American Society for Reproductive Medicine position statement on uterus transplantation: a committee opinion

Practice Committee of the American Society for Reproductive Medicine

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Following the birth of the first child from a transplanted uterus in Gothenburg, Sweden, in 2014, other centers worldwide have produced scientific reports of successful uterus transplantation, as well as more recent media reports of successful births. The American Society for Reproductive Medicine recognizes uterus transplantation as the first successful medical treatment of absolute uterus factor infertility, while cautioning health professionals, patient advocacy groups, and the public about its highly experimental nature. (Fertil Steril® 2018;110:605–10. ©2018 by American Society for Reproductive Medicine.)

KEY POINTS

- Uterus transplantation is an experimental procedure for the treatment of absolute uterus-factor infertility (UFI).
- Uterus transplantation should be performed within an Institutional Review Board (IRB)–approved research protocol.
- Uterus transplantation teams should be well-coordinated and multidisciplinary.
- Surgical training with animal models and/or cadaver labs is necessary prior to attempting transplantation in human subjects.
- The organ used during uterus transplantation can be from living or deceased donors.
- Transparent inclusion and exclusion criteria should guide selection of transplantation recipients.
- Standardized reporting on outcomes of uterus transplantation is desirable to assess the true risks, benefits, and outcomes associated with this procedure.
- Consistent with all organ transplantations, the Organ Procurement and Transplantation Network (OPTN)/United Network for Organ Sharing (UNOS) is the supportive organization for data collection. However, neonatal and long-term pediatric outcomes need to be collected.

BACKGROUND

Until the first live birth after uterus transplantation in Sweden in 2014, there were no treatment options available for women with an absent or nonfunctional uterus to carry their own child. Internationally, an attempt at uterus transplantation in 2000 resulted in the uterus being removed and another attempt in 2011 did not produce a live birth (1, 2). Women with UFI who have a nonfunctional or absent uterus historically have been advised to explore in vitro fertilization (IVF) with a gestational carrier (where legal), adoption, foster parenting, or to lead a life without children. The number of women with UFI is significant. In the United States, UFI affects 1%–5% of reproductive-aged infertile women and may result from major congenital uterus malformations (e.g., Mayer-Rokitansky-Küster-Hauser syndrome); benign, obstetrical, or oncologic hysterectomy; or an acquired uterus condition that leaves the uterus in situ but renders it nonfunctional such as severe Asherman syndrome (3, 4). It is not clear what percentage of these patients have an irreversible cause of UFI. Some women with UFI find adoption or the use of a gestational carrier impossible or unacceptable due to legal, religious, financial, or ethical concerns. Although the surgical approach to uterus transplantation is still in its infancy, there is widespread public interest and support for uterus transplantation and gestational

Received June 7, 2018; accepted June 12, 2018.

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Fertility and Sterility® Vol. 110, No. 4, September 2018 0015-0282/$36.00

https://doi.org/10.1016/j.fertnstert.2018.06.017

surrogacy (5–12). More than 30 uterus transplantations have been performed worldwide (13) as of the publication of this document, indicating the rapid tempo of developments in this field. There are several programs initiating or conducting clinical trials of uterus transplantation using both living and deceased donor models in the United States (14). There have been 11 reported deliveries worldwide, all through IVF, with 8 in Sweden, 2 in the United States, and 1 in Brazil (the first reported birth from a deceased donor), at the time of this writing. The mean gestational age at delivery in the Swedish trial of eight births was 35 weeks and 1 day with a birth weight of 2.5 kg. No birth defects were reported. The main obstetrical complications were preeclampsia and cholestasis. Follow-up between 2 months and 3 years has not revealed any significant infant disorders.

Composition of an Appropriate Research Team

Uterus transplantation is currently considered an experimental procedure and should not be performed outside of an IRB–approved research protocol. These trials should be listed on Clinicaltrials.gov. Due to the medical and surgical complexity of uterus transplantation as well as the need for long-term maternal-fetal-neonatal follow-up, these protocols appear to be most appropriate for tertiary medical centers. Teams embarking upon such protocols should be multidisciplinary with recommended representation as listed in Table 1. The primary surgeon/physician for the program should be clearly identified. This concept applies solely to the transplantation component and others will take the lead for the reproductive and obstetrical aspects of the procedure.

Uterus transplantation is unique in its temporary nature; the graft is not intended to last for the life of the recipient, only for as long as necessary to achieve childbearing goals. However, institutions must be prepared to follow a uterus transplantation recipient through four or more abdominal surgeries, including initial implantation of the uterus, one or more cesarean deliveries, and ultimate hysterectomy once childbearing is complete. For an individual recipient, this cycle may take several years to complete; therefore, ensuring the infrastructure for long-term follow-up is essential. Follow-up of the offspring will take even longer.

As a surgical team prepares for transplantation attempts in human subjects, surgical practice specific to uterus transplantation is required. Teams in both Sweden and the United States have prepared for human clinical trials with prior surgical training in rats, sheep, pigs, and nonhuman primates (15, 16). Surgical training and preparation may involve either large animal research or cadaver practice to optimize the surgical approach and team training for obtaining and implanting a uterus graft. The surgical complexity surrounding uterus transplantation lies mainly with the highly difficult dissection of the uterus vein, if used, to provide optimal drainage of the graft (17). As with all innovative surgical procedures, adaptations may be necessary to obtain optimal results (18, 19). Surgeons should possess considerable expertise in vascular dissection and anastomosis as well as navigating the pelvic, vaginal, and retroperitoneal pelvic anatomy. Transplantation teams and recipients must understand that postoperative complications such as graft thrombosis and infection may necessitate hysterectomy in the immediate postoperative period. In addition, other complications, such as graft rejection, may also occur prior to the recipient completing any pro creative treatment and childbearing. Psychosocial team members should have experience either with the psychosocial assessment and care of solid-organ transplant candidates and solid-organ donors or be willing to be mentored by psychosocial team members from existing uterus vascularized composite allograft (VCA) programs.

Issues of Ethics, Consent, and Subject Selection

Human uterus transplantation is considered a VCA, similar to transplantation of the face, limbs, abdominal wall, and other non-lifesaving organs. These transplants can be substantially life-enhancing. However, they do present unique ethical and logistical considerations. VCAs are regulated in a manner similar to other solid organs and require specialized consent to allow removal of the specified organ as well as its use in research. UNOS provides oversight for organ procurement organizations, which obtain the appropriate consent for VCAs from either the donor in living-donor transplants or the donor's family in deceased-donor transplants. Living donors should be specifically counseled regarding the risks of injury, as the hysterectomy required for a living-donor uterus transplantation approximates a radical hysterectomy and injuries have been reported to donors in all series of living donors to date (18, 19). Care should be taken to avoid undue emotional and psychological pressure in living donors, who are often family members of the recipient seeking transplantation. Recipients must be counseled carefully and thoroughly, as women hoping to achieve pregnancy are considered a vulnerable population. Counseling must highlight the experimental nature of this type of clinical research rather than potential pregnancy as the central focus. Recipients must be advised of both known and unknown risks of transplantation and the

TABLE 1

Recommended composition of the uterus transplantation team.

Team member
Reproductive endocrinologist
Transplant surgeon
Gynecologic surgeon
Maternal-fetal medicine specialist
Anesthesiologist
Infectious disease specialist
Psychiatrist or psychologist
Neonatologist
Pathologist
Radiologist
Bioethicist or professional with bioethics expertise
Social worker
Living donor advocate as described by UNOS regulations
Research nurse/coordinator
Transplant medicine specialist

ASRM. Uterus transplantation guidance. Fertil Steril 2018.