

Updates on Frozen Embryo Transfer



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Practices surrounding IVF cycles have evolved widely over the past 40 years. Cutting edge techniques several years ago have naturally been replaced by a range of protocols and procedures to take advantage of improved safety and efficacy profiles. Through application of vitrification techniques over slow freezing, embryo viability post thaw is significantly improved, creating space for other advantages of frozen embryo transfers (FETs) to emerge.

FETs improve success rates, perinatal risk profiles and maternal risk profiles. The advent of FETs collectively improved success rates as well as decreased pregnancy loss, both ultimately improving the number of live births.

Factors contributing to this increased success vary. One beneficial aspect of freeze-all cycles includes the ability to push oocyte development longer, rather than triggering when the first few follicles become large. This allows for more aggressive stimulation with higher oocyte yields. Studies have shown that while 19mm is an optimal size for retrieval, larger follicles yield good quality blasts in similar percentages. With a frozen transfer physicians can stimulate the ovaries more aggressively, particularly in high responder patients, without risking severe OHSS due to high numbers of follicles, higher estrogen levels, and the threat of continued elevated HCG in the setting of an ongoing pregnancy. Freeze-all cycles also permit preimplantation genetic testing (PGT) to be performed, and embryo selection for transfer improves with potential combination of multiple cohorts of available embryos. PGT tested embryos ensures obviously aneuploid embryos are not transferred. The impact of transferring clearly aneuploid embryos affects not only patient distress in an adverse outcome, but also the potential resultant desire for termination of an abnormal pregnancy that could have been avoided. Genetic testing also permits greater comfort in transferring

a single embryo, thereby cutting risk of multiple pregnancies down to spontaneous levels instead of the historically elevated multiple gestations associated with IVF.

Optimization of embryo-endometrial synchrony likely greatly contributes to improved success rates. With the presence of ovarian stimulation immediately prior to transfer, the endometrial development is altered, negatively impacting timing of appropriate endometrial histology and hormonal receptor regulation. The relative risks of perinatal complications significantly decrease with FETs. This is partly attributable to improved success rates and ability to do single embryo transfer of euploid embryos which minimizes the incidence of multiple gestations. In addition to the increase in singleton pregnancies, avoidance of perinatal complications remains significant even when comparing outcomes in singleton fresh vs. frozen cycles. Placental diseases, low birthweight and prematurity, ovarian hyperstimulation syndrome all decrease with frozen embryo cycles. With that said, hypertensive disorders of pregnancy are definitively higher with FETs and that factor should be accounted for while counseling patients.

Several protocols to optimize transfer are available. Programmed cycles employing supplemental estradiol and progesterone while suppressing follicular development allow for more specific control of the transfer date. Modified natural cycles combine a more physiologic follicle development while also maintaining control of key hormonal changes required for implantation. Natural cycles avoid the use of exogenous medications and take advantage of a completely unaltered uterine environment. No method is completely advantageous, however. Programmed cycles expose patients to additional medication, modified natural cycles and natural cycles may be difficult to optimize, and time appropriately and are more subject to the inconsistencies and inadequacies that required the patient to use fertility treatments in the first place. Currently, a heavily studied area is the risk posed by FETs of preeclampsia on the mother, and how specific protocols may or may not impact its incidence.

Cumulatively, FET increases success rates and safety profiles for patients due to increased ability to optimize oocyte stimulation practices, embryonic genetic testing, endometrial development, and timing of embryo transfer.