

A Single-center Experience of Kidney Transplantation from Donation after Circulatory Death: Challenges and Scope in India

Abstract

Donation after circulatory death (DCD) has never been attempted in India because of legal constraints and lack of guidelines for the withdrawal of life support in end-of-life situations. The present report describes the initial experience of transplantation of organs from DCD donors in a tertiary care center in India. Between 2011 and 2015, five donors had kidneys retrieved after cardiac arrest. These patients were declared dead after waiting for 5 min with no electrocardiographic signal on monitor following cardiopulmonary resuscitation (CPR), which was restarted in three patients till organ retrieval. All donors received heparin and underwent rapid cannulation of aorta, infusion of preservative cold solution, and immediate surface cooling of organs during retrieval surgery. 9/10 kidneys were utilized. Mean donor age was 29.6 ± 16.3 years, M:F 4:1 and mean age of recipients was 38.7 ± 10.8 years, M:F 7:2. Seven patients required dialysis in postoperative period. Mean postoperative day 0 urine output was 1.9 ± 2.6 L. Baseline creatinine achieved was 1.38 ± 0.35 mg/dl after a mean duration of 26.12 ± 15.4 days. Kidneys from donors where CPR was continued after the declaration of death ($n = 3$) had better recovery of renal function (time to reach baseline creatinine 21.2 ± 7.2 vs. 34.3 ± 23.7 days, baseline creatinine 1.36 ± 0.25 vs. 1.52 ± 0.45 mg%). In donors without CPR, one kidney never functioned and others had patchy cortical necrosis on protocol biopsy, which was not seen in the kidneys from donors with CPR. Kidneys from DCD donors can serve as a useful adjunct in deceased donor program. Continuing CPR after the declaration of death seems to help in improving outcomes.

Keywords: Deceased donor transplant, donation after circulatory death, kidney transplantation, India

Introduction

Donation after circulatory death (DCD) has become a well-accepted source of organs across the world. As the waiting list of patients needing organ replacement continues to grow and organ donations from brain dead donors have started to plateau or decline, there has been an increasing interest and utilization of organs from DCD donors.^[1] DCD has been divided into various categories as per modified Maastricht classification [Table 1] based on the circumstances in which donation happens and can be broadly classified into controlled or uncontrolled types.^[2-4] Uncontrolled DCD require immediate identification, consent, and retrieval of organs at a very short notice which raises many legal and ethical concerns. In addition, utilization of these organs requires extremely good infrastructure and a well-coordinated transplantation program. On the other hand, utilization of organs from controlled DCD

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has become a standard practice in developed countries where the donation can happen in a planned manner after elective withdrawal of support in a terminally ill patient. However, DCD has never been attempted so far in a systematic manner in India because of lack of clarity regarding the use of these organs in the Transplantation of Human Organs Act (THOA) 1994 and its subsequent modifications.^[5,6] In addition, there are no guidelines for withdrawal of life support in end-of-life situations, so utilizing organs from category III donors might be legally questionable in India. The present report describes the initial use of DCD organs from Maastricht category IV and V donors in a tertiary care center in India with a well-established organ transplant program and highlights the challenges of performing transplantation from DCD donors.

Materials and Methods

Between January 2011 and November 2015, organs were retrieved from forty-seven

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deceased organ donors at our center. 5/47 (10.6%) of these donors had organs retrieved after circulatory death. 4/5 (80%) were Maastricht category IV donors and one was a category V donor. Three of these patients had a cardiac arrest in Intensive Care Unit (ICU) after the initial examination by the brain death certification committee. One donor who had already been declared brain dead had a cardiac arrest while about to be shifted to operation theater for organ donation. One patient with end stage lung disease had a cardiac arrest in ICU. All patients were consented for organ donation before the cardiac arrest. Only kidneys were retrieved and used for transplantation, and the recipients were already identified and cross matching for transplantation was initiated before the cardiac arrest. The patients were declared dead after waiting for 5 min with no electrocardiographic activity on the monitor after 30 min of unsuccessful cardiopulmonary resuscitation (CPR). After declaration of death, donors received 500 units/kg of heparin intravenously. Chest compressions were restarted in three patients to maintain circulation and ventilation was continued till necessary arrangements could be made for organ retrieval. In the remaining two patients, CPR was discontinued and they were directly shifted to operation theater for removal of kidneys. All donors underwent rapid cannulation of aorta, infusion of cold preservative solution, and immediate surface cooling of organs during retrieval surgery. Prior femoral cannulation was not used in any patient. Warm ischemia time was calculated from the time of cardiac arrest till cannulation and perfusion of aorta. The recipients were explained the risks and underwent standard transplant procedure. All recipients except one were induced with antithymocyte globulin (thymoglobulin, Genzyme®). One patient who had hepatitis C viremia at the time of transplant received basiliximab (Simulect; Novartis®) induction. The immunosuppression in all patients comprised tacrolimus, mycophenolate mofetil/sodium, and steroids.

Results

Ten kidneys were retrieved from 5 DCD donors. The deceased donors demographics and other details are given in Table 2. Three donors had trauma with head injury as the cause of death, one was postoperative case of brain tumor, and one patient had end stage lung disease. One kidney had to be discarded as the recipient refused consent at an advanced stage, but the rest of the nine kidneys were utilized. Table 3 describes the recipient demographics and the postoperative allograft function. Mean age of the recipients was 38.7 ± 10.8 years, and the male:female ratio was 7:2. All patients except two required dialysis support in the immediate postoperative period. The postoperative day 0 output for the nine patients was 1.9 ± 2.6 L (range 25–7500 ml/day). The baseline creatinine achieved was 1.38 ± 0.35 mg/dl after a mean duration of 26.12 ± 15.41 days (range 10–60 days). The kidneys from donors where CPR was not continued after the declaration of death ($n = 2$) fared poorly when compared to those

Table 1: The modified Maastricht classification of donation after circulatory death

Category	Description	Circumstances
Type I	Dead on arrival (irreversible cardiac arrest on the street)	Uncontrolled
Type II	Unsuccessful resuscitation (includes patients brought into the emergency room while being resuscitated by the ambulance crew)	Uncontrolled
Type III	Imminent cardiac arrest in intensive care (ventilator switch-off)	Controlled
Type IV	Cardiac arrest during or after the brain death diagnostic procedure	Controlled
Type V	Unexpected cardiac arrest in intensive care	Uncontrolled

Table 2: Deceased donor donation after circulatory death demographics

Number of donors	5
Cause of death	
Trauma	3
Cerebral tumor	1
End stage lung disease	1
Mean age (in years) (range)	29.6±16.3 (18-51)
Male:female	4:1
Mean creatinine at admission (mg/dl)	1.14±0.15 (0.9-1.3)
Mean urine output before cardiac arrest (ml/h)	67±48.1 (25-150)
Mean warm ischemia time (min)	68±15.16 (56-78)
Mean cold ischemia time (h)	4.62±11.54 (3.5-13.1)

where CPR was continued ($n = 3$). One of these kidneys never functioned and the patient remained on dialysis till she received another kidney from a brain-dead donor. The other recipient of the same donor also had a suboptimal function and achieved a minimum creatinine of 2.0 mg%. Both the kidneys from other donor where CPR was withheld showed evidence of patchy cortical necrosis (upto 25%) on protocol biopsies done at postoperative day 7, but these kidneys eventually regained normal renal function. The mean creatinine in patients who received kidneys from donors where CPR was continued was 1.36 ± 0.25 mg% and for patients whose donors did not receive CPR was 1.52 ± 0.45 mg%. The patients who received kidneys for donors with CPR achieved their baseline creatinine earlier (21.2 ± 7.2 days) when compared to the other group (34.3 ± 23.7 days).

Discussion

At our institute, the first deceased donor organ donation, after THOA 1994, was performed from a brain dead donor in 1996. However, the number of deceased organ donations remained very limited till 2008 when serious efforts were made to strengthen the deceased program by our department. This resulted in increased number of organ

Table 3: Details of recipients and post-operative graft function

S No	Recipient	Age (in years)	Basic kidney disease	Sex	Induction	Day 0 urine output (in ml/24 hours)	Days to reach baseline creatinine	Baseline creatinine (in mg/dl)
1	UD	39	Glomerulonephritis	Female	ATG**	25	Primary nonfunction	
2	AS	22	Obstructive uropathy	Male	ATG	3450	60	2.0
3	VS	41	Glomerulonephritis	Female	ATG	7500	13	1.1
4	UC	49	Diabetes	Male	ATG	450	30	1.45
5	HS*	25	Glomerulonephritis	Male	Basiliximab	25	28	1.0
6	SKS*	54	Diabetes	Male	ATG	1150	21	1.3
7	AS*	31	Chronic interstitial nephritis	Male	ATG	4200	10	1.7
8	SK*	43	Glomerulonephritis	Male	ATG	470	20	1.38
9	KR*	45	Glomerulonephritis	Male	ATG	25	27	1.2

*CPR was continued in the donors, **ATG: Antithymocyte globulin

donations after brain death from 2 per year to nearly 20 per year till 2014 when again there was a sharp decline due to various reasons. During this period, it was thought to utilize the DCD donors to strengthen the organ donation program. DCD donors formed about 10% of all donors over the 3 years period but provided the necessary impetus to our program at a time when the donation rate had hit an all-time low. The early outcome of transplants from these donors was acceptable with 8/9 grafted kidneys (88%) achieving acceptable renal function as has been reported in the literature.^[7,8] However, delayed graft function in the immediate postoperative period was common due to effect of prolonged warm ischemia in the donor. Different strategies have been used to minimize ischemic damage to the organs after cardiac arrest till organ retrieval. In the present experience, CPR was continued in 3/5 patients and continuing CPR after death achieved some organ perfusion till the time patient was shifted to operating room and resulted in better function in these kidneys although numbers were too small to draw any statistical conclusion. Other options for minimizing ischemic insult to organs include the use of double balloon femoral cannulas, which can be inserted at the bedside even before cardiac arrest, and it can be used to perfuse the donor with cold preservative solution once cardiac arrest happens.^[9] These cannulas were not available at our hospital routinely, and these donations were not anticipated. However, it is encouraging to note that even with simple CPR, good outcomes can be expected. CPR is commonly used as a preservation technique in uncontrolled DCD donation till the time femoral cannulation and perfusion can be done. However, continuing CPR manually for 30–60 min is labor intensive and needs 3–4 medical personnel taking turns, while the necessary arrangements for organ retrieval can be made. Use of automatic CPR machines can circumvent this problem with equivalent outcomes.^[10] Other options to preserve organs include the use of extracorporeal membrane oxygenation (ECMO) machine. Subnormothermic perfusion with ECMO circuit has been recently shown to greatly improve the outcomes of DCD organs. In a study by Reznik *et al*, 47.7% (21/44) of kidneys showed immediate

function when perfusion on ECMO circuit was carried out after cardiac arrest and an extended warm ischemia time of 61.4 ± 4.5 min, which is remarkable as these organs would not have been used otherwise. In addition, there was no case of primary nonfunction.^[11] Using ECMO after the declaration of death poses an ethical dilemma as whether to consider the person on ECMO as dead or alive.^[12] Use of ECMO also requires additional cost and infrastructure, which may not be readily available in developing countries. Moreover, there are ethical concerns regarding pre-mortem interventions to improve the organ viability. Ideally, these interventions should never harm the donor and require informed consent.^[11,12] Pre-mortem interventions may include medications, such as anticoagulants, inotropes or vasodilators, and procedures, such as central venous catheter placement. Continuing CPR is the least controversial and invasive among any of the interventions being used for DCD.

In the present study, a 5 min period of no cardiac activity after cessation of CPR was taken to declare death. It is argued that for DCD to take place the cessation of circulatory function must be permanent but may not be irreversible. The cessation is permanent if cardiac activity will not resume on its own through autoresuscitation or as a result of CPR.^[13,14] Irreversibility requires that the function is incapable of being restored within the limits of current technology. However, irreversibility is not necessary for the declaration of death, and there is a consensus among different organizations supporting this argument.^[15] Within this framework, how much time must elapse to preclude autoresuscitation sufficiently is a significant concern. It is recommended waiting at least 2 min but not more than 5 min so that organs do not suffer irreversible damage.^[11,15] Maastricht category IV donor forms only a minority of DCD donors across different series and most of donations usually come from category III donors.^[8,16] There are countries such as Spain and France where category I donors form the majority whereas in countries such as Austria, Belgium, Netherlands, and Italy, category II donors are also considered.^[8,16,17] This difference is due to

different approaches to end-of-life care and to availability of ICU resources and need of organs. However, we could attempt DCD donations only in category IV and V because there are no guidelines in India to withdraw support in terminally ill patients who are not likely to become brain dead. During our experience, we came across families who realized the futility of continuing further medical care in their terminally ill patients and were distressed by continuing care in an irremediable situation. Some of them wanted to donate organs but since withdrawal of support could not be done, they either waited till the cardiac arrest to happen or took the patient home against medical advice. Our first DCD donor was a similar patient with end stage lung disease in whom lung transplant was not feasible. The patient had a cardiac arrest resulting from hemodynamic instability while on a ventilator but if end of life care guidelines are documented in our country, many more such potential organs could be utilized. It is high time that Indian medical fraternity and policy makers should come together to formulate guidelines which can be followed in such situations as is practiced elsewhere in the world. It will also rationalize the use of scarce medical resources such as ICU beds.

Use of DCD donors was possible at our hospital as our center has a well-established kidney transplant program with all facilities available locally. DCD donation is resource intensive as cardiac arrest is unpredictable, and there are limits of ischemia times beyond which the organs would become unusable. A lot of medical resources such as operation theater, ICU, transplant teams, coordinators, and patients have to respond to the situation in an urgent manner to make it a success. Therefore, DCD in India with the current laws would be possible only in a few centers with a well-developed deceased organ donation program. The development of better preservation methods immediately after cardiac arrest in future has the potential to encourage DCD organ donation in a big way, and the recent advances in normothermic organ perfusion as well as hypothermic machine perfusion of organs has been reported to reduce or reverse preservation-related injury which if implemented routinely can greatly increase this source of organs.^[12,18-20]

The limitations of this study include that it is an early experience with small numbers by a dedicated team of transplant surgeons, so generalization might be difficult. DCD is resource intensive and cannot be taken lightly. Delayed graft function is almost universal but ultimate recovery of kidney function is good. Withdrawal of care guidelines for terminally ill patients is desperately required for both promoting DCD donations and to provide a dignity of death in an end of life situation.

Conclusion

It can be stated that kidneys from donors after cardiac arrest can serve as a useful adjunct in deceased donor

program. Continuing CPR after declaration of death seems to help in improving outcomes in these patients.

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Conflicts of interest

There are no conflicts of interest.

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