Art of Operative Technique

Surgical techniques for cardiac allograft procurement and perfusion in controlled donation after circulatory death

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In the last decade, heart transplants using allografts from adult donors after circulatory death, in a controlled setting, controlled donation after circulatory death (cDCD) have been rapidly adopted and widely performed. The selection of retrieval methods has largely been determined by state or institutional guidelines concerning permissible postmortem procedures. A significant majority of cDCD heart recoveries have employed direct procurement and perfusion (DPP) followed by normothermic machine perfusion (NMP) for graft preservation. Another established method involves the thoracoabdominal normothermic regional perfusion (taNRP), which is then followed by either NMP or static cold storage. Processing, management and surgical techniques of heart allograft procurement after cDCD are herein described and discussed.

Keywords: Heart transplantation; controlled donation after circulatory death (cDCD); direct procurement and perfusion (DPP); normothermic regional perfusion (NRP); organ care system (OCS)

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Introduction and operative techniques

Evaluation and selection of donor hearts for transplantation

Heart transplantation from donors after circulatory death, in a controlled setting, controlled donation after circulatory death (cDCD) is primarily restricted to donors categorized under Maastricht Category 3 and controlled Category 4 (1,2). Typically, these donors have suffered severe brain injuries but remained viable long enough to be admitted to an intensive care unit and sustained on life support.

In cDCD, discontinuation of care is agreed when prosecution of treatment is deemed futile, thus evaluating availability for donation, through previous donor consent and/or non-opposition of relatives.

The criteria for selecting cDCD donors closely mirror those for donors after brain death (DBD), with the main distinction being the age limit for cDCD heart donation due to the increased vulnerability of older hearts to ischemic damage (1,2).

All potential donors should undergo an echocardiogram before the withdrawal of life-sustaining therapy (WLST) to evaluate heart function and rule out significant structural abnormalities such as valvular heart disease, regional wall motion abnormalities, or pathological left ventricular hypertrophy (1,2).

Pre-mortem coronary angiography may not always be possible before WLST, so an emphasis is placed on identifying risk factors for coronary artery disease. If there is suspicion of obstructive coronary disease, coronary angiography can be performed *ex situ* during normothermic machine perfusion (2).

Ideally, the potential donor would be located at the recipient's transplant center to facilitate the process, though this is often impractical, making remote hospital procurement more common.

Due to the heightened sensitivity of cDCD hearts to ischemic injury, it is advisable to withdraw life support in an environment that minimizes the time between death determination and the commencement of organ retrieval (1-5). Suitable locations include the intensive care unit, an anesthetic bay, or an operating room. Predicting a timely circulatory arrest can be challenging; however, factors such as a Glasgow Coma Scale score of 3, younger age, lack of spontaneous breathing, higher oxygen needs, use of vasopressors, absence of brainstem reflexes, and low arterial pH are associated with quicker circulatory arrest after WLST. If several factors suggest that circulatory death will not occur promptly, the transplant center might decide not to mobilize a retrieval team.

Following WLST, the cDCD donor heart inevitably experiences a period of global warm ischemia. The timing and duration of warm ischemia can vary significantly. In most successful cDCD heart transplants, the functional warm ischemic time (FWIT)—the interval from when the donor's systolic blood pressure drops below 50 mmHg to when circulation is restored via normothermic regional perfusion (NRP) or the organ is flushed with preservation solution in direct procurement—has been under 30 minutes. Preclinical studies show that exceeding 30 minutes of FWIT results in severe injury to the cDCD heart, likely leading to primary graft failure if transplanted (2). The total ischemic impact on a cDCD heart includes both the FWIT and cold ischemia periods necessary for implantation and potentially for transport (2-14).

Preparation and initial procedures

Hospitals handling potential cDCD donors should have a comprehensive institutional policy (2-12) (*Figure 1*). This policy should detail the criteria for determining cDCD eligibility, the procedures for WLST, the administration of comfort care, monitoring techniques, and the necessary time after the cessation of circulation (observation period) before declaring death.

Although the patient has not yet been pronounced dead, the focus must remain on providing compassionate end-of-life care, which should not be altered by the organ donation process.

It is standard practice to administer intravenous heparin at the time of WLST. Research is ongoing into other medications that might mitigate ischemia-reperfusion injury in donor organs, but no additional treatments are currently utilized (2). The practice of pre-WLST cannulation of arteries and veins to facilitate organ donation is contentious and would require explicit informed consent from the patient or their representative.

WLST, palliative care, and the official declaration of death should be carried out independently from the organ procurement teams, adhering to local and state regulations. Effective coordination and communication with the organ procurement teams are crucial.

After the ventilator is turned off, extubation is performed, and infusions are stopped, the patient's vital signs are meticulously monitored. Parameters such as heart rate, blood pressure, respiratory rate and peripheral oxygen saturation are communicated to the organ procurement teams, typically on a minute-to-minute basis. This data helps each team assess the viability of their respective organs and determine if circulatory arrest is imminent, prompting them to prepare the necessary equipment.

The FWIT starts when the systolic blood pressure falls below 70 to 50 mmHg. Some facilities also monitor peripheral oxygen saturation and begin the FWIT when this drops below 70%. However, peripheral oxygen saturation levels can be influenced by the state of peripheral perfusion and may not reliably reflect myocardial oxygenation.

Death is declared according to established procedures, with the absence of a pulse signifying circulatory arrest. Mechanical asystole observed via an intra-arterial line is commonly used to mark this moment. Electrical asystole, which typically occurs a few minutes later, is not necessary for declaring death.

Once the absence of a pulse and the observation period (which varies by region) are confirmed (1,2,14), the donor is transported to the operating room under the supervision of the organ procurement teams. Standard procedures for identity verification, skin preparation, and draping are completed if not already performed, and the process of multiorgan retrieval begins. Cardiothoracic and abdominal teams operate concurrently to conduct a median sternotomy and midline laparotomy.

While the FWIT concludes either with a cold flush in the case of direct procurement and perfusion (DPP) or with the reperfusion of the heart in NRP, according to local policies and/or regulatory matters, the total ischemic time

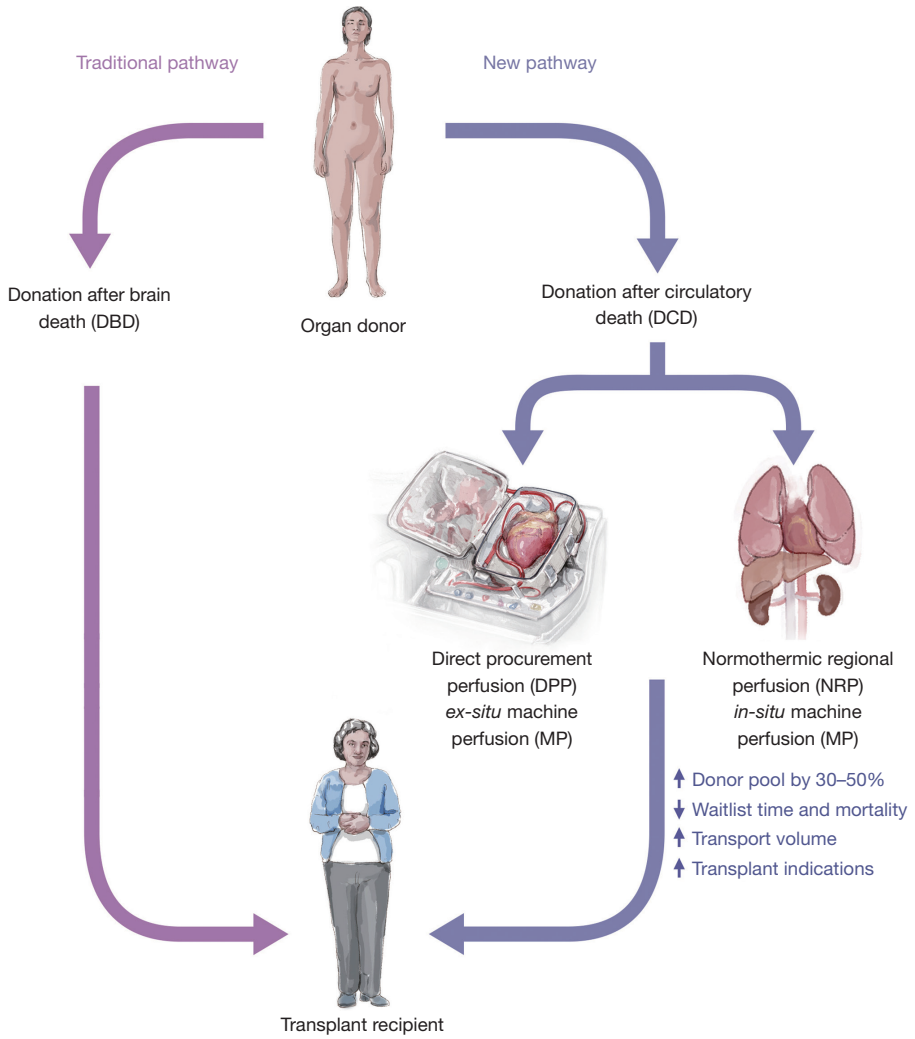

Figure 1 Traditional pathway (DBD) and new pathway (DCD) for heart graft procurement.

for the graft encompasses both the FWIT and the periods of cold ischemia needed for implantation and potentially for transport (2-13).

Procurement and machine preservation of cardiac allografts

One major challenge when using hearts from donors who have experienced circulatory death [donation after circulatory death (DCD)] is the warm ischemia that occurs after the cessation of life-support measures. To mitigate this, techniques have been developed for heart retrieval after cDCD to minimize additional ischemic damage and assess the heart's viability before implantation. The primary methods used are DPP (*Figures 1-3*) and NRP (*Figures 4,5*), with or without additional external perfusion (2-13).

For DPP, it is essential to gather between 1.1 and 1.5 liters of donor blood, which will be used as the perfusate, prior to starting the preservation flush. This blood is collected in a bag with 25,000 units of heparin, irrespective of whether heparin was given before death. It is also advised to add tirofiban (2 mg if the platelet count is below 300,000 and 3 mg if above 300,000) to prevent platelet activation and clot formation in the perfusion circuit. Following a rapid sternotomy and pericardiotomy, the right atrial appendage is incised for blood collection. Although traditional gravity-based methods are used, active suction into a cell salvage canister proves more efficient.

During blood collection, an antegrade cannula is placed in the aortic root to facilitate the introduction of preservation solution. After blood collection, a cross-clamp is applied, and preservation solution is infused in an antegrade manner, maintaining sufficient aortic root pressure. In the UK and Australia (2,6-12), modified St Thomas' solution with erythropoietin and glyceryl trinitrate is used; however, recent DCD trials in the US employing the DPP method have used Del Nido cardioplegia (2). If the lungs are not being procured, the heart is vented via the inferior vena cava and the right or left superior pulmonary vein.

For simultaneous heart and lung procurements, left heart venting is done through the left atrial appendage rather than the pulmonary veins. Once the myocardial preservation solution is delivered, a purse string is placed in the main pulmonary artery, and a pneumoplegia cannula is inserted to assist in preserving the lungs. Following the administration of cardioplegia, dissection begins with dividing the superior vena cava, inferior vena cava, and separating Sondergaard's groove. The procedure concludes by dividing the left atrium, leaving a small rim of atrial tissue with the pulmonary veins. Lung removal is performed by a separate surgeon to avoid delaying the normothermic *ex-situ* perfusion of the heart.

Once the preservation solution is administered, the heart is removed and prepared for normothermic *ex-situ* machine perfusion (13) (*Figures 2,3*). This technique allows for the reanimation and assessment of the donor

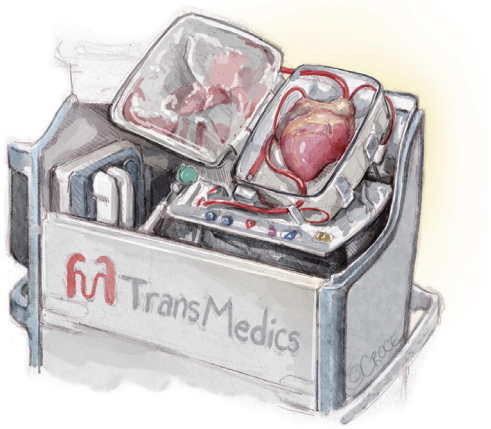

Figure 2 *Ex-situ* machine perfusion cardiac allograft preservation device.

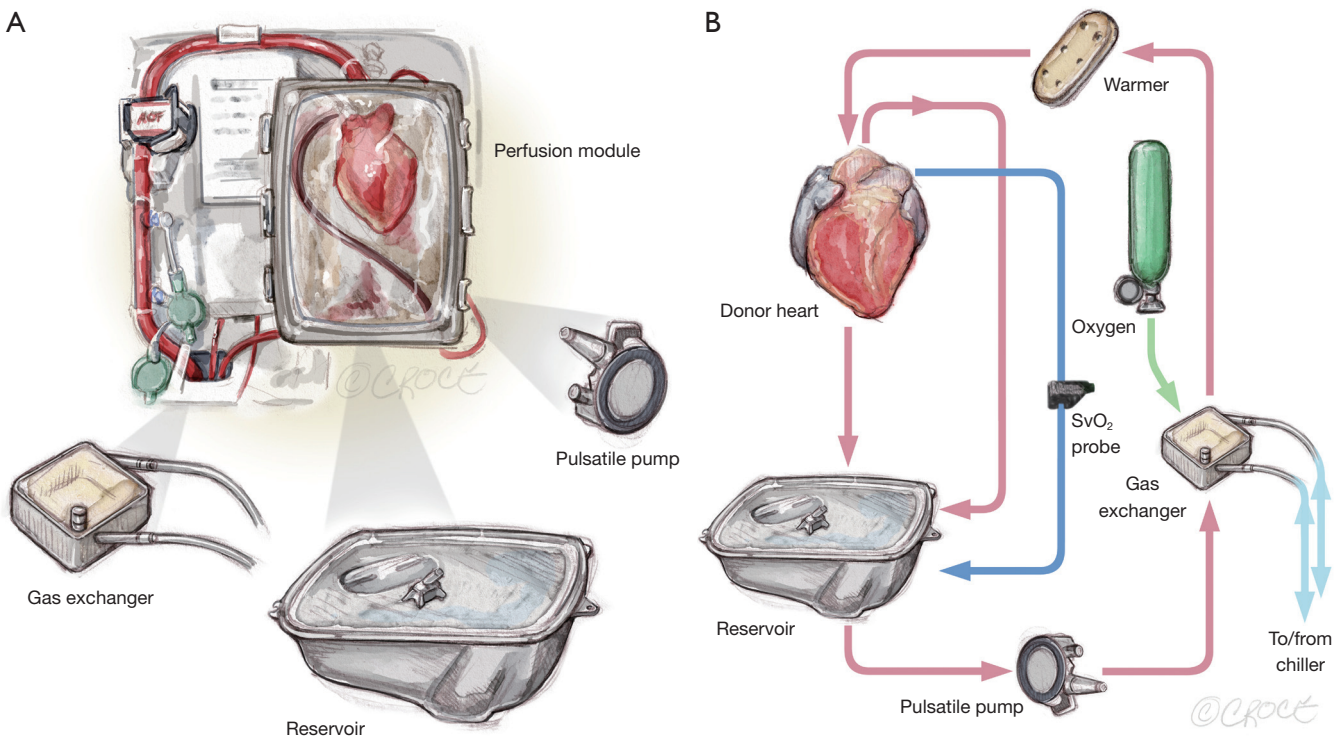

Figure 3 *Ex-situ* machine perfusion cardiac allograft preservation setting. (A) In the box; (B) out of the box. SvO_2, venous oxygen saturation.

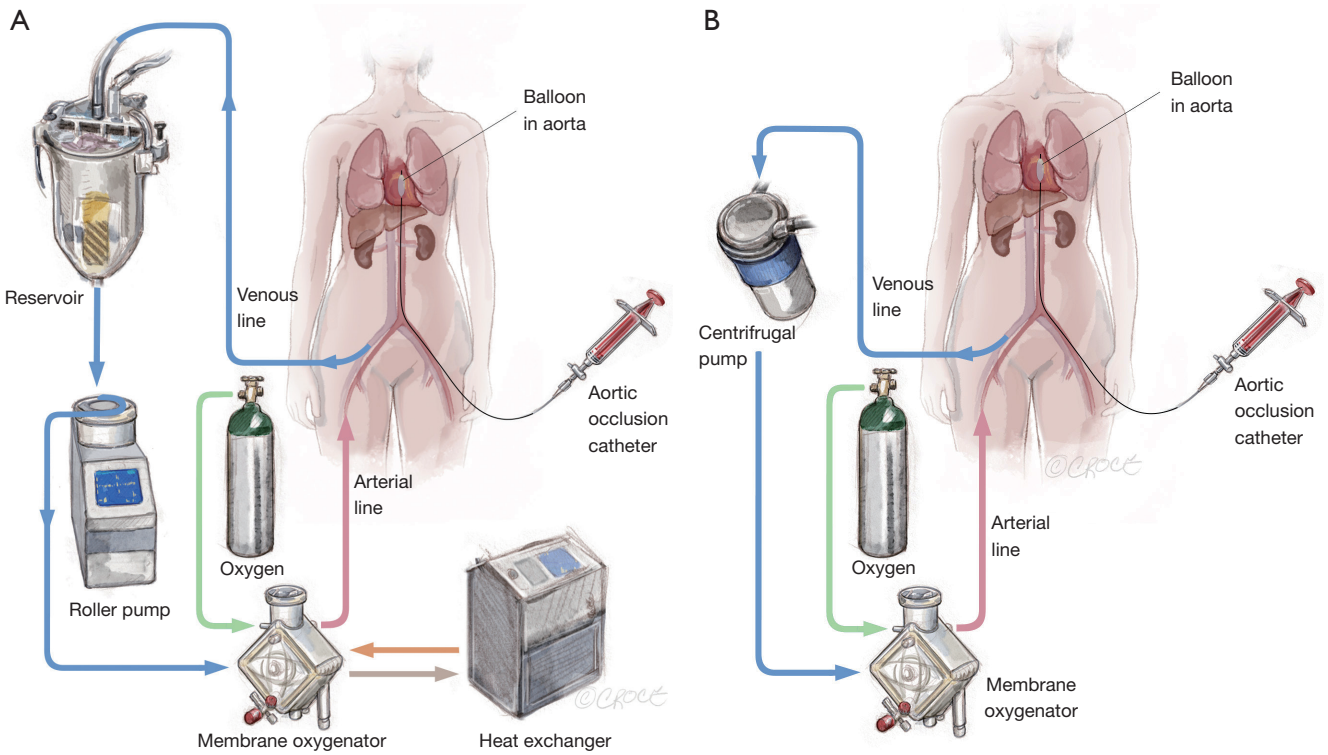

Figure 4 Arrangements for abdominal normothermic regional perfusion in donation after circulatory determination of death. (A) Open circuit; (B) closed circuit.

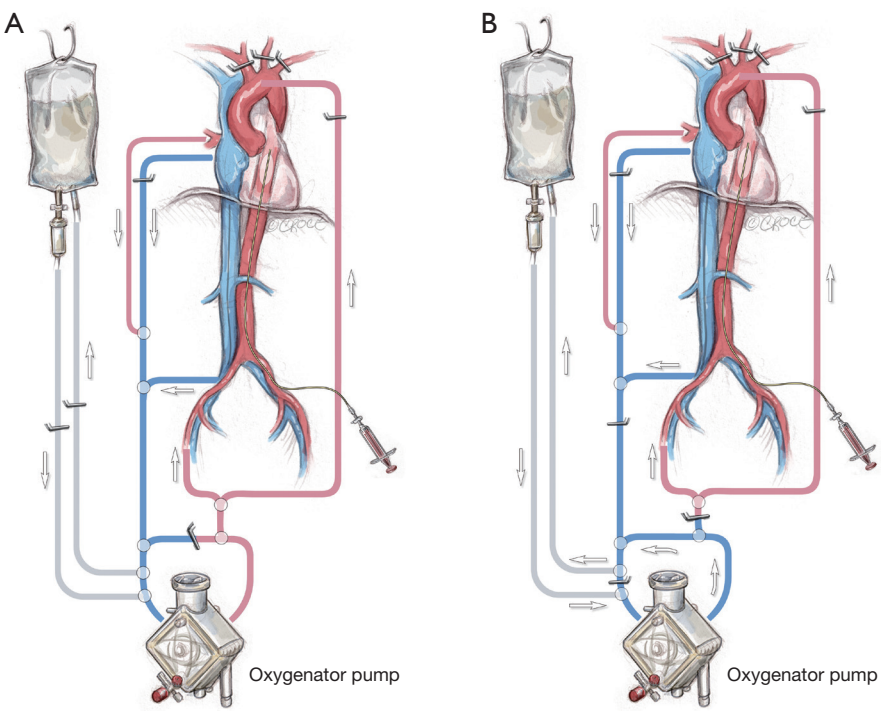

Figure 5 *In-situ* thoracoabdominal normothermic regional perfusion cardiac allograft preservation setting. (A) Circuit working; (B) circuit recirculation.

heart during transport. *Ex-situ* perfusion provides aortic inflow for coronary perfusion against a closed aortic valve, fully unloading the left heart. A left ventricular vent is inserted through the open left atrium and mitral valve to prevent perfusate accumulation and avoid distension or air embolism. If necessary, defibrillation can be performed, and epicardial pacing leads are used to manage the heart rate. Coronary blood flow, returning to the right atrium via the coronary sinus, is directed into the right ventricle and expelled into the pulmonary artery and cannula. Once stabilized on the *ex-situ* device, aortic pressures and flows are adjusted through modifications to pump flow and infusions of epinephrine or adenosine, maintaining the target parameters set by the manufacturer throughout the perfusion.

During the perfusion process, the viability and suitability of the allograft are evaluated based on various factors, including the FWIT, hemodynamic stability during *ex-situ* perfusion, and arterial and venous lactate levels and trends. While there is limited clinical data on the maximum acceptable FWIT, a FWIT of up to 30 minutes is generally considered acceptable and associated with outcomes comparable to those of DBD (2). Initial lactate levels in cDCD donors are typically higher than in DBD donors, but there is no universally applied lactate threshold. Most centers prefer to monitor overall lactate trends rather than relying on a fixed cutoff value.

The normothermic machine perfusion (NMP) platform also enables further evaluation of the allograft using techniques such as *ex-situ* angiography, if needed, and provides a perfusion time for organ transport and preservation >250 minutes as reported by the American Association for Thoracic Surgery 2023 Expert Consensus Document (2).

Once the heart is deemed suitable for transplantation, the recipient procedure can commence. Cooling of the heart during *ex-situ* perfusion is initiated using an external water heater cooler, bringing the donor heart to 18 ℃ before administering the cardioplegic preservation flush. The heart is then decannulated, removed from the device, and implanted into the recipient as usual.

NRP

Traditionally, the recovery of abdominal organs from donors after cDCD involved swift removal followed by standard cold storage. This approach included a phase of warm ischemia while confirming donor death post-withdrawal of life support, succeeded by additional ischemia during cold storage. This method has been associated with less favorable outcomes for liver and kidney transplants. The development of cDCD heart donation has introduced two primary strategies: *in-situ* (within the donor) and *ex-situ* (outside the donor) reperfusion techniques (*Figure 1*). *In-situ* reperfusion uses extracorporeal circulation to restore blood flow to the chest and abdominal organs, thus decreasing their ischemic period, while the cerebral circulation is excluded by occluding the aortic arch vessels. This method, referred to as taNRP (*Figures 4,5*), has demonstrated promising early results for heart, liver, and kidney transplants (2). However, additional extensive research is needed to evaluate if it provides a significant advantage over direct organ recovery.

In planned NRP procedures, donors are frequently positioned at the recipient hospitals, or a mobile team is dispatched to the donor location. Early experiences from institutions such as New York University and Papworth (2,6) underscore the benefits of having the donor and recipient in close proximity to reduce transport delays. However, in countries like the United States (US), Spain, and Belgium (2,6-12), it is more common to send a recovery team for distant taNRP procurements, with the retrieved heart being transported either via normothermic *ex-situ* perfusion or conventional cold storage.

During NRP, various medications may be employed to mitigate oxidative stress and warm ischemia. Although preclinical studies have explored several potential agents, current clinical practice includes steroids, N-acetylcysteine, erythropoietin, and mannitol (2-5). While data on the effectiveness of these agents is limited, no adverse effects on the recovered organs have been reported (2-12).

Typically, rapid cannulation follows the declaration of death and the administration of heparin prior to withdrawal. The most common technique involves sternotomy and central cannulation. For example, the methods used by Vanderbilt University and Papworth (6,7) involve initial cannulation of the right atrium and/or femoral vein to facilitate venous drainage and organ decompression, followed by arterial cannulation, which may occur in the chest, abdomen, or iliac/femoral arteries. An extracorporeal circuit may be used, with or without a venous reservoir. Although a full cardiopulmonary bypass (CPB) circuit offers considerable benefits, it is complex and may be supplemented with a cardiotomy and vacuum. A simpler extracorporeal life support (ECLS) circuit is more adaptable and portable for the recovery team. Details on circuit design are available from Vanderbilt and Papworth teams (2,6,7)

(*Figures 4*,*5*). Cerebral circulation is interrupted before initiating ECLS, typically by clamping the aortic arch vessels or, for abdominal organ NRP, by applying a direct cross-clamp or an endo-clamp via the femoral arteries to the descending thoracic aorta. Some groups also vent the distal arch vessels to eliminate collateral circulation. Sternotomy, cerebral exclusion, and cannulation are usually completed within 3 to 10 minutes. Thoracoabdominal perfusion begins with flow rates of approximately 2.5 to 3.0 liters per minute and pressures of 60 to 70 mmHg. Pressure can be adjusted pharmacologically or by clamping the common iliac arteries. Consideration should also be given to left ventricular venting to prevent distension and injury, which can be achieved with a left ventricular vent inserted via the right superior pulmonary vein or pulmonary artery vent.

A 20-minute period of taNRP helps restore energy stores in the ischemic heart (2-5). During this time, the heart is gradually weaned from the mechanical circuit, transitioning the cDCD donor into a more conventional heart-beating donor. An issue may arise if the donor's lungs are severely compromised, leading to hypoxia. Cardiac evaluations can be carried out using transesophageal echocardiography and a pulmonary artery catheter, which is inserted percutaneously into the right jugular vein or directly into the exposed innominate vein. These evaluations occur after the FWIT of cDCD organ donation. Coronary artery angiography and computed tomography scans have also been utilized during NRP (2). Biomarkers like perfusate lactate profiles are usually monitored while on NRP (2).

Collaborative efforts in graft procurement

The length of FWIT critically influences the post-transplant performance of both heart and liver grafts (2-5). Many factors impacting FWIT occur before the official death declaration and cannot be altered; therefore, it is imperative to enhance coordination among procurement teams to minimize the interval between incision and organ perfusion. Each additional minute of delay in starting perfusion can increase the risk of liver ischemic cholangiopathy by 16% (2-5).

Effective coordination between the abdominal and thoracic teams is essential before departing for the procurement site (2,14). Agreement on the timing and order of blood collection and abdominal flushing is crucial to avoid miscommunication and prevent organ loss. The abdominal team must determine whether to utilize taNRP or to postpone liver preservation until after the donor blood required for *ex-situ* heart perfusion has been collected. If the latter option is chosen, ensuring the donor's hematocrit is within the appropriate range (17–20%) for the *ex-situ* perfusate may necessitate pre-arrival transfusion. Organ procurement organizations should anticipate the need for additional equipment and personnel, including experienced staff, to minimize delays in organ reperfusion.

Upon arrival at the donor hospital, a final coordination meeting among all teams is essential before the withdrawal of life support. The specific procedures for cannulation, drainage, and perfusion depend on the chosen procurement technique. For NRP, the thoracic team is primarily responsible for initiating cardiopulmonary bypass and providing reperfusion to all organs. In contrast, with DPP, the thoracic and abdominal teams operate independently, managing their respective organs. Special attention is required for the reanimation and preservation of the heart using *ex-situ* perfusion methods.

In *ex-situ* heart perfusion, 1.5 liters of donor blood, free of preservation solutions, are needed for the organ care system (OCS) (13). The donor is positioned in the Trendelenburg position, and the heart team begins by accessing and cannulating the right atrium. Suction may be employed to expedite blood collection, which usually takes around one minute. While this is happening, the liver team can prepare for cannulation but should withhold the perfusate administration until the heart team has completed its procedures. Efficient teamwork is likely to shorten the FWIT and improve the quality of the transplanted organs, leading to more favorable outcomes (2,14).

Comments

Heart transplants using hearts from adult cDCD donors commenced in July 2014. Since then, approximately 450 such transplants have been carried out across Australia, Europe, and the US (2-14). The longest-surviving recipient has now surpassed seven years post-transplant (2,14). The selection of retrieval methods has largely been determined by state or institutional guidelines concerning permissible postmortem procedures. A significant majority of cDCD heart recoveries (over 80%) have employed DPP followed by NMP using the OCS (13). Another established method involves the taNRP, which is then followed by either NMP or static cold storage (*Figures 6*,7).

As experience with cDCD heart transplants grows, it is anticipated that this practice could potentially boost global heart transplant activity by up to 30% (2,14). Although

Figure 6 Temperature controlled cardiac allograft cold storage device.

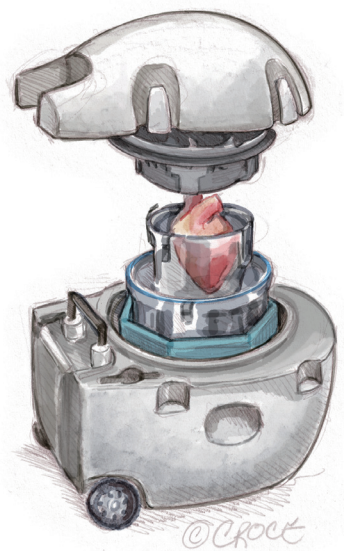

Figure 7 Temperature controlled cardiac allograft arrangement for cold storage.

the outcomes thus far are encouraging, the long-term results for recipients of cDCD heart transplants, especially in comparison to those receiving hearts from brain-dead donors (DBD), particularly concerning cardiac allograft vasculopathy and late graft failure, remain to be fully understood.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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