Abstract title: Anti-Müllerian Hormone (AMH) as a quantitative and qualitative marker of euploid blastocysts.

Study question:
Is AMH an effective tool to predict the percentage of euploid embryos and blastocyst formation irrespective of the age of the patient?

Summary answer:
Higher AMH levels are associated with a higher rate of euploid embryos and increased blastocyst formation on day 5.

What is known already:
AMH is an established marker of the ovarian reserve and it is strongly correlated with female age.

However, it has been suggested that AMH is not only a quantitative but also a qualitative biomarker of oocyte/embryo competence and it has been demonstrated that high AMH levels, e.g. due to the Polycystic Ovary Syndrome, are at increased risk of poor blastocyst development. Reduced ovarian reserve might be per se associated with decreased oocyte developmental competence leading to increased aneuploidy rates in embryos independent of the age of the patient.

Study design, size, duration:
A retrospective analysis was performed between March 2017 and August 2018 including couples planned for Preimplantation Genetic Testing for Aneuploidies (PGT-A).

Patients were split into two groups and were analyzed individually; (i) the fresh group comprised of couples who underwent PGT-A with only fresh oocytes (n=516) and (ii) the vitrified group (n=184) in which vitrified oocytes were accumulated from 1.97 (±1.26) previous ovarian stimulation cycles, as a strategy to increase the number of potential euploid embryos.

Participants/materials, setting, methods:
Vitrification and warming were performed with the Cryotop method (Kitazato, Biopharma). Trophectoderm biopsy samples were subjected to Next Generation Sequencing (NGS) to screen the cells. AMH serum levels (ng/ml) were determined using a commercial fully automated assays Elecsys® (Roche) and values >5 were excluded. Blastulation rate was defined as the number of fertilized embryos capable of cavitating on day 5.
Linear regression analysis was conducted to verify the predictability of AMH values and the percentage of euploid embryos and blastulation rate on day 5. A Poisson regression model was used to correlate AMH levels with the number of euploid embryos according to the number of embryos biopsied.

In the fresh group, average maternal age was 35.8 years (± 5.95), AMH 1.95ng/ml (±1.27), 54% (±33%) blastulation rate on Day 5, 46% (±35%) euploid rate. Higher AMH values were found to have a statistically significant effect on the percentage of euploid embryos (p=0.001) and blastocyst formation on day 5 (p<0.001) as well as for the number of euploid embryos (p<0.001).

In the vitrified group, average maternal age was 38.55 (± 5.35), AMH 1.2ng/ml (±1.06), 8.43 (±5.57) MII oocytes warmed, 86% (±21%) survival rate, 34% (±33%) blastulation rate on day 5, 31% (±39%) euploid rate. As in the fresh group, higher AMH values were found to have a statistically significant effect on the percentage of euploid embryos (p=0.009) as well as for the number of euploid embryos (p=0.003). However, no significant differences were found between higher AMH levels and blastocyst formation (p=0.249).

Limitations, reasons for caution:
Retrospective design of the study.

Wider implications of the findings:
The independent relationship between AMH and the percentage of euploid embryos suggests that AMH is not only a quantitative but also a qualitative biomarker of oocyte-embryo competence. As the effect of AMH on blastocyst formation is lost after oocyte vitrification, the use of oocyte accumulation should be further evaluated.

Trial registration number:
N/A

Keywords:
pgt-a
AMH
oocyte vitrification
euploidy rate