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Uterus Transplantation: The Ethics of Using Deceased vs. Living Donors

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Abstract

Research teams have made considerable progress in treating absolute uterine factor infertility through uterus transplantation, though studies have differed on the choice of either deceased or living donors. While researchers continue to analyze the medical feasibility of both approaches, little attention has been paid to the ethics of using deceased versus living donors as well as the protections that must be in place for each. Both types of uterus donation also pose unique regulatory challenges, including how to allocate donated organs; whether the donor / donor's family has any rights to the uterus and resulting child; how to manage contact between the donor / donor's family, recipient, and resulting child; and how to track outcomes moving forward.

Keywords

organ transplantation; reproductive technologies; informed consent; regulatory issues; rationing / resource allocation

Introduction

Absolute uterine factor infertility (AUI) affects 1/500 women of reproductive age, or approximately 85,000 women in the United States (U.S.) (Johannesson et al. 2014) and 1.5 million women worldwide (Flyckt et al. 2017). These women either lack a uterus for congenital (ex. Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome) or iatrogenic (ex. hysterectomy for cervical cancer, leiomyoma, uncontrolled postpartum bleeding) reasons, or they possess a uterus that is nonfunctional due to some anatomical or physiological defect (ex. intrauterine adhesions, severe adenomyosis, congenital uterine malformation). At present, three options exist for women with AUI to attain parenthood: (1) adoption, (2) gestational surrogacy, and (3) uterus transplantation. Of these, uterus transplantation is the only option that provides an opportunity for both genetic and gestational motherhood. Unfortunately, access to all three options is limited. Adoption can be a long and difficult administrative procedure, surrogacy is expressly allowed in only 14 American states

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(Finkelstein et al. 2016) and outright banned in much of Europe and the Middle East (Twine 2015), and uterus transplantation remains in the clinical trial stage.

The first human uterus transplant occurred in Saudi Arabia in 2000 when a 46-year-old woman undergoing hysterectomy for benign ovarian cysts donated her uterus to a 26-year-old woman who previously had a hysterectomy for postpartum bleeding. Unfortunately, the donor suffered ureteral injury and the graft failed in the recipient (Fageeh et al. 2002). After this failure, another human uterus transplant was not performed until 2012 when a Turkish team transplanted the uterus of a 22-year-old brain-dead donor into a 23-year-old recipient with MRKH syndrome. The woman became pregnant after in vitro fertilization (IVF) but the pregnancy miscarried in the first trimester (Akar et al. 2013). It was not until 2014 that a Swedish team achieved the first live birth after uterus transplantation (Brännström et al. 2015) followed by four additional births (Keuhn 2017). For all 9 recipients, living donors were used, 5 of whom were the recipient's mother. Although one donor suffered ureteral injury, the procedure had a 78% overall success rate for recipient grafts (Brännström et al. 2014).

Spurred by this progress overseas, American institutions have begun their own clinical trials. The birth of the first U.S. baby born from a uterus transplant took place in November, 2017 as part of Baylor University Medical Center's 10-patient clinical trial with living donors (Sifferlin 2017) (Keuhn 2017). The Cleveland Clinic is currently conducting a 10-patient clinical trial with deceased donors (Flyckt et al. 2017). According to clinicaltrials.gov, the University of Pennsylvania is also preparing to begin a trial with deceased donors, and the University of Nebraska Medical Center and Brigham and Women's Hospital are developing their own trials with living donors. Despite their different logistical approaches with respect to living or deceased donors, these national and international teams all stipulate that transplantation be transient with uterus removal after childbirth to avoid lifelong immunosuppression.

Although there is ample literature addressing the general ethical and regulatory issues surrounding uterus transplantation, little attention has been paid to the ethical and regulatory issues related to choice of donor. While the Turkish and Cleveland Clinic teams are using deceased donors, the Saudi, Swedish, and Baylor University teams have chosen to rely on living donors. Given this discordance, it is important to examine the ethical considerations involved in donor selection, as well as the protections that must be in place for each donor type. Both types of uterus donation also pose unique regulatory challenges, including how to allocate donated organs; whether the donor / donor's family has any rights to the uterus and resulting child; and how to manage contact between the donor / donor's family, recipient, and resulting child. Additionally, both types of donation require outcome monitoring to ensure safety, access to relevant risks and prognosis for informed consent, and comparison of the procedure's efficacy depending on the source of the uterus.

Deceased Donation

The U.S. operates under an explicit consent, or "opt in," system wherein "cells, tissues, or organs may be removed from a deceased person if the person had expressly consented to

such removal during his or her lifetime” (World Health Organization 2010, 230). If there is no clear consent or opposition to donation from the deceased, permission is obtained from a legally specified surrogate. Although the 1968 Uniform Anatomical Gift Act (UAGA) gave adults a right to donate their organs postmortem “without subsequent veto by others” (Institute of Medicine 2006, 19), the U.S. did not have a formal system to govern deceased donation until it passed the National Organ Transplant Act (NOTA) in 1984. The Act prohibited the sale of organs and established the Organ Procurement and Transplantation Network (OPTN), which the United Network of Organ Sharing (UNOS) has managed since it was awarded the initial contract in 1986. As the OPTN administrator responsible for fairly allocating organs, managing the recipient waitlist, and compiling national transplant records, UNOS oversees 58 organ procurement organizations (OPOs). When a donated organ becomes available, the OPO works with the family and hospital to determine consent; evaluate medical eligibility; and coordinate recovery, preservation, and transportation while UNOS algorithms determine the potential recipient (Institute of Medicine 2006).

Moral Justification

Deceased organ donation for life-saving organs is morally based in the principles of rescue ethics. According to the rule of rescue, a moral responsibility exists to save endangered human life whenever possible. Thus, if one can donate organs after death to save other individuals, one has a duty to do so because postmortem organ removal involves no physical risks, costs, or inconvenience to the donor, and the ability to save lives justifies desecration of the deceased’s body (Howard 2006). However, due to the principles of autonomy and respect for persons, organs may only be removed from deceased individuals who gave explicit consent for donation or from individuals whose families have given surrogate consent.

While the ability to save lives justifies desecration of the deceased’s body, it is not immediately clear that the ability to improve quality of life does the same. At first blush, the rule of rescue poses a dilemma in that uterus transplantation is not a life-saving procedure. A thorough philosophical discussion regarding this point is outside the scope of the current manuscript. Nonetheless, science and society at large have permitted donation of other quality-of-life donations, including vascular composite allografts (VCAs) for face and arm transplantation. As such, it seems that society has broadened the justification for deceased organ donation from the rule of rescue to a more general appeal to beneficence. Now, not only is deceased organ donation justified for saving endangered human life whenever possible, but also for improving the quality of human life whenever possible.

Infertility has negative psychological effects (Luk and Loke 2015), and in one study, more than half of the women seen for pre-infertility treatment consultation described their infertility as the most upsetting experience of their lives (Freeman et al. 1985). Furthermore, when infertility results from cancer or its treatment, some patients describe their loss of fertility as causing as much emotional pain as the cancer itself (Neiman et al. 2007). As presented elsewhere more extensively, uterus transplant thus holds significant quality-of-life-improving potential and deceased uterus donation may be justified by a general appeal to beneficence (Arora and Blake 2014).

Of course, unlike face and arm transplants, uterus transplant is ephemeral in nature. However, the time-limited nature does not change the ethical decision-making in terms of beneficence. Despite its removal after childbirth to avoid lifelong immunosuppression, the transplanted uterus still serves the same purpose in the recipient for which it was biologically intended and donated. Furthermore, although the transplant is temporary, its benefit lasts for a lifetime with the opportunity to experience gestation (plus the birth of a child if the pregnancy is successful). Therefore, despite its quality-of-life purpose and temporary nature, deceased uterus donation is morally justified by the principle of beneficence.

Consent

Given the principles of autonomy and respect for persons, the deceased donor or an appropriate surrogate must consent to donation. However, as noted by Arthur Caplan,

“few, if any, American women ever thought that the uterus might be one of the organs considered for donation when they signed a donor card. A woman might not prove as willing to donate her uterus as she would be to donate her heart or liver”

given that it is a non-vital organ and serves a reproductive purpose. (Caplan et al. 2007, 19). While we do not make any empirical claims regarding the donation intentions of American women, certainly a signed general donor card cannot provide sufficient consent for uterus donation at this point in time. Donate Life, the organization that coordinates the National Donate Life Registry, informs donors that they are consenting to the donation of specific organs (heart, lungs, kidneys, liver, intestines, and pancreas) and tissues (corneas, tendons, valves, veins, skin, and bones) (Donate Life 2017). Current organ donors have not given consent for uterus donation, and their consent cannot be ethically assumed.

Fortunately, VCA transplantation regulations have dealt with similar issues. Although VCAs are classified as organs, current consent to organ donation as recorded in donor registries or on donor cards does not include consent to VCA donation. U.S. OPTN policy declares that the “recovery of VCAs for transplant must be specifically authorized” (Organ Procurement and Transplantation Network 2017) and even some European countries that follow a presumed consent system require explicit consent for VCA donation (Rahmel 2014). The transplant community recognizes that VCA donation must not negatively affect donation of life-saving solid organs, so healthcare providers should only request VCA donation when it seems appropriate after receiving approval for general organ donation (Rahmel 2014). In line with these policies, Cleveland Clinic physicians obtained separate consent from the family for the first partial face transplant in the U.S. after the decision to donate traditional vital organs was made (Arora and Blake 2014). Although a full discussion of the ethical basis for distinct regulations and consent practices surrounding VCA donation is not within the scope of this manuscript, we agree with contemporary practice. Given the non-vital and potentially highly personal nature of these organs as well as the lack of empirical evidence demonstrating public awareness and desire to serve as donors for non-vital organs, separate and explicit consent practices should continue for VCA donation.

Therefore, because the uterus is a VCA donation, existing OPTN policy requires OPOs to obtain explicit consent for uterus donation. Some have questioned whether this consent should be given only by the deceased herself, claiming that

“given the public’s lack of familiarity with uterus transplantation and the unique ethical and legal considerations surrounding reproductive decision-making, surrogate consent is not now and may never be appropriate” (Woessner et al. 2015, 85).

Although caution is necessary given the personal and foundational nature of procreative liberty, that uterus donation has reproductive implications does not automatically make surrogate decision-making inappropriate. While the donated uterus will be used to carry a developing fetus, uterus transplant does not involve the passage of the deceased’s genetic material to offspring. It is also arguable that face transplants are much more personal in nature than uterus transplants. Nevertheless, given current uncertainty regarding the role of the uterine microenvironment in fetal development (Ng et al. 2013) (Salamonsen et al. 2009) and the public’s lack of familiarity with uterus transplantation, it is reasonable to be wary of surrogate decision-making for deceased uterus donation. It is difficult to argue that the deceased would have desired to donate her uterus when much of the public is not aware of the possibility of uterus donation. Furthermore, given the intensely personal nature of reproductive decision-making, surrogate decision-making is rarely used in other aspects of reproductive care such as assisted reproductive technology or termination of pregnancy (Blake 2013). However, as the field evolves and further information regarding the role of the uterine microenvironment, the public’s attitudes toward uterus transplantation, and donor’s views of uterus donation in the context of their own procreative liberty comes to light, reevaluation of this restriction is warranted.

Procurement

Procurement of the uterus as a non-vital organ should occur after procurement of vital organs. Harvesting of organs for quality-of-life transplants must not impinge upon the harvesting of organs for life-saving transplants given the severity and emergency of the latter. Although hand or forearm procurement for VCA transplantation is sometimes possible before or during the procurement of other life-saving organs given the use of a tourniquet and the 30-minute procedure length, this is often not the case for face donation because the procedure typically lasts between 7–12 hours (Rahmel 2014). The uterus may be retrieved within 18–90 minutes (Lavoué et al. 2017), but its location in the body may interfere with other organs and their blood supplies. Therefore, uterus removal should occur only after procurement of vital organs.

Living Donation

Although the dead donor rule provides a deontic constraint against removal of vital organs from living donors (Truog et al. 2013), living donors may donate non-vital organs such as the uterus if the supply from deceased donors is insufficient, or if transplant with organs from living donors is significantly more efficacious than transplant with organs from deceased donors. Unlike deceased donation, wherein no physical harm can come to the

donor, the ethical dilemmas surrounding living uterus donation revolve around the issue of subjecting a healthy person to harm for the benefit of another. Indeed, there are no medical benefits to the donor unless the healthcare team somehow discovers a previously unrecognized condition during the donor work-up. As a result, the moral justification for living uterus donation proves more challenging than that for deceased uterus donation, and necessitates that donors be fully informed regarding the medical and psychological risks. Given these risks, if in the future transplantation with deceased donor uteri appears equivalent to living uterus donation, and a sufficient number of uteri may be obtained from deceased donors, living uterus donation may eventually become obsolete (Williams 2016).

Unfortunately, determining the risks of living uterus donation is difficult given that a limited number of such surgeries have been performed to date. Although the two procedures are significantly different in terms of duration, approach, etc., the risks of simple total abdominal hysterectomy may instead be considered as a rough first estimate. Indeed, these risks are well known given that over 35% of women have a hysterectomy by age 60 (Olausson et al. 2014). As with all surgical procedures, clotting, bleeding, and death are potential complications (Mayo Clinic 2017), but more common complications specific to simple total abdominal hysterectomy include hemorrhage (1%), transfusion (2–12%), infection [fever of unknown origin (10–20%), surgical site (6.6–24.7%), wound side (4–8%), pelvis (3.2–10%), urinary tract (1.1–5%), pneumonia (0.4–2.6%)], bladder injury (1–2%), intestinal injury (0.1–1%), ureteral injury (0.1–0.5%), and vesicovaginal fistula (0.1–0.2%) (Kisu et al. 2012). The longer procedure time (10–13 hours) for living uterus donation compared to simple total abdominal hysterectomy may increase these complication rates; for example, 2/14 (14%) of living donors have suffered ureteral injury thus far, which is significantly higher than the 0.1–0.5% risk for simple total abdominal hysterectomy (Fageeh et al. 2002) (Brännström et al. 2014) (Keuhn 2017) (Kisu et al. 2012). Given that a uterus transplant harvesting surgery is significantly more complex and invasive than a simple hysterectomy or even a radical hysterectomy routinely performed for staging and treatment of gynecologic malignancies, the true incidence of complications remains unknown.

Beyond these immediate surgical complications, hysterectomy for uterus donation may also have long-term medical consequences that affect quality-of-life. For example, despite some disagreement in the literature (Atay et al. 2007), premenopausal women may be at increased risk for ovarian failure after hysterectomy and may require hormone replacement therapy for early menopause (Ahn et al. 2002) (Chan et al. 2005) (Moorman et al. 2011) (Nahás et al. 2003). There may also be some risk of sexual dysfunction after hysterectomy. Although most women experience unchanged or improved sexual function, a significant minority report sexual dysfunction (Thakar 2015) (Lonnée-Hoffmann and Pinas 2014).

Similarly, uterus donation poses some psychological risks to living donors that should be considered in a comprehensive analysis of the procedure. If we can extrapolate from other forms of living organ donation, the RELIVE study showed that approximately 4% of donors (99/2455) face an emotional, psychological, or substance use difficulty because of donation (Jacobs et al. 2015). In addition, some donors may feel guilty or that the procedure was a waste if the transplant fails (MacLeod 2003) (Tong et al. 2012). Regardless of whether the transplant fails or succeeds, donors' relationships with their recipients may change and

donors may come to regret their decision to donate. Indeed, some of the women desiring to participate as research subjects for uterus transplant previously had an elective hysterectomy thinking that they had finished having children, only to find a new partner with whom they now desire children (Catsanos et al. 2013).

Moral Justification

Given these risks, it is important to assess the degree to which we are putting an individual at risk for the benefit of another, transforming them from a healthy person into a patient. While organ transplant violates Hippocrates' "first, do no harm" as well as the Kantian principle by using the living donor as a means to an end, it is generally justified based on utilitarian ethics. However, it is unclear the degree to which this utilitarian calculus holds for an organ that is non-vital and temporarily needed.

Perhaps the simplest argument in support of living uterus donation lies in the principle of respect for autonomy, which requires us to acknowledge others' rights to hold views, make choices, and take actions based on their personal values and beliefs (Beauchamp and Childress 2009). Despite the physiological risks, donors may wish to donate because of perceived psychological and emotional benefits. Indeed, supporting research shows that donors experience lasting increases in self-esteem, happiness, and quality-of-life after donation (Clemens et al. 2006) (Wiedebusch et al. 2009) (Reese et al. 2015), and that they appreciate the chance to enjoy life with a loved one now restored to health (United Network of Organ Sharing Ethics Committee 1992). Family in particular receive a great psychological benefit from donation.

However, as a *prima facie* principle, respect for autonomy does not override the principle of nonmaleficence, and so it does not automatically justify living organ donation. There are two moral agents involved in the donation process, and the autonomy of physicians must also be respected as moral agents governed by the principles of beneficence and nonmaleficence (Spital 2001). Physicians have a fiduciary responsibility to only recommend and provide procedures that offer the patient, in this case, the potential donor, more good than harm (Delmonico and Surman 2003) (Spital 2002) (Spital 2004). Therefore, they have a moral obligation to override the potential donors' wishes when the risks of donation outweigh the benefits (Spital 2004) (Wright et al. 2004). That is, the probability of a successful transplant informs whether the potential donor will benefit psychologically and emotionally (Spital 2004). In this vein, current transplantation practice requires that donors not only consent to donation, but also be approved by the transplant center before being allowed to donate (Steiner 2007). This does not depreciate the value of donor consent, however; indeed, the donation process cannot proceed without it.

As long as these criteria are met, living uterus donation is justified. Given that uterus donation serves a quality-of-life-improving rather than a quality of life-saving purpose, the benefits to uterus donors may be less than those for kidney or liver donors. However, the uterus's non-vital nature also implies lower levels of risk to the donor, and so the benefits and harms remain sufficiently balanced when all criteria are met. Although their donation will not save the life of another, donors will still experience improved mental and emotional wellbeing from helping another give birth despite previously untreatable infertility. They

may also be able to enjoy a relationship with the offspring depending on the nature of their relationship with the recipient (Olausson et al. 2014). Therefore, even though uterus transplant has a quality-of-life rather than life-saving purpose, a favorable harm-benefit ratio for the donor may be achieved. However, if in the future transplantation with deceased donor uteri appears equivalent or even superior to living uterus donation, and a sufficient number of uteri may be obtained from deceased donors, living uterus donation may become obsolete to avoid the risks to living donors (Williams 2016).

Consent

Donor consent is necessary to morally justify living uterus donation, and so certain policies should be in place to ensure that such consent is appropriately informed. Discussing every element of informed consent is beyond the scope of this paper, but it is important to consider what specific information must be disclosed regarding uterus donation given the unique nature of the procedure. Guidelines written for the disclosure process with potential living kidney and liver donors by The Live Organ Donor Consensus Group (2000, 2920) provide a good basis for the disclosure process with potential living uterus donors and include the following:

- “Description of the evaluation, the surgical procedure, and the recuperative period
- Anticipated short- and long-term follow-up care
- Alternative donation procedures, even if only available at other transplant centers
- Potential surgical complications for the donor, citing the reports of donor deaths (even if never experienced at that transplant center)
- Medical uncertainties, including the potential for long-term donor complications
- Any expenses to be borne by the donor
- Potential impact of donation on the ability of the donor to obtain health and life insurance
- Potential impact of donation on the life-style of the donor, and the ability to obtain future employment
- Information regarding specific risks and benefits to the potential recipient
- Expected outcome of transplantation for the recipient
- Any alternative treatments (other than organ replacement) available to the recipient
- Transplant center-specific statistics of donor and recipient outcomes”

Teams providing uterus transplant should adhere to these standards at a minimum when disclosing to potential living uterus donors. Additional research ethics and consent issues such as the therapeutic misconception and the lack of long-term safety information for both donor and recipient must be clearly discussed.

Teams providing uterus transplants should also follow the protections incorporated into the donor evaluation process for potential living kidney and liver donors. As with the potential recipient, the team should have private conversations with the potential donor because her answers might change in the absence of friends and family. In this vein, the entire evaluation should be kept confidential and should be carried out by a team separate from that of the recipient. In particular, an independent living donor advocate should support the potential donor and ensure that she is fully informed. By evaluating external pressures, such as family members or the pressure to gestate in our pronatalist society (Catsanos et al. 2013), the donor advocate can also advocate for the potential donor's autonomy in making a voluntary decision regarding whether to donate. Additionally, the living donor advocate should be careful to safeguard the potential donor's right to opt out of donation at any time without disclosing why to the recipient. While establishing such space between the donor and recipient can be difficult, especially in cases of familial ties between the two parties, it is nevertheless essential to ensuring the ethicality of uterus donation from a living donor. Indeed, the recipient may otherwise pressure the potential donor, or the donor may make her donation contingent upon promises of a future relationship with the resulting child.

Challenges of Deceased vs. Living Donation

Despite these differences in the moral justifications of and consent processes for deceased and living uterus donation, some challenges affect both forms of donation, albeit in potentially different ways. These problems include how to allocate donated organs; whether the donor / donor's family has any rights to the uterus and resulting child; how to manage contact between the donor / donor's family, recipient, and resulting child; and how to track outcomes moving forward.

Allocation of Donated Organs

Allocation has traditionally been an issue in organ transplantation because demand exceeds supply. Although living donation typically occurs in a directed manner, from a family member or friend of the recipient, it may also occur in a non-directed manner from an anonymous individual. Therefore, allocation challenges can affect both deceased and living organ donation.

Early studies suggest that distributive justice issues are likely to greatly impact uterus transplantation given the limited supply of and the large demand for donated uteri. For example, a 6-month New York study identified only 150 multi-organ procurements from 1,800 eligible organ donors as potential procedures for uterus donation, and consent for donation was only given in 6% of cases (Del Priore et al. 2007). Although this might be due to the research purpose of these donations, it could also be because of the symbolic nature of the organ in terms of femininity and motherhood (Johannesson et al. 2014). Regardless of the reason, it is clear that uterus donation will not meet the potential demand from the large number of women with AUI; therefore, an allocation system must be in place.

How to allocate deceased and non-directed living donor uteri among potential recipients poses a unique problem because, although organ allocation is typically based on a combination of medical criteria (whether a good tissue match), geographic region

(depending on how long the organ remains viable outside of the body), and necessity, infertility is a disease without a scale, and so the principle of “sickest first” (Persad 2009, 424) does not apply. VCA transplantation regulation has dealt with a similar dilemma through a two-step selection and ranking process. In selection, all patients on the waiting list who are suitable for a specific organ are identified by comparing compatible blood types and similar physical characteristics to the donor. During ranking, an allocation sequence among all suitable recipients is determined based on geography and how long the recipient has already been waiting (Rahmel 2014) (Organ Procurement and Transplantation Network 2017). Applying such a ranking system to uterus transplantation seems unfair, however. Given the age restrictions on a woman’s reproductive potential, a woman who joins the list at a later age may not get a uterus until after she passes her reproductive years as organs are instead given to younger women who joined the list earlier. Furthermore, although anyone can be listed on multiple transplant lists in different OPO regions if they have the money for travel, temporary housing, etc., only wealthy individuals can afford this opportunity, and this allows them to get through the line faster (Givens 2015). Additional factors must be incorporated into the ranking process if we are to fairly allocate uteri from deceased donors.

To this end, Bayefsky and Berkman (2016) recently proposed a ranking system based on four factors:

1. Motivation to seek treatment – Women seeking treatment should not only want a functional uterus, but should also want to use that uterus to experience pregnancy and become a mother. They cannot simply want a uterus to restore bodily integrity.
2. Recipient age – Given the child-bearing purpose of the procedure, uterus transplant recipients should be of reproductive age, defined by Bayefsky and Berkman as between 20 and approximately 45. Women nearing the end of this age-range should be prioritized since they are approaching their last opportunity to have children, although time on the waiting list should also be factored in.
3. Child-rearing capacity – Because uterus transplantation implies childbirth, eligible patients should pass a criminal background check for child abuse and negligence. They should also meet a minimum level of financial ability to establish a safe environment for the future child. The process should not be discriminatory, however, and so the standards should be set at the bare minimum to avoid social justice issues. In this vein, marital/partner status and sexual orientation should not be considered.
4. Amount of infertility treatment required – Women should have lower priority on the list if they have a lower chance of successfully carrying a child to term in the transplanted uterus.

Although we largely agree with this system proposed by Bayefsky and Berkman (2017), we propose several additions:

- Priority if especially difficult to find an appropriate donor – For example, some patients are highly sensitized, meaning they have extremely high antibody levels that react to foreign tissue. Given the difficulty of finding an appropriate donor

for these patients, they should receive priority if an appropriate donor becomes available.

- Lower priority if have already given birth –Bayefsky and Berkman (2017) claim that women near the end of their reproductive years should receive priority by the fair innings argument. In the same vein, we contend that by the fair innings argument, women should receive lower priority if they have already gestated and given birth. Although some women will surely want multiple children, and they have every right to pursue such wishes, everyone should have a chance to gestate one child and give birth, and so priority should be given to individuals who have not yet had this opportunity.
- Comprehensive child-rearing capacity – Although Bayefsky and Berkman (2017) include child-rearing capacity, they describe this as a minimum level of financial stability and a criminal background check negative for child abuse and negligence. We propose a social work, psychology, or similar evaluation prior to being listed for uterus transplant to ensure a comprehensive assessment of ability to rear a child. Of course, imposing one's own view on what a "good mother" is should also be avoided, and rather the best interest and safety of the future child be paramount. For example, a women with alcohol use disorder should not be eligible for uterus transplantation until she achieves sobriety given the significant consequences of alcohol use during pregnancy to a fetus.
- Not listed if unable to procure an embryo via IVF – Given that the purpose of the transplant must be to give birth to a child, it makes sense that a requirement be the ability to procure an embryo. Such an absolute criterion is necessary because without an embryo, the recipient cannot give birth, which would defeat the purpose of the uterus transplant as an infertility treatment. Uterus transplant already requires IVF, so eggs should be harvested (either from the recipient or a donor) and embryos created (either with sperm from the partner or a donor) and cryopreserved prior to transplantation. Although use of fresh embryos was previously associated with a higher birth rate, rates of success with cryopreservation are now reaching rates comparable to those with fresh embryos (Doyle et al. 2017) (Keenan, et al. 2017) (Shah et al. 2016). Indeed, use of frozen embryos may even improve autologous transfer success rates because of the opportunity to delay transfer and thus avoid the non-physiologic endometrium that occurs during a stimulation cycle and is less favorable for implantation and placentation (Cedars 2016). Therefore, because the purpose of uterus transplant is to give birth to a child, and because frozen and fresh embryos produce similar live birth rates, embryos should be created and cryopreserved prior to uterus transplantation. If an embryo cannot be procured, the patient should not be listed as a potential recipient.

Together, Bayefsky and Berkman's criteria (2017) and these additions provide a comprehensive system to address the challenge of ranking potential uterus transplant recipients in the allocation process.

As an aside, the Montreal Criteria suggest that only genetic women should be permitted to receive a uterus transplant at this time (Lefkowitz et al. 2013). We agree that there are potential unexplored issues surrounding uterus transplant with a non-genetically female recipient – how to place the uterus in a nongynecoid pelvis, how to achieve adequate vascularization, how to manage hormone replacement to sustain implantation and pregnancy, etc. However, we encourage further research into this area and thus identify it as a research gap. Nevertheless, until clinical trials address this issue, we suggest that only genetic females receive uterus transplants out of concern for safety.

Donor Rights to the Uterus and Resulting Child

Given the ephemeral nature of uterus transplant, with removal of the organ at conclusion of the child-bearing process to avoid life-long immunosuppression, some living donors or families of deceased donors may view their donations as loans rather than as gifts. They may feel entitled to the donated uterus after removal from the recipient, or they may regret the donation in the first place and want to effectively “undo it.” Although this may seem unlikely, multiple living kidney donors have sued their recipients for return of the donated organ after their relationships with the recipient soured (HuffPost 2014) (Jennings 2012) (Millman 2009). That this “take-back” problem has been an issue with life-saving, permanent kidney transplants suggests that it might also be an issue with uterus transplant, particularly since the uterus is not a vital organ and will already be removed from the recipient after the conclusion of child-bearing. However, the donors and their families do not have a right to the uterus after donation. Once donated, the organ is the property of the recipient, and upon its removal, it is medical waste. This protocol must be made clear during the consent process for both living and deceased donation.

In additional, potential uterus donors and their families must recognize that donation does not entail any parental rights to children born from the donated uterus. According to the Uniform Parentage Act of 2000, for gestational surrogacy with a validated contract, the intended parents are the parents of the child (Uniform Law Commission 2002), and in the case of uterus transplantation, the claim to parenthood is even less for the donor than that for a gestational surrogate as there are no maternal bonds created through gestation and birth (Johnson v. Calvert 1993).

Beyond this discussion of parental rights, directed living donors (grandmothers, sisters, aunts, etc.) might expect more out of their relationship with the resulting child. Unlike the issue of parental rights, such feelings cannot be easily mediated by the legal system. However, just as the transplant team should ensure that donors understand they have no parental rights to the child, so should they ensure that the donor does not make her donation contingent upon promises of a future relationship with the resulting child.

Donor-Recipient-Child Contact

Like with all organ transplants, another potential challenge of uterus donation relates to contact between the families of deceased donors and their recipients, or between non-directed living donors and their recipients. However, in the case of uterus transplant, there is also the possibility that the child born from a uterus transplant may seek to contact the

deceased donors' family or non-directed living donor in the future. Logistically, this may be difficult for the transplant center and OPO to coordinate given the distance in time from the donation to when the child is old enough to understand his or her gestational and birthing history. However, should it still be possible to connect deceased donors' families or non-directed living donors with recipients and their children, this contact should, like all contact between organ recipients and deceased donors' families or non-directed living donors, remain anonymous unless both parties choose to identify themselves (United Network of Organ Sharing 2015). Deceased donors' families and non-directed living donors should not in any way be pressured to contact the child born through their donation given the sensitive nature of the situation. They might be uncomfortable speaking to someone born from within their or their loved one's womb despite being comfortable with its donation. In the same vein, children should not feel pressured if contacted by the donors' family as such contact may make them uncomfortable and introduce confusion regarding their background. Until children reach age 18, all contact from the deceased donors' family or the non-directed living donor should go through the child's parents (including the recipient as the child's mother) out of respect for their parental rights to choose when and what to tell the child about his or her mother's gestation and birthing process.

Tracking Donor Outcomes

Finally, a persistent problem in the field of transplantation is lack of knowledge of long-term living donor outcomes. Therefore, an international registry should be developed to monitor the procedure by maintaining detailed records of all living uterus donations and their corresponding recipient procedures and outcomes. Given the current experimental nature of uterus transplantation, this registry should also include data on deceased uterus donations, not so much as a protective mechanism for deceased donors, but so that this outcome data may be easily compared with living donor outcome data. Indeed, if transplantation with deceased donor uteri appears equivalent or even superior to living uterus donation, and a sufficient number of uteri may be obtained from deceased donors, living uterus donation may become obsolete (Williams 2016).

Conclusion

In conclusion, beneficence justifies deceased uterus donation despite its quality-of-life purpose and temporary nature, while the psychological and emotional benefits of donation currently justify living uterus donation despite its imposition of physical harm. If equivalent clinical success can be demonstrated with deceased donation and the supply of deceased organs is adequate to meet demand, living uterus donation would no longer be ethically appropriate. For deceased donation, medical teams must obtain consent from a donor at present and potentially a surrogate in the future. For living donation, medical teams must obtain consent from the donor. Although disclosure remains an important part of the informed consent process for both types of donation, it is absolutely critical that living donors fully understand the risks, benefits, and alternatives before making a voluntary decision with assistance from a living donor advocate. Living donors and the families of deceased donors should also understand that through the donation process, they have given up all rights to the donated uterus and to any children born from it.

From a policy perspective, UNOS should allocate donor uteri to people who desire to gestate and parent a child, can procure an embryo via IVF, and possess the minimal capacity to rear a child adequately in a manner that accounts for the recipient's age, ability to carry a pregnancy to term, number of previous children, and difficulty to match to a donor. As with other organ transplants, OPOs should facilitate anonymous contact between donors and recipients, but also between donors and resulting children. Given the new and experimental nature of uterus transplantation, an international registry should be developed to monitor the procedure by maintaining detailed records of both living and deceased uterus donations and their corresponding recipient procedures and outcomes.

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