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Editorial

Should brain-dead or living donors be used for uterus transplantation? A statement by the CNGOF French Uterus Transplantation Committee (CETUF)



The first birth of a healthy child in 2014 to a woman who had undergone uterus transplantation (UTx) under the care of Mats Brännström's team in Sweden astounded the medical world and the general public. This birth provided proof of concept for UTx after over a decade of scepticism in the medical community, and offered new hope to women with absolute uterine factor infertility (AUI). UTx has been expanding rapidly since then, with more than 38 uterus transplants performed worldwide and 12 healthy children born to uterus transplant recipients in Sweden, the USA, Brazil [1] and Italy (unpublished). Most uterus transplants are now performed in clinical trials, using either living or brain-dead donors. The teams from Sweden [2], Germany [3], China [4], Serbia [1] and India [1] have chosen to use living donors, usually a relative of the recipient, those from Cleveland [5] and Brazil [1] have opted for brain-dead donors, while the teams from Dallas [6] and Czech Republic [7] use both donor types. The feasibility of both models has been demonstrated, in terms of successful transplantation and the birth of a healthy child. The Swedish and Dallas teams use living donors [2,8]. This is the model that gave rise to the first live birth following UTx and with which the longest experience has been acquired. More recently, a Brazilian team obtained the first livebirth after brain-dead donor UTx [1]. Both models have had similar graft success rates—62% (18/29) for living donor UTx and 67% (6/9) for brain-dead donor UTx—although the data on the latter are more limited and very recent (first birth in 2018).

The two models have different drawbacks (risk of complications, organization, organ quality, and organ availability) that must be taken into account and managed when developing a UTx programme.

Influence of donor type on the risk of complications

UTx poses a number of risks to living donors, with complications such as ureteral injury requiring placement of a double J stent [9] or pyelostomy with ureteral reimplantation [2], transient defecation disorders, vaginal cuff dehiscence, and buttock pain [10]. The risk of ureteral complications for living donors is due to the fact that it is difficult to dissect the ureter away from the uterine veins running over and under it. This deep, delicate, time-consuming dissection makes uterus retrieval from a living donor a complex operation. It can take between 6 h (in the case of the Chinese team, using a robot-assisted minimally invasive approach [4]) and over 11 h 30 min (by the pioneering Swedish team, using an open approach [2]). The robot-assisted minimally invasive approach should lessen donor morbidity.

The living donor, who is commonly the recipient's mother, may also experience psychological sequelae, whether the uterus transplant succeeds or fails. Both scenarios can create feelings of guilt, and above all a sense of obligation to donate her uterus to her daughter. However, the study on the 9 women who underwent hysterectomy for UTx in the original Swedish series showed that, 12 months after surgery, irrespective of the events that occurred (perioperative complications, rejection, UTx failure), no psychosocial impact was demonstrated among the donors [11].

Uterus retrieval from a brain-dead donor during multi-organ procurement appears more reproducible than from a living donor, with no need for parametrial dissection. The uterus is simply removed en bloc, with its vasculature intact up to the internal iliac vessels. There are obviously no donor complications, and uterus retrieval surgery is shortened to about 19 min (range: 10–25 min) [12].

Influence of donor type on logistical management

Donor type has a profound effect on the logistical management of the surgeries involved. Two surgical teams are required for transplantation: one to retrieve the organ from the donor and a second to transplant it into the recipient. UTx surgery is always complex, with recipient surgery taking between 4 h 10 min [2] and 6 h [10]. In the brain-dead donor model, both donor and recipient surgeries are emergency operations, as their timing is dictated by the availability of a multi-organ donor. Emergency surgery carries a higher risk of surgical complications [13]. UTx, like any new surgical activity, requires an ability to adapt and memory skills, both of which can be impaired by tiredness and stress. The advantage of the living donor model is that both operations, including anaesthesia, can be planned in advance, which makes it possible to maximize the team's performance by assembling all the surgical expertise required (robotic gynaecological surgeon, transplant surgeon, vascular surgeon) on the same day. The brain-dead donor model is more onerous organizationally, due to the additional on-call arrangements required and difficulties in coordinating the multiple medical and surgical specialties involved. In fact, Limoges University Hospital's brain-dead donor UTx project has been suspended temporarily while the organizational and administrative issues such a project presents are resolved.

Influence of donor type on graft quality

Another advantage of using living donors is that a preoperative assessment can be conducted to ensure that the donor's uterus is functional. It is easy to find out her obstetrical history and perform

a cervical smear with HPV typing. A thorough morphological examination of the uterus is also performed, using pelvic ultrasonography to measure the uterus and endometrium and look for leiomyomata, and hysteroscopy to detect any uterine cavity abnormalities. The pelvic vasculature is evaluated to determine the diameter of the uterine arteries and to identify the presence of vascular disease by magnetic resonance angiography. The latter can only be performed on a living donor. Finally, the compatibility between donor and recipient may be greater in the living donor model, because the donor is usually related to the recipient (e.g. mother or sister) [2]. Furthermore, when a living donor is used, HLA compatibility between the donor and recipient can be determined in advance by crossmatching.

Such preoperative assessment maximizes the chances of a successful uterus transplant. In addition to it being difficult to thoroughly evaluate the uterus of a brain-dead donor, its quality may deteriorate during multi-organ procurement. This is because, as a non-vital organ, the uterus tends to be retrieved after the heart, liver and kidneys, which increases the cold ischaemia time. However, in animal and human studies of uterine resistance to warm and cold ischaemia, histological and functional impairment were only observed after at least 6 h or even 24 h of cold ischaemia, depending on the preservation solution used [14]. One advantage of brain-dead donors in terms of graft quality is that part of the internal iliac artery can be taken, which lengthens the vascular pedicles and facilitates the vascular anastomoses in the recipient.

Organ availability

Although the use of uterine grafts from brain-dead donors offers the enormous advantage of posing no surgical or psychological risk to the donor and none of the ethical problems associated with the procurement of organs from living donors, some studies have predicted that the potential demand among women with AUI will exceed the supply of uteri from this source. An estimated 1 in 500 women have AUI, corresponding to 30 000 women in France [15]. According to France's Biomedicine Agency, only 1770 multi-organ retrievals are performed each year in France and only 885 of these donors are women. Donor age is another constraint when selecting a uterus donor. The risk of vascular disorders in women over the age of 65 precludes them as a source of uterus grafts, yet they account for almost 40% of donors. There will not be enough suitable female brain-dead donors to satisfy the total demand among women with AUI.

In summary, living donors and brain-dead donors offer different advantages and disadvantages in a UTx programme. The advantages in terms of organization and clinical logistics, and potential improvements in the chances of success, argue in favour of a strategy based on living donors. On the other hand, the risk of complications for the living donor and the ethical problems this poses argue in favour of a brain-dead donor strategy. However, given the foreseeable shortage of uterus grafts, the two strategies will be complementary in routine clinical practice.

Disclosure of interest

The authors declare that they have no competing interest.

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