Rise of the machines: Normothermic regional perfusion use in heart transplantation in the United States

Doug A. Gouchoe, MD,[a,b] Divyaam Satija, BS,[a] Ervin Y. Cui, BS,[a,b] Jacob N. Schroder, MD,[c] Carmelo A. Milano, MD,[c] Muath Bishawi, MD,[d] Ammu V. Alvarez, MD,[a] Kukbin Choi, MD,[a] Matthew C. Henn, MD, MS,[a] Brent C. Lampert, DO,[e] Nahush A. Mokadam, MD,[a] Bryan A. Whitson, MD, PhD,[a,b] and Asvin M. Ganapathi, MD[f]

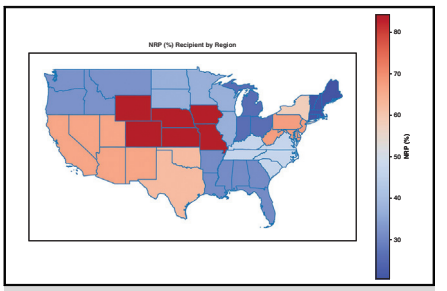
ABSTRACT

Background: Normothermic regional perfusion (NRP) and direct procurement and perfusion (DPP) allow for transplantation with donation after circulatory death (DCD) hearts. This study aimed to characterize the use of and variations in NRP and DPP for DCD transplants in the United States.

Methods: Heart transplants performed between December 1, 2019 and March 31, 2024, were identified from the United Network for Organ Sharing database. DPP and NRP procurement strategies were classified based on previously published methods. The groups were compared, and survival was assessed using Kaplan-Meier methods. Geographic and center variability was categorized using encrypted data.

Results: There were 595 NRP transplants and 625 DPP transplants. Distance traveled and out-of-body time were significantly lower for the NRP group ($P < .01$ for both). There were no significant differences in postoperative dialysis, stroke, or 1-year survival between the 2 groups; however, the rate of postoperative pacemaker placement was higher with NRP ($P < .05$). From 2019 to 2024, 54 of 61 centers (88.5%) used NRP, 50 of 61 centers (82%) used DPP, and 43 of 61 centers (70.5%) used both procurement techniques, with NRP the more popular DCD procurement technique. Geographically, NRP was more prevalent in regions 2, 5, and 8 used, whereas DPP was most prevalent in regions 1, 3, and 10.

Conclusions: The use of NRP is increasing in the United States, with tremendous growth seen since its introduction several years ago. Significant variation remains in the use of NRP and DPP, and further exploration of the impact of each procurement and preservation strategy on transplantation outcomes is needed. (J Thorac Cardiovasc Surg 2025;170:268-76)



Normothermic regional perfusion use in the United States.

CENTRAL MESSAGE

The use of normothermic regional perfusion has increased. Despite the existence of regional variation, it has similar short-term outcomes to other procurement strategies.

PERSPECTIVE

The use of normothermic regional perfusion use has increased tremendously since its introduction several years ago. Significant variation remains regarding the use of normothermic regional perfusion and direct procurement and perfusion, and further determination of the impact of each strategy on other organ procurement and primary graft function is necessary.

See Commentator Discussion on page 277.

From the [a]Division of Cardiac Surgery, Department of Surgery, The Ohio State University Wexner Medical Center, Columbus, Ohio; [b]COPPER Lab, The Ohio State University, Columbus, Ohio; [c]Division of Cardiac Surgery, Department of Surgery, Duke University Medical Center, Durham, NC; [d]Department of Surgery, Emory University, Atlanta, Ga; [e]Division of Cardiovascular Medicine, Department of Medicine, The Ohio State University Wexner Medical Center, Columbus, Ohio; and [f]Los Robles Regional Medical Center, Thousand Oaks, Calif.

This research was generously supported through the Jewel and Frank Benson Family Endowment and the Jewel and Frank Benson Research Professorship.

IRB approval 2018H0079.

Gouchoe and Satija contributed equally to this manuscript.

Read at the 104th Annual Meeting of The American Association for Thoracic Surgery, Toronto, Ontario, Canada, April 27-30, 2024.

Received for publication April 26, 2024; revisions received Nov 22, 2024; accepted for publication Dec 1, 2024; available ahead of print Dec 9, 2024.

Address for reprints: Asvin M. Ganapathi, MD, 227 West Janss Rd, Suite 340, Thousand Oaks, CA 91360 (E-mail: asvin.ganapathi@osumc.edu).

0022-5223/$36.00

https://doi.org/10.1016/j.jtcvs.2024.12.001

Abbreviations and Acronyms

CSS = cold static storage
DCD = donation after circulatory death
DPP = direct procurement and perfusion
EVP = ex vivo perfusion
ECMO = extracorporeal membrane oxygenation
NRP = normothermic regional perfusion
OPTN = Organ Procurement and Transplantation Network
UNOS = United Network for Organ Sharing

Scanning this QR code will take you to the table of contents to access supplementary information. To view the AATS Annual Meeting Webcast, see the URL next to the webcast thumbnail.

Transplantation is often the sole viable therapy for end-stage heart failure. Limited donor availability for heart transplantation has led providers to explore donation after circulatory death (DCD), with promising results.[1,2] Recently, 2 procurement strategies in DCD heart transplantation have been popularized: direct procurement and perfusion (DPP) and normothermic regional perfusion (NRP).

Although all DCD procurements start with withdrawal of life-sustaining treatment, subsequent circulatory arrest and an obligatory standoff period, which in the United States is 2 to 5 minutes,[3] procurement strategies differ in the timing of cardiectomy and transport of the heart. DPP involves immediate cardiectomy following the standoff period and subsequent perfusion with ex vivo machine perfusion (EVP; ie, direct procurement and perfusion).

In contrast, procurement with NRP begins with the establishment of extracorporeal circulation (centrally in most cases) with the use of extracorporeal membrane oxygenation (ECMO) and cessation of blood flow to the brain. The establishment of extracorporeal circulation ultimately affords clinicians dynamic in situ organ assessment to evaluate the heart's function and suitability for donation.[4] If the heart is deemed suitable for transplantation, it can be safely transported via cold static storage (CSS)[5] or EVP.[6]

NRP and DPP are still relatively new procedures, and investigations into the outcomes of subsequent heart transplantations are just now unfolding.[1,2,4,5,7-10] Here we aimed to characterize the use of and variation in NRP and DPP in the United States, a large country with a diverse population and an amalgamation of beliefs. We hypothesized that while NRP use has grown, both regional and center variations remain.

METHODS

Adult heart transplants were identified using data from the United Network for Organ Sharing (UNOS)/Organ Procurement Transplant Network (OPTN) database for December 1, 2019, to March 31, 2024. Recipients with a prior heart transplant or undergoing multiorgan transplant were excluded. Patients were then stratified according to procurement method: NRP or DPP. Method of procurement was determined based on previously published methods, in which NRP procurements were identified by an interval from circulatory standstill to cross-clamp of >30 minutes,[1,5,7,10] and DPP procurements were identified by an interval <30 minutes.[1,10-12] The study was deemed exempt from Institutional Review Board approval (IRB 2018H0079; January 1, 2018).

Continuous variables were assessed for normality using QQ plots and presented as mean ± standard deviation (SD) or median (interquartile range [IQR]). Continuous variables were compared using the parametric Student t test or nonparametric Kruskal-Wallis test, and categorical variables were compared using the χ^2 test. Unadjusted survival was assessed using Kaplan-Meier methods with the log-rank test. To determine regional trends, the region and recipient's state of permanent residence provided in the data file were used to identify where use of the organ occurred. Additionally, the state of the donor hospital was identified and used to examine variability. Changes in the trends of use were assessed using the Spearman rank correlation test. Finally, the Spearman correlation test was used to evaluate the relationship between median distance traveled and the proportion of NRP use per center, followed by a line of best fit to display the association. Missingness for all variables was calculated (Table E1), and no imputation was performed. All statistical analyses were performed with R version 3.6.2 (R Foundation for Statistical Computing). Statistical significance was set at $P < .05$ for all analyses.

RESULTS

A total of 625 (51.2%) DPP DCD transplant recipients and 595 (48.8%) NRP DCD transplant recipients who underwent lung transplantation between December 1, 2019, and March 31, 2024, were identified (Figure E1). There were no significant differences in age, sex, or race between the DPP and NRP groups. Additionally, there were no significant differences in baseline medical comorbidities, including body mass index, smoking history, glomerular filtration rate, and diagnosis, as well as no differences in pretransplantation mechanical circulatory support requirements. DPP DCD transplant recipients spent a median of 29 days (IQR, 9-155 days) on the waitlist, compared to a median of 28 days (IQR, 8-118.5 days) for NRP recipients ($P = .157$) (Table E2). There were no significant differences in age or sex between donors in the DPP and NRP groups; however, there were significantly higher proportions of black donors in the DPP group and of Hispanic donors in the NRP group ($P < .01$). Donors in the DPP group to have significantly higher creatinine levels, whereas donors in the NRP group had significantly higher ejection fractions ($P < .05$ for both). There were no additional significant between-group differences in baseline medical conditions or donor causes of death (Table 1). Over the study period, 90% of donor hearts that were recovered for transplantation using DPP eventually were transplanted, compared to 96.7% of NRP procured donor hearts ($P < .001$).

ADULT

TABLE 1. Donor demographics

Characteristic	Overall	DPP group (N = 625)	NRP group (N = 595)	*P* value
Age, y, median (IQR)	31 (24-37.2)	31 (25-37)	32 (24-38)	.272
Male sex, n (%)	1028 (84.3)	527 (84.3)	501 (84.2)	.999
Ethnicity, n (%)				.005
White	928 (76.1)	476 (76.2)	452 (76)	
Black	118 (9.7)	76 (12.2)	42 (7.1)	
Hispanic	142 (11.6)	58 (9.3)	84 (14.1)	
Asian	13 (1.1)	7 (1.1)	6 (1)	
Other	19 (1.6)	8 (1.3)	11 (1.8)	
Coronary artery disease, n (%)	10 (0.8)	2 (0.3)	8 (1.3)	.057
Smoking history, n (%)	133 (11.1)	72 (11.7)	61 (10.5)	.56
Recent cocaine use, n (%)	255 (28.5)	131 (27.8)	124 (29.2)	.689
Diabetes, n (%)	40 (3.3)	19 (3)	21 (3.5)	.749
Hypertension, n (%)	164 (13.5)	76 (12.2)	88 (14.9)	.202
BMI, median (IQR)	26.6 (23.5-31.1)	26.6 (23.5-31.1)	26.7 (23.5-31)	.998
Donor cause of death, n (%)				.109
Neurologic (seizure/CVA)	109 (8.9)	54 (8.6)	55 (9.2)	
Drug overdose	281 (23)	145 (23.2)	136 (22.9)	
Asphyxiation	138 (11.3)	81 (13)	57 (9.6)	
Cardiovascular	113 (9.3)	62 (9.9)	51 (8.6)	
Trauma (GSW/stab/blunt)	514 (42.1)	258 (41.3)	256 (43)	
Drowning	8 (0.7)	5 (0.8)	3 (0.5)	
Other	57 (4.7)	20 (3.2)	37 (6.2)	
Donor clinical infection, n (%)	978 (80.3)	497 (79.5)	481 (81.1)	.531
Donor creatinine, median (IQR)	0.8 (0.6-1)	0.8 (0.6-1)	0.7 (0.6-1)	.004
Donor alcohol use, n (%)	320 (27)	155 (25.3)	165 (28.9)	.188
Ejection fraction, %, median (IQR)	63 (60-66)	61 (58-65)	64 (60-68)	.007

DPP, Direct procurement and perfusion; *NRP*, normothermic regional perfusion; *IQR*, interquartile range; *BMI*, body mass index; *CVA*, cerebrovascular accident; *GSW*, gunshot wound.

Regarding transplant outcomes and characteristics, recipients in the NRP group underwent transplantation at centers with a higher overall total median center volume during the study period compared to the DPP group (median, 255 [IQR, 176-513] vs 228 [IQR, 177-513]; $P = .003$). Additionally, those in the DPP group had a significantly longer median out-of-body time (6 hours [IQR, 5-7.1 hours vs 3.8 hours [IQR, 2.9-5.3 hours]), as well as distance traveled to recipient hospital (389 [IQR, 186-596] nautical miles vs 237 [IQR, 65-505] nautical miles) ($P < .05$ for both). Postoperative hospital length of stay and rates of dialysis, stroke, and acute rejection before discharge did not differ significantly between the 2 groups ($P > .05$ for all); however, there was a significantly higher rate of pacemaker placement in the NRP group (2% vs 0.5%; $P = .043$) (Table 2). Additionally, there were no significant differences in cardiac output, mechanical circulatory support use, or primary graft dysfunction postoperatively (Table E3). Regarding survival, neither in-hospital mortality ($P = .604$) nor mid-term survival ($P = .63$) differed significantly between the 2 groups (Figure 1). Additionally, 90-day survival ($P = .55$) and 1-year survival ($P = .87$) were similar in the 2 groups (Figure E2).

Over the study period, there was a significant increase in the incidence of heart transplants from DCD donors, from only 0.2% of heart transplants in 2019 and to 18.2% in 2024. There was a consistent year-over-year increase in transplant numbers for both the DPP and NRP groups. The Spearman rank correlation analysis confirmed this statistically significant trend in both NRP ($P < .01$) and DPP ($P < .01$) use over time. The use of NRP rose from 19.8% in 2020 to 51.6% in 2023 ($P < .001$) (Figure E3), and since January 2023, it has been performed more frequently than DPP (Figure 2). Between 2019 and 2024, 61 centers used DCD hearts, 54 centers (88.5%) used NRP, and 50 centers (82%) used DPP (Figures 3 and E3). Eleven centers used only NRP, and 7 centers used only DPP (Table E4).

There was a significant difference in procurement technique among UNOS regions ($P < .01$), with UNOS regions 2, 5, and 8 using NRP more frequently and UNOS regions 1,

TABLE 2. Operative characteristics and postoperative outcomes

Variable	Overall	DPP group (N = 625)	NRP group (N = 595)	*P* value
Overall center volume, n, median (IQR)*	241 (176-513)	228 (177-513)	255 (176-513)	.003
Distance traveled, nautical miles, median (IQR)	311.5 (130-550)	389 (186-593)	237 (65-505)	<.001
Out-of-body time, h, median (IQR)	5.1 (3.5-6.5)	6 (5-7.1)	3.8 (2.9-5.3)	<.001
Length of stay, d, median (IQR)	16 (12-25)	17 (12-25)	16 (12-25)	.458
Postoperative dialysis, n (%)	214 (18.3)	112 (18.4)	102 (18.1)	.964
Postoperative stroke, n (%)	52 (4.4)	27 (4.4)	25 (4.4)	.999
Postoperative pacemaker, n (%)	14 (1.2)	3 (0.5)	11 (2)	.043
In-hospital mortality, n (%)	40 (3.6)	23 (3.9)	17 (3.2)	.604
Acute rejection before discharge, n (%)	163 (13.9)	92 (15.1)	71 (12.6)	.241
Year of transplant, n (%)				<.001
2019	7 (0.6)	6 (1)	1 (0.2)	
2020	101 (8.3)	81 (13)	20 (3.4)	
2021	186 (15.2)	96 (15.4)	90 (15.1)	
2022	299 (24.5)	142 (22.7)	157 (26.4)	
2023	523 (42.9)	253 (40.5)	270 (45.4)	
2024	104 (8.5)	47 (7.5)	57 (9.6)	

DPP, Direct procurement and perfusion; *NRP*, normothermic regional perfusion; *IQR*, interquartile range. *Overall center volume includes both donation after circulatory death and donation after brain death transplants.

3, and 10 using DPP more frequently. Regions 1, 5, and 11 used the most DCD heart allografts, with regions 1 and 11 generally using DPP and region 5 preferring NRP. Overall, regions 2, 6, and 10 had the lowest use of DCD heart allografts (Figures 4 and E4, Table E5). Analysis of state-level trends revealed a higher rate of NRP DCD transplants in Colorado, Tennessee, Pennsylvania, Nebraska, and California and higher rates of DPP DCD transplants in South Carolina, North Carolina, Connecticut, and Massachusetts (Figure 5, *A*; Table E6). Of note, recipients from Louisiana,

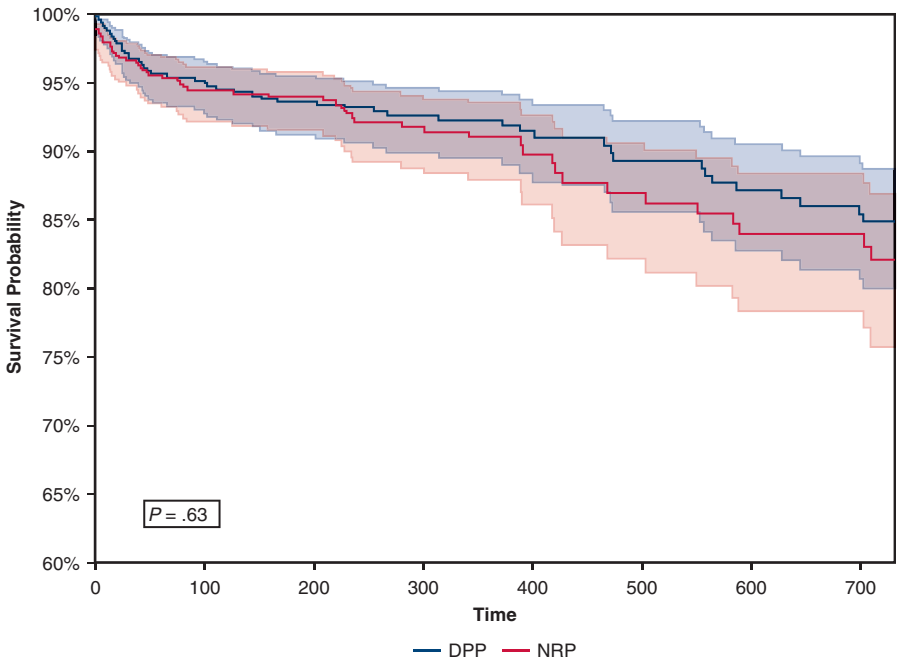


FIGURE 1. Survival among recipients. Plots show Kaplan-Meier survival estimates, with 95% confidence interval (*CI*) denoted by *shaded areas*. 90-day survival was 94.5% for the normothermic regional perfusion (*NRP*) group (95% confidence interval [*CI*], 92.1%-96.2%) and 95.2% for the direct procurement and perfusion (*DPP*) group (95% CI, 93.1%-96.7%), and 1-year survival in the 2 group was 91.1% (95% CI, 88.0%-93.5%) and 92.3% (95% CI, 90.0%-94.4%), respectively.

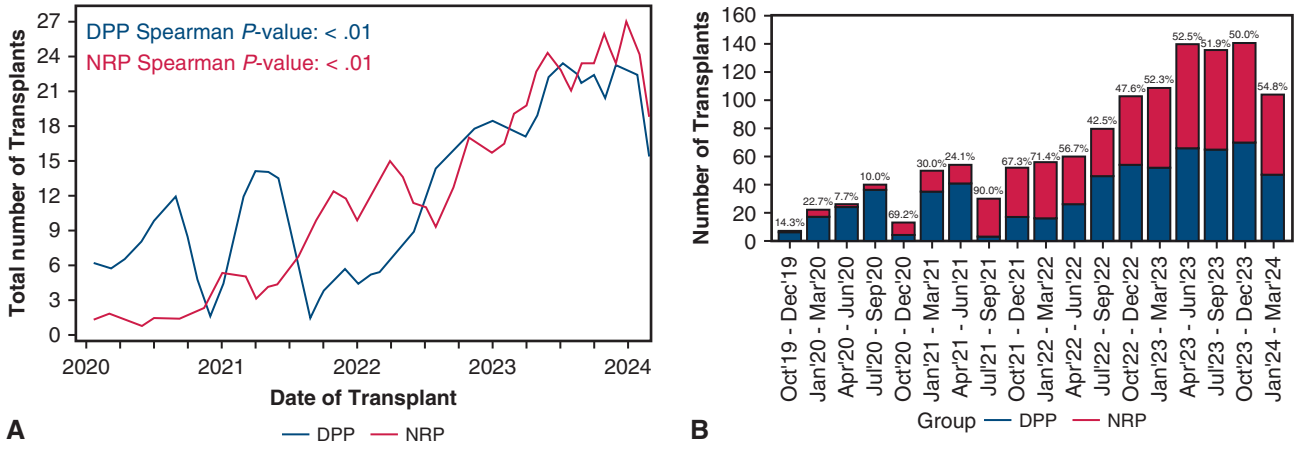


FIGURE 2. Trends in donation after circulatory death (*DCD*) heart procurement techniques. A, Linear trends in normothermic regional perfusion (*NRP*) and direct procurement and perfusion (*DPP*) use over time. B, Percentage of NRP procurements over time, noted above the *red* (NRP)/*blue* (DPP) bars.

Missouri and Oklahoma exclusively received NRP allografts; however, all these states had <10 DCD transplants. When analyzing specifically where DCD heart procurement occurred, procurement in Utah, Colorado and Nebraska was done more often using NRP, whereas procurement in Illinois, Massachusetts, South Carolina and Washington was done most frequently with DPP (Figure 5, *B*; Table E7).

DISCUSSION

With the increased use of DCD heart allografts, increasing attention has been focused on how these organs are used and their outcomes. Our analysis demonstrates that while there was a significantly higher rate of pacemaker placement in the NRP group compared to the DPP group, this did not affect in-hospital mortality or short-term survival, similar to results in previous reports.[2,4,9,10] Ultimately, despite these results, significant variations in NRP and DRP use at the regional and state levels exist within the United States. Our analysis of variations in the use of NRP reveals 3 important findings: (1) the use of NRP has increased significantly since 2020, and NRP is now used more frequently than DPP; (2) there is significant geographic variation in the use of NRP in terms of location of both donor and recipient; and (3) while many centers use

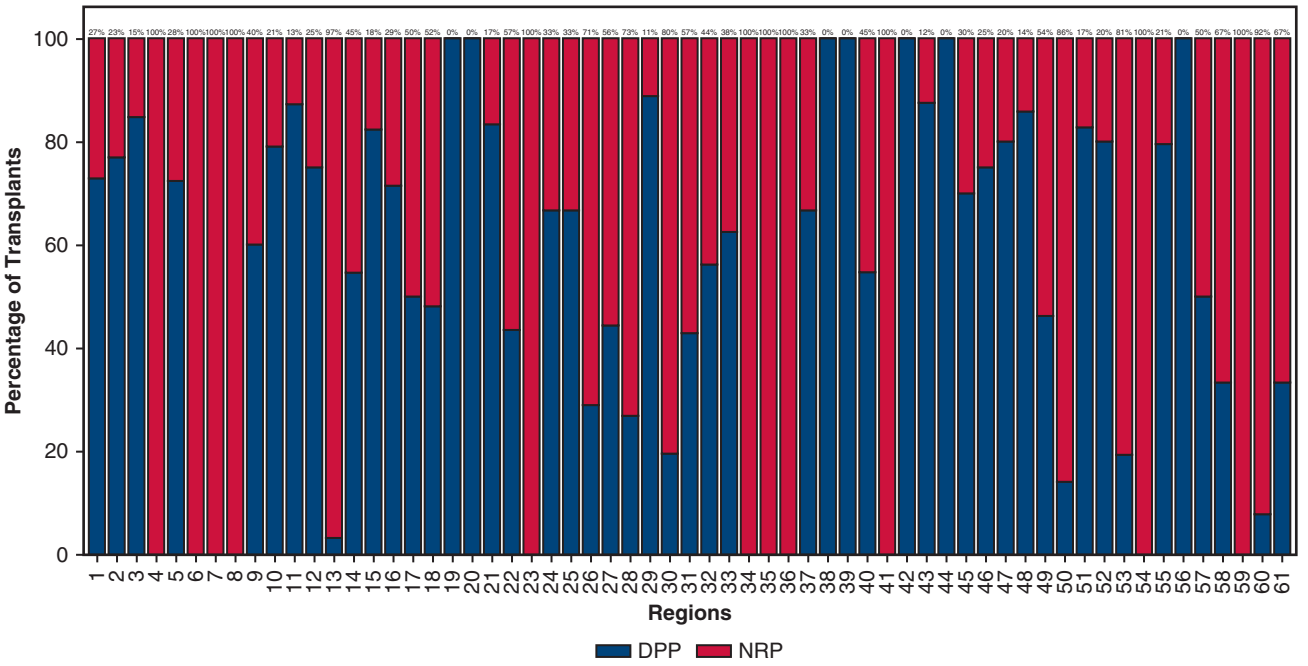


FIGURE 3. Center distribution of normothermic regional perfusion (*NRP*; *red*) and direct procurement and perfusion (*DPP*; *blue*) use.

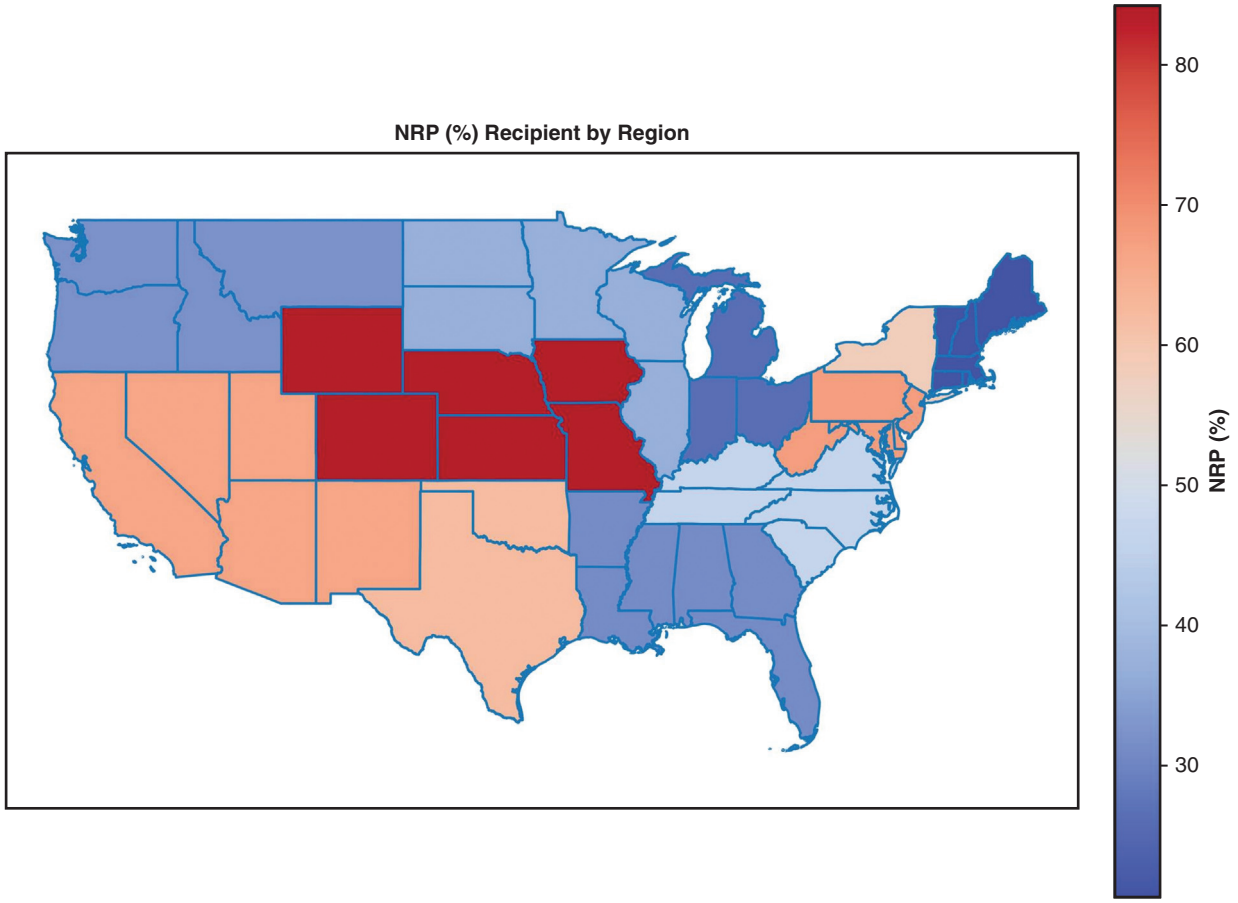


FIGURE 4. Normothermic regional perfusion (*NRP*) recipient utilization by region, UNOS regions 1 to 11.

both DPP and NRP, most tend to have a preference for one strategy over the other (Figure 6).

Regarding procurement strategies in DCD heart transplantation, center geography and regional variations in the use of DPP and NRP were noted. Although transplant center location was not available (only deidentified center data were available), the analysis did examine use based on the permanent address by state of the recipient and donor. Except for UNOS regions 9 and 11, all other regions had a clear preference (>60% of one procurement method)

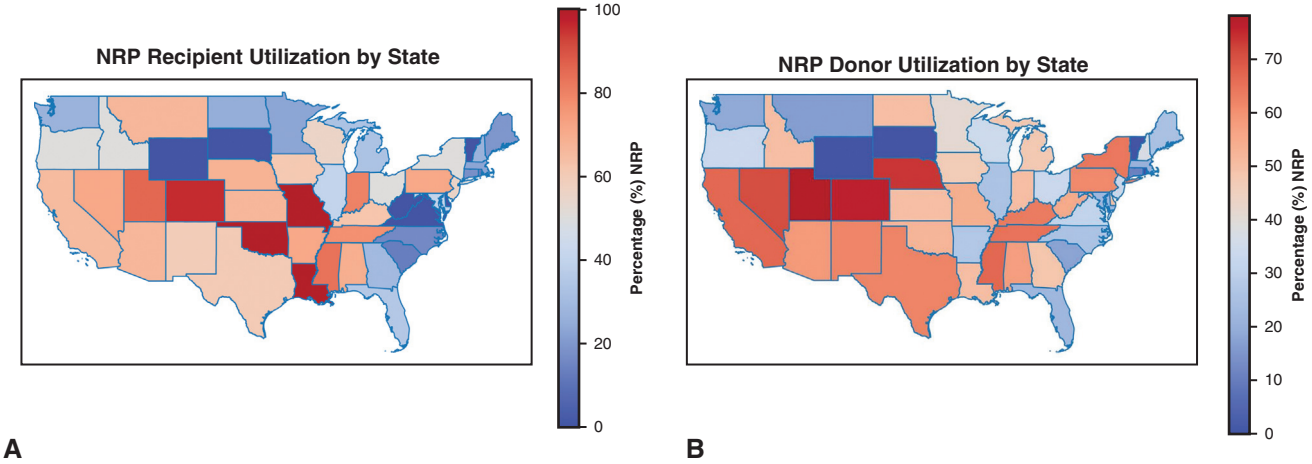


FIGURE 5. Use of normothermic regional perfusion (*NRP*) or direct procurement and perfusion (*DPP*) by state. A, State NRP use based on use of NRP allografts in recipients. B, State NRP use based on NRP donor state.

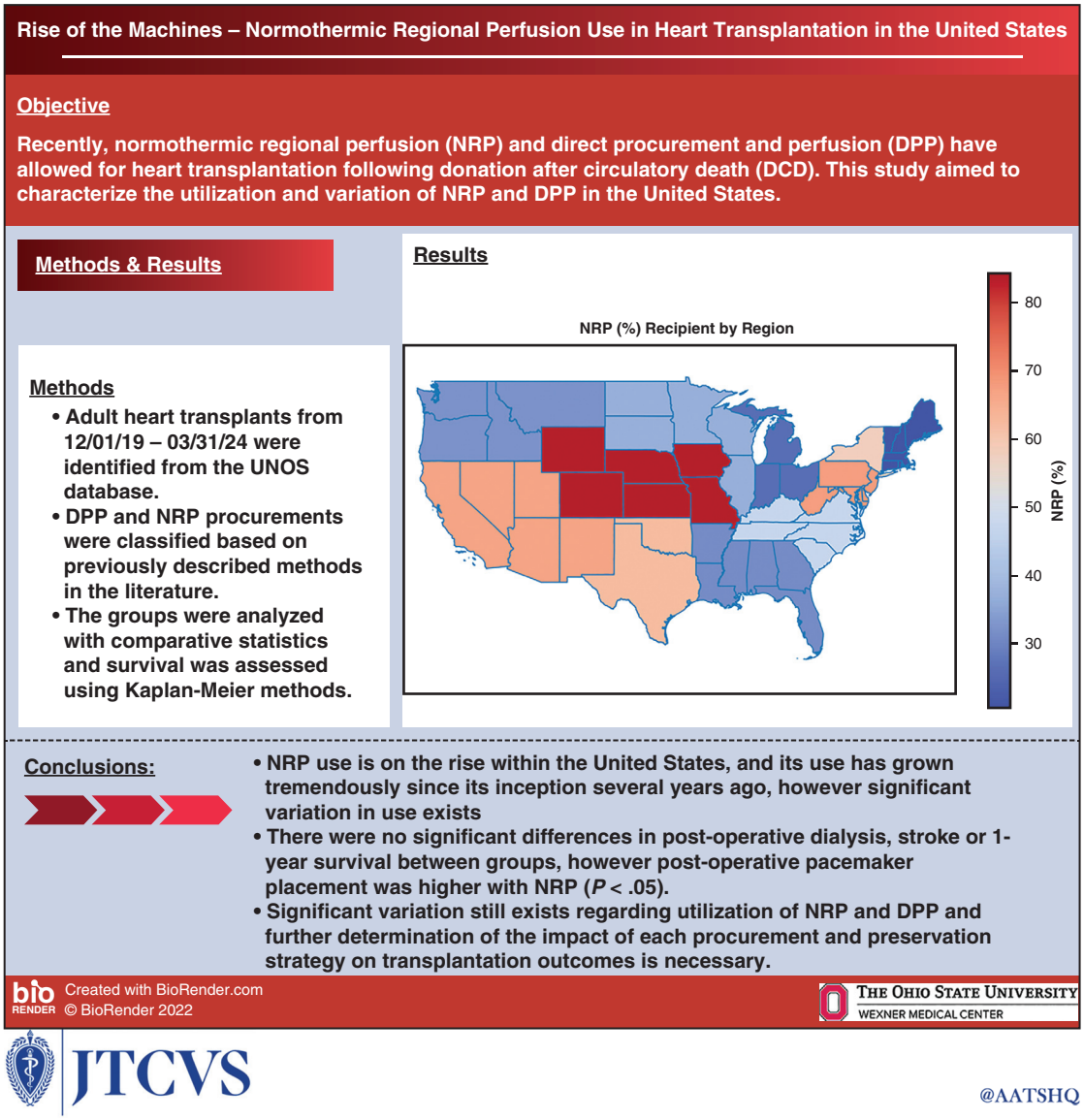


FIGURE 6. Graphical abstract depicting the study's objective, methods, results and conclusions.

for either NRP or DPP. It is unclear why these differences exist; however, travel distance for organs as well as ethical concerns (notably in region 1, where organ procurement organizations have been vocal in their expression of the overall ethical concerns surrounding NRP[13]) may impact these findings. Although there was some variation among East Coast regions, the majority of the Mountain West and West Coast used NRP, with the Pacific Northwest the notable exception. It was notable that the overall distance traveled and out-of-body time (or likely time between cross-clamping and recipient reperfusion for DPP with EVP) was significantly longer for DPP, suggesting that centers procuring organs from farther away may have a preference for DPP. However, the regional variations—particularly the fact that Western states prefer NRP—demonstrate otherwise. Given the shorter distance traveled in the NRP group, further research is needed to determine whether centers with shorter median travel distances are more likely to use NRP, and whether these centers are located in areas of higher population density, which potentially would facilitate closer donors. A preliminary plot of the median distance traveled compared to the percentage of NRP demonstrated a moderate correlation of distance to NRP use, with increased distance negatively associated with NRP use (Figure E5); however, more data are needed to confirm this potential association. Additionally, center-level policies and preferences may influence the procurement strategy.

Regarding center utilization, it is notable that although many centers use both DPP and NRP, most centers

demonstrate a clear preference for one strategy (82% with >60% use of one strategy). The data demonstrate that 49.2% of centers used DPP >60% of the time and 32.8% of centers used NRP >60% of the time. Also of note, although NRP was first used in early 2020, significant ethical concerns surrounding its use might have impacted centers' decisions regarding the optimal approach to DCD heart transplantation.[13] A center's views and comfort with DCD heart transplantation also may impact its choice of procurement strategy. For example, a center that feels strongly about observing cardiac function for a prolonged period following death or using an extended-criteria donor may prefer DPP with EVP to assess cardiac function over a longer period, as opposed to a center that is comfortable with the brief observational period associated with NRP. Transplant providers also must consider preservation following procurement with DPP or NRP. Namely, if a prolonged distance or out-of-body time is planned for recovery, EVP may be preferred because of its perceived association with mitigating ischemic effects, and thus DPP may be the preferred procurement method to reduce the equipment required. However, minimal significant differences in recipient and donor characteristics were noted between the 2 groups, indicating that these characteristics do not appear to be associated with a center's preferred procurement method. Finally, center volume may have a role in NRP and DPP preference, as higher-volume centers more often use NRP. Although this finding may be related to resource availability, the reason for significantly different center volumes between the groups is unclear, and further research is needed.

The procurement strategy's financial impact may be influential as well. Although we do not have financial data available, previous studies have suggested how cost impacted centers' decision to use one procurement strategy over another.[5] Over the period of analysis, DPP use followed a distinct pattern (a sharp reduction, followed by sharp increase then reduction, and then gradual increase) (Figure 2, *A*), which coincides with the timing of clinical trial enrollment and subsequent approval of the Heart Organ Care System by TransMedics in April 2022.[2] Therefore, centers that use primarily DPP potentially could have been early adopters of DPP and EVP. Early-adopting centers may have already purchased the reusable component (ie, the primary machine) and thus would be responsible only for the disposables, which may have encouraged the use of DPP. Conversely, the rise in NRP use may be related to the fact that institutions beginning a DCD program without having purchased an EVP machine may have preferred to use equipment that is already be part of their program. Finally, it is important to consider that as more centers use procurement services and local procurement, these factors may influence how NRP and DPP are used, particularly the costs of these services and equipment.

Finally, while transplant centers and organ procurement organizations may influence the choice of procurement method, surgeons also must consider the impact on other organs procured for transplant, namely the lungs and liver. Initial anecdotal experiences and data were concerning for damaging effects of NRP on the lungs due to pulmonary congestion.[14] Although current data suggest that DCD heart and lungs from the same donor can be used safely,[10] it has become apparent that proper procurement technique involves appropriately ventilating the lungs to minimize atelectasis, as well as venting of the pulmonary circulation with a pulmonary artery cannula.[4] Furthermore, regarding the liver and other abdominal organs, there also are data suggesting that NRP can help improve outcomes of these procurements,[2] and our analysis also shows that NRP has a significantly higher utilization rate compared to DPP. Although more data are needed to analyze the impact of DPP and NRP on other organ procurements, it is important that all procuring teams understand the planned operative procurement sequence to best increase organ utilization.

Limitations

This study has inherent limitations that affect any large database, including a lack of certain data, in particular definitive coding that clearly states whether a DCD donor underwent NRP or DPP. The accepted method for determining NRP or DPP use is a derivation and the best estimate of this perfusion technique, but is not a direct observation.[10] Additionally, the lack of reason for choice of DPP v. NRP limits the ability to understand why a particular procurement/preservation technique was utilized. Furthermore, the UNOS database's retrospective nature makes it subject to information and selection bias. Data on immediate function and the rate of primary graft dysfunction have a high rate of missingness in the UNOS database, limiting further outcome inferences regarding procurement and preservation techniques. The UNOS database does not clearly distinguish if CSS or EVP was used following procurement or the method of CSS. Consequently, determining the optimal preservation strategy for DCD donors is difficult, and we did not include data on preservation strategy; however, collection of such data will be important for future research. Additionally, given the relatively recent use of DCD hearts, the UNOS database does not have much granularity on total perfusion time or warm ischemic time in donors (specifically related to high missingness in time of death data) and/or recipients. The lack of significant survival data beyond 3 years also limits conclusions about the impact of procurement strategy on longer-term survival and other long-term outcomes. Finally, information on donor management as well as donor hospital resources was not available, and these data may have influenced the choice of a particular strategy.

CONCLUSIONS

NRP use is on the rise within the United States and has grown tremendously since its inception several years ago. Currently, it is the most widely used procurement method for DCD heart transplantation in the United States, with no differences in short- or mid-term survival compared to DPP. Regionally, significant variation in the use of NRP and DPP remains, owing to several possible factors, and more information is needed on the choice of procurement strategy, as well as the impact on overall organ utilization. Ultimately, further exploration of the impact of each strategy on other organ procurement, hospital-associated costs, feasibility of extended travel/procurement, and graft function is needed.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://www.aats.org/resources/rise-of-the-machines-normother-7031.

Conflict of Interest Statement

Dr Whitson serves on the Clinical Events Committee of TransMedics OCS. Dr Mokadan is a consultant and investigator for Abbott, Medtronic, Carmat, Xylocor, and SynCardia. All other 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.

References

1. Messer S, Cernic S, Page A, et al. A 5-year single-center early experience of heart transplantation from donation after circulatory-determined death donors. *J Heart Lung Transplant*. 2020;39(12):1463-1475. https://doi.org/10.1016/j.healun.2020.10.001
2. Schroder JN, Patel CB, DeVore AD, et al. Transplantation outcomes with donor hearts after circulatory death. *N Engl J Med*. 2023;388(23):2121-2131. https://doi.org/10.1056/NEJMoa2212438
3. Saemann L, Karck M, Korkmaz-Icöz S, Wenzel F, Szabó G. Ethical decision diagrams on donation after cardiocirculatory death heart transplantation considering organ preservation techniques. *Transplant Direct*. 2020;6(11):e617. https://doi.org/10.1097/txd.0000000000001075
4. James L, LaSala VR, Hill F, et al. Donation after circulatory death heart transplantation using normothermic regional perfusion: the NYU protocol. *JTCVS Tech*. 2022;17:111-120. https://doi.org/10.1016/j.xjtc.2022.11.014
5. Hoffman JRH, McMaster WG, Rali AS, et al. Early US experience with cardiac donation after circulatory death (DCD) using normothermic regional perfusion. *J Heart Lung Transplant*. 2021;40(11):1408-1418. https://doi.org/10.1016/j.healun.2021.06.022
6. Messer S, Page A, Axell R, et al. Outcome after heart transplantation from donation after circulatory-determined death donors. *J Heart Lung Transplant*. 2017;36(12):1311-1318. https://doi.org/10.1016/j.healun.2017.10.021
7. Smith DE, Kon ZN, Carillo JA, et al. Early experience with donation after circulatory death heart transplantation using normothermic regional perfusion in the United States. *J Thorac Cardiovasc Surg*. 2022;164(2):557-568.e1. https://doi.org/10.1016/j.jtcvs.2021.07.059
8. Dhital K, Ludhani P, Scheuer S, Connellan M, Macdonald P. DCD donations and outcomes of heart transplantation: the Australian experience. *Indian J Thorac Cardiovasc Surg*. 2020;36(Suppl 2):224-232. https://doi.org/10.1007/s12055-020-00998-x
9. Louca J, Öchsner M, Shah A, et al. The international experience of in-situ recovery of the DCD heart: a multicentre retrospective observational study. *EClinicalMedicine*. 2023;58:101887. https://doi.org/10.1016/j.eclinm.2023.101887
10. Kwon JH, Ghannam AD, Shorbaji K, et al. Early outcomes of heart transplantation using donation after circulatory death donors in the United States. *Circ Heart Fail*. 2022;15(12):e009844. https://doi.org/10.1161/circheartfailure.122.009844
11. Dhital KK, Iyer A, Connellan M, et al. Adult heart transplantation with distant procurement and ex-vivo preservation of donor hearts after circulatory death: a case series. *Lancet*. 2015;385(9987):2585-2591. https://doi.org/10.1016/s0140-6736(15)60038-1
12. Shudo Y, Benjamin-Addy R, Koyano TK, Hiesinger W, MacArthur JW, Woo YJ. Donors after circulatory death heart trial. *Future Cardiol*. 2021;17(1):11-17. https://doi.org/10.2217/fca-2020-0070
13. Wall AE, Fiedler A, Karp S, Shah A, Testa G. Applying the ethical framework for donation after circulatory death to thoracic normothermic regional perfusion procedures. *Am J Transplant*. 2022;22(5):1311-1315. https://doi.org/10.1111/ajt.16959
14. Zhou AL, Ruck JM, Casillan AJ, et al. Early United States experience with lung donation after circulatory death using thoracoabdominal normothermic regional perfusion. *J Heart Lung Transplant*. 2023;42(6):693-696. https://doi.org/10.1016/j.healun.2023.03.001

Key Words: normothermic regional perfusion, heart transplantation, donation after circulatory death

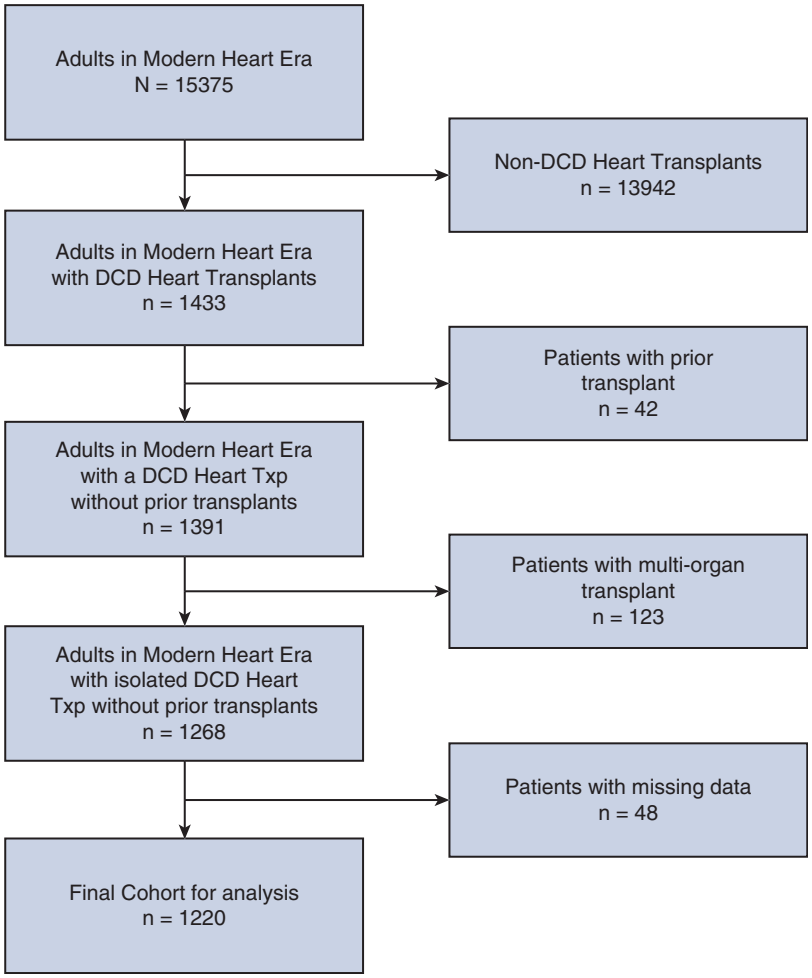


FIGURE E1. CONSORT diagram depicting study inclusion and exclusion criteria. *DCD*, Donation after circulatory death.

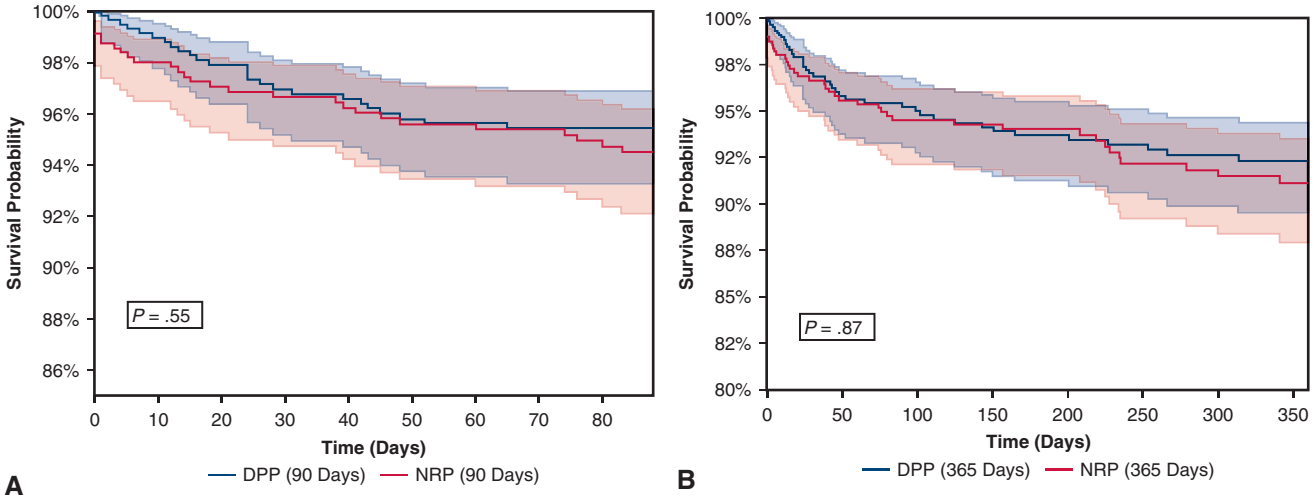


FIGURE E2. Kaplan-Meier survival estimates with 95% confidence intervals (*shaded areas*) at 90 days (A) and 1 year (B). *DPP*, Direct procurement and perfusion; *NRP*, normothermic regional perfusion.

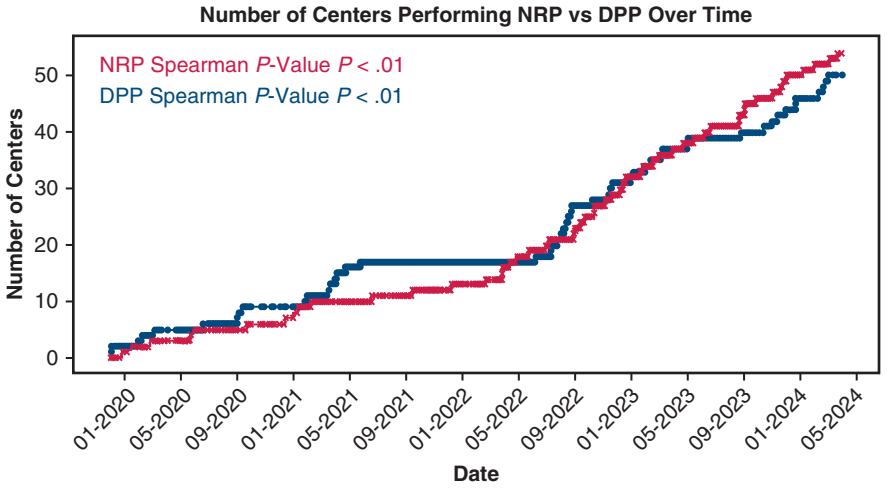


FIGURE E3. Trends in use of normothermic regional perfusion (*NRP*; *red*) and direct procurement and perfusion (*DPP*; *blue*) over time.

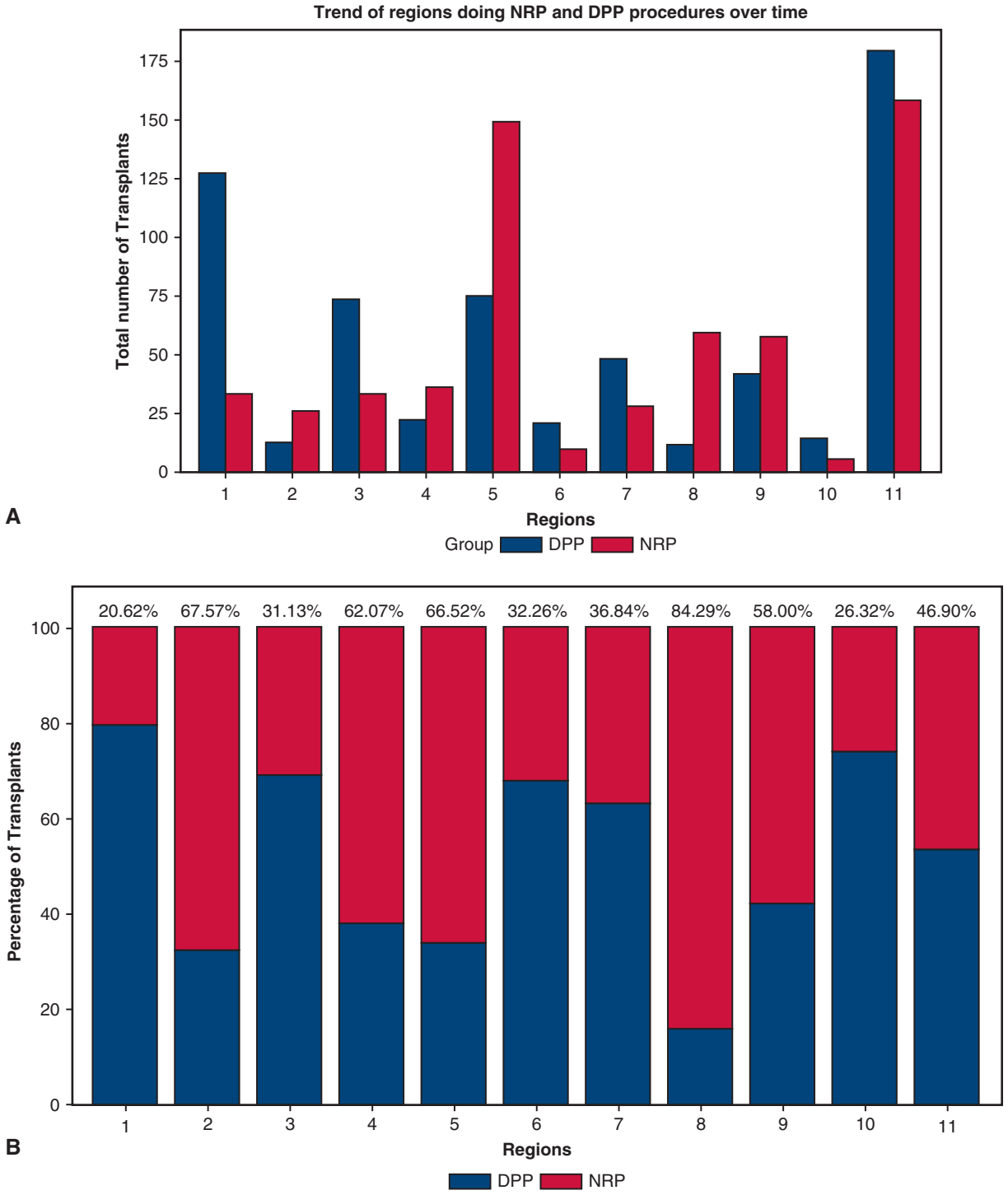


FIGURE E4. Total number of normothermic regional perfusion (*NRP*) and direct procurement and perfusion (*DPP*) transplants. A, Total number of transplants by region. B, Percentage of transplants by region.

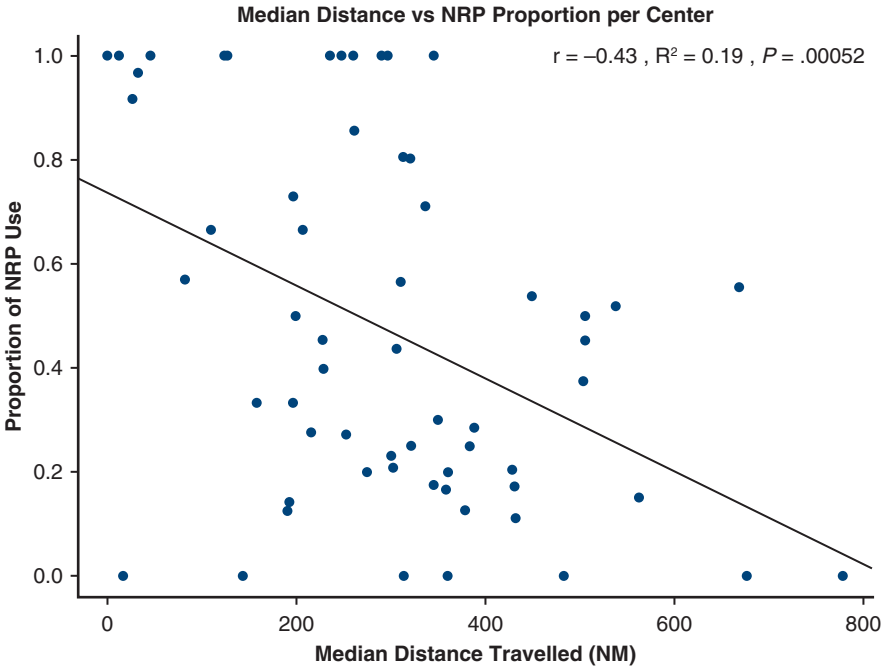


FIGURE E5. Scatterplot showing the relationship between the median distance traveled (NM) and the proportion of normothermic regional perfusion (*NRP*) use per center. The line of best fit shows a moderately negative correlation (Spearman r = −0.43; $R^2 = 0.19$) that was statistically significant ($P < .001$).

TABLE E1. Missingness

Variable	% missing
Recipient demographics and baseline characteristics	
Age (y)	0.00
Male sex	0.00
Race	0.00
BMI (kg/m^2)	0.08
Weight	0.08
Education level	3.44
Former smoker >20 pack-y	0.66
Diabetes	0.66
Creatinine (mg/dL)	3.52
GFR (mL/min/1.73 m^2)	3.69
Preoperative dialysis	0.00
Diagnosis	0.66
Blood group	0.00
IV inotropes	0.00
Mean pulmonary artery pressure (mm Hg)	5.82
Cardiac output	7.30
PCWP	9.26
PRA	0.00
Days on wait list	0.00
Preoperative mechanical support	0.00
Donor characteristics	
Age	0.00
Male sex	0.00
Ethnicity	0.00
CDC high risk	0.90
Coronary artery disease	0.00
Smoking history	2.05
Recent cocaine use	26.64
Diabetes	0.33
Hemoglobin A1C	78.28
Diabetes duration	97.13
Hypertension	0.57
BMI	0.00
Cause of death	0.00
Bloodstream infection	0.00
Clinical infection	0.16
Pulmonary infection	0.00
Creatinine	0.00
Alcohol use	3.03
Extracranial cancer	0.25
Myocardial infarction history	0.57
Antihypertensives 24 h before XC	0.08
Inotropes	0.00
Ejection fraction	0.33
Operative characteristics and postoperative outcomes	
Year of transplant	0.00
Sex mismatch	0.00
Yearly center volume average	0.00
Distance traveled (nautical miles)	0.00
Ischemia time (h)	4.34
Length of stay (d)	5.90
Postoperative dialysis	3.93
Postoperative stroke	4.02
Postoperative pacemaker	4.02
Acute rejection before discharge	3.93
In-hospital mortality	8.20
Acute rejection before discharge (simple)	3.93
Treated for rejection in first y	52.87
Cause of death	91.56
Status	0.00
Cardiac output 24 h	78.85
Cardiac output 72 h	82.46
Dobutamine at 24 h	74.75
Dobutamine at 72 h	74.75
Dopamine at 24 h	74.75
Dopamine at 72 h	74.75
ECMO at 24 h	73.36
ECMO at 72 h	73.36
Epinephrine at 24 h	74.75
Epinephrine at 72 h	74.75
Epoprostenol at 24 h	74.84
Epoprostenol at 72 h	74.75
Intra-aortic balloon pump at 24 h	73.36
Intra-aortic balloon pump at 72 h	73.36
Inhaled NO at 24 h	73.36
Inhaled NO at 72 h	73.36
Life support at 24 h	74.75
Life support at 72 h	74.75
LVEF at 24 h	74.67
LVEF at 72 h	74.75
Milrinone at 24 h	74.75
Milrinone at 72 h	74.75
PGD at 24 h	74.75
PGD at 72 h	74.75
RA pressure at 24 h	79.59
RA pressure at 72 h	80.90

BMI, Body mass index; *GFR*, glomerular filtration rate; *IV*, intravenous; *PCWP*, pulmonary capillary wedge pressure; *PRA*, panel reactive antibody; *CDC*, Centers for Disease Control; *XC*, cross clamp; *ECMO*, extracorporeal membrane oxygenation; *NO*, nitric oxide; *LVEF*, left ventricular ejection fraction; *PGD*, primary graft dysfunction; *RA*, right atrial.

ADULT

TABLE E2. Transplant recipient demographics

Characteristic	Overall	DPP group (N = 625)	NRP group (N = 595)	*P* value
Age, y, median (IQR)	57 (46-64)	56 (45-64)	57 (46-64)	.201
Male sex, n (%)	975 (79.9)	495 (79.2)	480 (80.7)	.569
Race, n (%)				.161
White	822 (67.4)	418 (66.9)	404 (67.9)	
Black	244 (20)	136 (21.8)	108 (18.2)	
Other	154 (12.6)	71 (11.4)	83 (13.9)	
BMI, kg/m^2, median (IQR)	28.2 (24.8-32)	28 (24.5-32.1)	28.2 (25.2-32)	.448
Former smoker, n (%)	534 (44.1)	280 (45)	254 (43.1)	.528
Diabetes, n (%)	367 (30.3)	191 (30.7)	176 (29.8)	.788
Creatinine, mg/dL, median (IQR)	1.1 (0.9-1.4)	1.1 (0.9-1.4)	1.1 (0.9-1.4)	.607
GFR, mL/min/1.73 m^2, median (IQR)	63 (49.2-82.2)	63.1 (49.2-82.8)	62.9 (49.2-80.5)	.555
Preoperative dialysis, n (%)	15 (1.2)	6 (1)	9 (1.5)	.538
Diagnosis, n (%)				.66
Ischemic dilated cardiomyopathy	339 (28)	167 (26.8)	172 (29.2)	
Nonischemic dilated cardiomyopathy	652 (53.8)	341 (54.8)	311 (52.7)	
Other	221 (18.2)	114 (18.3)	107 (18.1)	
Status, n (%)				.201
Status 1	38 (3.1)	22 (3.5)	16 (2.7)	
Status 2	457 (37.5)	253 (40.5)	204 (34.3)	
Status 3	209 (17.1)	97 (15.5)	112 (18.8)	
Status 4	344 (28.2)	165 (26.4)	179 (30.1)	
Status 5	3 (0.2)	1 (0.2)	2 (0.3)	
Status 6	168 (13.8)	86 (13.8)	82 (13.8)	
IV inotropes, n (%)	383 (31.4)	209 (33.4)	174 (29.2)	.129
Mean pulmonary artery pressure, mm Hg, median (IQR)	25 (19-33)	26 (19-34)	25 (19-33)	.2
Cardiac output, median (IQR)	4.3 (3.6-5.3)	4.3 (3.5-5.3)	4.4 (3.6-5.3)	.751
Days on wait list, median (IQR)	29 (9-139)	29 (9-155)	28 (8-118.5)	.157
Preoperative mechanical support, n (%)				.819
None	597 (48.9)	300 (48)	297 (49.9)	
Durable LVAD	329 (27)	169 (27)	160 (26.9)	
Pre IABP	181 (14.8)	93 (14.9)	88 (14.8)	
Temporary VAD	81 (6.6)	43 (6.9)	38 (6.4)	
BIVAD	9 (0.7)	5 (0.8)	4 (0.7)	
ECMO	23 (1.9)	15 (2.4)	8 (1.3)	

DPP, Direct procurement and perfusion; *NRP*, normothermic regional perfusion; *IQR*, interquartile range; *BMI*, body mass index; *GFR*, glomerular filtration rate; *IV*, intravenous; *LVAD*, left ventricular assist device; *IABP*, intra-aortic balloon pump; *VAD*, ventricular assist device; *BIVAD*, biventricular assist device; *ECMO*, extracorporeal membrane oxygenation.

TABLE E3. Additional operative and postoperative outcomes

Outcome	Overall	DPP group (N = 625)	NRP group (N = 595)	*P* value
Cardiac output at 24 h, median (IQR)	6.3 (5.3-7.6)	6.3 (5.3-7.3)	6.3 (5.3-7.7)	.85
Cardiac output at 72 h, median (IQR)	6.5 (5.5-7.9)	6.5 (5.4-7.9)	6.6 (5.5-7.8)	.667
ECMO at 24 h, n (%)	31 (9.5)	13 (8.3)	18 (10.7)	.577
ECMO at 72 h, n (%)	17 (5.2)	7 (4.5)	10 (6)	.722
IABP at 24 h, n (%)	42 (12.9)	15 (9.6)	27 (16.1)	.113
IABP at 72 h, n (%)	18 (5.5)	8 (5.1)	10 (6)	.924
PGD at 24 h, n (%)				.764
No	238 (77.3)	114 (75.5)	124 (79)	
Unknown	23 (7.5)	12 (7.9)	11 (7)	
Yes	47 (15.3)	25 (16.6)	22 (14)	
PGD at 72 h, n (%)				.959
No	251 (81.5)	124 (82.1)	127 (80.9)	
Unknown	25 (8.1)	12 (7.9)	13 (8.3)	
Yes	32 (10.4)	15 (9.9)	17 (10.8)	

DPP, Direct procurement and perfusion; *NRP*, normothermic regional perfusion; *IQR*, interquartile range; *ECMO*, extracorporeal membrane oxygenation; *IABP*, intra-aortic ballon pump; *PGD*, primary graft dysfunction.

ADULT

TABLE E4. Center distribution of DPP and NRP

Center	DPP, n	NRP, n	DPP, %	NRP, %	Total DCD transplants
1	16	6	72.73	27.27	22
2	10	3	76.92	23.08	13
3	78	14	84.78	15.23	92
4	0	6	0.00	100.00	6
5	21	8	72.41	27.59	29
6	0	14	0.00	100.00	14
7	0	4	0.00	100.00	4
8	0	2	0.00	100.00	2
9	3	2	60.00	40.00	5
10	19	5	79.17	20.83	24
11	110	16	87.30	12.70	126
12	3	1	75.00	25.00	4
13	1	30	3.23	96.77	31
14	6	5	54.55	45.45	11
15	14	3	82.35	17.65	17
16	10	4	71.43	28.57	14
17	1	1	50.00	50.00	2
18	13	14	48.15	51.85	27
19	3	0	100.00	0.00	3
20	9	0	100.00	0.00	9
21	5	1	83.33	16.67	6
22	10	13	43.48	56.52	23
23	0	2	0.00	100.00	2
24	2	1	66.67	33.33	3
25	2	1	66.67	33.33	3
26	11	27	28.95	71.05	38
27	4	5	44.44	55.56	9
28	7	19	26.92	73.08	26
29	8	1	88.89	11.11	9
30	21	86	19.63	80.37	107
31	3	4	42.86	57.14	7
32	18	14	56.25	43.75	32
33	15	9	62.50	37.50	24
34	0	5	0.00	100.00	5
35	0	7	0.00	100.00	7
36	0	27	0.00	100.00	27
37	2	1	66.67	33.33	3
38	2	0	100.00	0.00	2
39	1	0	100.00	0.00	1
40	23	19	54.76	45.24	42
41	0	4	0.00	100.00	4
42	2	0	100.00	0.00	2
43	7	1	87.50	12.50	8
44	1	0	100.00	0.00	1
45	7	3	70.00	30.00	10
46	9	3	75.00	25.00	12
47	28	7	80.00	20.00	35
48	6	1	85.71	14.29	7
49	6	7	46.15	53.85	13
50	1	6	14.29	85.71	7
51	24	5	82.76	17.24	29
52	8	2	80.00	20.00	10
53	32	133	19.39	80.61	165
54	0	1	0.00	100.00	1
55	27	7	79.41	20.59	34
56	3	0	100.00	0.00	3
57	1	1	50.00	50.00	2
58	10	20	33.33	66.67	30
59	0	1	0.00	100.00	1
60	1	11	8.33	91.67	12
61	1	2	33.33	66.67	3

DPP, Direct procurement and perfusion; *NRP*, normothermic regional perfusion; *DCD*, donation after circulatory death.

TABLE E5. Regional distribution of DPP and NRP

Region	DPP, n	NRP, n	DPP, %	NRP, %	Total DCD transplants
1	127	33	79.38	20.63	160
2	12	25	32.43	67.57	37
3	73	33	68.87	31.13	106
4	22	36	37.93	62.07	58
5	75	149	33.48	66.52	224
6	21	10	67.74	32.26	31
7	48	28	63.16	36.84	76
8	11	59	15.71	84.29	70
9	42	58	42	58	100
10	14	5	73.68	26.32	19
11	180	159	53.10	46.90	339

DPP, Direct procurement and perfusion; *NRP*, normothermic regional perfusion; *DCD*, donation after circulatory death.

ADULT

TABLE E6. Procurement type by recipient state

State	DPP, n	NRP, n	DPP, %	NRP, %	Total DCD transplants
Alabama	4	9	30.77	69.23	13
Arizona	4	8	33.33	66.67	12
Arkansas	2	5	28.57	71.43	7
California	57	108	34.55	65.45	165
Colorado	1	24	4.00	96.00	25
Connecticut	23	5	82.14	17.86	28
Delaware	0	0	0.00	0.00	0
Florida	42	23	64.62	35.38	65
Georgia	31	13	70.45	29.55	44
Hawaii	1	3	25.00	75.00	4
Idaho	2	2	50.00	50.00	4
Illinois	9	6	60.00	40.00	15
Indiana	2	8	20.00	80.00	10
Iowa	7	11	38.89	61.11	18
Kansas	1	2	33.33	66.67	3
Kentucky	9	15	37.50	62.50	24
Louisiana	0	2	0.00	100.00	2
Maine	21	5	80.77	19.23	26
Maryland	3	2	60.00	40.00	5
Massachusetts	53	16	76.81	23.19	69
Michigan	6	3	66.67	33.33	9
Minnesota	10	3	76.92	23.08	13
Mississippi	1	5	16.67	83.33	6
Missouri	0	6	0.00	100.00	6

(Continued)

TABLE E6. Continued

State	DPP, n	NRP, n	DPP, %	NRP, %	Total DCD transplants
Montana	1	2	33.33	66.67	3
Nebraska	7	15	31.82	68.18	22
Nevada	4	10	28.57	71.43	14
New Hampshire	11	4	73.33	26.67	15
New Jersey	8	10	44.44	55.56	18
New Mexico	2	3	40.00	60.00	5
New York	40	41	49.38	50.62	81
North Carolina	102	20	83.61	16.39	122
North Dakota	3	1	75.00	25.00	4
Ohio	4	4	50.00	50.00	8
Oklahoma	0	1	0.00	100.00	1
Oregon	3	3	50.00	50.00	6
Pennsylvania	10	25	28.57	71.43	35
Rhode Island	7	1	87.50	12.50	8
South Carolina	20	3	86.96	13.04	23
South Dakota	3	0	100.00	0.00	3
Tennessee	21	71	22.83	77.17	92
Texas	22	34	39.29	60.71	56
Utah	1	6	14.29	85.71	7
Vermont	2	0	100.00	0.00	2
Virginia	14	0	100.00	0.00	14
Washington	16	6	72.73	27.27	22
West Virginia	3	0	100.00	0.00	3
Wisconsin	13	16	44.83	55.17	29
Wyoming	0	0	0.00	0.00	0

DPP, Direct procurement and perfusion; *NRP*, normothermic regional perfusion; *DCD*, donation after circulatory death.

TABLE E7. Procurement type by state of donor hospital

State	DPP, n	NRP, n	DPP, %	NRP, %	Total DCD transplants
Alabama	6	8	42.86	57.14	14
Arizona	18	25	41.86	58.14	43
Arkansas	8	3	72.73	27.27	11
California	27	54	33.33	66.67	81
Colorado	13	41	24.07	75.93	54
Connecticut	8	1	88.89	11.11	9
Delaware	1	1	50.00	50.00	2
Florida	42	12	77.78	22.22	54
Georgia	16	15	51.61	48.39	31
Hawaii	0	0	0.00	0.00	0
Idaho	5	5	50.00	50.00	10
Illinois	20	7	74.07	25.93	27
Indiana	15	15	50.00	50.00	30
Iowa	8	7	53.33	46.67	15
Kansas	8	8	50.00	50.00	16
Kentucky	11	19	36.67	63.33	30
Louisiana	5	5	50.00	50.00	10
Maine	3	1	75.00	25.00	4
Maryland	7	2	77.78	22.22	9
Massachusetts	23	6	79.31	20.69	29
Michigan	22	20	52.38	47.62	42
Minnesota	10	7	58.82	41.18	17
Mississippi	3	6	33.33	66.67	9
Missouri	12	14	46.15	53.85	26
Montana	5	1	83.33	16.67	6
Nebraska	4	11	26.67	73.33	15
Nevada	5	12	29.41	70.59	17
New Hampshire	5	3	62.50	37.50	8
New Jersey	10	5	66.67	33.33	15
New Mexico	5	8	38.46	61.54	13
New York	22	39	36.07	63.93	61
North Carolina	52	18	74.29	25.71	70
North Dakota	1	1	50.00	50.00	2
Ohio	50	25	66.67	33.33	75
Oklahoma	10	11	47.62	52.38	21
Oregon	14	7	66.67	33.33	21
Pennsylvania	20	31	39.22	60.78	51
Rhode Island	3	0	100.00	0.00	3
South Carolina	14	3	82.35	17.65	17
South Dakota	2	0	100.00	0.00	2
Tennessee	14	26	35.00	65.00	40
Texas	43	70	38.05	61.95	113
Utah	4	14	22.22	77.78	18
Vermont	2	0	100.00	0.00	2

(Continued)

TABLE E7. Continued

State	DPP, n	NRP, n	DPP, %	NRP, %	Total DCD transplants
Virginia	11	5	68.75	31.25	16
Washington	13	3	81.25	18.75	16
West Virginia	5	6	45.45	54.55	11
Wisconsin	17	9	65.38	34.62	26
Wyoming	2	3	0.00	0.00	5

DPP, Direct procurement and perfusion; *NRP*, normothermic regional perfusion; *DCD*, donation after circulatory death.