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ORIGINAL RESEARCH

MECHANICAL CIRCULATORY SUPPORT/CARDIAC TRANSPORT

Early U.S. Heart Transplant Experience With Normothermic Regional Perfusion Following Donation After Circulatory Death

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ABSTRACT

BACKGROUND Heart transplantation following donation after circulatory death (DCD HT) has short-term survival outcomes comparable to donation after brain death and has led to a significant increase in transplantation volume. The U.S. experience with the normothermic regional perfusion (NRP) DCD HT procurement method has not been evaluated.

OBJECTIVES The aim of this study was to examine short-term outcomes associated with NRP vs direct procurement and perfusion (DPP) methods used during DCD HT in the United States.

METHODS The UNOS (United Network for Organ Sharing) registry was queried for all adult (age ≥18 years) heart recipients and corresponding donors of controlled DCD HT from January 2019-December 2023. Transplantations were stratified by NRP or DPP reperfusion methods. The primary outcome was overall survival.

RESULTS A total of 918 heart donors and recipients met inclusion criteria, including 622 (68%) DPP and 296 (32%) NRP transplantations. Unadjusted Kaplan-Meier survival analysis demonstrated improved short-term survival associated with NRP (log-rank $P = 0.005$). After adjustment, DCD HT with NRP was independently associated with improved survival (HR: 0.39 [95% CI: 0.22-0.70]; $P = 0.002$). A propensity-matched analysis similarly demonstrated a cumulative survival benefit to NRP (log-rank $P = 0.006$).

CONCLUSIONS In this largest national series of DCD HT procurement perfusion strategies, NRP is associated with improved short-term survival as compared with DPP. This study evaluates the U.S. early experience with DCD HT, and longer-term follow-up data are needed to further assess the impact of DPP and NRP methods on post-heart transplantation outcomes. (JACC Heart Fail. 2024;12:2073-2083) © 2024 by the American College of Cardiology Foundation.

Due to the mismatch of donor heart availability with the number of patients in need of heart transplantation, alternative donation and procurement methods have been evaluated in efforts to expand the donor pool. International experience[1-7] and a recent U.S. prospective randomized trial[8] of heart transplantation following donation after circulatory death (DCD HT) report short-term

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ABBREVIATIONS AND ACRONYMS

DCD HT = heart transplantation following donation after circulatory death

DPP = direct procurement and perfusion

LVAD = left ventricular assist device

MCS = mechanical circulatory support

NRP = normothermic regional perfusion

survival to be noninferior to that obtained with use of donation after brain death donors, suggesting that DCD HT is a viable transplantation strategy with potential to increase the donor pool. Notably, the adoption of DCD HT resulted in a 28% increase in the United Kingdom's donor pool.[9]

The risk of allograft injury during the warm ischemic time of a DCD HT procurement poses concerns regarding graft function upon implantation. To evaluate and enhance functional recovery following warm ischemia, 2 procurement reperfusion methods have been developed.[9,10] Direct procurement and perfusion (DPP) involves withdrawal of life-sustaining treatment and donor cardiectomy upon the confirmation of circulatory death; this method is routinely augmented with ex vivo perfusion and has been the prevailing strategy for DCD procurement in the United States. An alternative strategy, normothermic regional perfusion (NRP), uses extracorporeal circulation with the exclusion of the cerebral circulation to reperfuse and reanimate the donor heart in situ before cardiectomy.[10,11] Cited benefits of NRP include more rapid reperfusion after the period of warm ischemia for both the heart and abdominal organs, the ability to perform a physiological assessment of the allograft in situ, and cost-effectiveness.[9,11,12]

There has been recent increased clinical interest in the use of NRP; however, there is a lack of data regarding the U.S. national experience with this perfusion method. Therefore, we aimed to compare short-term recipient outcomes associated with NRP and DPP used during DCD heart procurement using a large national transplant registry.

METHODS

DATA SOURCE. The UNOS (United Network for Organ Sharing) OPTN (Organ Procurement and Transplantation Network) provided STAR (Standard Transplant Analysis and Research) files containing deidentified donor and recipient transplant data from January 2019 through December 2023. The database contains prospectively collected data on all solid organ transplantations performed in the United States during this period. This study was deemed exempt by the Institutional Review Board at Duke University.

STUDY POPULATION. The UNOS registry was queried for all adult (≥18 years of age) heart recipients and corresponding donors of controlled DCD HT from January 2019 to December 2023. This time period was selected as it coincides with the adoption of DCD HT in the United States. Recipients with prior transplants, undergoing multiorgan transplantation, and those with missing survival data were excluded from the analysis. We also excluded donors with a death to cross-clamp time >180 minutes or those with a missing time of death.

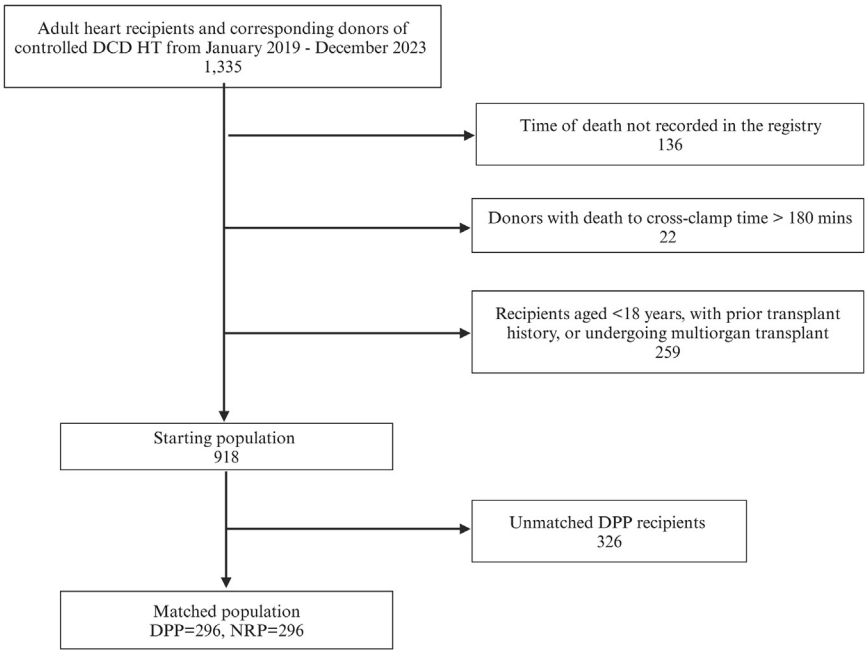
The reperfusion method used during DCD HT is not collected by UNOS; therefore, utilization of DPP and NRP were determined by using ancillary DCD data collected by UNOS. DPP and NRP redundant methods were distinguished by the length of time from circulatory standstill to cross-clamp for cold cardioplegia administration. DPP was defined as a death to cross-clamp time of <30 minutes; NRP was defined as a death to cross-clamp time between 31 and 180 minutes. This distinction between DPP and NRP procurements is assumed based on available published reports.[10,13-15] In addition, we performed a sensitivity analysis using our own center's patients and found that the time distinction used to identify DPP vs NRP reperfusion methods was accurate.

DATA ANALYSIS. Descriptive analysis of baseline donor and recipient characteristics was performed, stratified by perfusion strategy. Data are presented as median (Q1-Q3) for continuous variables and percent (count) for categorical variables, unless otherwise specified. Unadjusted comparisons between cohorts were performed using the Wilcoxon rank sum test for continuous variables and the Pearson chi square test or Fisher exact test for categorical variables, as appropriate. The Fisher exact test was used for analysis of variables with a small sample size and expected frequency <5.

Kaplan-Meier analysis was used to estimate unadjusted survival, with differences between cohorts assessed using the log-rank test. Adjusted post-transplant survival was modeled using a multivariable Cox proportional hazards model. Covariates were selected a priori based upon clinically relevant factors available within the data set and available degrees of freedom. In addition to procurement perfusion method used, covariates consisted of donor age, recipient age, recipient left ventricular assist device (LVAD) status, use of temporary mechanical circulatory support (MCS) before transplantation, and annualized heart transplant center volume. The proportional hazards assumption was assessed using the Schoenfeld test.

Propensity score matching was performed using a nearest neighbor algorithm and a standard caliper width of 0.1 of the SD of the propensity score. Patients were matched based on donor and recipient covariates including donor sex, age, body mass index,

FIGURE 1 Flowchart of Study Inclusion and Exclusion Criteria



The UNOS (United Network for Organ Sharing) registry was queried for all adult (≥18 years of age) heart recipients and corresponding donors of controlled heart transplantation following donation after circulatory death (DCD HT) from January 2019 to December 2023. After applying our exclusion criteria, the unmatched population consists of 918 recipients. Propensity matching resulted in 296 direct procurement and perfusion (DPP) recipients and 296 normothermic regional perfusion (NRP) recipients.

race/ethnicity, cause of death, and recipient sex, age, body mass index, race/ethnicity, medical condition at transplantation, waitlist status, heart failure etiology, and prior LVAD. Comparisons between post-matching cohorts were performed by examining standardized mean differences. Recipient survival was analyzed using the Kaplan-Meier method.

Two-sided values of $P \leq 0.05$ were considered statistically significant. All statistical analyses were performed using R software version 4.3.0 (R Foundation for Statistical Computing).

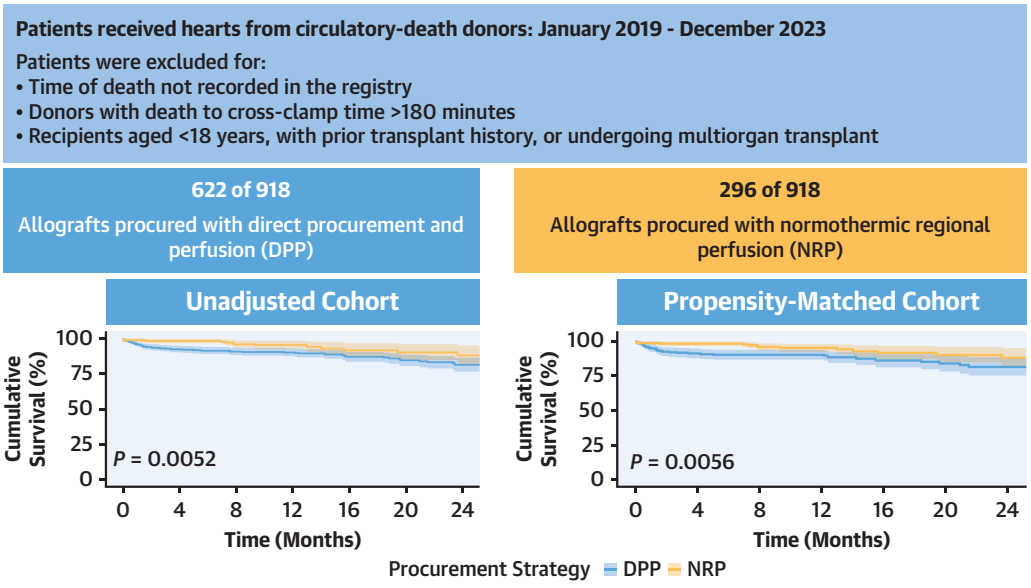
RESULTS

RECIPIENT AND DONOR CHARACTERISTICS. In total, 918 DCD HT recipients met inclusion criteria within the defined study period and were included for analysis, among which 622 (68%) and 296 (32%) received allografts that were perfused with DPP and NRP methods, respectively (**Figure 1, Central Illustration**). Among DCD donors who underwent heart procurement, the discard rate (number of hearts not transplanted divided by the total number of hearts recovered) was 9.6% for DPP and 1.4% for NRP.

Reported death to cross-clamp times are shown in **Figure 2**. Median time to cross-clamp was 7 minutes (Q1-Q3: 5-9 minutes) for DPP procurements compared with 72 minutes (Q1-Q3: 60-98 minutes) for NRP. As seen in the histogram, there are 2 distinct populations of donors on either side of the 30-minute cutoff time used for DPP vs NRP stratification.

Baseline characteristics of the donors and recipients are summarized in **Tables 1 and 2**, respectively. There were no significant differences between donor characteristics of allografts procured with DPP or NRP methods, importantly including heart function and donor cause of death. The median organ travel distance was significantly longer for DPP organs compared with NRP organs (400 miles vs 221 miles; $P < 0.001$). Recipients of NRP hearts were more likely to be older (median age 59 years vs 56 years; $P = 0.006$), have a history of malignancy (11.5% vs 7.1%; $P = 0.034$), and spend less time on the transplant waitlist (median 28 days vs 37 days; $P = 0.010$). Recipients of DPP hearts were more likely hospitalized and in the intensive care unit at the time of transplantation compared with NRP recipients ($P = 0.002$). DPP recipients were also more likely to

CENTRAL ILLUSTRATION **Kaplan-Meier Analysis of Overall Recipient Survival**



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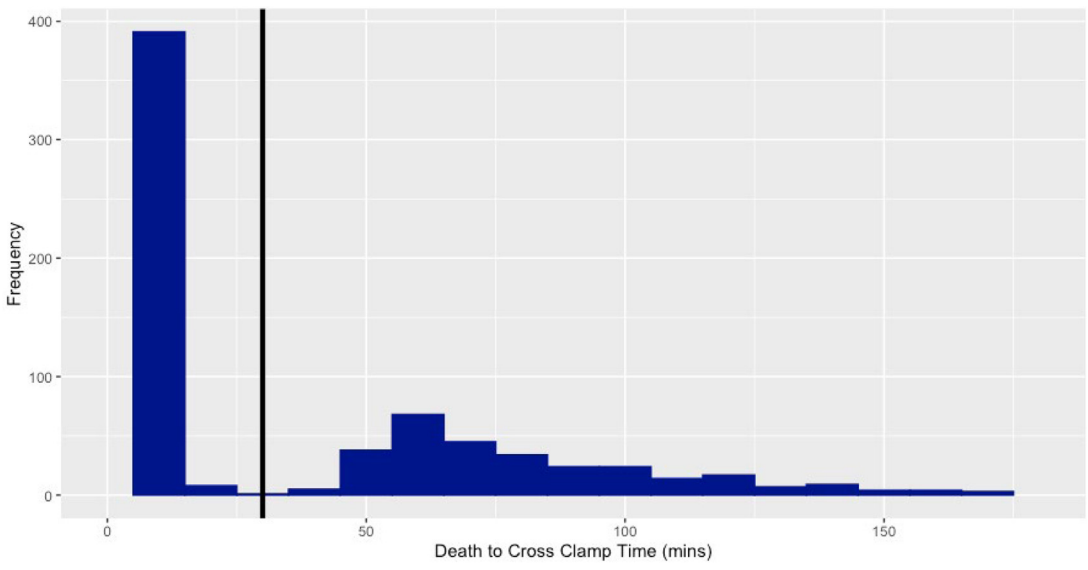
Study population and cumulative survival analysis of the unadjusted and propensity-matched heart transplantation following donation after circulatory death recipient cohorts, stratified by perfusion method. Shaded areas are 95% CIs.

FIGURE 2 **Time From Death to Cross-Clamp for DCD HT Donors**



The frequency distribution of death to cross-clamp times of the DCD HT donor population. The solid black line is at 30 minutes, which was used to define DPP and NRP reperfusion methods. Abbreviations as in Figure 1.

have an LVAD before transplant ($P = 0.002$) and more likely to receive a transplant at UNOS status 1 to 2 compared with NRP recipients, who were more likely to receive a transplant at status 4 to 6 ($P < 0.001$). There was no difference in temporary MCS need at the time of transplantation between DPP and NRP recipients.

PROPENSITY SCORE MATCHING. Propensity matching yielded 296 recipients who received a DPP allograft and 296 who received an NRP allograft. Donor and recipient characteristics are summarized in Supplemental Tables 1 and 2. The propensity-matched cohorts were well-balanced with absolute standardized mean differences <0.10 across the majority of covariates. We did not attempt to match patients based on the "time on waitlist" and "distance from the donor hospital" variables; after matching, these variables remained significantly different between the 2 cohorts.

SURVIVAL ANALYSIS. The unadjusted Kaplan-Meier survival curve for the study population is shown in Figure 3. In the unmatched cohort, NRP was associated with improved overall survival (log-rank $P = 0.005$). Thirty-day survival was 96.0% (95% CI: 94.1%-97.5%) among DPP recipients compared with 98.6% (95% CI: 97.2%-100.0%) among NRP recipients. One-year survival was 90.1% (95% CI: 87.4%-92.8%) among DPP recipients compared with 95.2% (95% CI: 92.3%-98.2%) among the NRP recipients. The Kaplan-Meier survival curve for the propensity-matched cohort is shown in Figure 4. In the matched cohort, NRP was also associated with improved cumulative survival (log-rank $P = 0.006$). Of note, when survival analysis is restricted to only patients who survived and have a minimum follow-up of 90 days, there is no significant difference in cumulative survival between the 2 cohorts (log-rank $P = 0.3$) (Supplemental Figure 1).

Cox proportional hazards regression was used to identify factors independently associated with mortality amongst recipients of DCD HT (Table 3). DCD transplantation using an NRP procurement method was associated with improved survival (HR: 0.39 [95% CI: 0.22-0.70]; $P = 0.002$). For low-volume transplant centers (<15 transplantations/year), mortality decreased as transplantation volume increased (HR: 0.73 [95% CI: 0.51-1.04]; $P = 0.082$). Transplant centers that performed >15 transplantations per year had an increase in mortality with increased transplant volume (HR: 1.87 [95% CI: 1.01-3.47]; $P = 0.047$). Donor and recipient age as well as pre-transplant LVAD or temporary MCS status were not associated with an elevated risk of mortality.

TABLE 1 Baseline Donor Demographics and Risk Factors

	DPP (n = 622)	NRP (n = 296)	*P* Value
Male	525 (84.4)	260 (87.8)	0.200
Donor age, y	30 (24-36)	31 (24-38)	0.369
Donor BMI, kg/m^2	26.4 (23.3-31.0)	27.1 (23.7-30.9)	0.261
Donor ethnicity			0.056
White	483 (77.8)	226 (76.4)	
Black	68 (11.0)	21 (7.1)	
Hispanic	57 (9.2)	41 (13.9)	
Other	13 (2.1)	8 (2.7)	
Donor history			
Cigarette use	64 (10.3)	32 (10.8)	0.900
Cocaine use	150 (24.1)	72 (24.3)	1.000
Alcohol abuse	166 (26.7)	73 (24.7)	0.566
Diabetes	19 (3.1)	5 (1.7)	0.322
LVEF	62 (59-65)	64 (60-68)	0.064
Donor cause of death			0.120
Anoxia	317 (51.0)	129 (43.6)	
Cerebrovascular/stroke	35 (5.6)	19 (6.4)	
Head trauma	245 (39.4)	133 (44.9)	
CNS tumor	1 (0.2)	3 (1.0)	
Other	24 (3.9)	12 (4.1)	
ABO blood type			0.636
A	187 (30.1)	98 (33.1)	
B	46 (7.4)	25 (8.4)	
AB	4 (0.6)	1 (0.3)	
O	385 (61.9)	172 (58.1)	

Values are n (%) or median (Q1-Q3).

BMI = body mass index; CNS = central nervous system; DPP = direct procurement and perfusion; LVEF = left ventricular ejection fraction; NRP = normothermic regional perfusion.

We conducted a subanalysis comparing outcomes from high-volume centers; a high-volume center was defined as performing >10 DPP or NRP perfusion methods on average annually. Of the 58 recipient centers included in our analysis, there were 3 high-volume DPP centers and 2 high-volume NRP centers. There is no cumulative survival difference between NRP recipients from a high-volume NRP center and DPP recipients from a high-volume DPP center (log-rank $P = 0.27$) (Figure 5).

UNADJUSTED SECONDARY OUTCOMES. Secondary outcomes in the unmatched cohort are summarized in Table 4. There were no differences in rates of drug-treated acute rejection before discharge and rates of rejection within 1 year of transplantation between the DPP and NRP recipient groups. Additionally, hospital length of stay, rates of new-onset dialysis, and follow-up ejection fraction were not significantly different between the 2 study groups. The median follow-up time at which left ventricular ejection

TABLE 2 Baseline Recipient Demographics and Risk Factors

	DPP (n = 622)	NRP (n = 296)	*P* Value
Male	484 (77.8)	241 (81.4)	0.243
Age, y	56 (44-63)	59 (49-65)	0.006
BMI, kg/m^2	27.9 (24.5-31.8)	28.7 (25.3-32.1)	0.058
Ethnicity			0.305
White	405 (65.1)	211 (71.3)	
Black	135 (21.7)	54 (18.2)	
Hispanic	66 (10.6)	24 (8.1)	
Other	16 (2.6)	7 (2.4)	
Recipient history			
Diabetes	182 (29.3)	94 (31.8)	0.488
Malignancy	44 (7.1)	34 (11.5)	0.034
Cerebrovascular disease	51 (8.2)	18 (6.1)	0.315
Heart failure etiology			0.172
Ischemic	154 (24.8)	89 (30.1)	
Non-ischemic dilated	344 (55.3)	146 (49.3)	
Other	124 (19.9)	61 (20.6)	
Recipient creatinine, mg/dL	1.1 (0.9-1.4)	1.2 (1.0-1.3)	0.328
Recipient bilirubin, mg/dL	0.7 (0.4-1.0)	0.7 (0.5-1.0)	0.505
Pre-transplant status			0.002
ICU	228 (36.7)	78 (26.4)	
Hospitalized, non-ICU	101 (16.2)	43 (14.5)	
Not hospitalized	293 (47.1)	175 (59.1)	
Medical therapy			
IV antibiotics in 2 wks before transplantation	33 (5.3)	16 (5.4)	1.000
IV inotropes before transplantation	201 (32.3)	83 (28.0)	0.217
LVAD before transplantation	269 (43.2)	96 (32.4)	0.002
Temporary MCS before transplantation	118 (19.0)	55 (18.6)	0.959
IABP	98 (15.8)	51 (17.2)	0.638
ECMO	11 (1.8)	2 (0.7)	0.312
Temporary VAD	15 (2.4)	3 (1.0)	0.241
ABO blood type			0.496
A	217 (34.9)	112 (37.8)	
B	62 (10.0)	36 (12.2)	
AB	19 (3.1)	8 (2.7)	
O	324 (52.1)	140 (47.3)	
Days on waitlist	37 (10-179)	28 (8-112)	0.010
Waitlist status at transplantation			<0.001
Status 1	17 (2.7)	4 (1.4)	
Status 2	248 (39.9)	77 (26.0)	
Status 3	103 (16.6)	50 (16.9)	
Status 4	166 (26.7)	107 (36.1)	
Status 5	3 (0.5)	–	
Status 6	85 (13.7)	58 (19.6)	
Distance from donor hospital to transplant center, miles	400 (182-593)	221 (41-406)	<0.001

Values are n (%) or median (Q1-Q3).

ECMO = extracorporeal membrane oxygenation; IABP = intra-aortic balloon pump; ICU = intensive care unit; IV = intravenous; LVAD = left ventricular assist device; MCS = mechanical circulatory support; VAD = ventricular assist device; other abbreviations as in Table 1.

fraction was determined was 588 days post-op for the DPP cohort (Q1-Q3: 366-792 days) vs 393 days for the NRP cohort (Q1-Q3: 363-720 days). Recipient causes of death are listed for each group; however, the numbers of patients are too small for any meaningful statistical analysis.

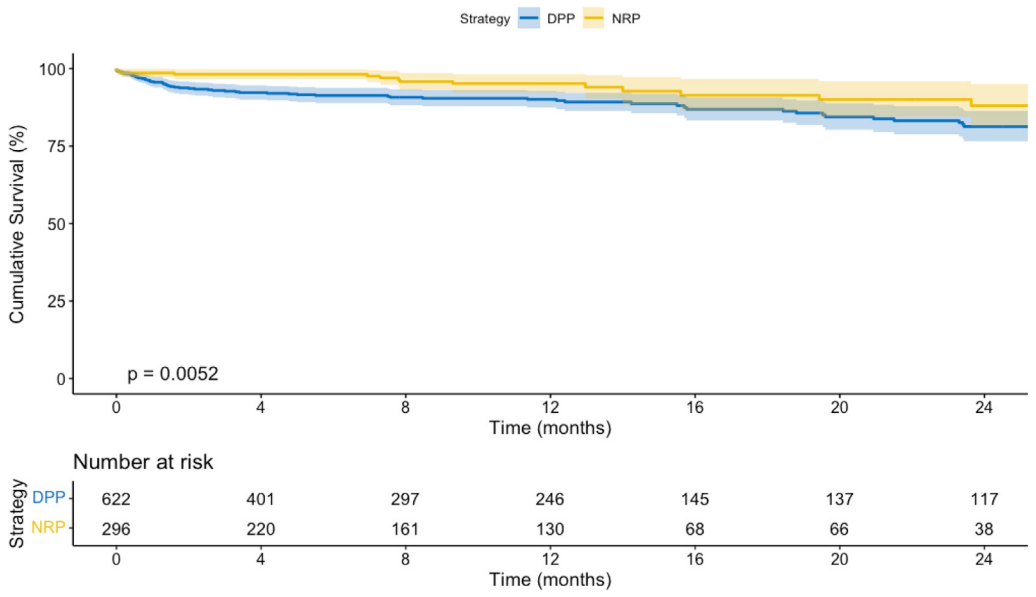
DISCUSSION

The demand for heart transplantation far exceeds the availability of donor hearts. Advancements in procurement and perfusion strategies have enabled adoption of DCD HT, a technique that has expanded the donor pool up to 30%.[9,16] The U.S. DCD HT experience began in 2019 and is still early. Thus, surveillance of outcomes continues to be necessary as adoption of the technique expands. The analysis presented here investigated short-term recipient outcomes, stratified by DPP and NRP procurement perfusion methods used for DCD HT in the United States.

With 918 patients, this report represents the largest registry analysis of DCD HT procurement perfusion methods in the United States since adoption of the DCD procurement strategy in 2019. In this analysis of the U.S. experience with NRP, there is a significant survival benefit for patients who received allografts procured with NRP, in both the unadjusted and propensity-matched cohorts. While the NRP recipients in the unmatched cohort are less ill at the time of transplantation than the DPP recipients, the survival benefit to NRP persists after propensity-matching. In addition, the NRP method is independently associated with improved survival among DCD HT recipients in Cox hazards analysis. Of note, there still remains a significant difference in the median organ travel distance in the propensity-matched cohort, with travel time significantly greater for the DPP group; therefore, it is difficult to conclude whether NRP could be used effectively in cases with greater travel distances.

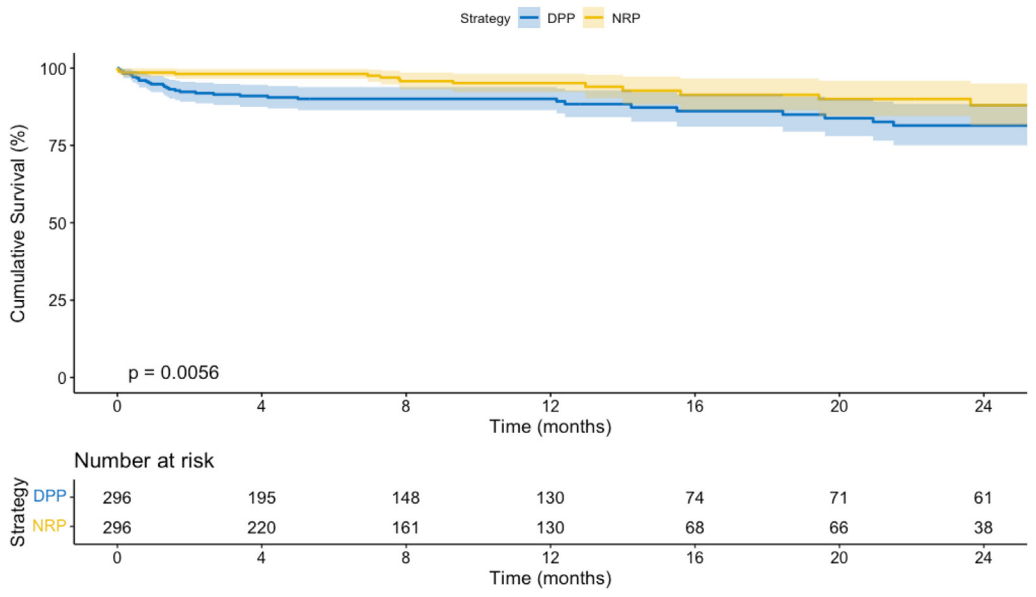
The results presented herein are the first to demonstrate improved short-term survival with the use of NRP. In a comparative analysis of DPP vs NRP use among 79 DCD HT allografts, the Papworth group demonstrated no difference in 1-year survival (P = 0.15) between the 2 cohorts.[5] Earlier and smaller U.S. retrospective series demonstrate comparable survival between the 2 perfusion strategies.[14,15,17] A recent multicenter retrospective study of 157 patients demonstrates similar early survival of NRP compared with DCD HT.[7] Although the Papworth group demonstrated a reduced frequency of dialysis and shorter hospital length of stay in the NRP cohort,[5] we did not see any significant difference in secondary clinical outcomes between the DPP and NRP cohorts evaluated in this study.

FIGURE 3 Kaplan-Meier Recipient Survival Analysis of the Unmatched Cohort



Cumulative survival analysis of the overall study population, stratified by allograft perfusion method. Shaded areas represent 95% CIs. Abbreviations as in Figure 1.

FIGURE 4 Kaplan-Meier Recipient Survival Analysis of the Propensity-Matched Cohort



Cumulative survival analysis of the propensity-matched cohort, stratified by allograft perfusion method. Shaded areas represent 95% CIs. Abbreviations as in Figure 1.

TABLE 3 Cox Proportional Hazards Model for Heart Transplantation Following Donation After Circulatory Death

		95% CI		
	HR	Lower	Upper	*P* Value
NRP	0.39	0.22	0.70	0.002
Donor age, per 5 y	0.95	0.82	1.08	0.422
Recipient age, per 5 y	1.05	0.96	1.15	0.285
LVAD before transplantation	1.46	0.94	2.27	0.094
Temporary MCS before transplantation	1.12	0.63	1.99	0.847
Transplant center annualized volume				
<15, per 5 transplantations	0.73	0.51	1.04	0.082
>15, per 5 transplantations	1.87	1.01	3.47	0.047

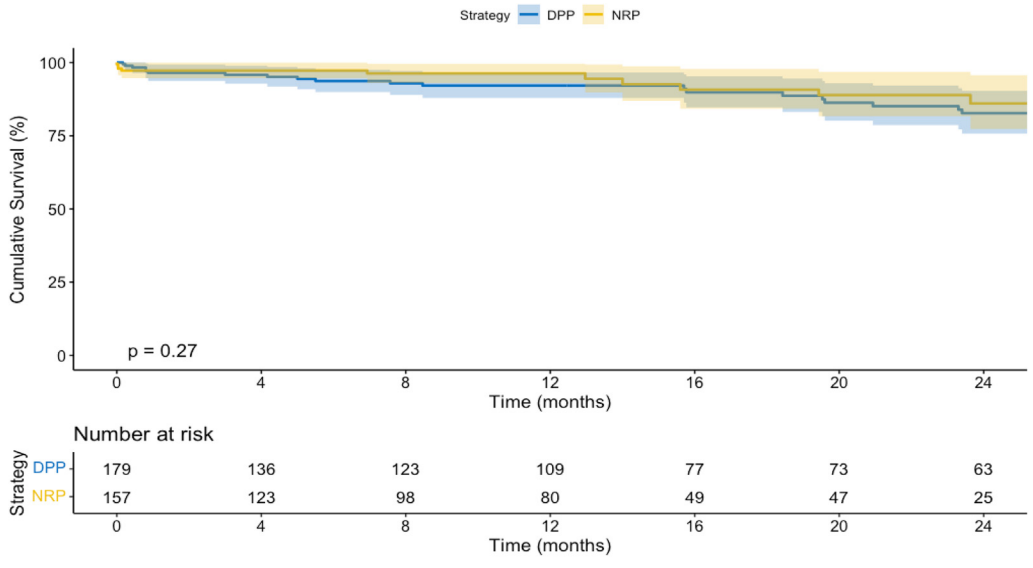
Abbreviations as in Tables 1 and 2.

Interestingly, we found that when short-term recipient outcomes were analyzed from only high-volume centers (>10 NRP/DPP annually), there was no longer a difference in cumulative survival between the DPP and NRP cohorts. These results may suggest that some of the survival difference seen between DPP and NRP may be driven in part by low-volume centers. The exact variables contributing to this discrepancy are outside the scope of this study and require further investigation. However, the equalization of survival may reflect optimization of the respective DPP and NRP protocols at these high-volume centers, which have mitigated graft losses.[13]

Beyond heart transplant-related outcomes, there may be additional important benefits to NRP that are not captured in this study. The UNOS registry does not provide any data pertaining to the choice of perfusion method or cost associated with each perfusion method. Additional studies will be needed to determine whether the choice between DPP and NRP is based purely on procurement team preference or donor hospital capability, or whether there are variables associated with the heart allograft not captured here that influence choice of perfusion method. Furthermore, there has been recent evidence to suggest improved abdominal organ quality following NRP as compared with DPP. Retrospective analyses of livers recovered with NRP demonstrated that the use of NRP was associated with less early allograft dysfunction, fewer anastomotic strictures, and significantly less ischemic cholangiopathy.[11,18-23] Kidneys recovered with NRP seem to have a lower risk of delayed graft function.[24-26]

Despite the reported benefits, the broader adoption of NRP has been met with several ethical concerns regarding its potential conflict with the definition of irreversible circulatory death. Australia does not currently permit NRP as the method is not congruent

FIGURE 5 Kaplan-Meier Recipient Survival Analysis of Transplants Performed at High-Volume Centers



Cumulative survival subanalysis of DCD HT recipients from high-volume centers. A high-volume center was defined as performing >10 DPP (n = 3 centers) or NRP (n = 2 centers) procurements on average annually. There is no significant difference between DPP or NRP survival at high-volume centers. Shaded areas represent 95% CIs. Abbreviations as in Figure 1.

with existing laws for DCD where death is defined as the irreversible cessation of blood circulation.[27] While the updated 2023 Canadian guidelines clarify that NRP does not violate the dead donor rule, NRP has still not been implemented in Canada.[28] In the United States, the legal definition of death is defined by the Uniform Declaration of Death Act, asserting that a person is dead after the irreversible cessation of cardiopulmonary and neurological function. The NRP technique involves the application of clamps to the head vessels in order to prevent restoration of any cerebral circulation and any reanimation of brain function; such a maneuver could be interpreted as securing brain death, which is not a conventional part of organ procurement from deceased donors. Although the ACP (American College of Physicians) issued a position paper in 2021 stating that NRP is unethical,[29] the American Society for Transplantation has refuted the ACP's position, stating that NRP recovery does not begin until after the patient is physiologically and legally dead, and that there is no intent to resuscitate the individual.[11,30,31] Ongoing discussion of the ethics surrounding NRP procurement will be necessary before the technique is widely adopted.

STUDY LIMITATIONS. First, DCD HT is still a novel procurement method in the United States with only short-term and medium-term patient follow-up data available. As such, further surveillance for long-term results beyond 1-year mortality are necessary. In addition, the primary stratification variable for this study (DPP vs NRP) was derived based on likely death to cross-clamp durations in the published reports, and may not be perfectly accurate. The distinction between DPP and NRP procurements was assumed based on: 1) reperfusion times >30 minutes are reported in the published reports for NRP; and 2) U.S. and international centers use organs procured with DPP only when functional warm ischemia is <30 minutes.[11,13] To further evaluate this distinction between perfusion methods, we performed a sensitivity analysis of our own institution's cohort, and found congruence with the literature-reported 30-minute cutoff point. A proportion of patients included in the cohort likely represents many of the patients who were enrolled in the DCD Heart Trial, which likely influenced the frequency of DPP relative to NRP procurements presented in this analysis.

Although propensity score matching was performed to balance the DPP and NRP recipient cohorts, as with any observational study, it is possible that unmeasured confounding variables are contributing to the survival difference between cohorts.

TABLE 4 Clinical Outcomes of the Unadjusted Recipient Cohort Stratified by Perfusion Method

	DPP (n = 622)	NRP (n = 296)	*P* Value
Length of hospital stay, d	17 (12-26)	16 (12-24)	0.257
Acute rejection episode before discharge	97 (15.6)	38 (12.9)	0.325
Treated with antirejection medication	58 (9.3)	25 (8.5)	0.459
Treated for rejection within 1 y	51 (8.2)	22 (7.4)	0.786
Post-transplant new onset dialysis	108 (17.4)	49 (16.6)	0.833
Most recent EF in follow-up[a]	60 (55-65)	60 (55-65)	0.780
Recipient cause of death			
Primary failure	6 (9.7)	2 (13.3)	
Acute rejection	2 (3.2)	–	
Chronic rejection	2 (3.2)	–	
Infection	13 (21.0)	4 (26.7)	
Cardiovascular	9 (14.5)	2 (13.3)	
Pulmonary	3 (4.8)	2 (13.3)	
Cerebrovascular	7 (11.3)	2 (13.3)	
Malignancy	1 (1.6)	–	
Multiple-organ failure	6 (9.7)	–	

Values are median (Q1-Q3) or n (%). [a]Available for 267 DPP and 139 NRP patients.
EF = ejection fraction; other abbreviations as in Table 1.

Furthermore, registry data are limited by variability and errors in data collection, especially for variables recently introduced in the data set, such as those characterizing DCD HT. Notably, the registry lacks granularity to fully characterize the DCD procurements, including hemodynamic and biochemical parameters, information regarding choice of DPP vs NRP methods, whether donor and recipient are collocated, and use of static cold storage vs ex vivo perfusion devices. It is assumed that the majority of NRP cases utilized static cold storage, but perfusion storage may have been employed for some cases and could impact outcomes. Additionally, the functional warm ischemic time for the DCD HT cases is not defined within the UNOS database, which may be an important predictive variable. Lastly, variables that capture whether primary graft dysfunction is present are not well-defined and are often missing from the data set. As the DCD HT experience grows and the registry is refined, further evaluation of these variables will be necessary.

CONCLUSIONS

Outcomes of the early experience for NRP in the United States demonstrate improved short-term survival with the use of NRP. However, this survival difference was not demonstrated among more experienced centers. Recipients who received allografts with NRP have similar short-term secondary

outcomes as those procured with DPP. Further evaluation and ongoing refinement of registry variables are necessary to determine long-term outcomes and delineate which clinical scenarios are best managed with each perfusion procurement method.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Following DCD, heart allografts are reperfused in order to enhance functional recovery after warm ischemia. In the United States, roughly 70% of DCD HT allografts are procured with the DPP method, while 30% are procured via the NRP method.

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: Among patients undergoing heart transplantation with DCD allografts, there appears to be a short-term survival benefit when the allograft is reperfused via NRP methods. In an unmatched cohort, 1-year survival of NRP recipients was 95%. Interestingly, cumulative survival is equivalent for DPP and NRP methods at high-volume centers.

TRANSLATIONAL OUTLOOK: Further work is needed to better identify which allografts or clinical scenarios will be best managed with each perfusion procurement method.

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APPENDIX For supplemental tables and a figure, please see the online version of this paper.