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Article

Comparing Procurement Methods in Donation after Circulatory Death Heart Transplantation: An Analysis of the UNOS Registry

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Abstract

Background: In donation after circulatory death (DCD) heart transplants, choosing an optimal procurement method between normothermic regional perfusion (NRP) and direct procurement and preservation on the TransMedics Organ Care System (OCS) remains an important consideration. Thus, we aimed to evaluate long-term outcomes between NRP and OCS in DCD heart transplants. **Methods**: Using the UNOS registry, we queried all adults (≥18 years old) undergoing DCD and donation after brain death (DBD) heart transplantation between December 2019 and September 2023. TransMedics OCS donors were defined by time from death to clamp ≤30 minutes. Comparatively, NRP donors were defined by time from death to clamp >30 minutes. Kaplan–Meier recipient and graft survival analyses were conducted. Multivariate Cox proportional hazard models were used to identify independent predictors of mortality. **Results**: We identified 11,767 DBD transplants, 507 OCS, and 265 NRP recipients. Acute rejection rates were not significantly different between groups ($p = 0.42$). However, significant differences in overall survival were identified between DBD, OCS, and NRP ($p = 0.019$). Nonetheless, this difference may be attributed to a significant decline in survival for OCS recipients at 3 years (60.7% vs. 78.8% for DBD vs. 83.3% for NRP). Moreover, there were significant differences in graft survival ($p = 0.02$), with NRP demonstrating superior outcomes at 3 years (83.3%) compared to 60.7% for OCS and 80.0% for DBD. **Conclusion**: Both procurement methods demonstrate comparable short-term survival and graft function. However, long-term outcomes are more favorable among NRP recipients than OCS and conventional DBD methods. Nevertheless, continued investigation is needed to understand why this mortality difference exists.

Keywords

donation after circulatory death; heart transplant; normothermic regional perfusion; donation after brain death; direct procurement and preservation; organ care system; ischemia time

Introduction

Orthotopic heart transplantation represents the gold standard for patients with end-stage heart failure [1,2]. With improved techniques for transplantation, perioperative care, and long-term immunosuppression therapies, survival has continued to extend beyond 10 years post-transplant [3]. However, the organ donor shortage remains a critical limiting factor in our ability to deliver heart transplants to more than 3000 patients on the waiting list in the United States [4]. While traditional donation after brain death (DBD) heart transplant remains the predominant strategy, transplanting donation after circulatory death (DCD) donors has been increasingly performed in the United States since 2019 with comparable outcomes to DBD [1,5–10]. In addition, DCD heart transplants have been shown to significantly increase donor organ pool and utilization [6,11].

DCD heart transplants are functionally different from DBD in that these donors experience asystole. Thus, the goal in optimizing DCD transplants is to (i) minimize warm ischemia time, (ii) transport hearts to the recipient without functional compromise, and (iii) assess functional capabilities before placing the allograft in the recipient. Currently, there are two widely used procurement strategies: normothermic *in-situ* regional perfusion (NRP) and direct procurement and preservation (DPP) using *ex-vivo* machine perfusion such as the Organ Care System (OCS) (TransMedics Inc., Boston, MA, USA). Recent studies have demonstrated comparable short-term outcomes between NRP and OCS in centers performing DCD heart transplants [1,6–9,12,13].

NRP has also proven more cost-effective than DPP [10]. However, the long-term survival and outcomes between NRP and OCS methods, especially relative to conventional DBD heart transplants, have yet to be examined. Thus, we aim to evaluate longitudinal utilization and long-term survival between NRP and OCS methods in DCD heart transplants compared to DBD.

Materials and Methods

Source of Data and Study Population

We utilized the United Network for Organ Sharing (UNOS) Standard Analysis and Research (STAR) database, which facilitates the Organ Procurement and Transplantation Network (OPTN). Due to the de-identified nature of the database, this study was deemed exempt from the Virginia Commonwealth University School of Medicine Institutional Review Board and complies with the International Society for Heart and Lung Transplantation (ISHLT) ethics statement. Due to the retrospective nature of the database, the need for informed consent for the study was also waived. We identified all adult patients (aged $\geq$18 years) listed for DCD and DBD heart transplants in the United States from December 1, 2019, to September 30, 2023. Patients who underwent multi-organ transplants or missing donor information were excluded. All donors were Maastricht class 3.

Determining Procurement Methodology

Since UNOS does not collect organ procurement techniques for each transplant case, we used the methodology established by Wall *et al*. [14] to distinguish between NRP and OCS. Death-to-cross clamp time $\leq$30 minutes was defined as OCS, while >30 minutes was defined as NRP [14]. However, given the concern that utilizing the 30-minute time mark may have misclassified a subset of patients, further subgroup analysis was performed to divide $\leq$30-minute group (OCS) into $\leq$10 minutes and >10 minutes and to divide the >30-minute group (NRP) into 31–40 minutes and >41 minutes.

Statistical Analysis

All recipients of heart transplants were stratified by the modes of their donor's death: DCD and DBD. DCD heart transplant recipients were further stratified into NRP and OCS. To better isolate the impact of procurement methods, NRP and DPP groups were compared within two sets of subgroups: with and without (presumed static cold storage) *ex vivo* machine perfusion on OCS. Recipient and matched donor characteristics were collected, with categorical variables reported as percentages and continuous variables reported as means with standard deviations (SD) or median with interquartile ranges (IQRs). The one-way analysis of variance (ANOVA) test was used to compare continuous variables following the Gaussian distribution.

In contrast, the Kruskal-Wallis test was used to compare continuous variables that do not follow the Gaussian distribution. Categorical variables were compared using Pearson's Chi-square test. Our outcomes of interest included recipient and primary graft survival at 30 days, 1-, and 3 years. We also analyzed postoperative outcomes such as length of hospital stay, acute rejection rates, and postoperative dialysis. The Kaplan-Meier method was used to plot and assess recipient and primary graft survival, and the log-rank test was used to compare cohort differences. We used multivariate Cox proportional hazard models to estimate the adjusted hazard ratios (HR) for NRP and OCS on the risk of mortality using recipient and donor comorbidities, donor cause of death, recipient diagnoses, age, sex, body mass index (BMI), and donor-recipient distance as covariates. All analyses were performed using R Statistical Software (version 4.3.1, R Core Team, 2020, Vienna, Austria). All p-values were based on two-sided statistical tests, with significance at $p < 0.05$.

Results

Baseline Recipient and Donor Characteristics

During the study period, 12,539 patients received isolated heart transplants, 507 of whom underwent DCD with OCS, 265 underwent DCD with NRP, and 11,767 underwent DBD. The number of DCDs has steadily increased since 2019, with most NRP used in 2022 compared to all previous years (Fig. 1).

Several differences in recipient characteristics were identified between cohorts (Table 1).

DCD NRP recipients were significantly older than DCD OCS and DBD groups ($p < 0.001$). Recipients of DCD NRP were much less likely to be females than other groups ($p < 0.001$) but had the highest BMI ($p < 0.001$). Both DCD OCS and NRP recipients were more likely to have diabetes compared to DBD recipients ($p = 0.004$). There were significant differences in primary cardiac diagnoses between groups ($p < 0.001$). Most notably, DCD NRP recipients were more likely to have required heart transplants due to ischemic cardiomyopathy compared to DCD OCS and DBD recipients. Importantly, DCD NRP recipients were least likely to have required pre-transplant circulatory support on extracorporeal membrane oxygenation (ECMO) compared to DCD OCS and DBD recipients ($p < 0.001$). We found no significant differences between groups' days spent on the waitlist ($p = 0.09$).

While donor BMI ($p = 0.79$) and age ($p = 0.31$) did not differ between groups, we found significant differences in the donor's mode of death between groups ($p = 0.0002$).

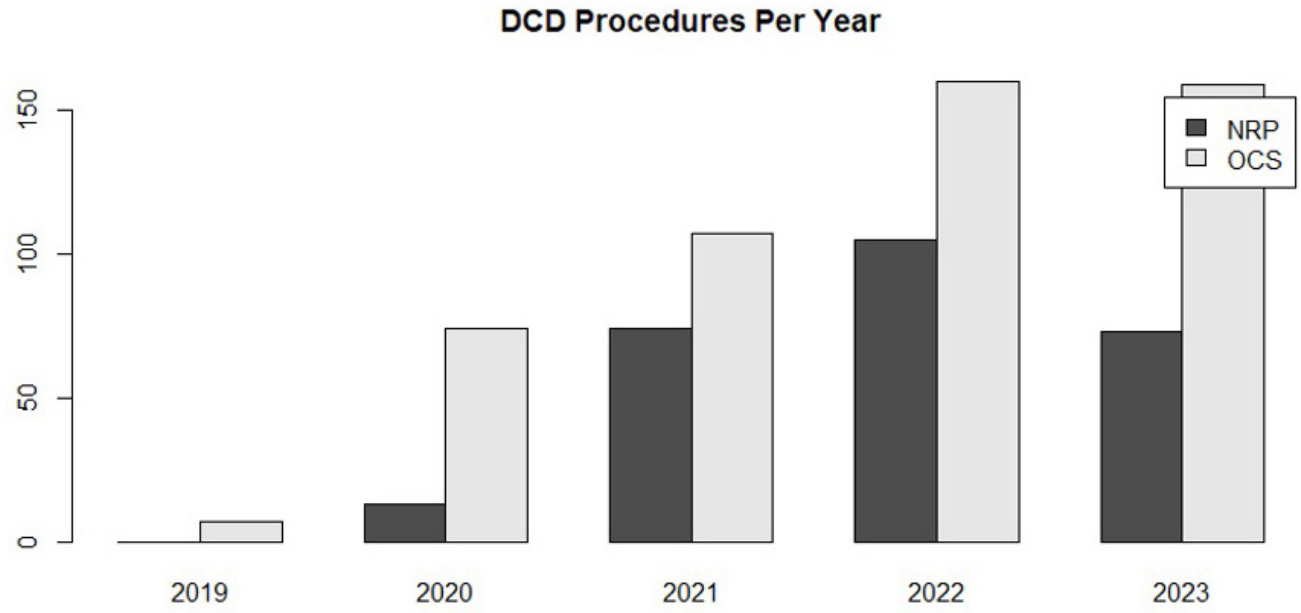

Fig. 1. The number of DCD heart transplants performed yearly from December 1, 2019, to September 30, 2023, was stratified by procurement methods (NRP vs. OCS). DCD, donation after circulatory death; NRP, normothermic regional perfusion; OCS, Organ Care System.

DCD NRP donors were less likely to have died by anoxia but much more likely to have experienced head trauma or central nervous system (CNS) tumor. As expected, there were significant differences between groups using *ex vivo* machine perfusion ($p < 0.001$). As expected, DCD OCS donors were most likely to have been preserved via *ex vivo* machine perfusion (79.68%). Notably, however, 33.21% of DCD OCS donor organs were also preserved via machine perfusion. DCD OCS donor organs traveled the shortest distance to the recipient transplant center than DCD OCS and DBD ($p < 0.001$).

Clinical Outcomes

There were significant differences in overall survival ($p = 0.019$) between groups (Fig. 2).

This is primarily attributed to the discrepancy in survival between DBD and DCD OCS donors ($p = 0.007$), particularly at 3 years (79.8% vs. 60.7%). There were no significant differences in overall survival between DBD and DCD NRP ($p = 0.47$) or DCD NRP and DCD OCS ($p = 0.094$). DCD NRP recipients experienced 98.2, 92.7, and 83.3% survival rates at 30-day, 1-, and 3-year intervals, respectively (Table 2).

We found significant differences in long-term graft survival ($p = 0.02$), with DCD NRP demonstrating 98.2, 92.7, and 83.3% survival at 30-day, 1-, and 3-year intervals compared to 95.9, 89.5, and 60.7% for DCD OCS at the same time intervals. There were no significant differences in acute rejection rates ($p = 0.42$). However, DCD OCS recipients were more likely to require postoperative dialysis ($p = 0.003$). We found substantial differences in length of hospital stay between groups ($p = 0.03$), with DBD (25.07 days) recipients requiring the most extended hospitalization compared to DCD OCS (22.60 days) and NRP (21.48 days).

Importantly, 33.21% of the DCD NRP group had also utilized OCS as a method of organ preservation. Thus, the impact of procurement methods (NRP vs. DPP) on recipient and graft survival were directly compared within subgroups of recipients whose hearts were either preserved via OCS or not. Among recipients of hearts which were preserved on OCS, we observed no significant differences in 3-year recipient ($p = 0.52$; Fig. 3A) and graft ($p = 0.41$, Fig. 3B) survival. However, among recipients of hearts which were not preserved on OCS, NRP conferred significant recipient ($p = 0.047$; Fig. 4A) and graft ($p = 0.046$; Fig. 4B) survival benefits at the 3-year time interval.

On multivariate Cox proportional hazard models, NRP was associated with significantly improved survival (HR 0.52, $p = 0.04$), while OCS was associated with increased risk of mortality (HR 1.44, $p = 0.01$) compared to conventional DBD (Table 3). However, *ex vivo* machine perfusion of the donor heart alone had no significant impact on survival (HR 1.02, $p = 0.37$). Furthermore, increased recipient age (HR 1.01, $p < 0.001$), BMI (HR 1.02, $p < 0.001$), and need for ventilator support at transplant (HR 2.12, $p < 0.001$) were associated with increased risk of mortality.

Furthermore, in DCD heart transplants, increased recipient age (HR 1.01, $p < 0.001$), BMI (HR 1.02, $p < 0.001$), and preoperative need for a ventilator (HR 2.12, $p < 0.001$) were associated with increased risk of mortality.

Table 1. Baseline recipient and donor characteristics by organ donation type and procurement methods.

Characteristics	DBD (N = 11,767)	DCD OCS (N = 507)	DCD NRP (N = 265)	*p*-value
Recipient Characteristics				
Age, Mean (SD)	46.67 (20.30)	53.17 (12.82)	54.73 (14.12)	<0.001
Females, N (%)	3517 (29.89%)	110 (21.70%)	52 (19.62%)	<0.001
BMI (kg/m^2), Mean (SD)	26.59 (5.85)	28.31 (4.88)	29.00 (5.00)	<0.001
Diabetes	2841 (24.14%)	149 (29.39%)	78 (29.43)	0.004
Primary Cardiac Diagnosis, N (%)				<0.001
Nonischemic Cardiomyopathy	6083 (51.70%)	278 (54.83%)	127 (47.92%)	
Ischemic Cardiomyopathy	2500 (21.25%)	124 (24.46%)	79 (29.81%)	
Hypertrophic/Restrictive Cardiomyopathy	947 (8.04%)	38 (7.49%)	18 (6.79%)	
Congenital Heart Disease	1194 (10.15%)	17 (3.35%)	8 (3.02%)	
Others/Unknown	1043 (8.76%)	50 (9.86%)	33 (12.45%)	
Days on Waitlist, Median (IQR)	34 (10–147.5)	40 (10–183)	30 (10–115)	0.09
ECMO at Transplant, N (%)	685 (5.82%)	8 (1.58%)	2 (0.75%)	<0.001
Ventilator at Transplant, N (%)	361 (3.07%)	1 (0.19%)	3 (1.13%)	<0.001
Donor Characteristics				
Age, Mean (SD)	29.65 (12.62)	30.03 (7.89)	29.81 (9.58)	0.79
Females, N (%)	3562 (30.27%)	75 (14.79%)	29 (10.94%)	<0.0001
BMI (kg/m^2), Mean (SD)	27.09 (6.73)	27.54 (6.18)	27.23 (6.92)	0.31
History of Cigarette Use, N (%)	1242 (10.87%)	46 (9.20%)	24 (9.19%)	0.35
Race and Ethnicity, N (%)				<0.0001
White	7039 (59.82%)	399 (78.70%)	204 (76.98%)	
Black	2141 (18.19%)	58 (11.44%)	15 (5.66%)	
Hispanic/Latino	2201 (18.70%)	41 (8.09%)	38 (14.33%)	
Others	386 (3.28%)	9 (1.78%)	8 (3.02%)	
Causes of Death, N (%)				0.0002
Anoxia	5572 (47.35%)	253 (49.90%)	121 (45.66%)	
Stroke	1304 (11.08%)	30 (5.92%)	19 (7.17%)	
Head Trauma	4592 (39.02%)	209 (41.22%)	114 (43.02%)	
CNS Tumor	43 (0.37%)	1 (0.19%)	2 (0.75%)	
Others	256 (2.18%)	14 (2.76%)	14 (5.28%)	
Ex-vivo Machine Perfusion, N (%)	332 (2.82%)	404 (79.68%)	88 (33.21%)	<0.001
LVEF (%), Mean (SD)	61.88 (6.80)	62.61 (7.06)	62.88 (7.11)	0.004
Donor-Recipient Distance (nautical miles), Median (IQR)	245 (110–407)	410 (193–609.5)	220 (28–406)	<0.001

Abbreviations: BMI, body mass index; CNS, central nervous system; DBD, donation after brain death; DCD, donation after circulatory death; ECMO, extracorporeal membrane oxygenation; OCS, Organ Care System; NRP, normothermic regional perfusion; LVEF, left ventricular ejection fraction; SD, standard deviation; IQR, interquartile range.

Table 2. Clinical outcomes of heart transplant recipients by matched organ donation type and procurement methods.

Outcomes	DBD (N = 11,767)	DCD OCS (N = 507)	DCD NRP (N = 265)	*p*–value
Acute Rejection, N (%)	1809 (15.37%)	79 (15.58%)	33 (12.45%)	0.42
Post-transplant Dialysis, N (%)	1548 (13.16%)	91 (17.95%)	43 (16.22%)	0.003
Length of Hospital Stay, Mean (SD)	25.07 (28.48)	22.60 (20.73)	21.48 (16.44)	0.03
Recipient Survival (%), Median (95% CI)				0.019
30–Days	97.1% (96.8–97.4%)	95.9% (94.0–97.8%)	98.2% (96.4–100%)	
1–Year	91.1% (90.4–91.6%)	89.5% (86.3–92.7%)	92.7% (88.7–96.9%)	
3–Years	79.8% (78.3–81.3%)	60.7% (46.7–78.9%)	83.3% (73.1–94.8%)	
Graft Survival (%), Median (95% CI)				0.02
30–Days	97.0% (96.7–97.4%)	95.9% (94.0–97.8%)	98.2% (96.4–100%)	
1–Year	91.0% (90.4–91.6%)	89.5% (86.3–92.7%)	92.7% (88.7–96.9%)	
3–Years	80.0% (78.5–81.5%)	60.7% (46.7–78.9%)	83.3% (73.1–94.8%)	

Abbreviations: CI, confidence intervals; DBD, donation after brain death; DCD, donation after circulatory death; OCS, Organ Care System; NRP, normothermic regional perfusion.

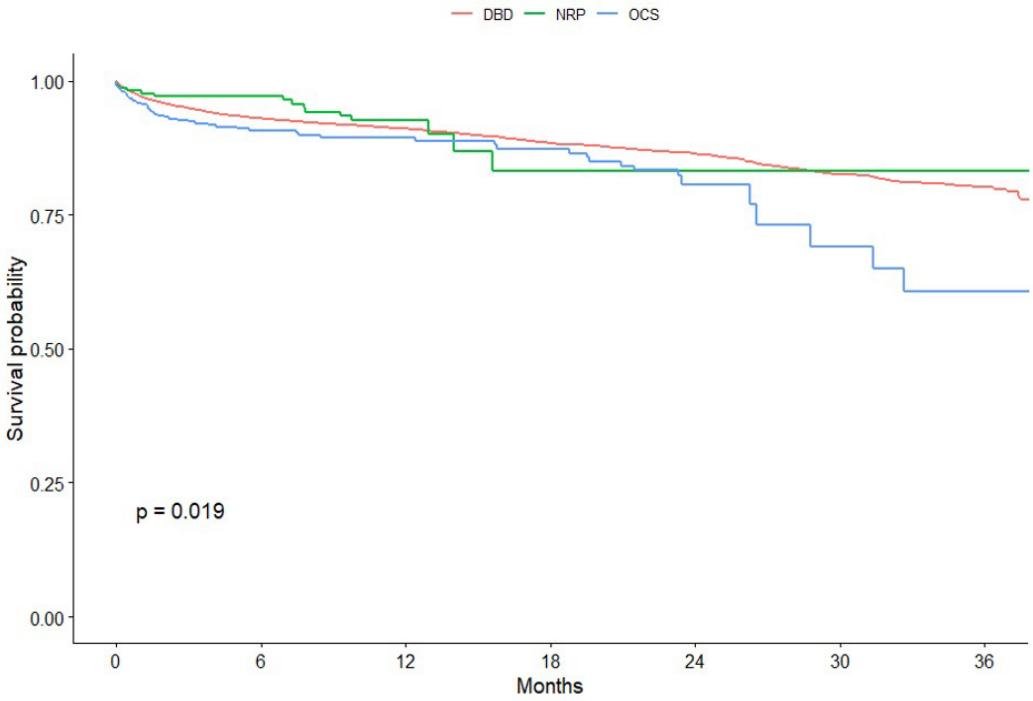

Fig. 2. Kaplan-Meier survival analyses between DBD, DCD NRP, and DCD OCS heart transplants. DBD, donation after brain death; NRP, normothermic regional perfusion; OCS, Organ Care System; DCD, donation after circulatory death.

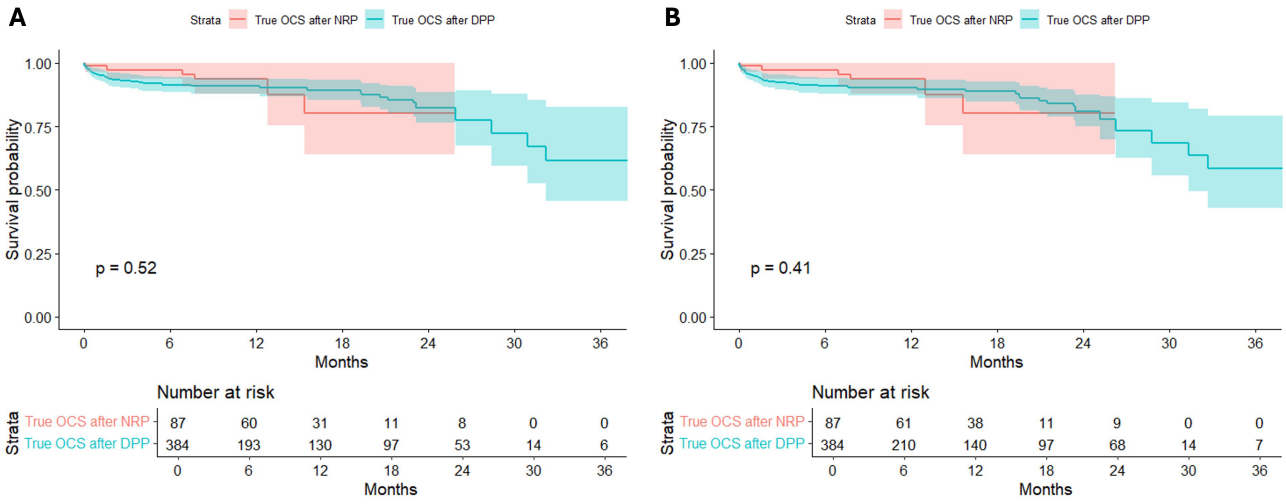

Fig. 3. Kaplan-Meier recipient (A) and graft (B) survival analyses between NRP and DPP among recipients of hearts preserved by *ex vivo* machine perfusion using OCS. Shaded regions indicate 95% confidence intervals; DPP, direct procurement and preservation; OCS, Organ Care System; NRP, normothermic regional perfusion.

Subgroup analyses between DCD NRP and OCS groups revealed a clear delineation between death-to-cross clamp times between the two procurement strategies (**Supplementary Fig. 1**).

Discussion

As DCD heart transplants become increasingly performed, many transplant centers may continue to evaluate DCD as a viable alternative to DBD. Choosing an optimal organ procurement and preservation method remains one of the most crucial decisions in improving recipient outcomes in DCD. In this study, we directly compared 3-year survival estimates between NRP and OCS procurement methods for all adult DCD heart transplants between 2019 and 2023, particularly in the context of conventional DBD heart transplants. Thus, this study represents the largest real-world cohort analysis of DCD heart transplants in the United States.

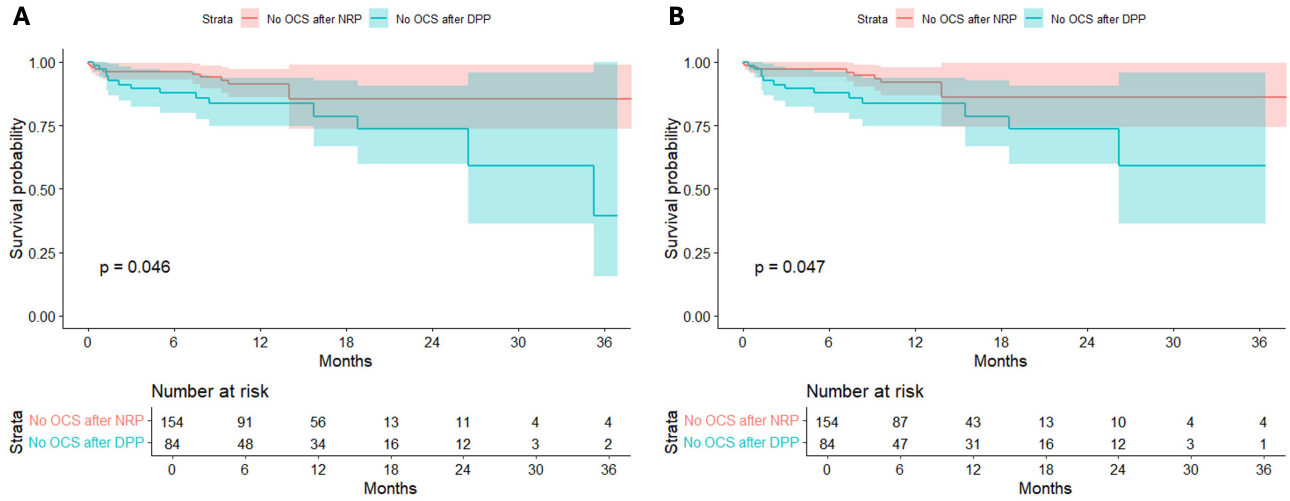

Fig. 4. Kaplan-Meier recipient (A) and graft (B) survival analyses between NRP and DPP among recipients of hearts that were not preserved by *ex vivo* machine perfusion using OCS. Shaded regions indicate 95% confidence intervals. DPP, direct procurement and preservation; OCS, Organ Care System; NRP, normothermic regional perfusion.

Table 3. Adjusted multivariate Cox regression analysis on mortality risk in DCD heart transplant.

Variables	Hazard Ratios	95% Confidence Intervals	*p*-value
Type of Donation/Procurement Methods (DBD as Reference)			
NRP	0.52	0.43–0.63	0.04
OCS	1.44	1.18–1.75	0.01
Recipient Age	1.01	0.83–1.23	<0.001
Recipient Sex (Male as Reference)	0.92	0.76–1.12	0.19
Recipient BMI	1.02	0.84–1.24	<0.001
Recipient on ECMO at Transplant	1.19	0.98–1.45	0.21
Recipient on Ventilator at Transplant	2.12	1.74–2.58	<0.001
Recipient Diabetes	1.09	0.9–1.33	0.23
Donor Organ Preserved via *Ex Vivo* Machine Perfusion	1.02	0.89–1.45	0.37

Abbreviations: BMI, body mass index; DBD, donation after brain death; DCD, donation after circulatory death; ECMO, extracorporeal membrane oxygenation; OCS, Organ Care System; NRP, normothermic regional perfusion.

Recipient and graft survival were broadly comparable between NRP and OCS at 30 days and 1 year. Importantly, our data indicates that the benefits of NRP over conventional DPP may be independent of organ preservation using OCS. However, after 3-years, recipients of DCD donor hearts procured and preserved via OCS experienced declining survival rates, particularly when compared to conventional DBD methods. In multivariate risk modeling, NRP conferred significant survival benefits, whereas OCS was associated with an increased risk of post-transplant mortality. However, this may be largely driven by the DPP methodology as opposed to the mode of organ preservation using OCS, as *ex vivo* machine perfusion for the heart alone had no impact on survival.

A recent study by Ran *et al*. [13] demonstrated similar findings in propensity score-matched analyses where NRP and OCS had comparable 1-year survival outcomes. Our findings extend these results to 3-years when survival trends diverge between NRP, OCS, and traditional DBD methods. While this may be due to significant differences in survival between DBD and OCS, our results may have more practical implications. In certain transplant centers and select patients, it may be more beneficial to offer DBD organs rather than DCD OCS organs, mainly if NRP is not a viable alternative. This is especially important as OCS is less cost-effective [8,15,16] and is associated with greater odds of organ nonuse or incomplete procurement runs [10]. NRP relies on a modified version of CPB but requires little in the way of more specialized equipment.

On the other hand, OCS requires the OCS system and single-use materials for each procurement. One cost analysis estimated each NRP transplant to cost about $4000, while OCS involved the console for $275,000 and single-use components costing between $40,000 and $55,000 [16]. Peled *et al*. [17] estimated the cost of *ex-situ* perfusion at about $57,000; in the case series of 15 patients who underwent successful NRP transplantation, the estimated savings were $850,000 compared to the anticipated cost of OCS. A

2024 single institution cost analysis estimated the cost per organ for NRP to be about $2550, compared to the cost for OCS, which was estimated at $80,000 per allograft. In other words, as the authors pointed out, a single OCS organ costs about as much as 31 organs procured with NRP [10]. Arguments can be made for the cost-benefit of earlier organ transplantation facilitated with DCD methodologies, especially compared with the anticipated costs of disease progression necessitating increased hospital and intensive care unit (ICU) admissions and mechanical circulatory support; however, the financial burden of OCS has likely delayed adoption by some centers [16–18].

Several previous studies have demonstrated the benefits of NRP in DCD heart transplants. A series of 15 patients transplanted via NRP with cold storage also showed positive outcomes. At 24 hours, cardiac indices were about 3.4 L/min/m^2, with LVEF >55 percent in all patients on postoperative day seven transesophageal echocardiogram. Of the 15 patients, three required temporary MCS postoperatively, but all were able to be weaned off and remained alive 30 days postoperatively. Of note, this study was the first to demonstrate good outcomes with longer ischemic times and in higher-risk donors, which suggests longer transport times may be feasible without needing *ex vivo* machine perfusion [15]. A notable advantage of NRP is the ability to perform a complete cardiac assessment before procurement, thus allowing surgeons to avoid procuring non-viable or borderline grafts and limiting the need for OCS [19]. On the other hand, functional evaluation of the donor's heart remains limited during direct procurement and preservation via OCS. In this strategy, much of the biochemical assessment of the heart function is relegated to arterial blood gasses and lactate trends, which may not correlate well with posttransplant graft survival [20]. In addition, NRP significantly reduces warm ischemic time, helping minimize the effects of ischemia-reperfusion injuries [21]. Ultimately, both procurement methods have advantages and disadvantages, and the decision between NRP and DPP with or without OCS should be made on a patient-by-patient basis. However, NRP should be the preferred procurement technique in DCD heart transplants to maximize recipient benefits even when OCS is not a viable option due to cost constraints.

The ethical debates surrounding the use of DCD merits further discussion. There is great heterogeneity regarding the definition of death, particularly when considering cultural and legal definitions with variations between countries and cultures. In NRP, a patient is pronounced dead secondary to circulatory arrest; following a standoff period, cardiac function is re-established for organ profusion and subsequent procurement. Clamping of arch vessels occludes cerebral perfusion and prevents travel of inflammatory mediators associated with brain death; however, there is a question of collateral facilitating perfusion [17]. In 2021, the American College of Physicians stated concern regarding the practice of NRP. The primary problem is that re-initiating circulation with successful resuscitation breached the definition of circulatory death [22]. The counterargument is that the surgical team ensures cessation of cerebral perfusion rather than inciting death. Animal studies have been performed demonstrating no meaningful cerebral activity.

Furthermore, when a variety of metrics are used to measure brain activity in donors, including nares perfusion and electroencephalogram (EEG) activity, the patients appear to remain brain dead despite reanimation of the heart [23]. Some centers routinely utilize cerebral perfusion monitoring; however, no standard guidelines exist [24]. A 2022 consensus statement from the ISHLT explored major ethical principles in the setting of NRP and offered the following recommendations: (i) the decision to donate must be an informed discussion with donor and family, with no element of coercion; (ii) appropriate measures should be taken to ensure donor comfort throughout the process; and (iii) determination of death must be carried out before transitioning to procurement [15,25].

A notable potential advantage of OCS over NRP is its ability to maintain normothermic perfusion over an extended period, which could enable donor organ procurement at distant sites. Previous studies have demonstrated optimal perfusion and allograft function for up to eight hours. This has shown to be of particular use when considering areas like Australia, where centers are very spread out and more extended distance travel may be necessary to facilitate procurements [6,7,26–28]. Finally, allograft function via biochemical evaluation is possible via lactate levels obtained from the aortic root and pulmonary artery cannula; levels greater than 5 mmol/L have been shown to predict post-transplant graft failure [29,30]. Monitoring of function can better enable the use of marginal grafts, also helping to expand the donor pool [31].

Finally, it is essential to acknowledge that most studies regarding OCS have only looked at short-term outcomes. Given the decreased three-year survival for OCS noted in this study, it is important to consider some mechanisms at play. Prolonged *ex-situ* perfusion has been associated with myocardial edema. However, this does not affect the graft or recipient in the short term; it may cause long-term effects by mediating an inflammatory response [31]. In a large retrospective study, Li *et al*. [32] noted increased rates of acute rejection across DCD donors compared to DBD donors, including in propensity-matched and subgroup analysis. Most patients in their cohort underwent DCD with OCS, with increased total ischemic time; ischemia is a well-established mediator of increased inflammatory cytokines. Long-term consequences of this initial inflammatory cascade may decrease overall survival [29,32]. However, this remains an area where considerable research is needed.

Limitations

First, it is retrospective and relies on the utilization of data from a registry, thus limiting the scope of information. Patients may have had significant comorbidities contributing to outcomes that could not be assessed given the methods. In addition, data was limited to patients within the United States, so outcomes from international centers with significant experience in both methods of DCD could not be included. Cutoff times were used as surrogates to assume OCS vs. NRP; however, it is possible that this was inaccurate; furthermore, there have been cases where grafts are procured via NRP and then stored on OCS, and authors were unable to account for this in statistics analysis. Additionally, time of death is not consistent between organ procurement organizations, with some reporting time of death after asystole and others reporting time of death after the standoff period. This means some patients may have been misclassified between the two groups. Finally, given the small sample size, confidence intervals were wide and continued to grow with more extended periods. Given the limited data available, it is difficult to interpret the decreased 3-year survival. The survival difference at three years may be due to chance alone and does not tell us definitively if there is a reduced survival given the wide confidence interval.

Conclusion

Using the UNOS database, we demonstrate that while short-term outcomes between NRP and OCS remain comparable in DCD heart transplants, NRP may confer additional survival benefits beyond three years post-transplant. On the other hand, OCS may be associated with an increased risk of mortality, particularly compared to conventional DBD heart transplants. As more transplant centers continue to consider DCD organs, the advantages and disadvantages of procurement strategies should be carefully evaluated to optimize outcomes for an ever-growing list of patients awaiting heart transplants.

Availability of Data and Materials

The data supporting this study's findings are available from UNOS/OPTN, but restrictions apply to their availability. These data were used under license for the current study and are not publicly available. Data are available from the authors upon reasonable request and with the permission of UNOS/OPTN.

Author Contributions

EB, GG, YCK: conceptualization, investigation, methodology, validation, visualization, writing-original draft, and writing-review and editing. MA: data curation, formal analysis, methodology, software, validation, and visualization. IFT, KBS, JC, VK, and ZAH: conceptualization, investigation, project administration, supervision, resources, writing-original draft, writing-review and editing. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

The study was carried out in accordance with the guidelines of the Declaration of Helsinki. As all data were de-identified, this study was exempt from the Virginia Commonwealth University School of Medicine Institutional Review Board. IRB approval was waived as the study was deemed exempt from review. Thus, no IRB approval number is relevant for this study.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.59958/hsf.8163.

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