Donation after circulatory death: the current state and technical approaches to organ procurement

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Purpose of review
In this review, we discuss the current state of donation after circulatory death (DCD). We define the DCD donor and describe the current protocols in management of the DCD patient. We then discuss current techniques in organ procurement of the lung and abdominal organs.

Recent findings
Although donation after brain death is preferable to DCD, recent data have demonstrated acceptable early outcomes in both thoracic and abdominal organ transplant. In spite of advancements in surgical techniques and organ preservation, much has yet to be learned to minimize warm ischemia time and reperfusion injury in the DCD population.

Summary
In light of the continually growing disparity between organ supply and demand, DCD has regained traction as a means to increase the donor pool.

Keywords
donation after circulatory death, kidney transplantation, liver transplantation, lung transplantation

INTRODUCTION

Prior to the adoption of the brain death criteria in 1968, most organ donations were from nonheart beating donors or donations after cardiac/circulatory death. Donation after brain death (DBD) became the standard as a result of better outcomes associated with the continued organ perfusion until procurement, when individual organs are reperfused and cooled. At present, most organ donations are of DBD donors or live donors. Yet, there remains an increasing demand for organs with a continually limited supply and a high number of deaths while on the waiting list (Fig. 1). According to the 2012 annual report of the US Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients, the mortality rates per 100 wait-list years for 2010–2012 is 15.4 for lung, 12.4 for heart, and 5.8 for liver [1–3]. Moreover, the problem of organ availability is compounded by the reality that not all procured organs are suitable for transplantation. According to the same US Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients annual report, of 8144 deceased donors, only 29.7% of hearts, 20.1% of lungs, 73% of livers, 75.1% of kidneys, 12.8% of pancreases, and 1.3% of intestines were transplanted [4]. These data highlight the continued need for organ donation and further advancements in techniques for organ recovery. As such, aggressive means to increase the donor pool are being employed and include utilization of live donors, expanded-criteria donors, and donation after circulatory death (DCD) donors, which now includes donation after assisted suicide/euthanasia in certain countries [5]. Additionally ex-vivo organ perfusion techniques are being developed to recover otherwise unsuitable organs for transplantation.

In the early 1990s, interest in DCD donors reemerged as a viable alternative to further circumvent the shortage of abdominal and thoracic organs [6]. Indeed, DCD has been attributed to a more than 20% increase in the deceased donor pool in some centers and has demonstrated comparable early transplant outcomes to those from DBD donors, particularly with kidney, liver, pancreas, and lung transplantation [7–11]. Heart transplantation from

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KEY POINTS

- Death after circulatory arrest has regained worldwide traction as a means to increase the donor pool of thoracic and abdominal organs.
- Early recognition of the potential DCD donor and coordination, communication, and planning are critical to ensure appropriate handling of the donor and optimal organ procurement and preservation.
- The 'hands-off' period of true warm ischemia is a limiting factor of DCD, as it affects outcomes, and remains a matter of debate.

DCD patients has been limited by the susceptibility of the heart to warm ischemic injury innate to the procurement protocols of the DCD population, particularly the 'hands-off' period [12]. Indeed, many factors must be considered in order to optimize graft function post-transplant. Such considerations include circumstances of circulatory arrest, donor hemodynamic state during withdrawal of care until declaration of death, and duration of warm and cold ischemic times.

In this review, we define the DCD donor and discuss current protocols in management of the DCD patient. We then discuss current techniques in organ procurement of the lung and abdominal organs.

DONATION AFTER CIRCULATORY DEATH DONOR

DCD is defined as that of patients who have suffered a catastrophic neurological injury, but do not meet criteria for brain death; or whose circumstances of death preclude formal declaration of brain death [13,14]. Once a patient is deemed a DCD donor, death must be established by the absence of circulation using cardiopulmonary criterion, and both cessation of function and irreversibility must be determined [14–16]. Death must precede organ recovery. Candidacy for DCD donation is based on clinical judgment and guided by evidenced-based algorithms that predict the likelihood of circulatory death within 2 h of withdrawal of life support. The University of Wisconsin and the United Network for Organ Sharing criteria are often referenced and provide a guide for potential candidacy of DCD donation [17,18].

Early recognition of the potential DCD donor and appropriate coordination, communication, and planning are critical to ensure appropriate handling of the donor and optimal organ procurement and preservation. This includes communication between the donor's intensive care team, the donor's next of kin, the organ procurement organization (OPO), anesthesia team, and the surgical members of organ recovery. All legal and ethical issues must be addressed and consents obtained; formal plans for donor management ahead of and during organ recovery must be agreed upon; the logistics and conduct of organ recovery in the operating room must be understood by all involved to ensure rapid procurement and organ reperfusion and preservation.

In 1995, the Maastricht classification system was established, which categorized DCD donors based on the circumstance of circulatory arrest: uncontrolled (categories I and II) and controlled

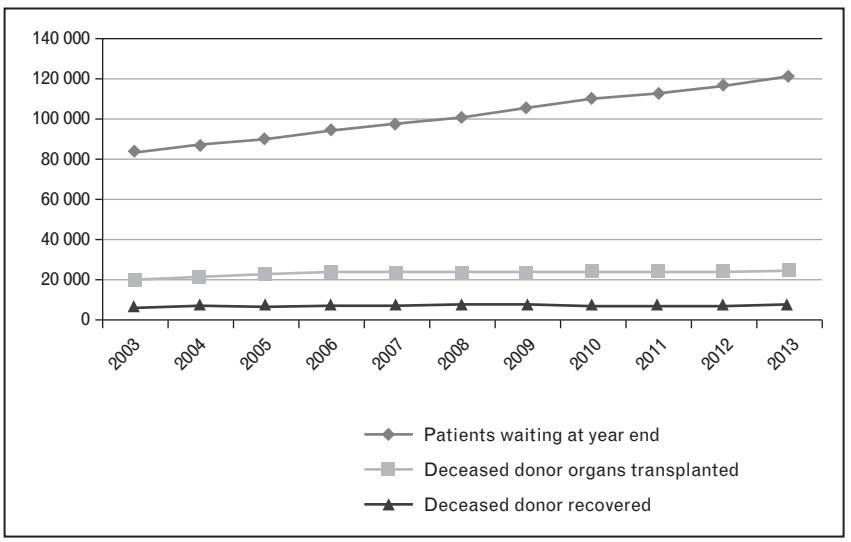

FIGURE 1. Data demonstrate continued growth of patients on waiting lists, whereas the numbers of recovered organs and transplant remain stagnant. Based on Organ Procurement and Transplantation Network data as of 15 December 2014. OPTN, Organ Procurement and Transplantation Network.

(categories III and IV) [19]. These criteria aim to provide insight into end-organ insult as a result of circulatory arrest and prolonged warm ischemia time and provide guidance of the optimal DCD donor. Currently, the majority of DCD donors in the USA, UK, Belgium, and The Netherlands are primarily category III, whereas category II DCD donors predominate in France and Spain [20,21]. The Maastricht classification system has been modified since its inception; most recently, it has been subcategorized into specific clinical scenarios of circulatory arrest and modified to reflect the acceptance of donation after euthanasia in several European countries (controlled, category V) (Table 1) [22–24]. Although only three European countries – Belgium, Luxemburg, and The Netherlands – currently accept donation after euthanasia, the practice has been recognized by Eurotransplant, an organization responsible for coordinating organ transplantation among several major European nations. In the initial Belgian experience with donation after euthanasia, four of the 17 DCD donors for lung transplant were euthanized; actuarial 1- and 3-year survival was 75% with reported excellent graft function [25]. In spite of such outcomes, donation after euthanasia remains a matter of great ethical and legal debate, and is beyond the scope of this review. Indeed, these legal and ethical caveats must be overcome in order for this class of DCD donors to demonstrate a significant impact on the donor pool.

PROCUREMENT PROTOCOL AND SURGICAL APPROACH

Several methods exist for rapid procurement; here we focus on lung and abdominal organ procurement using that of the University of Wisconsin method, as previously described in the literature [13,17].

Early recognition and proper management of the potential DCD donors are the first critical steps in optimal organ preservation. Discussion with the family regarding organ donation is made once the decision is made to withdraw care, and is performed by the patient's primary intensive care team. Once a DCD donor has been established, the OPO is contacted and detailed consents are obtained. Transplant recipient teams are then contacted. Once all legal and ethical issues have been addressed, the urgent time constraints of DCD procurement mandate appropriate assessment and management of the donor, definitive establishment and declaration of death, and appropriate steps are taken to minimize warm ischemia time ahead of and during procurement.

Once care is withdrawn, expiration must occur within 2 h or this would preclude the patient from being a donor. There is variability in this preclusion time as certain programs advocate a time of 60 min and others 90 min; this is dependent on the OPO protocol, the hemodynamic status of the donor, and whether the donor is a potential liver donor [11,13,26]. Withdrawal of care is often performed in the operating room or in the intensive care unit in

Table 1. Modified Maastricht classification reflecting assisted suicide

Modified Maastricht classification for donors after circulatory death	
Uncontrolled DCD	
I. Dead in the out-of-hospital setting	1A. Cardiocirculatory death outside the hospital with no witness. Totally uncontrolled
	1B. Cardiocirculatory death outside the hospital with witnesses and rapid resuscitation attempt. Uncontrolled
II. Unsuccessful resuscitation	2A. Unexpected cardiocirculatory death in the ICU. Uncontrolled
	2B. Unexpected cardiocirculatory death in the hospital (emergency room or ward), with witnesses and rapid resuscitation attempt. Uncontrolled
III. Awaiting cardiac arrest	3A. Expected cardiocirculatory death in the ICU. Controlled
	3B. Expected cardiocirculatory death in the operating room (withdrawal phase >30 min). Controlled
	3C. Expected cardiocirculatory death in the operating room (withdrawal phase <30 min). (Highly) controlled
Controlled DCD	
IV. Cardiac arrest while brain dead	4A. Unexpected cardiocirculatory arrest in a brain-dead donor (in the ICU). Uncontrolled
	4B. Expected cardiocirculatory arrest in a brain-dead donor (in the operating room or ICU). (Highly) controlled
V. Euthanasia	5A. Medically assisted cardiocirculatory death in the ICU or ward. Controlled
	5B. Medically assisted cardiocirculatory death in the operating room. Highly controlled

DCD, donation after circulatory death; ICU, intensive care unit. Reproduced with permission from [22].

the presence of family. The former is often preferred as it minimizes warm ischemia time that would otherwise be lost during transportation to the operating room and prepping of the patient for organ recovery. In some institutions, the transport period is incorporated into the mandatory 5-min 'hands-off' period after expiration and before organ recovery [20]. Prior to expiration and depending on local DCD protocol, consent may be obtained for interventions and administration of medications ahead of expiration. This includes administration of pharmacological agents to minimize ischemia/reperfusion injury [27]. To prevent thrombi, 300 U/kg of heparin is given; 10 mg phentolamine or 1 mg prostaglandin may be also be given via central line to reduce vasospasm and facilitate organ flush. There is a theoretical risk that heparin may hasten death, although this has never been shown; phentolamine may cause a transient drop in blood pressure; however, this is not believed to promote progression of circulatory death [13]. Nonetheless, if there is a concern that administration of any pharmacological agent may contribute to or hasten death, it should not be given; for example, a high risk of bleeding or critical hypotension warrants further discretion for the use of heparin and phentolamine, respectively. If consent is obtained, femoral artery and vein cutdown and cannulation may be performed under local anesthesia ahead of withdrawal of care, per local protocol, to allow for rapid organ recovery [14,28]. Chilled preservation solution is kept ready along with tubing primed for rapid infusion upon declaration of death.

Once all premortem interventions are performed and care is ready to be withdrawn, all recovery team members leave the room, and care is withdrawn under the guidance of the local management team with an OPO present. Hemodynamics are recorded on a minute-by-minute basis by the OPO until death is declared. A 5-min 'hands-off' period follows the declaration of death to ensure irreversibility of cardiopulmonary function ahead of commencement of the organ recovery process. The 'hands-off' period defines true warm ischemia time, which is the period between circulatory arrest and cold flush or direct organ perfusion; as such, the duration of the 'hands-off' period is critical and is of debate. A period of functional warm ischemia occurs during the agonal phase of dying, when mean perfusion pressures and arterial saturation progressively drop; systolic arterial pressures less than 50 mmHg and arterial saturation below 70% for greater than 20–30 min subject the end organs to additional insult in addition to the true warm ischemia time (Table 2) [29–31]. True warm ischemia time for the kidney and pancreas is 45–60 min, whereas for the liver, such ischemic time beyond 20–30 min is attributed to increased complications [14,15,29, 30,32–34]. The lungs are deemed less susceptible to ischemic injury as a result of continued cellular metabolism when reinflated; appropriate functional ischemic time for the lung is approximately 60 min, and is measured to the time of reinflation, rather than cold perfusion [12,31,35]. The metabolic demands of the heart make it the most susceptible to ischemic injury and have limited heart transplantation from DCD donors. Current evidence suggests warm ischemic times of up to 20 min, but not more than 30 min, may be feasible for heart transplantation from DCD donors [12,36–39]. According to the recent international guidelines on determination of death, the 'point of no return,' or autoresuscitation, is variable from 2 to 10 min [18]. As such, the exact time for the 'hands-off' period is debatable and varies from 2 min in some centers in the USA and Australia to upward of 20 min in Italy [12,15,40–42]. Both the American Society of Transplant Surgeons and the Society of Critical Care

Table 2. Acceptable functional ischemic times of DCD organs retrieval in the United Kingdom [31]

Organ	Minimum functional warm ischaemia time (min)	Comments
Kidney	120	A further 120 min in selected donors. DCD kidneys have a higher incidence of delayed graft function, but have similar long-term function to DBD grafts
Liver	30	May be limited to 20 min in suboptimal donors. Outcomes from DCD liver transplantation are acceptable, but there is greater postoperative morbidity and a higher incidence of graft failure and biliary complications compared with DBD grafts
Lung	60	Time to reinflation of the lungs rather than cold perfusion. DCD may represent an important source of additional lung grafts, particularly when combined with ex-vivo perfusion techniques
Pancreas	30	

UK functional warm ischaemia criteria for DCD organ retrieval. DBD, donation after brain death; DCD, donation after circulatory death. Reproduced with permission from [31].

Medicine currently recommend at least a 2-min waiting period in order to minimize warm ischemia time, whereas the Institute of Medicine recommends a 5-min period [14]. Once the 'hands-off' period has expired, the primary team declares death. The recovery team then enters the operating room, and if not performed premortem, the femoral artery is cannulated up to the aortoiliac junction and rapid cold preservation solution is circulated.

We now describe surgical techniques for lung and abdominal organ procurement.

For lung procurement, after sternotomy is performed, postmortem heparinization by cardiac massage is performed for risk reduction of microthrombi. The pericardium is then opened and the pulmonary artery is exposed. Ten milligram of phentolamine or 1 mg of prostaglandin is given directly into the pulmonary artery and circulated by direct cardiac massage for 1 min. The pulmonary artery is then cannulated with 6.5 F cannula directed at the pulmonary valve. Four liters of cold pulmoplegia solution with 10 mg/L of phentolamine are administered and vented through an incision in the left atrial appendage. The lungs can be ventilated to allow for even bilateral distribution of flush and pulmoplegia, although this should be done after 15 min of arrest to avoid inadvertent cardiac stimulation [11,43]. The pleurae are then opened and lungs inspected for adequacy of inflation and pulmoplegia flush; cold saline is poured into the chest during flush. The heart and lungs are removed *en bloc* with the lungs moderately inflated prior to stapling the trachea. The heart is removed on the back table. Two to 4 l of pulmoplegia solution with 10 mg/l of phentolamine are flushed retrograde through each of the pulmonary veins, and microthrombi are removed from effluent in the pulmonary artery. The lungs are separated with final inspection of quality of flush, inflation, and weight of each lung prior to final decision to begin recipient operation. Lungs are packed in cold sterile solution and ice in outer pack for transport.

Simultaneously, during median sternotomy, the abdomen is opened from xiphoid to the pubic symphysis. Cold preservation solution being circulated via femoral artery can be vented through an incision in the right atrium or the femoral vein during opening of chest and abdomen. The thoracic aorta is then clamped to ensure adequate flush of the abdominal organs. Two to 2 l of preservation solution are infused and the abdomen is filled with ice.

Once the flush is complete and the effluent is clear, retrieval of the abdominal organs *en bloc* proceeds. The esophagus is divided in the chest using a gastrointestinal anastomosis stapler, and dissection is started at the level of the right atrium and carried down to the aortic bifurcation. The organs then are placed in their anatomical position. The lateral attachments of the left and right colon are taken down. The ureters are identified and divided close to the bladder. The distal aorta and cava are divided just cephalad to the bifurcation. The sigmoid colon is then identified and divided using a gastrointestinal anastomosis stapler. The abdominal viscera is then removed *en bloc* and placed in a large basin with ice. The inferior mesenteric vein or a branch of the superior mesenteric vein is identified and cannulated, and 1 l of preservation solution is flushed through the portal system. The common bile duct is also identified and divided close to the duodenum and flushed with 50 ml of preservation solution. The gall bladder is opened and flushed with cold normal saline. The posterior wall of the aorta is opened longitudinally; the celiac, superior mesenteric artery, and renal artery orifices are identified. The celiac and SMA are flushed with 500 ml of preservation solution. The right and left renal arteries are also flushed with 500 ml of preservation solution. The organs are then stored *en bloc* in preservation solution at 4°C and transported to the transplant center for further back-table dissection.

CONCLUSION

In light of the continued disparity between organ supply and demand, the DCD approach has demonstrated appropriate outcomes and has gained traction in many transplant centers across the world. Strict adherence to local protocols and guidelines is essential for appropriate handling of ethical, legal, and medical issues in order to ensure proper donor management and optimal organ protection and preservation. This entails a multidisciplinary team approach involving the donor family members, the intensive care team, the OPO, the anesthesia team, and organ recovery teams; proper communication cannot be overemphasized.

Although advancements have been made in DCD transplantation, much is yet to be learned to further optimize organ protection by minimizing warm ischemia time and reperfusion injury. In spite of acceptable early outcomes in lung, kidney, liver, and pancreas transplantation, DBD remains the preferred donor option. Heart transplantation using DCD donors remains a challenge, but significant advancements suggest that this may be feasible in the near future [12]. To further optimize organ protection, extracorporeal membrane oxygenation during procurement is being employed by several centers to allow continued organ perfusion and unhurried procurement [44]. Additionally, ex-vivo

organ perfusion techniques are being developed to optimize graft recovery and preservation in lung, liver, kidney, and heart [45–48]. These techniques have demonstrated promising results that will further advance organ protection and recovery, and likely increase the donor pool.

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Conflicts of interest

There are no conflicts of interest.

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