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Is more better? A higher oocyte yield is independently associated with more day-3 euploid embryos

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Study question:

Is the number of oocytes retrieved (COCs) after ovarian stimulation for IVF independently associated with the number of day-3 euploid embryos?

Summary answer:

A higher oocyte yield is independently associated with more day-3 euploid embryos, although the expected benefit decreases significantly with advancing age

What is known already:

Ovarian stimulation represents a key step for the success of in-vitro fertilization cycles. Although, traditionally, ovarian stimulation aims at collecting more than one oocytes in order to increase the chance of pregnancy, there is evidence suggesting that excessive ovarian response leads to lower live birth rates. Furthermore, there is evidence suggesting that mild stimulation is associated with embryos of higher reproductive potential. Whether indeed a higher oocyte yield after ovarian stimulation is associated with the genetic composition of the resulting embryos and therefore with their reproductive potential is still largely unproven.

Study design, size, duration:

This is a multi-centered retrospective cohort study analysing all preimplantation genetic screening (PGS) cycles using day 3-biopsy and array-CGH (n=724) between March 2011 and December 2016 in 3 laboratories. Overall, 464 patients underwent 724 cycles of PGS for advanced maternal age (n=264), recurrent miscarriage (n=137), recurrent implantation failure (n=235), history of chromosomally abnormal children (n=44) and patient request (n=44). Cycles performed for genetic reasons (monogenic disease, parental chromosomal abnormality and gender selection) were excluded.

Participants/materials, setting, methods:

The primary outcome measure was the number of euploid embryos (EE) on day-3. Cycles with no embryo available for biopsy on day-3 were classified as having 0 euploid embryos. Statistical

analysis was performed using the generalized estimating equations framework and multivariate regression models to control for the clustering nature of the data while adjusting for potential confounders. Uncertainty around estimated effect sizes was expressed with either p-values or 95% CI.

Main results and the role of chance:

The mean age of patients was 38.8 (38.5-39.2) years and the BMI was 23.7 (23.2-24.2) kg/m^2. The mean number of COCs was 11.7 (11.1-12.2) and that of EE was 1.01 (0.88-1.14).

The univariate analysis identified a significant negative association of EE with female age ($p<0.001$), starting ($p<0.001$) and total dose of FSH ($p<0.001$) and duration of stimulation ($p=0.018$). The number of COCs exhibited a positive association with EE (coeff:+0.10, 0.08-0.13). Also, the indication for PGS was significantly associated with EE, with advanced age leading to significantly less EE than all other indications ($p<0.001$). No association was present between EE and BMI ($p=0.691$).

A multivariate regression GEE model including all the aforementioned variables as covariates as well as an interaction term between female age and number of oocytes revealed that the number of oocytes retrieved was still positively associated with EE (coeff:+0.40, 0.24-0.56). The interaction term was also highly significant (coeff:-0.01, $p<0.001$) indicating an effect modifying role of female age on the association of oocytes retrieved with EE. To produce one and two euploid embryos, 5 and 14 oocytes, respectively, are required at age 34, while 10 and 24 oocytes, respectively, are required at age 38.

Limitations, reasons for caution:

This study is retrospective and although every effort has been made to control for potential confounders, residual unknown bias cannot be excluded. Furthermore, the population analyzed in this study might not be completely representative of the general population undergoing IVF.

Wider implications of the findings:

These results provide an explanatory mechanism for the recently published positive association between the number of COCs and cumulative pregnancy. Also, they allow for a better understanding of the association between the number of COCs and EE in different age groups and can help clinicians optimise their ovarian stimulation strategy.

Trial registration number:

not applicable

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None