## **NEWS AND VIEWS**

## Uterus transplantation: advantages and disadvantages of a deceased donor

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Dear Editor,

First successful livebirth following uterus transplantation (UTx) from a deceased donor was recently reported by Ejzenberg et al. [1]. In 2014, Brännström et al. achieved the first successful delivery after UTx from a live donor [2]. To date, more than 50 UTx procedures have been performed worldwide, leading to more than 10 newborns after UTx from live donors. However, the report of successful livebirth after UTx from a deceased donor increases the potential of UTx for women with uterine factor infertility (UFI).

Most UTx procedures use a uterus from a live donor, but living-to-living UTx is a highly invasive surgery. Brännström et al. perfected their surgical technique in animal experiments for more than 10 years and conducted clinical studies of UTx in many women; however, the time of donor surgery in the first trial was still ~ 10 h and the blood loss was high [3]. This is because an extremely precise surgical procedure is required to remove a part of the deep uterine vein located in the pelvic floor and the internal iliac vein as drainage veins. Robot-assisted surgery has been performed for less-invasive surgery in living donors and novel operative procedures using the ovary or utero-ovarian vein as a drainage vein in place of the uterine vein have been developed [4, 5]. These methods reduce the operative time and bleeding volume, and consequently, should reduce risks for living donor UTx surgery in the future.

Despite the advances in living donor UTx, the guiding principles of organ transplantation still indicate that the organ should be collected from a deceased donor. The first UTx from a deceased donor was performed in Turkey in 2011 and the patient became pregnant, but had repeated

The greatest advantage of UTx from deceased donors is elimination of surgical stress in living donors. Resection of extended vascular pedicles of greater length than those from living donors and extraction of the uterus can be achieved in a faster procurement time. However, there are also several disadvantages. First, it is difficult to plan surgery. Management by multidisciplinary experts is necessary for UTx, since the procedure remains in the experimental stage, with careful preoperative preparation, patient selection, and sufficient informed consent required. These procedures are more difficult for UTx from deceased donors, which may explain why UTx from living donors is currently more common. Second, thorough preoperative screening is difficult for deceased donors. Living donors undergo preoperative uterine imaging and angiography by CT and MRI, and uterine cancer screening including HPV testing, Pap smear, and endometrial biopsy; however, these examinations are not fully performed due to the limited time for UTx from deceased donors. In addition, no details of medical history can be obtained. Third, ischemic time (particularly cold ischemic time) is longer than that in living donors. The uterus of a living donor is transferred to a recipient in the next operating room, whereas the uterus of a deceased donor may be transferred to a recipient in another institution. Furthermore, the uterus of a brain-dead multi-organ donor is not a vital organ and it is the final procurement after that of vital organs, resulting in an extended ischemic time. Fourth, vasoactive drugs including catecholamines are frequently administered to patients in the agonal stage; consequently, vascular insufficiency and systemic inflammatory changes may have negative effect on organs. Vasoactive drugs were administered to the deceased donor for 4 h before transplantation in Ejzenberg et al. [1].

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abortion and no livebirth [6]. UTx from deceased donors was then performed in the United States (Cleveland and Dallas) [7, 8] and the Czech Republic [9], but without subsequent livebirth, which raised a question of the feasibility of such transplantation.

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The final difficulty with UTx from a deceased donor is that microvessels located in tissues surrounding the uterus must be carefully ligated for transplantation. Failure to do so results in hemorrhage after reperfusion during recipient surgery. With regard to dissection and ligation in back-table preparation of the uterus of a deceased donor, it is difficult to find fine vessels around a white uterus that was washed out with organ-protecting solution. This makes vascular treatment before reperfusion in a deceased donor more difficult than that in a living donor. As stated in Ejzenberg et al. [1], the hemorrhage volume of the recipient was 1200 mL, indicating substantial blood loss, and most blood was lost from the transplanted uterus after reperfusion. Previous reports of UTx had hemorrhage volumes of the recipient ranging from 500 to 1000 mL in transplantation [3, 4, 9, 10], mainly due to bleeding around the uterus after reperfusion, rather than blood loss in vascular anastomosis. Furthermore, recipients had postoperative complications including retroperitoneal hematoma and hematoma surrounding the uterus [3, 10].

UTx from a deceased donor still has disadvantages to be resolved, but does not have the greatest problem in living-to-living UTx, which is the risk to the donor. Establishment of the proof of concept and feasibility of UTx from a deceased donor has opened up a new option, in place of adoption and surrogacy, for women with UFI. This major achievement constitutes a medical milestone in assisted reproduction and transplantation. This success is expected to motivate performance of UTx from deceased donors worldwide, and these cases will provide new evidence with regard to the safety and efficacy of UTx from a deceased donor.

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## **Compliance with ethical standards**

Conflict of interest The authors declare no competing interests.

**Human participants or animal experiments** This article does not contain any studies involving human participants or animals.

## References

 Ejzenberg D, Andraus W, Mendes LRBC, Ducatti L, Song A, Tanigawa R, Rocha-Santos V, Arantes RM, Soares-Jr JM,

- Serafini PC, Haddad LBP, Francisco RPV, D'Albuquerque LAC, Baracat EC (2018) Livebirth after uterus transplantation from a deceased donor in a recipient with uterine infertility. Lancet 392(10165):2697–2704
- Brännström M, Johannesson L, Bokström H, Kvarnström N, Mölne J, Dahm-Kähler P, Enskog A, Milenkovic M, Ekberg J, Diaz-Garcia C, Gäbel M, Hanafy A, Hagberg H, Olausson M, Nilsson L (2015) Livebirth after uterus transplantation. Lancet 385(9968):607–616
- Brännström M, Johannesson L, Dahm-Kähler P, Enskog A, Mölne J, Kvarnström N, Diaz-Garcia C, Hanafy A, Lundmark C, Marcickiewicz J, Gäbel M, Groth K, Akouri R, Eklind S, Holgersson J, Tzakis A, Olausson M (2014) First clinical uterus transplantation trial: a six-month report. Fertil Steril 101:1228–1236
- 4. Wei L, Xue T, Tao KS, Zhang G, Zhao GY, Yu SQ, Cheng L, Yang ZX, Zheng MJ, Li F, Wang Q, Han Y, Shi YQ, Dong HL, Lu ZH, Wang Y, Yang H, Ma XD, Liu SJ, Liu HX, Xiong LZ, Chen BL (2017) Modified human uterus transplantation using ovarian veins for venous drainage: the first report of surgically successful robotic-assisted uterus procurement and follow-up for 12 months. Fertil Steril 108:346–356
- Testa G, McKenna GJ, Gunby RT Jr, Anthony T, Koon EC, Warren AM, Putman JM, Zhang L, dePrisco G, Mitchell JM, Wallis K, Klintmalm GB, Olausson M, Johannesson L (2018) First live birth after uterus transplantation in the United States. Am J Transplant 18:1270–1274
- Erman Akar M, Ozkan O, Aydinuraz B, Dirican K, Cincik M, Mendilcioglu I, Simsek M, Gunseren F, Kocak H, Ciftcioglu A, Gecici O, Ozkan O (2013) Clinical pregnancy after uterus transplantation. Fertil Steril 100:1358–1363
- Richards EG, Flyckt R, Tzakis A, Falcone T (2018) Uterus transplantation: organ procurement in a deceased donor model. Fertil Steril 110:183
- Testa G, Anthony T, McKenna GJ, Koon EC, Wallis K, Klintmalm GB, Reese JC, Johannesson L (2018) Deceased donor uterus retrieval: a novel technique and workflow. Am J Transplant 18:679–683
- Chmel R, Novackova M, Janousek L, Matecha J, Pastor Z, Maluskova J, Cekal M, Kristek J, Olausson M, Fronek J (2018) Revaluation and lessons learned from the first 9 cases of a Czech uterus transplantation trial: four deceased donor and 5 living donor uterus transplantations. Am J Transplant. https://doi. org/10.1111/ajt.15096 (Epub ahead of print)
- Johannesson L, Wallis K, Koon EC, McKenna GJ, Anthony T, Leffingwell SG, Klintmalm GB, Gunby RT Jr, Testa G (2018) Living uterus donation and transplantation: experience of interest and screening in a single center in the United States. Am J Obstet Gynecol 218:331.e1–331.e7

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