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The Journal of Heart and Lung Transplantation

http://www.jhltonline.org

A national pilot of donation after circulatory death (DCD) heart transplantation within the United Kingdom

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Abbreviations: ARVC, Arrhythmogenic Right Ventricular Cardiomyopathy; CHD, Congenital Heart Disease; CLOD, Clinical Lead in Organ Donation; DBD, Donation After Brain Death; DCD, Donation After Circulatory Death; DCM, Dilated Cardiomyopathy; DPP, Direct Procurement and Perfusion; DWIT, Donation Withdrawal Ischaemic Time; ECMO, Extra Corporeal Membrane Oxygenation; ESMP, Ex-situ Machine Perfusion; FWIT, Functional Warm Ischaemic Time; HBI, Hypoxic Brain Injury; HCM, Hypertrophic Cardiomyopathy; IABP, Intra-Aortic Balloon Pump; ICH, Intracerebral Haemorrhage; IHD, Ischaemic Heart Disease; ICU, Intensive Care Unit; IQR, Interquartile Range; JIF, Joint Innovation Fund; MCS, Mechanical Circulatory Support; NHS, National Health Service; NHSBT, National Health Service Blood and Transplant; NHSE, National Health Service England; NORS, National Organ Retrieval Service); NRP, Normothermic Regional Perfusion; OCS, Organ Care System; PA, Pulmonary Artery; PGD, Primary Graft Dysfunction; PVR, Pulmonary Vascular Resistance; RBHT, Royal Brompton and Harefield Hospital; RCM, Restricted Cardiomyopathy; RPH, Royal Papworth Hospital; SD, Standard Deviation; TANRP, Thoraco abdominal normothermic regional perfusion; TBI, Traumatic Brain Injury; TPG, Trans Pulmonary Gradient; UK, United Kingdom; US, United States; VAD, Ventricular Assist Device; WLST, Withdrawal of Life Sustaining Therapy

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https://doi.org/10.1016/j.healun.2023.03.006

KEYWORDS:
heart;
transplant;
circulatory death;
circulatory determined death;
ex-situ heart perfusion system

BACKGROUND: The United Kingdom (UK) was one of the first countries to pioneer heart transplantation from donation after circulatory death (DCD) donors. To facilitate equity of access to DCD hearts by all UK heart transplant centers and expand the retrieval zone nationwide, a Joint Innovation Fund (JIF) pilot was provided by NHS Blood and Transplant (NHSBT) and NHS England (NHSE). The activity and outcomes of this national DCD heart pilot program are reported.

METHODS: This is a national multi-center, retrospective cohort study examining early outcomes of DCD heart transplants performed across 7 heart transplant centers, adult and pediatric, throughout the UK. Hearts were retrieved using the direct procurement and perfusion (DPP) technique by 3 specialist retrieval teams trained in ex-situ normothermic machine perfusion. Outcomes were compared against DCD heart transplants before the national pilot era and against contemporaneous donation after brain death (DBD) heart transplants, and analyzed using Kaplan-Meier analysis, chi-square test, and Wilcoxon's rank-sum.

RESULTS: From September 7, 2020 to February 28, 2022, 215 potential DCD hearts were offered of which 98 (46%) were accepted and attended. There were 77 potential donors (36%) which proceeded to death within 2 hours, with 57 (27%) donor hearts successfully retrieved and perfused ex situ and 50 (23%) DCD hearts going on to be transplanted. During this same period, 179 DBD hearts were transplanted. Overall, there was no difference in the 30-day survival rate between DCD and DBD (94% vs 93%) or 90 day survival (90% vs 90%) respectively. There was a higher rate of ECMO use post-DCD heart transplants compared to DBD (40% vs 16%, $p = 0.0006$), and DCD hearts in the pre pilot era, (17%, $p = 0.002$). There was no difference in length of ICU stay (9 DCD vs 8 days DBD, $p = 0.13$) nor hospital stay (28 DCD vs 27 DBD days, $p = 0.46$).

CONCLUSION: During this pilot study, 3 specialist retrieval teams were able to retrieve DCD hearts nationally for all 7 UK heart transplant centers. DCD donors increased overall heart transplantation in the UK by 28% with equivalent early posttransplant survival compared with DBD donors.

J Heart Lung Transplant 2023;42:1120−1130

In the United Kingdom (UK) donation after circulatory death (DCD) donors represent 40% of deceased donors.[1] The UK was an early pioneer in the use of heart transplants from DCD donors.[2] Following prolonged research,[3] the world's first DCD heart transplant using thoraco abdominal normothermic regional perfusion (TANRP)[2] was performed in Cambridge, UK. In quick succession, the first European DCD heart transplant utilizing the direct procurement and perfusion (DPP) technique,[4] and the world's first DCD heart transplant utilizing TANRP/cold storage was reported.[5] This was followed by the first pediatric DCD heart transplant using TANRP.[6] The UK was the first to describe combined DCD heart and kidney[4] and DCD heart lung transplants,[7] whilst also reporting the world's largest single center experience of both adult[8] and pediatric[9] DCD heart transplants. In addition the UK was first to describe combined abdominal NRP and direct procurement of the DCD heart.[10]

Following a service evaluation of DCD heart retrieval services at 2 transplant centers in 2015, a limited roll out of the DCD heart program began. The expansion relied on charitable donations to support individual transplant centers which was not sustainable in the longer term.

As several UK single center experiences expanded over the next 5 years it was evident that significant obstacles had to be overcome to attract national funding. These were namely equity of access to donor hearts for transplant recipients, agreed outcome reporting, sustainability, and the incorporation of a specialized ex situ machine perfusion service into the preexisting National Organ Retrieval Service (NORS).

To address these needs, a national joint innovation fund (JIF) pilot study was funded by National Health Service Blood and Transplant (NHSBT) and National Health Service England (NHSE). The activity and outcomes of this national pilot program, between September 7, 2020 and February 28, 2022, are reported.

Material and methods

Joint innovation fund (JIF)

The JIF Board was composed of clinical and managerial representatives, organ donation specialists, clinical leads in NORS, clinical leads in organ donation, statistics, quality, governance, operational and finance leads as well as devolved nation representatives and NHS Blood and Transplant and NHS England commissioners. The Board met quarterly to provide management and oversight of the pilot.

Offering sequence

Donors fulfilling the criteria outlined in Appendix 1, where consent was obtained from next of kin, were referred and hearts offered to recipient centers. The first offer was made to the transplant center in whose allocation zone the donor hospital was located. The order of the subsequent center offers followed the UK Heart Allocation Policy.[11] This contrasted with donation after

brain death (DBD) hearts which were offered through the super-urgent, urgent and nonurgent allocation tiers.

Retrieval teams

Three retrieval teams that had performed greater than 10 DCD heart retrievals were included within the pilot. The team consisted of 5 members; (1) surgeon, (2) surgical assistant, (3) scrub nurse, (4) ex situ machine perfusion practitioner and (5) organ perfusion specialist to manage heart and lung preservation solutions. Compared with the standard NORS team, the DCD retrieval team had 1 additional member. The on-call team provided a 7-day 24 hour rolling rota cover. The 3 retrieval teams were Royal Brompton and Harefield Hospital (RBHT) and Wythenshawe Hospital which provided 1 week cover each and Royal Papworth Hospital (RPH) which contributed 2-week cover each month.

Teams were funded to attend the donor hospital, retrieve and instrument the heart on the ex situ heart perfusion device and accompany the perfused heart to the transplant center, administer cardioplegia and hand the DCD heart to the implanting surgeon.

Retrieval technique

As part of the JIF pilot a national protocol was agreed.[12] No other antemortem interventions or medications are permitted in the UK. Currently the TANRP technique is restricted within the UK due to concern of collateral circulation, a factor which has greatly impacted the utilization of this technique in the UK. Similar debate is occurring within other countries.[13] Therefore, only the DPP technique was utilized for this study. Cases of combined abdominal normothermic regional perfusion with direct procurement and perfusion of the DCD heart were included. Following withdrawal, the retrieval team stood by for 2 hours until the potential donor arrested or was returned to the ICU. Following mechanical asystole, a 5-minute observation period was respected before death was declared.

Following declaration of death, the donor was transferred into theatre and prepped and draped. A rapid sternotomy was undertaken, Heparin administered and the donor exsanguinated. The donor blood was then added to the Organ Care System ex situ heart perfusion device, along with the propriety perfusion solution. 500 mls St Thomas's cold crystalloid cardioplegia supplemented with the postconditioning agents Erythropoietin and Glyceryl Trinitrate were then administered into the aortic root before the heart was removed from the donor.[14]

Two retrieval options were permitted for instrumentation of the donor hearts according to center experience:

Method A

Two of the teams followed the technique described by Messer/Large.[8] After the heart is removed the aorta is cannulated and a tie strap applied, a cannula is placed within the pulmonary artery (PA) and secured and the heart then perfused on the OCS device. A vent is then placed in the left atrial appendage. After the heart is perfused and vented the aortic cannula is then reinforced with 4 pledgeted sutures. Both left and right ventricles are left unloaded. The inferior and superior vena cava are both left open. The pulmonary artery cannula is left disconnected but allows blood to be channeled into the venous reservoir by gravity.

Method B

One team followed the technique as described by Dhital et al.[14] Following cardioplegia the heart is removed and the aorta is prepared with 4 pledgeted sutures on the back table. A suture is used to make a pursetring in the PA and a cannula inserted. The heart is then perfused on the OCS device. The left ventricle is vented before the superior vena cava is tied and the inferior vena cava oversewn. The pulmonary artery cannula is then connected and coronary sinus blood is then directed through 1/4'' tubing producing a partially loaded right ventricle.

For all teams, after retrieval, the heart was transported to recipient centers accompanied by a retrieval surgeon and perfusion device operator.

If the heart was deemed transplantable en route, this would be communicated to the recipient center to start the recipient procedure in order to minimize the OCS perfusion time.

Recipients

No restrictions were placed on DCD heart recipients in this trial in relation to urgency status, etiology of heart failure, transpulmonary gradient, or long-term ventricular assist device (VAD) or extra corporeal membrane oxygenation (ECMO). On arrival at the recipient center, once the implanting surgeon was ready for the donor heart, OCS perfusion would be discontinued and 1 liter of supplemented cold crystalloid cardioplegia was administered.[14]

There was no prescribed protocol on the cardio protection regime, if any, employed during the implant or the number of anastomosis undertaken before releasing the cross clamp. The immunosuppression regime was left at the discretion of each individual transplant center.

Statistical analysis

Data were extracted from the UK Transplant Registry held by NHSBT on June 14, 2022. Continuous data with normal distributions are expressed with means and standard deviations, and compared using Student's *t*-test, while continuous data with non-normal distributions are presented with medians and interquartile ranges (IQRs) and compared using Wilcoxon's rank-sum. Categorical data are summarized with counts and percentages and compared using the chi-square test or Fisher's exact test. Survival analysis was performed using the Kaplan−Meier method, and comparisons were tested using the log-rank test. Statistical significance was considered for $p < 0.05$. None of the studied patients were lost to follow-up. Missing data are explicitly stated in results. The data analysis was carried out using the SAS version 9.4 software.

Results

Retrieval team

Over the 18-month period there were changes to the retrieval team cover. After 7 months on the rota, Wythenshawe withdrew from the service due to staff redeployment during the coronavirus disease 2019 (COVID-19) pandemic. To cover this 1 week, a hybrid team was established which composed of 2 surgeons from RBHT and the rest of the 3 team members from RPH.

Offers and transplants

During the 18-month study period, 215 potential DCD hearts were offered of which 120 (56%) were accepted, Figure 1. There were 98 (46%) potential donors attended by a retrieval team and 77 (36%) proceeded to asystole. Out of the 57 (27%) DCD hearts that were placed on the OCS, 50 (23%) were transplanted. Of the 57 hearts placed on the OCS, the utilization rate was 87%. During the 18-month study period, 179 DBD hearts were retrieved using cold static storage and transplanted.

Donors and recipients

Of the transplanted DCD hearts, the mean donor age was 32±11 years, Table 1. The majority were male, (72%) which was a higher proportion in comparison to the DBD cohort (54%) $p = 0.04$. There were more hypoxic brain injury patients in the DCD group (56% vs 41%, $p = 0.01$) and more intracerebral hemorrhage patients in the DBD group (47% vs 24%, $p = 0.01$).

The median age of the DCD heart recipient was 48 (38-58) years old. There were more male DCD heart recipients in comparison to the DBD group, (82% vs 52%, $p = 0.003$). The median recipient height was 8 cm taller in the DCD group in comparison to the DBD group ($p = 0.0016$).

More patients on the nonurgent waiting list were transplanted with DCD hearts (42% DCD vs 24% DBD, $p = 0.04$), whilst more patients on the urgent heart transplant waiting list were transplanted with DBD hearts (56% DBD vs 40% DCD, $p = 0.04$).

There were no significant differences in donor and recipient baseline characteristics when comparing DCD hearts pre and during the JIF trial.

Of the DCD hearts transplanted, there were variations in transplant rates across the 7 transplant centers. During this study period, a large proportion of the DCD heart transplants (78%) were carried out by 3 transplant centers who performed 13 DCD heart transplants each. The other 4 centers only performed 11 DCD hearts transplants between them.

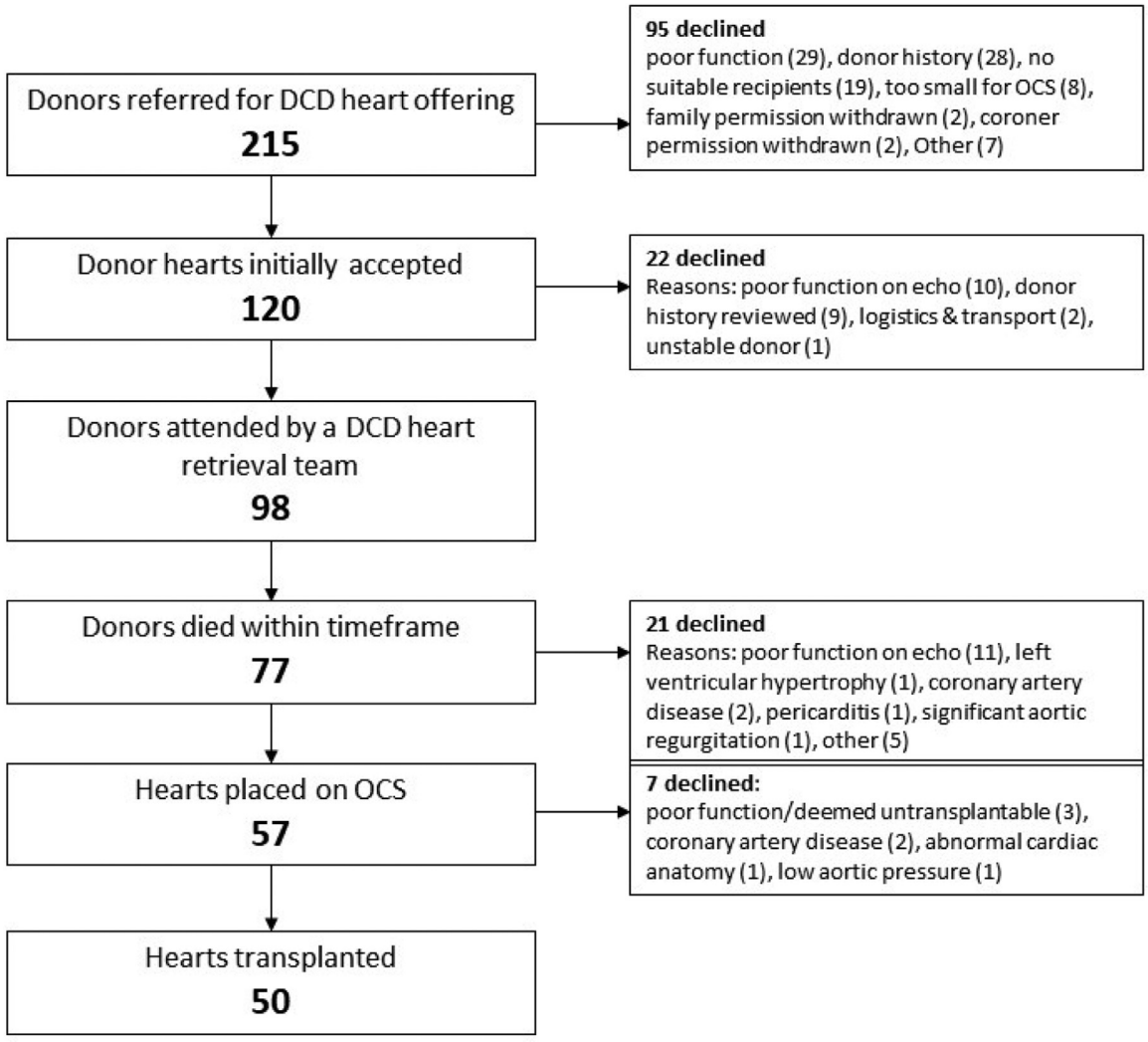

Figure 1 DCD Donors offered and transplanted.

Table 1 Recipient and Donor Demographics

	DCD pre-JIF and JIF			DCD vs DBD JIF period		
	Pre-JIF *n* = 125	JIF *n* = 50	*p* value	DCD *n* = 50	DBD *n* = 179	*p* value
Donor demographics						
Age, years Mean [Std DEV]	34 [11]	32 [11]	0.20	32 [11]	34 [13]	0.33
Sex male, *n* [%]	104 [83]	36 [72]	0.14	36 [72]	97 [54]	**0.04**
Blood group						
A, *n* [%]	41 [33]	18 [36]	0.51	18 [36]	64 [36]	0.64
B, *n* [%]	8 [6]	5 [10]		5 [10]	12 [7]	
O, *n* [%]	75 [60]	26 [52]		26 [52]	101 [56]	
AB, *n* [%]	1 [1]	1 [2]		1 [2]	2 [1]	
Cause of death						
HBI, *n* [%]	53 [42]	28 [56]	0.27	28 [56]	74 [41]	**0.01**
TBI, *n* [%]	17 [14]	6 [12]		6 [12]	8 [4]	
ICH, *n* [%]	41 [33]	12 [24]		12 [24]	84 [47]	
Tumor, *n* [%]	2 [2]	2 [4]		2 [4]	2 [1]	
Thrombosis, *n* [%]	5 [4]	2 [4]		2 [4]	6 [3]	
Other, *n* [%]	7 [6]	0 [-]		0 [-]	5 [3]	
Height, cm [Std DEV]	176 [9]	175 [10]	0.55	175 [10]	172 [11]	0.05
Recipient demographics						
	Pre-JIF *n* = 125	JIF *n* = 50	*p* value	DCD *n* = 50	DBD *n* = 179	*p* value
Age, years [IQR]	52 [40-59]	48 [38-58]	0.08	48 [38-58]	46 [31-56]	0.32
Sex male, *n* [%]	100 [80]	41 [82]	0.93	41 [82]	104 [58]	**0.0033**
Blood group						
A, *n* [%]	55 [44]	26 [52]	0.18	26 [52]	83 [46]	0.37
B, *n* [%]	12 [10]	9 [18]		9 [18]	20 [11]	
O, *n* [%]	53 [42]	14 [28]		14 [28]	68 [38]	
AB, *n* [%]	5 [4]	1 [2]		1 [2]	8 [4]	
Diagnosis						
IHD, *n* [%]	22 [18]	5 [10]	0.29	5 [10]	29 [16]	0.74
CHD, *n* [%]	4 [3]	5 [10]		5 [10]	16 [9]	
DCM, *n* [%]	65 [52]	29 [58]		29 [58]	101 [56]	
HCM, n [%]	12 [10]	6 [12]		6 [12]	13 [7]	
RCM, *n* [%]	4 [3]	1 [2]		1 [2]	8 [4]	
other, *n* [%]	18 [14]	4 [8]		4 [8]	12 [7]	
Urgency						
Nonurgent, *n* [%]	70 [56]	21 [42]	0.09	21 [42]	43 [24]	**0.04**
Urgent, *n* [%]	45 [36]	20 [40]		20 [40]	100 [56]	
Super-urgent, *n*[%]	10 [8]	9 [18]		9 [18]	36 [20]	
Height, cm [IQR]	174 [167-179]	176 [167-180]	0.74	176 [167-180]	168 [159-175]	**0.0016**
Creatinine, mmol/liter, [IQR][a]	99 [84-121]	93 [77-129]	0.52	93 [77-129]	89 [69-112]	0.26
Missing	*5*	*1*		*1*	*8*	
Pre-tx VAD/ECMO, *n*[%]	37 [30]	16 [32]	0.90	16 [32]	59 [33]	0.90

CHD, congenital heart disease; 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, ischaemic heart disease; IQR, interquartile range; NRP, normothermic regional perfusion; RCM, restrictive cardiomyopathy; TBI, traumatic brain injury; VAD, ventricular assist device; VHD, valvular heart disease; pre-tx, pretransplant; ECMO, extra corporeal membrane oxygenation; StdDEV, standard deviation.

The significance of the bold values in the table is statistical significance of p value <0.05.

[a]Creatinine at listing for transplantation.

Outcomes

The thirty-day survival rate for DCD heart transplantation in the JIF era was 94% which was comparable to that of both the pre-JIF trial era, (97%, $p = 0.39$) and the contemporary DBD heart cohort (93%, $p = 0.77$), Table 2. The 90-day JIF era survival rate (90%) was also comparable to that of pre-JIF (91%, $p = 0.72$) and that of DBD cohort (90%, $p = 0.99$), Figure 2. The 1-year survival rate for the study was 84% which was identical to that of DBD (84%, $p = 0.91$) and similar to that of the pre-JIF era (86%, $p = 0.60$).

In comparison to DBD heart transplants, there was a much higher incidence of ECMO support posttransplant in the JIF DCD trial group (40% vs 16%, $p = 0.0006$). In comparison to the pre-JIF era, although there were fewer intra-

Table 2 Posttransplant Recipient Outcome

	DCD pre-JIF and JIF			DCD vs DBD JIF period		
	Pre JIF *n* = 125	JIF *n* = 50	*p* value	DCD *n* = 50	DBD *n* = 179	*p* value
Survival						
30-day, % [95% CI]	97 [92-99]	94 [83-98.]	0.39	94 [83-98]	93 [88-96]	0.77
90-day, % [95% CI]	91 [85-95]	90 [77-96]	0.72	90 [77-96]	90 [84-93]	>0.99
1 year, % [95% CI]	86 [79-91]	84 [64-93]	0.60	84 [63-93]	84 [76-90]	0.91
Mechanical circulatory support posttransplant						
IABP, *n* [%]	31 [25]	4 [8]	**0.02**	4 [8]	17 [10]	0.96
ECMO, *n* [%]	21 [17]	20 [40]	**0.0021**	20 [40]	29 [16]	**0.0006**
VAD, *n* [%]	5 [4]	2 [4]	-	2 [4]	7 [4]	>0.99
Posttransplant outcomes						
Ventilation, days [IQR]	2 [1-6]	4 [2-12]	**0.02**			
Missing	*14*	*9*				
Hemofiltration, *n* [%]	63 [51]	29 [60]	0.36	29 [60]	79 [45]	0.08
Missing	*2*	*2*		*2*	*3*	
ICU stay, days [IQR]	7 [4-14]	9 [7-19]	**0.03**	9 [7-19]	8 [5-14]	0.13
Missing	*11*	*9*		*9*	*23*	
Hospital stay, days [IQR]	24 [19-34]	29 [22-44]	0.13	29 [22-44]	27 [21-37]	0.47
Missing	*15*	*12*		*12*	*33*	
Treated rejection episode in 30 days, *n* [%]	9 [7]	4 [8]	0.76	4 [8]	25 [14]	0.41
Missing	*2*	*2*		*2*	*3*	
Treated rejection episode in 90 days, *n* [%]	16 [14]	4 [9]	0.61	4 [9]	38 [24]	0.06
Missing	*10*	*7*		*7*	*22*	

DBD, donation after brain death; DCD, donation after circulatory-determined death; ECMO, extra corporeal membrane oxygenation; IABP, intra-aortic balloon pump; ICU, intensive care unit; IQR, intra quartile range; JIF, joint innovation fund; VAD, ventricular assist device.

The significance of the bold values in the table is statistical significance of p value <0.05.

aortic balloon pumps post-DCD transplant in the JIF era (8% JIF vs 25% pre-JIF, $p = 0.02$), there was a much higher incidence of ECMO support post-DCD transplant (40% JIF vs 17% pre-JIF, $p = 0.002$).

This higher rate of posttransplant ECMO utilization was reflected in the posttransplant outcomes in the JIF era with DCD heart transplant recipients spending longer on the ventilator, (4 days JIF vs 2 days pre-JIF, $p = 0.02$) and longer duration in the ICU (9 days JIF vs 7 days pre-JIF, $p = 0.03$). There was no difference in hospital stay or treated rejection episodes. There was no significant difference between DBD and the JIF DCD heart transplant outcomes in relation to ICU stay (DCD 9 days vs 8 days DBD, $p = 0.13$) or hospital stay (DCD 29 days vs 27 days DBD, $p = 0.47$).

Ischemic timings

When comparing ischemic timings, pre- and postintroduction of the JIF there was no significant difference in ischemic times with the exception of the time from cardioplegia delivery to reperfusion on the OCS device, which was 3 minutes longer during the JIF period. (10 minutes pre-JIF vs 13 minutes JIF, $p = 0.03$).

The JIF ischemic times by retrieval technique were also compared, Table 3. When comparing method A versus method B, those retrievals that employed abdominal NRP and DCD heart retrieval were excluded (as potentially they could take longer), leaving 25 DCD hearts retrieved with method A versus 20 hearts with method B. There was no significant difference in the treatment withdrawal to confirmation of death between the methods A and B (19 minutes, $p = 0.91$). Method B had a longer time from treatment withdrawal to blood reperfusion compared to method A (42 minutes vs 36 minutes, $p = 0.0016$) and a longer time from donor systolic blood pressure <50 mm Hg to donor heart reperfusion, (33 minutes versus 25 minutes $p = 0.0026$). There was no significant difference in the time from donor asystole to delivery of cardioplegia (13 minutes) between the 2 techniques ($p = 0.23$). It took on average 6 minutes longer to reperfuse the heart via method B following the delivery of cardioplegia ($p = 0.0001$). There was no significant difference in OCS perfusion time between the 2 methods (A 258 vs B 249 minutes, $p = 0.34$).

The donor and recipient characteristics of the hearts retrieved across the 2 different methods were found to be comparable, Table 4, with the exception of recipient age which was older in method B. There was no significant difference in short term recipient outcomes by retrieval center with similar ECMO and VAD rates post-transplant, Table 5. The 30-day survival by method was 100% for method A vs 85% for method B, $p = 0.07$, Table 5.

Discussion

This is the first study to describe the early outcomes of a nationally funded DCD heart transplant program with hearts retrieved by direct procurement and ex situ machine perfusion using a national specialist retrieval service.

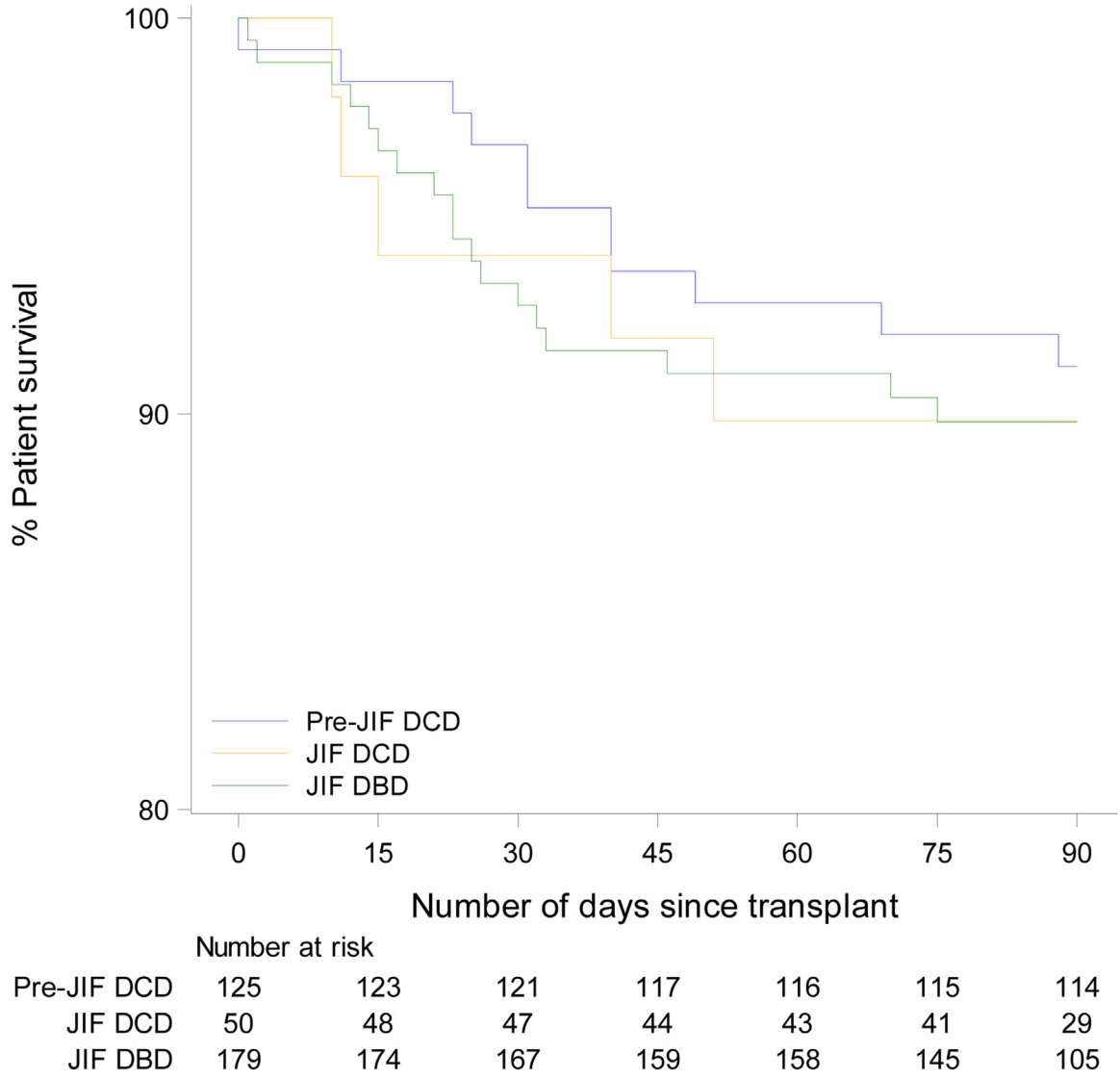

Figure 2 Ninety-day survival for pre-JIF DCD, JIF DCD and JIF DBD recipients.

The national DCD heart transplant program increased heart transplant activity by 28% whilst the primary outcome of 90-day survival (90%) was comparable with both DBD (90%) and DCD heart retrieval (90%) performed by single UK centers before the national JIF study.[8] There was a high utilization rate of DCD hearts (88%) in the study which was higher than single center experiences described by both Papworth (76%)[8] and most recently Sydney (72%).[15] A possible reason for such a high utilization rate is that retrieval teams had already overcome their learning curve and had the confidence to transplant hearts where lactate trends had previously been unhelpful.[16]

A surprising outcome of the study was that the post-transplant ECMO rate was significantly high at 40%. This was both higher than DBD (16%) and pre-JIF DCD heart era (17%). This rate of severe PGD requiring ECMO in this series is the highest ever reported by other early single center experiences; Papworth 18%[8] and Sydney 31%,[17] and is more than double reported by the recent US multicenter trial of DCD hearts of 14% to 16%.[18]

There are several possible explanations for this high rate of severe primary graft dysfunction. When the ECMO utilization rate per transplant center was investigated it was evident that 3 transplant centers with low experience of DCD heart transplantation had a 100% ECMO rate posttransplant, Table 6. Although DCD hearts have been proven to have comparable short-term outcomes in comparison to DBD,[8,15] they are still vulnerable to further ischemic insults during implant. There is variation across the UK in donor heart protection during implantation from continuous antegrade or retrograde cold blood cardioplegia during implantation, with some adding ''hot shot'' to the extreme of no cardioplegia at all. Implant times can vary from being very short from where just the left atrium and aortic anastomosis are performed before releasing the cross clamp to the other extreme where all the vascular anastomoses are completed before releasing the aortic cross clamp. Therefore, a further way to reduce the rate of severe PGD would be an agreed national protocol to adopt an implant technique minimizing the warm ischemic time. Potentially a further way to reduce the high incidence of ECMO would be for the more mature

Table 3 DCD Donor Heart Ischemic Timings

	Pre-JIF $n = 125$	JIF $n = 50$	Difference	p value
WLST to confirmation of death, min [IQR]	18 [14-22]	19 [17-20]	1	0.51
Missing	*8*	*3*		
[DWIT] WLST to blood reperfusion, min [IQR]	40 [33-59]	39 [35-46]	1	0.82
Missing	*14*	*12*		
[FWIT] SBP <50 mm Hg to reperfusion, min [IQR]	27 [24-37]	28 [24-34]	1	0.91
Missing	*30*	*3*		
Time from asystole to delivery of cardioplegia, min [IQR]	13 [10-14]	13 [11-14]	0	0.21
Missing	*31*	*6*		
Time from SBP <50 mm Hg to delivery of cardioplegia, min [IQR]	15 [13-18]	17 [14-19]	2	0.06
Missing	*45*	*12*		
[CIT] Time from cardioplegia to reperfusion, min [IQR]	10 [8-13]	13 [9-19]	3	**0.03**
Missing	*35*	*15*		
Asystole to blood reperfusion, min [IQR]	24 [21-30]	26 [24-30]	2	0.35
Missing	*14*	*12*		
OCS perfusion time, min [IQR]	242 [200-300]	258 [216-306]	16	0.22
Missing	*10*	*2*		

Ischemic times by retrieval method in JIF period

	Method A $n = 25$	Method B $n = 20$		p value
WLST to confirmation of death, min [IQR]	19 [17-20]	19 [18-20]	0	0.91
Missing	*3*	*0*		
[DWIT] WLST to blood reperfusion, min [IQR]	36 [33-38]	42 [38-47]	6	**0.0016**
Missing	*6*	*5*		
[FWIT] SBP <50 mm Hg to reperfusion, min [IQR]	25 [22-27]	33 [26-37]	8	**0.0026**
Missing	*0*	*2*		
Time from asystole to delivery of cardioplegia, min [IQR]	13 [12-14]	13 [11-13]	0	0.23
Missing	*3*	*3*		
Time from SBP <50 mm Hg to delivery of cardioplegia, min [IQR]	18 [14-19]	17 [13-19]	1	0.70
Missing	*8*	*4*		
[CIT] Time from cardioplegia to reperfusion, min [IQR]	9 [8-11]	15 [15-19]	6	**0.0001**
Missing	*7*	*7*		
Asystole to blood reperfusion, min [IQR]	24 [19-28]	28 [26-32]	4	**0.0008**
Missing	*6*	*5*		
OCS perfusion time, min [IQR]	258 [228-302]	249 [186-301]	9	0.34
Missing	*0*	*2*		

CIT, cold ischemic time; DWIT, donation withdrawal ischemic time; FWIT, functional warm ischemic time; IQR, interquartile range; JIF; joint innovation fund; OCS, Organ Care System; SBP, systolic blood pressure; WLST, withdrawal of life sustaining treatment.

The significance of the bold values in the table is statistical significance of p value <0.05.

DCD heart transplant centers sharing their experience and learning and supporting less experienced centers as well as aiming for a joint national implant protocol.

Variation also exists in the national DCD heart retrieval protocol in both the way the DCD heart is procured and cannulated on the OCS. This variation has resulted in the average time from donor systolic blood pressure < 50 mm Hg to heart re-perfusion for the hearts in method B to be 8 minutes longer than method A. Although this prolonged ischemic time did not translate into higher ECMO rates (Table 5), the lower 30-day survival may reach significance as the program expands. (85% method B compared to 100% method A, $p = 0.07$). The Papworth experience would suggest that the best outcomes for DCD hearts are achieved when the FWIT is below 30 minutes.[19] A learning point from this study has been to have an evidence based, single national agreed protocol in order to minimize all ischemia times.

The Sydney experience has shown that time from asystole to administration of cardioplegia is an important factor with times over 15 minutes associated with higher rates of ECMO.[17] In a recent update of the Sydney experience, they report reducing ECMO rates post DCD heart transplant from 35% to 8% in the most recent era.[15] They have attributed this to avoiding hearts with >15 minutes from asystole to delivery of cardeoplegia and adding Tirofiban which aids blood collection buts also may have a cardioprotective role.[15]

A challenge of the national program has been sustaining manpower whilst maintaining expertise in the specialized teams. After time, the Wythenshawe team left the program due to a shortage of perfusion staff during the COVID-19 pandemic resulting in a hybrid team from the other centers. This

Table 4 JIF Donor and Recipient Demographics by Retrieval Technique

	Method A *n* = 25	Method B *n* = 20	*p* value
Donor demographics			
Age, years [Std DEV]	34 [11]	30 [11]	0.49
Sex male, *n* [%]	16 [64]	16 [80]	0.33
Blood group			
A, *n* [%]	10 [40]	8 [40]	-
B, *n* [%]	2 [8]	2 [10]	
O, *n* [%]	12 [48]	10 [50]	
AB, *n* [%]	1 [4]	0 [-]	
Cause of death			
HBI, *n* [%]	14 [56]	12 [60]	0.75
TBI, *n* [%]	2 [8]	3 [15]	
ICH, *n* [%]	6 [24]	5 [25]	
Thrombosis, *n* [%]	2 [8]	0 [-]	
Tumor, *n* [%]	1 [4]	1 [4]	
Height, cm [Std DEV]	174 [11.4]	178 [8.1]	0.10
Recipient demographics			
Age, years [IQR]	46 [25-51]	55 [46-59]	**0.04**
Sex male, *n* [%]	19 [76]	18 [90]	0.27
Height, cm [IQR]	176 [166-180]	176 [167-179]	0.84
Blood group			
A, *n* [%]	15 [60]	10 [50]	0.64
B, *n* [%]	3 [12]	5 [25]	
O, *n* [%]	6 [24]	5 [25]	
AB, *n* [%]	1 [4]	0 [-]	
Diagnosis			
IHD, *n* [%]	2 [8]	4 [20]	0.67
CHD, *n* [%]	4 [16]	1 [5]	
DCM, *n* [%]	13 [52]	12 [60]	
HCM, *n* [%]	4 [16]	2 [10]	
RCM, *n* [%]	1 [4]	0 [-]	
other, *n* [%]	1 [4]	1 [5]	
Urgency			
Nonurgent, *n* [%]	11 [44]	8 [40]	-
Urgent, *n* [%]	9 [36]	8 [40]	
Super-urgent, *n* [%]	5 [20]	4 [20]	
Creatinine, mmol/Liter, [IQR][a]	90 [77-129]	97 [84-116]	0.78
Missing	*0*	*0*	
Pre-tx VAD/ECMO, n[%]	9 [36]	6 [30]	0.76

CHD, congenital heart disease; 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; IQR, interquartile range; RCM, restrictive cardiomyopathy; TBI, traumatic brain injury; VAD, ventricular assist device; VHD, valvular heart disease; pre-tx, pretransplant; ECMO, extra corporeal membrane oxygenation; StdDEV, standard deviation.

The significance of the bold values in the table is statistical significance of p value <0.05.

[a]Creatinine at listing for transplantation.

Table 5 JIF Posttransplant Recipient Outcomes by Retrieval Technique

	Method A *n* = 25	Method B *n* = 20	*p* value
Survival			
30-day, % [95% CI]	100 [-]	85 [60 - 95]	0.07
90-day, % [95% CI]	91 [67 - 98]	85 [60- 95]	0.51
1 year, % [95% CI]	91 [67 - 98]	74 [48 - 92]	0.38
Mechanical circulatory support posttransplant			
IABP, *n* [%]	3 [12]	1 [5]	0.62
ECMO, *n* [%]	11 [44]	8 [40]	-
VAD, *n* [%]	0 [-]	1 [5]	0.44
Posttransplant outcomes			
Ventilation, days [IQR]	5 [2-20]	3 [2-12]	0.70
Missing	*6*	*1*	
Hemofiltration, *n* [%]	16 [67]	11 [55]	0.54
Missing	*1*	*0*	
ICU stay, days [IQR]	10 [4-24]	9 [7-19]	0.56
Missing	*6*	*3*	
Hospital stay, days [IQR]	28 [18-46]	32 [28-66]	0.27
Missing	*6*	*5*	
Treated rejection episode in 30 days, *n* [%]	2 [8]	2 [5]	-
Missing	*1*	*1*	
Treated rejection episode in 90 days, *n* [%]	3 [13]	0 [-]	0.26
Missing	2	*4*	

DBD, donation after brain death; DCD, donation after circulatory-determined death; ECMO, extra corporeal membrane oxygenation; IABP, intra aortic balloon pump; ICU, intensive care unit; IQR; intra quartile range; JIF, joint innovation fund; VAD, ventricular assist device.

resulted in the transplant practitioners and ex situ practitioners in Papworth being on call for 3 weeks in 4. Unless properly resourced, this would be unsustainable. To address this a further UK retrieval team has been trained in DCD heart retrieval. It became clear during the pilot that the scarcity of clinically trained perfusionists (that can run a cardiopulmonary bypass machine) could have a significant impact on the sustainability of DCD heart retrieval in the long term. The pilot has shown that nurse practitioners and other clinical professionals can be successfully trained to operate the OCS.

Currently DCD hearts are offered on the basis of allocation zone. DCD hearts are not offered on the basis of urgency of recipient. Consequently, the results for the pilot have shown that DCD hearts have been transplanted in more nonurgent patients than urgent patients in comparison to DBD. This has resulted in centers transplanting hearts for recipients stable at home where it could have been used to transplant a clinically more urgent recipient in another center on temporary mechanical circulatory support. Nevertheless, this approach allowed newer centres with relatively little or no experience to apply the caution that the more experienced centres had employed during their early days of DCD heart transplantation, whilst experienced centres could transplant into urgent/super-urgent recipients.

Table 6 ECMO for Severe Primary Graft Dysfunction by Implanting Centre

Centre	A	B	C	D	E	F	G	*p* value
Number of DCD heart transplants	13	13	13	3	1	3	4	
ECMO, *n* [%]	7 [54]	3 [23]	2 [15]	3 [100]	1 [100]	0 [-]	4 [100]	**0.0013**

Limitations

The limitations of the study are that it is a small observational pilot that was restricted to 18 months. Only short-term outcome data is known and there was some missing data with respect to key variables.

Conclusion

This pilot has shown that UK DCD heart retrieval can be performed successfully by teams trained in ex situ heart perfusion to serve all national transplant centers. The program delivered 30-day, 90-day and 1 year survival that is comparable to DBD heart transplants and previously reported single center experiences whilst increasing overall hearts transplant activity by 28%.

Disclosure

The authors have no conflicts of interest to declare.

This research was funded by the National Health Service Blood and Transplant and National Health Service England.

Appendix 1. Donor Inclusion and Exclusion Criteria

- Maastricht Category III and IV DCD donors
- Consent for heart donation
- Age up to 50 years (up to the day before the 51st birthday)
- Weight > 50kg—routine inclusion
- Weight between 40 and 50 kg—inclusion under certain circumstances
- No valvular abnormalities and left ventricular ejection fraction >50% on transthoracic echocardiogram before WLST
- WLST close to theatre
- Expected death within 4 hours of WLST
- Previous midline sternotomy
- Valvular heart disease
- Congenital heart disease
- Significant coronary artery disease
- Chronic atrial fibrillation
- Insulin dependent diabetes
- Virology: HIV +
- Current IV drug abuse
- Tumor with high risk of transmission according to NHSBT and SABTO guidelines
- Coronary artery disease: history of chronic stable angina, myocardial infarction, CABG or percutaneous coronary intervention (PCI)
- Median sternotomy for cardiac surgery
- LVEF $\leq$30%
- Myocarditis
- Lyme disease
- Primary cerebral lymphoma
- All secondary intracranial tumors
- Any active cancer with evidence of spread outside affected organ within 3 years of donation
- Malignant Melanoma
- Active (not in remission) hematological malignancy (myeloma, lymphoma, leukemia)
- Definite, probable or possible case of human transmissible spongiform encephalopathy (TSE including CJD and vCJD, individuals whose blood relatives have had familial CJD, other neurodegenerative diseases associated with infectious agents.
- Tuberculosis: active and untreated or during first 6 months of treatment. (Organs can be considered for transplant if the donor has received a minimum of 6 months of appropriate antituberculous treatment, unless the isolate is found to be drug-resistant).
- West Nile Virus (WNV) infection
- HIV disease (not HIV infection only
- A history of infection with Ebola virus
- Bacillus anthracis (Anthrax)
- Dengue Virus
- Proven Corona Virus without recovery (Corona Virus infection includes COVID-19, SARS and MERS)
- Rabies
- Yellow fever
- Viral hemorrhagic fevers - including Lassa, Ebola, Marburg and CCHF viruses
- Chikungunya virus (Donation can be considered 6 months postrecovery)
- Progressive Multifocal Leukoencephalopathy (PML)
- Zika virus (Donation may be considered 6 months after recovery)
- Systemic infection with candida/aspergillus/other fungi/endemic mycoses

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