Gestational carrier use in assisted reproductive technology: what can it tell us about the uterine role in infertility?

In this issue, Dr. Gayathree Murugappan and colleagues (1) provide a detailed analysis of 10 years of Society for Assisted Reproductive Technology (SART) data on gestational carrier and nongestational carrier (autologous uterus) assisted reproductive technology (ART) cycle outcomes. Over the 10 years, SART reported 1,337,721 cycles that met their inclusion criteria, of which 24,269 (1.81%) used a gestational carrier's uterus. In brief, the authors found that use of a gestational carrier uterus during ART cycles resulted in statistically significantly better implantation, clinical pregnancy, and live-birth rates as compared with the use of an autologous uterus. They reported an impact of infertility diagnosis, in that ART cycles due to only male factor infertility were similarly successful with gestational carrier or autologous uteri. They also discovered an interesting interaction with age, in that women aged 40 or older using their own oocytes had a greater improvement in live births with use of a gestational carrier uterus than did younger women. Finally, they were able to examine frozen-thawed versus fresh embryo transfer cycles, and noted that the greatest relative improvement in live-birth pregnancy success with the use of a gestational carrier uterus occurred in frozen thawed cycles in which an oocyte donor was used as the oocyte source.

This analysis differs in several key findings from a recent Centers for Disease Control and Prevention paper analyzing gestational carrier cycles reported in the United States over the same 10-year time period (2). Perkins et al. found significant improvements (but to a less impressive degree) with use of gestational carriers, with greater relative improvements in cycles using autologous oocytes. Of note their analysis was limited to only the last 5 years of their data collected, failed to adjust for body mass index, and excluded all frozen thawed transfer cycles. Despite the methodological differences, both studies documented statistically significant improvements in live-birth pregnancy rates (adjusted odds ratios 1.28–1.48) with the use of a gestational carrier uterus.

Since Sauer, Paulson, and Lobo (3) published their landmark study showing the results of oocyte donation in recipient women older than age 40 years as equivalent to younger women, the prevailing dogma in our field has been that reproductive female aging is almost entirely ovarian in origin. This current analysis casts doubt upon that belief and highlights the importance of the uterine role in implantation and fertility. Certainly this comes as no surprise to those of us unfortunately accustomed to consultations with patients who have failed the repeated transfer of euploid embryos without any obvious anatomic uterine defects.

Gestational carriers have been selected for their proven reproductive success, as most programs will only consider carriers who are of normal weight, have no serious medical conditions, have had at least one successful term birth with no major obstetric complications, and have no history of infertility or recurrent miscarriage. They are the Olympians of reproduction. The current study supports our diagnostic acumen, as there was no statistically significant benefit to using these "reproductively elite uteri" when only male factor infertility and no female factors were listed. Thus, in the cases in which the female partner was judged to be completely normal, their own reproductive performance was not significantly different from the gestational carriers. In all other cases, however, use of a gestational carrier uterus was associated with statistically significant improvements in ART success.

Recent work on the gene expression profile (4) during the window of implantation along with studies of the microbiome of the uterine cavity (5) in fertility and in cases of reproductive failure has added to a much older literature on the histologic assessment of endometrial receptivity. Of course we are taught that the appearance of pinopodes during the window of implantation is a marker of a receptive uterus, suggesting that some physiologic normalcy is important. This has remained true even after we learned that dating the degree of decidualization of the endometrium by histologic criteria was no longer a valid or useful test in infertile women. The current study lends strength to the assertion that we need to develop better methods of assessing the functional reproductive competence of the uterus in ART if we are to truly achieve maximum success. This work suggests that uterine reproductive functionality may also deteriorate with advancing age, although to a lesser degree than ovarian function declines. It remains to be seen whether endometrial/uterine receptivity assessment will move into the forefront of our evaluations before ART, or whether it will remain as an investigation of last resort for those with repeated ART cycle failures.

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https://doi.org/10.1016/j.fertnstert.2017.11.025

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