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; IHD, Ischaemic Heart Disease; 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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A National Pilot of Donation After Circulatory Death (DCD) Heart Transplantation Within the United Kingdom

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A National Pilot of Donation After Circulatory Death (DCD) Heart Transplantation Within the United Kingdom

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Abstract

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 centres 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 programme are reported.

Methods:

This is a national multi-centre, retrospective cohort study examining early outcomes of DCD heart transplants performed across 7 heart transplant centres, adult and paediatric, throughout the UK. Hearts were retrieved using the direct procurement and perfusion (DPP) technique by three 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 7th September 2020 to 28th February 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 centres. DCD donors increased overall heart transplantation in the UK by 28% with equivalent early post-transplant survival compared with DBD donors.

Keywords
Heart; transplant; circulatory death; circulatory determined death; ex-situ heart perfusion system

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)

IHD (Ischaemic Heart Disease)

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)

Introduction:

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 utilising the direct procurement and perfusion (DPP) technique,[4] and the world's first DCD heart transplant utilising TANRP / cold storage was reported.[5] This was followed by the first paediatric 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 centre experience of both adult[8] and paediatric[9] DCD heart transplants. In addition the UK was fist to describe combined abdominal NRP and direct procurement of the DCD heart.[10]

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

As several UK single centre 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 specialised *ex situ* machine perfusion service into the pre-existing 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 programme, between 7th September 2020 and 28th February 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 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 centres. The first offer was made to the transplant centre in whose allocation zone the donor hospital was located. The order of the subsequent centre 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 non-urgent 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 one additional member. The on-call team provided a 7-day 24 hour rolling rota cover. The three retrieval teams were Royal Brompton and Harefield Hospital (RBHT) and Wythenshawe Hospital which provided one week cover each and Royal Papworth Hospital (RPH) which contributed two-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 centre, 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 utilisation of this technique in the UK. Similar debate is occurring within other countries.[13] Therefore, only the DPP technique was utilised 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. 500mls St Thomas' s cold crystalloid cardioplegia supplemented with the post conditioning 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 centre 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 channelled 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 four 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 ¼" tubing producing a partially loaded right ventricle.

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

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

Recipients:

No restrictions were placed on DCD heart recipients in this trial in relation to urgency status, aetiology of heart failure, transpulmonary gradient, or long-term ventricular assist device (VAD) or extra corporeal membrane oxygenation (ECMO). On arrival at the recipient centre, once the implanting surgeon was ready for the donor heart, OCS perfusion would be discontinued and 1 litre 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 centre.

Statistical Analysis:

Data were extracted from the UK Transplant Registry held by NHSBT on 14th June 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 summarised 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 eighteen-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 COVID19 pandemic. To cover this one 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 utilisation 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 haemorrhage 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 non-urgent 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 was variations in transplant rates across the 7 transplant centres. During this study period, a large proportion of the DCD heart transplants (78%) were carried out by three transplant centres who performed 13 DCD heart transplants each. The other 4 centres only performed 11 DCD hearts transplants between them.

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 ninety-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 one-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 post-transplant in the JIF DCD trial group (40%vs 16%, p=0.0006). In comparison to the pre-JIF era, although there were fewer intra-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 post-transplant ECMO utilisation was reflected in the post-transplant 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).

Ischaemic Timings

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

The JIF ischaemic 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 mins, p=0.91). Method B had a longer time from treatment withdrawal to blood re-perfusion compared to method A (42 mins vs 36 mins, p=0.0016) and a longer time from donor systolic <50mmHg to donor heart re-perfusion, (33 mins versus 25mins p=0.0026). There was no significant difference in the time from donor asystole to delivery of cardioplegia (13minutes) between the two 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 two methods (A 258 versus B 249 minutes, p=0.34).

The donor and recipient characteristics of the hearts retrieved across the two 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 centre 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 programme with hearts retrieved by direct procurement and ex situ machine perfusion using a national specialist retrieval service.

The national DCD heart transplant programme 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 centres before the national JIF study.[8] There was a high utilisation rate of DCD hearts (88%) in the study which was higher than single centre experiences described by both Papworth (76%) [8] and most recently Sydney (72%).[15] A possible reason for such a high utilisation 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 centre experiences; Papworth 18% [8] and Sydney 31%,[17] and is more than double reported by the recent US multicentre trial of DCD hearts of 14-16%.[18]

There are several possible explanations for this high rate of severe primary graft dysfunction. When the ECMO utilisation rate per transplant centre was investigated it was evident that three transplant centres with low experience of DCD heart transplantation had a 100% ECMO rate post- transplant,

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 ischaemic 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 minimising the warm ischaemic time. Potentially a further way to reduce the high incidence of ECMO would be for the more mature DCD heart transplant centres sharing their experience and learning and supporting less experienced centres 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 < 50mmHg to heart re-perfusion for the hearts in method B to be 8 minutes longer than method A. Although this prolonged ischaemic time did not translate into higher ECMO rates (Table 5), the lower thirty-day survival may reach significance as the programme 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 minimise all ischaemia 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 from 35% to 8% in the most recent era.[15] They have attributed this to avoiding hearts with >15minutes 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 programme has been sustaining manpower whilst maintaining expertise in the specialised teams. After time, the Wythenshawe team left the programme due to a shortage of perfusion staff during the COVID19 pandemic resulting in a hybrid team from the other centres. This 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. In order 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 non-urgent patients than urgent patients in comparison to DBD. This has resulted in centres transplanting hearts for recipients stable at home where it could have been used to transplant a clinically more urgent recipient in another centre on temporary mechanical circulatory support.

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 centres. The programme delivered 30-day, 90-

day and 1 year survival that is comparable to DBD heart transplants and previously reported single centre experiences whilst increasing overall hearts transplant activity by 28%.

Funding

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

Declaration of Competing Interest

None

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 40-50kg – inclusion under certain circumstances • No valvular abnormalities and left ventricular ejection fraction >50% on transthoracic echocardiogram prior to 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 • Tumour 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≤30% • Myocarditis • Lyme disease • Primary cerebral lymphoma • All secondary intracranial tumours • Any active cancer with evidence of spread outside affected organ within 3 years of donation • Malignant Melanoma - please refer to section below on when donors with malignant melanoma may be considered • Active (not in remission) haematological malignancy (myeloma, lymphoma, leukaemia) • 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 anti-tuberculous 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 haemorrhagic fevers - including Lassa, Ebola, Marburg and CCHF viruses • Chikungunya virus (Donation can be considered 6 months post recovery) • 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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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]	
Tumour, 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						
Non-Urgent, 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,	10 [8]	9 [18]		9 [18]	36 [20]	

n[%]						
Height, cm [IQR]	174 [167-179]	176 [167-180]	0.74	176 [167-180]	168 [159-175]	**0.0016**
Creatinine, mmol/L, [IQR]*	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, pre-transplant; ECMO, extra corporeal membrane oxygenation; StdDEV, standard deviation; IQR, interquartile range; *Creatinine at listing for transplantation

Table 2. Post-Transplant 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 Post-Transplant						
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
Post Transplant 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; IABP, intra aortic balloon pump; ECMO, extra corporeal membrane oxygenation, JIF; joint innovation fund; VAD; ventricular assist device, ICU, intensive care unit; IQR; intra quartile range

Table 3. DCD Donor Heart Ischaemic 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<50mmHg 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<50mmHg 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*		
Ischaemic 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<50mmHg 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<50mmHg 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*		

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

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			0.75
HBI, n [%]	14 [56]	12 [60]	
TBI, n [%]	2 [8]	3 [15]	
ICH, n [%]	6 [24]	5 [25]	
Thrombosis, n [%]	2 [8]	0 [-]	
Tumour, 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			0.64
A, n [%]	15 [60]	10 [50]	
B, n [%]	3 [12]	5 [25]	
O, n [%]	6 [24]	5 [25]	
AB, n [%]	1 [4]	0 [-]	
Diagnosis			0.67
IHD, n [%]	2 [8]	4 [20]	
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			-
Non-Urgent, n [%]	11 [44]	8 [40]	
Urgent, n [%]	9 [36]	8 [40]	
Super-Urgent, n [%]	5 [20]	4 [20]	
Creatinine, mmol/L, [IQR]*	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, ischaemic heart disease; IQR, interquartile range; NRP,;

RCM, restrictive cardiomyopathy; TBI, traumatic brain injury; VAD, ventricular assist device; VHD, valvular heart disease; pre-tx, pre-transplant; ECMO, extra corporeal membrane oxygenation; StdDEV, standard deviation; IQR, interquartile range; *Creatinine at listing for transplantation

Table 5. JIF Post-Transplant 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 Post-Transplant			
IABP, n [%]	3 [12]	1 [5]	0.62
ECMO, n [%]	11 [44]	8 [40]	-
VAD, n [%]	0 [-]	1 [5]	0.44
Post Transplant Outcomes			
Ventilation, days [IQR] ***Missing***	5 [2-20] *6*	3 [2-12] *1*	0.70
Hemofiltration, n [%] ***Missing***	16 [67] *1*	11 [55] *0*	0.54
ICU stay, days [IQR] ***Missing***	10 [4-24] *6*	9 [7-19] *3*	0.56
Hospital stay, days [IQR] ***Missing***	28 [18-46] *6*	32 [28-66] *5*	0.27
Treated rejection episode in 30 days, n [%] ***Missing***	2 [8] *1*	2 [5] *1*	-
Treated rejection episode in 90 days, n [%] ***Missing***	3 [13] 2	0 [-] *4*	0.26

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

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

Figure 1. DCD Donors Offered and Transplanted

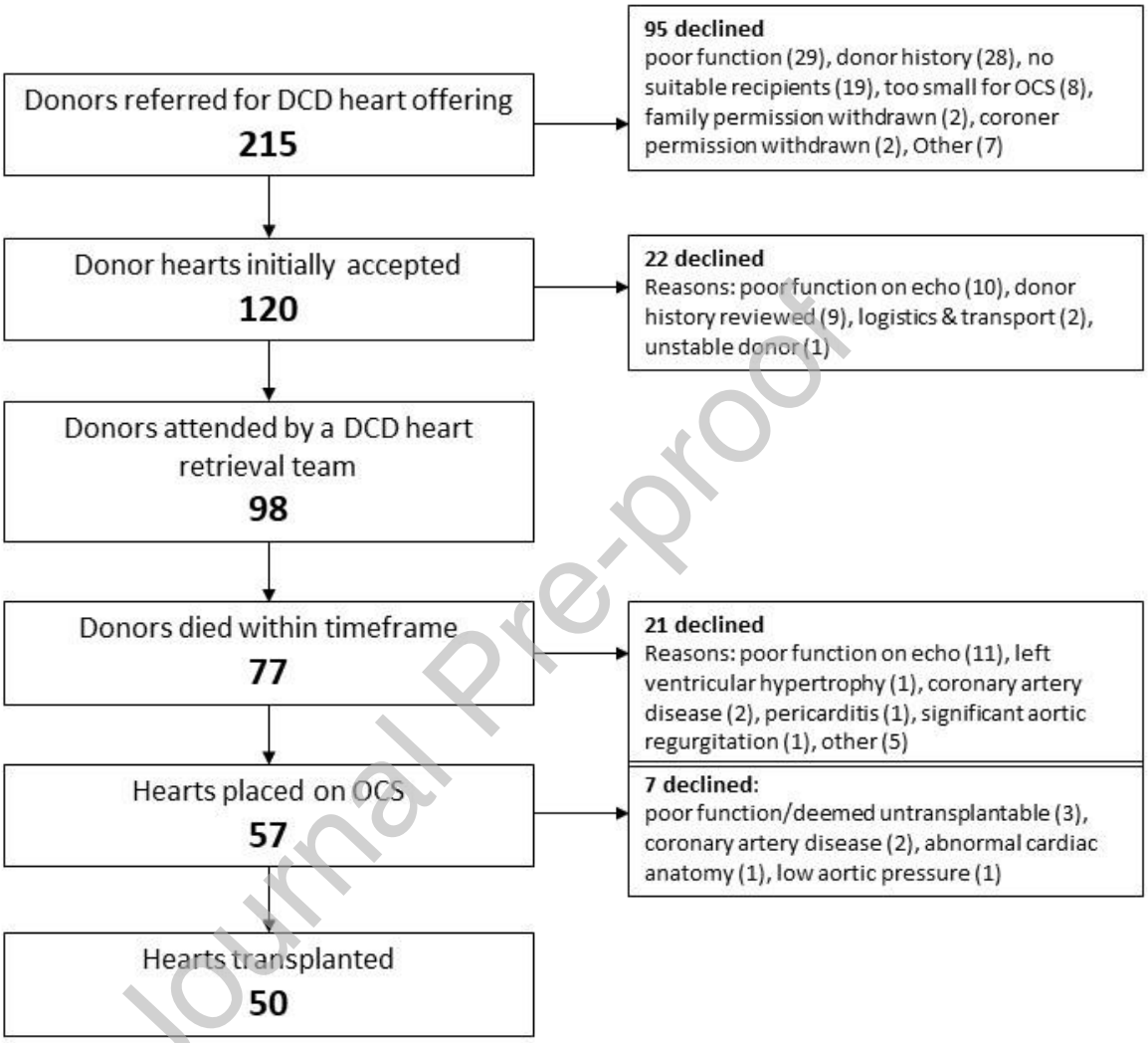
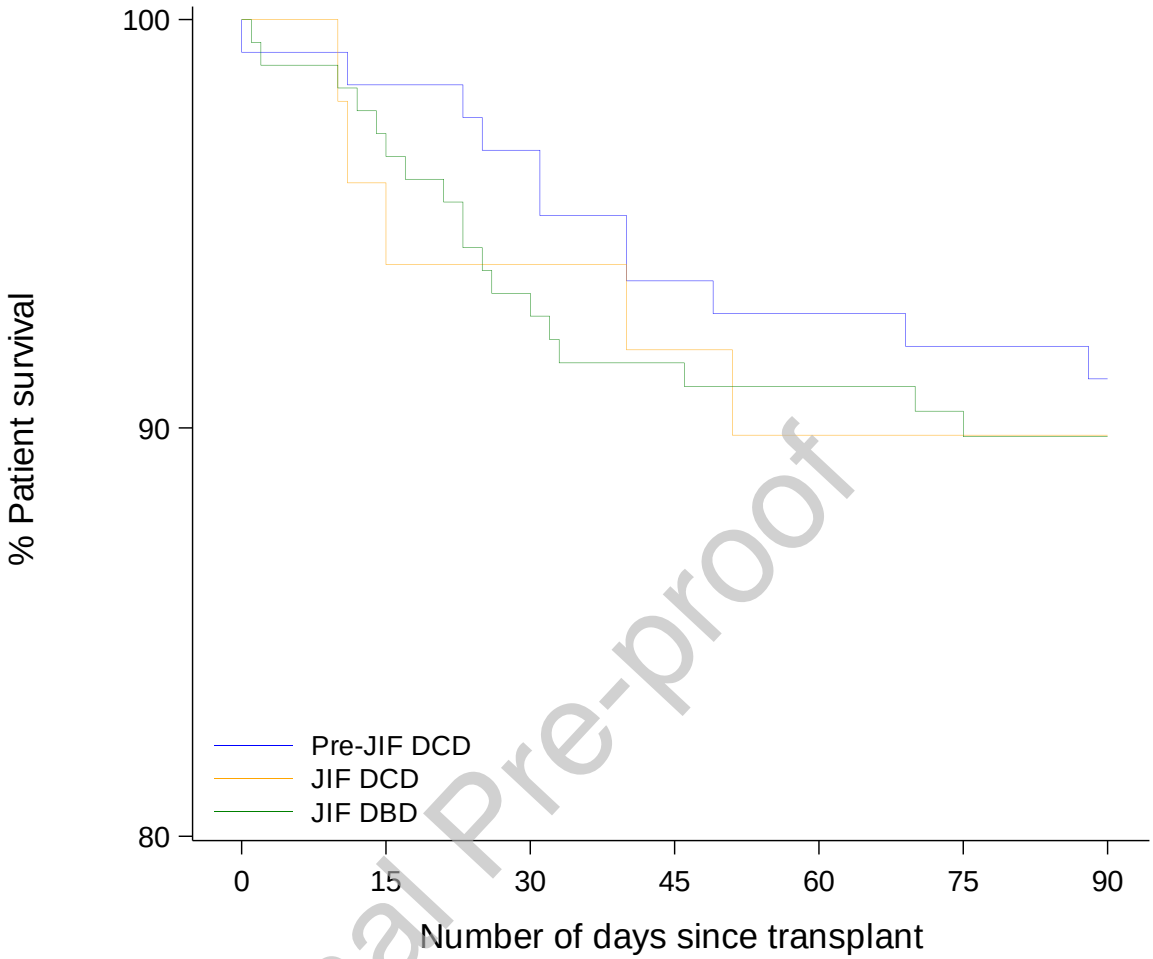


Figure 2. 90 day survival for pre-JIF DCD, JIF DCD and JIF DBD recipients



Number at risk							
Pre-JIF DCD	125	123	121	117	116	115	114
JIF DCD	50	48	47	44	43	41	29
JIF DBD	179	174	167	159	158	145	105