References


Gayathree Murugappan* and Ruth Bunker Lathi
Division of Reproductive Endocrinology and Infertility, Stanford University, Stanford, CA, USA

*Correspondence address. E-mail: gayathreem@gmail.com
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Reply: The value of cytogenetic analysis of the product of conception before preimplantation genetic screening

Sir,

Thank you for your letter regarding our recent publication, Intent to treat analysis of in vitro fertilization and preimplantation genetic screening versus expectant management in patients with recurrent pregnancy loss (Murugappan et al., 2016). We agree, as you have stated, that aneuploidy plays a significant role in clinical miscarriage as well as in recurrent pregnancy loss. Miscarriage in RPL patients, however, may have multiple other contributing factors, and this has been discussed in the literature. The authors of the letter highlight a study by Ogasawara in 2000 demonstrating that abnormal karyotypes in products of conception (POCs) become less frequent as the number of miscarriages increases (Ogasawara et al., 2000). Manquard et al. has demonstrated that the rate of aneuploidy in POCs from RPL patients is not significantly higher than aneuploidy rates seen in sporadic miscarriages, suggesting that an additional factor may have a role in contributing to clinical miscarriage in RPL patients (Manquard et al., 2010). In a 2012 study by Ogasawara, the cumulative live birth rate in women with prior aneuploidy in POC was 71.9% compared with a 44.7% live birth rate in women with prior euploid losses (Sugjura-Ogasawara et al., 2012). This was a good prognostic sign for both expectant management and possibly for IVF–PGS. In patients with two consecutive miscarriages with the first loss being aneuploid, 32 of 42 or 76% had a second aneuploid loss, suggesting that the karyotype results of one miscarriage do not always predict the results of the second miscarriage or predict if the patient is at higher risk of aneuploidy conception.

The authors of the letter suggest using POC karyotyping to identify RPL patients with a clear history of chromosome aneuploidy and offer PGS to this subset of the RPL population. We acknowledge that a limitation of the study was that karyotype information on POC from previous miscarriages was not available for the majority of RPL patients in the study, and we were therefore unable to report this. Furthermore, due to the retrospective nature of the study design, the patients were included in the PGS cohort if they expressed a desire to pursue treatment. While karyotypes should ideally be obtained after every clinical miscarriage, there are many barriers to performing this in clinical settings so providers often need to counsel patients without this information. Within an idiopathic RPL population, we agree that some patients may benefit more than others from PGS over expectant management. Our study, however, was not designed to identify the subset of RPL patients for whom PGS may provide the greatest incremental benefit over expectant management. Our goal was to capture the actual use of PGS, not perfect use of the technology. While many studies of PGS report live birth rates per euploid embryo transferred, we wished to convey that not every RPL patient who desires to perform PGS arrives to the point of transferring a euploid embryo. We did report that older patients with DOR are at higher risk of treatment failure with PGS. In our current management of RPL patients, PGS may very well be offered to patients in whom it is unnecessary. Our hope was to convey that expectant management is an alternative and equally successful treatment strategy.

As we continue to scrutinize our utilization of PGS in the RPL population, we would be very interested to see RPL patients risk-stratified and PGS being offered to those patients with a proven history of aneuploidy to determine if these patients in fact receive the greatest benefit from this technology. Comparing IVF and PGS to expectant management is challenging, as there are many factors that influence success rates of each option. We hope that prospective studies include an intent to treat as well as expectant management arm, as patients who are at risk of not reaching euploid embryo transfer with IVF and PGS may have a higher live birth rate with expectant management. In addition, future studies should include data about POC karyotype, maternal age, ovarian reserve and number of miscarriages to help identify groups that are most likely to benefit or be harmed by the use of PGS.

References


Gayathree Murugappan* and Ruth Bunker Lathi
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Reply: Should we also work on an international informed consent for endometriosis surgery?

Sir,

We read with great interest the letter to the editor by Dr David Soriano concerning our recently published article ‘Consensus on recording deep endometriosis surgery: the CORDES statement’, Vanhie et al. (2016). In his letter, Dr Soriano highlights the need for a consensus on an international consent form for endometriosis surgery.

The main goal of the CORDES statement was to provide an instrument for standardized recording of all relevant aspects of deep endometriosis in surgical trials. Although the development of an international informed consent was not within the scope of our project, all co-authors agree that an international consent form for endometriosis surgery would be very useful in daily clinical practice and might lead to an improvement of the preoperative workup.

The systematic review of the literature concerning deep endometriosis, which formed the basis of the CORDES papers, showed that there is an enormous variation in published data on complication rates, success rates and recurrence rates in deep endometriosis surgery. This is due to the lack of standardized definitions, inadequate reporting and the very diverse surgical techniques used. Clearly, results related to clinical outcome after surgery are largely dependent on the population studied, e.g. primary intervention or secondary intervention, and this patient population is often inadequately characterized. In our view, the lack of good information from high quality trials impedes the development of an international consent form at present.

Based on our experience, the development of an internationally accepted consent form, applicable in a wide range of countries, will require a long and difficult consensus process. As stated earlier, this was not the ambition of the authors publishing the CORDES statement, but may be a next step for these authors, or for other groups like the World Endometriosis Society, European Endometriosis League and/or Society for Endometriosis and Endometrial Disorders.

Reference
