Surgical and logistical concerns for ex vivo–based perfusion strategies for “donation after circulatory death” multiorgan recovery

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Organ recovery following donation after circulatory death (DCD) has been successfully developed and refined over the past 2 decades to expand the donor pool of kidneys, livers, and lungs. 1,2 Compared with donation after brain death (DBD), DCD organs are exposed to additional warm ischemia. However, aided by emerging ex vivo organ perfusion technology, encouraging results have recently been reported for DCD livers, lungs, and kidneys. 3-6 This technology has recently been adopted by pioneering DCD heart transplant programs, first in Australia 7 and then validated in the United Kingdom. 8 Although greater rates of primary graft dysfunction (PGD) requiring extracorporeal membrane oxygenation have been reported, early outcomes in patient survival among DCD heart transplants have been comparable with those of DBD heart transplants. 9

Two general approaches to DCD donor heart recovery have been adopted. 7,8,10-13 The normothermic regional perfusion (NRP) technique involves restoring circulation to the entire donor but surgically excluding the brain by clamping the aortic arch blood vessels. NRP allows the teams an ability to resuscitate and assess the donor’s organs in a fully loaded and working state. Organ recovery is then performed in a manner otherwise identical to standard DBD procurement, using traditional cold storage.

In contrast, direct procurement with ex vivo perfusion (DPEP) for the heart requires a rapid collection of donor blood, a step specific to DCD heart procurement. This is followed by an in situ cold preservation flush and a mildly hypothermic (34°C) ex vivo perfusion strategy similar to those most commonly deployed for abdominal organs and lungs using the Organ Care System device (OCS; Transmedics, Andover, Mass). 11

DCD heart recovery using OCS Heart System was developed for DBD donors and has received approval from the Food and Drug Administration for this indication. 14 While there are ongoing legal, ethical, and regional controversies regarding the NRP approach, 15 DPEP using OCS for DCD heart transplantation avoids these. The device was investigated in Australia and the United Kingdom and has been examined in a clinical trial in the United States since 2019. Herein, we share our current practices in terms of effective communication, procedural tips, and handling

CENTRAL MESSAGE
Expanding multiorgan recovery from donation after circulatory death to include the heart presents logistical and technical challenges. Optimal collaboration among recovery teams is crucial.

See Commentary on page 57.
DCD-related regional policies and events for DPEP DCD heart recovery based on our experience in the United States.

ASSESSMENT OF LIKELIHOOD OF PROGRESSION TO DONATION

There is no clear, nor uniform definition of the warm ischemic time (WIT). One of the criteria used in the selection of DCD donors is the time of withdrawal of life-sustaining treatment (WLST) to antegrade flush (“total” donor warm ischemic time: tDWIT). Currently, many transplant centers moved to focus on the “functional” donor warm ischemic time (fDWIT), which defines the time from the onset of organ ischemia (an arterial blood pressure or peripheral blood oxygen saturation below a certain value) to antegrade flush. This allows for the evaluation of additional organs and is considered a better predictor of clinical outcomes after DCD transplantation.

Iyer and colleagues reported in their animal study that impaired functional, biochemical, and metabolic recovery was seen following resuscitation of DCD porcine hearts exposed to WITs of greater than 20 minutes. Pharmacologic postconditioning using Celsior solution (Waters Medical Systems, Rochester, Minn) extends the tolerance of DCD hearts to warm ischemia by approximately 10 minutes, allowing complete functional recovery of hearts up to 30 minutes of WITs in porcine hearts. The OCS DCD Heart trial sets the fWIT threshold as 70% of peripheral blood oxygen saturation or 50 mm Hg of systolic blood pressure and a time limit of 30 minutes before the heart would be excluded from the trial, so this threshold has gained general acceptance across centers for DPEP. For liver transplantation, acceptable limits and definitions for organ ischemia vary among centers; however, the majority of liver programs in the United States consider an allowable tDWIT or fDWIT of up to 30 minutes.

Lungs and kidneys exhibit a clinically acceptable PGD rate after relatively longer tDWITs. Accordingly, some programs will accept organs after a 90- or even 120-minute tDWIT. The definition of WIT and allowable WIT for each organ should be discussed beforehand and agreed upon by all organ recovery teams. The donor’s hospital policy with respect to tDWIT limits and definition circulatory death also needs to be confirmed in advance.

The first step in considering any DCD heart offer is assessing the likelihood of progression to organ recovery. Although there is no established evidence-based, algorithm for predicting cardiac death within less than 30 minutes of fDWIT, certain parameters may be useful. Munshi and colleagues reviewed 15 studies associated with time to death after WLST. Across the 7 prediction tools proposed, only a few were validated in a separate cohort, and most had only moderate sensitivity and primarily focused on time to death within 60 minutes. The parameters most consistently associated with more rapid progression to cardiac death across a variety of different populations were Glasgow Coma Scale score ≤4; spontaneous breathing rate below ventilator settings and absence of other brain stem reflexes; severe lung dysfunction (high oxygen or positive end-respiratory pressure requirement); and hemodynamic instability (high-dose vasopressor or inotrope requirement).

Existing models apply broadly to DCD donors, but the DCD heart donors are a more specific subset so these studies have to be interpreted carefully. We screen DCD heart offers to ascertain the existence/degree of spontaneous breathing and remaining brain reflexes on the donors. In our experience, if the respiratory drive and other brainstem functions are mostly preserved, the donor is less likely to progress to circulatory arrest within 30 minutes of heart ischemia. Although distance from the organ recovery site and consequences associated with prolonged travel time are neutralized by use of the OCS technology, related logistical barriers, such as transportation costs as well as donor organ quality (metabolic condition, inotrope requirements, echocardiographic findings), and recipient factors (listing status/urgency, degree of sensitization, and other competing factors for organ offer, such as blood type or size) influence the initial decision to accept or reject a distant DCD organ offer.

THE LOCATION WHERE EXTUBATION IS PERFORMED

In our experience, most hospitals permit donor extubation in the operating room (OR). However, in some cases, hospital practice or policy or family request dictates that the donor is extubated outside of the OR. Sterile preparation and draping of the surgical field may be performed even if the donor will be extubated outside of the OR. All tubing, including suction tubing, lines for preservation solutions, and the blood collection line for OCS are assembled and positioned ahead of time. Organ-recovery teams should accommodate requests from the family, the organ procurement organization representative, or the clinician assigned to establish a time of death to have one arm extended and/or the face exposed for the benefit of the donor’s family if they’ll be present for WLST. After draping, an additional sterile drape is then placed over the entire surgical field, and the top drape at the patient’s head can be pulled caudad, maintaining the aseptic field underneath.

For out-of-OR extubation, the options for sterile preparation, draping, and performing surgery on the intensive care unit bed should be considered as donor hospital/facility policy allows. If not permitted, the time for transportation to the OR, sterile preparation and draping, and tubing setup for suction and preservation solution will need to be accounted for in determining the allowable WIT. When possible, the WIT may be minimized by transporting the
donor to the OR during the “no-touch” interval before death declaration. Drapes and flush tubing can be set up ahead of time using sterile basins on rolling stands with suction passed off and already connected ready to quickly move to the operative field.

**HEART TEAM PREPARATIONS BEFORE EXTUBATION**

Preparation of heart team equipment before extubation is essential for successful DCD heart recovery. After the OR huddle among all teams (Table 1), all equipment required for every step is prepared aseptically on a Mayo stand or table that is rapidly accessible to the heart team (Table 2, Figure 1). In addition to the Mayo stand, a separate back table for OCS disposables and sterile instruments is also required. To avoid unnecessary expenses, the opening of sterile supplies needed to attach the heart to the OCS device is delayed until cardioplegia is initiated within 30 minutes of fDWIT.

Once preparations are completed in the OR, extubation can proceed. Thirty thousand units of heparin is generally administered to the donor through a secure intravenous access catheter before extubation.

**DETERMINATION OF TIME TO RECOVER ORGAN FOR DCD**

Following the first determination by the responsible provider that the donor’s circulation has ceased, a “no-touch interval” is required to confirm the absence of spontaneous recovery of respiratory or cardiac function. The “no-touch interval” varies from 2 to 5 minutes according to local hospital policy or, less often, is determined by local organ procurement organization protocols.22 Loss of phasic activity on an arterial waveform is a typical proxy for onset of circulatory arrest, and a period of ‘pulseless electrical activity’ often precedes electrocardiographic silence by several minutes; hospital policy dictates how this pulseless electrical activity interval is considered with respect to the time at which death is declared. Practically, provided that 5 minutes is required for each no-touch time and additional time is needed following skin incision to initiate cardioplegia; these several aggregate minutes need to be subtracted from the allowable WIT. Functionally this means that the initial determination of circulatory arrest must occur within 20 minutes of ischemia onset not to exceed 30 minutes of fDWIT.

**THE OPERATIVE FLOW FOR DCD HEART DPEP**

Importantly, cardioplegia and abdominal antegrade flush should both be initiated within 3 to 5 minutes after the end of the no-touch period. Heart procurement procedures are initiated simultaneously with the standard abdominal DCD procedures, as previously reported.1,23 The operative

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**TABLE 1. Huddle topics in DCD multiple organ recovery with ex vivo perfusion strategies: Information needs to be shared in advance**

| Definitions of WIT for each organ: tDWIT vs fDWIT |
| Location where donor is prepared for surgery and extubated |
| Deciding how/whether to prep and drape beforehand |
| The timing and amount of heparin to be given |
| Duration of no-touch period |
| Flow of operation/interaction among teams: time to start abdominal flush; venting strategy; location of aortic crossclamp (descending vs abdominal aorta), etc |
| Agreement between heart and liver teams on how long the liver team will be willing to delay antegrade flush for blood collection |
| Designate OPO time-keeper to track and communicate critical intervals: heparin; start of fDWIT (WLST); start of fDWIT (SpO2 <70% or SBP <50 mm Hg for heart); start of no-touch time (asytolic); end of WIT (start of antegrade flush) |

**TABLE 2. The equipment checklist for DCD heart DPEP**

1. Assembled sternal saw
   - Preferred blade direction; battery charged or air power on, as applicable
2. Instruments to open chest for RA drain/cardioplegia/Ao X-C
   - Knife #10; straight or curved Mayo scissors; DeBakey forceps (3); chest retractor; blue towels; pericardial retraction stitch (2-O Silk); needle holder
3. Assembled blood collection kit
   - Connections tight, stop-cock ports sealed, to avoid air entrainment and an airlock during collection
4. Cardioplegia kit
   - Cardioplegia tubing and connector (assembled); cardioplegia needle; cardioplegia stitch, snare, and snaps; needle holder
5. Instruments for procedure
   - Knife #11; curved Mayo or Metzenbaum scissors; O or 2-O silk ties; Ao X-C; Satinsky clamp (if needed to grab atrial appendage); vascular clamp (if needed for IVC clamp)
6. Suction systems/ice slash
   - Four suction systems, at least 2 attached to Poole suction tips; sufficient topical slush ice available for chest and abdominal teams.

RA, Right atrial; Ao X-C, aortic crossclamp; IVC, inferior vena cava.

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WIT, Warm ischemic time; tDWIT, total donor warm ischemic time; fDWIT, functional donor warm ischemic time; OPO, organ procurement organization; WLST, withdrawal of life-sustaining treatment; SpO2, peripheral oxygen saturation; SBP, systolic blood pressure.
steps for the heart procurement, previously described by Connellan and Dhital,\textsuperscript{11} are summarized in Table 3.

DCD heart procurement introduces several technical aspects that differ from isolated abdominal DCD organ recovery (Video 1; Table E1).

1. Abdominal antegrade flush initiation must be delayed until heart team donor blood collection is completed to avoid a high potassium concentration in the OCS perfusion system. After blood collection (generally $<3$ minutes from incision), the abdominal team may start abdominal antegrade flush via the infrarenal abdominal aorta while the heart team places a cardioplegia cannula. The process of blood collection can be difficult and create points of disagreement, which will be discussed further herein.

2. Until the supraceliac abdominal aorta or thoracic descending aorta is crossclamped, initiation of abdominal antegrade flush pressurizes the thoracic aorta partially, simplifying cardioplegia catheter placement, and delivers some antegrade flush to heart since the ascending aorta is not immediately clamped.

3. Once the cardioplegia is initiated and the ascending aorta is crossclamped, an additional aortic crossclamp may be applied to the supradiaphragmatic aorta through the left chest if requested by the abdominal team, with care taken not to compromise cardioplegia delivery.

4. If the lungs are also being recovered, additional procedures should be followed. The donor is reintubated during sternotomy and ventilation with low tidal volume can be resumed after the initiation of cardioplegia. This must

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**FIGURE 1.** The operating room setting for multiorgan recovery using an ex vivo perfusion strategy in donation after circulatory death. This is at the moment blood is being drained for OCS. Before withdrawal of treatment, each surgical team sets up a separate table for the instruments that would be required between a skin incision and an administration of antegrade flush.
not be done before cardioplegia administration, as ventila-
tion can restore a cardiac rhythm. Venting is done by
making a large incision in the left atrial appendage to
minimize pulmonary congestion, as this is a primary
cause of PGD in lungs after DCD. If the lungs are not be-
ing recovered, venting is most easily done by dividing
the pulmonary veins. Antegrade flush through the pul-
monary artery is delayed until after cardioplegia has
begun and is confirmed. When this has commenced, an
appropriate site for cannulation is chosen on the distal
main pulmonary artery (PA). Since perfusion on OCS re-
quires a purse-string suture in the cuff of the PA, leaving
enough length of PA for this suture is critical. If the lung
team also plans to use OCS, they can use a portion of the
proximal descending thoracic aorta to construct a single
PA cuff to cannulate for OCS. After both cardioplegia
and pulmonary antegrade flush, the heart explant is
done with careful attention to structures that have
usually been separated before crossclamp in a DBD
recovery but not in this case, most notably separating
the right PA from the back of the aorta and superior
vena cava.

**BLOOD COLLECTION PROCESS AND PITFALLS**

Successful perfusion of the heart on OCS depends on the
collection of adequate blood (1.1 L) before any organ ante-
grade flush enters the donor.\textsuperscript{11,24} This is the most chal-
"\textsuperscript{11,24}"\textsubscript{11,24}lenging part of DCD heart recovery using DPEP. Some
flexibility on the part of the abdominal team may be justifi-
able based on a recent study using the United Network for
Organ Sharing database, which showed that there was no
difference in posttransplant outcomes between DCD liver
transplants from donors with tDWIT <30 minutes and
tDWIT between 30 and 40 minutes.\textsuperscript{3} Nevertheless, given
the close relationship between WIT and liver PGD, the
abdominal team should not be asked to significantly delay
initiating antegrade flush delivery to the abdominal organs.
It is important to complete blood collection before adminis-
tration of any antegrade flush to the patient. High-potassium
in priming blood can reduce contractility of heart on the
OCS device, which might affect lactate clearance and heart
recovery. Moreover, an inadequate priming volume can also
be problematic as even recently banked red blood cells
(RBCs) typically have high potassium concentrations, and
are acidic, and the citrate–phosphate–dextrose–adenine
used to prevent clotting in banked blood products efficiently
chelates calcium and magnesium. Nevertheless, as a pre-
caution, 2 units of RBC could be held in reserve in case
of insufficient blood collection. If banked blood is
required due to insufficient donor blood retrieval, they
should be prepared by washing to remove excess potassium
whenever possible. This process can be accomplished by
heart recovery team in advance, or at donor hospitals if an
autologous OR blood recovery system is available.\textsuperscript{25} If
banked blood is used, extra attention should be paid to the
electrolytes in the circuit prime as supplements will likely
be required.

The surgeon and surgical assistant must agree on specific
roles; usually, the assistant controls the drainage cannula,
evacuates airlock from the cannula and connector tubing
if needed to start collection, and passes off the collection
apparatus. The assistant generally prepares the suction
tubing and cardioplegia line as well while the surgeon opens
chest.

The abdominal surgeons will usually be ready to initiate
their organ antegrade flush within 3 minutes of the skin inci-
sion. To avoid substantial delay for the abdominal team, the
heart surgeons should aim to start blood drainage within 60–
90 seconds after skin incision and to finish within 3 minutes.
The Trendelenburg position can increase venous return and
expedite this process when siphoning, although is typically

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**TABLE 3. The operative steps for DCD heart DPEP**

| Step | Description |
|------|-------------|
| 1.   | Sharp midline incision to expose anterior sternum from suprasternal notch to xiphoid |
| 2.   | Open sternum in midline with sternal saw |
| 3.   | Place and open sternal retractor |
| 4.   | Incise midline pericardium from the diaphragm to just below the innominate vein |
| 5.   | Incise RA appendage or lateral wall (no purse-string suture), finger occlusion |
| 6.   | Place 34-French cannula via RA incision |
| 7.   | Collect 1.2-1.5 L of donor blood by gravity; Trendelenburg, heart massage if necessary |
| 8.   | Vent LA, manually decompress ventricles |
| 9.   | Place cardioplegia purse-string suture in ascending aorta |
| 10.  | Place cardioplegia cannula in ascending aorta, snare, deair |
| 11.  | Initiate antegrade cardioplegia |

RA, Right atrial; LA, left atrium.

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**VIDEO 1.** An initial part of the surgical procedure for DCD heart procure-
ment using an ex vivo perfusion strategy is presented. Successful collabo-
ration is promoted by awareness on each procurement team of the other
team’s operative flow, key issues, and essential surgical goals. Video avail-
able at: https://www.jtcvs.org/article/S2666-2507(21)00761-6/fulltext.
not needed if using active suction. However, the liver team appropriately feels the urgency to proceed expeditiously when the liver WIT approaches 30 minutes.\(^6,26\) If the liver WIT exceeds 25 minutes at the time of skin incision, our team will allow the liver team to proceed with the abdominal antegrade flush whenever they are ready. In this situation, we recommend clamping the inferior vena cava (IVC) in the pericardium before starting the abdominal flush. This allows the heart team to continue with the blood collection. A prolonged blood collection time, however, should be avoided to prevent hemodilution or hyperkalemia in the OCS circuit, which can result from azygous and collateral venous return. Of note, unless the heart team clamps the intrapericardial IVC, the abdominal team should not vent the abdominal IVC during blood collection by the heart team, since this will interfere with donor blood drainage. However, if the IVC is clamped in the chest, venous drainage must be accomplished in the abdomen by the abdominal procurement team.

A single-stage venous cannula is provided by the manufacturer (Transmedics, Andover, Mass) for right atrial blood collection. Alternatively, a dual-stage cannula can be another option; however, a dual-stage cannula can be a problem if IVC clamp is required. Passive drainage with direct manual heart massage using a large bore single-stage cannula usually yields sufficient blood for OCS device priming, and decompresses the heart and abdominal venous system before the abdominal team initiating the antegrade flush. While vacuum assistance can also be employed, we use passive siphon as our standard procedure, which minimizes the potential risks of hemolysis and hyperkalemia due to cavitation.

Heart and liver WIT must be tracked by a member of the organ recovery team, and the teams kept updated until antegrade flushes are initiated. The heart and liver teams should agree on a specific time delay for blood collection after which the abdominal team will be allowed to start their antegrade flush.

CONCLUSIONS

There are important differences between DBD and DCD procurements, and critical time constraints create potential contrasting priorities between thoracic and abdominal surgical procurement teams with the time delay for the abdominal antegrade flush due to OCS blood collection. Effective communication, careful advanced preparation, and inter-team coordination are the keys to successful multi-organ DCD procurement.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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|                          | Heart                                      | Lung                                      | Liver/kidney                  |
|--------------------------|--------------------------------------------|-------------------------------------------|------------------------------|
| Skin incision            |                                            |                                           |                              |
| Sternotomy/open pericardium |                                            |                                           |                              |
| Blood collection from RA: Aim to complete within 3 minutes after skin incision | Reintubation by anesthesia team           | Abdominal aortic cannulation         |                              |
|                          |                                            | Notify heart team before flushing         |                              |
| Cardioplegia needle placed | LA or PV vent                              | Abdominal antegrade flush (tDWIT vs fDWIT: <30 minutes) |                              |
| Cardioplegia; Ao X-C (fDWIT: <30 minutes) | PA cannulation at distal main PA | Supraceliac Ao X-C: infradiaphragmatic vs supradiaphragmatic | IVC vent if desired |
|                          | Lung antegrade flush                       |                                           |                              |
|                          | Ice slush into each cavity                 |                                           |                              |
|                          | Similar flow to DBD procurement            |                                           |                              |

RA, Right atrium; LA, left atrium; PV, pulmonary vein; tDWIT, total donor warm ischemic time; fDWIT, functional donor warm ischemic time; Ao X-C, aortic crossclamp; IVC, inferior vena cava; PA, pulmonary artery; DBD, donation after brain death.