Preimplantation genetic testing for aneuploidy in patients under 37: easy come, easy go

Open your eyes, look up to the skies and see! This month's article by Mejia et al. (1) adds to the growing and ever-convincing body of evidence, both prospective and retrospective that indicates that preimplantation genetic testing for aneuploidy (PGT-A) in a young cohort (<37 years) does not improve reproductive outcomes.

Mejia et al. (1) reviewed 31,900 patients from the Society for Assisted Reproductive Technology Clinic Outcome Reporting System database aged 21–37 years who were undergoing their first autologous oocyte retrieval from 2014–2016. Of these, 2,538 were classified as undergoing PGT-A. The cohort was subdivided by age, with 2 groups: <35 and 35–37 years of age. The primary outcome of the study was the cumulative live birth rate. A generalized linear model including age, body mass index, number 2 pro nuclear embryos available for transfer, number of embryos transferred, and the length of follow-up was used to calculate adjusted odds ratios (aOR) and 95% confidence intervals (95% CI).

Patients in the PGT-A group were on average older, had a higher diminished ovarian reserve, and were more likely to have >1 diagnosis of infertility. There were also differences between cycle characteristics between groups, with those using PGT-A having a higher average total follicle-stimulating hormone dose and higher use of intracytoplasmic sperm injection. Overall, Mejia et al's (1) results are consistent with the largest trials and meta-analyses that have been performed on this topic to date (2–4). The cumulative live birth rate is no different in women 35–37 years of age who transfer tested vs. untested embryos (66.6% vs. 62.5%; aOR: 0.92, 95% CI: 0.83–1.01).

But these findings are not new—several randomized studies have failed to demonstrate a cumulative live birth benefit for PGT-A in patients <37 years of age. This makes good intellectual sense because it is well established that euploidy rates are highest in the age range. Screening for aneuploidy in a population at low risk for aneuploidy is unlikely to be a fruitful endeavor. What is novel about this study is that they found that PGT-A in women <35 years of age was associated with a lower cumulative live birth rate compared with the transfer of untested embryos (70.6% vs. 71.1%; aOR: 0.82, 95% CI: 0.72 –0.93). Although causality cannot be established, several investigators have postulated that this may be because of reduced reproductive potential from traumatic trophectoderm biopsy, freezing and thawing cycles, extended blastocyst culture, and our ability to interpret mosaic results that may deprioritize viable embryos from the transfer.

One finding from this study that is worth highlighting is the association of reduction in miscarriage with PGT-A in women 35–37 years of age (aOR: 0.77, 95% CI: 0.61–0.98). Miscarriage is a physically and psychologically difficult outcome for so many of our patients. The decision to use PGT-A for the sole purpose of miscarriage reduction in this age group is a deeply personal one that requires shared decision-making with patients. Although embryonic chromosomal aneuploidy accounts for a large portion of reproductive failure, it is not the sole driver of recurrent miscarriage. A discussion of the added cost, increased time to pregnancy, and potentially increased risk of hypertensive disorders of pregnancy with trophectoderm biopsy should all be thoroughly discussed.

Overall, the results of this study add to the growing literature that informs clinicians as to who is not a good candidate for PGT-A. Data from Mejia et al. (1) suggest that PGT-A in women <35 years of age is associated with a lower cumulative live birth rate compared with the transfer of untested embryos and offers no benefit to those aged 35–37 years. It is ok that PGT-A does not provide uniform benefits across all age groups—we already know which age groups stand to benefit the most from aneuploidy screening. It is our job to apply these data and individualize the use of PGT-A for the patient in front of us to maximize its potential. We think it is time to leave PGT-A for women <37 years behind and face the truth. Let's use PGT-A smarter, not more often, and certainly not for everyone.

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