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SPECIAL FEATURE

Outcome after heart transplantation from donation after circulatory-determined death donors

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KEYWORDS:
heart;
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direct procurement and perfusion

BACKGROUND: The requirement for heart transplantation is increasing, vastly outgrowing the supply of hearts available from donation after brain death (DBD) donors. Transplanting hearts after donation after circulatory-determined death (DCD) may be a viable additive alternative to DBD donors. This study compared outcomes from the largest single-center experience of DCD heart transplantation against matched DBD heart transplants.
METHODS: DCD hearts were retrieved using normothermic regional perfusion (NRP) or direct procurement and perfusion (DPP). During NRP, perfusion was restored to the arrested heart within the donor with the exclusion of the cerebral circulation, whereas DPP hearts were removed directly. All hearts were maintained on machine perfusion during transportation. A retrospective cohort of DBD heart transplants, matched for donor and recipient characteristics, was used as a comparison group. The primary outcome measure of this study (set by the United Kingdom regulatory body) was 90-day survival.
RESULTS: There were 28 DCD heart transplants performed during the 25-month study period. Survival at 90 days was not significantly different between DCD and matched DBD transplant recipients (DCD, 92%; DBD, 96%; $p = 1.0$). Hospital length of stay, treated rejection episodes, allograft function, and 1-year survival (DCD, 86%; DBD, 88%; $p = 0.98$) were comparable between groups. The method of retrieval (NRP or DPP) was not associated with a difference in outcome.

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CONCLUSIONS: These results suggest that heart transplantation from DCD heart donation provides comparable short-term outcomes to traditional DBD heart transplants and can serve to increase heart transplant activity in well-selected patients.
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In 2017, we mark the 50th anniversary of the first successful human heart transplant. Since then, almost 120,000 patients worldwide have benefited from this operation, returning a nearly normal quality of life to those with end-stage heart failure while extending life by an average of 11.9 years.[1]

In 1967, Barnard transplanted a heart from a "non-heart-beating" or donation after circulatory-determined death (DCD) donor, because brain death had not been legally recognized.[2] As brain death became legally accepted over the course of the next decade, it brought with it 2 advantages.[3–5] Beating hearts from donation after brain death (DBD) donors could be functionally assessed before procurement, allowing for selection of only optimal donor hearts, and more importantly, donor organs were not subject to the detrimental effect of warm ischemia. By avoiding this injury, the simple preservation method of cold storage became routinely used to transport DBD hearts between the donor and recipient hospitals.

During the last 2 decades, the number of suitable DBD heart donors has plateaued while the number of patients diagnosed with heart failure continues to increase. As a result, the waiting list for heart transplantation has tripled in the United Kingdom (UK), with fewer than half receiving a transplant within 3 years of being listed.[6]

To address this rapidly increasing gap between supply and demand, surgeons were forced to not only extend the acceptance criteria for DBD hearts but also reexplore DCD heart transplantation. Until recently, anxieties concerning the unquantifiable warm ischemic injury after cardiac arrest, coupled with the inability to assess function of the asystolic heart, have been major hurdles to transplanting DCD hearts.

This was challenged in 2008 when a group in Denver, Colorado, reported the successful transplantation of 3 DCD pediatric hearts using simple cold storage.[7] Their protocol included ante-mortem heparin administration, colocation of the donors and recipients, and reduction of the standard observation period required between asystole and the declaration of death to 75 seconds. This was controversial, and stands in comparison to the UK, where ante-mortem interventions and ante-mortem drugs are prohibited, colocation is a rarity, and the observation period is legally defined at 5 minutes.[8]

In 2015, a group from Sydney, Australia, reported 3 successful DCD heart transplants.[9] Instead of cold static storage, DCD hearts underwent normothermic blood perfusion during transportation from donor to recipient hospitals. Cardiac function was not assessed, and lactate metabolism was used as a surrogate marker of heart quality.

In 2016, we established a protocol for DCD heart transplantation based on normothermic regional perfusion (NRP) of the donor heart.[10] This technique, first described in 2009, restored coronary perfusion within the cadaver after exclusion of the cerebral circulation.[11] This permitted a functional assessment of the DCD heart, providing the confidence to embark on a program of DCD heart transplantation within the UK.

Although a few isolated case series in the modern era have shown that DCD heart transplantation is possible,[7,9,10,12] this approach must be proven to be at least equivalent to the current standard of care with DBD hearts. In this study, we sought to address this issue by comparing DCD and DBD heart transplant outcomes.

Methods

Study description

This was a single-center observational matched cohort study comparing consecutive patients who received transplants of DCD donor heart between February 1, 2015, and March 31, 2017, vs matched recipients who received transplants of DBD donor hearts between February 1, 2013, and March 31, 2017. The DBD cohort period was extended to allow accurate matching given the heterogeneity of donors and recipients. There was no difference in implant technique or immunosuppressive regimens during this period. Two techniques were used to retrieve donor DCD hearts: normothermic regional perfusion (NRP) or direct procurement and perfusion (DPP). DCD hearts were then transported continually perfused on the Organ Care System (OCS; TransMedics, Andover, MA). DBD hearts all underwent the current standard of direct procurement and cold storage until transplantation. The study protocol was approved by Papworth Hospital Clinical Practice Committee and National Health Service Blood and Transplant (NHSBT). A specialist nurse in organ donation obtained consent from the donor next of kin.

The donors

DCD heart donors were restricted to Maastricht category III donors, defined as expected death after the withdrawal of life-supportive therapy (WLST).[13] The decision to withdraw treatment was based on futility of treatment and made by a multidisciplinary team in conjunction with the patient's family from whom consent for DCD heart donation was obtained. Criteria for DCD heart donation are summarized in Table 1. A local physician undertook WLST in the intensive care unit (ICU) or in the anesthesia room. The donation warm ischemic time (DWIT) was measured from WLST and the functional warm ischemic (FWIT) time (the duration of presumed organ malperfusion) was measured from

Table 1 Criteria for Heart Donation After Circulatory-Determined Death

Inclusion criteria	Exclusion criteria
Category III DCD donor	Previous cardiac surgery
Participating DCD donor hospital	Previous midline sternotomy
Age ≥18 to ≤ 57 years old	Known coronary heart disease
Consent for donation from next of kin	Known congenital heart disease
Expected death within 4 hours of WLST	Previous myocardial infarct
WLST in anesthesia room or ICU	Insulin-dependent diabetes
No valvular abnormalities on echocardiogram	Epinephrine infusion
Ejection fraction > 50% before WLST	Dobutamine infusion
	Norepinephrine > 0.3 μg/kg/min
	Active malignancy
	Hepatitis B antigen-positive
	Hepatitis C antibody-positive
	Malignant melanoma
	All secondary intracerebral tumors
	Human immunodeficiency virus
	Primary intracerebral lymphoma
	Creutzfeldt-Jacob disease
	Tuberculosis

DCD, donation after circulatory-determined death; ICU, intensive care unit; WLST, withdrawal of life-supportive therapy.

when the systolic blood pressure fell below 50 mm Hg. After mechanical asystole (loss of a pulse), a 5-minute observation period was respected before confirmation of death according to national guidelines.[14] Donors were then transferred to the operating theater for multiorgan retrieval commencing with a midline sternotomy and the subsequent delivery of heparin into the right atrium and pulmonary artery.

Portable normothermic machine perfusion

The OCS is currently the only commercially available means of continuous normothermic perfusion of the heart during transportation.[15] The Langendorff coronary perfusion system allows the heart to beat but not eject and is therefore incapable of a functional assessment.[16] Paired arterial and venous blood samples are taken periodically to monitor lactate.

DPP protocol

A large cannula was inserted into the donor right atrium and blood drained for priming of the OCS. Thereafter, 500 ml cold cardioplegic solution (St Thomas No. 2), supplemented with 2,500 IU erythropoietin and 50 mg glyceryl trinitrate, was administered into the aortic root before retrieval and instrumentation on the OCS.[17] DWIT and FWIT were considered to have ceased upon reperfusion of the heart on the OCS.

NRP protocol

The protocol for NRP was prepared in collaboration with the UK Donor Ethics Committee and the authority for organ donation and retrieval within the UK National Health Service Blood and Transplant (NHSBT). NRP was limited to the original 3 donor hospitals that were close to our center originally involved in the research phase. After declaration of death, cannulae were inserted into the ascending aorta and right atrium before perfusion was restored to the thoracoabdominal organs for transplantation, with exclusion of the cerebral circulation. Functional assessment was done after weaning from NRP using a pulmonary artery flotation catheter and transesophageal echocardiogram. Acceptance criteria included an ejection fraction ≥ 50% and a cardiac index ≥ 2.5 liters/min/m^2 with left and right atrial pressures ≤12 mm Hg. Donor blood for priming of the OCS was collected before cardioplegic arrest, as above.

DBD hearts

Before acceptance, DBD beating hearts were functionally assessed using a pulmonary artery flotation catheter and transesophageal echocardiogram. Acceptance criteria were identical to hearts weaned from NRP. Hearts were arrested with 1 liter St Thomas No 2 cardioplegic solution and cold stored at 4°C during transportation.

The recipients

Recipients for DCD heart transplantation were selected from the heart transplant waiting list at Papworth Hospital. Patients were excluded if they had a high transpulmonary gradient > 12 mm Hg or pulmonary vascular resistance > 3 Wood units, a known risk factor for primary graft dysfunction. Potential patients were given an information leaflet and consented for both DCD and DBD heart transplantation.

The transplants

All hearts were transplanted orthotopically using the bicaval technique. Immunosuppression in both groups included induction with anti-thymocyte globulin and maintenance immunosuppression with tacrolimus, mycophenolate mofetil, and prednisolone.

Outcomes

The primary outcome was 90-day survival. Secondary outcomes included cardiac performance, the requirement for mechanical, inotropic, and ventilator support, number of treated rejection episodes, and the ICU and hospital lengths of stay.

Statistical analysis

Analysis was performed using R 2016 software (Core Team, The R Foundation for Statistical Computing Vienna, Austria). Continuous data are summarized with medians and interquartile ranges (IQR) and categoric data with counts and percentages. Paired data were analyzed using the Wilcoxon signed rank test for continuous data, the McNemar exact test for dichotomous categoric data, and the Stuart Maxwell test for contingency tables containing more than 2 rows/columns. Independent data were analyzed using the Wilcoxon rank sum test for continuous data and the Fisher test for categoric data. Statistical significance for the primary outcome was set at p-values of ≤ 0.05. For secondary outcomes, in addition to unadjusted p-values, Benjamini-Hochberg correction was also used to prevent false positives. Owing to the small sample size, matching was achieved on a descriptive basis by an independent blinded reviewer using donor variables (age, sex, height) and recipient variables (sex, etiology, pre-transplant ventricular assist device, transpulmonary gradient and pulmonary vascular resistance). Survival analysis was performed using the non-parametric Kaplan-Meier method and log-rank test.

Results

There were 40 potential DCD donors attended during the study (Figure 1). Thirty-five donors arrested within 4 hours after WLST, with 17 donor hearts undergoing NRP and 18 undergoing DPP. Three DCD hearts were declined in the DPP group after being instrumented on the OCS: 1 due to severe left ventricular hypertrophy, 1 due to a rapidly rising lactate, and 1 due to a subsequently detected abdominal malignancy. Four DCD hearts in the NRP group were declined during in situ NRP: 1 due to poor function and the other 3 due to palpable coronary artery disease. Coronary angiography of the donor heart is not available in the UK. Two recipients were excluded from our analysis: 1 transplanted NRP donor heart did not undergo perfusion on the OCS device because the donor and recipient were uniquely colocated, and 1 DPP recipient underwent combined heart-kidney transplantation. At the time of writing, both of these latter recipients are alive and well $>$ 1 year post-transplant.

DCD vs DBD

Twenty-six isolated DCD hearts were transplanted in the study period for analysis: 12 NRP and 14 DPP (Figure 1). Donor and recipient characteristics are described in Table 2. The transplanted median DCD donor age was 35 years (IQR, 31–38 years) compared with a median age of 38 years (IQR, 30–50 years) for the matched DBD group, which was not significantly different ($p = 0.24$). There was no significant difference in donor blood group or donor norepinephrine requirement. The only significant difference in unmatched characteristics between the groups was cause of death ($p = 0{\cdot}03$). The most common cause of death was hypoxic brain injury in the DCD group and intracerebral hemorrhage in the DBD group.

Outcomes

The overall 90-day survival was 92% in the DCD group and 96% in the DBD group ($p = 1.00$; Figure 2). Although, DCD 30-day survival was 100%, 1 recipient died on Post-Operative Day (POD) 31 from primary graft dysfunction. In this case, the heart was retrieved from a 34-year-old donor using the DPP technique. No palpable coronary artery disease was identified at retrieval. After reperfusion on the OCS, the donor heart appeared satisfactory, with falling perfusate lactate levels. The heart failed to support the circulation after transplantation, and the recipient required extracorporeal membrane oxygenation (ECMO) mechanical support. This was complicated by a catastrophic intracerebral hemorrhage on POD 31. The post-mortem examination revealed severe non-calcific coronary artery

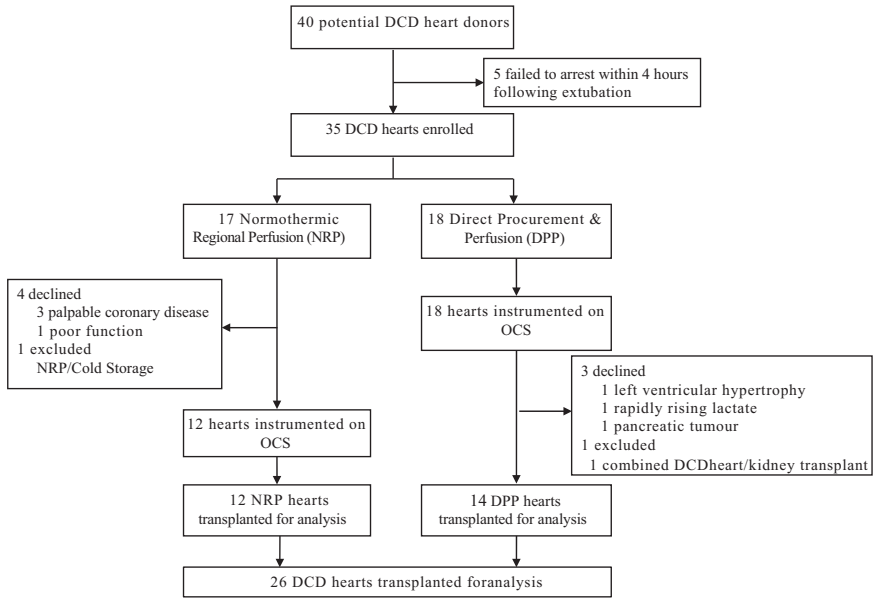

Figure 1 Flow chart of donor heart enrollment. DCD, donation after circulatory-determined death; OCS, Organ Care System, TransMedics, Andover, MA.

Table 2 Donor and Recipient Demographics

	DCD vs DBD			DCD procurement method		
Variable[a]	DCD ($n = 26$)	DBD ($n = 26$)	p-value[b]	NRP ($n = 12$)	DPP ($n = 14$)	p-value[b]
Donor demographics						
Age, years	35 (31–38)	38 (30–50)	0.24	37 (33–42)	35 (26–36)	0.15
Male sex	22 (85)	17 (65)	0.12	9 (75)	13 (93)	0.31
Blood group						
O	18 (69)	15 (58)	0.69	8 (67)	10 (71)	0.82
A	7 (27)	9 (35)		4 (33)	3 (21)	
B	1 (4)	2 (8)		0 (0)	1 (7)	
Cause of death						
HBI	13 (50)	6 (23)	0.03	3 (25)	10 (71)	0.10
ICH	7 (27)	12 (46)		5 (42)	2 (14)	
TBI	5 (19)	2 (8)		3 (25)	2 (14)	
Other	1 (4)	6 (23)		1 (8)	0 (0)	
Height, cm	174 (169–180)	177 (168–183)	0.87	173 (169–179)	174 (170–181)	0.59
Norepinephrine, μg/kg/min	0.02 (0.00–0.15)	0.07 (0.00–0.34)	0.46	0.02 (0.00–0.14)	0.04 (0.00–0.16)	0.89
Recipient demographics						
Age, years	57 (44–61)	59 (51–61)	0.22	58 (49–60)	55 (44–61)	0.69
Male sex	22 (85)	21 (81)	0.18	10 (83)	12 (86)	0.31
Blood group			0.83			0.84
O	13 (50)	13 (50)		5 (42)	8 (57)	
A	11 (42)	9 (35)		6 (50)	5 (36)	
B	2 (8)	3 (12)		1 (8)	1 (7)	
AB	0 (0)	1 (4)		0 (0)	0 (0)	
Height, cm	174 (171–178)	172 (167–178)	0.61	174 (169–176)	175 (172–180)	0.42
TPG, mm Hg	7 (6–8)	7 (5–8)	0.83	8 (7–8)	7 (5–8)	0.32
PVR, Wood units	2.0 (1.5–2.2)	1.9 (1.5–2.3)	0.89	2.1 (1.7–2.2)	1.8 (1.4–2.2)	0.33
Diagnosis						0.12
DCM	15 (58)	15 (58)	0.48	9 (75)	6 (43)	
HCM	5 (19)	3 (12)		2 (17)	3 (21)	
RCM	0 (0)	2 (8)		0 (0)	0 (0)	
IHD	4 (15)	5 (19)		0 (0)	4 (29)	
VHD	1 (4)	1 (4)		1 (8)	0 (0)	
ARVC	1 (4)	0 (0)		0 (0)	1 (7)	
Pre-transplant VAD	6 (23)	6 (23)	1.00	1 (8)	5 (36)	0.17

ARVC, arrhythmogenic right ventricular cardiomyopathy; DBD, donation after brain death; DCD, donation after circulatory-determined death; DCM, dilated cardiomyopathy; DPP, direct procurement and perfusion; HBI, hypoxic brain injury; HCM, hypertrophic cardiomyopathy; ICH, intracerebral hemorrhage; IHD, ischemic heart disease; NRP, normothermic regional perfusion; PVR, pulmonary vascular resistance; RCM, restrictive cardiomyopathy; TBI, traumatic brain injury; TPG, transpulmonary gradient; VAD, ventricular assist device; VHD, valvular heart disease.

[a]Continuous values are reported median (interquartile range) and categoric data as number (%).

[b]The unadjusted p-values are displayed between groups.

disease. A DCD heart transplant recipient died on POD 88 after readmission with an opportunistic fungal infection having been discharged on POD 30. A third DCD heart recipient died on POD 291 of antibody-mediated rejection having initially been discharged from the hospital on POD 23. One recipient in the DBD group required ECMO support because of primary graft dysfunction and died of multiorgan failure on POD 34.

Early post-transplant hemodynamic data are described in Table 3. The DCD hearts had better early cardiac performance after transplantation on similar support in the ICU, with a higher median cardiac index (2.5 vs 2. 0 liters/min/m^2, $p = 0.04$). The difference in use of ventilatory or mechanical support was not significant. There was a trend towards shorter hospital stay for the DCD group (20 vs 27 days, $p = 0{\cdot}09$). No difference was seen in the number of treated rejection episodes between the groups. To date, there are 12,749 days of cumulative survival in the DCD group (range, 31–896 days). After adjusting for multiple testing (Benjamini-Hochberg), only the initial cardiac output remained significantly better in the DCD group ($p = 0.03$).

NRP vs DPP

The NRP and DPP donors did not differ significantly in age, sex, blood group, height, or cause of death. There was no difference in the median time to declaration of death after WLST between NRP and DPP (18 vs 19 minutes, $p = 1.00$). However, compared with DPP, NRP was found to have a shorter DWIT by 13 minutes and FWIT by 9 minutes

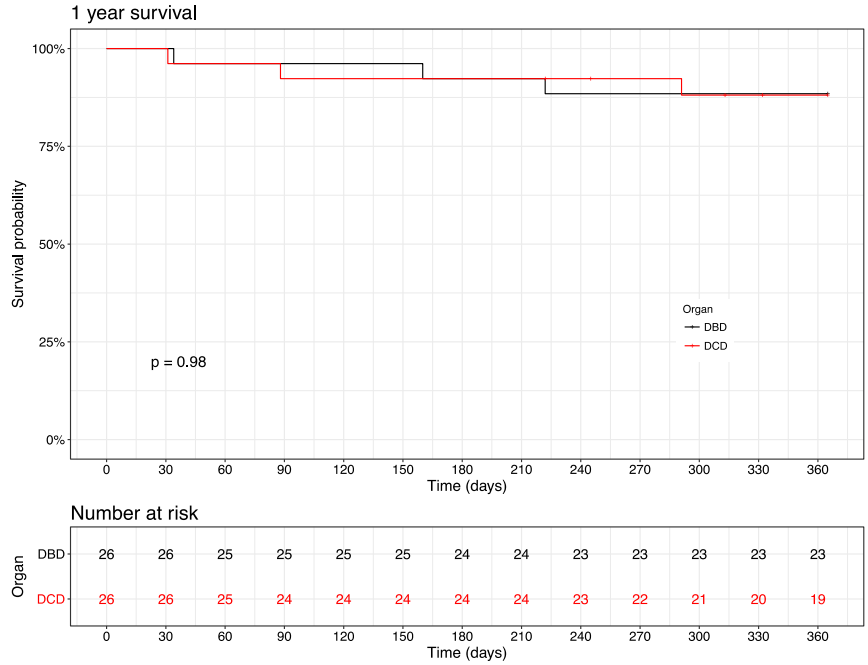

Figure 2 Kaplan-Meier survival of donation after circulatory-determined death (DCD) and donation after brain death (DBD) heart transplantation.

(Table 4). The difference in the median time on OCS support between the 2 groups (NRP, 170 minutes; DPP, 241 minutes) is explained geographically through the proximity of the NRP participating centers to our hospital.

There was no difference between NRP and DPP for post-transplant outcomes relating to mechanical or pharmacologic support, ventilation duration, or duration of ICU or hospital lengths of stay.

Discussion

This study found the use of DCD donors resulted in an equivalent 90-day survival to that seen in contemporary DBD practice. In addition, early cardiac output was better in the DCD group. This may be explained by the elimination of cold ischemia during transportation; however, when cold storage and machine perfusion of DBD hearts were compared in the Randomized Study of Organ Care System Cardiac for Preservation of Donated Hearts for Eventual Transplantation (PROCEED II) trial, no difference in clinical outcome was seen.[18] Other possible explanations to account for our findings include the avoidance of the detrimental effect of brain death on heart function in the DCD group and possible ischemic pre-conditioning during WLST.

When methods of DCD heart retrieval were compared, there was no difference in clinical outcomes between DPP and NRP. However, both techniques have advantages and disadvantages. The main advantages to NRP are earlier reperfusion and formal functional assessment. This assessment of organ quality after the declaration of death has allowed us to push the boundaries of DCD donation, enabling safe access to the extended criteria DCD heart donor. We have increased DCD donor age to $>$ 55 years and the donation withdrawal ischemic time (DWIT) up to 169 minutes. Despite this, the use of ECMO support after transplantation was only 12% in our series. In comparison, other centers where donor age has been limited to 40 years and the DWIT limited to only 30 minutes report post-transplant ECMO support of up to 30%.[9] Importantly, the use of NRP has influenced our practice to be less reliant on lactate as a marker for organ quality and thereby increased our organ utilization without compromising outcomes.[19]

In addition to minimizing the warm ischemia of the donor heart, NRP has the benefit of early reperfusion of donor abdominal organs with evidence of improved outcomes compared with cold static storage for liver and kidney transplants.[20] Although NRP may add to the overall theater time for multiorgan retrieval, this technique eliminates the need for rushed DCD organ retrieval, which may reduce the risk of iatrogenic organ damage.

The main drawback of NRP is that as a result of the varying definitions between countries relating to the declaration of death, it is not currently scalable internationally.[21] Such ethical variation is also encountered in other aspects of DCD donation, such as ante-mortem heparinization, ante-mortem cannulation, and the legally defined observation period from mechanical asystole to the declaration of death, which can vary from 2 to 20 minutes. Through extensive debate over the last decade in the UK between the public, ethicists, intensivists, surgeons, and the legal profession, NRP has been accepted into current practice. In addition, countries with established abdominal NRP programs have expressed an interest in thoracoabdominal NRP with a view to further increase organ utilization to include both the heart and lungs.

Overall, NRP is technically more demanding and is more resource intensive. NRP costs an additional $4,000 for each

Table 3 Heart Transplant Outcomes

	DCD vs DBD			DCD procurement method		
Variable[a]	DCD ($n = 26$)	DBD ($n = 26$)	p-value[b]	NRP ($n = 12$)	DPP ($n = 14$)	p-value[b]
Survival						
30 days	26 (100)	26 (100)	1.00	12 (100)	14 (100)	1.00
90 days	24 (92)	25 (96)	1.00	12 (100)	12 (86)	0.48
Cardiac performance						
Cardiac index, liters/min/m^2	2.5 (2.1–2.7)	2.0 (1.8–2.4)	0.04	2.5 (2.4–2.7)	2.5 (1.7–2.8)	0.62
Cardiac output, liters/min	4.9 (4.0–5.2)	3.9 (3.2–4.4)	0.006	5.0 (4.3–5.1)	4.6 (3.4–5.5)	0.60
MAP, mm Hg	71 (64–78)	66 (60–70)	0.08	69 (64–78)	70 (69–78)	0.79
CVP, mm Hg	10 (8–11)	11 (9–12)	0.10	10 (8–11)	9 (8–11)	0.57
PAP diastolic, mm Hg	14 (12–17)	15 (12–19)	0.65	13 (12–17)	16 (13–18)	0.43
Mechanical support						
IABP	7 (27)	4 (15)	0.51	2 (17)	5 (36)	0.39
ECMO	3 (12)	1 (4)	0.63	1 (8)	2 (14)	1.00
VAD	1 (4)	0 (0)	1.00	0 (0)	1 (7)	1.00
Pharmacologic Support						
Dopamine, μg/kg/min	4.8	5.0	0.04	5.1	4.8	0.15
Adrenaline, μg/kg/min	0.04	0.04	0.65	0.04	0.03	0.73
Norepinephrine, μg/kg/min	0.01	0.03	0.09	0.00	0.00	0.43
Post-transplant outcomes						
Ventilation duration, days	0.9 (0.5–3.3)	1.8 (0.7–2.5)	0.84	0.6 (0.4–1.1)	2.5 (0.5–3.6)	0.06
Length of stay, days						
Intensive care unit	5 (3–8)	7 (4–9)	0.49	5 (4–5)	6 (3–10)	0.67
Hospital	20 (17–28)	27 (21–34)	0.09	19 (17–27)	20 (19–27)	0.58
Hemofiltration	8 (31)	7 (27)	0.51	2 (17)	5 (36)	0.39
Ejection fraction,[c] %	63 (58-63)	63 (62-63)	1.00	62 (58-65)	62 (60-63)	1.00
Treated rejection	9 (35)	15 (58)	0.15	4 (33)	5 (36)	1.00

CVP, central venous pressure; DBD, donation after brain death; DCD, donation after circulatory-determined death; DCM, dilated cardiomyopathy; DPP, direct procurement and perfusion;
ECMO, extra corporeal membrane oxygenation; IABP, intraaortic balloon pump; MAP, mean arterial pressure; PAP, pulmonary artery pressure; VAD, ventricular assist device.

[a]Continuous values are median (interquartile range) or as indicated, and continuous values as number (%).

[b]Unadjusted p-values are displayed between groups.

[c]Determined by transthoracic echocardiogram, with the first echocardiogram performed in the outpatient clinic.

DCD heart assessed due to equipment and personnel. However, at a cost of $38,000 per OCS module, this upfront cost is easily offset in our experience because all NRP donor hearts have been used once assessed and accepted for transplantation. In comparison, 17% of DPP hearts were turned down for transplantation after perfusion on the OCS at a potential cost of $114,000. This rate of turn down is in keeping with the experience of other units practicing DPP for DCD heart retrieval.[9]

The main advantage of the DPP approach is that it can be incorporated into existing DCD procurement programs with minimal disruption. The technique is relatively simple to perform and easily disseminated to other centers. No additional blood products are needed, and a smaller team

Table 4 Ischemic Timing for Donation After Circulatory-Determined Death Hearts

	NRP	DPP	
Variable[a]	($n = 12$)	($n = 14$)	p-value[b]
Withdrawal to death, minutes	18 (13-21)	19 (15–23)	1.00
DWIT, minutes	24 (21-28)	37 (33-42)	0.003
FWIT, minutes	17 (15-19)	26 (23-31)	<0.001
OCS perfusion time, minutes	170 (140-179)	241 (210–280)	0.003
Implant duration, minutes	32 (31-35)	37 (34–46)	0.03

DWIT, donation withdrawal ischemic time; FWIT, functional warm ischemic time; OCS, Organ Care System, TransMedics, Andover, MA.

[a]Values are median (interquartile range).

[b]p-values are displayed between groups.

is required. The main disadvantage is the inability to directly assess heart function, and therefore, more emphasis is placed on surrogate markers of organ function such as lactate.

Our conclusions are limited by a small sample size, lack of randomization, and fixed prescription of NRP participating hospitals. Although we have taken precautions to minimize variability between groups by limiting practice to our single center over a similar time period, a randomized controlled trial comparing DBD and DCD heart transplantation would be required to prove non-inferiority. However, such a trial would not be accepted ethically given the severe scarcity of donor hearts.

Although we report comparable short-term and midterm results between DBD and DCD heart transplantation, the longer-term results are unknown. The effects of prolonged warm ischemia and machine perfusion on the coronary endothelium and the development of cardiac allograft vasculopathy have yet to be determined.

Previous forecasts predicted DCD heart transplantation may increase heart transplant activity by 17% to 30%.[22–25] During the study period, 84 DBD heart transplants were performed at our institution with a total of 28 additional DCD heart transplants, increasing our overall heart transplant activity by 33%. We believe that the adoption of DCD heart transplantation, whether retrieved by NRP or DPP, can be safely implemented into widespread routine clinical practice.

Disclosure statement

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