chicago, IL; [2]Indiana University School of Medicine, Indianapolis, IN; [3]University of California at Davis, Davis, CA.

OBJECTIVE: Lipid-stimulated inflammation is increased in PCOS independent of obesity.[1] We evaluated the effect of saturated fat ingestion on nuclear factor-κB (NFκB) activation, inhibitory-κB (IκB) protein content and tumor necrosis factor-α (TNFα) mRNA content from mononuclear cells (MNC) of normal weight women with PCOS with and without AA, compared with normal weight body composition-matched ovulatory controls; and their relationship with HCG-stimulated ovarian androgen secretion and insulin sensitivity.

DESIGN: Cross-sectional study

MATERIALS AND METHODS: We studied 14 normal weight women with PCOS (7 with & 7 without AA) diagnosed on the basis of oligo-amenorrhea and hyperandrogenemia and 14 normal weight ovulatory controls (7

with & 7 without AA) ages 18-40. AA was defined as the % ratio of truncal fat to total body fat measured by DEXA that was 2SD above the mean of controls without AA. NFκB activation, IκB protein content and TNFα mRNA content were respectively quantified by electrophoretic mobility assay, Western blotting and RT-PCR in MNC isolated from blood samples drawn fasting and 2, 3 and 5 hours after dairy cream ingestion (100 ml). Androgens were measured by RIA from blood samples drawn fasting and 24, 48 and 96 hours after HCG administration (5000 IU). Insulin sensitivity was derived by IS_{OGTT}.

RESULTS: Compared with controls, the change from baseline (%) in NFκB activation and TNFα mRNA content increased ($p<0.02$) and IκB protein content decreased ($p<0.0001$) in both PCOS groups at 2 hours (NFκB – with AA: 27±4 vs. 4±5, without AA: 23±4 vs. -17±1; TNFα – with AA: 23±6vs. -13±3, without AA: 26±9 vs. -8±9; IκB – with AA: -35±2 vs. 18±5, without AA: -30±4 vs. 17±5) and 3 hours (NFκB – with AA: 25±4 vs. 2±4, without AA: 20±4 vs. -16±1; TNFα – with AA: 25±12 vs. -14±3, without AA: 29±15 vs. -14±6; IκB – with AA: -41±2 vs. 23±6, without AA: -35±5 vs. 20±5), and returned to baseline at 5 hours (NFκB – with AA: 1±1 vs. 0±1, without AA: 1±1 vs. -1±1; TNFα – with AA: 2±12 vs. -7±4, without AA: 2±6 vs. -3±6; IκB – with AA: -1±1 vs. 1±1, without AA: -1±1 vs. 1±1). Compared with controls, both PCOS groups exhibited greater ($p<0.05$) HCG-stimulated area under the curve (AUC) for testosterone (T) (with AA: 6466±775 vs. 3858±531, without AA: 6157±1026 vs. 3064±587) and androstenedione (A) (with AA: 501±35 vs. 307±24, without AA: 516±38 vs. 300±36). For the combined groups, the lipid-stimulated incremental AUC (iAUC) for NFκB activation and TNFα mRNA content was positively correlated with HCG-stimulated androgen AUC (NFκB – T: $r=0.53$, $p<0.006$; A: $r=0.62$, $p<0.0009$; TNFα – T: $r=0.41$, $p<0.05$; A: $r=0.55$, $p<0.004$). IS_{OGTT} was negatively correlated with the lipid-stimulated iAUC for NFκB activation ($r= -0.39$, $p<0.05$) and TNFα mRNA content ($r= -0.48$, $p<0.02$), and positively correlated with the lipid-stimulated iAUC for IκB protein content ($r=0.53$, $p<0.006$).

CONCLUSIONS: Lipid-stimulated NFκB activation and TNFα mRNA content are increased and lipid-stimulated IκB protein content is decreased in PCOS independent of AA. We speculate that this proinflammatory phenomenon in PCOS promotes hyperandrogenism and insulin resistance, and is further perpetuated by AA.

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P-938 3:30 PM Wednesday, October 21, 2020

EXOSOMES DERIVED FROM HUMAN UMBILICAL CORD MESENCHYMAL STEM CELLS PROMOTE PROLIFERATION OF ENDOMETRIAL STROMAL CELL.

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OBJECTIVE: To investigate whether the exsomes derived from Umbilical cord mesenchymal stem cells (UCMSCs) could improve the regeneration of endometrium in an experimental model of thin endometrium.

DESIGN: Randomized, control trial, animal research.

MATERIALS AND METHODS: UCMSCs were isolated and characterized. UCMSC-exos were extracted by differential ultracentrifugation and identified by western blots, transmission electron microscopy, and nanoparticle tracking analysis. A thin endometrium rat model was established by infusing ethanol into the uterine cavity of Sprague-Dawley rats. In all, 24 rats with thin endometrium and 12 normal rats were divided into 3 groups: (1) normal group, (2) experimental group transplanted with UCMSC-exos into uterine cavity, and (3) control group transplanted with saline into the uterine cavity. Three rats were killed at time 0 h, 7 d, 14 d and 28 d and bilateral uterus were obtained at each time points for the subseqent experiments. Morphological changes were determined by hematoxylin-eosin staining or Masson staining.The amount of fibrosis, vascularisation, inflammation and immunohistochemical staining with vascular endothelial growth factor (VEGF), Bcl-2 and Caspase-3 level were evaluated in the endometrial tissues.

RESULTS: The isolated UCMSC-exos had a typical cup-shaped morphology with a monolayer membrane, expressed the specific exosomal markers Alix, CD63, and TSG101 and were approximately 60 to 200 nm in diameter. The rats in group2 had a significantly thicker endometrial lining and exhibited higher expression of cytokeratin, vimentin than that of group3 ($P < .05$), which were similer with group 1. The amount of fibrosis, VEGF were similar between group1 and 2. In group2, comparing to group3, show less fibrosis but upregulated VEGF staining and Bcl-2 level was observed, while Caspase-3 level was downregulated($P < .05$).

CONCLUSIONS: UCMSC-Exos improved the proliferation of endometrium. UCMSC-Exos upregulated VEGF, Bcl-2 level as well as downregulated Cleaved Caspase-3 level and activated the PTEN/AKT signaling pathway to regulate the proliferation and antiapoptosis. Thus, UCMSC-Exos could be used as a potential treatment to promote endometrial repair.

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SUPPORT: None

P-939 3:30 PM Wednesday, October 21, 2020

COVID-19 PANDEMIC EFFECT ON EARLY PREGNANCY – ARE MISCARRIAGE RATES ALTERED, IN ASYMPTOMATIC WOMEN?.

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OBJECTIVE: To evaluate the effect of the COVID-19 pandemic state on early, 1st trimester pregnancies, in light of a link described between war-induced stress and adverse pregnancy outcomes.

DESIGN: Retrospective cohort study conducted in a University fertility center.

MATERIALS AND METHODS: All 1ST trimester viability scans done since the COVID-19 shut down, March13-May 6, 2020 (Study group), and between March 1-May 17, 2019 (pre-pandemic Control), were reviewed. Early 1st trimester pregnancy outcomes (Viable pregnancy, Arrested pregnancy including biochemical pregnancy loss and miscarriage, and ectopic pregnancy (EP)) were measured. A multivariate analysis was performed to control for significant confounders. Power analysis revealed that a sample size of 58 patients per group has a 90% power with a 15% difference in outcomes and α=5%. The study group denied symptoms of COVID-19.

RESULTS: 113 women were scanned in the study, and 172 in the control periods (5-11 weeks gestational age). The groups had similar demographics, gestational history, fertility diagnosis and treatment characteristics (Table). No significant differences were noted in the rate of recurrent pregnancy loss (RPL). Viable clinical pregnancy rates were not different between the groups (76.1% vs. 80.2% in the pandemic and pre-pandemic groups p= 0.41). No significant difference was seen in number of 1st trimester miscarriage (14.2% vs 12.8% p=0.76), biochemical pregnancies (3.5% vs 1.7% p=0.34), or in total miscarriage rate (22.1% vs 16.9% p=0.32), nor in EP rates (0.9% vs 2.3% p=0.36)

Mean serum TSH levels were higher in the control but fell in the normal range for both groups. Use of donor sperm was higher in the control and may have favored lower miscarriage rates in that group.

CONCLUSIONS: The COVID-19 pandemic environment does not seem to affect early first-trimester miscarriage rates in asymptomatic patients.

Characteristic	Study(n=113)	Pre-pandemic Control (n=172)	*P*-value
Female Age, Years, mean±SD	36.5 ± 4.5	37.2 ± 5.4	0.28
RPL History, N(%)	15 (13.3)	15 (8.7)	0.22
Fertility diagnosis, N(%)			
Unexplained	24 (21.4)	32 (19.6)	0.21
Male Factor	36 (32.1)	58 (35.6)	
Tubal factor	5 (4.5)	11 (6.8)	
Polycystic ovarian syndrome	21 (18.8)	25 (15.3)	
Decreased ovarian reserve	23 (20.5)	20 (12.3)	
Endometriosis	1 (0.9)	4 (2.5)	
Base line testing, median(IQR)			
AMH ng/ml	2.5 (1.0 – 4.4)	2.5 (1.2 – 5.4)	0.75
TSH mIU/L	1.3 (0.9 – 1.8)	1.7 (1.2 – 2.3)	0.001
Antral follicular count (AFC)	16 (9 – 29)	14 (9 – 25)	0.27
Total motile sperm count, median(IQR)	18 (6 – 43)	12 (5 – 47)	0.23
Sperm donation, N (%)	2 (1.8)	17 (9.9)	0.01
Pregnancy, N (%)			
Spontaneous	34 (30.1)	54 (31.4)	0.97
IUI	34 (30.1)	51 (29.7)	
IVF	45 (39.8)	67 (38.9)	
ICSI (percentage of IVF patients)	31 (79.5)	52 (77.6)	0.82
Blastocyst transferred	39 (86.7)	56 (83.6)	0.65

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QUANTITATIVE DETECTION OF BIOLOGICALLY RELEVANT ANTI-MULLERIAN HORMONE (AMH) AND PROGESTERONE IN HUMAN HAIR SAMPLES. Alice K. Crisci, BS,[1] Brian Ring, PhD,[1] Sarthak Sawarkar, MS,[2] Yolanda Cabello, PhD,[3] Laura Garcia-Calvo, PhD,[2] Maria Hebles Duvison, PhD,[4] Carmen Ochoa Marieta, MD,[5] Maria Jose Figueroa-Garcia, Embryologist,[6] Laura García De Miguel, Gynecologist,[7] Santiago Munne, PhD,[1] Manuel Alvarez-Rodríguez, PhD,[2] Manel Lopez-Bejar, PhD.[8] [1]MedAnswers, San Pedro, CA; [2]Universitat Autònoma de Barcelona, Barcelona, Spain; [3]Hospital Ruber Juan Bravo, Madrid, Spain; [4]Ginemed Sevilla, Sevilla, Spain; [5]CER Santander, Santa Cruz de Bezana, Spain; [6]HC Marbella International Hospital, Marbella, Spain; [7]Clinica Tambre, Madrid, Spain; [8]Western University of Health Sciences, Pomona, CA.

OBJECTIVE: Anti-Mullerian Hormone (AMH) and progesterone are used as biomarkers in assessing fertility and readiness for assisted reproductive procedures, usually measured in blood samples. The objective of this study was to determine if biologically relevant quantities of AMH and progesterone in human hair samples could be assessed.

DESIGN: The study design was prospective in nature. A total of (n=152) human female participants between the ages of 18-65 years were included in the study over a period of 10 months (recruitment ongoing).

MATERIALS AND METHODS: Sample collection was performed in a clinical setting, with blood and hair samples collected from patients. Hair follicles were not required, with a minimum of 100mg of hair cut from the participants. A doctor or a clinical technician measured the antral follicle count (AFC) by ultrasound. Biologically active AMH and progesterone was extracted from hair using a proprietary method. Hormone presence in hair extract was confirmed in a set of samples using Western Blotting. Hormones were measured in plasma and hair extract by ELISA.

RESULTS: AMH was detected via ELISA (n=95 in hair, 42 in plasma), and confirmed on a set of samples via western blots on denatured gel with bands at 70kDa. An average level of 9.37 pg/ml (95%CI 6.77-12) was detected in hair and 3.68 ng/ml (95%CI 2.79-4.56) in plasma in age-group <25 yrs. This is in contrast to the age group >39 years, within which a mean of 3.02 pg/ml (95%CI 2.19-3.85) AMH detected in hair and 0.92 ng/ml (95%CI 0.43-1.41) in plasma samples. AMH in hair did not significantly associate with measurements in plasma (effect size 0.19, p value 0.0852). AMH measured in hair correlated with age more strongly than plasma AMH (p-value =1.26 x10-5 (hair), p-value 0.088 (plasma)). AMH levels in hair were also strongly associated with AFC when corrected for hair weight, with an effect size of 3.75 (95% CI: 1.7; 5.8), and P value of 0.0168. Progesterone was measured via ELISA (n=76 in hair, n=91 in plasma) via ELISA. The association between progesterone in plasma and hair was significant (p value of 0.0298, p value of 0.013 when adjusted for hair weight).

CONCLUSIONS: We found that progesterone and AMH could be detected in human hair samples, and levels of AMH in hair were positively associated with maternal age and antral follicle count. The stronger association of AMH in hair versus plasma with age and AFC suggests that, though AMH is relatively stable during the monthly cycle, acute measurements of AMH may have variability that may make measurement via hair samples of greater utility for assessing reproductive health. Hair is a medium that can accumulate biomarkers over several weeks, while serum is an acute matrix that can represent only current levels. Detection of steroid hormones in hair has been used in neuroendocrinological studies in human and animals. However AMH measurements in hair are not currently employed for clinical purposes. In addition to this benefit, assessing reproductive hormone via a non-invasive method may allow an increased adoption of the use of these hormones in addressing reproductive health.

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FOLLICULAR-PHASE SINGLE-DOSE GNRH AGONIST PROTOCOL VS GNRH ANTAGONIST PROTOCOL IN PATIENTS WITH REPEATED IVF FAILURE. Rui Huang, MD, PhD, Xing Yang, Ph.D., Qian Li, Master. The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: To compare the clinical outcomes between follicular-phase single-dose gonadotropin-releasing hormone (GnRH) agonist protocol and GnRH antagonist protocol in patients with repeated IVF failure.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: The IVF cycles conducted on 764 patients with repeated IVF failure (No. of previous failed IVF cycle>=2) and normal ovarian reserve (AMH >1.1ng/ml) from Jun. 2017 to Dec. 2019 were included in this retrospective cohort study. The follicular-phase single-dose GnRH agonist protocol, in which 3.75 mg Triptorelin was administrated on cycle day 2 and exogenous gonadotropin (Gn) was initiated 4 weeks later, was applied in 303 patients and GnRH antagonist protocol utilized in the remaining 461 patients. The clinical outcomes, including stimulation duration, total dose of exogenous Gn, No. of oocytes retrieved, No. of transferrable embryos, clinical pregnancy rate and miscarriage rate between the two groups were compared respectively. P<0.05 was considered as statistical significance.

RESULTS: No significant difference was observed in basic characteristics between two groups. Comparing with the antagonist group, both the stimulation duration and the total Gn dose were significantly longer and higher in the agonist group. More oocytes and transferrable embryos were obtained, and the clinical pregnancy rate per fresh embryo transfer cycle was significantly higher in the agonist group. The basic and cycle characteristics were listed in the following table.

CONCLUSIONS: In patients with repeated IVF failure, follicular-phase single-dose GnRH agonist protocol resulted in a significantly higher clinical pregnancy rate than antagonist treatment, implying that single-dose GnRH agonist treatment may offer additional benefits for this specific group of patients.

SUPPORT: This work was supported by theÂ Natural Science Foundation of Guangdong Province (No.2019A1515011764).

	GnRH agonist protocol (n=303)	GnRH antagonist protocol (n=461)	*P* value
Age (y)	33.61±3.58	33.95±3.94	0.231
BMI (Kg/m^2)	22.20±5.49	22.03±2.94	0.186
Infertility duration (y)	5.67±3.26	5.36±3.31	0.209
AMH (ng/ml)	3.29±2.08	3.39±3.18	1.000
No. of previous IVF cycles	2.62±1.04	2.62±1.33	0.952
Gn initiation dose (IU)	235.07±58.80	229.00±59.36	0.164
Stimulation duration (d)	11.02±1.85	8.49±1.45	<0.01
Dose of Gn (IU)	2633.45±783.82	1937.08±586.31	<0.01
No. of oocytes retrieved	12.12±5.95	9.79±6.44	<0.01
No. of transferrable embryos	4.24±3.50	3.57±3.23	<0.01
No. of good-quality embryos	3.30±3.12	2.82±2.96	0.03
No. of embryos transferred	1.79±0.51	1.84±0.44	<0.01
No. of cycles with fresh embryo transfer	181	197	
Clinical pregnancy rate (%)	53.60	34.01	<0.01
Miscarriage rate (%)	20.62	14.93	0.354

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THE POSITION OF POINT OF HATCHING (POH) AND ITS ANGLE VIS-À-VIS THE INNER CELL MASS IS A ROBUST CRITERIA FOR SELECTION OF HATCHING BLASTOCYST FOR ENHANCED LIVE BIRTH RATES IN IVF CYCLES. Bindu N. Chimote, M.Sc., M.Phil, Ph.D.(Biochemistry); M.Sc. Clinical Embryology (Leeds-UK),[1] Nishad N. Chimote, M.Sc.,[2] Amogh N. Chimote, M.D.,[2] Riju A. Chimote, M.D.,[2] Natchandra Manoharrao Chimote, M.Sc., Ph.D.[3] [1]Consultant Clinical Embryologist, Nagpur, India; [2]Vaunshdhara Fertility Centre, Nagpur, India; [3]Scientific Director, Vaunshdhara Fertility Centre, Nagpur, India.

OBJECTIVE: Hatching of blastocyst from zona pellucida is extremely essential for implantation and live birth. It has been arbitrarily believed that the point of hatching (POH) should be diagonally opposite the inner cell mass (ICM). However, there is no documentation yet of the impact of angle of POH vis-à-vis ICM on the implantation (IR) and live birth rates (LBR) in vitro. We aimed at measuring the actual angle of POH and evaluating its correlationship with IVF outcomes.

DESIGN: Retrospective analysis of single hatching blastocyst transfer cycles carried out from 2014 to 2019. To avoid any bias due to blastocyst quality, we retrospectively included cycles involving transfer of only Grade AA or Grad AB hatching blastocysts. The angle formed between the imaginary tangent from the midpoint of ICM arc and the line from this ICM midpoint to POH, drawn on the photographic image of blastocyst, constituted our angle of POH. Cycles were classified into three groups on the basis on angle POH as Group A (0-30°), Group B (31-60°) and Group C (61-90°).

MATERIALS AND METHODS: Serum βhCG was measured on day 8 post blastocyst transfer. A βhCG value > 25 mIU/ml was considered as positive indication of pregnancy. Gestational sac with foetal cardiac activity on ultrasound at 6th week gestation confirmed clinical pregnancy. Missed abortion was defined as a spontaneous loss of cardiac activity after 6 weeks gestation. IR and LBR were also evaluated. Data was analysed using the graph pad prism V software. P<0.05 was considered significant. The statistical power of our study is >85%.

RESULTS: An overall comparison between pregnant and non-pregnant groups showed no significant difference in the angle of POH (56 vs. 53). However, interesting results were obtained when transfer cycles were classified on the basis of POH angle. Of the total 2350 hatching blastocysts evaluated, n=440 (18.7%), n=800 (34%) and n=1110 (47%) belonged to Group A, Groups B and Group C respectively. The clinical pregnancy rate differed significantly between the 3 groups (20.45% vs. 36.25% vs. 37.4%, One way ANOVA p<0.0001) respectively.

Significant differences were observed (Group C >Group B >Group A) in degree of blastocyst expansion (One way ANOVA p=0.0068) and gradation of trophoblastic (TE) cells (p<0.0001) whereas there was no difference in ICM grades between the 3 groups.

The IR was significantly lower (20%, p<0.0001) in Group A compared to that in Groups B and C. Although the implantation rates in both Groups B and C were comparable (36 vs. 38%, p>0.05); the rates of missed abortion were significantly higher in Group B compared to Group C (5 vs. 1.8%, p<0.0001). The live birth rates were significantly higher in Group C compared to Group B (37% vs. 30%, p=0.031).

CONCLUSIONS: The angle at which point of hatching originates vis-à-vis the ICM greatly influences IVF outcomes. Thus, in addition to morphometric evaluation of blastocyst, it is imperative to assess the angle of POH as a selection criteria so as to minimize the chances of missed abortion and to enhance live birth rates in IVF cycles.

References: nil

SUPPORT: None

P-943 3:30 PM Wednesday, October 21, 2020

DIAGNOSTIC EFFICIENCY OF BLASTOCYST CULTURE MEDIUM IN NONINVASIVE PREIMPLANTATION GENETIC TESTING (NIPGT). Jingbo Chen, M.D. candidate,[1] Lei Jia, PhD,[1] Shujing He, MM,[2] Cong Fang, Ph.D.[1] [1]Reproductive Medicine Research Center, Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; [2]The Sixth Affiliated hospital of Sun Yat-Sen University, Guangzhou, China.

OBJECTIVE: To evaluate the diagnostic efficiency of spent blastocyst culture medium (BCM) in noninvasive preimplantation genetic testing (niPGT) by comparing the karyotype concordance with corresponding inner cell mass (ICM) among initial trophectoderm (TE) biopsy, TE re-biopsy and BCM sampling.

DESIGN: Re-analysis aneuploid/mosaic blastocysts donated for research by couples.

MATERIALS AND METHODS: A total of 26 blastocysts with aneuploid (n=23) or mosaic diagnosis (n=3) were donated for research from 12 couples with indications of preimplantation genetic testing for chromosomal structural rearrangements (PGT-SR) or preimplantation genetic testing for aneuploidy (PGT-A), at Reproductive Medicine Research Center of the Sixth Affiliated Hospital of Sun Yat-Sen University, from July 2018 to July 2019. TE and ICM were biopsied (5-10 cells) in a routine procedure; TE was re-biopsied (more than 10 cells) at other sites of trophectoderm compartment. The MALBAC single-cell whole genome amplification (WGA) method was used to amplify DNA from all cells and BCM samples. Embryos were diagnosed as euploid, aneuploid or mosaic by NGS results. Embryos were classified as mosaic if the level of mosaicism ranged from 40% to 70%, while less than 40% was labeled as euploid and more than 70% as aneuploid. But for chr13, chr16, chr18 and chr21 chromosomes, the criterion for mosaicism was set to be 30%. The primary outcomes of this study, concordance rates with ICM biopsies, were compared among groups (initial TE biopsies, TE re-biopsies and BCM samples). The karyotype concordance of each two groups was defined as the presence of the same abnormal chromosome, especially in the target chromosome in different testing results compared. The clinical concordance of all four samples was defined as the concordance in embryo diagnosis, such as uniform aneuploid or not. To assess the diagnostic efficiency of BCM sample, false positive rate (FPR), false negative rate (FNR), sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) were calculated according to the corresponding ICM results. Statistical analyses were performed with the Chi-Square test, Yates' correction, or Fisher's exact test accordingly when comparing frequencies or proportions. All statistical analysis was performed using SPSS 22.0. $P<0.05$ was considered as significant.

RESULTS: For 23 embryos diagnosed as aneuploid by initial TE biopsy, 78.3% of initial TE samples, 87.0% of TE re-biopsies and 78.3% of BCM samples were concordant with corresponding ICM samples ($P>0.05$); but for 3 mosaic embryos, the concordance rates with ICM of these three groups were 0%, 100% and 100% ($P<0.05$), respectively. With the corresponding ICM result as the true result, sensitivity of both niPGT-A and initial TE were 100%; but the FPR of initial TE was higher than that of niPGT-A (100% vs. 0, $P=0.100$).

CONCLUSIONS: NiPGT-A using spent BCM had similar diagnostic efficiency as TE-biopsy PGT-A. And in case of mosaic embryos, niPGT-A using BCM may be more reliable for predicting the karyotypes of ICM than initial TE biopsy.

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FIBROTIC CHANGES IN TRANSGENDER OVARIES DUE TO TESTOSTERONE EXPOSURE. Anamika Ratri, BA, Riley Mickelsen, BS, Meredith Gray, MD, Nika C. Gloyeske, MD, Courtney A. Marsh, MD, MPH, Lane K. Christenson, PhD. University of Kansas Medical Center, Kansas City, KS.

OBJECTIVE: Transgender men (TGM) undergo extensive testosterone (T) exposure as part of gender conformation therapy. Androgens have well known impacts on the HPG axis as well as direct effects on the ovary. Reports conflict on whether TGM ovaries have characteristics of PCOS, which can also heighten T levels in the patient. Elevated androgens and aging can both increase collagenization of the ovary. In this study, we evaluated ovarian morphologic differences in young and old TGM patients, examining fibrosis of the tissue. Ovarian fibrosis could impede ovulation, which may lead to problems with fertility.

DESIGN: Ovarian fibrosis in TGM was compared to age-matched cisgender (CG) ovaries. All patients were divided into two age groups, young ($\leq$35 yr) and old (>36 yr). Fibrosis was detected by histological quantitation of picrosirius red (PSR) staining.

MATERIALS AND METHODS: Ovaries from young and old TGM patients (n=5/3, respectively) were collected during gender confirming surgeries. Ovaries from young and old CG donors (n=3/4, respectively) were obtained from patients undergoing oophorectomy for benign reasons. All samples were collected following KUMC IRB approval. Ovaries were fixed in 4% formaldehyde, processed and embedded in paraffin. 7μm-thick histological sections were stained with 0.1% PSR/0.1% Fast Green. Four randomly selected cortical areas of each ovarian section were imaged at 10x using bright field microscopy. PSR staining intensities were quantified using ImageJ per NIH recommended methodology. One-Way AVOVA ($p<0.05$) followed by LSD means separation tests were completed using SPSS program. To correct for heterogeneity of variance, data was log transformed.

RESULTS: Young (29$\pm$2.0yr) and old (40.0$\pm$0.7yr) TGM patients underwent 34.8$\pm$4.2mo and 40.6$\pm$39.2mo of T-therapy, respectively; note one old TGM patient was exposed for 119mo. Age matched young and old CG patients were 31$\pm$2.0 and 36$\pm$0.5yr of age. Ovarian PSR staining levels in young TGM patients were higher (292,184$\pm$122,991 $p<0.05$) compared to young CG donors (39,154$\pm$14,643). Ovaries from old TGM also showed increased PSR staining, (98,775$\pm$17,887) compared to old CG (34,359$\pm$5,540; $p<0.05$). TGM ovaries had few large follicles, which were atretic, whereas CG ovaries typically contained a few large healthy follicles.

CONCLUSIONS: This study establishes quantitatively that long-term testosterone exposure increases collagen deposition within young and old TGM ovarian tissue compared to CG age matched tissues. Our findings indicate a lack of multiple follicles in TGM ovaries, which diverges from several prior observations that TGM ovaries exhibited a PCOS-like morphology. Increased number of subjects will clarify whether age of TGM and duration of T-therapy impacts the extent of ovarian fibrosis. By understanding the time frame of ovarian fibrosis, this may give TGM greater control over fertility as they transition.

SUPPORT: None

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NOVEL AND UNIQUE KEY MARKERS IN THE INFLAMMATORY PATHWAYS FOR GENITAL TUBERCULOSIS (GTB). Madhavi M. Panpalia, MS,[1] Trupti Mehta, DGO, DNB,[1] Shiva Chettiar, Ph.D.,[2] Alpesh Patel, Ph.D.,[2] Sapna Agarwal, MD,[1] Jyotshna Palgamkar, DGO, DNB,[1] Swapneil R. Parikh, DNB,[3] Firuza Rajesh Parikh, MD DNB PhD.[1] [1]Jaslok Hospital and Research Centre, Mumbai, India; [2]Genexplore Diagnostics and Research Centre, Ahmedabad, India; [3]Kasturba Hospital of Infectious Diseases, Mumbai, India.

OBJECTIVE: To identify novel and unique diagnostic markers for the presence of Genital Tuberculosis (GTB).

DESIGN: Infertile women suspected of GTB were included in the study. An array of tests including endometrial biopsies for TB culture, nested TB-PCR, Immunocytochemistry, TNF alpha, P27, $\alpha_1\beta_3$integrins and evaluation of CD138 and endoscopy including either laparoscopy and or hysteroscopy was carried out. Those confirmed with GTB by two or more parameters were considered as TB positive and those with either one or none of the parameters positive were considered to be TB negative. Expressional analysis was performed on the same sample of the endometrial biopsy that had been collected. Pathway analysis to establish markers associated with TB and integrated pathways differentially associated to normal physiology were mapped.

MATERIALS AND METHODS: A total of 97 samples were subjected to diagnostic tests mentioned above. Results were tabulated to differentiate between TB positive and TB negative samples. Based on the screening tests, 34 samples were positive and 63 were negative. All these samples were subjected to custom designed gene expression analysis by microarray technique using Agilent G3 scanner and results were analysed on GeneSpring 14.9 software (Strand Lifescience). Data was normalized and those with fold chain more than 2 were considered for further analysis. Expression fold change of TB positive samples was compared to TB negative samples with respect to focused inflammatory pathway analysis comprising of 1052 genes. Through literature survey, a total of 1052 genes were identified as associated with inflammatory pathways and data of expression analysis was compared to these genes.

RESULTS: Bioinformatics analysis of the study revealed that 129 genes were differentially regulated in TB positive endometrial tissue as compared to TB negative endometrial tissue. Further, expression of 47 genes was statistically significant and considered for further pathways and marker identification analysis. Results showed that apart from innate immune response pathways like MAPK and cytokine pathways, we observed that genes involved in cell migration, Adhesion-Extravasation, G-protein coupled receptor pathways were also altered in TB positive endometrium thus, explaining the associated infertility.

CONCLUSIONS: Early detection of GTB is important in salvaging reproductive potential. GTB has a detrimental impact on female fertility. However its diagnosis by conventional methods is at times difficult in this form of extra-pulmonary TB and delay in diagnosis can negatively impact on future fertility. The present study has identified novel markers in the form of differential expression of 52 genes involved not only in classical inflammatory response pathways but pathways associated with inflammatory dysfunction in GTB.

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EMBRYONIC EVENTS AND NOT UTERINE EVENTS ARE ASSOCIATED WITH PREGNANCY OUTCOMES IN A DECEASED DONOR UTERUS TRANSPLANT PROGRAM: PRELIMINARY RESULTS. Elliott G. Richards, MD,[1] Marjan Attaran, M.D.,[2] Cynthia M. Austin, M.D,[2] Cristiano Quintini, MD,[3] Andreas G. Tzakis, MD,[3] Tommaso Falcone, M.D.[4] [1]Cleveland Clinic Foundation, Cleveland, OH; [2]Cleveland Clinic, Beachwood, OH; [3]Cleveland Clinic, Cleveland, OH; [4]Cleveland Clinic, Cleveland, OH.

OBJECTIVE: Uterus transplantation is an emerging treatment for absolute uterine factor infertility. The majority of uterus transplants to date have utilized living donors (LDs). Only a few sporadic case reports exist with deceased/cadaveric donors (DDs), an approach with prolonged graft ischemia times. Our objective is to determine whether pregnancy rates are similar in DD to LD uterus transplantation.

DESIGN: Prospective trial of DD uterus transplantation.

MATERIALS AND METHODS: Candidates with absolute uterine factor infertility underwent extensive screening and testing. In vitro fertilization was performed prior to uterus transplantation. DDs were matched to potential recipients by ABO compatibility and CMV status. First embryo transfers were attempted at six months post-transplant.

RESULTS: Eight DD uterus transplantations in total were attempted, with four patients achieving pregnancy (two with live born children by cesarean hysterectomy and two with ongoing pregnancies), two additional patients

with uterus still in situ but with recurrent implantation failures, and two patients experiencing postoperative complications necessitating graft hysterectomy prior to embryo transfer attempt. For those achieving pregnancy, the average baseline anti-mullerian hormone was 4.9±3.0, compared to 1.3±0.1 for the non-pregnant group. The average number of frozen embryos prior to transplant was 8.5 (6.62 frozen blasts per IVF cycle) in the pregnant group and 5.0 (1.88 frozen blasts per IVF cycle) in the nonpregnant group. All donors were multiparous except two (one recipient with recurrent implantation failure and one with early graft loss). Average cold ischemia time in minutes was 255±115 in the pregnant group and 324±47 in the non-pregnant group. All six patients with graft survival had onset of menses within 34 days of transplant. Average endometrial thickness at embryo transfer was 9.8±1.9 mm in the pregnant group and 10.3±1.7 mm in the non-pregnant group. The average total number of transfers performed was 1.25±0.5 in the pregnant group and 4±1.4 transfers thus far in the nonpregnant group.

CONCLUSIONS: Our series is the largest trial of DD uterus transplantation to date. Preliminary data show similar rates of key success milestones (graft survival, pregnancy, live birth) as in LD series. DD recipients with multiple implantation failures had poorer IVF outcomes pre-transplant, suggesting that failures to conceive are due to embryo factors and not endometrial function. Given this, candidates for uterus transplantation should meet stringent criteria of number of cryopreserved blastocysts before undergoing a uterus transplant procedure.

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CONTINUOUS AND INTERMITTENT AEROBIC TRAINING DID NOT CHANGE TELOMERE LENGTH, ALTHOUGH IT REDUCES HYPERANDROGENISM AND ANTROPOMETRIC INDEXES IN POLYCYSTIC OVARY SYNDROME. Cristiana Libardi M. Furtado, PhD,[1] Victor Barbosa Ribeiro, PhD,[2] Daiana CC. Pedroso, PHD,[3] Gislaine S. Kogure, PhD,[4] Rui A. Ferriani, MD, PhD,[4] Rodrigo T. Calado, MD, PhD,[4] Rosana M. dos Reis, MD, PhD.[4] [1]Federal University of Ceara, Fortaleza, Brazil; [2]Federal Institute of São Paulo, Jacareí, Brazil; [3]FERTILITY CENTER OF RIBEIRÃO PRETO - CEFERP, RIBEIRAO PRETO, Brazil; [4]Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, Brazil.

OBJECTIVE: To evaluate the effects of continuous (CAT) and intermittent (IAT) aerobic exercises on telomere length and the implications on anthropometric, hormonal and metabolic parameters of PCOS.

DESIGN: Randomized controlled clinical trial.

MATERIALS AND METHODS: 87 PCOS women were stratified randomly according to body mass index (BMI) into CAT (n=28), IAT (n=29) and non-training control group (n= 30). Aerobic exercises were performed on a treadmill, three times per week for four months. Telomere length was evaluated using qPCR and anthropometric, hormonal and metabolic parameters were measured, before and after 16-week of training or observation. Statistical analyses were carried out using SAS 9.0 software.

RESULTS: CAT and IAT did not change telomere length or the inflammatory biomarkers homocysteine and c-reactive protein after 16 weeks of training in PCOS. However, a negative correlation was observed between telomere length and age (p=0.0324) and BMI (p=0.0192). Booth exercises reduced waist circumference (CAT, p=0.045 and IAT, p=0.014) and testosterone levels (CAT, p=0.032 and IAT, p=0.019). Specifically, CAT reduced hip circumference (p=0.032) and cholesterol (p = <0.01) and low-density lipoprotein levels (LDL, p=0.03), and IAT decreased the waist-hip ratio (p=0.012) and free androgen index (p=0.037). In the controls, WC (p=0.049) and total cholesterol (p=0.010) increased after the observation period.

CONCLUSIONS: Four months of CAT or IAT did not change telomere length and inflammation in PCOS. Both protocols are important treatment strategies for women with PCOS, reducing anthropometric indexes and hyperandrogenism, and the CAT was effective in the control of lipid parameters in PCOS.

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P-948 3:30 PM Wednesday, October 21, 2020

DEVELOPMENT AND VALIDATION OF A NOVEL MAIL-IN SEMEN ANALYSIS SYSTEM AND THE CORRELATION BETWEEN ONE HOUR AND DELAYED SEMEN ANALYSIS TESTING. Mary Katherine Samplaski, MD,[1] Owen Falk, MS,[2] Stan Honig, MD,[3] David Shin, MD,[4] William J. Matthews, BS,[5] James Smith, MD, MS.[6] [1]University of Southern California, Los Angeles, CA; [2]Fellow, San Francisco, CA; [3]Yale University, New Haven, CT; [4]Hackensack University Medical Center, Hackensack, NJ; [5]Fellow Health Inc., San Francisco, CA; [6]University of California, San Francisco UCSF, San Francisco, CA.

OBJECTIVE: To compare the results of standard one hour and delayed semen analysis (SA) testing to establish the effectiveness of a novel mail-in SA system.

DESIGN: Prospective cohort.

MATERIALS AND METHODS: Men undergoing SA in the San Francisco Bay Area were recruited for SA testing with social media advertisements. One-hour SA (World Health Organization 5th edition), then repeat SA testing (on the same sample) was performed, at multiple time points over 52 hours utilizing a novel technique for maintaining sperm viability.

RESULTS: 164 subjects were recruited with a subset of 26 for the validation portion of the study. One hour SA on 104 ejaculates from these 26 patients demonstrated mean semen volume 2.82 ml (SD±1.08 ml), sperm concentration of 75.0 million/ml (SD±36.6 million/ml), total motility of 59.8% (SD±9.1%), and normal morphology of 11% (SD±2.7%). With up to 52 hours of observation and 4 subsequent SA measurements per ejaculate, sperm concentration was found to remain stable, motility declined by 0.39% per hour, and normal morphology declined by 0.1% per hour (Table 1. Measured 1 hour and calculated motility (correlation coefficient (CC) 0.87) and morphology (CC 0.82) were strongly correlated. The low coefficient of variation within concentration (3.9%), motility (3.0%), and morphology (4.7%) measurements exceeded minimal FDA standards (10.0%) for SA testing.

CONCLUSIONS: This novel, mail-in, CLIA-approved SA testing system demonstrates a high degree of correlation between 1-hour SA testing and delayed SA testing. This test was highly reproducible with coefficient of variation exceeding current FDA standards for sperm concentration, motility and morphology. This test is particularly applicable given recent needs for social distancing, concerns for rising prevalence of male infertility and possible patient concerns regarding privacy and embarrassment with face-to-face communication with a medical laboratory staff. Reliable home produced,

TABLE 1. Baseline Semen Parameters and Mean Change Per Hour with Repeated Measurements up to 52 Hours from Production (N= 104 ejaculates from 26 subjects)

	Mean	Median	Min	Max	Mean Change per Hour*	95% CI**	
Volume (ml)	2.82	2.5	1.5	6.0	N/A	N/A	
Concentration (million sperm/ml)	75.0	74.4	9.3	162.0	0.05	-0.09	0.19
Motility (%)	59.8	61	34	77	-0.39%	-0.044%	-0.35%
Normal Morphology (%)	11	11	5	18	-0.10	-0.11%	-0.09%

*Samples incubated in 5ml sperm media at random moderate temperatures. Semen analysis performed at least 3 times up to 52 hours after production.
**Concentration P=0.29; Motility P < 0.0001; Morphology P < 0.0001

mail-in testing may increase access to SA testing and allow a reproductive specialist to address any identified abnormalities in a timely manner.

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ABSENCE OF COVID-19 VIRUS WITHIN AN ACTIVE IVF LABORATORY USING STRICT PATIENT SCREENING AND SAFETY CRITERIA. Sandeep K. Rajput, PhD,[1] Shaihla A. Khan, PhD,[1] Benjamin B. Goheen, BS,[1] Heidi J. Engelhorn, MS,[1] Deirdre M. Logsdon, M.S.,[1] Courtney K. Grimm, MS,[1] Rebecca Kile, MS,[1] Rachel C. West, PhD,[1] Ye Yuan, PhD,[1] William B. Schoolcraft, MD,[2] Rebecca L. Krisher, PhD,[1] Jason E. Swain, PhD, HCLD.[2] [1]CCRM Colorado, Lone Tree, CO; [2]CCRM Fertility Network, Lone Tree, CO.

OBJECTIVE: In the early stages of the COVID-19 pandemic, most IVF clinics stopped the majority of patient treatment cycles to minimize the risk of disease transmission. When ASRM and other professional societies recommended resumption of treatments, procedures were put into place to ensure patient and staff safety. However, the risk of SARS-CoV-2 viral exposure and potential cross contamination within the IVF laboratory remains largely unclear. The objective of this study was to assess the true risk of exposure to SARS-CoV-2 in an active IVF laboratory when strict patient screening procedures are in place.

DESIGN: Prospective analysis.

MATERIALS AND METHODS: Prior to restarting IVF treatments, a COVID-19 safety protocol was implemented. Patients and staff were required to wear masks, fill out a symptom-based questionnaire daily, have their temperature taken, and practice social distancing in patient waiting areas. Each female patient undergoing transvaginal oocyte retrieval (TVOR) was required to have a negative SARS-CoV-2 RNA test 3-4 days prior to the procedure. Male partners were not tested. All cases examined utilized ICSI. The first tube of follicular fluid aspirated during TVOR (FF), culture media drops following removal of embryos on day 5 (M), and vitrification solution (VS) after blastocyst cryopreservation were analyzed. Self-inactivating replication incompetent lentivirus particles containing the single stranded viral RNA genome were immediately inoculated into each sample after collection as a positive control for viral RNA stability, prior to direct RNA isolation (M, VS) or sample concentration (FF). For FF, cell debris was removed by centrifugation and filtration (0.22 um) prior to concentration of virus particles with an Amicon filter. RNA was isolated using the optimized QIAamp viral RNA minikit, RNA quantity and quality determined, and cDNA synthesized using SuperScript IV VILO master mix. A multiplex TaqMan-based qPCR assay was developed for SARS-CoV-2 and lentivirus RNA (detection limit 5 SARS-CoV-2 copies/qPCR reaction and 50 viral copies/2 mL sample), and used to test all diagnostic samples. SARS-Cov2 synthetic RNA and lentivirus RNA were used as an RT-qPCR positive control. Samples with no amplification of lentivirus genome were removed from the analysis (false negative).

RESULTS: In total, culture medium from 30 patients, vitrification solution from 98 patients, and follicular fluid from 156 patients were analyzed. All samples were negative for the presence of SARS-CoV-2 viral RNA.

CONCLUSIONS: With stringent safety protocols in place, including patient testing and use of ICSI, the presence of SARS-CoV-2 RNA can be avoided in the IVF laboratory. Importantly, this study does not indicate that virus from an actively infected patient cannot be found in follicular fluid or make its way into the IVF lab. However, it does provide reassurance that with proper patient testing and safety measures, cross-contamination of the virus between gametes and embryos (including within liquid nitrogen storage dewars), as well as exposure of embryologists, is minimal.

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TRANSCRIPTOMIC AND GENOMIC SEARCH OF ENDOMETRIAL RECEPTIVITY MARKERS IN WOMEN WITH RECURRENT IMPLANTATION FAILURE. Wan Tinn Teh, MBBS, MRMed, FRANZCOG, PhD,[1] Peter AW. Rogers, BSc, PhD.[2] [1]Melbourne IVF, East Melbourne, VIC, Australia; [2]University of Melbourne, Parkville, VIC, Australia.

OBJECTIVE: The primary aim was to perform differential gene expression (DGE) of endometrium to identify receptivity genes that are associated with implantation failure. The secondary aim was to interrogate recent endometrial genome-wide association studies (GWAS) data to identify expression quantitative trait loci (eQTLs) for receptivity genes that had been identified through the DGE study.

DESIGN: Transcriptomic and genomic studies of secretory phase endometrium.

MATERIALS AND METHODS: Women with history of subfertility were recruited from the Royal Women's Hospital and Melbourne IVF in Australia. Clinical outcomes were followed up for at least 3.5 years. Participant were then assigned into recurrent implantation failure (RIF) group or control group. We defined RIF as absence of pregnancy after >3 embryo transfers (ETs) with high quality embryos or the transfer of ≥10 cleavage stage embryos (or ≥5 blastocysts) in multiple transfers. Controls were women who had been pregnant within the last 2 years or who had conceived during the follow-up period after participation in the study.

Endometrial biopsy and venesection were performed at LH plus 6 (+/- 1 day). Gene expression array of the endometrium was performed using Illumina Human HT-12 v4.0. DNA isolated from blood samples was analysed on HumanCoreExome chips and Infinium PsychArray. Gene expression data was normalized for cycle stage.

RESULTS: There were 31 participants in the control group, and 41 participants in the RIF group. Participants in the RIF group had significantly more previous unsuccessful ETs (p=0.00), higher total number of embryos transferred (p=0.00) and shorter average menstrual cycle length (p=0.04). No other significant differences were noted between the two groups.

Initial DGE analysis showed significant differences in expression of some genes between the control and RIF groups after correction for cycle stage. However, after correcting for multiple testing, there were no genes with significantly different expression between the two groups (FDR = 0.9999).

The top 100 differentially expressed genes from the RIF group were compared with a published gene expression signature for endometrial receptivity (Koot et al. 2016). Two common genes were identified - *SMAD9* and *NR5A2*. Naïve calculation showed that these two genes were likely not significant, and due solely to chance.

52 endometrial samples from this study were incorporated in a larger cohort of endometrial samples for endometrial eQTL analysis (Fung et al. 2018). Five cis-eQTLs were identified – *PIGP*, *MYOM2*, *RER1*, *POLR2J*, *SCHIP1* in the top 100 differentially expressed genes for the RIF group.

CONCLUSIONS: Our results demonstrate in conjunction with the published literature that no consistently reproducible endometrial genes linked to implantation failure have yet been identified. The identification of true genetic association requires a large sample size and replication in different populations. RIF due to reduced uterine receptivity is not a common occurrence, hence recruitment of subjects with true endometrial implantation failure is challenging.

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PERFLUORINATED COMPOUND (PFC) EXPOSURE IN OVARIAN GRANULOSA CELLS ALTERS GAP JUNCTION GENE EXPRESSION. Henry P. Mishek, Medical Student, Kendra L. Clark, PhD, John S. Davis, PhD. University of Nebraska Medical Center, Omaha, NE.

OBJECTIVE: Perfluorinated compoundc (PFCs) are synthetic chemicals that are persistent in the environment and bioaccumulate in humans and animals. These substances are ubiquitous in drinking water, cookware, stain repellents, food storage, packing materials, and cosmetics. Perfluorooctanoic acid (PFOA) is the most commonly detected PFC and has been associated with reduced fecundity and infertility. Ovarian gap junctions facilitate the transfer of various nutrients, ions, metabolites, and nucleotides between follicular cells and the oocyte. It is possible that PFOA mediates its effects by disrupting gap junction intracellular communication (GJIC) between granulosa cells or altering expression of gap junction-related genes. In this experiment, we aim to determine the effects of perfluorooctanoic acid (PFOA) exposure on connexin-43 (CX43) gene expression and GJIC in granulosa cells.

DESIGN: This study utilized a dye coupling method to assess GJIC in HGrC1 cells, an immortalized human granulosa cell line, after 24-hour (24h) exposure to environmentally relevant concentrations of PFOA.

MATERIALS AND METHODS: Previous work in this lab has shown that environmentally relevant concentrations (1-10 μM) of PFOA stimulate HGrC1 cell proliferation as early as 24 hours. Therefore, we utilized

concentrations of 1μM, and 10μM to assess GJIC with the vehicle dimethyl sulfoxide (DMSO, <0.1%) used as control. Cells were grown to confluence and then treated with PFOA for 24h. Luciferase Yellow (LY) and Rhodamine-dextran (RhoD) dyes were loaded into cells using the scrape load technique. Cells were incubated with the dyes for 5 minutes with subsequent washes to remove any residual dye, fixed, then imaged with confocal microscopy. The degree of dye migration was assessed using ImageJ. RNA was isolated and real-time qPCR was performed to quantify CX43 gene expression.

RESULTS: Preliminary results showed that treatment with 10 μM PFOA significantly ($P < 0.025$) reduced the distance traveled by the dye compared with vehicle treated controls. qPCR analysis determined that 1μM PFOA induced a 2.1-fold increase in CX43 transcripts relative to vehicle control.

CONCLUSIONS: Few studies have been reported using environmentally relevant concentrations of PFOA to elucidate the relationship between PFOA exposure and impaired ovarian processes. This study uses concentrations that are relevant to levels reported in human serum. Initial results indicate that PFOA reduces GJIC which may affect granulosa and follicle function. The increase in CX43 mRNA suggests a possible compensatory mechanism in response to PFOA exposure.

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RELATIONSHIP BETWEEN THE DURATION OF EQUILIBRATION STEP OF THE VITRIFICATION AND CHANGES ON ABUNDANCE AND COMPOSITION OF OOCYTE MEMBRANE LIPIDS.

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OBJECTIVE: Volumetric damages and cytotoxicity due to cryoprotectants exposure are time-sensitive in the vitrification process and can trigger the lipid remodeling of the plasma membrane. Here, we investigate the effects of exposure time to equilibration solution (ES) on membrane lipid profile of C57BL/6J mice oocytes using *MRM-profiling*, a sensitive exploratory method for lipidomics of oocytes and embryos[1]. We also assessed the effects of supplementing ES with antioxidants and unsaturated fatty acids. Experimental groups included oocytes equilibrated with Irvine Scientific (IRV), a commercial standard vitrification medium; Tvitri-4 (T4) produced in small scale for research by INVITRA®, and Tvitri-4 supplemented with L-carnitine (LC) and oleic and linoleic fatty acids (FA) (T4-LC/FA; Patent n. BR102019013697-9).

DESIGN: Experimental study.

MATERIALS AND METHODS: Oocytes were randomly divided in 7 groups: non-exposed (NE) and exposed to either 10-minute equilibration step (ES10) according to the manufacturer's procedure or 7-minute equilibration step (ES7), using IRV, T4, or T4-LC/FA media. After equilibration, oocytes were washed in methanol: H2O and lipids extracted with methanol. Diluted lipid extracts were flow injected into the triple quadrupole spectrometer with electrospray ionization (ESI). Relative ion intensities were used for univariate (ANOVA, fold-change, t-test, volcano plot) and multivariate analysis (PCA, PLS-DA, cluster analysis). Most informative lipids were sorted out using statistical significance of $p<0.05$ or partial least square discriminant analysis (PLS-DA) variables of importance (VIP) scores>1.

RESULTS: One-way ANOVA showed PC (38:8) differently represented among NE, ES7 and ES10 groups, upregulated in T4-LC/FA oocytes. In ES7 groups, two by two comparisons between IRV, T4 and T4-LC/FA using volcano plot (p-value$\leq$0.05; fold-change$\geq$2.0) detected 4, 5, and 4 significant lipids between IRV vs. T4, IRV vs. T4-LC/FA, and T4 vs. T4-LC/FA, respectively, with the PEo(36:1) overrepresented in IRV (fold-change=12.5). In ES10 groups, were detected 11, 19 and 4 lipids differentially represented among IRV vs. T4, IRV vs. T4-LC/FA, and T4 vs. T4-LC/FA, respectively. PLS-DAVIP scores identified in IRV oocytes 8 free- fatty acids, phosphatidyletanolamine PEo(36:1), phosphatidylcholines PCo(32:0) and PC(36:3), phosphatidylserines PS(14:1), PS(16:0), PS(30:2), PSo(40:5), and phosphatidylinositols PI(22:4) and PI(40:8) among the top features, whereas unsaturated PC and SM predominated in T4 and T4-LC/FA oocytes. Significant lipids observed between T4 and T4-LC/FA pointed oleic (18:1) and linoleic (18:2) acids upregulated in T4-LC/FA oocytes exposed for 10 min to ES.

CONCLUSIONS: The duration of the equilibration phase changed the abundance and composition of membrane lipids. Phospholipids were upregulated at 10-minute exposure to ES, except in IRV oocytes. The oleic and linoleic acids used as supplements in T4-LC/FA medium were promptly detected in the oocytes and seem contribute to better preserving membrane phospholipids during cell equilibration.

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IDENTIFICATION AND CHARACTERIZATION OF HUMAN ENDOMETRIAL STROMA CELL-DERIVED EXOSOMES BY PROFILING THE PROTEIN COMPONENTS.

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OBJECTIVE: To characterize and investigate the exosomes composition present in the pathogenesis of endometriosis.

DESIGN: We collect and purified exosomes that were derived from human eutopic and ectopic endometrioal stromal cells (EuESCs and EcESCs). We employed a proteomic approach to profile the protein composition of ESCs and comparison the EuESCs-exos and EcESCs-exos protein to evaluate the role of exosomes on endometriosis pathogenesis.

MATERIALS AND METHODS: Exosomes were isolated from ESCs culture supernatant by a combination of differential centrifugation. ESCs-exos obtained were extensively characterized using western blot to identify specific exosomal markers , transmission electron microscopy (TEM), and nanoparticle tracking analysis (NTA) to identify specific exosomal structure and size. The proteomics profiling of exosomes derived from ESCs via UPLC-MS/MS. Identified exosomes protein were analysed using Ingenuity Pathway Analysis (IPA) to determine the associated functions and pathways. We performed the XTT assays, migration assay and angiogenesis to examine the function of exosome protein.

RESULTS: A total of 105 proteins were identified from EuESCs-exos and EcESCs-exos by UPLC- MS/MS analysis. Among these, 36 proteins were different in EcESCs-exos compared to EuESCs-exos. We noted that ANXA2 was as one of the potential candidate expression protein in EcESCs-exos. The identified proteins were subjected to IPA for pathway prediction and function annotations. The data showed that ANXA2 were closely associated with cell morphology, amino acid metabolism, cell cycle, cell to cell signaling and interaction, and cellular assembly and organization. The data show that ANXA2 was high expression in EcESCs-exos, suggesting that exos-ANXA2 were association with endometriosis. We found that exos-ANXA2 increased cell growth, motility and angiogensis. It indicated that exos-ANXA2 was involved in regulating endometriosis. Our data suggest the function of ANXA2 mediated by exosomes can regulate cell proliferation and motility of ESCs, which can imply in endometriosis pathogenesis.

CONCLUSIONS: In conclusion, we demonstrate a function of ANXA2 in endometriosis pathogenesis mediated by exosomes, and through regulation of the ERK/STAT3 pathway and angiogenesis in endometriosis.

SUPPORT: This work is supported by MOST Taiwan [grant number 108-2314-B-037-069-MY3].

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IMPACT OF ADJUVANT CHEMOTHERAPY OR TAMOXIFEN ALONE ON THE OVARIAN RESERVE OF YOUNG WOMEN WITH BREAST CANCER: A PROSPECTIVE LONGITUDINAL STUDY.

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OBJECTIVE: To determine the longitudinal impact of adjuvant chemotherapy and tamoxifen-only treatments on the ovarian reserve recovery patterns of women with breast cancer by using a ultra-sensitive Anti-Mullerian Hormone (AMH) assay.

DESIGN: Multi-Center Prospective Longitudinal.

MATERIALS AND METHODS: One-hundred.-and-forty-two women with a primary diagnosis of breast cancer were prospectively followed with serum AMH assessments before the initiation, and 12, 18 and 24 months after the completion of adjuvant chemotherapy or the start of tamoxifen-only treatment. The chemotherapy regimens were classified into Anthracycline-Cyclophosphamide-based (AC-based) and Cyclophosphamide-Methotrexate+5-Fluorouracil (CMF). Longitudinal data were analyzed by mixed effects model for treatment effects over time, adjusting for baseline age and BMI.

RESULTS: Both chemotherapy regimens resulted in significant decline in ovarian reserve compared to the tamoxifen-only treatment ($p<0.0001$ either regimen vs. tamoxifen for overall trend). The AMH levels sharply declined at 12 months and the level of decline did not differ between the two chemotherapy groups ($p=0.53$).There was no significant recovery from 12 to 18 and 18 to 24 months after the completion of AC-based or CMF regimens ($p=0.97$). While the mean/median AMH level was 0.34/0.09 ng/dl at the 12-month time point, it was 0.40/0.06 ng/dl and 0.42/0.07 ng/dl at 18- and 24-month time points for the AC-based regimens group. These values were 0.11/0.03, 0.12/0.02 and 0.20/0.03 at the 3 time points for the CMF group. These mean levels are substantially below the threshold for normal ovarian reserve, which is generally 1.1 ng/mL or higher for the age group. AMH levels remained undetectable in 20% (15/76) vs. 38% (5/13) of women in the AC-based regimens vs. CMF groups at 24 months ($p=0.16$ from Fisher exact test). In contrast, tamoxifen-only treatment did not significantly alter the age-adjusted serum AMH levels over the 24-month follow up. Likewise, the use of adjuvant tamoxifen following AC-based regimens did not affect AMH recovery.

CONCLUSIONS: Our study is the first to assess ovarian reserve changes with serum AMH in a prospective longitudinal fashion, with multiple time points up to 24-month post-completion of chemotherapy, and in comparison with tamoxifen-only treatments. It shows that both AC-based regimens and CMF significantly compromise ovarian reserve, without a recovery beyond 12 months post-chemotherapy. In contrast, tamoxifen-only treatment does not alter serum AMH levels. The latter also indicates that the ovarian reserve of women who are on long-term tamoxifen treatment can be reliably assessed by serum AMH. This study provides novel information which will be useful in counseling young women with breast cancer for fertility preservation and in assessing post-chemotherapy ovarian damage and recovery.

SUPPORT: This study was supported by RO1 HD053112 from the Eunice Kennedy Shriver. National Institute of Child Health and Human Development (NICHD), and National Cancer Institute.

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SHOULD THERE BE AN "AI" IN TEAM?: EMBRYOLOGISTS IMPROVE SELECTION OF HIGH IMPLANTATION POTENTIAL EMBRYOS WITH THE AID OF AN ARTIFICIAL INTELLIGENCE ALGORITHM.

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OBJECTIVE: A deep learning artificial intelligence (AI) algorithm has been demonstrated to outperform embryologists in identifying euploid embryos destined to implant with an accuracy of 75.3% (1). While initial AI selection results are promising, this method of selection is completely driven by an algorithm and does not factor in the visual assessment of an embryologist. Our aim was to evaluate the performance of highly trained embryologists in selecting top quality day 5 euploid blastocysts with and without the aid of a deep learning algorithm.

DESIGN: Before and after.

MATERIALS AND METHODS: A non-overlapping series of 200 sets of Day 5 euploid embryo images with known implantation outcomes was distributed to 14 highly trained embryologists from multiple centers in the US. They were asked to select which of two embryos to transfer from each set. The same 200 sets of embryos, but with indication of which embryo in each set had been identified by the algorithm was then distributed and they were again asked to select which to transfer. Paired t-test and receiver operating curves were performed in Stata to compare the percent of embryos with successful implantation selected by embryologist visual assessment alone to those selected with aid of the algorithm.

RESULTS: Embryologists provided with AI results selected embryos which successfully implanted in 76.5% of cases compared to 69.5% for those selected using visual assessments alone ($p<0.019$). All 14 embryologists improved in their ability to select embryos with the aid of the AI algorithm with a mean percent improvement of 11.1% (range 1.4% to 15.5%). Accuracy of selection improved after addition of AI as well. The AUC (95% CI) for embryo selection by an embryologist alone compared to the same embryologist with AI was 0.69 (0.62-0.75) and 0.76 (0.70-0.82) respectively ($p<0.016$). There were no differences in degree of improvement by embryologist level of experience (junior, intermediate, senior).

CONCLUSIONS: The incorporation of an AI framework for blastocyst selection enhanced the performance of trained embryologists in identifying PGT-A euploid embryos destined to implant. A large randomized controlled trial is warranted to confirm that embryologists in combination with AI can improve in-vitro fertilization outcomes by selecting embryos with higher implantation potential than the current method of visual assessments alone.

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SUPPORT: SUPPORT: This work was partially supported by the Brigham Precision Medicine Developmental Award (Brigham Precision Medicine Program, Brigham and Women's Hospital), Partners Innovation Discovery Grant (Partners Healthcare), and R01AI118502, and R01AI138800.

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OLDER OLIGOASTHENOZOOSPERMIC MEN HAVE ALTERED TELOMERE BIOLOGY AND LESS CHANCES THAN CONTROLS FOR ASSISTED REPRODUCTIVE TECHNOLOGY OUTCOMES (ART).

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OBJECTIVE: The male factor accounts for half of the infertility cases that request ART. Beyond known causes, such as genetic, metabolic, endocrine, infectious or anatomic, new pathways could enlighten the 30% unexplained cases of male infertility. Because the telomere pathway affects organ function, due to telomere attrition with age, it is a good candidate to explain idiopathic infertility. Telomeres consist of DNA tandem repeats, which are bound by a protein complex, known as shelterin, which localize at the ends of linear chromosomes, safeguarding chromosome integrity. While in somatic differentiated cells telomere lenght (TL) decreases with age, spermatozoa show long telomeres. The objective of the study is to evaluate whether the telomere pathway is associated with low quality sperm parameters and ART outcomes.

DESIGN: Analytic prospective cohort study.

MATERIALS AND METHODS: 80 males were recruited between 2018 and 2019 from IVIRMA Madrid. The cohort includes two different age groups, younger than 25 and older than 40, composed of normozoospermics (NZ) or oligoasthenozoospermics (OAZ) men (25 people per group). Leukocytes and spermatozoa were extracted and then, evaluated for TL and TRF1 levels by Quantitative Fluorescent In Situ Hybridization followed by image acquisition using high resolution confocal microscope. CY3-fluorescent intensity (telomeres) was analyzed with the Definiens software. Seminal and IVF s parameters were assessed according to IVIRMA standard protocols.

RESULTS: In blood, a tendency to higher TL in young NZ compared with OAZ was observed. In addition, a lower percent of long telomeres was observed in OAZ (30% vs 45.26%, $p = 0.015$). Interestingly, a trend towards telomere lengthening with age was observed in NZ spermatozoa from both

age groups. TL was similar in young groups while in older groups TL was statistically significantly different (134.6 ± 15.95 a.u vs 113.6 ± 12,99 a.u, NZ and OAZ respectively, $p = 0.035$). Moreover, an accumulation of critically short telomeres was found in older OAZ (3.28 % vs 11.68 %, NZ and OAZ respectively; $p = 0.043$). To analyse telomere protection, TRF1 levels were studied. In blood, younger OAZ showed lower levels of TRF1 (317.3 ± 49.93 a.u vs 267.7 ± 40.02 a.u, NZ and OAZ respectively; $p = 0.010$) and accumulated a higher percent of low TRF1 levels at telomeres (16.9% vs 25.22 %, $p = 0.001$). Regarding ART outcomes, a lower rate of fertilization per Metaphase II oocytes (0.358 ± 0.072 vs 0.811 ± 0.019, $p < 0.0001$) and a higher rate of abortion (0.277 ± 0.188 vs 0.014 ± 0.014, $p = 0.032$) was found in older OAZ after intracytoplasmic sperm injection using donor oocytes and transfer.

CONCLUSIONS: OAZ patients have a shorter systemic TL already detectable at young age and also patent in sperm at older ages, possibly due to telomere unprotection with low levels of TRF1. Therefore, in OAZ patients, alteration of telomere biology could cause the premature aging of the reproductive system. Additionally, older OAZ had worse ART outcomes in contrast with NZ, suggesting that correct TL maintenance is a potential molecular marker of sperm quality to consider at older ages, before performing ART.

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THE IMPACT OF THE COVID-19 PANDEMIC IN TERMS OF QUALITY OF LIFE AND DISTRESS IN INFERTILITY, A QUESTIONNAIRE STUDY.

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OBJECTIVE: The COVID-19 pandemic has an impact on daily life as well as fertility care. Evidence supports the notion that infertility causes substantial emotional distress and has a significant impact on a person's quality of life. The effects of the COVID-19 pandemic on experiencing emotional distress in subfertile patients compared with their pre pandemic situation are unclear. In this study the impact of the restrictive consequences of COVID-19 in terms of emotional distress and infertility related quality of life is investigated, by comparing the pre pandemic emotional distress in a cohort of men and women at time of the first consultation in our fertility clinic with distress and quality of life during the COVID-19 pandemic.

DESIGN: An online questionnaire study regarding couples with an indication for IVF, whose treatment was, due to the restrictive measures of the COVID-19 pandemic, interrupted or postponed without knowledge of the length of time.

MATERIALS AND METHODS: Pre pandemic, all patients in our clinic received the SCREENIVF questionnaire during their first consult as a standard procedure (T0). After closure of our clinic in March due to the restrictive consequences, were patients invited by email, on the 16th of June 2020, to participate in an online questionnaire study (T1). Consenting participants provided demographic information and completed the validated FertiQoL and SCREENIVF questionnaires.

Mean scores were compared using the Paired-Samples T Test, while the McNemar test was used on paired nominal data.

RESULTS: From the 336 invited patients, 120 responded. More women (n=79) than men (n=41) agreed to participate in the study. Of the 120 participants, 72 (60%) completed the SCREENIVF at T0. We analyzed the difference between scores at T0 and T1 of those 72 participants. At T1, the mean score of the SCREENIVF was higher in the domains Anxiety, (mean score T0 4.0±3.2 vs T1 5.3±3.5, p=0.002), and Helplessness (mean score T0 10.7±3.0 vs T1 12.7±4.7, p<0.001). There was no significant difference in the domains Social support and Acceptance. In the domain depression, the mean score was higher at T0 (mean score T0 6.2±4.7 vs T1 3.7±3.2, p<0.001). The number of participants scoring high at risk of emotional distress on the different domains of the SCREENIVF was higher at risk on T0 (29.2% vs 11.1%, p=0.011).

During COVID-19 pandemic, the total score of the FertiQoL off all participants was 71.1(± 12.5). Women had lower total FertiQoL scores (68.7 ± 11.4) than men (75.8 ± 13.8; P = 0.003); this was true for each domain (except Relational).

CONCLUSIONS: This study shows the impact of the COVID-19 pandemic on emotional distress, especially revealed by more feelings of anxiety and helplessness. Meanwhile, patients' level of depression showed a decrease in times of pandemic compared to the time of the first consultation. Those results might be explained with the thought that due to the pandemic there is more loss of control (i.e. related to anxiety) than loss of hope (i.e. related to depression). We need to address the increased feelings of anxiety and helplessness in our patients.

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ASSOCIATIONS AMONG MORPHOLOGICAL PARAMETERS, CLINICAL FACTORS AND EUPLOID BLASTOCYST FORMATION.

João Paolo Bilibio, PhD,[1] Pânila Longhi Lorenzzoni, MsC,[2] Arivaldo José Conceição Meireles, PhD.[3] [1]Federal University of Pará, Belém, Brazil; [2]Federal University of Rio Grande do Sul, Porto Alegre, Brazil; [3]Pronatus Human Reproduction Clinic, Belém, Brazil.

OBJECTIVE: To evaluate the association among embryonic morphological parameters, clinical factors and euploid blastocyst formation.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: There were a total of 430 blastocyst embryos that underwent PGT-A by next-generation sequencing (NGS) from 135 patients who underwent intracytoplasmic sperm injection (ICSI) during the study period, June 2018 to June 2019. Embryo biopsy occurred on D5 or D6 according to the blastocyst morphology. Only blastocyst embryos with a visible inner cell mass and with a degree of expansion greater than 2 were submitted to biopsy. After embryo biopsy, all fragments were sent for PGT-A. After the results were obtained, statistical analysis was performed to assess the association of the risk of aneuploidy with the characteristics of embryonic development and the couple's clinical infertility factors.

RESULTS: Of 422 blastocysts, 200 (47.4%) were euploid, and 222 (52.6%) were aneuploid. Women over 38 years old were more likely to form aneuploid embryos (OR: 3.4, CI: 2.2-5.4, P<0.001). Poor ovarian reserve (OR: 3.3, P<0.001), increased male age (39.0 versus 40.7, P=0.019), and decrease in the percentage of sperm with normal morphology (2.5% vs. 1.9%, P=0.047) were associated with aneuploidy. Type C trophoectoderm (TE) and type C inner cell mass type were associated with a

TABLE 1. Predictive value, likelihood ratio, sensitivity, and specificity for diagnosis of embryo aneuploidy

	Pretest prevalence	PPV	NPV	LR+	LR-	Sensitivity (%)	Specificity (%)
Two factors							
Maternal age > 38 years + ICM type C	52.6	81.8	49.6	4.0	0.9	12.0	97.0
Maternal age > 38 years + TE type C	52.6	88.6	51.4	7.0	0.8	17.4	97.5
Three factors							
Maternal age > 38 years + TE type C + ICM type C	52.6	85.0	48.8	5.1	0.9	7.6	98.6

PPV: Positive predictive value; *NPV: Negative predictive value; LR: Likelihood ratio; ICM: Inner cell mass; TE: Trophoectoderm.*

high risk of embryo aneuploidy with an OR of 4.1 (CI: 2.2-7.7, P<0.001) and (OR: 1.7, CI: 1.01-3.0, P=0.048), respectively. Logistic regression analysis revealed maternal age and type C TE as the main risk factors for aneuploidy. Among combinations of factors (table 1), the best marker for the risk of aneuploidy was maternal age above 38 years combined with an embryo with trophoectoderm type C, which had a positive predictive value of 88.6% and specificity of 97.5%.

CONCLUSIONS: The trophoectoderm and inner cell mass type C are the major embryo risk factors for aneuploidy, explaining approximately 71% and 60% of the risk, respectively. Among clinical factors, advanced maternal and paternal age (greater than 38 and 36 years, respectively), antral follicle (< 5), and low percentage of sperm with normal morphology increased the risk of embryonic aneuploidy.

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IS UNIVERSAL SCREENING OF IVF PATIENTS FOR SARS-COV-2 JUSTIFIED? Daniel S. Seidman, MD,[1] Arik Kahane, MD,[2] Adrian Shulman, MD,[1] Eyal Schiff, MD,[1] Tal Shavit, MD[1] [1]Assuta Medical Center, Ramat-Hachayal, Tel-Aviv, Israel; [2]Assuta Medical Center, Rishon LeZion, Israel.

OBJECTIVE: Resuming all ART treatments in Israel, following the COVID-19 lockdown put into effect on March 22, 2020, was fraught with concern, as the pandemic is still raging. One of the safety measures implemented was universal screening for SARS-CoV-2 of all ART patients. Our aim was to assess the usefulness of this measure.

DESIGN: Cohort study.

MATERIALS AND METHODS: All women initiating ART treatment from May 1st, through July 17, 2020, at one of the two IVF Units of the Assuta Medical Centers, were required to undergo screening with nasopharyngeal swabs and a quantitative polymerase-chain-reaction test to detect SARS-CoV-2 infection. All women with symptoms of Covid-19 or those with recent exposure to an infected person were not allowed to commence ART treatment. Since almost all of the IVF cycles performed at our centers are fully covered by the Israeli national health insurance, treatment is very accessible, and thus we believe that our sample is representative of the country's COVID-19 prevalence.

RESULTS: A total of 4,259 asymptomatic women underwent ART treatments at the Assuta Medical Centers, 2,787 ovum pick-ups and and 1,472 frozen embryo transfers. Overall, 23 women (0.54%) tested positive for SARS-CoV-2. The rate of women who tested positive was similar in our IVF center in Tel-Aviv, 11 of 2,299 women (0.48%), and in our more southern Rishon Lezion center, 12 of 1,970 (0.61%). An additional 11 women had to cancel their IVF treatment as their male partner was tested positive for SARS-CoV-2. Only a fifth of the positive patients came from cities declared by the Ministry of Health as Covid-19 hotspots.

CONCLUSIONS: Our use of universal SARS-CoV-2 testing in all ART patients initiating ART treatment revealed that at this point in the pandemic in central Israel, one in 200 asymptomatic women starting an ART treatment cycle was positive for SARS-CoV-2. This ratio is approximately 10 times lower than the current rate among women screened in Israel due to Covid-19 related symptoms or exposure to a positive person. The potential benefit of universal testing for Covid-19 includes the ability to protect patients and health care staff during these challenging times by lowering the risk of novel coronavirus exposure in the ART clinic. However, universal screening may burden the limited testing resources and may lead to less vigilant use of personal protective measures.

SUPPORT: None

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CAN WE DIAGNOSIS ENDOMETRIOSIS WITH A PHONE APP? NEZHAT ENDOMETRIOSIS ADVISOR MOBILE APPLICATION AS A PREDICTOR FOR ENDOMETRIOSIS IN PATIENTS EXPERIENCING PELVIC PAIN, INFERTILITY OR UNEXPLAINED INFERTILITY. Janelle M. Jackman, MBBS,[1] Anuj Vaid, BA,[2] Shruti Agarwal, DO,[1] Azadeh Nezhat, MD,[3] Camran Nezhat, MD.[3] [1]Camran Nezhat Institute, Center for Special Minimally Invasive and Robotic surgery, Stanford University Medical Center, Palo Alto, CA; [2]Drexel University, Philadelphia, PA; [3]Camran Nezhat Institute, Center for Special Minimally Invasive and Robotic surgery, Stanford University Medical Center, University of California San Francisco, Palo Alto, CA.

OBJECTIVE: Endometriosis has a debilitating impact on women's lives, including severe pain, infertility and interference with daily life. For most women with endometriosis, the diagnosis is often missed, misdiagnosed and it is usually takes years before the right diagnosis is made. The first step in alleviating the adverse sequelae on endometriosis is to promptly and accurately diagnose it. Unfortunately, there is usually a delay especially in women with lower socioeconomic background as the diagnosis is made surgically. Our study is to evaluate the positive predictive value (PPV) of Nezhat Endometriosis Advisor

mobile application questionnaire as a noninvasive screening test for the diagnosis of endometriosis in patients experiencing severe or chronic pelvic pain, recurrent pregnancy loss, or unexplained infertility.

DESIGN: Retrospective study design.

MATERIALS AND METHODS: Retrospective cohort study at a university-affiliated private practice. Inclusion criteria were women who had no previous surgical diagnosis of endometriosis who utilized the app and was scheduled for laparoscopic surgery due to history. Patients then underwent laparoscopic

surgery with an indication of diagnosing and treatment of suspected endometriosis. The primary outcome

measured was the PPV of Nezhat Endometriosis Advisor mobile application questionnaire to the

surgical diagnoses of endometriosis. Statistical analysis was performed using SPSS v.25.0.

RESULTS: 30 patients met the inclusion criteria so far for our on going study. 95.0% of patients who had a screening test result of 90% or more on the app, had a surgical pathology confirmed diagnosis of endometriosis. However 100% of the patients who had a screen result of >90% on the app, had visual diagnosis of endometriosis at different stages at the time of surgery. The 8% who did not have pathological confirmation of endometriosis, had fibrosis diagnosed which may be due to late presentation of endometriosis example burnt out endometriosis presentation. The PPV of the screening questionnaire for endometriosis was 95.0%. In patients with app scores between 75-90%, pathology confirmed endometriosis 80% of times. Few patients who had diagnostic surgery despite low scores, endometriosis was confirmed in less than 10% of the cases. All patients had complete resolution or improved symptomatology after surgery.

CONCLUSIONS: Nezhat Endometriosis Advisor mobile application questionnaire has a high PPV of 95% for diagnosing endometriosis and can help identify a patient population that may require surgical treatment for pelvic pain or unexplained infertility. This will be helpful as it may lead to earlier presentation of endometriosis which will help with treatment and management. This is also very beneficial to patients in lower socioeconomic demographics who may not have easy access to healthcare and may otherwise suffer for a long time with pain or infertility before a diagnosis is made. More research is needed to determine the continued accuracy of the app in different patient population and demographics.

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A COMPREHENSIVE COVID-19 RISK MITIGATION STRATEGY FOR SAFE PATIENT CARE AND STAFF WELLNESS DURING A GLOBAL PANDEMIC. Mandy G. Katz-Jaffe, PhD,[1] Lauren Henry, BS,[1] Nathan McCubbin, BS,[1] Rachel Tucci, BS,[1] Rachel S. Mann, BS, MS,[1] Susanna McReynolds, PhD,[1] William B. Schoolcraft, MD[2] [1]Colorado Center for Reproductive Medicine, Lone Tree, CO; [2]CCRM Colorado, Lone Tree, CO.

OBJECTIVE: In the midst of the COVID-19 epidemic and the estimation that the vast majority of the population remains susceptible to SARS-CoV-2 infection, a comprehensive risk mitigation strategy to identify asymptomatic and pre-symptomatic carriers is key to providing safe clinical care during fertility treatment. The objective of this study was to evaluate the efficiency of a combined triage protocol and molecular testing for active SARS-CoV-2 viral infection for both patients and staff from a multi-site IVF network.

DESIGN: Prospective study.

MATERIALS AND METHODS: A symptomatic triage was performed whereby all patients were contacted by phone for the presence of COVID-

19 symptoms or if they had been in contact with someone suspected or confirmed to be positive for the virus. Only patients determined to be at low risk for COVID-19 were allowed to enter the clinic for fertility treatment. Both patients and staff were required, upon arrival at the clinic, to wear a mask, complete a symptom-based questionnaire, record body temperature, and keep a safe social distance of more than 6 feet at all times. Any individual recording a fever over 100.4^{O}F and/or two or more symptoms was instructed to stay/return home for self-quarantine. Specimen collection for viral screening involved an anterior nare sampling method and storage in a FDA approved viral transport medium. Viral RNA was isolated using the MagMAX™ Viral/Pathogen II (MVP II) Nucleic Acid Isolation Kit (Thermo Fisher Scientific). Molecular testing for active SARS-CoV-2 viral RNA infection was performed using the FDA emergency use authorized TaqPath™ RT-PCR COVID-19 test (Thermo Fisher Scientific) for every patient within 3-5 days prior to oocyte retrieval or an attempt to achieve a pregnancy, and for all staff bi-weekly. Positive cases were reported to each respective local State Health Department.

RESULTS: Of the 2,074 patients tested for COVID-19 between May and July 2020 across nine fertility clinics in the US, only 3 (0.15%) were found to be positive for SARS-CoV-2 viral RNA infection. In all cases the patients were asymptomatic and passed the triage protocol. PCR testing of staff bi-weekly identified 6 positive cases. All but one indicated having one or two mild symptoms. There were no recorded community transmissions among either patients to staff or between staff members.

CONCLUSIONS: A comprehensive risk mitigation strategy that includes a combined triage protocol, safe social distancing and molecular testing for active SARS-CoV-2 viral RNA infection in both patients and staff enables early detection and isolation of infected asymptomatic or pre-symptomatic individuals, thereby creating a safe environment for patient care and staff welfare during the global COVID-19 pandemic.

SUPPORT: None

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SEMINAL TEX-101 MAY PREDICT RESTORATION OF SPREMATOGENESIS AFTER VARICOCELECTOMY IN AZOOSPERMIC MEN WITH PALPABLE VARICOCELE.

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OBJECTIVE: around 40% of men with non-obstructive azoospermia (NOA) and palpable varicocele may benefit from varicocelectomy with appearance of sperms in ejaculate. Testicular histopathology predicts the outcome of varicocelectomy and men with hypospermatogenesis or late maturation arrest have better prognosis compared to men with early maturation arrest or Sertoli cell only (SCO) syndrome.

Testis expressed protein (TEX-101) is a seminal plasma protein that shed from testicular germ cells and it has been found to be significantly lower in men with SCO in compare with other NOA subtypes.

We aimed to assess the predictive role of seminal TEX-101 in recovery of sperms in ejaculate after varicocelectomy.

DESIGN: Prospective cohort.

MATERIALS AND METHODS: Forty male patients with NOA and palpable bilateral varicocele were subjected to seminal TEX-101 by ELISA (Wuhan Fine Biotech Co., Ltd. China), serum gonadotropins and total testosterone evaluation, followed by sub-inguinal microsurgical varicocelectomy. Two seminal analyses were performed in 3- and 6-months follow-up periods to assess appearance of sperms in ejaculate.

Mann Whitney test was used to compare pre-operative seminal TEX-101, FSH, LH and testosterone between the group of men with observed sperms in ejaculate during follow-up (group 1) and men with persistent azoospermia (group 2). Receiver operating curve (ROC) test was used to calculate a cut-off value and diagnostic indices (sensitivity and specificity) of pre-operative seminal TEX101.

RESULTS: After varicocelectomy, spermatozoa were found in the ejaculate of 10/40 (25%) through the follow-up (7 patients at the 3-months follow-up and additional 3 patients at 6-months follow-up). In these ten patients (G1), no significant differences were observed in pre-operative testicular volume or serum testosterone levels in compare with patients with persistent azoospermia during follow-up period (G2).

Pre-operative seminal TEX-101 was significantly higher in G1 in compare with G2 (p=0.014), while serum FSH and LH were significantly higher in G2 (p=0.001, p=0.01 respectively), as shown in table (1).

TABLE (1).

	G1 (n=10)	G2 (n= 30)	P value
TEX101 (ng/ml)	13.5 (7.5-22.3)	9.8 (2.8-18.2)	**0.014**
FSH (mIU/ml)	5.1 (3.5-9.2)	13.9 (3.5-31.2)	**0.001**
LH (mIU/ml)	4.2 (2.4-6.5)	6.3 (2.7-27)	**0.01**
Total testosterone (nmol/L)	5.1 (2.2-13)	4.5 (1.9-10.8)	0.818

Data are expressed as median (range).

Area under curve using ROC was 0.76 and a cut-off value of ≥9.9 ng/ml showed sensitivity of 90% and specificity of 57% in pre-operative TEX-101 prediction of recovery of sperms.

CONCLUSIONS: Pre-operative seminal TEX-101 can be used as a predictor for recovery of sperms in the ejaculate after varicocelectomy in men with NOA and palpable varicocele.

NCT04397887.

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EFFECT OF HORMONAL CONTRACEPTION ON ILLNESS SEVERITY IN WOMEN WITH POSITIVE SARS-COV2 TESTS.

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OBJECTIVE: To evaluate if hormonal contraception affects illness severity in SARS-CoV2 positive women.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Chart review of reproductive age (12-49 yo) women who tested positive for SARS-CoV2 at a tertiary medical center from March 28-April 27, 2020. Exclusion criterion was pregnancy. Women using hormonal contraception were compared to patients not using hormonal contraception. Patients were not contacted to confirm contraception. The primary outcome was hospital admission rate. Secondary outcomes included a composite score for illness severity and clinical signs of infection (Table 1). Multivariable logistic regression was used to control for differences at baseline. Results are reported as adjusted odds ratio (aOR) with a 95% confidence interval (CI). Calculated p values $\leq$ 0.05 were statistically significant.

RESULTS: A total of 2044 women were screened for SARS-CoV2. Of the 132 positive women, 46 used hormonal contraception: levonorgestrel IUD (n=9; 19.6%), injectable progestin (n=2; 4.35%), oral progestin (n=3; 6.52%), oral contraceptive (n= 24; 52.1%), transdermal patch (n=4; 8.70%), vaginal ring (n=4; 8.70%) and 86 did not use hormonal contraception. The rate of hospitalization for SARS-CoV2 was low for users and non-users of hormonal contraception (2.3% vs. 3.8%, respectively) and was not statistically different between groups. There was no difference between the rate of symptoms and clinical signs of infection between groups.

CONCLUSIONS: Sex hormones may play a significant role in regulating immune response and can impact disease state. We provide preliminary evidence that use of hormonal contraception does not have a significant effect on the illness severity in SARS-CoV2 as measured by hospitalization.

TABLE 1. Primary and secondary outcomes

	Hormonal contraception (n= 44)a	Not on hormonal contraception (n=79)a	Adjusted OR (95% CI)
Primary Outcome			
Hospital admission	1 (2.3)	3 (3.8)	0.99 (0.68-1.44)
Clinical Signs			
Composite score of illness severity[b]	1 (2.3)	2 (2.5)	0.98 (0.67-1.43)
Heart rate > 100 beats/min	4 (9.1)	3 (3.8)	0.99 (0.68-1.45)
Respiratory rate > 22 breaths/min	1 (2.3)	1 (1.3)	0.97 (0.67-1.42)
Urine output < 0.5 mL/kg/hr	1 (2.3)	1 (1.3)	0.97 (0.66-1.42)
Lactate > 3 mmol/L	0	0	c
Temperature > 100.4 °F	6 (13.6)	8 (10.1)	0.98 (0.67-1.42)
WBC > 12,000 or < 4,000 / mm^3	0	0	c
Intubation	0	0	c

Data are shown as n/N (%) unless otherwise specified [a] n=2 & n=7 patients excluded in the hormonal vs. not hormonal groups, respectively, due to no data on hospital admission [b] Components of the composite: hypoxia (O2 < 94%), > than 50% lung involvement on imaging, respiratory failure, respiratory shock, multiorgan dysfunction, death [c] Unable to perform logistic regression due to cells with 0 counts

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TOLL-LIKE RECEPTOR-2 AND TISSUE INHIBITOR OF MATRIX METALLOPROTEINASE-2 GENETIC VARIANTS AS PREDICTORS OF TOBACCO-MEDIATED FEMALE INFERTILITY AMONGST *MYCOBACTERIUM TUBERCULI*-POSITIVE ASIAN INDIAN COHORT. Saumya Pandey, M.Sc., Ph.D. Indira IVF Hospital, Udaipur, India.

OBJECTIVE: Tobacco-consumption is a significant predictor of metabolic-perturbations in female reproductive physiology, including endometriosis/stillbirths/miscarriages/infertility worldwide. Targeting Toll-like receptor-2 and Tissue Inhibitor of Matrix Metalloproteinase-2 genetic polymorphisms in demystifying the underlying genetic/cellular/molecular basis of tobacco-mediated female infertility amongst Asian Indian cohort is an immunotherapeutically attractive strategy for cost-effective infertility management. This study aimed to evaluate the role of TLR-2(-196 to -174del) and TIMP-2 (-418G>C) [rs8179090] gene-polymorphisms in susceptibility to tobacco-mediated infertility amongst Asian Indian women.

DESIGN: Prospective case-control (1:1) hospital-based study.

MATERIALS AND METHODS: 100 Asian Indian *Mycobacterium tuberculi*-positive infertility patients (>35 years) and 100 unrelated/age-matched/*M. tb.*-negative/married (parity: 2-4 children) female controls of similar ethnicity were enrolled (sample-size calculation using Quanto); *M. tb.*-positivity was assessed using Gene-Expert/TB-Gold PCR-testing. Endometrial thickness was determined using Color-Doppler imaging. Genomic DNA extraction from peripheral blood samples collected from study subjects (N=200) was carried out using salting-out method. TLR-2/TIMP-2 genotyping was performed using polymerase chain reaction-based restriction fragment length polymorphism. Self-reported tobacco-usage was ascertained using bilingual Questionnaire in English/Hindi dialects. Statistical data-analysis was performed using multivariate logistic regression analysis with Bonferroni's corrections for multiple comparisons in stratified subgroups (SPSS ver.16.0).

RESULTS: The findings demonstrated no significant association between TLR-2 (-196 to -174del) and TIMP-2 (-418G>C) gene-polymorphisms and risk of developing *M. tb.*-mediated infertility in the study-population; stratified-analysis using case-only study-approach revealed no effect of TLR-2/TIMP-2 polymorphisms on *M. tb.*-positive infertile patients (N=100) with thin endometrium <6.0 mm; recombinant Granulocyte-Colony-Stimulating-Factor infusion (300 mcg) significantly increased endometrium thickness (p>0.05). TLR-2 and TIMP-2 genetic variants modulated the risk in infertile patients who smoked/chewed tobacco (55% tobacco-users) with borderline association (p=0.046); TLR-2 ins/del genotype showed strong association (OR=1.9 [95%CI=1.1-3.3]) with tobacco-usage in infertile women with *M. tb.*-positivity. Overall, the study demonstrated lack of association between TLR-2 and TIMP-2 gene-polymorphisms and infertility susceptibility in women of Asian Indian ethnicity.

CONCLUSIONS: The study highlighted the significance of TLR-2/TIMP-2 genetic variants in tobacco-mediated infertility susceptibility in Asian Indian women providing fascinating avenues for future development of TLR-2/TIMP-2 predictive biomarkers in stratifying *M. tb.*-positive infertile patient-populations.

SUPPORT: None

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PRETERM BIRTH SUBTYPES BY FERTILITY STATUS AND FERTILITY TREATMENT: A POPULATION-BASED COHORT STUDY. Yimin P. Wang, MSc,[1] Jessica Pudwell, MSc, MPH,[1] Joel G. Ray, MD, MSc,[2] Yingwei Peng, PhD,[1] Maria P. Velez, MD, PhD[1] [1]Queen's University, Kingston, ON, Canada; [2]St. Michael's Hospital, Toronto, ON, Canada.

OBJECTIVE: To evaluate preterm birth (PTB) subtypes, according to both fertility status and infertility treatment (IT).

DESIGN: Retrospective cohort study using linkage of universal health databases from Ontario, Canada.

MATERIALS AND METHODS: Included were all singleton births, April 2006-March 2014. Exposure categories were defined as spontaneous conception (reference); subfertility (history of an infertility consult billed as ICD-9 code 628 in the absence of IT); non-invasive IT (ovulation induction or intrauterine insemination); and invasive IT (IVF or ICSI). PTB outcome subtypes were classified as spontaneous or provider-initiated (iatrogenic). Modified Poisson regression generated risk ratios (RR) for the association between exposure categories

TABLE. Risk of preterm birth subtypes according to exposure by fertility status and fertility treatment

	Relative risk of preterm birth (95% CI)		
Exposure category	Any preterm birth	Spontaneous preterm birth	Provider-initiated preterm birth
Spontaneous conception	1.00 (ref)	1.00 (ref)	1.00 (ref)
Subfertility	1.16 (1.13 to 1.20)	1.15 (1.10 to 1.19)	1.23 (1.16 to 1.31)
Non-invasive IT	1.27 (1.17 to 1.36)	1.19 (1.09 to 1.31)	1.48 (1.29 to 1.69)
Invasive IT	1.63 (1.52 to 1.75)	1.40 (1.27 to 1.53)	2.35 (2.09 to 2.64)

and risk of PTB. Models were adjusted by inverse probability weighting, accounting for age, parity, obesity, smoking, hypertension, diabetes, income quintile, rurality and immigration status.

RESULTS: A total of 723,810 deliveries were included, of which 646,926 (88.3%) were by spontaneous conceptions; 68,822 (9.4%) in women with subfertility; 9024 (1.2%) by non-invasive IT; and 8038 (1.1%) by invasive IT. IT exposed women were significantly more likely to be older, nulliparous, obese, and have diabetes and chronic hypertension. PTB rates were 6.0% in women with spontaneous conceptions, 7.7% in those with subfertility, 8.0% with non-invasive IT, and 10.8% following invasive IT. Compared to women who had spontaneous conception, the RR of any PTB rose by degree of IT invasiveness (see Table). This was especially so for the outcome of provider-initiated PTB (Table).

CONCLUSIONS: Infertility, and its treatments, are associated with a higher risk PTB, especially provider-initiated PTB. Accordingly, strategies to reducing the risk of provider-initiated PTB are recommended.

SUPPORT: Canadian Institutes of Health Research (CIHR)

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PLOIDY STATUS AND DEVELOPMENTAL POTENTIAL OF HUMAN BLASTOCYSTS CONTAINING NONDIVIDING BLASTOMERES OR FRAGMENTATION. Yimin Shu, MD, PhD, Jun Yang, Ph.D. Wake Forest University School of Medicine, Winston Salem, NC.

OBJECTIVE: Nondividing blastomeres are arrested cells that are excluded from developing embryos and remain outside the developing blastomeres at morula stage, leading to decreased blastocyst formation and blastocyst quality. Although remaining developing cells try to compensate the cell loss, very little data is available regarding its ploidy status and further developmental potential.

DESIGN: This retrospective data analysis involved infertility patients undergoing PGT-A through NGS in an academic IVF Program between January 2015 and February 2020.

MATERIALS AND METHODS: Artificial shrinkage of blastocoel by laser during the biopsy process allows us an opportunity to carefully observe the presence and extent of nondividing blastomeres/fragmentation under zona pellucida. We define a nondividing blastomere as an embryonic cell arrested during the first four embryonic divisions (2- to 16-cell stage). To differentiate fragmented polar bodies from real embryo fragmentation, only blastocysts with 10% or above fragmentation were defined as fragmented embryos. Biopsied trophectoderm cells were analyzed with NGS by CooperGenomics. The primary outcome measures are euploid/aneuploid rates. Clinical outcomes following transfer of euploid embryos were also investigated. Embryo implantation was defined as detection of a gestational sac and fetal heart beat.

RESULTS: Among 2891 biopsied blastocysts from 512 PGT-A cycles of 427 patients, 1945 did not have nondividing blastomere/fragmentation (67.3%) and 946 had (32.7%). Blastocysts without nondividing blastomeres had a significantly higher chance to be euploid (48.9% vs 40.6%, $p < 0.001$). This trend was also observed for each age group (<35, 35-37, 38-40, and >=41). On the other hand, higher percentage of euploid embryos containing nondividing blastomeres had complex chromosomal abnormalities (3 or more chromosomal abnormalities) (17.4% vs 10.2%). Embryo implantation rate of those euploid blastocysts without nondividing blastomeres was significantly higher than those with nondividing blastomeres (70.0% (255/366) vs 57.3% (75/131), $p<0.01$). More euploid blastocysts without nondividing blastomeres implanted for each patient group (<35, 35-37, >=38) (73.0%, 72.0%, and 60.2% respectively) as compared to those with nondividing blastomeres/fragmentation (66.1%, 55.6%, and 40% respectively) but their differences were not significant. Among the 28 euploid blastocysts with fragmentation, 19 implanted (67.9%). However, when there were 3 or more nondividing blastomeres in an euploid blastocyst, implantation rate (14/32, 43.8%) significantly decreased as compared to those with 1 or 2 nondividing blastomeres (42/74, 56.8%).

CONCLUSIONS: Our results showed that embryos with arrested nondividing blastomeres can maintain euploid and result in live births. However, its further developmental potential is compromised if remaining developing cells could not efficiently compensate the early cell loss. Our findings provide new insights regarding the extent to which blastocysts containing arrested blastomeres are capable of producing ongoing pregnancies.

SUPPORT: None.

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SHEDDING LIGHT ON THE PSYCHOLOGICAL AND DEMOGRAPHIC PREDICTORS OF GAY AND BISEXUAL MEN'S DESIRE FOR PARENTHOOD AND PREFERRED TIMING OF PARENTHOOD. Hoi Yan Celia Chan, PhD,[1] Yuen Kiu Georgina So, MSc,[2] Yu Te Huang, PhD[2] [1]The University of Hong Kong, Hong Kong, Hong Kong; [2]The University of Hong Kong.

OBJECTIVE: In spite of improved accessibility of ART to parenthood in some parts of the world, sexual minority individuals still face significant psychosocial barriers in actualising their desire to become parents. Having internalized negative beliefs about homosexuals and lacking social support from LGBT communities are detrimental to the mental well-being of sexual minority individuals. However, little is known whether these factors influence gay and bisexual men's decision to parent. The study addressed how internalized homophobia, minority stress, and connectedness with the LGBT community influenced Taiwanese gay and bisexual men's desire for and preferred timing of parenthood?

DESIGN: A cross-sectional online survey was conducted in May 2018, the time before legalisation of same-sex marriage in Taiwan. 1,381 Taiwanese men self-identified as either gay or bisexual were recruited.

MATERIALS AND METHODS: Primary outcomes of interest were whether respondents wish to have children (yes vs. no) and whether they wish to children before or after 35 years. Importance of childbearing, internalized homophobia, minority stress, LGBT community connectedness, and a select set of demographic variables were treated as predictor variables and entered into two hierarchical binary logistic regression models for estimation of parenthood desire and timing of parenthood, respectively.

RESULTS: Overall 74% of respondents reported a desire to have children. Wanting children was associated with being bisexual (β=0.94, p< .001), having a university degree (β=0.69, p< .01), and being in a more satisfactory relationship among those who have a partner (β=0.04, p< .001). Higher perceived importance of childbearing to the self (β=1.49, p< .001), the relationship with one's partner (β=0.40, p< .01) and parents (β=0.25, p< .01), but not importance of childbearing to one's partner, was associated with greater odds of wanting children. While controlling for these variables, higher levels of internalized homophobia uniquely predicted greater parenthood desire (β=0.03, p< .05), while minority stress and LGBT community connectedness were not significant predictors. A second set of analyses were performed to examine factors associated with the preference to delay parenthood. Age is the only demographic factor predicting the wish to delay parenthood (β=0.16, p< .001). Respondents who reported higher levels of community connectedness with the LGBT community had a greater tendency to wish to have children after the age of 35 (β=0.07, p< .01). Neither perceived importance of childbearing, internalized homophobia or minority stress played a role in predicting the wish to delay parenthood.

CONCLUSIONS: Gay and bisexual men's desire for and preferred timing of parenthood are influenced respectively by levels of internalized stigma and connectedness with the LGBT community. More systematic efforts should be directed at exploring factors that underline gay and bisexual men's perceived self-competence as parents, paying particular attention to internalized homophobia and LGBT community connectedness affecting parenthood decisions.

References: Nil

SUPPORT: Nil

P-968 3:30 PM Wednesday, October 21, 2020

RELATIONSHIP BETWEEN TEMPORAL CHANGES OF ENDOMETRIAL BLOOD FLOW IMPEDANCE IN A NATURAL AND HORMONE REPLACEMENT CYCLE AND PREDICTION OF PREGNANCY DURING VITRIFIED-WARMED EMBRYO TRANSFER. Toshifumi Takahashi, M.D., Kuniaki Ota, M.D. Fukushima Medical University, Fukushima, Japan.

OBJECTIVE: Frozen-thawed embryo transfer (ET) is performed in a natural or hormone replacement therapy (HRT) cycle for endometrial preparations. However, how to determine which endometrial preparation method is suitable for the individual is unknown.This study was to examine the relationship between the temporal changes in endometrial blood flow impedance during natural and HRT cycles and clinical outcomes in vitrified-warmed ET.

DESIGN: A single-center retrospective observational cohort study.

MATERIALS AND METHODS: This study was approved by the institutional review board of the Fukushima Medical University. This study

included a total of 60 women, 28 with natural and 32 with HRT cycles, who underwent vitrified-warmed ET. Uterine radial artery resistance index (RA-RI) was measured during the natural and HRT cycles at the early follicular phase, days of the human chorionic gonadotropin trigger during a natural cycle or start of progesterone administration during the HRT cycle, and the day of ET. The association between the RA-RI at the different measurement point and the pregnancy were examined in the natural and HRT cycles by univariate analysis and multivariate logistic analysis. Receiver-operating characteristic analysis was used to determine the cut-off value of the RI with respect to pregnancy in natural and HRT cycles. The area under the curves (AUC) and their 95% confidence intervals (CI) were calculated.

RESULTS: The clinical pregnancy rates of the natural and HRT cycles were 32.1% and 34.4%, respectively. In the univariate analysis, the RA-RI at the early follicular phase was significantly lower in the pregnant group than that in the non-pregnant group in the natural but not HRT cycle (P=0.04). In the multivariate logistic analysis, the RA-RI at the early follicular phase was an independent predictive factor for pregnancy in the natural but not HRT cycle (P=0.02). The odds ratio for pregnancy was 0.7 (95% CI, 0.52–0.95) when the levels of RA-RI at the early follicular phase was increased by 0.01 in the natural cycle. With the natural cycle, the area under the receiver-operating characteristic curves for the RA-RI at the early follicular phase with a threshold of 0.68 was 0.75 (95% CI, 0.57–0.93). The positive predictive and negative predictive values were 0.53 (95% CI, 0.37–0.59) and 0.92 (0.74–0.99), respectively.

CONCLUSIONS: With the natural cycle, the RA-RI at the early follicular phase was associated with pregnancy, and this might have a potential in predicting pregnancy in vitrified-warmed ET cycles. Our findings suggest that RA-RI at the early follicular phase might be an effective and useful tool in choosing natural or HRT cycles for vitrified-warmed ET. This provides a clue to the individualization of the choice of an endometrial preparation method during the frozen-thawed ET.

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"EVALUATION OF DUAL TRIGGER (GNRH AGONIST PLUS HCG) VS HCG IN IMPROVING IVF CYCLE OUTCOME IN NORMAL RESPONDER GROUP- A PROSPECTIVE RANDOMIZED CLINICAL STUDY. Ritika Gupta, MBBS, DNB (OBGY) FELLOWSHIP IN REPRODUCTIVE MEDICINE,[1] Sanjay Makwana, MBBS, MS, DIPLOMA IN REPRODUCTIVE MEDICINE,[2] Rahul K. Sen, MSC, PHD[3] [1]FELLOW, VASUNDHARA HOSPITAL AND FERTILITY CENTER, JODHPUR, INDIA, GURUGRAM, India; [2]MEDICAL DIRECTOR VASUNDHARA HOSPITAL AND FERTILITY CENTER, JODHPUR, INDIA, JODHPUR, India; [3]chief embryologist, vasundhara hospital, jodhpur, JODHPUR, India.

OBJECTIVE: To assess role of Dual trigger (GnRH agonist plus Human chorionic gonadotropin) vs Human chorionic gonadotropin (hCG) in optimizing GnRH antagonist IVF- ICSI cycle outcome in normal responder group.

DESIGN: A Prospective randomized clinical study.

MATERIALS AND METHODS: Normal responder patients were allocated in two groups: case group who has received dual trigger (GnRH agonist (Triptorelin 0.2 mg) + rec-HCG (Ovitrel 250 μg) and control group who has received rec-hCG (Ovitrel 250 μg) only for ovulation trigger. Follicular aspiration was done 35 hr after trigger. Outcome variables measured were no. of follicles $>$ 15 mm on trigger day, no. of COCs retrieved, no. of M II oocytes retrieved, proportion of MII Oocyte (MII oocyte/ total no of oocyte), no. of day 3 good quality embryos, positive β -hCG cases, implantation rate, clinical pregnancy rate (CPR).

RESULTS: Total 100 patients were included for study: 50 in study and 50 in control group. Both groups were similar in terms of age (28.62 vs 28.54, P= NS), BMI (24.27vs 24.49, P=NS), AMH (2.53vs2.69, P=NS), AFC (11.48vs12.02, P =NS). There was no significant difference in duration and etiology of infertility, length of stimulation and no. of follicles $>$ 15 mm on trigger day between case and control group. Total no. of OCC retrieved in case and control group was 10.92$\pm$2.59 and 10.54$\pm$2.96 respectively. There was no significant (p$>$0.7) difference in no. of oocytes between dual and hCG trigger group(P value=0.7, NS). There was significantly higher no. of MII oocytes (7.24$\pm$2.60 vs 6.68$\pm$2.28, P value=0.02) in dual trigger as compared to hCG trigger group. Proportion of MII oocytes (65.62 vs 62.85, P= 0.03) was significantly higher in dual trigger group. There was no significant difference in no. day 3 embryos (5.42vs 4.82, P value=0.25,NS), implantation rate (23.56 vs 21.35, P value=0.07,NS) and CPR(36.73 vs 34.7, P value=0.36,NS) between both groups. Though, clinical pregnancy rate was slightly higher in dual trigger group but difference was not significant.

CONCLUSIONS: Dual trigger improves the no. and proportion of MII oocytes as compared to hCG trigger alone in normal responder group. The promising effect of dual trigger in improving oocyte maturity may potentially be utilized in improving IVF cycle outcome. Further larger prospective trials are needed for validation of beneficial effect of dual trigger in normal responder patient in future.

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IMPACT OF 2008 AND COVID-19 ECONOMIC RECESSIONS ON FERTILITY TREATMENTS AND LIVE BIRTHS. Fady I. Sharara, M.D.,[1] Piotr Gromski, PhD,[2] Andrew D. A. C. Smith, PhD,[3] Deborah A. Lawlor, PhD,[4] Scott M. Nelson, MD, PhD[2] [1]Virginia Center for Reproductive Medicine, Reston, VA; [2]University of Glasgow, Glasgow, United Kingdom; [3]University of the West of England, Bristol, United Kingdom; [4]MRC Integrative Epidemiology Unit at the University of Bristol, Bristol, United Kingdom.

OBJECTIVE: The economic and reproductive medicine response to the COVID-19 pandemic in the United States has reduced the affordability and accessibility of fertility care. We sought to determine the impact of the 2008 financial and the COVID-19 recession on fertility treatments and cumulative live-births.

DESIGN: prospective projection modeling.

MATERIALS AND METHODS: We examined annual US natality, CDC IVF cycle activity and live birth data from 1999 to 2018 encompassing 3,286,349 treatment cycles, to estimate the age-stratified reduction in IVF cycles undertaken after the 2008 financial recession, with forward quantitative modelling of IVF cycle activity and cumulative live-births for 2020 to 2023.

RESULTS: The financial recession of 2008 caused a four-year plateau in fertility treatments with a predicted 53,026 (95% CI 49,581 to 56,471) fewer IVF cycles and 16,872

(95% CI 16,713 to 17,031) fewer live births. A similar scale of economic recession would cause 67,386 (95% CI: 61,686 to 73,086) fewer IVF cycles between 2020 and 2023, with women younger than 35 years overall undertaking 22,504 (95% CI 14,320 to 30,690) fewer cycles, as compared to 4,445 (95% CI 3,144 to 5749) fewer cycles in women over the age of 40 years. This equates to overall 25,143 (95% CI: 22,408 to 27,877) fewer predicted live-births from IVF, of which only 490 (95% CI 381 to 601) are anticipated to occur in women over the age of 40 years.

CONCLUSIONS: The COVID-19 recession could have a profound impact on US IVF live-birth rates in young women, further aggravating pre-existing declines in total fertility rates.

SUPPORT: None

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ALTERED FOLLICULAR FLUID MICRO RNA PROFILES IN POLYCYSTIC OVARIAN SYNDROME MAY SERVE AS PREDICTIVE BIOMARKERS OF OOCYTE MATURATION STAGE. Tamar Matitashvili, MD,[1] Sezgi Arpag, MSc,[2] Seifeldin Sadek, MD,[1] Gerard Celia, Jr., PhD,[1] Laurel Stadtmauer, MD, PhD,[1] Anca Dobrian, PhD[2] [1]Jones Institute, Norfolk, VA; [2]Eastern Virginia Medical School, Norfolk, VA.

OBJECTIVE: Our objective was to define extracellular vesicle's (EV) miRNA cargo in follicular fluid (FF) of polycystic ovarian syndrome (PCOS) and control patients to determine: potentially novel mechanistic pathways responsible for oocyte maturation and to establish correlations between EV miRNA cargo and oocyte maturation stage that could lead to discovery of novel biomarkers.

DESIGN: Prospective pilot study.

MATERIALS AND METHODS: Our study included 6 women diagnosed with PCOS based on Rotterdam criteria and 6 non-PCOS controls matched for age and BMI. Patients in both groups were on the standard gonadotropin releasing hormone antagonist protocol for controlled ovarian stimulation.

FF was obtained from the first punctured follicle in each ovary during oocyte retrieval, and further processed for isolation of small EVs using a commercially available kit. Following RNA extraction, miRNA composition was quantitated using the nanoString nCounter FLEX Analysis platform. Oocytes isolated from each of the individual follicles were scored for maturity staging, after the removal of cumulus cells. Comparisons between the two groups were performed using the Kruskal-Wallis test and correlations

between miRNA expression and clinical parameters were done using Spearman's non-parametric test.

RESULTS: In vitro fertilization cycle (IVF) characteristics, number of oocytes and blastocytes were not statistically different between the PCOS and control groups. FF-EVs were similarly in numbers and total amount of mRNA cargo. Out of 828 human miRNAs screened in the FF, expression of 19 miRNAs were above the detection limit. 7 miRNAs (miR-502-5p, miR-603, miR-548aa, miR-548t-3p, miR-1246, miR-548n, miR-627-5p and miR-4531) were exclusively found in PCOS samples and 2 miRNAs (miR-21-5p and miR-411-5p) were detectable in the non- PCOS group only. MiR-1253 and miR-302d-3p were present in both groups and were significantly lower in the PCOS group ($p<0.03$).

Using ingenuity pathway analysis (IPA) we identified 3930 potential miRNA-regulated target genes. One of the validated target genes of miR-302d-3p is FOXL-2, which is upregulated in the presence of miR-302d-3p. FOXL-2 is a transcription factor known to be involved in ovarian development. Knockout of FOXL-2 leads to formation of cystic follicles with an androgen predominant environment, which is a feature of PCOS.

To examine association between follicular fluid EV-miRNAs and oocyte maturity we compared FF samples that had metaphase II (MII) oocytes to those that had metaphase I (MI) or germinal vesicle. FF that contained MI oocytes had less miR-302d-3p compared to samples with MII oocytes ($p<0.01$).

CONCLUSIONS: MiR-302d-3p level in EVs of FF might become a potential biomarker used to predict oocyte maturity or fertilization rate in IVF subjects, including PCOS patients. Future studies focused on miR-302d-3p in oocyte development and further validation of this EV miRNA in FF could lead to a promising new biomarker to predict fertility rates or oocyte quality. This and other miRNAs can also reveal new pathways responsible for oocyte maturation arrest in PCOS patients.

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SARS-COV-2 HERD IMMUNITY, INFECTIVE AND NAÏVE INCIDENCE IN FERTILITY CLINICS AFTER PANDEMIC LOCKDOWN. A MULTICENTER STUDY. Russell A. Foulk, MD,[1] Denny Sakkas, PhD,[2] Refik Kayali, PhD,[3] Diana Valbuena, MD, PhD,[4] Carlos Simon, MD, PhD,[5] Juliana Cuzzi, PhD[3] [1]Utah Fertility Center, Pleasant Grove, UT; [2]Boston IVF, Waltham, MA; [3]Igenomix US, Miami, FL; [4]Igenomix, Paterna (Valencia), Spain; [5]Igenomix Foundation, INCLIVA, Valencia, Spain; Department of Obstetrics and Gynecology, Valencia University, valencia, Spain; Department of Obstetrics and Gynecology, BIDMC, Harvard University, Boston, MA- USA Boston, U.S.A., Valencia, Spain.

OBJECTIVE: COVID19 was declared a global pandemic by the WHO in March, 2020 and lockdown was imposed to a third of the world's population. Now, determining the transmission potential and immune status among sheltering in place asymptomatic patients and clinical staff resuming their activity is crucial. Here, we report herd immunity, infective, and naïve incidence for SARS-CoV-2 after the lockdown period, among asymptomatic medical personnel and patients in two US ART centers located in states with different COVID19 incidences.

DESIGN: Prospective multicenter study (ClinicalTrials.gov NCT04466644).

MATERIALS AND METHODS: A total of 339 asymptomatic individuals (personnel and patients) were analyzed from June 18 to July 30, 2020 in two ART centers reopening after lockdown following CDC safety guidelines. In Clinic A (Utah Fertility Center), located in a low prevalence State (312 cases per 100,000 on 06/01/2020), 154 individuals were analyzed. In clinic B (Boston IVF), in a high prevalence scenario (Massachusetts, 1,462 cases per 100,000 on 06/01/2020), 185 individuals were tested. Asymptomatic individuals attending or working in the indicated clinics were tested by RT-PCR on nasopharyngeal swab for SARS-CoV-2 RNA detection (Thermofisher, Waltham, MA, USA), and for IgG quantification on blood samples (Abbott Inc, Scarborough, ME, USA), following FDA-Emergency Use Authorization protocols. IRB approval was obtained from WIRB Protocol #20201490.

TABLE 1. Incidence of immune, infective, and naïve individuals for COVID19.

	IMMUNE RT-PCR (-)/ IgG(+)	INFECTIVE RT-PCR (+)	NAÏVE RT-PCR (-)/IgG (-)
CLINIC A	**0.65%** (1/154)	**0.65%** (1/154)	**98.7%** (152/154)
CLINIC B	**2.2%** (4/183)	**0.5%** (1/183)	**97.3%** (178/183)

RESULTS: From 339 asymptomatic individuals tested, the percentage of non-informativity was 0 for RT-PCR and 0.6% (2 out of 339) for the IgG test. Only those individuals with informative results for both tests (n= 337) are presented.

CONCLUSIONS: In the population investigated, our results suggest that the impact of the pandemic is far from reaching the level required to achieve herd immunity (i.e., 50% of a population). Therefore, transmission remains a risk since potential infectivity is present in 0.6% of the asymptomatic population tested. This figure was maintained despite their different geographical locations and the adherence to CDC guidelines of the IVF clinics involved. Interestingly, the two PCR+ individuals were IgG + suggesting virus persistence or reinfection that, if tested by serology alone, would be considered immune. These results together with the high incidence of naive individuals draws attention for the implementation of a consistent program of testing for COVID19 as a means of preventing reemerging outbreaks in our fertility centers.

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IMPACT OF ENDOCRINE DISRUPTOR LEVELS FOUND IN URINE AND FOLLICULAR FLUID ON CLINICAL PARAMETERS OF IVF PATIENTS IN A EUPLOID SET/FET CYCLE. Andrea Palomar, MSc,[1] Roberto Gonzalez-Martin, MSc,[1] Caroline Zuckerman, BS,[2] Christine V. Whitehead, BSN, RN,[2] Richard Thomas Scott, Jr., MD,[2] Francisco Dominguez, Ph.D.[1] [1]IVI Foundation - ISSLaFe Biomedical Research Institute, Valencia, Spain,; [2]IVI RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: Exposure to certain exogenous compounds associated with lifestyle habits has become a risk factor that could threaten reproductive success. This heterogeneous group of compounds known as endocrine disruptors (ED), which are present in the patient's daily intake, such as phytoestrogens (daidzein, genistein), parabens (beauty products) and phthalates (daily use plastics) play a major role in infertility-related problems. As there is a pressing need to investigate the effect EDs have on human reproduction, this research aimed to detect a set of non-persistent ED in urine and follicular fluid (FF) samples of women undergoing infertility treatment to establish its impact on IVF clinical parameters.

DESIGN: 60 patients attending IVI-RMA New Jersey undergoing an euploid single frozen embryo transfer (SET/FET) after PGT-A analysis were included in this study. All patients recruited were age 18 to 42 years old and had a BMI of 18.5 to 29.9 kg/m^2. Urine collected at oocyte retrieval and FET as well as FF from patients were analysed by liquid chromatography coupled to mass spectometry (HPLC-MS) for mono(2-ethylhexyl) phthalate (MEHP), methyl-paraben (m-Par), propyl-paraben (p-PAR), daidzein and genistein. These measurements were correlated with pre-implantation IVF clinical parameters.

MATERIALS AND METHODS: Patients included underwent PGT-SET/FET cycles following standard protocols. Measurements of ED levels in FF and urine collected at two different time-points were performed by HPLC-MS (Triple Quad 1290-6460, Agilent) with internal standards for each compound tested. Urine ED levels were normalized by creatinine and measured by Jaffe reaction (R&D Systems). Number of oocytes retrieved, oocyte maturation, fertilization, blastocyst development and aneuploid rates were correlated with ED levels using Poisson regression models.

RESULTS: Among all compounds and clinical outcomes analyzed, only MEHP levels show an outstanding relative effect on the number of oocytes recovered in patients. Specifically, MEHP found in FF showed the highest relative effect over number of oocytes recovered (-31.37; [95% CI: -53.57, -9.17]; $p=0.0056$). This effect is also observable in urine collected at the oocyte retrieval (-9.37 [-17.15, -1.59]; $p=0.0182$). The impact of MEHP levels is maintained in urine collected at the time of embryo transfer, although the relative effect is lower (-1.16; [-2.65, 0.32]; $p=0.1247$) possibly due to its non-persistent nature. No significant effect was found in fertilization, blastocyst development or aneuploid rates in these patients.

CONCLUSIONS: This study suggests that among all EDs found in urine and FF of the patients, high levels of MEHP correlates with fewer retrieved oocytes, thus threatening the chances of reproductive success. Urine and FF levels of MEHP at the time of oocyte retrieval may indicate the damaging effect of this compound on oocyte development. Therefore, it is essential to reduce the patient's exposure to this kind of compound during ovarian

stimulation to minimize its impact on the number of oocytes retrieved to allow maximum optimization of IVF treatments.

SUPPORT: This research is supported by predoctoral contract for training in research into health (PFIS; PI/00009), APOTIP/2018/010, Miguel Servet Contract (CPII18/00002) and ISCIII FIS project (PI17/00931)

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MAY AUTOIMMUNE DISEASE BE A PREDICTOR FACTOR OF INFERTILITY IN WOMEN WITH ENDOMETRIOSIS? Larissa Milani Coutinho, Doctorate student, Gabriel Duque Pannain, Medical doctor, Luzia Ribeiro Nasser Salomão, Medical doctor Universidade Federal de Juiz de Fora, JUIZ DE FORA, Brazil.

OBJECTIVE: Although endometriosis physiopathology has not been totally clarified yet, it must be a multifactorial disease and immune pathways may take part of the onset and progression of the disease. A recent meta-analysis has suggested that patients with endometriosis are at higher risk to have at least one other immune condition, such as rheumatoid arthritis (RA), autoimmune thyroid disorder (ATD), inflammatory bowel disease (IBD). Maybe the high levels of inflammation related to endometriosis might be associated to an imbalance of immune response. Infertility is a frequent consequence of endometriosis. Although the mechanisms capable to explain endometriosis-associated infertility remain obscure, studies have shown that inflammatory and immune factors may take a role in the process as well. We aimed to investigate whether autoimmune diseases could be associated to the occurrence of infertility in patients with endometriosis.

DESIGN: A retrospective study was performed at a Public University Hospital, by analyzing medical records of all the 162 patients with a diagnosis of endometriosis, followed up in the Endometriosis specific outpatient clinic, since its creation, in February 2017, until March 2020.

MATERIALS AND METHODS: After excluding patients with other causes of infertility aside endometriosis, patients that had never tried to conceive and those who had achieved pregnancy after a surgical treatment, the remaining patients were divided in two groups: fertile (n=61) and infertile (n=86). The two groups were analyzed for socio demographic variables as well as features related to the disease and the association with autoimmune disease. Among autoimmune diseases, we observed patients with hypothyroidism (5), type 1 diabetes (4), ulcerative colitis (2) and rheumatoid arthritis (1).

RESULTS: It was a sample composed by 162 women aged between 19 and 53 years old with an average age of 35.2 years and standard deviation of 7.23. After analyzing the two groups, we calculated logistic regression to verify whether it is possible to correlate the variable presence of autoimmune disease with the infertility outcome. For autoimmune disease, the confidence interval was from 1.194 to 17.802 to 95% with a p-value of 0.027, corroborating that there is a correlation between autoimmune diseases and infertility in patients in this sample. We also calculated the prevalence ratio in these patients, which was higher in patients with autoimmune disease than in those without (mean of 1.527, being 1.439 the lower and 1.615 the upper bound with 95% confidence interval).

CONCLUSIONS: Despite of the scarcity of data associating endometriosis and autoimmune disease, the coexistence of such conditions might be related to a greater difficult in achieving pregnancy. Maybe patients presenting both diagnosis should be advised to pay special attention to their reproductive plans, by avoiding postponing either natural attempt to get pregnant or fertility treatments when indicated. For those women with no current plans to conceive, an interesting strategy would be to offer the possibility of performing social oocyte cryopreservation.

SUPPORT: No financial support was given.

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ASSESSING FERTILITY AWARENESS IN WOMEN IN AN INNER NEW YORK CITY HOSPITAL. Janelle M. Jackman, MBBS,[1] Fernando Polanco, MD,[2] Shelena Ali-Bynom, M.D., M.P.H,[3] Natasha Fievre, MD[3] [1]Camran Nezhat Institute, Center for Special Minimally Invasive and Robotic surgery, Stanford University Medical Center, New York, CA; [2]Providence Hood River Hospital, Hood River, OR; [3]The Brooklyn Hospital Center, Brooklyn, NY.

OBJECTIVE: Maternal age is the single most important determinant of fertility. Ovarian function declines as women age and fertility naturally declines around mid-thirties.However childbearing has increased between the ages of 35 to 39 years. Increased maternal age may also affect maternal and fetal health, leading to permanent chronic conditions. Fertility literature has suggested that female fertility and reproduction biology awareness is poor. This is especially true for women in lower socioeconomic groups and minorities who may not have access to health care education. This study aimed to look at fertility awareness in women at a single NYC community hospital.

DESIGN: An anonymous cross sectional survey administered in an OB-GYN clinic at a single NYC community hospital.

MATERIALS AND METHODS: An anonymous cross sectional survey was administered at an OBGYN clinic between April and July 2019. Patients participated voluntarily and their participation implied consent. They were asked a series of 28 fertility related questions and all information was anonymous. Inclusion criteria was all willing women at the clinic over the age of 18 years old. Statistical analysis utilized descriptive statistics, the Students t-test for equality of means and linear regression. Probability outcomes <0.05, were statistically significant.

RESULTS: There were 66 patients who participated in the survey. African Americans ethnicity made up 66% of the patients, 24% were Hispanic and 10% comprised of Caucasian, Middle Eastern and Asian. Around 92% had greater than high school education. The majority of patients,73% knew that complications increased in pregnancies in women greater than 35 years. However, an alarming 28% believed that age did not affect fertility and 59% of them stated if they knew, they would have began childbearing earlier. Patients with a history of infertility were slightly more knowledgable on age and infertility but this difference was not statistically significant. Our results showed that nulliparous patients were less educated about age of decreased fertility (0% vs 13%) compared to multiparous patients, however overall there was a low correct response to this question (11%).

CONCLUSIONS: Our results show that there is a need for greater education regarding the decline in fertility in women with respect to age and other factors that affect fertility. This will assist in women being able to make well informed family planning decisions. Factors such as our race, ethnicity and socioeconomic status should not play a role in health care access or education. More research is needed to fully understand the barriers to health and health education as well to determine ways to decrease health disparities and ensure patients are knowledgeable about their fertility and health.

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CLINICIAN TRAINING NEEDS IN REPRODUCTIVE HEALTH COUNSELING FOR SEXUAL AND GENDER MINORITY AYA WITH CANCER. Gwendolyn P. Quinn, Ph.D.,[1] Amani Sampson, B.A.,[1] Ash B. Alpert, M.D.,[2] Rhyan Jenifer Toledo, BA,[1] Megan E. Sutter, PhD,[3] Paige W. Lake, MPH,[4] Matthew B. Schabath, Ph.D.,[4] Susan T. Vadaparampil, Ph.D.[4] [1]NYU Langone School of Medicine, New York, NY; [2]URMC, Rochester, NY; [3]NYU Langone Health, New York, NY; [4]Moffitt Cancer Center, Tampa, FL.

OBJECTIVE: Adolescent and young adults (AYA) with cancer have distinct psychosocial needs, with reproductive health being a chief concern. Reproductive health includes fertility, contraception, romantic relationships, body image, sexuality and disease prevention. Along with the unique needs of AYAs with cancer, health disparities exist among sexual and gender minority (SGM) AYAs, and there is a gap in clinician training. Our NCI-funded R25 Enriching Communication skills for Health professionals in Oncofertility (ECHO) provides reproductive health communication training to psychologists, social workers, nurses, and physician assistants who provide care for AYA people diagnosed with cancer. To refine our curriculum to address the unique needs of SGM AYAs with cancer, we conducted a survey of prior ECHO trainees to evaluate knowledge and comfort in obtaining sexual orientation and gender identity (SOGI) information from patients and providing reproductive health counseling.

DESIGN: A 28-item electronic survey was distributed to 601 prior ECHO trainees.

MATERIALS AND METHODS: Quantitative items assessed: SOGI data collection at their institution; SGM AYA cancer-related health knowledge; adequacy of ECHO training for SGM AYAs; desire for additional training; comfort discussing reproductive health with SGMs; and confidence in knowledge of SGM health needs *(pre- and post-survey)*. Response options ranged from 1=strongly agree to 5=strongly disagree, or 'prefer not to answer. Total knowledge score was computed and ranged from 0=no correct responses to 7=all correct. Self-perceived comfort and confidence were assessed with regard to specific patient subgroups (i.e., gay/lesbian; bisexual/queer; and trans/nonbinary patients). Four open-ended items invited respondents to describe personal experiences, reservations, and suggestions for improving SGM AYA cancer care. Quantitative responses were summarized with descriptive statistics. Paired t-tests were used to analyze changes in confidence. Content analysis was applied to qualitative responses.

RESULTS: Of the 346 who completed the survey (58% response rate), only 7.4% correctly answered all knowledge questions (M=3.76, SD=1.72). One-third thought ECHO training adequately addresses SGM needs, and the majority (89%) wanted additional training in SGM reproductive health. Confidence in knowledge of SGM health was neutral in all subgroups prior to survey completion (M=3.05, SD=1.02), but reduced significantly for bisexual/queer (ΔM=-0.21 $t(307)$=4.70, $p<.001$) and transgender/nonbinary health(ΔM=-0.12 $t(307)$=2.66, $p=.008$). Open-ended responses focused on experiences caring for SGM AYAs with cancer; training needs; and appreciation for the survey.

CONCLUSIONS: Results demonstrate a need to refine ECHO curriculum to include SGM reproductive health concerns and strong desire for SGM content among trainees. We are developing a module to improve reproductive health communication for the care of SGM AYAs with cancer and survivors.

SUPPORT: NCI 3R25CA142519-09S1

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IMPACT OF AMBIENT TEMPERATURE ON OVARIAN RESERVE AMONG WOMEN FROM A FERTILITY CLINIC.

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OBJECTIVE: In most mammalian species, heat stress caused by high ambient temperatures has a deleterious effect on reproductive function including impaired follicular growth. Recent climate projections predict that heat waves will increase in frequency, intensity, and duration, necessitating the need to better understand the relationship between temperature and reproductive health in humans. Our objective was to determine the effect of ambient temperature and extreme weather events on antral follicle growth among women attending an infertility clinic.

DESIGN: Our prospective cohort study included 632 women attending the Massachusetts General Hospital Fertility Center (2005-2015) who had an antral follicle count (AFC) measured with transvaginal ultrasonography.

MATERIALS AND METHODS: We collected data on the daily average, maximum, minimum, and apparent temperatures at a woman's residential address for the 90 days prior to their antral follicle scan using information from the Parameter-elevation Regressions on Independent Slopes Model at a 4 km^2 resolution. Heatwaves and cold spells were defined as $\geq$3 consecutive days where the maximum temperature exceeded the 99th or fell below the 1st percentile for the region, respectively. We evaluated the association of AFC with ambient temperature and extreme weather events using Poisson regression, adjusting for relative humidity, fine particulate matter exposure, age, education, smoking status, year and month of AFC, and diagnosis of diminished ovarian reserve and ovulation disorders.

RESULTS: High ambient temperatures during 3 months prior to antral follicle scan (corresponding to exposure during the preantral to preovulatory stages of follicular development) were associated with lower AFC. Specifically, a 1°C increase in average maximum temperature was associated with a -1.6% (95% CI -2.8, -0.4) lower AFC. Associations remained negative, but were attenuated, for average maximum temperature exposure in the month (-0.9% 95% CI -1.8, 0.1) and 2 weeks (-0.8 95% CI -1.6, 0.0) prior to antral follicle scan. The negative association between average maximum temperature and AFC was stronger among women who had their antral follicle scans performed November through June, where average maximum temperatures ranged from 0 to 23 °C, rather than during the summer months (July-October). Exposure to a heatwave in the 3 months prior to AFC was associated with a -7.2% (95% CI -14.9, 1.3) lower AFC while exposure to a cold spell was associated with a 14.3% (95% CI 2.0, 28.2) higher AFC.

CONCLUSIONS: Exposure to higher than average temperatures, particularly outside of the summer months, were associated with lower ovarian reserve. These preliminary results raise concern that rising ambient temperatures worldwide may result in accelerated reproductive aging among women.

SUPPORT: This work was funded in part by P30ES000002, R01ES009718, R01ES022955, and R00ES026648 from NIEHS and RD-834798 and RD-83587201 from US EPA.

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A CROSS-SECTIONAL SURVEY OF TAIWANESE GAY AND BISEXUAL MEN'S PARENTHOOD DESIRES AND PREFERRED MEANS OF FAMILY FORMATION.

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OBJECTIVE: Desires for parenthood and knowledge about the means to parenthood are important determinants of reproductive behaviours. Despite ART and adoption becoming more accessible in select parts of the world, sexual minority individuals consistently report lower desire for parenthood and anticipated higher levels of stigma surrounding parenthood than did heterosexual individuals. While there is a burgeoning literature on parenthood orientations, attitudes and demographic composition among same-sex couples, gay men, and, to a larger extent, bisexual men, are significantly under-represented. The study investigated the parenthood desires and preferred methods of family formation among Taiwanese gay and bisexual men before legalization of same-sex marriage in Taiwan.

DESIGN: A cross-sectional online survey was administered to Taiwanese men who self-identified as gay or bisexual recruited through social media. Data collection took place before legalization of same-sex marriage in Taiwan in May 2018.

MATERIALS AND METHODS: Respondents completed an online survey with a list of items relating to their parenthood desires, preferred method(s) of family formation, and reproductive awareness for respondents who endorsed surrogacy and ART as a preferred method. Men who self-identified as transgender, queer and asexual were precluded from analyses due to small cell sizes, yielding a final sample of 1,381 men. Variables were compared between age and other demographic groups using independent-samples t-tests or chi-squared tests.

RESULTS: Respondents were on average 27, the majority were homosexual, employed, university-educated, and non-religious. Among the 1,023 (74%) respondents who desire to have children, they desire to have two children, and to have the first child at 32 years and the last child no later than 43 years. Adoption was the most preferred method of family formation (83%), followed by surrogacy and ART (73%) and marriage with an opposite sex (12%). Surrogacy and medically assisted reproduction is more frequently desired among men aged 35 or above (82% in men aged >35 vs. 69% in men aged 18-24, $p<.05$), and among men who preferred to have the first child after 35 years (77% first child after 35 years vs. 61% first child before 35 years, $p<.05$). However, among those who preferred surrogacy and assisted reproduction, only 6% had ever received semen analysis, and over 17% had no knowledge of the legality of surrogacy arrangements in Taiwan. Further, bisexual men were more likely than homosexual men to endorse marriage with an opposite sex as a preferred method of family formation (36% vs. 6%, $p<.001$). Preferred method of family formation is not correlated with relationship status or education level.

CONCLUSIONS: The majority of gay and bisexual men wish to have children via adoption or surrogacy and ART albeit reporting low reproductive awareness. The rarity of fertility-optimising behaviours and inadequate awareness of legality issues in this Taiwanese sample highlights the importance for accessible fertility- and treatment-/adoption-related resources among sexual minority communities.

References: Nil

SUPPORT: Nil

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NOVEL INDICES FOR THE EVALUATION OF OBESITY IN ERECTILE DYSFUNCTION PATIENTS. Sujith M. Jose, MBBS, MS, MCh, Vaibhav Vishal, MBBS, MS, MCh, Alphonse Jithin Jayan, MBBS, MS, MCh. Urology Resident, calicut, India.

OBJECTIVE: The association between Metabolic Syndrome (MetS) and erectile dysfunction(ED) is bidirectional. Inflammatory mediators from the visceral fat induce oxidative damages in the penile microvasculature resulting in ED. Waist circumference(WC) is not a reliable indicator of visceral fat as it includes subcutaneous fat also. Greater prevalence of MetS in Asian men compared to African-American men with the same WC is due to the relatively higher levels of visceral fat in them. Visceral Adiposity Index (VAI) and Lipid Accumulation Product (VAP) are novel indices that include functional parameters along with anthropometric parameters and gives better assessment of visceral adipose dysfunction.The purpose of the study is to investigate the potential link between these novel indices and ED severity.

DESIGN: Observational Cross-sectional study.

MATERIALS AND METHODS: In this study,ED patients were divided into mild ED group (score >11) and severe ED group (score ≤11) based on International index of Erectile Function-5 scores. WC, Body Mass Index(-BMI) and lipid profile were obtained and VAI, LAP were calculated using formulas, VAI=WC/[39.68+(1.88×BMI]×triglycerides/1.03×1.31/high density lipoprotein and LAP=[WC–65]×triglycerides.Mean, standard deviation and p values were calculated using appropriate formulas and p value<0.05 was accepted as statistically significant.

RESULTS: Of 116 men included in the study, 60 had mild ED and 56 had severe ED. Mean age was 51.83±6.2 for mild ED group and 52.16±5.8 for severe ED group. Mean VAI was statistically significantly higher in severe ED group compared to mild ED group (8.452±2.33 vs 4.753 ±1.52 ;p <0.001). Mean LAP was also significantly higher in severe ED group (89.427±31.48 vs 52.21± 29.96;p< 0.001). Interesting, difference in WC(95.5±9.5 vs 95±8.5 ; p =0.146) and BMI(26.48± 3.72 vs 24.67 ± 4.15; p= 0.363)was not statistically significant among two groups.Mean serum estradiol level showed a statistically significant difference among two groups (110.4 ± 43.8 vs 99.87 ± 45.7 ; p<0.001).

CONCLUSIONS: VAI and LAP have stronger correlation with ED severity than single antrapometric tools.Severe ED patients have higher estradiol level compared to mild and moderate ED patients due to their higher visceral fat and VAI. Considering the simplicity and reliability, these novel indices should be included in the evaluation of obese ED patients.

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RISK FACTOR ANALYSIS FOR SARS-COV-2 SERO-POSITIVITY WITHIN ASSISTED REPRODUCTIVE. Nicolás Prados, PhD MSc,[1] Cristina González-Ravina, PhD,[2] Vanessa Vergara, MD,[1] Javier Herrero, MSc,[1] María Cruz, PhD,[1] Antonio Requena, PhD, MD.[1] [1]IVIRMA Global Headquarters, Madrid, Spain; [2]IVIRMA Global Headquarters, Sevilla, Spain.

OBJECTIVE: Making decisions about how to fight the SARS-CoV-2 pandemic without completely disrupting our activity requires better tools that inform the extent of transmission. Understanding risk factors of virus susceptibility could help us to establish intervention policies. The objective of our work is to assess risk factors and seroprevalence in our patients in order to plan evidence-based strategies.

DESIGN: Multicenter retrospective, anonymized cohort analysis performed in 11 private clinics belonging to the IVIRMA group in Spain.

MATERIALS AND METHODS: Between April 27th and June 26th, 2020, 6140 individuals undergoing an assisted reproductive treatment were tested for SARS-CoV-2. Before tested, a symptomatic triage had been carried out and only patients classified with a negative triage attended the clinic for further testing. SARS-CoV-2 specific IgG and IgM antibodies in serum were detected using EDI Novel Coronavirus COVID-19 ELISA kit (Epitope Diagnostics, USA) according to the manufacturer's instructions. We divided our clinics into two different geographic areas: region A (seroprevalence <5%) and region B (seroprevalence >5%) based on the results obtained in our population. Statistical analyses were performed using the Statistical Package for Social Sciences 19.0 (IBM Corporation, Armonk, NY, USA).

RESULTS: Of the 6140 persons tested for SARS-CoV-2, 4470 (72.8%) were women and 1670 (27.2%) men. Over the course of the study, 42 (0.7%) tested positive for SARS-CoV-2 IgM antibodies. Seropositivity does not vary significantly with age and we did not observe differences regarding gender or blood group. However, we found that individuals with negative rhesus (Rh) factor had a slightly greater risk of being seropositive (RR 2.5 [129-2.13]) than those Rh positive. There are no differences in the percentage of people in the active phase of the disease depending on the geographical area (RR 0.8 [0.43-1.52]). However, when we analysed the data according to time, the rate of positive individuals does not vary throughout the weeks in region A, while for the region B the incidence of IgM drops significantly (p=0.003) from the first week of the study (3.7%) to the last (0.0%), which would indicate decline of the virus transmission over time. When we analysed the seropositivity rate according the partner's serological status, the data showed that there is approximately 10 times more incidence of being positive IgG in couples than in random population.

CONCLUSIONS: We show that in areas with higher prevalence of the disease, the percentage of IgM positive individuals is also higher. Also, there is a greater risk of being infected when the couple is already seropositive. No differences were observed according the age and there is higher prevalence in Rh-negative individuals.

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IDENTIFICATION OF NOVEL MUTATIONS IN CANDIDATE GENES ASSOCIATED WITH POLYCYSTIC OVARY SYNDROME (PCOS) IN WOMEN WITH ARAB ETHNICITY. Maha Al-Khaduri, MD FRCSC,[1] Fatima Ahmed Al Kindi, Bsc, Msc,[2] Yahya Tamimi, Msc, Phd,[2] Ammar Hamed Nomani, Bsc,[2] Yahya M. Al-Farsi, MD Phd.[2] [1]College of Medicine, Sultan Qaboos University, Muscat, Oman; [2]College of Medicine, Sultan Qaboos University, Al Khodh, Oman.

OBJECTIVE: There is a genetic component to the etiology of Polycystic Ovary Syndrome (PCOS) with candidate genes identified by Genome-wide studies in Chinese and European populations. However, in Middle Eastern populations, where genes are expected to be concentrated due to prevalence of consanguineous marriages, this is not yet explored. To our knowledge this is the first study analyzing 11 candidate genes by exome sequencing in women of Arab ethnicity diagnosed with PCOS.

DESIGN: Prospective case control study.

MATERIALS AND METHODS: A sample size of 49 cases and 49 controls was estimated for a significance level of 5% at 60% power, with minor allele frequencies of 12% and 1% in cases and controls respectively with a 1:1 ratio. We recruited 50 cases and 50 controls (Omani women) from the Gynecology clinic at Sultan Qaboos University Hospital in Oman. All cases fulfilled the Rotterdam criteria for PCOS. Controls were randomly selected from non-pregnant women within reproductive age who were not diagnosed with PCOS. Genetic disorders, congenital adrenal hyperplasia, androgen secreting tumors, Cushing syndrome, and hyperprolactinemia were excluded. The data collected included family history of PCOS, parental consanguinity, biochemical laboratory test results, physical examination and pelvic ultrasound findings. Targeted Exome Sequencing using a custom gene panel of 11 genes [LEPR, THADA, LHCGR, FSHR, YAP1, SUOX, DENND1A, VDR, VEGFA, CYP1A1, KISS1] was conducted on DNA extracted from blood samples of cases and controls then data was analyzed using ANNOVAR software to identify variants with a frequency less than 1%.

RESULTS: Family history of PCOS was significantly higher among cases (46.9%) than controls (16.0%), P=0.001. Parental consanguinity was prevalent in both cases (26.6%) and controls (38%). Infertility, an-ovulation, Luteinizing hormone, anti-Mullerian hormone, total Testosterone and Thyroid Stimulating Hormone (TSH) were significantly higher among cases (P<0.05). There was an association between TSH and fasting insulin (OR=1.30). We found three nonsynonymous variants in the LEPR gene, two of which were predicted by SIFT software to be harmful (pathogenic). In the THADA gene, one nonsynonymous mutation, found in three patients was predicted to be pathogenic, in addition to one novel non-frameshift deletion found in one patient. A controversial novel nonsynonymous variant was found in the LHCGR gene, predicted as neutral, and disease-causing mutation by SIFT software, and mutation tester, respectively. Another nonsynonymous variant was found to be novel, and pathogenic in the FSHR gene. Moreover, in the YAP1 gene, a nonsynonymous variant was detected and predicted by SIFT and other software to be neutral (nonpathogenic). Two nonsynonymous variants were found in the SUOX gene, with one of the variants reported in Clinvar with uncertain significance related to sulfite oxidase deficiency condition. The other variant was found to be tolerated with no effect on protein function.

CONCLUSIONS: We report Novel mutations in THADA, LHCGR and FSHR genes in Omani women of Arab ethnicity diagnosed with PCOS.

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PREGNANCY OUTCOMES IN FEMALE PATIENTS EXPOSING TO CYCLOSPORIN VERSUS TACROLIMUS AS PRIMARY IMMUNOSUPPRESSION AFTER SOLID ORGAN TRANSPLANTATION: A SYSTEMATIC REVIEW AND META-ANALYSIS.

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OBJECTIVE: Tacrolimus and cyclosporin are both calcineurin inhibitors (CNIs) recommended as first-line immunosuppressants for solid organ transplantation, we aim to compare the influences of tacrolimus and cyclosporin on pregnancy outcomes for female transplant recipients.

DESIGN: Systematically review of observational studies comparing pregnancy outcomes of tacrolimus and cyclosporin as primary immunosuppression after solid organ transplantation.

MATERIALS AND METHODS: A comprehensive literature search was conducted between January 1, 2000 and March 20, 2020 according to the database of PubMed, EMBASE, and Web of Science. The following combination of text terms was searched in [Title]: Transplant / Transplants / Grafts / Graft / Transplantations / Transplantation, and Pregnancy / Pregnancies / Gestation / Pregnant / Gravidity / Gravidities. Weighted mean difference (WMD) and odds ratio (OR) was calculated to compare continuous and dichotomous variables respectively with 95% confidence intervals (CIs). Publication bias was estimated by funnel plots. Quality of study was assessed according to the modified Newcastle-Ottawa scale.

RESULTS: 24 observational studies including a total of 1492 pregnant post-transplant recipients were identified in our analysis. Tacrolimus-treated recipients experienced lower risk of gestational hypertension (44.6% vs 29.0%; OR:1.58; 95% CI,1.20-2.08; $P < 0.01$) and infections (24.7% vs 13.6%; OR:1.87; 95% CI, 1.25-2.80; $P < 0.01$). Cyclosporin-treated recipients showed a lower incidence of abortions (16.7% vs 25.5%; OR: 0.59; 95% CI, 0.41-0.86; $P < 0.01$), gestational diabetes (2.3% vs 9.3%; OR: 0.24; 95% CI, 0.13-0.44; $P < 0.00001$) and cesarean section (41.7% vs 48.8%; OR:0.71; 95% CI, 0.54-0.93; $P = 0.01$). Additionally, cyclosporin performed better regarding the live birth rate (78.4% vs 70.8%; OR: 1.43; 95% CI, 1.08-1.87; $P = 0.01$). There were no significant differences in the incidences of preeclampsia, postpartum rejection, preterm delivery and low birth weight.

CONCLUSIONS: Cyclosporin is safer in delivery outcomes, while tacrolimus is associated with lower risk of maternal complications except gestational diabetes.

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EVALUATING THE UTILITY OF A GLOBAL WEBINAR FOR MENTORING MEDICAL STUDENTS AND OB-GYN RESIDENTS IN REI.

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OBJECTIVE: The aim of this study is to evaluate the effectiveness of a live Q&A webinar on improving trainees' access to mentorship and knowledge of the path to becoming a reproductive endocrinology and infertility (REI) physician.

DESIGN: Prospective Paired Cohort Study.

MATERIALS AND METHODS: US and international medical students and OBGYN residents participated in a global live Q&A webinar featuring REI physicians and fellows. Webinar surveys were given and a total of 161 pre-webinar and 73 post-webinar surveys were reviewed. After application of exclusion criteria, 70 pre- and post-webinar surveys were compared. Paired nonparametric tests (Wilcoxon Signed-Rank Test) were performed to assess whether post-webinar knowledge was significantly different from pre-webinar knowledge.

RESULTS: In total, 268 people registered for the webinar and 162 attended live (60%). The majority of the 70 respondents who completed both surveys were female (90%) and MD medical students (80%). Of the respondents, only 31% reported their home institution had an REI fellowship program and 37% an affiliated REI office. Only 34% had previously shadowed an REI physician and 23% had rotated in an REI office. Thirty-three percent reported it was not easy and 13% it was extremely not easy to find research opportunities within the field of REI in medical school or residency, while 14% reported it was easy, and 39% unsure. Seventy-seven percent reported receiving minimal advice about a career in REI from their medical school or residency program, while 22% reported receiving some advice, and 1% extensive advice.

After the webinar, participants were more likely to report that social media can be utilized by trainees to connect with REI physicians to find networking and mentoring opportunities ($P = .022$) and they were more likely to use social media (ex. Instagram) to network with physicians and potential mentors ($P = .041$). When asked to what extent they agree that their interest in REI increased due to this webinar, 39% strongly agreed, 43% agreed, 13% were unsure, and 6% disagreed.

Overall, after the webinar, more trainees reported a better understanding of what the field of REI entails ($P = <.00001$), the path required to become an REI ($P = <.00001$), opportunities to find mentors in the field of REI ($P = <.00001$), opportunities at medical school or residency conducive to learning more about REI ($P = <.00001$), and applying for rotations in the field of REI ($P = <.00001$).

CONCLUSIONS: Most medical students and OBGYN residents have difficulty finding mentorship and research opportunities within the field of REI as many institutions do not provide trainees with opportunities to learn about the specialty. A webinar featuring REI physicians and fellows can provide the much-needed mentorship for trainees to help increase their interest in REI and provide them with advice regarding pursuing a career in the field. Additionally, trainees can utilize social media to connect with REI physicians and fellows to find mentorship, research, and networking opportunities within the specialty.

SUPPORT: None

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OOCYTE VITRIFICATION CAN ALTER OOCYTE AND EMBRYO REPAIR PROCEEDS IN CONFRONTING WITH SPERM DNA DAMAGE.

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Parameters	Untreated Sperm	0.2 LD50 treated Sperm	0.3 LD50 treated Sperm
Round spermatids	44.47±10.55[a]	35.29±16.89[b]	37.05±15.51[b]
Elongated spermatids	36.84±11.97[a]	31.04±16.67[b]	28.89±12.98[b]
Spermatogonial stem-cells	10.89±5.90	12.44±6.17	12.36±6.40
Concentration (M/ml)	10.72±5.77	7.13±3.47	6.34±2.30
	Non-vitrified Oocytes		
Fertilization rate (%)	96.42±9.44	96.77±6.32	89.11±16.16
Blastocyst rate (%)	56.01±18.40	32.40±20.04	21.80±14.58
	Vitrified Oocytes		
Fertilization rate (%)	96.75±8.59	86.84±18.61	93.67±11.71
Blastocyst rate (%)	27.26±18.91	13.54±12.92	9.66±13.30

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OBJECTIVE: Oocyte vitrification has different effects on mitochondrial function, gene expression and overexpression of repair proteins after vitrification and warming. Examining the capability of vitrified oocyte to repair sperm DNA fragmentation was the main objective of this research.

DESIGN: Non-vitrified and vitrified Cumulus-Oocyte-Complexes (COCs), were inseminated with Intact and two models of DNA fragmented sperms. Subsequent embryo development was followed until blastocyst stage. Pursuit of repair procedure was done by following changes in *Rad51* expression between different groups in zygote and blastocyst stage.

MATERIALS AND METHODS: Male mice were intraperitoneally injected with tert-Butyl hydroperoxide (tBHP) with 0.2 and 0.3 LD50 dosages for 14 days. Testis and epididymal sperm assessed by histology and TUNEL assay analysis. Obtained COCs from superovulated mice were vitrified and saved in LN2 on Cryotop for 2 weeks. Following warming, COCs were inseminated by DNA fragmented sperms. Expression level of *Rad51* was assessed with qRT-PCR in zygote and blastocyst stage.

RESULTS: Decreasing number of round and elongated spermatids and increasing number of spermatogonial stem cells, also decreasing sperm concentration of both treated groups indicated that tBHP injection reduced meiosis division. Sperm DNA fragmentation index in both treated groups was more than 20%, but in untreated group was less than 20%. Fertilization rate was not different between the groups; although, both sperm DNA damage and oocyte vitrification led to significant decrease in blastocyst formation. Moreover, zygotes derived from 0.3 LD50 sperms crossed with non-vitrified oocytes down-regulated *Rad51*; in contrast, 0.3 LD50 sperm with vitrified oocyte up-regulated the same gene. In blastocyst stage, 0.3 LD50 sperms with non-vitrified oocytes up-regulated *Rad51*; on the other hand, this gene was down-regulated in 0.3 LD50 sperms fertilized with vitrified oocytes (P-value<0.05). All data showed by mean±SD.

CONCLUSIONS: Oocyte vitrification and sperm DNA damage not only reduce blastocyst formation but also altered sperm repair *Rad51* gene expression.

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ESTABLISHING PAIN SCALES FOR GYNECOLOGIC PROCEDURE USING A NOVEL VAS APP. Lauren Y. C. Au, BA,[1] Wakako Horiuchi, BS,[1] Jasmine Tyson, MS,[1] Mary Tschann, PhD, MPH,[2] Bliss Kaneshiro, MD, MPH.[1] [1]University of Hawaii, Honolulu, HI,; [2]Society of Family Planning, Denver, CO.

OBJECTIVE: The pain experienced during procedures like intrauterine device (IUD) insertion, is a function of both the level of pain experienced and the duration the pain is felt. Some interventions may diminish the level of pain but prolong the procedure. In these instances, whether a given intervention provides benefit to the patient is difficult to assess. Researchers often use a traditional visual analog scale (VAS) where a patient makes a mark along a line to indicate the level of pain they experience, but these measurements only provide a snapshot of the patient's pain. The continuous VAS (cVAS) app records both pain scores and the duration of time an individual experiences various levels of pain. Our goal was to understand the feasibility of using the cVAS app during IUD insertion and to compare these measurements to a traditional VAS.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: We recruited 33 patients who were 18 years of age or older having an IUD insertion. Patients were oriented to the cVAS app prior to the procedure. During the procedure, the patient held the tablet, with the app loaded, and traced their finger along the line throughout the procedure according to the pain level experienced. Procedure milestones were logged on a synchronized app by a research assistant in the room and data was sent to a secure database. After the procedure, patients indicated overall pain on a paper-based 100 mm VAS and provided qualitative data about the amount of pain experienced and ease of use of the app. Without reviewing patient data, the provider who performed the procedure indicated the overall pain the patient experienced during the procedure on a paper-based 100 mm VAS. A cVAS pain score was calculated for each patient by graphing the level of pain recorded on the app on the y-axis and time on the x-axis. Area under the curve (AUC) was calculated and correlated with the patient reported VAS, provider estimated VAS, and maximum pain recorded on the cVAS app.

RESULTS: Of the 33 patients enrolled, 28 provided enough data for analysis (5 had missing or incomplete data). Mean procedure time was 4.94 minutes (sd=4.60, range 1.48 to 20.8). Mean overall patient reported and provider estimated VAS was 40.8 mm (sd=24.3, range 5.5 to 98.0) and 41.0 mm (sd=23.0, range 1.0 to 94.0), respectively. Mean maximum cVAS score recorded was 56.5 mm (sd=28.1, range 12 to 100) and mean AUC was 7005.8 (sd=6394.7, range 462.6 to 21919.3). Patient reported VAS score correlated strongly with AUC (r=0.53). Maximum cVAS score correlated moderately with AUC (r=0.47). Provider estimated VAS score correlated weakly with AUC (r=0.15). AUC correlated well with the amount of pain patients reported qualitatively. All patients found the app easy to use.

CONCLUSIONS: While this pilot app requires further refinement, the AUC represents a novel and accurate representation of patient pain levels. Using the cVAS in studies to investigate interventions to decrease pain with IUD insertion could result in the development of better techniques to reduce pain and improve patient satisfaction.

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DIFFERENT PROTEOMICS ANALYSIS INDICATES METFORMIN AS A NOVEL THERAPY TO AMELIORATE ENDOMETRIAL RECEPTIVITY OF ENDOMETRIOSIS. Xin Huang, Doctor,[■] Wei Huang, Professor,[2] Li Xiao, Doctor,[3] Ying Long, Doctor.[3] [1]West China Second Hospital; Key Laboratory of Birth Defects and Related Diseases of Women and Children, Ministry of Education, Sichuan University, Chengdu, China; [2]West China Second University Hospital of Sichuan University, Chengdu, China; [3]■.

OBJECTIVE: Endometriosis reduces female fecundity, decreased endometrial receptivity should be responsible for the pathogenesis. Metformin inhibited the growth of ectopic lesions, while the effect of metformin on eutopic endometrium of endometriosis has not been reported. This study aims to identify whether metformin can ameliorate endometrial receptivity of women with endometriosis and endometriosis model mice.

DESIGN: Compare protein expression of eutopic endometrium of minimal/mild endometriosis patients after 2 months treatment of Metformin (1000mg/d) and verify biomarkers associated endometrial receptivity that upregulated after Metformin treatment.

MATERIALS AND METHODS: Protein expressions profile of eutopic endometrial tissues from participants with minimal/mild endometriosis in secretory phase were analyzed by liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) based proteomics with data-independent acquisition (DIA) workflow. Up-regulated endometrial receptivity associated markers were screened out after metformin treatment in paired endometria. Parallel reaction monitoring (PRM) and immunochemistry were used for validation these markers. Endometria of endometriosis mice model on day 4 of pseudopregnancy were used for measured above screened markers, LIF and integrin $\alpha v\beta 3$ expression.

RESULTS: Compared to baseline, 149 differentially expressed proteins were detected in the endometria after metformin therapy. Insulin-like growth factor-binding protein 7 (IGFBP-7), α-antitrypsin (AAT), apolipoprotein D (ApoD), Rho GDP-dissociation inhibitor 1 (Rho-GDI), brain form glycogen phosphorylase (PYGB) and Cathepsin B (CTSB) that associated with endometrial receptivity had up-regulated after metformin therapy ($P<0.05$); while the expressions of those protein had no significant change in non-received controls. Up-regulated expression of IGFBP-7 and ApoD had been validated by PRM. IGFBP-7 and integrin$\beta 3$ were up-regulated after metformin treatment in endometria of endometriosis mice model during window of implantation.

CONCLUSIONS: Our study revealed that metformin may ameliorate expression of proteins related to endometrial receptivity in women with minimal/mild endometriosis and endometriosis mice model. Metformin could be used as potentially novel therapy to improve endometrial receptivity of infertile women with endometriosis.

SUPPORT: The study was funded by National Key R&D Program of China (Grant number: 2017YCF1001200).

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ASSESSING THE CHANGE IN INFERTILITY PATIENT'S SOCIAL MEDIA USE DURING COVID-19 RELATED CLINIC CLOSURES.

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BACKGROUND: Instagram is a popular app and social media networking platform that is utilised by patients to obtain and share health information.

OBJECTIVE: To assess whether infertility patients changed or altered their user engagement on Instagram in the time period around fertility clinic closure and reopening during the Covid-19 pandemic.

DESIGN: Content Analysis.

MATERIALS AND METHODS: The Instagram native insights analytics tool was used to analyse five social media accounts used by three independent Fertility Nurse Consultants in the United Kingdom (UK). Posts were examined between 1/03/20 - 02/07/20 for comments, likes, reach, profile visits, sharing and saving, growth and engagement, together with audience subdivision by gender, age and geography.

RESULTS: 436 posts were identified, saved by users 388 times generating 1834 profile visits. Average increases were noted in: followers 266%, comments 700%, likes 225%, reach 311% and user engagement 176%. Users were 89.2 % female and 10.8% male, predominantly from the UK, United States and Portugal. The age demographic was: Female $<$ 24 years $<$ 4%, 25 – 34 years 43%, 35 – 44 years 41.8%, 45 – 54 years 6.8%, $>$ 55 years 4.4% and Male $<$ 24 Years 8.6%, 25 – 34 years 33.2%, 35 – 44 years 37%, 45 – 54 years 11.8%, $>$ 55 years 9.4%.

Posts with the highest user engagement contained factual information regarding fertility clinics closure and reopening, validating increased anxiety concerning the impact of delay on chances of conception and managing negative thinking and uncertainty. Recurring themes in patients' comments related to information provided by fertility clinics. For example, 'I called my clinic yesterday and all I got was we have absolutely no idea', 'we haven't heard a peep from our clinic since lock down', 'I just want to hear from my clinic if they are opening or not', 'I am normally pretty resilient but this has floored me'.

As a result of increased user engagement and direct messaging, all five social media accounts posted daily to keep up with demand. They also participated in homogeneous podcasts, commenced support webinars and engaged with followers in real time weekly Instagram Live sessions. One account commenced a support group which had a 95% weekly engagement rate.

CONCLUSIONS: The results of this study indicate that Infertility patients increasingly relied on Instagram to manage their expectations surrounding treatment suspension, which they perceived as providing information and a support network that they felt was missing from their health provider.

Moving forwards, as Covid-19 continues to cause uncertainty, it is clear that fertility clinics should offer an additional psychological aspect to care, providing regular, updated information that matches patient preferences to their needs.

The authors are aware of the limitations and reason for caution with this study. Only five Instagram accounts were analysed. Therefore, only a small amount of data was available, with a particular user segment, which may not be indicative of the whole population.

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COVID CONCEPTION CATASTROPHE?: THE EXPERIENCE OF FERTILITYIQ USERS.

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OBJECTIVE: To assess concern about COVID-related clinic exposure, pregnancy risks, and treatment cancellations in a sample of infertility patients across the United States.

DESIGN: Analysis of a cross-sectional survey.

MATERIALS AND METHODS: FertilityIQ, an online educational platform, surveyed its 53,600 users via email between 05/27/2020-06/30/2020 to better understand their experiences with the delay of fertility care due to the COVID-19 pandemic. 13,490 email recipients opened the email and 1,730 women participated in the survey. Survey questions included the collection of demographic information (i.e., U.S. state of residence, age, gender, fertility diagnosis, and annual household income) and both quantitative and qualitative questions about fertility and the COVID-19 pandemic.

RESULTS: Two thirds of respondents were 31-40 years old. Of the women who responded, 43% were planning to start treatment immediately and 35% were actively undergoing fertility treatment when the pandemic began. Twenty-one percent chose to delay their own treatment and 58% had treatment postponed by their providers. Of the 943 women whose clinic delayed their treatment, 86% (n= 809) felt sad, but 67% (n= 630) agreed with the delay. Women with a higher income were more likely to agree with the decision to postpone ($P=0.019$). In addition, women with diminished ovarian reserve were more likely to feel sad about the COVID-related treatment delays ($P = 0.007$); age was associated with feelings of anger due to the delay ($P = 0.03$) and being "highly concerned" that the delay would affect pregnancy outcomes ($P = 0.006$). Overall, 46% of women were comfortable undergoing treatment during the pandemic, while 39% were unsure. Half of all women were "somewhat concerned" about pregnancy risks and 19% were "not concerned". Additionally, 38% were "not concerned" about exposure to COVID in the clinic, whereas 59% were "highly concerned" about treatment cancellation. The vast majority of women felt it was "highly important" that their clinic practice social distancing (71%). In regards to the financial burden, 33% of women were "highly concerned" about paying for treatment during the economic downturn whereas 29% were "not concerned". Importantly, 44% of women were "highly concerned" about their partner not being present during their treatment.

CONCLUSIONS: As expected, the majority of women were concerned and sad about delays in their fertility treatment during the COVID pandemic. Concerns include pregnancy risk, exposure risk, and having their partners present during their care. Both age and a diagnosis of diminished ovarian reserve were associated with emotional distress by these delays. A wide spectrum exists in the number of women with and without these concerns, and thus, additional education is needed for these patients to ensure their understanding of COVID exposure and potential pregnancy risks. Lastly, we recommend the provision of emotional support to fertility patients affected by the cancellation of fertility care and/or ongoing distress due to the COVID-19 pandemic.

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CHROMOSOMAL STRUCTURAL REARRANGEMENTS IN COUPLES DOES NOT INFLUENCE THE RATE OF MOSAICISM IN THEIR EMBRYOS.

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OBJECTIVE: To investigate whether the rate of mosaicism in preimplantation embryos is influenced by the chromosomal structural rearrangements in couples and the sex of the translocation carrier in preimplantation genetic testing (PGT).

DESIGN: A single center retrospective study performed between June 2018 and June 2020.

MATERIALS AND METHODS: The study included the data analysis of 754 blastocysts from 231 couples detected with Next Generation Sequencing(NGS). The cut-off values for reporting mosaic levels in our laboratory ranged from 40% to 70% .

According to the couples' chromosome karyotype, blastocysts were divided into three groups: reciprocal translocation carriers(N=442), Robertsonian translocation carriers(N=104), and couples with normal karyotype(N=208). The mean female age in all groups was similar and statistically non-significant(30.6±4.1, 31.2±2.7 and 31.0±5.0 for reciprocal translocation carriers, Robertsonian translocation carriers and couples with normal karyotype, 30.5±4.0 and 30.9±4.4 for male and female carriers). Statistical analyses were performed with IBM SPSS statistics 22.0 (SPSS, Inc., Chicago, IL). Independent-Sample T test and Chi-square test was used as appropriate. All statistical analysis was performed using SPSS 22.0. $P<0.05$ was defined as a statistically significant difference.

RESULTS: The mosaicism rate of reciprocal translocation carriers, Robertsonian translocation carriers and couples with normal karyotype were 4.30%(19/442), 10.58%(11/104) and 6.73%(12/208), respectively. There was no statistical significance in the mosaicism rate of reciprocal translocation carriers and couples with normal karyotype (4.30% vs. 6.73%, P=0.118). And Robertsonian translocation carriers were not statistically prone to have more mosaic embryos than couples with normal karyotype (10.58% vs. 6.73%, P=0.238).

When considering the sex of the translocation carrier, in reciprocal translocation group, the mosaicism rate of male carriers and female carriers was 5.19%(14/270) and 2.86%(5/172) respectively without statistical difference(P=0.250). The mosaicism rate of male Robertsonian translocation carriers and female Robertsonian translocation carriers was 14.55%(8/55) and 6.12%(3/49) respectively, and there was no statistical significance, too(P=0.163).

CONCLUSIONS: The frequency of mosaic embryos was not influenced by the chromosomal structural rearrangements in couples. Chromosomal translocation carriers generated more aneuploidy embryos, but they did not tend towards generating more mosaic embryos compared with couples with normal karyotype. And the sex of the translocation carrier did not influence the mosaicism rate, too. The possible reason is that reciprocal or Robertsonian translocation may not lead to errors in mitotic divisions during embryo early development.

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THE EFFECT OF SMOKING ON PREGNANCY COMPLICATIONS IN WOMEN WITH THE POLYCYSTIC OVARIAN SYNDROME (PCOS): A STUDY OF ALMOST 15,000 WOMEN.

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OBJECTIVE: The risk of pregnancy complications in patients PCOS is increased, including; pregnancy induced hypertension, preeclampsia, preterm birth and gestational diabetes mellitus (GDM). In the non PCOS population, prenatal smoking is associated with preterm birth, placental abruption, intra-uterine growth restriction and an inverse relationship with pregnancy induced hypertension (PIH). It remains unclear whether an association between smoking and GDM exists with studies reporting confliction results. We sought to investigate whether there is an association between pregnancy complications and smoking in women with PCOS.

DESIGN: This is a retrospective population-based study utilizing data from the HCUP-NIS over 11 years from 2004 to 2014. A dataset of all deliveries between 2004 and 2014 inclusively was created. Each patient was included only once. Women with PCOS were identified; of them 631 smokers and 14,251 none smokers.

MATERIALS AND METHODS: The HCUP-NIS is comprised of hospital inpatient stays submitted by institutions throughout the entire country and is representative of ~ 20% of admissions to US hospitals across 48 states and the District of Columbia. A multivariate logistic analysis was done adjusting for any statistically significant confounding effect ($p<0.05$).

RESULTS: While the risks of preterm premature rupture of membranes, preterm delivery (aOR 1.22 CI 0.77-1.93), placental abruption (aOR 1.08 CI 0.37-3.15), and PIH (aOR 1.01 CI 0.69-1.48) were not higher in smoking PCOS subjects, a significant association between smoking and diabetes mellitus (both GDM (aOR 1.46; 95%CI 1.01-2.10) and pregestational diabetes mellitus (6.5% vs. 4.0%, p=0.003)) was detected. There were no significant statistical differences in the rate of operative vaginal delivery or cesarean section. Risks of maternal infections and thrombotic complications and neonatal outcomes (small for gestational age, intrauterine fetal demise and congenital anomalies) were comparable.

CONCLUSIONS: Among women with PCOS who smoke the risk of gestational diabetes is increased; however, the expected decrease in PIH and specifically preeclampsia did not occur possibly due to the inherent risks of the syndrome itself.

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LINE 1 COPY NUMBER DECREASES AND TELOMERE LENGTH INCREASES WITH AGING IN SPERM CELLS.

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OBJECTIVE: Telomeres, repetitive sequences and associated proteins which cap and protect chromosome ends, undergo attrition with age in most tissues, providing an aging clock. Unlike other tissues, sperm telomeres increase rather than decrease with paternal age. The function of age-related sperm telomere elongation remains poorly understood. In yeast, mice and humans, telomeres can cause reversible silencing of genes, called the telomere position effect (TPE). We hypothesize that telomere elongation may help suppress Long Interspersed Nuclear Element 1 (L-1), a retrotransposon which becomes active in the germ line and can contribute to human genetic variation and genomic instability. Here we compare L-1 copy number in sperm samples from older and younger men to investigate the effect of paternal age and telomere elongation on L-1.

DESIGN: Prospective case-control study.

MATERIALS AND METHODS: Sperm samples (n=25) were donated for research by consenting men, aged 32-55, undergoing treatment at NYU Langone Fertility Center (NYUFC). Baseline semen parameters were evaluated, and samples processed by swim-up. Sperm genomic DNA was obtained using DNeasy Blood & Tissue Kit, QIAGEN® following manufacturer's recommended protocol, with an additional lysis step using X2 buffer (20 mM Tris-Cl, pH 8.0, 20 mM EDTA, 200 mM NaCl, 4% SDS); 80 mM dithiothreitol (DTT) and 12.5 μL/mL Proteinase K. Average sperm telomere length (STL) was assayed by mmqPCR and L-1 copy number by qPCR. Linear regression with Pearson Correlation Coefficient characterized the relationships between age, STL and L-1 copy number. Comparisons between old (age $\geq$ 45 years) and young men (age $\leq$ 40 years) were performed by t-test or Wilcoxon Test using GraphPad Prism 8 software. P-value < 0.05 was considered significant.

RESULTS: STL was positively correlated with age ($r^2 = 0.2851$; $p = 0.006$), as previously reported. STL from older (age $\geq$ 45 years, n: 5; Mean: 1.398 ± 0.3715) was significantly longer than younger men (age $\leq$ 40 years, n: 13, Mean: 0.9749 ± 0.1319) ($p = 0.0002$ Wilcoxon Test). L1 copy number in sperm decreased significantly with paternal age ($r^2 = 0.1585$; $p = 0.048$). T-test showed this effect was even more pronounced when comparing old (age $\geq$ 45 years, n=5; Mean: 0.8505 ± 0.1176) vs. young men (age $\leq$ 40 years, n=13, Mean: 1.012 ± 0.0885) ($p < 0.0001$).

CONCLUSIONS: We confirm increasing sperm telomere length with advancing paternal age. L1 copy number, in contrast, decreases significantly with paternal age, as sperm telomeres lengthen. Telomere elongation in the male germ line may represent a surveillance mechanism to repress retro transposition and maintain genomic instability. De repression of L-1 has been implicated in neuropsychiatric syndromes, so it will be of interest to determine whether failure of this mechanism contributes to the paternal age effect on neuropsychiatric syndromes.

SUPPORT: Coordination for the Improvement of Higher Education Personnel (CAPES, Finance Code: 001, Brazil; Grant number 88887.371487/2019-00 to TSB), Brazilian National Council for Scientific and Technological Development (CNPq, Brazil; Grant number 204747/2018-0 to FBK) and the Stanley H. Kaplan Fund of the NYU Grossman School of Medicine (to DLK).

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ADULT WEIGHT CHANGE IN RELATION TO SEMEN QUALITY AMONG MEN ATTENDING AN ACADEMIC FERTILITY CENTER. Vibha Singhal, MD,[1] Irene Souter, MD,[2] Jorge E. Chavarro, MD, Sc.D.[3] [1]MGH Weight Center, Boston, MA; [2]Massachusetts General Hospital, Harvard Medical School, Boston, MA; [3]Harvard School of Public Health, Boston, MA.

OBJECTIVE: In adults, obesity is associated with changes in some semen parameters especially sperm concentration. Most obesity related complications are influenced by the duration of obesity and age of onset. However, it is unclear if the degree of weight change during adult life has any impact on semen parameters. To address this question, we examined the association between weight changes during adult life and semen parameters.

DESIGN: Cohort Study.

MATERIALS AND METHODS: We recruited men in subfertile couples presenting to the Massachusetts General Hospital Fertility Center. Participants filled standardized questionnaires and provided a semen samples on site. We calculated weight change since age 18 years as the difference between current measured weight and self-reported weight at age 18 years, and classified men as weight stable (+2 to -2 kg), weight loss (<-2kg), weight gain below the median (+2 to 14kg) and weight gain above the median (>+14kg). We computed odds ratios (95%CI) of semen parameters below WHO reference limits using logistic regression adjusted for age, smoking status and abstinence time and separately for current and age 18 years body mass index (BMI). Last, we evaluated whether associations differed according to BMI at age 18.

RESULTS: We examined 845 men who were mainly Caucasian (86.6%), had a median (IQR) age of 36 (33-40) years, BMI of 27 (25-30) kg/m^2, and weight change since age 18 years of 14 (8-22) kg. Compared to men with stable weight, men who lost weight had (odds ratio [95%CI]) 3.2 (1.1-9.6) higher odds of low sperm morphology and 4.9 (1.6-15) higher odds of low motility. These estimates did not change substantially in models additionally controlling for current BMI or BMI at age 18 years. Men who had gained weight also had increased odds of semen parameters below WHO reference limits, but these estimates did not reach statistical significance. In models stratified by BMI at age 18 years, men who were overweight or obese at age 18 years and subsequently lost weight had a greater odds of sperm morphology (6.3 [0.9-40]) and motility (10.8 [1.6-71]) below WHO reference limits compared to men who were overweight/obese at age 18 and did not lose weight, whereas the relations of weight loss with morphology and motility were substantially weaker among men who were normal weight at age 18: 2.2 [0.4-11] and 1.8 [0.3-9.9], respectively.

CONCLUSIONS: Weight loss during adulthood among men with overweight/obesity at age 18 years is associated with increased odds of below reference sperm morphology and motility in men attending an academic fertility center. This finding is consistent with literature of semen abnormalities after weight loss surgery which suggests, at best, no benefit and in some cases harm of weight loss on markers of spermatogenesis. An important limitation of the study is the lack of information on the modality and rate of weight loss and if it was associated with any nutritional deficiencies. Clarifying the implications of these findings for future fertility of young men with obesity is critical.

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BLASTOCYST MOSAIC RATES DEMONSTRATE A DECREASING TREND WITH MATERNAL AGE. Liz R. Dulle, BS,[1] Jessi Anderson, MPH,[1] MacKenzie Purdy, MD.[2] [1]Vios Fertility Institute, Chicago, IL; [2]Vios Fertility Institute, Swansea, IL.

OBJECTIVE: Since chromosomal abnormalities increase drastically with maternal age while mosaicism, which occurs when there are 2 or more genetically different sets of cells in the body has not conclusively demonstrated change with age, we analyzed if there is a change in mosaic embryos with age.

DESIGN: A retrospective analysis was performed to determine if the percent of mosaicism was related to maternal age when undergoing an in vitro fertilization cycle (IVF) using Preimplantation Genetic Testing-Aneuploidy (PGT-A) with Next Generation Sequencing (NGS).

MATERIALS AND METHODS: Mosaic results were obtained for 2,597 embryos that underwent biopsy from 1/2019 to 6/2020 at two IVF centers. Patient age was separated into four categories: <35, 35-37, 38-40, and >40. All embryos were tested by using NGS and reports were given to the provider as euploid, aneuploid, mosaic or no results. The standard cut-off for reporting mosaicism was >20% abnormal cells in a sample and <80% abnormal. Statistical analysis was performed by chi-square testing and Cochran-Armitage trend test, assessing for a linear trend in the proportions across the age groups.

RESULTS: Based on 2,597 embryos biopsied, 121 (5%) were noted to be mosaic. Mosaicism based on age demonstrated: <35 age group, 78/1,414 (6%), 35-37 age group, 26/567 (5%), 38-40 age group, 10/375 (3%), and > 40 age group, 7/234 (3%). When comparing the four groups p=0.0611 for chi-square test and p=0.0095 for Cochran-Armitage test for trend.

TABLE 1. Mosaic samples compared to non-mosaic samples based on age

	<35	35-37	38-40	>40	Total
Mosaic	78 (6%)	26 (5%)	10 (3%)	7 (3%)	121 (5%)
Not Mosaic	1,336	541	365	234	2,476
Total	1414	567	375	241	2,597

CONCLUSIONS: We generally think of genetic abnormalities in the form of an all or nothing process but based on the timing of genetic changes there can be discordance of cell types leading to mosaicism. Many studies have demonstrated that abnormal meiotic division increases substantially with maternal age, but this has not been demonstrated for mosaic changes. With the development of PGT-A with NGS we can assess mosaic rates and trend with increasing age. In this large multi-site study, we determined that there is a trend toward decreasing mosaic rates with maternal age.

SUPPORT: None

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AN EVALUATION OF COMMERCIAL FERTILITY APPS: ALGORITHMIC PREDICTIONS AND USERS' PERCEPTIONS. Mayara Costa Figueiredo, MS,[1] H. Irene Su, M.D., M.S.C.E.,[2] Yunan Chen, PhD.[1] [1]University of California, Irvine, Irvine, CA; [2]University of California San Diego, La Jolla, CA.

OBJECTIVE: Fertility apps have been increasingly used to predict ovulation and fertile window, but it is unclear how these predictions are made (e.g., what indicators are used, how cycles are calculated) and how users perceive and trust them. The goal of this study is to evaluate current commercially available fertility apps focusing on their algorithmic feedback and users' experiences. More often patients are bringing apps to clinical appointments, so it becomes critical to analyze the type of support apps offer and how patients interact with their predictions.

DESIGN: We evaluated 30 best rated fertility apps obtained from the two main app stores, analyzing algorithmic feedback, app features, and user reviews of the selected apps.

MATERIALS AND METHODS: Each app was evaluated using a single dataset simulating four months of regular fertility cycles, including data for period dates, temperature, ovulation, and cervical mucus. Two researchers inputted the data in each app, analyzing how different types of data may visibly change the predictions of ovulation date and fertile window. Finally, user reviews from the app stores were qualitatively analyzed to surface users' experiences and perceptions of interacting with the fertility predictions.

RESULTS: Predictions varied considerably among apps. The first day of the fertile window varied by five days, with 13 apps predicting the same start day. Ovulation day varied by five days, with 19 apps predicting the same day and 2 apps not providing predictions. Length of fertile window ranged from 3 to 14 days (mean=7.167, sd=2.036). The start day of periods affected the

fertility predictions of 29 out of 30 apps (96.66%). Among the 30 apps, 20 provided ovulation tracking features but entering ovulation data only affected the prediction of 13 apps (65%). Similarly, temperature and cervical mucus tracking were present in 25 and 22 apps but entering temperature and mucus data affected predictions in only 6 (24%) and 1 app (4.54%) respectively. The analysis of app reviews suggests users have mixed reactions towards the apps, some fully trust algorithmic predictions, but many are confused about how the apps make predictions and why the predictions are incorrect comparing to the results of OPKs, or inconsistent with other fertility apps they use.

CONCLUSIONS: Our study reveals substantial inconsistencies in fertility predictions among the popular fertility apps we reviewed. Other than period dates, most data tracked by users do not lead to changes in predictions, which suggests that indicators that may require daily and disciplined work are not used. Our analysis show that the lack of clear description of what data are used in making fertility predictions can cause potential tracking burden, distrust of fertility technologies, or over-trust in predictions that may not be accurate. These issues may further affect users' fertility experiences and their interactions with healthcare providers. This study shows fertility technologies have to be designed more transparent with regard to their algorithmic feedback and to make the uncertainty intrinsic to fertility more visible to users.

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DEVELOPING A DECISION SUPPORT TOOL TO DETERMINE OPTIMAL NUMBER OF EUPLOID EMBRYOS BANKED TO ACHIEVE A DESIRED FAMILY SIZE. Devora Aharon, MD,[1] Cory Weinfeld, MS,[2] Alan B. Copperman, MD,[1] Erkan Buyuk, MD.[1] [1]Icahn School of Medicine at Mount Sinai, New York, NY; [2]Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: As women get older, the likelihood for pregnancy decreases: the chance of live birth (LB) after one IVF cycle at the age of 40 is 23%, but it declines to 4% at the age of 43, an 83% decrease.[1] This poses a challenge in particular for women above 35 who desire more than one child. After delivery of the first baby, the chance for pregnancy through a new IVF cycle will most likely be decreased. Ideally, women would bank the total number of euploid embryos needed to complete their family at a younger age. It is currently unknown how many euploid embryos need to be frozen for patients to achieve their ideal number of children. The aim of this study is to develop a decision support tool to inform patients about the number of euploid embryos that would result in a high likelihood of achieving their desired family size.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All patients who underwent single euploid frozen-thawed embryo transfer (FET) from January 2013 through October 2019 were included. The probabilities of one and 2 LB according to cumulative number of single euploid FET performed were calculated. Data were stratified by SART age group. Events of monozygotic splitting that resulted in twin LB were counted as 2 LB.

RESULTS: 4,169 single euploid FET cycles were included in the study. Overall, 69% of patients who attempted for one baby achieved a LB, and 67% of patients who attempted for two children achieved two LB. 78.8% of patients who transferred 2 euploid embryos achieved 1 LB and 13.1% achieved 2 LB (Table 1). The likelihood of 1 LB and 2 LB increased to 92.5% and 39.7% after 3 FETs, and to 97.9% and 71.7% after 4 FETs, respectively.

CONCLUSIONS: The goal of achieving two live births increased by 81% when 4 embryos were transferred compared to 3, indicating that patients who desire two children would be advised to bank at least 4-5 euploid embryos. Patient-focused decision support tools are now possible due to big data; a calculator will be built incorporating patient-specific factors to determine how many euploid embryos patients should bank in order to achieve their desired family size.

References: 1. SART 2017 National Data

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TIMING OF INITIATING GNRH ANTAGONIST DOWN-REGULATION IN IVF CYCLES AFFECTS CLINICAL OUTCOMES OF PCOS PATIENTS. Li Yujie, Doctor. Sixth Affliated Hospital of Sun Yat-sen University.

OBJECTIVE: Whether the timing of use of gonadotropin-releasing hormone (GnRH) antagonist down-regulation for IVF cycles affects pregnancy outcomes of polycystic ovary syndrome (PCOS) patients?

DESIGN: Retrospective cohort study of 1008 PCOS patients undergoing first IVF cycles using GnRH antagonist protocol from January, 2014 to December, 2019

MATERIALS AND METHODS: According to the dominant follicle size on the day of GnRH antagonist administration, the included patients were divided into three groups: Group A, dominant follicle diameter (DFD) < 10mm; Group B, 10mm ≤ DFD < 14mm; Group C, DFD ≥ 14mm. The parameters regarding demographic and clinical characteristics, ovarian stimulation characteristics, clinical outcomes including number of oocytes retrieved, top quality embryo number, clinical pregnancy rate, live birth rate, etc were compared among different groups.

RESULTS: The age, anti-Mullerian hormone level and body mass index were comparable among different groups. Total FSH dosage of Group A (1492.7IU) was more than Group B (1292.7IU) and Group C (1243.6IU). Group A needed longest FSH stimulation duration and GnRH antagonist duration (9.6days, 5.1days, respectively), then group B (8.9days, 4.8days, respectively), then group C (8.27days, 3.4days, respectively). Progesterone level on HCG day was higher in group B (1.00ng/ml) than in group A (0.88ng/ml) and group C (0.75ng/ml). The number of oocytes retrieved was highest in group B (18.3), then group A (16.3) and the lowest in group C (14.5). The number of fertilization embryos, transferable embryos, top-quality embryos and blastocysts in group B (10.8, 8.7, 7.2, 3.1, respectively) were more than in group C (8.5, 7.2, 5.9, 1.6, respectively), while comparable in group A (9.7, 8.2, 6.8, 3.3, respectively). Following the patients' first embryo transfer (ET) cycles, although there were no significant differences in the rate of chemical pregnancy, clinical pregnancy nor live birth in fresh or frozen ET cycles, the live birth rate of group C was the lowest (fresh ET, frozen ET: group A, 50.0%, 52.7%;group B, 48.0%, 54.7%;group C, 46.5%, 46.3%, respectively).

CONCLUSIONS: For PCOS patients, initiating GnRH antagonist when dominant follicle diameter between 10mm to 14mm could reduce FSH dosage, shorten FSH stimulation duration, retrieve more

TABLE 1. Likelihood of achieving 1 or 2 LB according to number of euploid single FET performed

SART group	A (<35)		B (35-37)		C (38-40)		D (41-42)		E (>42)		All patients	
Euploid SET #	1 LB	2 LB	1 LB	2 LB	1 LB	2 LB	1 LB	2 LB	1 LB	2 LB	1 LB	2 LB
1	52.1%	0.7%	49.9%	0.9%	50.4%	0.7%	48.4%	0.8%	49.4%	1.5%	50.6%	0.8%
2	80.8%	11.2%	78.4%	12.7%	77.5%	15.7%	76.0%	14.3%	75.9%	13.3%	78.8%	13.1%
3	93.8%	36.1%	93.2%	44.7%	91.2%	40.4%	92.0%	42.5%	87.2%	30.9%	92.5%	39.7%
4	98.6%	75.0%	97.9%	74.1%	97.6%	71.0%	97.1%	67.8%	96.7%	60.0%	97.9%	71.7%
5	99.5%	91.5%	99.5%	93.0%		88.9%	99.1%	84.3%	97.8%	81.8%	99.2%	89.6%
6		97.3%	99.9%	98.2%			100%	91.8%	99.4%	90.3%	99.8%	96.6%
7			99.9%	99.1%							99.9%	98.9%
8			99.9%	99.1%							99.9%	99.2%
9			100%	100%							100%	100%

oocytes, get more top-quality embryos and achieve higher live birth rate in IVF cycles.

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IDENTIFICATION OF WOMEN AT HIGH RISK FOR GYN HEREDITARY CANCERS MADE SIMPLE.

Bailey Gill McGuinness, MD,[1] John Wagner, MD.[2] [1]NYU Winthrop Hospital, Mineola, NY; [2]Huntington Hospital, Huntington, NY.

OBJECTIVE: The purpose of this project was to create and trial a screening form to be used in the out-patient setting to identify high-risk carriers for GYN hereditary cancer genes, such as BRCA, Lynch Synd., etc. This screening tool can be applied in internal medicine, OB/GYN and subspecialties, like REI. Early identification of genetic carriers allows for the opportunity to use PGT to prevent transfer of embryos carrying cancer genes when undergoing IVF.

The form identifies women who qualify for hereditary cancer screening and referrals to breast health programs (BHP) for consultation, increased surveillance, chemo-prophylaxis or prophylactic surgery. Several genetics companies promote forms that simplify the National Comprehensive Cancer Network (NCCN) guidelines for hereditary GYN cancer screening, such as this form. However, this is the only available form that combines NCCN guidelines with the Gail Model, which calculates a women's lifetime breast cancer risk.

DESIGN: Quality improvement project.

MATERIALS AND METHODS: Stage 1: The form was used in an OB/GYN office in East Northport, NY for one month. During this time, feedback from attendings, staff and patients was used to edit the form until the form was deemed not only accurate but user-friendly.

Stage 2: The form was introduced at an OB/GYN practice in Garden City, NY. Success of the form was measured by the number of patients identified who met criteria either for genetic testing or for referral to the local BHP, defined by an elevated Gail Model score. 6-week control (4/8/19 to 5/17/19) and study (5/21/19 to 7/5/19) periods were compared.

Descriptive statistics were performed.

RESULTS: During the control period prior to introduction of the form, there were 171 annual and new-patient visits, of which zero patients were identified as candidates for genetic testing or referred to the BHP. During the 6-week period following introduction of the form, 197 annual and new-patient visits were performed and 141 of these patients (71%) were screened with the form. One patient was unable to complete the form due to lack of family history. 11% of patients met criteria for referral to genetic counselors for testing and 7.8% of patients met criteria for referral to the BHP.

Physicians described the form as a tool to learn the NCCN guidelines. The form generated income for physicians who coded and billed for performing cancer screening or genetic counseling. Patients benefitted from appropriate referrals with significant clinical implications. Both patients and physicians described the form as simple to complete and navigate.

CONCLUSIONS: Identification of women at high risk for GYN hereditary cancers allows for appropriate referrals to genetic counselors for testing and to BHPs for cancer screening and prevention. Identifying genetic carriers prior to undergoing IVF is vital due to available technology, such as PGT, to prevent transfer of carrier positive embryos. This form proves to be user-friendly, accurate, income generating, and clinically relevant, as evidenced by continued use of this form beyond completion of the study.

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MITOCHONDRIAL DNA CONTENT IS NOT A USEFUL METHOD TO PREDICT THE REPRODUCTIVE OUTCOME OF EUPLOID BLASTOCYSTS.

Mariana Gomez Peña, BSc,[1] Laura J. Kopcow, MD,[1] Fabio L. Sobral, Physician,[1] Marcos Horton, Physician,[2] Mercedes Papayannis, BSc,[1] Evelyn De Martino, BSc,[1] Ignacio De Zuñiga, Physician,[3] Alejandro Oubiña, Physician,[1] Claudio Bisioli, MSc.[1] [1]Pregna Medicina Reproductiva, Buenos Aires, Argentina; [2]Juncal 3490, CABA, Argentina; [3]Pregna medicina reproductiva, Buenos Airesl, Argentina.

OBJECTIVE: To evaluate if the assessment of mitochondrial DNA (mtDNA) content is a useful tool to predict implantation and pregnancy performance in frozen euploid blastocysts transfer cycles.

DESIGN: Retrospective comparative study.

MATERIALS AND METHODS: One hundred and eighty-two elective single frozen blastocyst transfers after preimplantation genetic testing for aneuploidy (PGT-A) and mtDNA content assessment via next generation sequencing (NGS) were performed between May 2016 and October 2019. Euploid blastocysts for transfer were selected based on standard morphological criteria and independently of the mtDNA content result. Blastocysts transferred were grouped according to the value of a mtDNA content score (MS) as following: group A (MS < 18.19, N $= 30$), group B (MS $= 18.19$ to 24.15, N $= 55$) and group C (MS $= 24.15$ to 50.58, N $= 94$). Three of the studied blastocysts had MS > 50.58 and were excluded from the study. Study groups were comparable regarding patients' age, indication for PGT-A and proportion of good quality blastocysts. Student's t and Chi-squared tests were used as appropriate.

RESULTS: No differences were observed between groups regarding implantation, clinical and ongoing pregnancies and miscarriage rates (table 1).

TABLE 1. Outcomes results between groups

Study groups	A	B	C
Implantation	43.3 (13/30)	45.4 (25/55)	37.2 (35/94)
Clinical Pregnancies	43.3 (13/30)	43.6 (24/55)	35.1 (33/94)
Miscarriages	15.3 (2/13)	12.5 (3/24)	18.2 (6/33)
Ongoing pregnancies	36.7 (11/30)	38.2 (21/55)	28.7 (27/94)

CONCLUSIONS: Our study did not find any differences in mtDNA content with regards to embryo implantation or pregnancy outcomes. A bigger sample size would be crucial to confirm these preliminary results.

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THE SUPPRESSIVE EFFECT OF CELASTROL ON GROWTH OF ENDOMETRIOSIS IN VITRO IS ASSOCIATED WITH ANTAGONISM OF ESTROGEN RECEPTOR ACTIVITY.

Jingjie Li, M.D,[1] Pan Chen, PhD,[2] Jiayu Lin, Bachelor,[1] Xiaoyan Liang, M.D.[1] [1]the Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; [2]the First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: Celastrol is a quinine methide triterpenoid derived from the root of *Trypterigium Wilfordii*, which has been used in the oriental medical settings to treat various inflammatory and neurodegenerative disorders. We firstly explored its role in the growth of endometriosis in vitro.

DESIGN: Pharmacologic interventions in primary cultured human endometriotic stromal cells.

MATERIALS AND METHODS: Primary cultured human endometriotic stromal cells were prepared from ectopic endometrium of 15 patients with endometriosis undergoing laparoscopy at the Sixth affiliated Hospital of Sun Yat-sen University from January 2018 to May 2020. The cells were incubated with Celastrol at concentrations of 0.1μM, 1μM and 10μM for 24 hours, and the cell viability, proliferation ability and apoptosis were detected by MTT assay, BrdU incorporation assay and Caspase-Glo luminescent-based assays respectively. Dual luciferase activity assay with transient transfection of an ERE-tk-Luc reporter was applied in measuring the effect of Celastrol on estrogen receptor (ER) activation.

RESULTS: Celastrol dose-dependently inhibited the viability of human primary endometriotic stromal cells, and 35.2 % of cell viability was observed at 10μM of Celastrol. Similarly, the Brdu assay proved that the cells proliferation ability was also inhibited by Celastrol dose-dependently, with 34.8% decrease seen in 10μM. Furthermore, Celastrol induced a significant upregulation of caspase-3 activity in endometriotic stromal cells, and 3.61 folds of maximum increase was observed at 10μM. Besides, the dual luciferase reporter gene assay demonstrated that Celastrol inhibited activation of ER in a dose-dependent manner, and 10μM of Celastrol led to 12.7% of ER activity as compared to that in vehicle group.

CONCLUSIONS: Celastrol inhibits the cell viability and proliferation, while induces the apoptosis of human primary endometriotic stromal cells. The effects are associated with the antagonism of ER activity.

SUPPORT: Chinese Universities Scientific Fund of Sun Yat-sen University (NO.19ykpy04)

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WOMEN WITH ENDOMETRIOSIS-ASSOCIATED INFERTILITY HAVE DECREASED LIVE BIRTH RATES AFTER FROZEN EMBRYO TRANSFER – ANALYSIS OF THE "EIVF" DATABASE. Alex Finlinson, MD,[1] Henok G. Woldu, PhD,[2] Judy E. Stern, PhD,[3] Albert L. Hsu, MD.[4] [1]The Center For Health Analytics For National and Global Equity, Columbia, MO; [2]Dartmouth-Hitchcock, Lebanon, NH; [3]Department of Obstetrics and Gynecology; University of Missouri, Columbia, MO; [4]■.

OBJECTIVE: To determine whether women with surgically-confirmed endometriosis have decreased live birth rates after frozen embryo transfers (FETs), compared with either male factor or tubal factor infertility.

DESIGN: Retrospective analysis FETs in Massachusetts between 2003-2019, from the "eIVF" database.

MATERIALS AND METHODS: FET cycles in women with surgically-confirmed endometriosis were compared with those in couples with either male factor infertility or tubal factor infertility. Women were only classified as endometriosis if they had a surgical record of endometriosis of the uterus, ovary, fallopian tube, pelvic peritoneum, or rectovaginal septum. Any women who were noted to have clinical endometriosis that was not surgically confirmed, were excluded from analysis.

For the male factor analysis, couples with both endometriosis and male factor infertility were excluded; similarly, for the tubal factor analysis, couples with both endometriosis and tubal factor infertility were excluded; this resulted in different numbers of patients with surgically-confirmed endometriosis in these two analyses. Mean ages and BMI between the two groups were compared using the two sample t-test. Chi-square test and multivariable logistic regression were used to assess differences in live birth rates between surgically-confirmed endometriosis and either male factor or tubal factor infertility. Odds Ratios (OR) and 95% CI of the ORs were extracted from the fitted models. Two sided alpha level of 0.05 was used to determine statistical significance.

RESULTS: We compared 3,441 FET cycles in women with surgically-confirmed endometriosis to 11,510 FET cycles in couples with male factor infertility; groups had similar average age (35.1 vs 35.0, P=0.1947) and BMI (25.7 in both groups, P=0.527). Women with surgically-confirmed endometriosis had a 25% chance of live birth, compared with a 37% chance of live birth with male factor infertility (P<0.0001). Adjusting for age and BMI, the odds of live birth was 76% higher in male factor infertility (OR =1.76, 95% CI [1.61-1.91]), compared to women with surgically-confirmed endometriosis.

We compared 2,995 FET cycles in women with surgically-confirmed endometriosis to 4,558 cycles in couples with tubal factor infertility. The chance of live birth was 24% for surgically-confirmed endometriosis vs 28% for the tubal factor infertility group (P=0.0011). Adjusting for age and BMI, the odds of live birth were 26% higher in women with tubal factor infertility (OR 1.26, 95% CI [1.13-1.41]), in comparison to surgically-confirmed endometriosis.

CONCLUSIONS: Compared with either male factor or tubal factor infertility, surgically-confirmed endometriosis is associated with lower odds of live birth in couples undergoing FET.

References: n/a

SUPPORT: n/a

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THE STATE OF FERTILITY PRESERVATION COUNSELING FOR WOMEN WITH CYSTIC FIBROSIS REPORTED BY CYSTIC FIBROSIS PROVIDERS. Sigrid Ladores, PhD, RN, PNP, CNE, FAAN, Leigh Ann Bray, PhD, RN, CNL, Janet Brown, MSN, RN, Caitlin Campbell, BSN, RN, Peng Li, PhD, Jessica Corcoran, PhD, CRNP, CPNP-PC. University of Alabama at Birmingham, Birmingham, AL.

OBJECTIVE: Fertility preservation (FP) counseling is part of comprehensive care provided to women of childbearing age undergoing oncologic treatments; however, this is not standard for patient populations with other chronic conditions. The purpose of this study was to examine the current state of FP counseling for women with cystic fibrosis (CF) from the perspective of their healthcare providers, with the goal of identifying the gaps, barriers, and facilitators to implementation of counseling in clinical practice. This knowledge can lead to the development of FP guidelines for women with CF and enhance shared decision making by broadening their reproductive options.

DESIGN: This study utilized a quantitative, exploratory, cross-sectional design.

MATERIALS AND METHODS: Healthcare providers (e.g., physicians, nurse practitioners, clinic coordinators, pharmacists, social workers, nurses) were recruited from CF Foundation accredited clinics throughout the United States and via snowball sampling. Participants completed a web-based, anonymous FP survey with 39 items that took approximately 30 minutes to complete. Participants received $20 for their participation. The descriptive statistics were provided using R software.

RESULTS: Fifty healthcare providers completed the survey (M_{age}= 40.8, SD=11.1). The majority of the healthcare providers were female (n=45). Despite the fact that 92% (n=46) of the providers felt that FP discussions should be standard for all female patients with CF, 28% (n=14) of providers reported that FP topics were not discussed with female patients with CF at any age. Most providers felt that initiation of FP discussions was the responsibility of the healthcare team (n=34), but some felt that patients should initiate the FP discussions (n=11). Lack of knowledge (n=17) and lack of time (n=12) were the two most substantial barriers to FP discussions by healthcare providers. According to the providers, the two best facilitators for FP discussions in clinic would be having national guidelines or standards (n=41) and integrating partnerships with sexual and reproductive health specialists (n=39) as part of comprehensive CF care delivery. Having educational materials to foster FP discussions between providers and patients was another facilitator reported (n=50). Healthcare providers preferred having educational information and resources shared via online format (n=46) and written pamphlets (n=44).

CONCLUSIONS: Fertility preservation counseling is an important part of comprehensive care for women with CF; however, many women do not receive FP information. This national sample of CF healthcare providers reported that they lacked the knowledge and time to discuss FP with their patients. Removing the barriers and optimizing the facilitators to encourage FP discussions between women with CF and their providers will broaden these women's reproductive options by facilitating fully informed decision making to improve overall health outcomes.

SUPPORT: This study was supported by a grant from the National Institute of Child Health and Health Development.

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HUMAN PAPILLOMAVIRUS INFECTION GENOTYPE IN INFERTILE WOMEN AND ITS IMPACT ON REPRODUCTIVE OUTCOMES OF INTRAUTERINE INSEMINATION. Yujie Li, Doctor. Sixth Affiliated Hospital of Sun Yat-sen University.

OBJECTIVE: The purpose of this study was to evaluate the prevalence, genotype of HPV infection in women attending assistant reproductive treatment and to assess the relationship between HPV infection and outcome of intrauterine insemination (IUI).

DESIGN: A observational study in a tertiary hospital in southern China

MATERIALS AND METHODS: During December 2019 and July 2019, cervical-swab samples were collected for detecting HPV from 1743 infertile women seeking for assistance at the assisted reproductive technology center (ART). 28 HPV genotypes were detected, including 18 high-risk HPV (hrHPV) genotypes (types 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73 and 82), and 10 low-risk HPV (lrHPV) genotypes (types 6, 11, 40, 42, 43, 44, 54, 61, 81 and 83). We evaluated the prevalence of HPV in infertile women and evaluated associations between HPV and IUI reproductive outcome.

RESULTS: 181 (10.38%) of the 1743 infertile women tested positive for HPV. Of these, 117 (64.64%) tested positive only for high-risk subtypes, 51 (28.18%) tested positive only for low-risk subtypes, and 13 (7.18%) tested positive for both high- and low-risk subtypes. Overall, 7.46% of all patients tested (130/1743) were positive for a high-risk type. The most common HrHPV genotype was HPV52 (2.29%), followed by HPV16 (1.03%), HPV58 (0.98%), HPV51 (0.80%). For the LrHPV genotypes, the most common type was HPV44 (1.15%), followed by HPV81 (0.57%), HPV42 (0.52%).The prevalence of HPV infection was higher in the age group of 41-50 years (14.94%) than in the age group of 21-30 years (9.33%) and 31-40 years (9.73%). For women undergoing IUI, the chemical pregnancy rate of hrHPV infection group (27.27%), lrHPV infection group (25.0%) were higher than non-HPV infection group (12.85%).

CONCLUSIONS: 10.38% of the infertile women tested positive for HPV, of these 71.82% were positive for a high-risk type. The most common HPV genotype was HPV52 for HrHPV and HPV44 for the LrHPV. For those undergoing IUI, HPV infected women benefit more than non-HPV infected women.

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AURKC PATHOGENIC SINGLE NUCLEOTIDE VARIANTS ARE NOT INCIDENT IN ABORTED FETUSES WITH ANEUPLOIDY. Amin - Khosravani, Researcher,[1] Masood Bazrgar, Assistant Professor,[2] Maryam Eslami, Assistant Professor,[3] Amir Amiri-Yekta, Sr., Associate Professor.[2] [1]Faculty of Advanced Science and Technology, Tehran, Iran (Islamic Republic of); [2]Reproductive Biomedicine Research Center, Tehran, Iran (Islamic Republic of); [3]Applied Biotechnology Research Center, Tehran, Iran (Islamic Republic of).

OBJECTIVE: AURKC pathogenic single nucleotide variants are not incident in aborted fetuses with aneuploidy

DESIGN: A main cause of infertility is recurrent miscarriage; additionally a considerable portion of miscarriages occur due to chromosomal abnormalities with/without risk of aneuploidy recurrence.

Although fetal aneuploidy is associated with maternal age, it is incident in young women. AURKC protein kinase is an essential factor in the cell cycle and its dysfunction can reduce the accuracy of chromosome segregation.

MATERIALS AND METHODS: We collected 50 DNA samples of aborted fetuses with confirmed aneuploidy by QF-PCR and/or array CGH method. In order to rule out advanced maternal age as a contributing factor in fetal aneuploidy, samples from mothers older than 36 years were not included. We focused on two pathogenic single nucleotide variants (SNVs) of the Exons 5 and 6 of AURKC gene in Exon 6, rs397515484 and rs121908654 using Sanger sequencing method by analyzing the results with FinchTV software.

RESULTS: In 50 samples, there was no evidence of heterozygosity and homozygosity of rs397515484 and rs121908654 pathogenic SNVs

CONCLUSIONS: Considering that the targeted mutations were not observed in 50 samples, these SNVs (rs397515484 and rs121908654) do not seem to be prioritized for future screening of aneuploidy origin in parents with a history of abortion due to aneuploidy.

P-1004 3:30 PM Wednesday, October 21, 2020

COVID-19 AND ART OUTCOMES. Isaac J. Chamani, M.D.,[1] David H. McCulloh, Ph.D.,[2] James A. Grifo, MD, PhD,[3] Frederick L. Licciardi, M.D.[4] [1]Baylor College of Medicine, Houston, TX; [2]NYU Langone Fertility Center, New York, NY; [3]NYU Langone Prelude Fertility Center, New York, NY; [4]NYU Langone Health, New York, NY.

OBJECTIVE: The ongoing COVID-19 pandemic has disrupted the normal methods of communication used by physicians and patients, as well as the standard protocols and procedures by which medical clinics operate. Pandemic related stresses may have also influenced patient's fertility goals and/or their ovarian response. We questioned whether these changes resulted in any unanticipated effects in the treatments and outcomes of ART patients.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Patients who underwent GnRH-antagonist IVF cycles from January 2020 through June 2020 at NYU Fertility Center, a period in New York City over which the COVID-19 pandemic escalated and life in the city drastically changed as a result of new social distancing measures, were separated by month of treatment and compared with patients from the corresponding month in the prior year (January 2019 through June 2019). Patient age, AMH, days gonadotropin, #oocytes retrieved, #oocytes matured, #fertilized, #blastocysts, and #euploid embryos were compared using Student's T-test.

RESULTS: 1881 patients were compared over the parallel six-month periods. Clinic visits were markedly decreased over the months of March and April of 2020, when the pandemic was at its peak in NYC and treatments were suspended as per the ASRM pandemic guidelines. There were no differences in age, AMH, #oocytes retrieved, #mature oocytes, or #fertilized between the two years. In April of 2020 there were significantly more blastocysts per patient, as compared to April of 2019, however, in May and June of 2020 there were significantly fewer euploid embryos per patient, as compared to May and June of 2019 (see table).

CONCLUSIONS: In the months following the end of the COVID-19 treatment suspension, there were no apparent differences in patient characteristics or the quantitative responses to stimulation. However, there was a significant qualitative difference as expressed in the number of euploid embryos. It remains unclear if or how the pandemic is related to this difference.

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DOES CULTURING EMBRYOS IN THE TIME LAPSE INCUBATOR IMPROVE THE EMBRYO QUALITY AND PREGNANCY OUTCOME DURING IVF/ICSI TREATMENT? Alex C. Varghese, Ph.D,[1] Maria Teresita Lao, MSc,[1] Nnenna Maduabum, MD,[2] Essam S. N. Michael, M.D., FRCSC,[1] Kannamannadiar Jayaprakasan, Ph.D.[3] [1]Astra Fertility Clinic, Mississauga, ON, Canada; [2]University of Nottingham, Nottingham, United Kingdom; [3]Department of Obstetrics and Gynaecology, Derby, United Kingdom.

OBJECTIVE: To evaluate whether the use of time-lapse incubator (TLI) improve embryo quality and IVF outcome in comparison to standard trigas benchtop incubator.

DESIGN: A retrospective study in a tertiary fertility unit.

MATERIALS AND METHODS: Women aged <40 years undergoing IVF treatment from Jan 2018 to June 2019 were included. Poor responders with <4 oocytes retrieved and those needed treatment with surgical sperm retrieval for severe male factor were excluded. Mature oocytes, retrieved from 297 patients, were inseminated. Inseminated oocytes were cultured to the blastocyst stage either using a TLI (GERI Plus) with a single step media (n=188) or in a conventional Planer BT-37 Bench top incubator with sequential culture and Day-3 media change (n=109). 161 participants underwent fresh embryo transfer with one (70.2%) or two (29.8%) embryos. The outcome measures were usable blastocysts, proportion of top quality cleavage stage embryos and blastocysts, pregnancy rates and live birth rates. The Mann Whitney-U test was used to compare the demographics and the Chi-square test and the relative risk analysis were used to compare binary outcome variables.

RESULTS: The mean (±SD) age of the participants were similar in the study and the control groups (33.1± 3.8 vs 32.8± 3.8 years). Table 1 shows the comparison of outcome variables. Day-3 compaction rate and the

	Year	N	Age	AMH	#Oocytes	#Mature	#Fertilized	#Blasts	#Euploid
January	2019	190	37.1	2.8	14.8	8.4	6.5	3.2	2.0
	2020	235	36.5	2.7	15.7	7.9	6.0	3.2	2.1
February	2019	159	36.6	2.8	15.7	9.2	7.1	3.7	2.7
	2020	194	36.9	2.6	15.8	8.7	6.6	3.3	2.1
March	2019	177	36.9	2.4	13.2	7.5	5.6	3.2	2.2
	2020	90	36.6	2.8	15.0	6.9	5.1	2.7	2.3
April	2019	169	36.6	2.6	16.0	8.2	6.2	3.0*	2.2
	2020	34	36.8	2.5	15.3	11.4	8.1	5.1*	3.0
May	2019	141	36.7	2.4	16.1	8.7	6.5	3.5	2.4*
	2020	170	36.5	2.6	15.3	9.0	6.6	3.5	1.2*
June	2019	160	37.0	2.4	14.9	7.5	5.6	3.0	2.3*
	2020	176	36.5	2.4	14.4	7.0	5.4	2.7	1.0*

*indicates $p < .05$ for comparison between 2019 and 2020 values

	GERI Plus(n=188)	PLANER (n=109)	P-value
Gr.I & II embryos on D-3	80.9% 1637/2022	85.46% 1005/1176	0.24
Compaction on D-3	19.88% 402/2022	5.44% 64/1176	<0.001
Useable Blastocysts	64.59% 1306/2022	62.33% 733/1176	0.27
Top quality blastocysts (AA, AB, BA)	13.80% 279/2022	6.03% 71/1176	<0.001
CPR (sET+dET)*	31/64 (48.4%)	31/71 (43.6%)	0.58
LBR (sET+dET)*	29/64 (45.3%)	26/71 (36.6%)	0.31
CPR (sET)*	25/48 (52.0%)	15/44 (34.0%)	0.82
LBR (sET)*	23/48 (47.9%)	14/44 (31.8%)	0.12

*Pregnancy outcome data not available for all the participants.

proportion of top-quality blastocysts were higher in the TLI group. However, the pregnancy and live birth rates were similar.

CONCLUSIONS: While the proportion of compacted embryos on day 3 and of top-quality blastocysts developed were higher with TLI culture system, the live birth rates were similar between the two groups, albeit a better trend with TLI. A large randomized trial is warranted to evaluate this research question further.

P-1006 3:30 PM Wednesday, October 21, 2020

IMPROVEMENT IN THE BLASTOCYST FORMATION AND SUBSEQUENT CLINICAL PREGNANCY RATES FOLLOWING THE USE OF COLD-PLASMA BASED AIR PURIFICATION SYSTEM IN THE EMBRYO CULTURE LABORATORY. Satish Manohar Patki, Sr. M.D.,[1] Rajvi H. Mehta, Ph.D.[2] [1]Patki Hospital, IVF Consultant, Kolhapur, India; [2]Trivector Boimed LLP, Mumbai, India.

OBJECTIVE: To study the effect of installation of a cold-plasma based air purification system in the embryo culture laboratory on the quality of air and the effect on the blastocyst formation and subsequent clinical pregnancy rate.

DESIGN: After clearance by our Institutional Ethical Committee, a cold-plasma based air purification system was installed in the embryo culture laboratory which already had a well-maintained Heating Ventilation Air-Conditioning (HVAC) System. The ambient air quality, with specific reference to microbial contamination, volatile organic compounds (VOC) and particulate matter (PM) was compared before and after the installation of this air purification system. The blastocyst formation rate and clinical pregnancy rates was also compared during these two time frames.

MATERIALS AND METHODS: A portable Novaerus NV-1050 air purification system which consists of cold plasma technology along with activated carbon and HEPA filters was installed in embryo culture laboratory. The microbial count was determined weekly while the VOC and PM counts were monitored daily at the same time of the day.

410 patients underwent IVF procedures during 6 months. Of these, 199 patients underwent IVF before (Group I) and 211 patients (Group II) after the installation of Novaerus air purification system. Patient characteristics such as age, indication for IVF, ovarian stimulation protocol, fertilization techniques, embryo culture conditions, embryo transfer techniques and luteal support were similar in both the groups.

Embryos were cultured till the blastocyst stage and the percentage of excellent quality blastocyst formed per oocyte was recorded. All the blastocysts were vitrified and embryo transfer was performed after two months. The clinical pregnancy rate per embryo transfer was calculated in each group. The data was compared using unpaired t-test, with the help of SPSS software version 21.

RESULTS: No microbial growth was detected in both the groups. The levels of VOC, PM, Blastocyst formation and clinical pregnancy rate is tabulated.

CONCLUSIONS: The addition of a cold plasma based air purification system to the culture laboratory with an existing HVAC system significantly reduces the VOC levels and results in a significant increase in the blastocyst formation and clinical pregnancy rates. It could be an adjunct in the laboratory in these COVID times where there is an increased use of VOC releasing sanitizers.

P-1007 3:30 PM Wednesday, October 21, 2020

QUALITY OF ONLINE INFORMATION PROVIDED BY FERTILITY CLINIC WEBSITES: COMPLIANCE WITH BRAZILIAN MEDICAL COUNCIL (CFM) AND AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE (ASRM) GUIDELINES. Marcia C. Ferreira, MD, PhD, Caio Nobuyoshi Koga, Medical student, Marcela Chagas Lima Mussi, Medical student, Pollyanna Faria Fradico, Medical student, Marcia M. Carneiro, MD, PhD. UNIVERSIDADE FEDERAL DE MINAS GERAIS, Belo Horizonte, Brazil.

OBJECTIVE: To evaluate fertility clinic websites registred in the11th Report of the National Embryo Production System Platform (SisEmbrio 2017) in Brazil regarding their compliance with the 2004 American Society for Reproductive Medicine (ASRM) and the Brazilian Medical Council (CFM) guidelines for advertising and to survey the general features of their websites and social media.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: We performed a cross-sectional online evaluation to obtain data on the SiSembrio registered clinics websites using 2004 ASRM guidelines for advertising (Success rates published; Presence of data to support success rate ;Comparison marketing; Live birth rate (LBR) reported ;Method of calculating LBR; LBR for time period given ;Success rates based on age and diagnosis; Experimental/Investigational nature of

Parameter	Group I	Group II	Significance level/P Value
Mean Particle Matter Count	200 (SD ± 11.25)	195 (SD ± 10.37)	0.245
Mean VOC levels(ppb)	12.2 (SD ± 3.2)	7.5 (SD ± 2.6)	0.003
Mean Blastocyst formation rate	45.5 % (SD ± 6.9)	60.5 % (SD ± 5.3)	0.0009
Mean Clinical pregnancy rate	53.26% (SD ± 8.9)	66.35% (SD ± 7.1)	0.001

procedure defined) and compliance with CFM guidelines (practice director visible with respective council number; no information on treatments' costs, no photos of patients shown nor success stories with patient identification) for advertisement. The general characteristics of these fertility clinics websites and their social media were also assessed.

RESULTS: All 163 SiSEmbrio-registered clinics were evaluated; 155 (95,1%) had functional websites (8 public, 153 private, 8 public, 2 no information).Social media participation was as follows: WhatsApp 87(87;53.3%) Facebook (143 ;87.7%) and Instagram (135;82.8%) while 84 (51.5%) had other social media (YouTube, Linkedin and Twitter). Regarding CFM recommendations only 49 (31.6%) displayed a registered director, 84(54.1%) showed patients photos either on their sites and/or social media as well as success stories. No clinic announced prices and only one offered an exclusive treatment. Success rates were published on 51(32.9%) and only 18(11.6%) used their own data whereas 7 (4.5%) displayed success rates by age. No clinic showed LBR. All clinics offered IVF and 131 explained the procedure to patients. Social fertility preservation was offered by 127(81.9%) and oncofertility by 122 (78.7%). Preimplantation genetic diagnosis was available in 85 (54.8%), oocyte donation in 67(43.25), surrogacy in 51 (32.9%) and semen donation in 44 (28.4%) and only 35 (22.6%) had andrologists.

CONCLUSIONS: Online Information provided by fertility clinics in Brazil is heterogeneous. A significant proportion of the SisEmbrio-registered fertility clinics websites do not follow some aspect of ASRM and CFM guidelines for advertising. As websites and social media are widely used by patients to obtain health information, increased dissemination and awareness of the guidelines is highly recommended.

SUPPORT: None

P-1008 3:30 PM Wednesday, October 21, 2020

PREDICTING PROBABILITY OF CUMULATIVE LIVE BIRTH BASED ON BOTH BASELINE INFORMATION AND PROTOCOLS OF CONTROLLED OVARIAN STIMULATION. Jing Liu, Prof., Qi Wan, Dr., Jihua Huang, Dr., Xingyu Lv, Dr., Xiangqian Meng, Dr., Huan Xu, Dr., Ying Zhong, Prof. Chengdu Xi'nan Gynecology Hospital, Chengdu, China.

OBJECTIVE: To develop a prediction model for the probability of cumulative live birth from one initiated assisted reproductive technology (ART) cycle based on couples' baseline characteristics and controlled ovarian stimulation (COS) protocols. Therefore, we sought to create a clinical prediction model for counseling and COS protocol selection.

DESIGN: A retrospective cohort study.

MATERIALS AND METHODS: From Jan 2012 to Mar 2016, all women at age of 19-39 years old with at least 5 antral follicle count (AFC) underwent just one complete ART cycle with long GnRH-agonist, depot GnRH-agonist, modified long GnRH agonist and GnRH-antagonist protocols in Chengdu Xi'nan Gynecology Hospital were included, and followed up to Mar 2018. Couples with chromosome abnormality were excluded. Cumulative live birth was defined as first live birth resulting from one initiated ART cycle, including cycles in which fresh and/or frozen embryos were transferred, until one delivery with a live birth occurs or until all embryos are used, whichever occurs first. A multivariate stepwise logistic regression model was used to predict the probability of cumulative live birth. The accuracy of the model was then tested using a receiver operating characteristic curve (ROC).

RESULTS: 6862 patients with 6862 complete ART cycle were enrolled with a 72.89% overall cumulative live birth rate (CLBR), namely 5002 cycles cumulatively had live birth. Predictors in the model were female's age (-0.07, 95% CI:-0.09∼-0.05, P<0.001), height (0.06, 95% CI:0.05∼0.08, P<0.001), weight (-0.01, 95% CI:-0.02∼0.00 , P=0.005), duration of infertility (-0.06, 95% CI:-0.08∼-0.04 , P<0.001), number of previous ART cycle (-0.60, 95% CI:-0.79∼-0.41 , P<0.001), basal AFC (0.08, 95% CI:0.07∼0.09, P<0.001), basal FSH (-0.09, 95% CI:-0.12∼-0.06, P<0.001) and COS protocols [long GnRH-agonist (reference category), depot GnRH-agonist (-0.08, 95% CI:-0.64∼0.48, P=0.785), modified long GnRH agonist (-0.69, 95% CI:-0.96∼-0.43 , P<0.001), GnRH-antagonist protocols (-0.12, 95% CI:-0.71∼0.47, P=0.696)]. The area under the curve (AUC) for ROC was 0.708.

CONCLUSIONS: This model provides a scientific predicting method for probability of cumulative live birth, thus help doctors give patients more accurate counseling and select more suitable COS protocol.

SUPPORT: This study was supported by the China Health Promotion Foundation's ART Research Program of Young and Middle-aged Physicians.

P-1009 3:30 PM Wednesday, October 21, 2020

IS BLASTOCYST DEVELOPMENTAL RATE A GOOD PREDICTOR OF ONGOING PREGNANCY RATE IN EUPLOID BLATOCYSTS? Silvia De Frutos Sánchez, MSC,[1] Marta Ariza Lopez, MSC,[1] Fernando Bronet, PhD,[2] Eva María Martinez, MSC,[1] Maria Gaytan, PhD,[1] Ma Del Carmen Nogales, MSC,[1] Ma José de los Santos, PhD.[3] [1]IVI RMA Madrid, Madrid, Spain; [2]IVI Madrid, Madrid, Spain; [3]IVIRMA Valencia, Valencia, Spain.

OBJECTIVE: To determine whether onoing pregnancy rate (OPR) is affected by bastocyst developmental rate (trophoectoderm biopsy on day 5 or on day 6) in euploid embryos with the same morphological quality.

DESIGN: Retrospective, observational and multicenter cohort study.

MATERIALS AND METHODS: Patients who underwent PGT-A or PGT-SR cycles, dated from May 2016 to February 2019, in IVI Madrid, IVI Valencia and IVI Barcelona were included. A total of 5648 euploid embryos (biopsied on day 5 and on day 6) were divided into six different grups according to their morphological quality, wich are further divided acording to the biopsy day. Statistical program SPSS was used to find significant differences in OPR among analized groups (Table 1).

All biopsied blastocysts were hatching or hatched. Blastocysts were divided as followed: 427 in Group 1 (AA), 792 in Group 2 (AB/BA), 2921 in Group 3 (BB), 1477 in Group 4 (BC/CB/CC), 21 in Group 5 (AC) and 10 in Group 6 (CA).

RESULTS:

	OPR DAY 5	OPR DAY 6	p	N (D5+D6)
GROUP 1 BH(i) AA	55,50%	50,48%	ns	427
GROUP 2 BH(i) AB/BA	56,76%	51,28%	ns	792
GROUP 3 BH(i) BB	53,90%	46,23%	**0,0455**	2921
GROUP 4 BH(i) BC/CB/CC	45,26%	34,68%	**< 0,0001**	1477
GROUP 5 BH(i) AC	40%	33,33%	ns	21
GROUP 6 BH(i) CA	50%	33,33%	ns	10

CONCLUSIONS: Excelent and good blastocysts (Groups 1 and 2) have similar OPR, regardless the day of the biopsy. However, average and poor blastocysts (groups 3 and 4) showed lower OPR on Day 6. We can conclude that blastocyst developmental rate can affect OPR only when the morphological embryo qality is average or poor.

*As the number of embryos included in Groups 5 and 6 were too small, they have not been considered for conclusions.

P-1010 3:30 PM Wednesday, October 21, 2020

PROOF OF CONCEPT OF A TREATMENT FOR HUMAN OOCYTE MATURATION ARREST;TRANSVAGINAL OVARIAN NEEDLE INJURY PRECEEDING LETROZOLE PRIMING IN VITRO MATURATION. Safak Hatirnaz, MD,[1] Ebru Hatirnaz, MD,[1] Alper Basbug, MD,[2] Michael H. Dahan, M.D.,[3] Kaan Hatirnaz, LİCENCE STUDENT.[4] [1]Medicana International Hospital, Samsun, Turkey; [2]DÜZCE UNIVERSITY, DÜZCE, Turkey; [3]Division of Reproductive Endocrinology and Infertility, McGill University Health Care Center, Montreal, QC, Canada; [4]ONDOKUZ MAYIS UNİVERSİTY SCHOOL OF SCİENCE, SAMSUN, Turkey.

OBJECTIVE: We aim to present the proof of concept of a novel targeted treatment strategy; transvaginal ovarian needle injury (TVOI) preceeding letrozole priming in vitro oocyte maturation (Letrozole IVM) for women suffering from repeated in vitro fertilization failures due to oocyte maturation arrest (OMA).

DESIGN: This study is designed as a proof of concept study.

MATERIALS AND METHODS: 7 cases were treated with TVOI-Letrozole IVM protocol.

TVOI –Letrozole IVM protocol was desinged to address all mechanisms involved in the maturation arrest process of oocytes.

TVOI is the puncture under mild sedation or anesthesia with a 17 gauge aspiration needle with 10-20 punctures in each ovary.This procedure can be performed 1-6 months before letrozole priming IVM procedure.The aim of TVOI is to activate the follicles from the primordial follicular pool and to distrupt any inhibiting factors if present in the ovary

Letrozole,an aromatase inhibitor induces endogenous FSH secretion secondary to the reduced estrogen levels. The resultant increased androgens may promote follicular/oocyte growth and maturation.

IVM was selected as the treatment of choice in cases with OMA because unknown intrafollicular factors can be hypothesized to either promote apoptosis of the oocytes or may cause oocyte maturation issues.

The combination of these methods was named as TVOI-Letrozole IVM protocol

SPSS 23.0 (IBM Corporation, Armonk, NY, USA) was used for the statistical analysis of the data.The quantitative data were expressed as median and range (minimum–maximum) and categorical variables were expressed as number (%).

RESULTS: Seven out of fifteen women completed their TVOI-Letrozole IVM cycles.

The clinical and laboratory course of all participants(including treated and untreated patients) were shown in Table 1.

One woman with two IVF failures due to OMA a the MI stage gave birth to a healthy baby.

Another women with seven failed IVF attemts due to Mixed OMA(GV,MI and immature MII oocytes) gave birth to a healthy baby.

Embryo transfer was succesfully performed in a woman with mixed OMA who had five times failed IVF history but pregnancy can not be achieved.

In one woman with a history of five failed IVF attempts dueto MI OMA was treated with our protocol but we failed to achive MI-MII transition in this case.

In a woman with a family history of ZP1 mutation,we applied TVOI and letrozole priming IVM for diagnostic purpose and zona free oocytes without any maturation (GV OMA) was determined.

In one woman with Primary amenorrea with normal AMH value our protocol managed to retrieve one GV and one MI oocytes for the first time in her life but failed to mature the eggs.

In one woman with 4 failed IVF attempts due to mixt OMA ,one oocyte was succesfully fertilized for the first time but arrested at PN stage.

CONCLUSIONS: OMA is accepted to be untreatable by autologous oocytes currently .Targeted treatment like TVOI-Letrozole IVM may show in overcoming OMA in selected cases.Studies are warranted to clarify mechanisms of OMA and of how TVOI Letrozole functions.This case series presents the first livebirths with autologous oocytes in OMA.

SUPPORT: No financial support for this study

P-1011 3:30 PM Wednesday, October 21, 2020

HP-HMG IN MONOTHERAPY IMPROVES CLINICAL OUTCOMES IN YOUNG WOMEN. María Cruz, PhD, Maria Eugenia Ruiz, PhD. IVIRMA Global Headquarters, Madrid, Spain.

OBJECTIVE: To evaluate the efficacy of HP-hMG ovarian stimulation in young women to tailor ART protocols to meet patient needs and improve the likelihood of a positive outcome in real world setting.

DESIGN: Multicenter retrospective, anonymized cohort analysis performed in 11 Spanish clinics from the IVI group.

MATERIALS AND METHODS: Study population:women < 38 years old receiving monotherapy with HP-hMG (n=1744) or rFSH (n=3316). Patients underwent short GnRH antagonist protocol, 0.25 mg daily doses from day 6 of stimulation. On day cycle 2/3, they received daily rFSH α/β or HP-hMG, with FSH:LH activity ratio 1:1. Initial doses were based on weight and BMI according to the experience of clinicians. . A single dose of 0.1 mg GnRH agonist was used for triggering. Embryo transfer was performed on day 3 or 5 where applicable. ANOVA and Chi-squared statistical analysis was performed.

RESULTS: Assuming the limitations of the study design**,** we observed significant differences in age (33.1±0.1 vs 34.1±0.2 y, p<0.001), AMH levels (3.7±0.4 vs 2.9±0.5 ng/ml, p=0.002) and AFC (14.1±2.0 vs 12.7±1.5 follicles, p=0.031) favoring rFSH vs HP-hMG group. Number of retrieved oocytes was significantly higher with rFSH vs HP-hMG (13.1±0.4 vs 10.0±0.3, p<0.001). as well as MII (9.2±0.5 vs 7.1±0.2, p<0.001). However, despite these poorer biomarkers of ovarian response HP-hMG can improve the efficiency of the cycle since there are no significant differences in the usable blastocyst rate in any of the ratios analyzed. Clinical outcomes are also significantly better for HP-hMG vs rFSH: clinical pregnancy (57.1% vs 54.1% p=0.045) and live birth (45.8% vs 42.1% p=0.043) rates, respectively.

CONCLUSIONS: We can establish the possibility that the LH activity mainly provided by hCG of postmenopausal origin only, might improve the proficiency of the cycle. The HP-hMG group got a more effective MII/oocyte ratio. In addition, the initial differences in the number of oocytes retrieved with rFSH disappeared, as there were no differences in usable blastocyst rate according to the number of retrieved oocytes, MII or fertilized oocytes. We might also assume the hCG-driven LH activity improves embryo quality, since stimulation with HP-hMG significantly increases clinical outcomes not only in clinical pregnancy rate but in live birth rate, which is ultimately the parameter that determines the true success of the treatment. HP-hMG vs rFSH data of well-designed randomized control trials can be here confirmed in antagonist setting in a real-world scenario.

SUPPORT: No

P-1012 3:30 PM Wednesday, October 21, 2020

UTILIZATION OF GONADOTROPIN-RELEASING HORMONE AGONIST (GNRHA) TRIGGER IN GNRH ANTAGONIST CYCLES: DOES THE TIME INTERVAL FROM LAST ANTAGONIST ADMINISTRATION MATTER? Anat Hershko Klement, MD,[1] Efrat Esh Broder, MD,[1] Amy Solnica, RN MSN,[1] Hananel G. E. Holzer, MD,[1] Judith Frei, RN MSN,[2] Jigal Haas, M.D.,[2] Raoul Orvieto, MD.[2] [1]Hadassah Mt. Scopus, the Hebrew university, Jerusalem, Israel; [2]Sheba medical center, Tel Aviv university, Ramat Gan, Israel.

OBJECTIVE: To evaluate the efficiency of GnRHa trigger in GnRH antagonist cycles with regard to the time interval from the last antagonist administration to trigger injection.

DESIGN: A cohort encompassing two IVF clinics was assembled: we included GnRH antagonist IVF cycles in which GnRH agonist (GnRHa) trigger was used alone for final oocyte maturation or GnRHa trigger as a surrogate trigger along with hCG (dual trigger). Oocyte retrieval took place 36 hours after trigger injection. One clinic adhered to a 12-14 hour interval between last antagonist administration and trigger, while the other clinic practiced shorter intervals.

MATERIALS AND METHODS: All cycles were assessed retrospectively and analyzed according to the time interval between the last GnRH antagonist exposure to the triggering injection time. Group1 included patients with a 12-14 hour interval, Group 2 included patients with an 8-10 hour interval and Group 3 included patients with a 4-6 hour interval. LH levels were measured 12 hours post trigger injection. The study was approved by a local Institutional Review Board.

RESULTS: 78 patients were included in Group 1, 164 in Group 2, and 54 in Group 3. Roughly 40% of patients were triggered by the dual trigger and statistical analysis was split according to the triggering modality in order to avoid the bias related to the use of agonist trigger in cases prone to OHSS. For the entire study population, mean and median post-trigger LH levels were 66.7±41.4 mIU/ml, 61.2 4 mIU/ml respectively. No previous data exists regarding post trigger LH level in respect to the antagonist schedule: we found that LH levels were significantly higher in group 2 (55.8±28.5 Group 1, 77.0±49.4 Group 2, 59.2±29.5 Group 3, p= 0.01), but no correlation between the absolute LH level to the number of oocytes retrieved or to the oocyte maturation rate (p= 0.4 and 0.6 respectively) for both triggering modalities. In a multivariate Poissonian model for oocyte number, neither time interval from antagonist, nor absolute LH levels were significant predictors for the outcome, while age, as expected, was (p <0.001).

CONCLUSIONS: GnRH antagonist administration timing before GnRH agonist trigger does not seem to affect the triggering efficiency in intervals between 14 to 4 hours prior to the GnRH agonist utilization. In these time intervals, the conventional 0.2 mg GnRH agonist dose is sufficient for displacing the GnRH antagonist and triggering final follicular maturation. To the best of our knowledge, this is the first study looking into the efficiency of GnRHa trigger in GnRH antagonist cycles, with regard to the time interval from the last antagonist administration to trigger injection. Further prospective randomized controlled studies are warranted to support our conclusion.

SUPPORT: None

P-1013 3:30 PM Wednesday, October 21, 2020

WHEN AND WHERE DURING COVID-19: THE EFFECT OF AT-HOME SEMEN COLLECTION ON SPERM PARAMETERS, FERTILIZATION RATE, AND BLASTOCYST RATE. Caitlin R. Sacha, MD, Stylianos Vagios, MD, Karissa C. Hammer, MD, Victoria W. Fitz, MD, MSCR, Irene Souter, MD, Charles L. Bormann, PhD. MGH Fertility Center and Harvard Medical School, Boston, MA.

OBJECTIVE: In order to maintain social distancing and reduce risk of transmission of coronavirus disease 2019 (COVID-19) amongst patients at an academic fertility center, semen collection for semen analyses and treatments such as intrauterine insemination (IUI) and in vitro fertilization (IVF), were converted to "at home." Our aim was to assess whether at-home semen collection altered sperm parameters, fertilization rates, or day 5 usable quality blastocyst rates in patients undergoing IVF.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Semen parameters and embryo outcomes were compared in 42 patients between their IVF cycle prior to COVID-19 (on-site "clinic" collection) and their subsequent cycle after COVID-19 protocols necessitated "at-home" collection. On-site collection was performed in a room adjacent to the andrology laboratory, and processing occurred within approximately 30 minutes. The post-COVID-19 collections were performed at home with the standard specimen cup, delivered to the andrology laboratory within 2 hours of collection, and then processed. Patient demographics, semen parameters, fertilization rate (number of 2 pronuclear embryos/number metaphase II oocytes), and day 5 usable quality blastocyst rate (number transferable and freezable blastocysts/number 2 pronuclear embryos) in fresh transfer cycles were compared between clinic and at-home collections from each patient with a paired T-test. The effect of time between semen production and processing on sperm parameters and embryo outcomes was assessed with linear regression modeling.

RESULTS: Mean male age was 38.1 years in the clinic group and 38.9 years in the at-home group ($p < 0.001$). On average, men were abstinent for 2.9 days (SD 1.3) in the clinic group and 3.3 days (SD 3.6) in the at-home group ($p = 0.576$). Mean time to semen processing was 34.0 minutes (SD 11.4) in the clinic group and 78.7 minutes (SD 28.5) in the at-home group ($p < 0.001$). Semen concentration, percent motility, total motile count, and forward progression score were similar between the clinic and at-home groups. While there was no change in sperm parameters by the amount of time to processing in clinic samples, those collected at home demonstrated an increase in motility of 0.357% ($p = 0.002$), an increase in total motile count by 1.6 million ($p = 0.007$), and an increase in forward progression score of 0.01 ($p = 0.006$) for each extra minute from production to processing. There were no differences in mean fertilization rates (clinic 77.0%, SD 22.5 vs. at-home 77.9%, SD 18.2; $p = 0.813$) or usable day 5 blastocyst rates (clinic 47.2%, SD 21.3 vs. at-home 54.6%, SD 24.8; $p = 0.218$). Longer time between semen production and processing had no effect on fertilization rates or day 5 usable quality blastocyst rates.

CONCLUSIONS: Our data suggest that at-home semen collection within 2 hours of processing does not negatively impact sperm parameters or embryo outcomes within the same patient. Therefore, at-home collection is a reasonable alternative to on-site collection in clinics seeking to encourage increased social distancing of patients during the COVID-19 pandemic.

SUPPORT: None

P-1014 3:30 PM Wednesday, October 21, 2020

PATERNAL EXPOSURE TO NON-ESSENTIAL HEAVY METALS AFFECTS EMBRYO EFFICIENCY INDICATORS IN INTRACYTOPLASMIC SPERM INJECTION (ICSI) CYCLES: EVIDENCE IN FAVOR OF A PARADOXICAL EFFECT. Johnny Awwad, M.D., HCLD, Carol Sukhn, PhD, Akram Ghantous, PhD, Nour Assaf, BS, Ghazi Zaatari, MD. American University of Beirut Medical Center, Beirut, Lebanon.

OBJECTIVE: While preconception health remains an essential component of fertility counseling, the association between paternal exposure to pollutants and reproductive endpoints in intracytoplasmic sperm injection (ICSI) cycles remains uncertain and poorly explored. The primary aim of this study was to address this existing data gap and generate hypotheses by identifying associations between paternal levels of non-essential metals in blood and semen, and reproductive endpoints in ICSI cycles.

DESIGN: This is a prospective cohort study of heterosexual couples undergoing ICSI treatment using autologous oocytes at a university fertility center. Ninety-five heterosexual couples undergoing fresh ICSI cycles were evaluated.

MATERIALS AND METHODS: Metal levels (lead Pb, cadmium Cd, arsenic As, mercury Hg, barium Ba, and uranium U) in semen and blood samples from male partners were analyzed using Ion-Coupled Plasma-Mass Spectrometry (ICP-MS; Agilent 7500 ce, Agilent Technologies, Germany) equipped with cell dynamic range. Adjusted associations between paternal concentrations of metals and embryo-level outcomes (embryo quality/fragmentation score, cleavage, and implantation) were evaluated using multiple linear regression models and natural log transformed metal data. Associations between paternal exposure and reproductive endpoints (live births) were investigated using modified Poisson regression employing a sandwich variance estimator after adjusting for co-variates.

RESULTS: High blood Cd, As and U levels in men were associated with significantly lower proportions of cleaved embryos ($\beta = -0.30$; 95% CI: -0.11, -0.02; $P = 0.01$) ($\beta = -0.26$; 95% CI: -0.16, -0.11; $P = 0.02$) ($\beta = -0.22$; 95% CI: -0.24, -0.02; $P = 0.05$), respectively. Counterintuitively, paternal blood and semen Pb concentrations were positively associated with higher embryo implantation ($\beta = 0.26$; 95% CI: 0.01, 0.22; $P = 0.03$) ($\beta = 0.25$; 95% CI: 0.03, 0.14; $P = 0.04$), respectively. Semen U concentrations were also positively associated with embryo implantation ($\beta = 0.27$; 95% CI: 0.01, 0.19; $P = 0.03$). Paternal metal concentrations in both body compartments did not predict the likelihood of livebirth in ICSI treatment cycles.

CONCLUSIONS: These findings highlight the potential effects of sperm metal exposure on embryo efficiency indicators after ICSI, laying support to possible molecular pathways which could impact specific pre- and post-implantation embryonal events. This may point to the likelihood of a transgenerational effect of paternal exposure to pollutants with long-term bearing on obstetrical and postnatal outcomes. These results also underline a paradoxical favorable association between specific metal pollutants at low-exposure levels and some reproductive outcomes, shedding light on different pattern effects through pathophysiologic pathways unique to each trace element. Whereas counseling of women is common practice in fertility care, this study emphasizes the importance of paternal health on reproductive outcomes in ICSI treatment cycles and the need for more male partner inclusive counseling in fertility practice.

SUPPORT: Medical Practice Plan MPP - American University of Beirut

P-1015 3:30 PM Wednesday, October 21, 2020

COMPARISON OF THE EMBRYO QUALITY OBTAINED AFTER AN UNSTIMULATED AND STIMULATED CYCLE IN THE SAME INFERTILE PATIENT UNDERGOING *IN VITRO* FERTILIZATION. Elena Labarta, MD PhD,[1] Cristina Rodriguez-Varela, M.Sc,[1] Marcos Meseguer, PhD,[1] Lorena Bori, M.Sc,[1] Arantza Delgado, PhD,[2] Amparo Mercader, PhD,[1] Belén Aparicio-Ruiz, PhD,[1] Ernesto Bosch, MD, PhD.[1] [1]IVI-RMA, Valencia, Spain; [2]Embryologist, Valencia, Spain.

OBJECTIVE: To analyze if ovarian stimulation increases the rate of aneuploidy compared to what occurs in the natural basal state.

We compared the probability of a MII oocyte becoming an euploid blastocyst in a natural and stimulated cycle in the same patient.

DESIGN: Prospective cohort study comparing embryo quality after a modified natural (MNC) and a stimulated cycle (SC) in the same infertile IVF patient. Registration Number: NCT03128580.

MATERIALS AND METHODS: Patients provided written informed consent prior to any procedure. No exogenous gonadotropins were given in the MNC. The requirement to continue in the study was to obtain at least one MII oocyte in the MNC. The SC consisted of a fixed combo GnRH antagonist protocol with a daily dose of 225 IU of rFSH and 75 IU of hp-HMG. In both cycles, ovulation was triggered 36h prior to oocyte retrieval with triptoreline (0.1mg) when at least one (MNC) or 3 follicles (SC) >=17 mm were observed.

Embryo quality was assessed through morphological (following the ASEBIR criteria), morphokinetic (by time-lapse technology) and genetic evaluation (using NGS for the embryo chromosomal analysis).

Student's t tests and ANOVA were used for quantitative variables, for comparisons between 2 or more than 2 groups, respectively. $\chi 2$ was used for categorical variables. Correlation between quantitative variables was evaluated by Pearson's correlation analysis. P-value<0.05 is considered statistically significant.

Sample size was calculated assuming a 5% difference in the % of euploid embryos/ MII in favor of the MNC. Assuming that at least 2 MII oocytes are

obtained in the SC, 70 patients were needed to reach a statistical power of 80% and a 95% confidence level in a single-tailed test where the upper limit of the CI excludes a 10% difference (80 patients considering a 15% loss rate). After an interim analysis, the study was discontinued after a stochastic curtailment analysis.

RESULTS: From 54 recruited patients, 40 obtained MII oocytes in both cycles. Intra-patient comparison showed a similar proportion of euploid embryos per MII oocyte (16.1% in MNC and 18.6% in SC; p>0.05). The number of oocytes needed to obtain one euploid blastocyst was 6.2 MII in MNC and 5.4 MII in SC (p=0.68). Aneuploidy rates were 64.7% vs 52.4%, respectively (p=0.30).

No differences were observed in the morphological classification (p=0.89), whereas morphokinetic evaluation showed that tPNf, t3, t5, t6, t7, t8, t9+,tSC, and t5-t2 were significantly faster in the SC (p<0.05).

The mean number of euploid embryos was significantly higher in the SC (2.4 vs 0.2; p=0.000). A linear relation was found between the number of oocytes and the number of euploid blastocysts obtained (R=0.659; 0=0.00).

CONCLUSIONS: Ovarian stimulation has no negative effect on oocyte and embryo quality. Aneuploidy rate, the number of MII needed to obtain an euploid blastocyst, and embryo quality are comparable between the natural and the stimulated cycle. The implication of the faster division times observed in the SC is yet to be determined.

Ovarian stimulation offers a significantly higher number of euploid embryos without diminishing embryo quality.

SUPPORT: Research grant award from FINOX (Forward initiative 2016)

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REDUCTION OF BACTERIAL COLONY FORMING UNITS IN AN OBSTETRICS OPERATION THEATRE USING COLD-PLASMA BASED DIELECTRIC BARRIER DISCHARGE AIR PURIFICATION SYSTEM. Milind RAMCHANDRA. Ubale, M.D.,[1] Rajvi H. Mehta, Ph.D.[2] [1]Rajiv Gandhi Medical College & Chatrapati Shivaji Maharaj Hospital, Thane, India; [2]Trivector Boimed LLP, Mumbai, India.

OBJECTIVE: To evaluate the effectiveness of the cold-plasma based dielectric barrier discharge (CP-DBD) based air purification system on the number of bacterial colony forming units in an obstetrics operation theatre (OBOT).

DESIGN: Air samples were taken to determine the bacterial load before and 7, 14 and 21 days after the installation of the CP-DBD based air purification system in the OBOT; the unit was switched off on Day 21 and air samples were taken on Day 28. The number of bacterial colony forming units were compared on different days to determine the effect of the CP-DBD air purification system on the bacterial load.

MATERIALS AND METHODS: This study was carried out in the OBOT of a municipal public hospital. Air samples were taken from the OBOT (Pre, Day 0) at 0, 1, 2, and 4 hours. The CP-DBD based air purification system Novaerus-1050 was installed in the OBOT and air samples were taken at 0, 1, 2 and 4 hours on Day 7, 14, 21 days (Post). The Novaerus unit was switched off after taking the samples on Day 21 and 4 air samples at 0, 1, 2 and 4 were taken on Day 28. The number of individuals present in the OBOT on that particular day was also noted. The air samples were cultures on Blood agar and Sabouraud's Dextrose agar plates and incubated at at 37^0 C for 48 hours and 30 days respectively. The number of bacterial colony forming units for each air sample were determined in the Blood agar as well as Sabourauds Dextrose Agar plates. The data for Day 0, 7, 14, 21 and 30 was tabulated and and compared.

RESULTS: There was significant reduction in bacterial colony count /ml in post- I compared to pre-I air sampling. Fluctuation in post- I colony count at 0 ,1, 2, 4 hours was observed during each intervention day that is on 0, 7, 14, 21 days. However in all intervention days the 4 hours CFU showed reduction in bacterial colony counts as compared to 0 hour colony count. At day 28, there was increase in colony counts at every reading (0, 1, 2, 4 hours) as compared readings taken on day 0, 7, 14, 21 days when air purifier was operational. The mean CFU decreased from 21 on Day 0 to 10, 7, 5 on Day 7, 14 and 21 respectively. After switching off the CP-DBD air purification system, the mean CFU increased to 18 on Day 28.

CONCLUSIONS: The results indicate that continuous usage of cold plasma based air purifier system can decrease and consistently maintain low microbial load in the operation theaters. This system would be very useful in OBOTs of public hospitals which work 24 x 7 and therefore are higher risk of microbial contamination.

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INCREASED AVERAGE OF SPERM HEAD AREA (ASHA) IS A NOVEL SPERM PARAMETER ASSOCIATED WITH HIGHER INCIDENCE OF SPERM ANEUPLOIDY. Miguel Ruiz-Jorro, MD, MSc, PhD,[1] Minerva Ferrer-Buitrago, BSc, PhD,[1] Juan Jesús Bataller-Sánchez, BSc, MSc,[1] Antonio Barberá-Alberola, MSc,[1] Xavier Vendrell-Montón, BSc, PhD,[2] Carmen Calatayud-Lliso, MD, MSc, PhD.[1] [1]CREA. Medicina de la Reproducción S.L., Valencia, Spain; [2]Ascires Sistemas Genómicos, Paterna-Valencia, Spain.

OBJECTIVE: To evaluate the association between the average sperm head area (ASHA) and altered sperm aneuploidy rate in male infertility.

DESIGN: A total of 147 patients who showed normal sperm aneuploidy rates were used as a control to determine the cut-off value for ASHA. A retrospective study was further performed to calculate the incidence of sperm aneuploidy in infertile patients with a suspected risk of sperm aneuploidy: Recurrent implantation failure or pregnancy loss (RIF; RPL), or testicular failure (Study Group 1; n=250). The intra-patient variability of ASHA was compared to other sperm parameters: concentration, motility and morphology. Moreover, the sperm aneuploidy rate was prospectively assessed in a total of 22 patients with increased ASHA values, who showed normal testicular function, normal FSH values (4,81±2,83 mUI/ml), and absence of RIF or RPL. Sample size was adjusted to detect at least 30 % difference in sperm aneuploidy rate compared to published data in reference population of infertile men (15.0 %), and for a power calculation of 95.

MATERIALS AND METHODS: All participants signed an informed consent form. ASHA cut-off value was established according to the value at percentile 95. Chi-squared statistic was used to asses frequency distribution. Two semen samples were analyzed per patient according to WHO-V-manual. Sperm concentration, motility, morphology and ASHA were evaluated using the CASMA software ISAS. Samples were stained using the Diff-quick kit. Sperm aneuploidy was determined by FISH analysis (5 chromosomes) using Metafer-4 software.

RESULTS: ASHA cut-off value was established as $\geq$14,8 μm2 in the control group. Group 1 revealed an increased incidence of altered FISH (41.2%) compared to the reference value (15.0%). The mean ASHA value in group 1 was 12.9 $\pm$ 1.3 μm2, whereas the mean ASHA value in the subgroup of patients with altered FISH was 13.2 $\pm$ 1.4 μm2. ASHA values showed lower intra-patient variability (p<0.002) and higher positive predictive value to detect altered FISH (73.9%) than other sperm parameters such as concentration (56.5%), total sperm count (58.8%) and morphology (46.7%). The predictive value of ASHA to detect sperm aneuploidy was further validated in a prospective analysis (Group 2). Sperm parameters in group 2 were: concentration (20.8 $\pm$ 26.5 million sperm/ ml), % total motility (45.0 $\pm$14.6) and % normal morphology (1.6 $\pm$0.7). The mean ASHA value in group 2 was 15.2 $\pm$ 0.6 μm2, and the incidence of sperm aneuploidy was significantly increased compared to the reference value of 15.0% (p<0.05).

CONCLUSIONS: Our study describes ASHA as a sperm parameter with low intra-patient variability. Prospective data revealed that patients presenting with idiopathic infertility, who show ASHA values > 14,8 μm^2 have a high risk to carry chromosomal aberrations in sperm. Our results indicate that altered ASHA is an indicator to request a FISH analysis from the first sperm evaluation.

These findings provide new insights in the field of androgenetics and male infertility, since ASHA might contribute to reduce the time to advise PGT-A, and consequently, the time to conceive in some infertile couples.

References: Fluorescent in situ hybridization ofÂ human sperm: diagnostics, indications, and therapeutic implicationsRamasamy, Ranjith et al.Fertility and Sterility, Volume 102, Issue 6, 1534 - 1539

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PREGNANCY LOSS RATES AFTER SINGLE, EUPLOID FROZEN-THAWED EMBRYO TRANSFER IN THE COVID-19 ERA. Eric Flisser, MD,[1] Devora Aharon, MD,[2] Dmitry Gounko, MA,[1] Alan B. Copperman, MD.[2] [1]Reproductive Medicine Associates of New York, New York, NY; [2]Icahn School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: Data on the impact of COVID-19 on early pregnancy is extremely limited, and patients and practitioners remain cautious about initiating pregnancy in areas of high SARS-CoV-2 transmission.[1-4] In April 2020,

during the peak of the pandemic, the prevalence of COVID-19 among New York State residents was estimated to be 22.7%, consisting largely of asymptomatic infection.[5] If SARS-CoV-2 is pathogenic to early pregnancy, an increase in loss might be expected given this high transmission. The objective of this study is to determine if an increase in early pregnancy loss occurred in patients undergoing single euploid frozen embryo transfer (FET) during the height of the COVID-19 pandemic.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The study took place at an academic tertiary care center with offices throughout New York City. All single euploid FET cycles performed from January-May of 2017-2020 were included. Cycles with FET in 2017-2019 were compared to those with FET performed in the corresponding time period in 2020. Baseline characteristics included age, oocyte age, AMH, BMI, and endometrial thickness. Pregnancy loss rate (PLR), or loss after the presence of serum βhCG $\geq$2.5 mIU/mL, and clinical pregnancy loss rate (CLR), loss after a gestational sac was seen on ultrasound, were compared between January-May, 2017-2019 and January-May, 2020, in aggregate as well as for each corresponding month individually. Comparative statistics and multivariable logistic regression were used.

RESULTS: 2629 single euploid FET cycles were included in the study: 2070 from Jan-May, 2017-2019 and 559 from Jan-May, 2020. Positive pregnancy rates were 73.7% in January-May, 2017-2019 and 77.6% in January-May, 2020. Baseline characteristics were similar. No differences were seen in PLR or CLR when comparing FET from January-May, 2017-2019 to FET from January-May, 2020. No differences were seen in PLR or CLR when comparing individual months in 2017-2019 to 2020. On multivariable logistic regression, when controlling for oocyte age, AMH, BMI, and endometrial thickness, FET in January-May 2017-2019 was associated with a higher odds of pregnancy loss compared to January-May 2020 (OR 1.32, 95% CI 1.02-1.73, p=.039). No difference was seen in CLR between these groups (OR 1.34, 95% CI 0.92-1.97, p=.13). No differences were seen in PLR or CLR comparing each month individually in the two time periods.

CONCLUSIONS: This data is reassuring that early pregnancy loss rates were not increased during widespread SARS-CoV-2 transmission. A decrease in PLR in January-May 2020 compared to prior years might be attributable to selection against treatment of patients with known risk factors for severe infection. While in the absence of universal screening for SARS-CoV-2, which at the time was neither available nor recommended, this data does not exclude a possible impact of infection on pregnancy loss, it suggests that screening patients for elevated temperature, symptoms, and exposure may be effective in maintaining established early pregnancy success rates. This data may help guide clinics in regions experiencing a surge in virus transmission.

SUPPORT: None

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P-1019 3:30 PM Wednesday, October 21, 2020

IS COH /IUI AN EFFECTIVE TREATMENT IN OLDER WOMEN AND MALE PARTNERS WITH DECREASED TOTAL MOTILE SPERM COUNTS?

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OBJECTIVE: To assess the effect of the total motile sperm count (TMSC) on the success of controlled ovarian stimulation (COH) and intra uterine insemination (IUI) in women 38-42 years-of-age. Current literature suggests women 35-40 years of age have no pregnancies when TMSC $\leq$5mil at COH/IUI [1, 2].

DESIGN: Retrospective cohort study, included women who underwent IUI with stimulation at a University Reproductive Centre between 2009-2018.

MATERIALS AND METHODS: A database from all women aged 38-42 years old who underwent IUI with stimulation at a University Reproductive Centre between 2009-2018. Including stimulation with clomiphene citrate, letrozole or gonadotropins and divided into TMSC 5.01-10.0 mil and $\leq$5.00 mil. The main outcome was clinical pregnancy rate, defined as fetal heart beat by ultrasound, per stimulation cycle. Statistics were compared with multivariate logistic regression, t-tests or chi-squared tests.

RESULTS: A total of 397 cycles of IUI were included, of which, 190 cycles with TMSC 5.01-10.0 and two hundred and seven cycles with TMSC $\leq$5.00. There were no statistical differences in the basic characteristics between the two groups including: age (P=0.2), gravidity (P=0.7), parity (P=0.6), basal FSH (P=0.2), basal E2 (P=0.4), antral follicular count (P=0.5) and the number of mature follicles stimulated (P=0.2). As designed, TMSC was 7.6$\pm$1.5 mil in the first group and 2.4$\pm$1.6 mil in the second group (P<0.0001). The clinical pregnancy rate per cycle in the 5.01-10.00 TMSC group was 9.5 % vs. 3.4% when TMSC $\leq$5.00 (P=0.01). When evaluating only women 40-42 years of age (99 women in the 5.01-10.00 TMSC group and 95 in the group of TMSC $\leq$5.00); the pregnancy rates were not statistically different between the two groups (7% vs. 7.3%, P= 0.082), nor was the clinical pregnancy rate (5% VS. 5.2%, P=0.7).

CONCLUSIONS: Women 38-39 years-of-age have poorer outcomes at COH/IUI when TMSC $\leq$5 million than if it is greater. Once a woman is 40 years of age this effect is lost. With mild male factor infertility, women 38-39 years of age have respectable outcomes at COH/IUI. Clinical pregnancy rates are just 5% irrelevant of sperm quality in women 40-42 years of age performing COH/IUI with male factor infertility.

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GNRH ANTAGONIST PROTOCOL WAS SUPERIOR TO MILD STIMULATION PROTOCOL IN CONTROLLED OVARIAN STIMULATION IN PATIENTS WITH DISCORDANCE BETWEEN ANTI-MÜLLERIAN HORMONE CONCENTRATION AND ANTRAL FOLLICLE COUNT.

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OBJECTIVE: To evaluate the laboratory and clinical outcomes between GnRH antagonist and mild stimulation protocols in patients with discordance between anti-Müllerian hormone (AMH) concentration and antral follicle count (AFC).

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: This study was conducted in the Reproductive Medical Center of the First Affiliated Hospital of Kunming Medical University during Jan 2016 to Dec 2019. This study included 130 infertile couples with female AMH<1.1 ng/mL and AFC$\geq$7 , 65 couples received GnRH antagonist protocol and another 65 age and BMI-matched couples received mild stimulation protocol treatment.Laboratory and clinical outcomes were compared between GnRH antagonist cycles and mild stimulation cycles. The primary outcomes included the no. of aspirated oocytes and cumulative clinical pregnancy rate. The secondary outcomes included the cycle cancellation rate and the no. of good-quality embryos.

RESULTS: During the study period, a total of 220 patients received 303 GnRH antagonist and mild stimulation cycles in our reproductive center. 130 cycles (65 in each group) were enrolled by using propensity score matching with age and BMI. Mean female age in GnRH antagonist and mild stimulation groups were 36.2 and 36.4 years, respectively (p=0.84). Mean male age (37.0 vs. 38.0 years), female BMI (23.5 vs. 23.3 kg/m2), AMH (0.76 vs. 0.74 ng/mL) and AFC (8.8 vs. 8.4) were all similar between these two groups (p=0.37, 0.73, 0.58 and 0.25, respectively). After adjusting for a series of

potential demographical and clinical confounders, we found 2.1 more oocytes were aspirated in GnRH antagonist cycles compared with mild stimulation cycles [adjusted mean (95% CI): 4.7(4.2-5.3) vs. 2.8(2.4-3.2), p<0.001]. Good-quality embryos were also significantly more in GnRH antagonist cycles than mild stimulation cycles [1.6 (1.2-2.2) vs. 1.1(0.8-1.5), p=0.014]. The cycle cancellation rate was non-significantly lower in in GnRH antagonist cycles than mild stimulation cycles (0% vs. 3.1%, p=0.13). The cumulative clinical pregnancy rate in GnRH antagonist cycles was higher than that in mild stimulation cycles [30.0% (20.0%-42.7%) vs. 21.8% (13.8%-33.8%), whereas the difference was non-significant (p=0.29).

CONCLUSIONS: We concluded that GnRH antagonist protocol may be superior to mild stimulation protocols in women with low AMH (<1.1 ng/mL) but moderate AFC (≥7). Due to the retrospective nature and the limited no. of sample size, population and multi-center based study and RCTs are warranted to provide stronger evidence.

SUPPORT: This study was supported by the China Health Promotion Foundation's ART Research Program of Young and Middle-aged Physicians.

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RECOMBINANT LUTEINIZING HORMONE (LH) SUPPLEMENTATION IMPROVES CONTROLLED OVARIAN HYPERSTIMULATION OUTCOME IN WOMEN WITH LOW LH CONCENTRATION DURING MID- AND LATE-FOLLICULAR PHASE. Tian Tang, M.D., Yuechao Lu, M.D., Junliang Guo, M.D., Wei Huang, Professor. West China Second Hospital; Key Laboratory of Birth Defects and Related Diseases of Women and Children, Ministry of Education, Sichuan University, Chengdu, China.

OBJECTIVE: To examine the role of rLH supplementation in patients undergoing assisted reproductive technology (ART). We therefore compared the effect of rFSH vs rFSH+rLH on controlled ovarian hyperstimulation (COH) characteristics and ART cycle outcome.

DESIGN: A retrospective cohort study was conducted for all cases on ART cycle outcome with the use of either rFSH or rFSH+rLH.

MATERIALS AND METHODS: From January 2018 to January 2019, 163 patients (52 with rLH and 111 without rLH) were enrolled in this study : 1. Main causes of infertility attributable to tubal, idiopathic, or male factors; Regular menstrual cycle; Normal uterine cavity. 2. Serum levels of LH (Follicle reached 12mm of the ovarian cycle) ≤4 IU/l. 3.Underwent COH utilizing GnRH-antagonist protocol. Propensity score matching (PSM) was used to reduce confounding, baseline characteristics between two groups were matched. The primary outcome measures were number of oocytes retrieved and number of embryos available. The secondary outcome measure is clinical pregnancy rate in fresh embryo transfer cycle.

RESULTS: PSM resulted in 98 patients (49 in each group) for analysis. Baseline characteristics, including age, BMI, AMH, basal FSH, basal LH, LH on day of stimulation start, LH on day of follicle reach 12mm and LH on day of triggering, did not differ significantly between two groups. Women accepted rFSH+rLH for stimulation had significantly higher number of oocytes retrieved (12.24 ± 8.13 vs 8.27 ± 5.98, P=0.007) and higher number of embryos available (4.20 ± 2.75 vs 2.98 ± 2.47, P=0.022) than rFSH alone.

	rFSH alone (n=49)	rFSH+rLH (n=49)	P value
Baseline Characteristics			
AGE	31.67 ± 4.86	31.45 ± 5.22	0.826
BMI	21.78 ± 2.89	21.18 ± 2.46	0.274
AMH	4.71 ± 4.44	4.68 ± 4.86	0.977
LH on day of follicle reach 12mm	1.51 ± 0.83	1.45 ± 0.96	0.745
Basal FSH	5.98 ± 3.12	7.24 ± 4.69	0.123
Basal LH	7.44 ± 10.19	6.17 ± 4.57	0.431
LH on day of stimulation start	4.55 ± 4.14	3.69 ± 2.68	0.237
LH on day of triggering	5.72 ± 29.52	1.93 ± 2.52	0.373
Outcome Measures			
Number of oocytes retrieved	8.27 ± 5.98	12.24 ± 8.13	0.007
Number of embryos available	2.98 ± 2.47	4.20 ± 2.75	0.022
pregnancy rate (%)	32.35 (11/34)	44 (11/25)	0.521

Women in rFSH+rLH group had higher clinical pregnancy rate (44.0% vs 32.4%, P=0.521) but showed no significant difference compared with rFSH group.

CONCLUSIONS: Supplementation of rLH was suggested to bring more oocytes and embryos and it might potentially increase the clinical pregnancy rate. Our data supports rLH supplementation improves controlled ovarian hyperstimulation outcome in women with low LH concentration (≤ 4 IU/l) during mid- and late-follicular phase. Further studies are needed to confirm these findings.

SUPPORT: This work was supported by Chengdu Science and technology project (2019-YF05-00250-SN).

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IN VITRO FERTILIZATION OUTCOMES OF BLACK PATIENTS COMPARED TO WHITE PATIENTS IN A MIDWEST COHORT. Jean-Claire Powe Dillon, MD, MPH,[1] Caitlin Elizabeth Martin, MD, MS,[1] Patricia T. Jimenez, MD,[2] Joan Riley, PhD, HCLD,[3] Kenan Omurtag, MD.[4] [1]Washington University School of Medicine, St. Louis, MO; [2]Washington University in St. Louis, Saint Louis, MO; [3]Washington University in St. Louis, St. Louis, MO; [4]Washington University St Louis School of Medicine, St. Louis, MO.

OBJECTIVE: To identify disparities in IVF cycle outcomes and parameters between black and white patients at a single center.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: Data from 2016-2019 was obtained from clinical records at Washington University in St Louis. Women undergoing their first fresh IVF cycle at the clinic were included. All analyses were performed with IBM SPSS Statistics software (version 26). The data was analyzed using chi-square, Fisher's exact test, or student's T-test where appropriate**.** Multinomial logistic regression was used for assessing live birth rate, controlling for body mass index (BMI) and age.

RESULTS: There were 1054 white patients (93.6%) and 72 black patients (6.4%) identified. The mean age was similar for black patients compared to white patients (34.4 years vs. 33.3 years, p = 0.083). The mean BMI was statistically higher for black patients when compared to white patients (31.3 vs. 27.7, p < 0.001). Tubal factor (33.3% vs. 12.2%, p < 0.001) and uterine factor (6.9% vs. 1.1%, p= 0.003) infertility was more common amongst black patients compared to white patients. The stimulation regimens for IVF were similar between groups. Black patients were statistically more likely to use preimplantation genetic testing of their embryos (n=6, 8.3% vs. n=23, 2.2%, p=0.008). Black women were more likely to have more embryos available to freeze compared to white patients (4.36 vs. 3.41 embryos, p = 0.001), however the live birth rate was lower amongst black patients compared to white patients, which persisted when controlling for BMI and age (n=15, 20.8% vs. n=352, 33.4%, AOR 0.510 95% CI 0.279-0.930, p = 0.030). The number of patients whose pregnancies resulted in spontaneous abortions were not statistically different amongst both groups (black n=5, 6.9% vs. white n=65, 6.2%, p=0.799).

CONCLUSIONS: Despite advances in reproductive medicine, disparities exist between black and white patients undergoing IVF. In a midwestern cohort, despite freezing more embryos, the live birth rate was overall lower in black women undergoing their first IVF cycle at our center compared to white women, when controlling for BMI and age. Risk factors for poorer pregnancies outcomes were identified to be higher in our black patients, such as BMI and uterine factor, however additional analysis needs to be completed to identify these relationships further. Black patients were more likely to have embryos to cryopreserve and use preimplantation genetic testing when compared to white patients, which warrants investigation of cumulative live birth rate amongst the groups. A subanalysis of insurance coverage on this new cohort will also provide needed socioeconomic insights related to access and outcomes.

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WHERE DO CRYOPRESERVED EMBRYOS END UP AFTER A POSITIVE PREGNANCY TEST? Edgardo Young, Jr., PhD,[1] Laura Isa, Medical Doctor,[1] Sofia Garcia Argibay, Medical Doctor,[1] María Pía Zappacosta Villarroel, Medical Doctor,[1] Roberto Inza, Medical Doctor,[1] Alberto Valcarcel, PhD.[2] [1]IFER, Ciudad Autonoma de Buenos Aires, Argentina; [2]IFER, Ciudad Autónoma de Buenos Aires, Argentina.

AGE	DESTINATION		LBR	MR	*P*
<35 (n = 93)	Not used Embryos		46/68 (67,6%)	4/25 (16%)	p <0,0001
	Used Embryos	Taken to unknown site	5/22 (22,7%)	1/21 (4,8%)	p = 0,1853
		Taken to another center		1/21 (4,8%)	
		Embryo transfer	17/22 (77,3%)	19/21 (90,5%)	p = 0,4121
35-39 (n= 103)	Not used Embryos		43/63 (68,3%)	7/40 (17,5%)	p <0,0001
	Used Embryos	Taken to unknown site	4/20 (20%)	3/33 (9%)	p = 0,4048
		Taken to another center	3/20 (15%)	2/33 (6%)	p = 0,3536
		Donation	1/20 (5%)		
		Embryo transfer	20/12 (60%)	28/33 (84,8%)	p = 0,0541
>40 (n= 49)	Not used Embryos		17/31 (54%)	1/18 (5,5%)	p <0,0006
	Used Embryos	Taken to unknown site	6/14 (42,8%)	1/17 (5,88%)	p = 0,0281
		Embryo transfer	14/8 (57%)	16/17 (94,1%)	p = 0,0281

OBJECTIVE: To report what happens with vitried surplus embryos after IVF in patients with a positive pregnancy test, carrying out an analysis according to age and final evolution of the pregnancy.

DESIGN: Retrospective descriptive study.

MATERIALS AND METHODS: We analyzed 245 embryo transfer cycles, performed between January 2013 to December 2017, in 235 patients with a positive pregnancy test and who vitried surplus embryos. All the patients underwent treatment with their own oocytes. The variables studied were: age, miscarriage rate (MR) and live birth rate (LBR). We compared the destination of the cryopreserved embryos according to the patient's age and pregnancy evolution. Statistical analysis was performed with Fisher's exact test.

RESULTS: 20% of the IVF cycles (n=49) were performed in women older than 40 years, 42% between 35 and 39 (n =103) and 38% in women younger than 35 (n= 94). Average age was 35.8 ± 4.1 years. 859 embryos were cryopreserved (3.5 ± 1.9 cryopreserved embryos/patient). Average search time for surplus embryos was 20.5 ± 17.9 months, rising to 36.9 ± 14.9 months after delivery and decreasing to 8.7 ± 7.8 months after miscarriage (P<0.0001). Up to date there are 118 (48.2%) patients whose cryopreserved embryos have not been transferred yet. Signficant differences were found in the three groups in using the cryopreserved embryos according to whether or not they had delivery.

CONCLUSIONS: Half of the surplus cryopreserved embryos in assisted reproductive technologies are not transferred. Regardless of the age of the patient, all groups showed the same behavior regarding the utilization of the cryopreserved embryos after delivery. It is essential to advise couples who perform assisted reproductive technologies, with a good probability of success (regardless of the patient's age), about the responsibility that embryonic cryopreservation entails. Argentine legislation has limitations regarding the availability of cryopreserved surplus embryos. We believe that Public Health policies related to this issue should be re evaluated based on these results.

SUPPORT: None

P-1024 3:30 PM Wednesday, October 21, 2020

NOMOGRAM FOR THE CUMULATIVE LIVE BIRTH RATE IN LOW PROGNOSIS PATIENTS ACCORDING TO POSEIDON CRITERIA: A RETROSPECTIVE COHORT STUDY OF 4494 PATIENTS IN CHINA. Pengfei Qu, Ph.D, Wenhao Shi, M.D. Northwest Women's and Children's Hospital, Xi'an, China.

OBJECTIVE: A small number of prediction model have been previously developed to predict the success of infertility treatment. However, the studies of prediction model for low prognosis patients are limited. The aim of this study was to develop and validate a nomogram for the cumulative live birth rate (CLBR) in low prognosis patients using a single center database in China.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We reviewed the clinical data of 4494 low prognosis patients according to POSEIDON criteria who underwent in vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI) treatment between 2014 and 2018 at Assisted Reproduction Center of Northwest Women's and Children's Hospital, Northwest China. Of the eligible participants, 70% were randomly assigned to the training set, while the remaining 30% were assigned to the external validation set. Multivariate analysis using the Logistic regression model was performed.

RESULTS: Multivariate analyses revealed that female age, female body mass index (BMI), antral follicle count (AFC), male infertility, uterine factor infertility, and basal serum follicle stimulating hormone (FSH) level were significant factors for CLBR in low prognosis patients. An area under the receiver operating characteristic curve (AUC) in the prediction model was 0.70 (95% CI 0.68 to 0.72) in the training cohort. The validation set showed good discrimination with an AUC of 0.68 (95% CI 0.65 to 0.71). Additionally, Hosmer-Lemeshow chi-square statistic was 5.931 (P = 0.655).

CONCLUSIONS: We developed and validated a nomogram to predict CLBR in low prognosis patients using a single center database in China. The validated nomogram to predict CLBR could be a potential tool for IVF counselling in low prognosis patients.

P-1025 3:30 PM Wednesday, October 21, 2020

APPLICATION OF THE CRYOPIECE SYSTEM FOR CRYOPRESERVATION OF RARE HUMAN SPERMATOZOA. Wenlong Su, MS,[1] Lei Jia, PhD,[2] Shujing He, MM,[3] Zhiqiang Zhang, master's degree,[4] Cong Fang, Ph.D.,[2] Xiao-yan Liang, PhD.[4] [1]Sixth Affiliated hospital of Sun Yat-Sen University, Guangzhou, China; [2]Reproductive Medicine Research Center, Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; [3]The Sixth Affiliated hospital of Sun Yat-Sen University, Guangzhou, China; [4]The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: To investigate the clinical efficacy of cryopiece system for cryopreserving rare human spermatozoa from patients with severe male-factor infertility.

DESIGN: Retrospective study.

MATERIALS AND METHODS: Cryopreservation of small numbers of human spermatozoa with cryopiece system was performed at the Reproductive Medicine Center of the sixth affiliated hospital of Sun Yat-Sen University between August 2019 and July 2020. Cryopreservation procedure was as follows: The liquefied ejaculated semen or testicular tissue which was dissected with two 1 mL-syringe needles, was centrifuged at 300g for 5 min. And the re-suspended deposit was loaded on the micro-strips. Spermatozoa were captured using ICSI injection pipette and added to 0.5μL droplet of cryoprotective solution on a cryopiece. After holding upon liquid nitrogen vapor for 15 min, the cryovial with a cryopiece was plunged into liquid nitrogen. On the day of oocyte retrieval, the cryopiece was placed on the ICSI dish with 37°C immediately. The recovery rate, fertilization rate and clinical outcomes were analyzed to evaluate the clinical efficacy of cryopiece system.

RESULTS: In total, 125 spermatozoa from 7 patients (44% motile) were vitrified. 107 spermatozoa were warmed for ICSI; the sperm recovery was 100%. The motile sperm rate per recovered spermatozoa was 31.4%. The 2PN fertilization rate was 60.9%, the cleavage rate was 85.7% and the rate of transferable embryo on D3 was 60.9%. The clinical pregnancy rate following fresh embryo transfer was 100% (2/2).

CONCLUSIONS: Hence, we draw the conclusion that the cryopiece system was a simple constructed and highly efficient carrier that used for vitrification of small numbers of human spermatozoa in micro-droplets.

SUPPORT: Medical Scientific TechnologyÂ Research Foundation of GuangdongÂ Province of China (A2020226); National Natural Science Foundation of China (81871214); NationalÂ Key R&D Program of China (2017YFC1001603)

P-1026 3:30 PM Wednesday, October 21, 2020

OLEANOLIC ACID INHIBITS PROLIFERATION AND ANGIOGENESIS AND PROMOTES APOPTOSIS IN HUMAN ENDOMETRIOTIC STROMAL CELLS. Jingjie Li, M.D.,[1] Pan Chen, PhD,[2] Xiaoyan Liang, M.D.[1] [1]the Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; [2]the First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: Oleanolic acid (OA) is a pentacyclic triterpenoid that has long been used as an effective drug in treating hepatitis, but its role in endometriosis remains unclear, our study aims to investigate the effect of OA in endometriosis progression in vitro.

DESIGN: Pharmacologic interventions in human endometriotic stromal cells.

MATERIALS AND METHODS: Patients with ovarian endometriosis undergoing laparoscopy were recruited at the Sixth affiliated Hospital of Sun Yat-sen University from January 2018 to May 2020. Primary human endometriotic stromal cells that isolated from ectopic endometrium (endometriotic tissue, n=12) were exposed to 20μM, 40μM, 60μM and 80μM of OA for 24 h. MTT assay, BrdU incorporation assay and Caspase-Glo luminescent-based assay were performed to detect cell growth and apoptosis. Enzyme-linked immunosorbent assay was carried out to measure expression of vascular endothelial growth factor (VEGF).

RESULTS: OA reduced the viability of stromal cells in a dose-dependent manner, 60 and 80 μM of UA treatment led to a decrease in the endometriotic stromal cell viability to 64.2% and 53.3%, respectively ($p < 0.05$), as compared to the viability in the vehicle. BrdU assay confirmed that the growth inhibition effect of OA started at 40 μM and increased up to 80 μM (22.5% of that in the vehicle group). Caspase-3 activity was also promoted dose-dependently, and 2.3-, 5.8-, 18.7-, and 89.6-fold of increase were found in the four concentration groups. Besides, OA inhibited the secretion of the proangiogenic factor VEGF in endometriotic stromal cells, 40μM, 60μM and 80μM of OA remarkably downregulated the levels of VEGF in supernatants by 29.5%, 44.7% and 73.6%, respectively.

CONCLUSIONS: OA plays a role in suppressing the survival of human endometriotic stromal cells by inhibiting proliferation and angiogenesis and promoting apoptosis.

SUPPORT: Chinese Universities Scientiic Fund of Sun Yat-sen University (NO.19ykpy04)

P-1027 3:30 PM Wednesday, October 21, 2020

ZIKA VIRUS INFECTION AND MALE FERTILITY TWO YEARS AFTER A MAJOR OUTBREAK: PRELIMINARY FINDINGS. Filipe Tenorio Lira Neto, MD MSc,[1] Marina Cadena Matta, PhD,[1] Alexandre de Freitas Cavalcanti Filho, MS,[1] Leuridan Cavalcante Torres, Sr., PhD,[1] Peter N. Schlegel, M.D.,[2] Shuibing Chen, PhD,[2] Gilbert J. Wise, MD.[2] [1]Instituto de Medicina Integral Prof. Fernando Figueira, Recife, Brazil; [2]Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY.

OBJECTIVE: Evaluate the effects of the ZIKV epidemic in the male reproductive function in a cohort of fertile men two years after a major outbreak in Brazil.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: We enrolled 39 fertile men who attended the urology an outpatient clinic at Recife - Brazil for vasectomy. All subjects completed an epidemiological questionnaire, underwent standard semen analysis, sexual hormone levels measurement, and ZIKV serologic tests. Based on their serologic tests results, subjects were divided in two groups, a ZIKV negative (Z-) group and a ZIKV positive group (Z+). Epidemiological, clinical and laboratory variables were compared between both groups.

RESULTS: There were 25 (64%) ZIKV positive subject based on positive serum IgG anti-ZIKV antibodies; no subject showed IgM anti-ZIKV antibodies or viral RNA by PCR in semen samples. There were no significant differences between the groups regarding demographic and clinical data, but a few variables deserve mention. Overall, only 7 subjects reported ZIKV infection symptoms in the last two years, a small number compared to the overall prevalence of ZIKV of positive serologic test. The proportion of participants that reported symptoms was higher in the Z+ group when compared to the Z- group (24% and 7% respectively). Fever, myalgia, headache and cutaneous rash were the symptoms described. There were no known neurologic sequelae in patients or first-degree family members. The Z+ group had a clinically significant higher incidence of mosquito bites than the Z- group, although without statistically significance. In addition, semen analysis parameters and hormone levels showed no differences between the groups.

CONCLUSIONS: The prevalence of serum IgG anti-ZIKV antibodies was high in this cohort of fertile men, despite a low prevalence of ZIKV infection symptoms. There was no statistical difference in semen parameters or hormone between the groups. Screening of all male infertility patients should be considered in areas with high risk of exposure to Zika Virus.

SUPPORT: None

P-1028 3:30 PM Wednesday, October 21, 2020

DESCRIPTIVE DIFFERENCES IN FERTILITY TREATMENT USAGE AFTER THE START OF THE COVID-19 PANDEMIC: A PILOT STUDY - FEELINGS ABOUT INFERTILITY IN RESPONSE TO THE COVID-19 EPIDEMIC (FIRE). Ijeoma N. Iko, M.D., Amanda Adeleye, M.D., A. Musa Zamah, M.D., Ph.D. The University of Chicago, Chicago, IL.

OBJECTIVE: Prior research has demonstrated that economic health has an influence on the utilization of assisted reproductive technology (ART). It is indisputable that the United States (US) economy has been negatively impacted by the novel coronavirus (COVID-19) pandemic. However, there is limited data on how the pandemic has affected patient interest in fertility treatment and limited data on how concern about infectious disease and physical health may affect family building decisions. We hypothesized that there would be a decrease in interest in fertility treatments due to the COVID-19 pandemic. The aim of this pilot study was to assess if the experience of COVID-19 in the US has influenced intentions to pursue fertility treatment.

DESIGN: Prospective internet-based survey.

MATERIALS AND METHODS: An internet based survey, administered through Redcap was used to assess demographics, concern about COVID-19, fertility treatment prior to and after statewide lockdowns which became widespread on March 15th 2020. The pilot survey was administered June 1st to July 31st 2020 to infertile participants between the ages of 18-43 years. The CloudResearch platform was used to recruit participants and administer the survey. COVID-19 related questions were derived from the validated COVID concern survey. Summary statistics are presented. Institutional Review Board approval was obtained.

RESULTS: The pilot survey was completed by 55 participants (female =46, 83.6%; male=9, 16.4%) from 23 states. The mean age was 29.6 years (+/- 7.6). The majority were White (78%), non-Hispanic (92.7%), with varying education levels, 45.5% (25/55) with some college education, 20% with a bachelor's degree (11/55) and 14.5% with graduated education (8/55). The majority of participants were "somewhat concerned" that they would lose their current job in the next 12 months (41.4%). While the majority believed that COVID-19 had spread widely in the US (32.7%) and had "inflicted serious damage in the area that" they lived (38.2%), most individuals felt that they could protect themselves from the virus (48.2%).

Prior to the pandemic, 29.1% (n=16) participants sought ovulation induction medications, 16.4% (n=9) sought intrauterine insemination and 9.1% sought (n=5) in vitro fertilization (IVF). The remainder of patients were contemplating treatment. After the pandemic, 13 patients were no longer interested in fertility treatment. The majority of patients, 53% (n=7) stated "I am worried about the coronavirus/COVID-19" as the primary reason they discontinued treatment, compared to several other reasons including spontaneous conception, financial concerns, and lack of partner support.

CONCLUSIONS: COVID-19 is an important consideration for people who discontinue treatment; however, it may not deter the majority of patients who seek care. Data is part of an ongoing larger prospective study.

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SUPPORT: None

P-1029 3:30 PM Wednesday, October 21, 2020

DIFFERENT TREATMENT MODALITIES FOR MANAGEMENT OF CAESAREAN SCAR ECTOPIC PREGNANCY: A SINGLE-CENTER EXPERIENCE. Dania Al-Jaroudi, MD, MHA,[1] Saeed Marzoq Baradwan, MD, SBOG, ABOG, MRCPI, MRCOG2,[2] Saud Aboudi, MBBS.[3] [1]King Fahad Medical City, Riyadh, Saudi Arabia. Reproductive Endocrine and Infertility Medicine Department, Riyadh, Saudi Arabia; [2]Health Plus Fertility and Women's Health Center, Jeddah, Saudi Arabia; [3]Department of Obstetrics and Gynecology, King Fahad Medical City, Riyadh, Saudi Arabia, Riyadh, Saudi Arabia.

OBJECTIVE: This study aims to evaluate the outcomes of the different treatment modalities used in CSP treatment at a single center.

DESIGN: This is a retrospective case series study that was conducted; all women who diagnosed with CSP between January 2013 and November 2019 in Women's Specialized Hospital, King Fahad Medical City.

MATERIALS AND METHODS: The clinical characteristics, diagnosis, different treatment modalities, and clinical outcomes were analyzed.

RESULTS: Twenty-seven cases of CSP were identified during the study period. The mean maternal age was 36.55 years (range, 23-47 years). The gestational age at diagnosis ranged between 5 weeks and 5 days to 13 weeks and 6 days. All diagnoses were made by ultrasound. Fetal heartbeat was present in 10 cases (37.03%). The most commonly used method for first-line treatment was medical treatment. A total of 14 patients (51.85%) were treated with systemic methotrexate (MTX), Three (11.1 %) intra-sac and systemic MTX, and Two (7.4 %) intra-cardiac potassium chloride (KCl) along with systemic MTX, five (18.51%) cases had expectant management, one case initially treated with Laparotomy Wedge resection, and one case treated with Uterine artery embolization (UAE) and systemic MTX. A total of 20 (74.07%) patients were treated successfully with first-line treatment. Seven (25.92%) patients needed additional second line treatment. Among them, only one case had surgical intervention. None of the women in medical treatment group experienced any side effects. Overall, the mean β -hCG resolution time was 60.85 days (range, 28 - 95 days).

CONCLUSIONS: The treatment of CSP should be individualized based on risk factors. Diagnosis and management of CSP need expertise and a multidisciplinary approach to prevent complications. Early diagnosis and management of cesarean scar ectopic pregnancy remains the mainstay for a successful outcome.

SUPPORT: NONE

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