Normothermic regional perfusion in donation after circulatory death compared with brain dead donors: Single-center cardiac allograft outcomes

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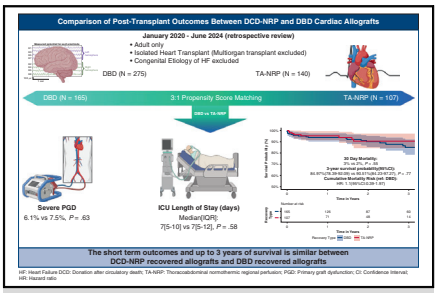
ABSTRACT

Objective: We sought to provide a single-center analysis of our normothermic regional perfusion (NRP)-recovered donation after circulatory death (DCD) heart transplant outcomes compared with a historical control group of donors of donation after brain death (DBD). We hypothesized that postoperative short-term outcomes and long-term survival trends are comparable in DCD-NRP and DBD cardiac allografts.

Methods: All adult heart-only transplants performed at our institution between January 2020 and June 2024 were retrospectively reviewed. Recipients were stratified into 2 groups: DCD-NRP and DBD. Propensity score matching was used to compare postoperative short and long-term outcomes. Kaplan-Meier was used to evaluate survival.

Results: Four hundred fifteen recipients met the inclusion criteria: 275 (63%) in the DBD group and 140 (37%) in the DCD-NRP group. In the propensity score-matching model there were no differences in severe primary graft dysfunction, mechanical circulatory support, right heart dysfunction, vasoactive inotropic scores, and 30-day mortality. There was also no difference in 1- and 3-year survival between groups.

Conclusions: In our single-center study, we found no differences in short and long-term outcomes between cardiac allografts from NRP-DCD compared with DBD donors. As such, NRP-recovered donors may be considered equivalent in terms of recipient outcomes to DBD donors. (J Thorac Cardiovasc Surg 2025;170:585-93)



Outcomes for allografts recovered by NRP and DBD are similar.

CENTRAL MESSAGE

Short- and long-term outcomes between cardiac allografts from normothermic regional perfusion in donation after circulatory death compared with brain dead donors are similar.

PERSPECTIVE

NRP for DCD heart recovery provides a physiologic in situ assessment and decreased cost compared with direct procurement and perfusion recovery methods. However, direct comparisons of NRP to DBD cardiac allografts are limited. This study suggests that NRP-DCD allograft recipients have similar post-operative morbidity and survival outcomes to DBD allografts and can be used to expand the donor pool.

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Abbreviations and Acronyms

DBD = donation after brain death or brain dead donor
DCD = donation after circulatory death
DPP = direct procurement and perfusion
HCV = hepatitis C virus
ICU = intensive care unit
PGD = primary graft dysfunction
NRP = normothermic regional perfusion
VIS = vasoactive inotropic scores

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Cardiac transplantation remains the gold standard in the treatment of end-stage heart failure, offering a potential lifeline to those with few other options. In recent years, donation after circulatory death (DCD) heart transplantation has proven to be a viable avenue for increasing the number of available cardiac allografts.[1] DCD hearts have been recovered either with direct procurement and preservation (DPP), or with normothermic regional perfusion (NRP). Early in the DCD experience, DPP was the only option, and randomized controlled trials have shown that DPP can yield outcomes similar to donation after brain death (DBD) donors.[2] A combined analysis from our institution of both DPP- and NRP-recovered allografts also showed no difference when compared with DBD.[1]

NRP has become increasingly popular due to its ability to provide a physiologic in situ assessment of the donor organ, as well as its decreased cost compared with DPP recovery methods with commercially available devices.[3,4] However, direct comparisons of NRP to DBD cardiac allografts are limited. An international multicenter analysis has demonstrated that outcomes of recipients of cardiac allografts recovered with NRP are equivalent to DBD with regard to 30-day, 1-year, and 5-year survival, and NRP use was responsible for a 23% increase in transplant center activity.[5] As an international study, it inherently included a wide variation in donor and recipient population as well as variable recovery and implant techniques.

Our institution has 1 of the world's largest experiences with NRP. As such, we sought to provide a single-center analysis of our NRP heart transplant outcomes compared with a historical DBD control group from our own institution. We hypothesized that postoperative short-term outcomes and long-term survival trends are comparable in NRP and DBD cardiac allografts.

METHODS

Study Population

To compare posttransplant outcomes and survival between allografts recovered using NRP in DCD donors and the traditional DBD recovery method, we retrospectively reviewed all adult heart-only transplants performed at our institution between January 2020 and June 2024. For NRP, this encompassed all procedures performed since our adoption of this technique. For DBD, this also included extended criteria brain-dead donors. Heart transplant cases due to congenital etiology and multiorgan transplants were excluded. Recipients were stratified into 2 groups based on the recovery method: DCD-NRP and DBD.

Data Definitions and Study Outcomes

NRP was the default recovery method for DCD donors secondary to cost associated with DPP, whereas DPP was only used when NRP was not permitted by the recovery hospital. DCD cases using DPP recovery cases were excluded. For the NRP technique, a sternotomy was performed followed by insertion of a right atrial cannula and a direct aortic cannula. Our modified extracorporeal circuit was then used to initiate NRP. The NRP protocols used in this study have been previously described in the literature.[1,4]

Our center used University of Wisconsin solution for preservation until January 21, 2021, after which Del Nido solution was adopted for all allografts. Data on recipient and perioperative implantation characteristics, as well as early allograft outcomes and follow-up time, were extracted from electronic medical records. Donor and explant procedure information was obtained from UNet (United Network for Organ Sharing).

The primary outcome of interest was the incidence of severe primary graft dysfunction (PGD), defined using the International Society for Heart and Lung Transplantation consensus criteria.[6] Other outcomes included ventilation time, vasoactive inotropic scores (VIS); cardiac indices at 24 and 72 hours; left ventricular ejection fraction at 7 days; intensive care unit (ICU) and hospital lengths of stay; and survival at 30 days, 1 year, and 3 years. This study was approved by the Institutional Review Board (241909; August 2024) at Vanderbilt University Medical Center.

Statistical Analysis

The distribution of recipient, donor, and procedural characteristics between the 2 groups was summarized as medians (first and third quartiles) for continuous variables and counts (percentages) for categorical variables. Statistical comparisons were performed using the Mann-Whitney *U* test for continuous variables and the Fisher exact test for categorical variables. The *P* values from these tests were extracted and used to construct summary tables. Outcomes between the 2 groups were compared using univariate logistic regression for categorical outcomes and generalized additive models for continuous outcomes.

To ensure a fair comparison, 3:1 propensity score matching was performed using the nearest-neighbor technique with a caliper of 0.3 to preserve the sample size. The propensity score model included donor and recipient baseline characteristics such as donor and recipient age, sex, body mass index, predicted heart mass, sex mismatch, race, blood group status, diabetes, hypertension, waitlist status, heart failure etiology, prehospitalization status, prior sternotomies, recipient preoperative creatinine level, retransplant status, preoperative mechanical circulatory support, donor cause of death, donor distance, and donor hepatitis C virus (HCV) exposure status. The propensity score model achieved an area under the curve of 84%. The standardized mean difference <15% was considered acceptable between the matched cohorts and <10% was considered ideal.

Univariate regression analyses were then repeated on the matched population.

In 2023, our center made a practice change and began using a 10 °C storage system (10 °C) as a static cold storage alternative to ice. Therefore, we adjusted for 10 °C use in subsequent analyses and reported the adjusted results.

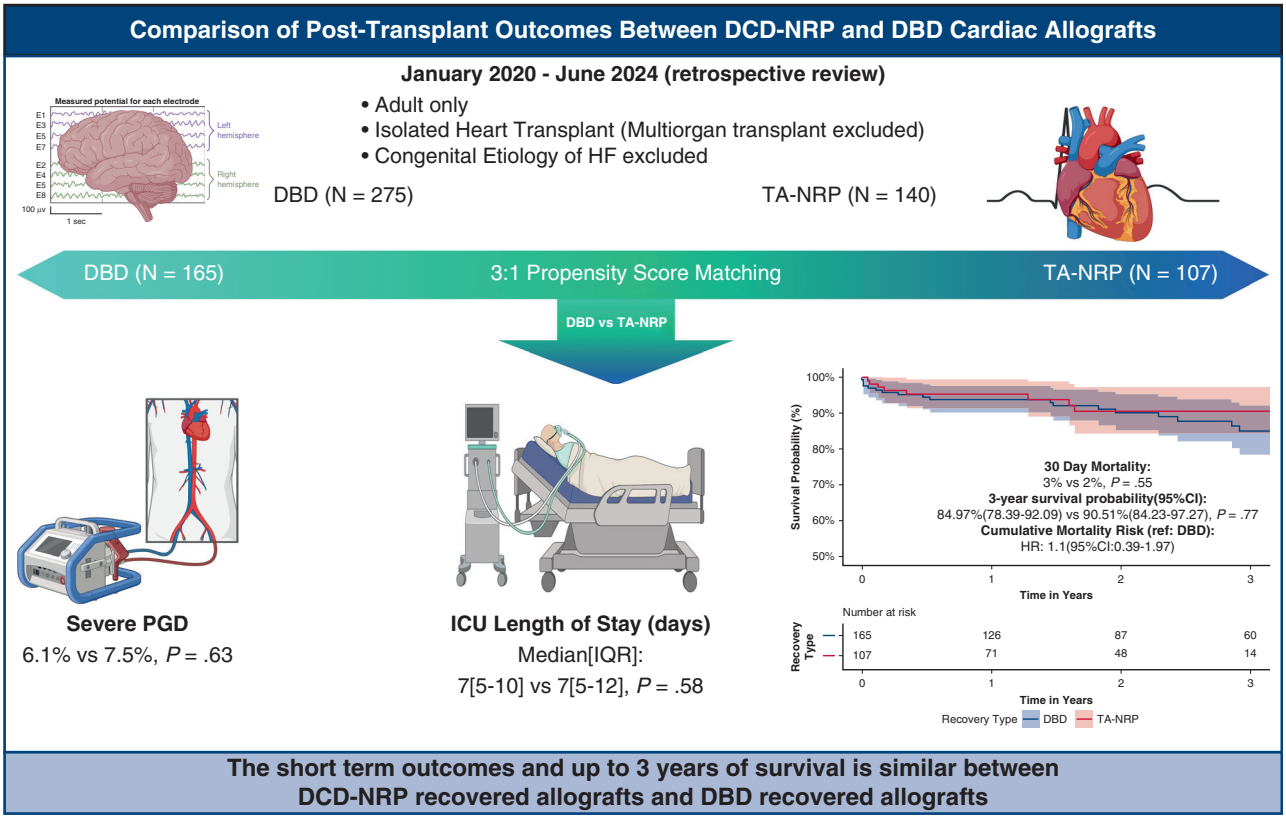
For survival outcomes, a Cox proportional hazards model was used on both matched and unmatched datasets. Kaplan-Meier survival curves were constructed for both groups in the unmatched and matched populations. To validate survival estimates and account for potential information bias, a post hoc 1-year survival sensitivity analysis was performed. This analysis excluded patients who were lost to follow-up or had not yet reached 1-year follow-up from the time of their procedure. All analyses were conducted using R version 4.4.1 (R Foundation for Statistical Computing), with $\alpha = 0.05$ considered statistically significant.

RESULTS

During the study period, 415 recipients met the inclusion criteria. Of these, 275 (63%) received allografts recovered from DBD donors, and 140 (37%) received allografts recovered from DCD donors using NRP (Figure 1).

Donor Characteristics

Compared with DBD donors, DCD donors recovered with NRP were younger (27 years; interquartile range [IQR], 22-36 years vs 32 years; IQR, 25-40 years; $P = .0002$), more likely to be male (82% vs 67%; $P = .001$), and more likely to be White (83% vs 64%; $P = .0004$) (Table 1). The prevalence of hypertension (15.7% vs 22.5%; $P = .03$) and diabetes mellitus (2% vs 7%; $P = .02$) was lower among NRP donors compared with DBD donors. Death due to cerebrovascular accident or intracerebral hemorrhage was higher in DBD donors (13% vs 5.7%; $P = .03$). Additionally, donor left ventricular ejection fraction was slightly higher in the NRP group (60%; IQR, 58.8%-65% vs 60%; IQR, 55%-65%; $P = .01$).



HF: Heart Failure DCD: Donation after circulatory death; TA-NRP: Thoracoabdominal normothermic regional perfusion; PGD: Primary graft dysfunction; CI: Confidence Interval; HR: Hazard ratio

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FIGURE 1. Central picture/graphical abstract. *DCD*, Donation after circulatory death; *NRP*, normothermic regional perfusion; *DBD*, donation after brain death; *TA-NRP*, thoracoabdominal normothermic regional perfusion; *PGD*, primary graft dysfunction; *ICU*, intensive care unit; *IQR*, interquartile range; *HR*, hazard ratio.

TABLE 1. Donor characteristics

Variable	Unmatched population			Matched population		
	TA-NRP (n = 140)	DBD (n = 275)	*P* value	TA-NRP (n = 107)	DBD (n = 165)	*P* value
Donor age (y)	27 (22.3-36)	32 (25-40)	**<.001**	27.1 (23-37)	29 (23-36)	.72
Male donor sex male	115 (82.1)	185 (67.3)	**.001**	85 (79.4)	121 (73.3)	.31
Donor BMI	26.4 (22.7-31.1)	26.6 (22.7-32.7)	.54	26.4 (23.5-30.9)	27 (22-33.7)	.62
Donor LVEF (%)	60 (58.8-65)	60 (55-65)	.01	60 (55-65)	60 (55-65)	.62
White donor race	116 (82.9)	177 (64.4)	**<.001**	87 (81.3)	123 (74.5)	.42
Donor blood type O	83 (59.3)	164 (59.6)	>.99	64 (59.8)	99 (60)	.99
Donor hypertension	22 (15.7)	62 (22.5)	.03	20 (18.7)	33 (20)	.88
Donor diabetes	3 (2.1)	20 (7.3)	.02	3 (2.8)	7 (4.2)	.74
Donor smoking >20 pack-y	13 (9.3)	40 (14.5)	.21	11 (10.3)	17 (10.3)	>.99
Donor HCV exposure	12 (8.6)	68 (24.7)	**<.001**	12 (11.2)	30 (18.2)	.57
Donor inotropes	3 (2.1)	11 (4)	.40	2 (1.9)	5 (3)	.61
Donor cause of death			**<.001**			.46
CVA/ICH	8 (5.7)	36 (13.1)		7 (6.5)	14 (8.5)	
Blunt trauma	48 (34.3)	45 (16.4)		30 (28)	34 (20.6)	
Anoxia/hypoxia	42 (30)	111 (40.4)		35 (32.7)	65 (39.4)	
Cardiac arrest/CPR attempt	67 (47.9)	162 (58.9)	.09	56 (52.3)	96 (58.2)	.46
Donor distance (nautical miles)	240 (139-439)	311 (157-450)	.25	249 (139-444)	249 (139-431)	.81
Predicted heart mass ratio	0.95 (0.84-1.1)	0.96 (0.83-1.1)	.93	0.95 (0.84-1.1)	0.97 (0.83-1.1)	.74

Values are presented as n (%) for categorical variables and median (interquartile range) for continuous variables. Bold values indicate that are statistically significant ($P < .05$). *TA-NRP*, Thoracoabdominal normothermic regional perfusion; *DBD*, donation after brain death; *BMI*, body mass index; *LVEF*, left ventricular ejection fraction; *HCV*, hepatitis C virus; *CVA*, cerebrovascular accident; *ICH*, intracerebral hemorrhage; *CPR*, cardiopulmonary resuscitation.

Recipient Characteristics

The recipient populations were largely similar between the 2 groups, except for differences in waitlist status and prehospitalization (Table 2). More DBD recipients had a waitlist status of 1 or 2 compared with NRP recipients (38.9% vs 17.1%; $P < .0001$), and a greater proportion of DBD recipients were prehospitalized (47.6% vs 26.4%; $P < .0001$).

Procedural Characteristics

The total ischemic time (postallograft recovery) was comparable between NRP and DBD allografts (NRP: 215 minutes; IQR, 184-239 minutes vs DBD: 205 minutes; IQR, 175-250 minutes; $P = .49$) (Table 3). A 10 °C cooler as a static cold storage method was used more frequently in the NRP group compared with the DBD group (29% vs 17%; $P = .02$). We have also summarized our donor ischemic times pre-NRP (Table E1). In addition, the number of declined cardiac allografts was significantly higher in the NRP group compared with the DBD group (23 out of 163 [14.1%] vs 17 out of 292 [5.8%]; $P = .005$) (Table E2).

Outcomes

The incidence of severe PGD requiring venoarterial extracorporeal membrane oxygenation was not significantly different between the DBD and NRP cohorts (NRP: 8% vs DBD: 5.5%; $P = .33$) (Table 4). However, severe right ventricular depression postbypass was more common in the NRP group (6.4% vs 1.8%; $P = .02$). The VIS at 24 hours (NRP: 16.6; IQR, 12.7-23 vs DBD: 11.5; IQR, 8.13-14.6; $P = .95$) and 72 hours (NRP: 6; IQR, 3.75-9.29 vs DBD: 5.86; IQR, 4-9.99; $P = .51$) were comparable between the groups. The cardiac index at 24 hours (NRP: 3.22; IQR, 2.7-3.7 vs DBD: 3.1; IQR, 2.6-3.6; $P = .09$) and left ventricular ejection fraction at postoperative day 7 (NRP: 62%; IQR, 55%-69% vs DBD: 65%; IQR, 55%-70%; $P = .88$) were also similar. ICU length of stay (7 days; IQR, 5-11 days in both groups; $P = .72$) and hospital length of stay (NRP: 17 days; IQR, 13-26 days vs DBD: 17.5 days; IQR, 13-25.8 days; $P = .71$) were comparable.

Within 30 days, 4 recipients (2.8%) in the NRP group and 9 recipients (3.2%) in the DBD group died ($P = .81$). Cumulative 1-year mortality rates were also similar (NRP: 7.8% vs DBD: 6.8%; $P = .75$) (Figure E1). The median follow-up time was 26 months (IQR, 11-40 months), which was significantly shorter in the NRP group (21 months; IQR, 11-34 months) compared with the DBD group (28 months; IQR, 12-43 months; $P = .001$). The 1-year survival probabilities were 97.14% (95% CI, 94.42%-99.94%) for the NRP group and 96.73% (95% CI, 94.65%-98.85%) for the DBD group. At 3 years,

TABLE 2. Recipient characteristics

Variable	Unmatched population			Matched population		
	TA-NRP (n = 140)	DBD (n = 275)	*P* value	TA-NRP (n = 107)	DBD (n = 165)	*P* value
Age at transplant (y)	57.6 (46.6-64.2)	58.1 (48.4-64.4)	.51	58.8 (48.7-65.4)	57.4 (47.4-64.5)	.71
Male recipient sex	116 (82.9)	195 (70.9)	**.008**	88 (82.2)	123 (74.5)	.18
Recipient BMI	29.8 (26.2-34)	29.4 (25.7-33.2)	.18	29.6 (26.1-33.9)	29.4 (26.3-32.9)	.63
White recipient race	107 (76.4)	187 (68)	.1	79 (73.8)	122 (73.9)	.87
Recipient blood type O	69 (49.3)	131 (47.6)	.86	52 (48.6)	80 (48.5)	.93
Diabetes mellitus	58 (41.4)	107 (38.9)	.89	42 (39.3)	67 (40.6)	.89
Hypertension	105 (75)	192 (69.8)	.16	79 (73.8)	119 (72.1)	.89
Female to male mismatch	11 (7.86)	36 (13.1)	.14	10 (9.4)	17 (10.3)	.84
Prior sternotomy	75 (53.6)	151 (54.9)	.93	59 (55.1)	94 (57)	.80
Prehospitalized	37 (26.4)	131 (47.6)	**<.001**	33 (30.8)	64 (38.8)	.69
Retransplants	8 (5.7)	16 (5.8)	>.99	6 (5.6)	10 (6)	.92
Transplant status 1 or 2	24 (17.1)	107 (38.9)	**<.001**	22 (20.6)	44 (26.7)	.31
Ischemic cardiomyopathy	44 (31.4)	85 (30.9)	.98	34 (31.8)	54 (32.7)	.96
Preoperative creatinine, mg/dL	1.18 (0.97-1.38)	1.24 (0.99-1.58)	.051	1.2 (0.99-1.46)	1.2 (0.94-1.5)	.99
Preoperative LVAD	44 (31.4)	74 (26.9)	.36	32 (29.9)	54 (32.7)	.69
Preoperative ECMO	2 (1.4)	13 (4.7)	.10	2 (1.9)	8 (4.9)	.32

Values are presented as n (%) for categorical variables and median (interquartile range) for continuous variables. Bold values indicate that are statistically significant ($P < .05$). *TA-NRP*, Thoracoabdominal normothermic regional perfusion; *DBD*, donation after brain death; *BMI*, body mass index; *LVAD*, left ventricular assist device; *ECMO*, extracorporeal membrane oxygenation.

survival probabilities were 89.67% (95% CI, 84.12%-95.59%) for the NRP group and 87.41% (95% CI, 82.76%-92.33%) for the DBD group (Cox hazard ratio, 1.1; 95% CI, 0.56-2.16; $P = .8$).

Propensity Score-Matched Analysis

In the 3:1 propensity score-matched cohort (N = 272; NRP = 107, DBD = 165) (Figure 2), baseline donor and recipient characteristics were balanced, and results were adjusted for 10 °C cooler use (Tables 1-3). Using NRP did not increase the incidence of severe PGD compared with DBD (odds ratio, 1.32; 95% CI, 0.46-3.83; $P = .6$) (Table 4). There was also no difference in right heart depression ($P > .05$). VIS at 24 and 72 hours also showed no significant differences between groups ($P > .05$).

The 1-year survival probabilities in the matched cohort were 95.28% (95% CI, 91.34%-99.41%) for NRP recipients and 93.78% (95% CI, 90.11%-97.59%) for DBD recipients (Figure 3). At 3 years, survival probabilities were 90.51% (95% CI, 84.23%-97.27%) for NRP recipients and 84.97% (95% CI, 78.39%-92.09%) for DBD recipients. The adjusted Cox hazard ratio for 3-year survival was 1.06 (95% CI, 0.4-2.2; $P = .54$). The outcome comparison for the matched population is summarized in Table 4.

Post Hoc 1-Year Survival Sensitivity Analysis

In the post hoc sensitivity analysis, including only patients who completed at least 1 year of follow-up (NRP: 103, DBD: 220), there was no significant difference in 1-

TABLE 3. Preservation and implant characteristics

Procedure characteristics	Unmatched population			Matched population		
	TA-NRP (n = 140)	DBD (n = 275)	*P* value	TA-NRP (n = 107)	DBD (n = 165)	*P* value
Static cold storage type, 10 °C cooler	41 (29.3)	47 (17.1)	**.02**	33 (30.8)	25 (15.2)	**.01**
Cold ischemic time (min)	168 (142-191)	159 (133-198)	.48	169 (142-190)	156 (133-195)	
Warm ischemic time (min)	49 (32-60)	46 (34-58)	.55	48.5 (32-60.8)	47 (33-57.5)	.55
Ischemic time (min)	215 (184-239)	205 (175-250)	.49	214 (192-240)	205 (174-246)	.28
Implant bypass length (min)	144 (117-175)	135 (105-170)	.08	146 (117-178)	136 (105-166)	.08

Values are presented as n (%) for categorical variables and median (interquartile range) for continuous variables. Bold values indicate that are statistically significant ($P < .05$). *TA-NRP*, Thoracoabdominal normothermic regional perfusion; *DBD*, donation after brain death.

TABLE 4. Posttransplant outcomes

Postoperative outcome	Unmatched population			Matched population		
	TA-NRP (n = 140)	DBD (n = 275)	*P* value	TA-NRP (n = 107)	DBD (n = 165)	*P* value
Severe PGD*	11 (7.9)	15 (5.5)	.33	8 (7.5)	10 (6.1)	.63
Vasoactive inotropic score at ICU arrival	16.6 (12.7-23)	16.7 (12.4-22.5)	.86	16.9 (12.7-23.2)	17.3 (13.3-23.2)	.52
Vasoactive inotropic score at 24 h	10.7 (8.14-14.9)	11.5 (8.13-14.6)	.95	11.7 (8.7-15.2)	11.8 (9.8-15.8)	.17
Cardiac index at ICU	2.76 (2.3-3.25)	2.7 (2.19-3.4)	.62	2.8 (2.3-3.3)	2.61 (2.17-3.3)	.72
Cardiac index at 24 h	3.22 (2.7-3.7)	3.1 (2.6-3.6)	.09	3.2 (2.7-3.7)	3.1 (2.6-3.61)	.56
LVEF postbypass <45%	21 (15)	21 (7.6)	**.02**	15 (14)	12 (7.27)	.08
Postbypass RV depression	9 (6.4)	5 (1.8)	**.02**	6 (5.6)	3 (1.8)	.12
ICU length of stay (d)	7 (5-11)	7 (5-11)	.72	7 (5-12)	7 (5-10)	.58
Hospital length of stay (d)	17 (13-26)	17.5 (13-25.8)	.71	17 (13.5-26)	17 (13-24)	.44
Ventilation time (h)	12 (9.06-22.2)	13.3 (8.43-24.5)	.88	12.9 (9.55-31)	13.8 (8.43-28.8)	.091
Mortality risk†	1.1 (0.56-2.16)	Reference	.80	1.1 (0.39-1.97)	Reference	.77
1-y Survival‡	94.25 (90.47-98.2)	94.34 (91.58-97.17)		95.28 (91.34-99.41)	93.78 (90.11-97.59)	
3-y Survival‡	89.67 (84.12-95.59)	87.41 (82.76-92.33)		90.51 (84.23-97.27)	84.97 (78.39-92.09)	
30-d Mortality	4/140 (2.8)	9/275 (3.2)	.81	2/107 (1.9)	5/165 (3)	.55

Values are presented as n (%) for categorical variables or median (interquartile range) for continuous variables, unless otherwise noted. Bold values indicate that are statistically significant ($P < .05$). *TA-NRP*, Thoracoabdominal normothermic regional perfusion; *DBD*, donation after brain death; *PGD*, primary graft dysfunction; *ICU*, intensive care unit; *LVEF*, left ventricular ejection fraction; *RV*, right ventricle. *Venoarterial extracorporeal membrane oxygenation at 24 hours. †Mortality risk calculated using Cox regression model. Values are presented as hazard ratio (95% CI). ‡Survival probabilities estimated using Kaplan-Meier analysis. Values are presented as probability (95% CI).

year survival probabilities between the groups (NRP: 92.2%; 95% CI, 87.2%-97.5% vs DBD: 93.2%; 95% CI, 89.9%-96.6%; $P = .65$) (Figure 4).

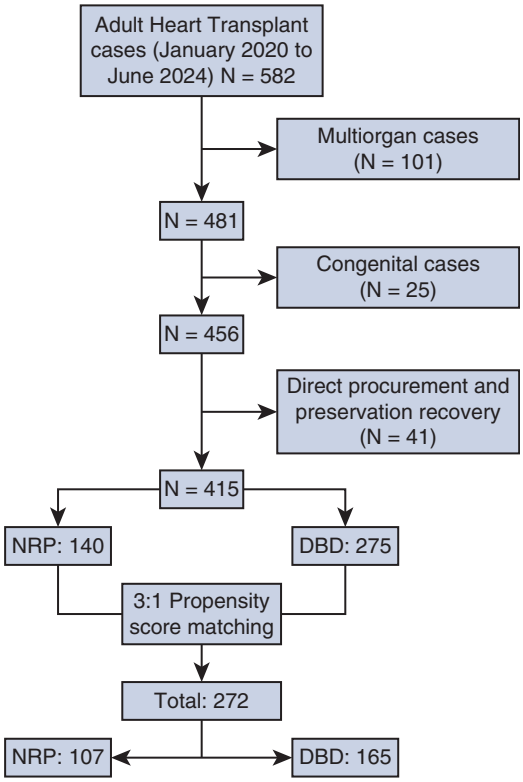


FIGURE 2. Patient selection flowchart. *NRP*, Normothermic regional perfusion; *DBD*, donation after brain death.

DISCUSSION

NRP has been shown provide excellent solid organ transplant outcomes that rival those of DBD.[7] For this reason, NRP for recovery of DCD allografts is rapidly becoming a favored approach for many transplant programs. Previously, we questioned whether the same phenomenon occurs in cardiac allografts by comparing DBD and DCD recoveries (ie, including both NRP and DPP).[1] However, due to the low sample size at that time, we could not perform a stratified analysis to draw direct comparisons of NRP or DPP versus DBD. This study builds on our prior work by attempting to achieve a more uniform comparison with less variation and has a larger single-center sample size with additional long-term data.

This single center analysis involves 1 of the largest-volume NRP programs in the world, spanning a cumulative follow-up time of 885 patient-years. In this study, we demonstrate remarkably similar early postoperative outcomes and long-term (3 years) survival compared with DBD donors. In our baseline-matched population, the incidence of PGD was similar between the 2 groups. Other outcomes, including the need for mechanical circulatory support, inotrope dependence, and ICU length of stay, were also comparable. We did observe a higher incidence of right heart dysfunction in the NRP group compared with the DBD group in the unmatched population. Despite this, there was still no difference in the incidence of PGD nor need for mechanical support. Our institution's practice is to manage this using a stepwise fashion of increasing inotropes and the addition of pulmonary vasodilators followed by select use of mechanical circulatory support. Using

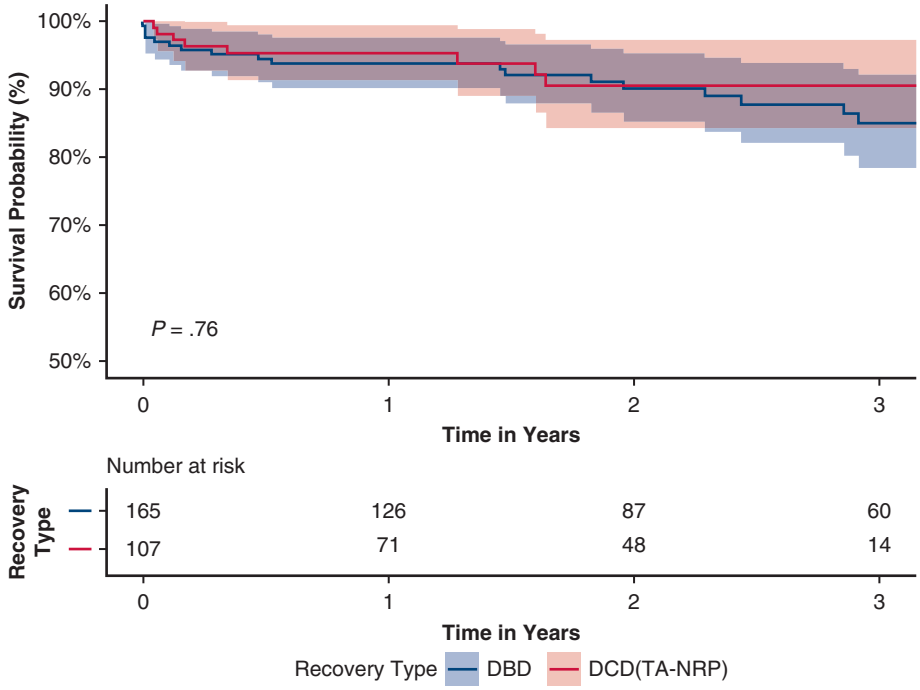


FIGURE 3. Kaplan-Meier survival curves (95% CI shown) for the matched population. Recipients with thoracoabdominal normothermic regional perfusion (*TA-NRP*) recovered allografts show no difference in survival compared with recipients with donation after brain death (*DBD*) recovered allografts. (Log rank *P* value = .76). *DCD*, Donation after circulatory death.

propensity score matching, we observed no significant differences in short- and long-term recipient outcomes between groups, including rates of right heart dysfunction. This in-depth evaluation of early allograft outcomes complements previous international multicenter studies (n = 153) that examined long-term outcomes between

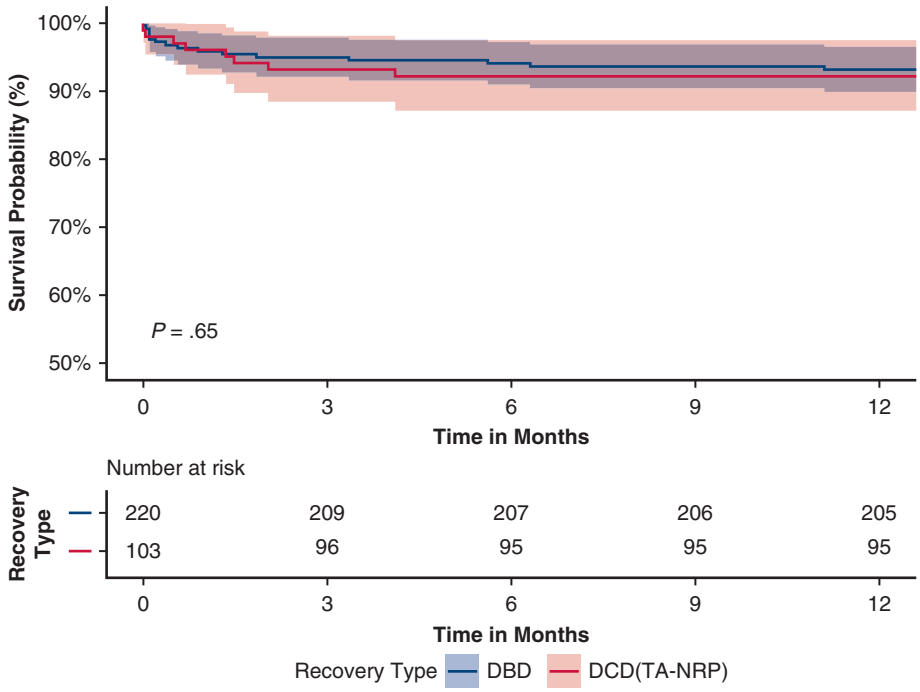


FIGURE 4. Kaplan-Meier survival curves (95% CI shown) for population with documented 1-year complete follow-up. Recipients with thoracoabdominal normothermic regional perfusion (*TA-NRP*) recovered allografts show no difference in survival compared with recipients with donation after brain death (*DBD*) recovered allografts. (Log rank *P* value = .65). *DCD*, Donation after circulatory death.

DBD and NRP recipients and demonstrated no difference in 30-day, 1-year, and 5-year survival.[5] Our study provides a more uniform comparison, by avoiding the wide variation in donor and recipient populations, as well as variable recovery and implant techniques in the prior multicenter studies that include programs from across the world.

One reason why early recipient outcomes may be similar between DBD and NRP cardiac allografts is intraoperative organ selection. NRP allows for in situ evaluation, similar to DBD donors, where the heart can be visually examined and evaluated in a fully loaded state. As such, NRP mimics the in-person evaluation and assessment of the cardiac allograft that occurs during DBD recoveries,[4,8,9] which may allow optimum selection of cardiac allografts before transplant.

It is also worth highlighting that NRP donors were younger in age than DBD donors in this study; however, this was expected. Early in our NRP experience, we only accepted donors who were younger than age 35 years given that there was typically no coronary artery evaluation in these DCD donors. As the study period proceeded, this restriction was relaxed, and we gained comfort with expanding our age range for NRP donors. Given that DBD donors were older, it would naturally follow that there was a higher incidence of hypertension and smoking in this cohort. The higher incidence of HCV-exposed donors in the DBD cohort can also be explained by our institutional practices because we were 1 of the earliest utilizers of HCV-positive cardiac allografts.[10,11] For this reason, we had access to DBD donors that may have been turned down at other centers due to HCV status. In addition, there were more women in the DBD recipients, which is the reason for the higher acceptance of female donor hearts in the DBD group. However, even in female recipients, there was a higher percentage of male donors used in the NRP group likely because more male donors were available. A lower percentage of female donors utilized may be intrinsic to the DCD process because this has been observed in other studies.[5]

There was also a difference in the waitlist status of the recipients. As 1 of the first centers to adopt DCD donation, we were able to use DCD allografts to transplant many of our recipients who were far down the waitlist and otherwise might not have received frequent offers. Given these differences, we used propensity score matching to adjust for these baseline differences between the 2 groups to minimize confounding bias.

This study reinforces that a period of warm ischemia (after extubation of the potential donor) can be well tolerated by the donor cardiac allograft. Although there were concerns about the influence of warm ischemia on the donor allograft early during the DCD experience,[12] we have shown that this ischemia can be rapidly reversed with in situ resuscitation and does not seem to result in a functional detriment to the cardiac allograft. Preclinical data by Sanchez-Camara and colleagues[13] demonstrated that the functional warm ischemic time, alone, does not appear to influence myocardial energetics. However, an asystolic period of 10 minutes appears to be a critical time point beyond which mitochondrial function and myocardial energetics rapidly decline.[13] Assuming a 3- to 5-minute standoff period after declaration of death, we reperfuse NRP hearts within 5 minutes to remain within this 10-minute period. Despite these studies, this 10-minute period can perhaps be pushed even further, as we had 19 patients with an asystolic warm ischemic time >19 minutes. This also has been shown in Italian studies highlighting where a 20-minute standoff of period is required. Despite this, acceptable outcomes have been achieved.[14] Additional studies are required to further investigate the influence of asystolic warm ischemic time on short- and long-term recipient outcomes after heart transplantation.

It is also worth highlighting the use of the Organ Care System after NRP compared with NRP to static cold storage. In their original cohort of patients, the Papworth group utilized the Organ Care System after NRP in scenarios where patients were not co-located in the same hospital.[15] In the United States, this practice has evolved and become very different. At present, the majority of centers using NRP for DCD cardiac allograft use static cold storage following cardiac allograft explant from the donor. To help circumvent the second arrest period, which is currently performed in both standard DPP and current NRP techniques, the beating-heart Organ Care System technique has evolved. At present, it has only been reported by 1 center and appears to have good outcomes.[16] However, further studies are required to further evaluate this technique.

Limitations

This study is a single-center, retrospective, observational analysis, which inherently carries the limitation of potential unmeasured confounders. Although there were differences in donor and recipient characteristics between groups with the DBD group having higher associated disorders, we attempted to account for these using propensity score matching. In addition, we made several clinical practice changes during the study period, including conversion to del Nido as a preservation solution and 10 °C preservation, which may have influenced our results. Despite accounting for these differences and protocol changes over time, residual confounding bias remains a possibility. Furthermore, as a single-center analysis, the findings are influenced by institutional practices and may be subject to selection bias, limiting the generalizability of the results to other centers or broader populations. We must also highlight that NRP is logistically complex, requiring substantial coordination between the donor hospital, procurement teams, perfusionists, and the organ procurement organization. Successful

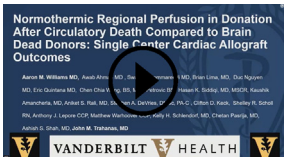
implementation depends on the agreement and collaboration of all involved parties. As such, this may limit the ability to replicate this technique.

CONCLUSIONS

Donor selection is among the most crucial decisions during the transplant process. After reviewing our data, NRP-recovered donors are considered equivalent to DBD donors in terms of recipient outcomes at our institution. However, larger, multicenter, prospective, longitudinal trials are necessary to further assess whether any differences in outcomes exist.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://www.aats.org/resources/observed-survival-trends-in-he-10012.



Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: heart transplant, normothermic regional perfusion, donation after circulatory death, brain dead donor, survival, primary graft dysfunction

ADULT

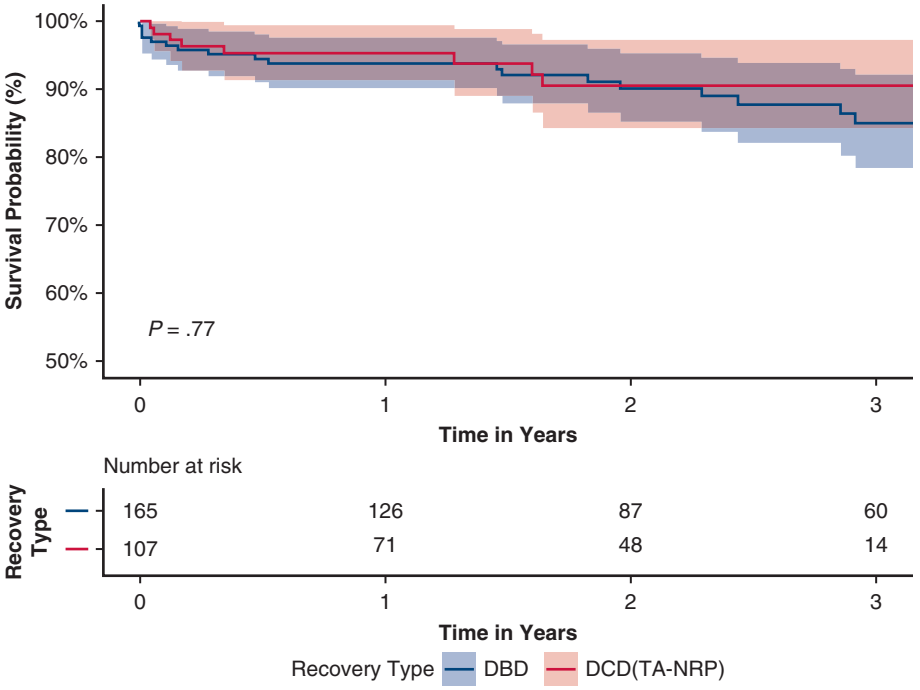

FIGURE E1. Kaplan-Meier survival curve (95% CI shown) for the unmatched population. Recipients with thoracoabdominal normothermic regional perfusion (*TA-NRP*) recovered allografts show no difference in survival compared with recipients with donation after brain death (*DBD*) recovered allografts. (Log rank *P* value = .77). *DCD*, Donation after circulatory death.

TABLE E1. Donation after circulatory death warm ischemic time intervals after withdrawal of life support

NRP interval	Result
Extubation to pump (DWIT min)	26 (21-32)
Agonal to pump (FWIT) based on Spo2 <80 (min)	22 (17.5-29)
FWIT based on SBP <80 mm Hg (min)	14 (11-18)
FWIT based on SBP <50 mm Hg (min)	12 (10-15)
Asystole to pump (AWIT) (min)	8 (7-10)

Values are presented as median (IQR). *NRP*, Normothermic regional perfusion; *DWIT*, donor warm ischemic time; *FWIT*, functional warm ischemic time; *SBP*, systolic blood pressure; *AWIT*, asystolic warm ischemic time.

TABLE E2. Recovery attempts and declined allografts rate comparison between normothermic regional perfusion (NRP) and donation after brain death (DBD)

Donor calls attended* (N = 507)	TA-NRP (n = 213)	DBD (n = 293)	*P* value
Recovery attempt made	163 (76.5)	292 (99.7)	<.001
Accepted allografts	140/163 (85.9)	275/292 (94.2)	.005
Declined allografts	23/163 (14.1)	17/292 (5.8)	
Declined reasons			–
Allograft quality	14/23 (60.9)	17/17 (100)	
Technical	9/23 (39.1)	0 (0)	

Values are presented as n (%). *This number excludes allograft recoveries for multiorgan and/or congenital etiology transplant.