RBM ONLINE

ELSEVIER

Letter

Response: how PGS/PGT-A laboratories succeeded in losing all credibility

To the Editor

We read with interest the correspondence by Gleicher et al. (2018) raising concerns and criticism regarding the application of preimplantation genetic testing for aneuploidy (PGT-A) in clinical practice. We agree with the observation that its current use is not supported by sufficient evidence regarding analytical and clinical validity/utility as recommended by the ACCE model, a guide to evaluating new genetic tests (https://www.cdc.gov/genomics/gtesting/ACCE/). This should raise concern among professional societies and health care authorities. Indeed, since the publication of our manuscript, the Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology (2018) have issued a Committee Opinion on the use of PGT-A. They conclude that the value of PGT-A as a universal screening test for all IVF patients has yet to be determined as published studies have important limitations including questions regarding appropriate patient selection and testing platforms. Nonetheless, they do acknowledge that the use of 24-chromosome testing is associated with higher birth rates after aneuploidy testing and single embryo transfer among favourable-prognosis patients and therefore has the potential to decrease the incidence of multiple gestations. With all its limitations, they envision that PGT-A will likely be a part of a future multidimensional approach to embryo screening and selection.

Regarding embryos detected as 'mosaic', they note that viable euploid pregnancies have been achieved with such embryos, albeit at lower rates. Chromosomal mosaicism is a real biological phenomenon that may present at any point along the reproductive genetic spectrum: from as early as the pre-implantation stage and throughout gestation as detected by prenatal diagnosis. When encountered, mosaicism often poses clinical uncertainties and dilemmas. For those who deal with prenatal diagnosis, like the authors, this is commonplace. If PGT-A continues to be practiced, even if only in the setting of randomized controlled trials, mosaicism will continue to be detected and therefore guidance is required on how best to deal with this phenomenon. This was the sole purpose of our study. It does not provide support for the efficacy of PGT-A, or lack thereof. It does not recommend or condemn its very use, nor does it suggest the use of one technology over the other. In lieu of sufficient data from PGT-A, we based our scoring algorithm for prioritizing mosaic embryos on an extrapolation from well-established prenatal diagnosis data. The algorithm does not take into account the degree of mosaicism as there is currently insufficient data to determine such a threshold.

We agree with Gleicher et al. (2018) that PGT-A remains a screening test and therefore, in absence of robust analytical validations of the various technologies, an embryo with an 'intermediate' result suggesting mosaicism cannot be reliably classified as a mosaic (true positive) rather than a technical artefact (false positive). It is precisely for this reason that our evidence-based algorithm provides a tool for decision-making and patient counselling in circumstances where mosaicism is suspected in the preimplantation stage, regardless of technology.

REFERENCES

Gleicher, N., Kushner, V.A., Barad, D.H., 2018. How PGS/PGT-A laboratories succeeded in losing all credibility. Reprod. Biomed. Online 37, 242–245.

Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology, 2018. The use of preimplantation genetic testing for aneuploidy (PGT-A): a committee opinion. Fertil. Steril. 109, 429–436.

Francesca Romana Grati, Gloria Gallazzi, Lara Branca, Federico Maggi, Giuseppe Simoni
Cytogenetics and Medical Genetics Unit, TOMA Advanced Biomedical Assays S.p.A., Busto Arsizio VA, Italy
E-mail address: fgrati@tomalab.com

Yuval Yaron
Prenatal Genetic Diagnosis Unit, Genetic Institute, Tel Aviv Sourasky Medical Center and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

https://doi.org/10.1016/j.rbmo.2018.06.020