Applying classic surgical tenets in the complex world of uterine transplantation

We have viewed, with great interest, the video article "Techniques for Successful Vaginal Anastomosis in the Uterine Transplant Patient" by Rehmer (1). This video reviews the process of uterus transplantation with specific focus on a technique for successful vaginal anastomosis of the recipient vaginal cuff with vaginal tissue of the donor specimen. The described technique uses a series of interrupted horizontal mattress sutures tied on the abdominal side of the anastomosis to evert the tissue edges. A return to classic surgical tenets, tissue edge eversion, and tension minimization improve the anastomotic closure. Additional key components include preoperative vaginal dilation for the recipient and ensuring a 1 cm or greater vaginal cuff margin on the donor tissue.

The goal of this technique is to reduce the occurrence of postsurgical vaginal stricture thereby facilitating efflux of menstrual blood and easing the process for cervical biopsies and embryo transfers. In a series of 20 cases of uterine transplantation, 40% required postoperative dilation of the vaginal anastomosis due to stricture formation (2), therefore developing techniques to reduce its occurrence is beneficial to patients. The originally described technique for anastomosis did involve a 1–1.5 cm margin of donor vaginal tissue, which was accomplished with a continuous suture rather than interrupted horizontal mattress stitches (3). The continued dissemination of surgical techniques as they evolve at different institutions will be invaluable in moving the field forward.

There are some questions that arise after observing the technique. Given that the uterine transplantation procedure is already a lengthy surgery lasting 10+ hours for the recipient, is this approach to the vaginal anastomosis of such benefit that it warrants prolonging surgical time? Report of the outcomes and incidence of vaginal stricture requiring dilation after introduction of this technique would be helpful in determining whether it should become the routine anastomotic closure. Additionally, there is interest in moving toward minimally invasive approaches for both donor and recipient surgeries. Would this interrupted mattress suture anastomosis translate to a robotic approach if it proves to be superior in reducing stricture?

As the optimization of surgical techniques used for uterus transplantation progresses, it is important to continue to review the state of this experimental therapy and its implementation in patient care. Uterus transplantation is an experimental treatment for absolute uterine factor infertility. The first transplantation was completed in 2000 in Saudi Arabia and, although it was technically successful, it resulted in hysterectomy 3 months later after graft necrosis. 2013 marked the beginning of the uterine transplantation trial in Sweden and the first successful live birth after transplantation occurred in 2014. The field has progressed rapidly over the past 6 years with multiple centers in North America and around the world now performing the procedure as part of and outside of clinical trials. There have been approximately 52 completed uterine transplantations worldwide as of April 2020 (4).

The 52 transplantations reported as of April 2020 have been done with a majority of specimens originating from living donors. There is approximately a 30% rate of graft failure, although that seems to be decreasing over time. In those with successful transplantations, the percentage that achieve at least one pregnancy is 37%. A subsequent case series from September 2020 reports a higher rate of pregnancy approaching 80% among successful transplantations at their institution (2). It should be recognized that all women in these studies had excellent ovarian function and many blastocysts were frozen before transplantation. Pre-eclampsia was the most frequently reported obstetric complication, occurring in 20% of patients. Surgical and postoperative complications have been reported and can be significant, including vascular issues such as limb ischemia and hemorrhage, as well as pelvic infection. The estimated overall complication rate is 23% (4). The previously mentioned case series included three bladder injuries, one episode of hemorrhagic shock, and one patient with lower extremity ischemia requiring a femoral-femoral bypass. Additionally, elevated creatinine levels have been observed in these individuals on immunosuppression.

The majority of individuals who have undergone uterine transplantation have congenital absence of the uterus as the cause of absolute uterine factor infertility. There is discussion of the potential for transplantation to be applied in other situations including transgender family building and additional causes of uterine factor infertility, such as adenomyosis, severe Asherman's disease, and prior cesarean hysterectomies. It will be interesting to see success and complication rates in patients who underwent a prior hysterectomy due to other pathologies as pre-existing adhesions and anatomic differences of pelvic vasculature may increase the risk of surgical complications.

Despite promising results in small case series, there remain significant concerns. This is a transplantation surgery done for a quality-of-life issue. It involves all of the risks of multiple major surgeries and immunosuppression and does not guarantee pregnancy. There are alternatives, such as gestational surrogacy and adoption, that do not incur the same risks to the recipient and the donor (if a living donor is used). The medical cost of a uterine transplantation in the United States is likely upward of $200,000 and is paid for currently by institutional funding and private grants. There are additional incurred costs by the patient including time off from work and the cost of moving to be in close proximity to the institution providing the service. Surveys of individuals who have applied to the ongoing trials of uterine transplantation, the vast majority of whom have congenital absence of the uterus, have found that these patients view uterine transplantation much more favorably as an option for family building compared with gestational surrogacy or adoption (5). Their primary concerns are privacy, choice, and control.

In the face of these challenges and unanswered questions, there remains significant patient and provider interest in this burgeoning practice, indicating that we will only continue to see it performed. It will be interesting to see acceptance rates

in countries where gestational surrogacy is prohibited, and tightly regulated, competing private health insurance companies, and government subsidies that control reimbursement for treatments. Even in the United States with mandated insurance coverage of fertility services, gestational surrogacy is typically not covered, making it unlikely that private insurances will agree to cover uterine transplantation. This means that access, already a major concern with fertility care, will be limited to the few wealthy individuals who can afford it or to those academic centers that have grants and philanthropy to continue this important work. Continued development and dissemination of surgical techniques as done here by Rehmer, as well as publication of data supporting that these techniques minimize risks and reduce complications, will be of utmost importance for increasing acceptance and coverage of this practice. Likewise, rigorous reporting of all transplantation-related outcomes by an international registry will be pivotal for the future of this field.

We commend the authors of this video on their effort to share their knowledge and experience to advance the practice of uterine transplantation. We are excited to see how this technology unfolds. We also encourage everyone to await further reporting of outcomes from more surgical trials before widely advocating and promoting what is still an evolving procedure.

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