Deceased Donor availability for uterus transplantation in Australia.

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AIM: To establish the feasibility of a deceased donor UTx program in Australia. Would enough uteri be available? Could the current international inclusion criteria be used in the Australian setting?

BACKGROUND:

Uterus Transplantation (UTx) is a new treatment option for women with absolute uterine factor infertility (AUFI). Uterine infertility affects around 1-5% of the female population.(1) The first successful live birth following UTx was announced in Sweden in 2015.(2) Subsequently more than 70 procedures have been completed and 32 live births reported in the literature.(3,4)

Internationally, most UTx procedures use a living donor (LD) model where there is a greater opportunity for donor screening and team preparation due to capacity for scheduling.(3) However, the risk to a LD cannot be ignored. in 2017, the first live birth using a deceased donor (DD) was announced in Brazil, proving success is possible from both donor models.(5) To date 17 DD procedures and 5 livebirths have been reported (3-6)

Debate remains over which donor model is more ethical and feasible, but a significant issue other than LD risk, raised by several research teams relates to organ availability in both models, with not all women having an available LD. Therefore, would enough DD uteri be available for a deceased donor only program?

Prior to initiation of a UTx program in Australia, it is essential to establish the potential number of deceased donor uteri that could be available and create the donor inclusion criteria suitable for the Australian setting.

Table 1: Current international DD inclusion criteria (Sweden, USA, Czech Republic).(7-9)

	Summary of International deceased donor inclusion criteria
1.	Female (all)
2.	Aged under 60 years (Czech Republic); Age under <55years (Sweden); *Age 16*-45yrs (USA)
3.	No previous malignancy of the uterus or other organ or tissue (all)
4.	No previous hysterectomy or major abdominal surgery (including caesarean section) (Sweden and Czech Republic); Caesarean section was not an exclusion in the USA.
5.	Brain-dead donors (all)
6.	Multi-Organ Donor (all)
7.	Normal BMI (USA)
8.	No systemic disease (Sweden, USA)
9.	*At least one normal full-term pregnancy (>37wks) and childbirth (Sweden); No abortions/miscarriages; Desirable in USA criteria*
10.	*Inclusion: Regular menstruation(USA) Exclusion: uterine disease (fibroids >1cm; pelvic inflammatory disease, endometriosis or adenomyosis; anatomic uterine anomalies*
11.	*Acceptance of organ donation prior to death (Sweden)*
12.	*Cytomegalovirus (CMV) status: positive serology for CMV are only used for recipients who are also serology positive for CMV.*

METHODS:

Using data provided from the NSW Organ and Tissue Donation (OTDS) service, a retrospective analysis was performed on 'all' donors between 2018-2020 and compared with current international trial UTx donor inclusion criteria (see table 1). A subgroup analysis was performed including gender, age, brain-death and multiorgan donor status, to establish the potential number of previous donors that may also have been eligible uterine donors.

RESULTS:

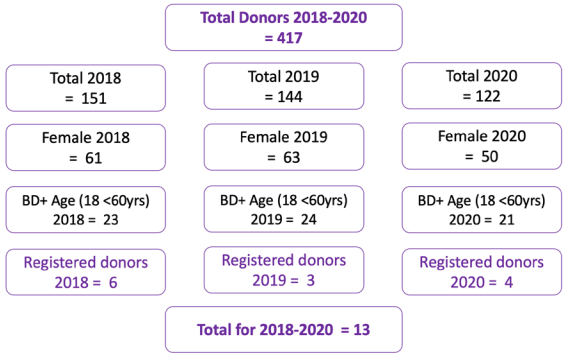

Figure 1: Results potentially available uterus donors (*OTDS donor data 2018-2020*)

There were a median of 144 (range 122-151) total organ donors between 2018-2020. All donors were compared with the current international UTx criteria (see Table 1). Of total donors, 41.9% were female, half met the age criteria under 60-years, 68.6% were donation after brain death and 96% were multi-organ donors. No donors had a malignancy or major abdominal surgery.

Using the current international UTx criteria (see Table 1), we estimate that 23 (range 21-24) potential donors may have been eligible for uterus donation annually. However, in Australia, both registered and unregistered donor families are approached for organ donation. If the criteria was limited to only 'self-elected donation' (ie the donor registered for organ donation prior to death), in the three-year period the overall eligibility would reduce to only 13/417 donors (3.1%) in the three-year period, or on average 4 donors a year. Moreover, criterion 9-12 were not available to assess, so hypothetically, this number could reduce even further.

CONCLUSION

An Australian UTx programme would provide women with AUFI the opportunity to carry their own genetic child. There will be ongoing debate around donor model of choice, which will only be answered as more UTx procedures occur and outcomes shared.

As with all transplant programs, donor availability is a limitation for both models. From this retrospective analysis it appears a DD only program may be possible if unregistered and nulliparous donors are included. However, a combined LD/DD program would be justifiable until the 'need versus availability' ratio and donor risk profiles, are more fully appreciated.

The criteria selected for DD inclusion needs further consideration prior to the establishment of a clinical program in Australia to maximise organ availability but ensure optimum graft outcomes leading to live births.

Working closely with the OTDS around donor conversations, (ie how best to approach senior available next of kin) will help increase availability but also ensure the sustainability and preservation of both current organ donations and UTx in the future.

REFERENCES

1. Milliez,J.(2009).Uterine transplantation: FIGO Committee for the Ethical Aspects of Human Reproduction and Women's Health. Int J Gyn Obst;106(3): 270-270.
2. Brännström, M et al. (2015). Livebirth after uterus transplantation. Lancet; 385 (9968): 607-616
3. Brännström, et al.(2021). Uterus transplantation worldwide: clinical activities and outcomes. Curr Opin Organ Transp; 26(6):616-626
4. Flyckt, et al.(2020). First birth from a deceased donor uterus in the United States: from severe graft rejection to successful cesarean delivery. Am J Obstet Gynecol; 223(2).143-151.
5. Ejzenberg, et al.(2018). Livebirth after uterus transplantation from a deceased donor in a recipient with uterine infertility. Lancet; 392 (10165): 2697-2704
6. Fronek, et al.20201.Human Uterus Transplantation from Living and Deceased Donors: Interim Results of the First 10 Cases of the Czech Trial. Clin Med;10(4).
7. D'Amico, et al. (2021).Uterus Recovery from Deceased Donor: Simple Techniq Securing Safety of Vital Organs and Uterus Graft. J Am Surg; 232(3):e1-e6
8. Fronek et al.(2015). Uterus Transplantation from Live Donors and from Deceased Donors: Clinical Study(UTxLD/DBD):Identifier NCT03277430.
9. Brännström. (2018) Uterus Transplantation from Deceased Donor - Gothenburg III. Identifier NCT03581019