Connecting the dots between oocyte quantity and quality in diminished ovarian reserve

Jaswa et al. (1) present their extensive preimplantation genetic testing for euploidy (PGT-A) experience between 2010 and 2019. In >1,150 women aged 19–42 with 8,000 biopsied blastocysts, the authors compare euploidy rates in women with or without diminished ovarian reserve (DOR). After controlling for age, the DOR group had a 24% reduced odds of a biopsied blastocyst being euploid compared with the non-DOR group. However, no differences in rates of live births per transfer were noted with or without DOR after euploid single embryo transfer. Strengths of this study include the large sample size in a single academic center and use of the Bologna criteria as a definition of DOR, although those designated with DOR had more mean metaphase II oocytes (i.e., 8.4) than expected. Limitations of the study design include a lack of specific details regarding ovarian reserve markers (antimüllerian hormone [AMH] and antral follicle count) and the heterogeneity of using a mixed variety of different methods of PGT-A analysis (single nucleotide polymorphism array, array comparative genomic hybridization, and next generation sequencing). In addition, there are inherent limits of reporting live birth rate per transferred embryo where only cycles with at least one blastocyst for biopsy were included in the analysis, and those cycles that did not have a blastocyst worthy of biopsy were excluded from the denominator. Despite these limitations, this study offers valuable insight into the age-old question of whether or not oocyte quantity and quality are concurrently reduced in women with DOR (1).

These findings raise both important theoretical and practical considerations when discussing a model to explore the reduced quantity and quality question. Let us investigate the theoretical consideration first. The PGT-A model contributes a significant piece to the puzzle of whether DOR reflects an oocyte aging process being tied to both changes in quantity and quality. This is reflected by the increase in the percentage of aneuploidy embryos, which indirectly reflects the increased rate of oocyte meiotic errors. Another model offering an independent line of evidence is the use of serum AMH to predict cumulative live birth rate (CLBR) in women with DOR independent of age. Such a noninvasive model associated with a less costly approach potentially offers a less confounded line of evidence of a concomitant reduction in oocyte quantity and quality occurring in DOR. In the AMH model, outcomes are less subject to selection bias when reported as CLBR per cycle start. Such evidence comes from a recent study examining whether serum AMH predicts CLBR in women with DOR independent of age (2). It addresses the question posed by Jaswa et al. (1) and supports a similar conclusion to the PGT-A model. Higher CLBRs in women with DOR are noted with higher AMH values independent of age, indirectly supporting the concept of a greater percentage of euploid embryos resulting in a greater CLBR per cycle start. Thus, two different approaches by two independent investigating teams support the concomitant decrease in both oocyte quantity and quality concept in DOR.

Furthermore, although there were no observed differences in miscarriage rates based on DOR reported in the Jaswa et al. study (1), there are reports of an inverse correlation between AMH and risk of miscarriage in women attempting natural conception (3) and those undergoing ART, independent of age (4). These data further support the concept that there is both a reduction in quantity and quality of oocytes and resultant embryos present in women with DOR as assessed by AMH independent of age.

As previously mentioned, although the study by Jaswa et al. (1) did not examine the correlation between PGT-A euploidy embryos and AMH, such studies have been attempted in the past but have had limited sample size and used early developed and less consistent assay methods (5). If a strong correlation were demonstrated between euploidy embryos and a contemporary automated AMH assay, this would offer a practical approach to predict the number of expected euploid embryos obtained by PGT-A before starting a given cycle. This information could assist in counseling and setting expectations as to how many cycles may be required to obtain the desired number of euploid embryos for ultimate transfer and cryopreservation. This would be useful for both patients and physicians before planning to embark upon a process as labor-intensive as PGT-A.

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