



Review Article

Heart transplantation after the circulatory death; The ethical dilemma

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ABSTRACT

Donors after brain death (DBD) have been the major source of organ donation due to good perfusion of the organs. However, owing to the mismatch in demand and supply of the organ donors and recipients, donors after circulatory death (DCDDs) has increased recently all over the world. Kidneys, liver, and lungs are being used for transplantation from DCDDs. Recently, heart transplantation from DCDDs has been started, which is under the firestorm of scrutiny by the ethicists. The ethical dilemma revolves around the question whether the donors are actually dead when they are declared dead by cardiocirculatory death criteria for organ procurement. The subsequent literature review addresses all the perspectives by differentiating between the donation methods known as DBDs and DCDDs, explaining the implications of the dead-donor rule on the organ donation pool, and categorizing the determinants of death leading to separation of the arguments under the two methods of donations.

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1. Introduction

The key to distinguish between different perspectives is that one needs to understand the number of perspectives and what the reasons of their existence are. The subsequent literature review addresses all those perspectives by differentiating between the donation methods known as donors after brain death (DBD) and donors after circulatory death (DCDD), explaining the implications of the dead-donor rule (DDR) on the organ donation pool, and categorizing the determinants of death leading to separation of the arguments under the two methods of donations. The aforementioned perspectives when studied intricately remain equivocal among bioethicists, transplantation experts, physicians, donors, and the general public.

In the current age of organ infiltration due to infectious diseases, it has become pertinent to widen the organ pool available for transplantation but the means to do that have posed quite a many ethical dilemmas. The deontological argument proposes that the means to an end are supposed to be in line with the morality

associated to them. Laws and norms against homicide forbid killings done for any purpose, including killings done to obtain organs to save the lives of others. These laws and norms apply even if the person is unconscious, extremely debilitated, or very near death.¹ DDR supports what Robertson has stated in his excerpt by stating that organ donors must be dead before organs procurement, and organ procurement itself should not lead to the death of the donor.¹ Whereas, utilitarianism concentrates on the weight of the ends, without caring about the means, thus supporting the DCDD protocols which when practiced for procurement of any organ after cessation of circulation rendered irreversible clearly violates the DDR. However, it is not just a matter of clear cut propositional and oppositional arguments, the entire issue of heart transplantation after the death of the donor is a classical debate of deontology versus utilitarianism.

The sole purpose of using organs from both DBD and DCDD is to transplant them into a deserving patient battling with death from a patient who has just been declared dead. This process is struck with several technicalities, out of which the first one is to determine the criteria of death: whether the donor's cause of death was irreversible or permanent and whether the donor's death was caused due to the cessation of circulation of blood to the organs or by cessation of brain function. Second, the organ procurement method used to prevent warm ischemia time to the heart to maintain

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perfusion. Moreover, keeping the transplantation either in line with the more popular DDR or otherwise, ethically justified.

2. Determinants of death

Before the 20th century, physicians deemed a patient dead once the body started to putrefy, became livid, and/or attained rigor mortis but that was not an era of organ transplantation, thus medical science had not developed as such to give physicians a chance to procure a patient's organs to be utilized later. It was only after the first kidney transplant in 1954, physicians understood the importance of perfusion of the organs even after a person has died. This led to discovery of different criteria to determine death which revolved around the cessation of circulation or the cessation of brain function.

To understand these criteria, one needs to be acquainted with the biophilosophical context of two words, “irreversibility” and “permanence”. The biological definition of death requires irreversibility of the death. According to the Uniform Determination of Death Act, death is defined as (a) irreversible cessation of circulatory and respiratory functions or (b) irreversible cessation of brain death. Irreversibility denotes that if these functions stop, they cannot be restarted, no matter what available technologies are used, whereas permanence refers to the practice that these functions will not recover and they will not restart spontaneously, and no medical efforts would be used to restart them. It can be significantly noticed that, whereas, “irreversibility” of cessation of brain function is the key to deem a patient dead on one side, the “permanent” cessation of circulatory and respiratory flow is enough to determine one's death on the other side.

Determination of death in the modern era was dependent on the interdependent triad of irreversible cessation of respiration, circulation, and brain function, but with the age of discovery moving forward, medical intervention, such as cardiopulmonary resuscitation or extracorporeal membrane oxygenation (ECMO), mechanically re-establishes respiration and circulation even when the brain has been considered irreversibly damaged by an electroencephalograph or other brain functioning tests. Cessation of circulation and respiration, therefore, serves as a valid surrogate indicator for cessation of all clinical brain functions in the absence of therapeutic interventions that re-establish circulation and oxygenation.²

The ethical dilemma arises when the physicians have to call time of death, because after the call has been made, no intervention can take place to revert the condition of the patient. Some hearts can autoresuscitate even after stopping; therefore, the absolute issue is to decide on a time period (standoff period) after which the physician can call it, and the transplant team can procure the organs. Although De Vita et al³ showed in their study that autoresuscitation is not possible after 65 s of absent heartbeat (asystole), it varies between 2 and 5 min as was suggested by the Ethics Committee of the American College of Critical Care Medicine and Society of Critical Care Medicine in 2001, because their study contained a smaller confidence interval because of a sample size of less than 200 patients.² However, ethical review boards of different hospitals have formulated their own criteria to determine the standoff period. Another question that troubles the ethicists when it comes to determination of death is to conform to the DDR. That can only happen when health professionals practicing DCDD abandon irreversibility for permanent cessation of circulatory flow because in waiting for irreversible cessation, the organs might lose perfusion, and the use of medical intervention may revive some or the other organ of the patient making it difficult to determine death. Understanding the distinction between the permanent and irreversible cessation of functions helps resolve important

conceptual and practical problems in death determination that have been introduced by DCDD.

3. DBD vs DCDD

DBD have been the major source of organ donation due to better perfusion of the organs until their retrieval for transplantation. However, owing to the mismatch in demand and supply of the organ donors and recipients, organ DCDD has increased recently all over the world. DCDD donors constitute varying proportions of the deceased donor pool in different countries with regard to their medical practices, social attitudes, and legal parameters. In the Netherlands, Australia, and the United Kingdom, DCDD accounts for a large proportion of donation protocols, up to one-third in the latter two; whereas in other countries such as Germany and Portugal, the rates of DCDD are low.⁴ In Spain, DCDD is less than 10% and only limited to uncontrolled DCDD.⁵ In the USA, most states have adopted the Uniform Determination of Death Act (UDDA) or a very close variant. The UDDA explicitly appeals to irreversibility, not permanence, regarding individuals with cessation of circulatory and respiratory functions as dead.⁶ Kidneys, liver, and lungs were being used for transplantation from DCDDs. Hearts, however, being the most susceptible to ischemic injury were the organs which were not considered viable for transplantation as it is the arrest of the heart which contributes to the cessation of circulation. DCDD donors can be differentiated by the Belgian modified Maastricht Classification into controlled and uncontrolled. According to this classification, uncontrolled patients include those who were dead before arrival at the hospital; hence, no resuscitation was attempted (category I) and those in whom resuscitation was attempted but was unsuccessful (category II). Controlled patients include those in whom circulatory death is imminent following withdrawal of cardiopulmonary assistance (category III), those who undergo cardiac arrest after the determination of brain death (category IV), and those who grant access to medically assisted death via euthanasia (category V).⁷ Nonetheless, since the 1970s, many corrections have been made, and heart transplantations from DCDDs are giving competitive results with respect to transplantations from DBDs, although under the firestorm of scrutiny by the ethicists.⁸ The conundrum of morality revolves around the question if the donors are actually dead when they are declared dead by cardiocirculatory death criteria for organ procurement. To minimize warm ischemic injury to the heart, heart DCDD protocols have been devised, which are not entirely uniform throughout various centers. They include (a) minimizing the standoff period, which is defined as the time between circulatory arrest and death declaration, (b) *ex vivo* perfusion, (c) cold fluid infusion, and (d) the use of organ preservation techniques including ECMO.

As opposed to the DBD hearts, DCDD hearts have already sustained enough ischemic damage and would be unable to withstand additional damage during the cold storage. Therefore, a specific approach needs to be employed for DCDD heart transplantation focusing on organ resuscitation reducing the effects of warm ischemia and preventing additional ischemia and organ reconditioning. To achieve this, two methods of DCDD heart resuscitation have been used, the direct procurement and perfusion (DPP) method and the normothermic regional perfusion (NRP) approach. DPP involves the use of cardioplegics to reduce the detrimental effects of ischemic injury. The application of hypothermic cardioplegics has been a standard in the procurement of hearts from DBD donors; however, owing to the already existent ischemic injury, the delivery of warm cardioplegics has been employed to improve recovery and optimize resuscitation in DCDD hearts.^{9,10} The NRP protocol includes reperfusion of donor blood following initiation of venoarterial ECMO and has been shown to improve

cardiac resuscitation because of the existing buffers and energy stores in the donor blood that aid recovery.¹¹ The NRP approach also allows assessment of direct myocardial function and suitability by measuring cardiac output via a pulmonary catheter and a transesophageal echocardiography evaluation.

The organ care system (OCS) preserves the donor heart in a perfused warm oxygenated condition during transfer from the donor to the recipient. The TransMedics organ care system is the only clinically available device; it allows for an extended out of body time of at least 8 h reducing the deleterious effects of cold ischemic storage and allowing increased distances for organ procurement. The Randomized Study of Organ Care System Cardiac for Preservation of Donated Hearts for Eventual Transplantation (PROCEED II) trial assessed the use of cold storage against continuous perfusion for transportation of DBD organs.¹² Although the mean total preservation time for OCS was longer than cold storage, the outcomes for both groups of patients were the same which proved the efficiency of OCS for long-term preservation. The function of marginal organs has been enhanced by the use of OCS, extending the donor pool by allowing previously unsuitable organs to be used for transplantation and also reducing chances of a failure. The Harefield group used the OCS to use organs previously deemed unfit as well as selecting high-risk recipients and reported a markedly improved short-term outcome and transplant activity particularly in patients with Left Ventricular Assist Device (LVAD) implants and previous sternotomies.¹³

The ethical dilemma arises when healthcare professionals have to choose to practice one of the two organ transplantation protocols, out of DBD and DCDD, depending on the state laws, hospital laws, patient consent, and physician bias. In the end, both methods have their ethical pros and cons; thus, Table 1^{14,15} explains the arguments in proposition and opposition of “ethical dilemmas of heart transplantation after circulatory death,” which will be supported by quoting the studies performed by researchers to prove their sides of the perspective sequentially.

4. Different perspectives of ethicists

For the researchers intricately seeking prominent results, based on the arguments mentioned in Table 1,^{14,15} there are a few approaches: (a) accept DDR fully and follow pursuit of DBD, (b) abandon DDR and follow absolute DCDD protocols, and (c) seek a middle ground between DDR and DCDD without contradicting

either. Examples of studies following one of the three options are mentioned in the following paragraph.

Dalle Ave et al have promoted the very controversial DCDD and tried to find a middle ground between DDR and DCDD. After studying four DCDD protocols at centers in Cape Town,¹⁶ Denver,¹⁷ Cambridge,¹⁸ and Sydney,¹⁹ they proved how protocols at Sydney were in line with the DDR; they suggested that heart DCDD protocols do not violate the DDR only if the criterion of death is based upon permanence rather than irreversibility.²⁰ Irreversibility denotes that the function cannot be reversed; however, ECMO can restore circulation long after the circulatory arrest. In addition, it is uncertain that how long we should wait to confirm that the brain's function has been irreversibly lost. Moreover, they suggested using longer stand-off period (minimum of 5 min) to ensure that the possibility of autoresuscitation has elapsed and all brain functions have been lost. Also, the use of any method that can restart the brain circulation should be forbidden. Thus, ECMO can be used only, if the brain circulation has been excluded by either positioning a cross-clamp on the aortic arch²¹ as done in the Cambridge study¹⁸ or by using an inflated thoracic aortic balloon.²² Dalle Ave et al analyzed six criteria of death to study DCDD protocol and how many out of them are in line with DDR. This is summarized in Table 2.

On the other hand, Nair-Collins et al suggested the complete abandonment of DDR instead of muddling through and devising a new criterion of death based on permanence.²³ In a survey, which clearly mentioned that removal of one's organs would be the direct cause of their death, 70% of the US adults confirmed to donate their organs if their brain was damaged.²³ Hence, after the valid informed consent, the donors should be able to donate vital organs under general anesthesia. This would ensure respecting the patient wishes as well as help in expanding the donor pool. Similarly, Truog emphasized on two points, keeping the patient away from suffering and respecting their choice of organ donation.²⁴ He suggested that the patients with extensive brain injuries and/or those who have chosen to withdraw life support should be allowed to donate the organs under anesthesia. Hence, we should forgo DDR which is built upon the illusion of bright line between dying process and organ procurement.

In retrospect, Mandell et al²⁵ have stressed upon the importance of DDR and argued that it is prudent to live in a world, where the public is skeptical and trust that the surgeon will not harvest their organs until they are fully dead, a constant fear studied in focus

Table 1
Debate over ethical dilemmas: pros and cons of DCDD protocols.

Proposition arguments of DCDD protocols	Opposition toward DCDD protocols
Better perfusion of the heart and other organs because of shorter stand-off period.	In the event of uncontrolled unsuccessful resuscitation, cannulation and perfusion has to be started before next of kin arrives and even though the donor's consent was involved, a physician's duty is first to prioritize the living. No absolute determination of irreversible death; thus, value of life decreases according to cultural ethicists.
Informed consent of the patient and the right to donate under general anesthesia.	Physician bias has been noted against stigmatized donor groups such as handicapped patients when it came to treating them. ⁵
Increases the organ transplantation pool by recovering a larger number of organs due to better perfusion.	Public skepticism and fear fed leading to mistrust over surgeons and transplantation enterprises.
The quality of the harvested organ is better because of shortened warm ischemia time.	DBD is totally compatible with the DDR.
If permanent cessation of circulation or brain function is taken into account, complies with the DDR ensuring faith within the ethicists.	Physicians may inappropriately withhold sufficient sedative or analgesic medication to prevent pain maybe to increase organ viability.
Prevents patients to feel pain or suffering which is normative in the process of CPR and ventilation proposed by DBD protocols to revive circulation and respiration because irreversible cessation of brain function has not been attained.	Compromised end-of-life (EOL) care so to speed up the process of dying for the donor to harvest their organs. ⁶
Transplantation frequencies increase in countries such as Japan which do not recognize brain dead donors as a donor can donate upon circulatory cessation.	In DBD, organ recovery is slower in 3–4 h, but in situ.
In DCDD, organ recovery is en bloc but in a rapid 1–2 h.	

CPR, cardiopulmonary resuscitation; DBD, donors after brain death; DCDD, donors after circulatory death; DDR, dead-donor rule.

Table 2
Criteria for the determination of death and their justification with respect to the DDR.

Criteria for death in DCDD protocols	Justification with respect to the DDR
Irreversible cessation of all bodily cells function or organs	Death is declared 2–10 min after cessation of cardiopulmonary circulation in practice and some body cells have not lost function in that time; therefore, this criterion violates DDR.
Irreversible cessation of heart function	Irreversible damage to heart function causes circulation to stop, and as no medical intervention is used, the heart cannot be transplanted.
Irreversible cessation of brain function	The use of brain death tests can prove loss of brain function but cannot prove its irreversibility. This is incompatible with the DDR.
Permanent cessation of brain function	It will ensure no medical intervention is used, and thus, after a standoff period is monitored to allow a possibility of autoresuscitation and awareness has passed, the organ is procured. This is compatible with the DDR.
Irreversible cessation of circulation	This violates the DDR as the function of the heart can be recovered by CPR and circulation can be restored by ECMO.
Permanent cessation of circulation	It will ensure no medical intervention is used and thus, after a standoff period is monitored to allow a possibility of autoresuscitation, the organ is procured. This does not violate the DDR.

CPR, cardiopulmonary resuscitation; DCDD, organ donation after circulatory death; DDR, dead-donor rule; ECMO, extracorporeal membrane oxygenation.

group analyses. They have rendered the suggestions of Truog baseless and tried to instil trust in the transplantation enterprises. Even Bernat et al in 2008 have emphasized the need for ethical implications in the controversial field of transplantation and how the maintenance of DDR as an anchor should be analogous to morals like the physician to declare death cannot be part of the transplantation team.²⁶

In the midst of numerous arguments over DBD versus DCDD and their compliance with DDR, we feel that the recently published article by Dalle Ave et al seems to start solving the problem. They proposed a new term, “donation after brain circulation determination of death”, which can be defined as permanent cessation of brain functions, determined by the permanent cessation of brain circulation in cases of circulatory arrest or irreversible cessation of brain circulation due to brain injury raising intracranial pressure.²⁷ The patients can provide informed consent to donate their organs on the basis of understanding this criterion of death.

5. Conclusion

The debate remains unresolved. The leaders of critical care, neurology, transplantation communities, and all other stakeholders should come together and try to make a consensus which establishes acceptable boundaries and maintain the public confidence in the integrity of the transplantation practices, keeping in mind their philosophical, cultural, and religious beliefs.

Conflicts of interest

All authors have none to declare.

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