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Transplant & Mechanical Support: Short Report

Outcomes of Donation After Circulatory Death Heart Transplantation Using Normothermic Regional Perfusion

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ABSTRACT

BACKGROUND Donation after circulatory death (DCD) with cardiopulmonary bypass for thoracoabdominal normothermic regional perfusion (TA-NRP) has led to increased use of donor hearts. Rejection rates and long-term survival outcomes are not known.

METHODS A single-center retrospective cohort review of patients who underwent DCD heart transplantation from January 2020 to December 2023 was performed. Donor and recipient characteristics, operative characteristics, and posttransplantation outcomes were analyzed. Subgroup analysis comparing co-localized vs distant donors and recipients was performed. The primary end point was 1-year survival. Secondary end points included incidences of primary graft dysfunction (PGD), cardiac allograft vasculopathy (CAV), rejection rate, and overall mortality. Our TA-NRP protocol has remained the same, consisting of sternotomy, ligation of aortic arch vessels, establishment of cardiopulmonary bypass, reintubation, resuscitation of the heart, and cold static storage during transport.

RESULTS In total, 32 recipients underwent DCD heart transplantation, including 26 isolated hearts, 3 heart-lungs, and 3 heart-kidneys. The median age was 56 years for recipients and 39 years for donors; 21 donors and recipients were co-localized, whereas 11 were distant. One-year survival was 100%. Two patients required mechanical circulatory support for PGD. Four patients experienced grade 2R acute cellular rejection. Five patients had grade 1 CAV at 1 year. On subgroup analysis, distant donors and recipients had longer warm (47 vs 30 minutes; $P < .005$) and cold (213 vs 76 minutes; $P < .005$) ischemia times, without any other differences.

CONCLUSIONS Outcomes after DCD heart transplantation using TA-NRP remain encouraging with acceptable rates of rejection, PGD, CAV, and survival at 1 year.

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Heart transplantation is considered a definitive therapy for patients with advanced heart failure. According to the Organ Procurement and Transplantation Network/Scientific Registry of Transplant Recipients 2021 Annual Data Report, the number of new listings increased to 4373 in 2021, which is the largest increase in the past decade.[1] Donation after circulatory death (DCD) has gained popularity over time, despite early

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Abbreviations and Acronyms

CAV = cardiac allograft vasculopathy
CPB = cardiopulmonary bypass
DBD = donation after brain death
DCD = donation after circulatory death
ECMO = extracorporeal membrane oxygenation
LVEF = left ventricular ejection fraction
TA-NRP = thoracoabdominal normothermic regional perfusion
PGD = primary graft dysfunction
WLST = withdrawal of life-sustaining therapy

IN SHORT

- Early outcomes of donation after circulatory death heart transplantation with the thoracoabdominal normothermic regional perfusion protocol are excellent.
- Hearts procured from older donors also showed similar outcomes.
- No differences in postoperative graft function, length of stay, and inotropic support were noted in the subgroup analysis of co-localized vs distant donors.

concerns of severe ischemia-reperfusion injury during withdrawal of life-sustaining therapy (WLST) and inability to assess the heart's viability after procurement.[2] One method to allay these concerns has been the introduction of thoracoabdominal normothermic regional perfusion (TA-NRP), during which extracorporeal membrane oxygenation (ECMO) is used to establish in situ reperfusion of the heart and other organs with oxygenated blood after isolation and ligation of the aortic arch vessels.[3] With this method, warm ischemia time is minimized, metabolic derangements are corrected, and the heart is evaluated under nearly physiologic conditions and transported with use of either cold static storage or a heart preservation system.[4] Here, we report our updated outcomes of DCD heart transplantation using TA-NRP, now considering both co-localized and distant donors.

MATERIAL AND METHODS

DATA SOURCE, STUDY POPULATION, AND OUTCOMES. This is a single-center retrospective cohort review of adult (aged ≥18 years) patients who underwent DCD heart transplantation from January 2020 to December 2023. The study was approved by the NYU institutional review board on December 11, 2023 (#s23-01570) with a waiver for patient consent. The primary source of data collection was electronic medical record chart review. A total of 241 patients underwent heart transplantation during the study period. Of these, 209 underwent heart transplantation by donation after brain death (DBD) donors. The remaining 32 patients underwent heart transplantation by DCD donors and compose the final cohort of this review. All patients underwent transplantation by our institution's TA-NRP protocol, which has been described previously (Figure).[5]

Demographic data of the recipients included age, sex, body mass index, and cause of heart failure; preoperative mechanical circulatory support use was also analyzed. Demographic data of the donors included age, sex, body mass index, and pertinent clinical history. Donor location (either co-localized or distant) was also tabulated. Operative variables including time from WLST to TA-NRP, time from skin incision to initiation of cardiopulmonary bypass (CPB), total donor CPB time, total warm ischemia time, and total cold ischemia time were analyzed. Left ventricular ejection fraction (LVEF) before and after TA-NRP was evaluated along with any presence of right ventricular dysfunction. The primary end point was 1-year survival. Secondary end points included overall mortality, incidence of primary graft dysfunction (PGD), incidence of rejection, and cardiac allograft vasculopathy (CAV) at 1 year. Other outcomes included extubation <24 hours, length of postoperative inotropic support, acute kidney injury, postoperative LVEF, and postoperative length of stay.

STATISTICAL ANALYSIS. Data analysis was conducted with Microsoft Excel (Microsoft Corporation). Continuous variables are presented as mean ± SD or median and interquartile range. Categorical variables are presented using frequency and percentages. For subgroup analysis, Student *t*-test was used to compare normally distributed continuous variables between groups, and the Mann-Whitney *U* test was used for nonnormally distributed continuous variables. All tests were 2 sided, with an α level of .05 considered to indicate statistical significance.

RESULTS

BASELINE DEMOGRAPHIC DONOR AND RECIPIENT CHARACTERISTICS. During the study period, a total of 38 donors were evaluated for TA-NRP and potential DCD heart procurement. Four donors did not die within the allotted time after WLST (120 minutes). Intraprocedural complications occurred in an additional 2 donors. The first

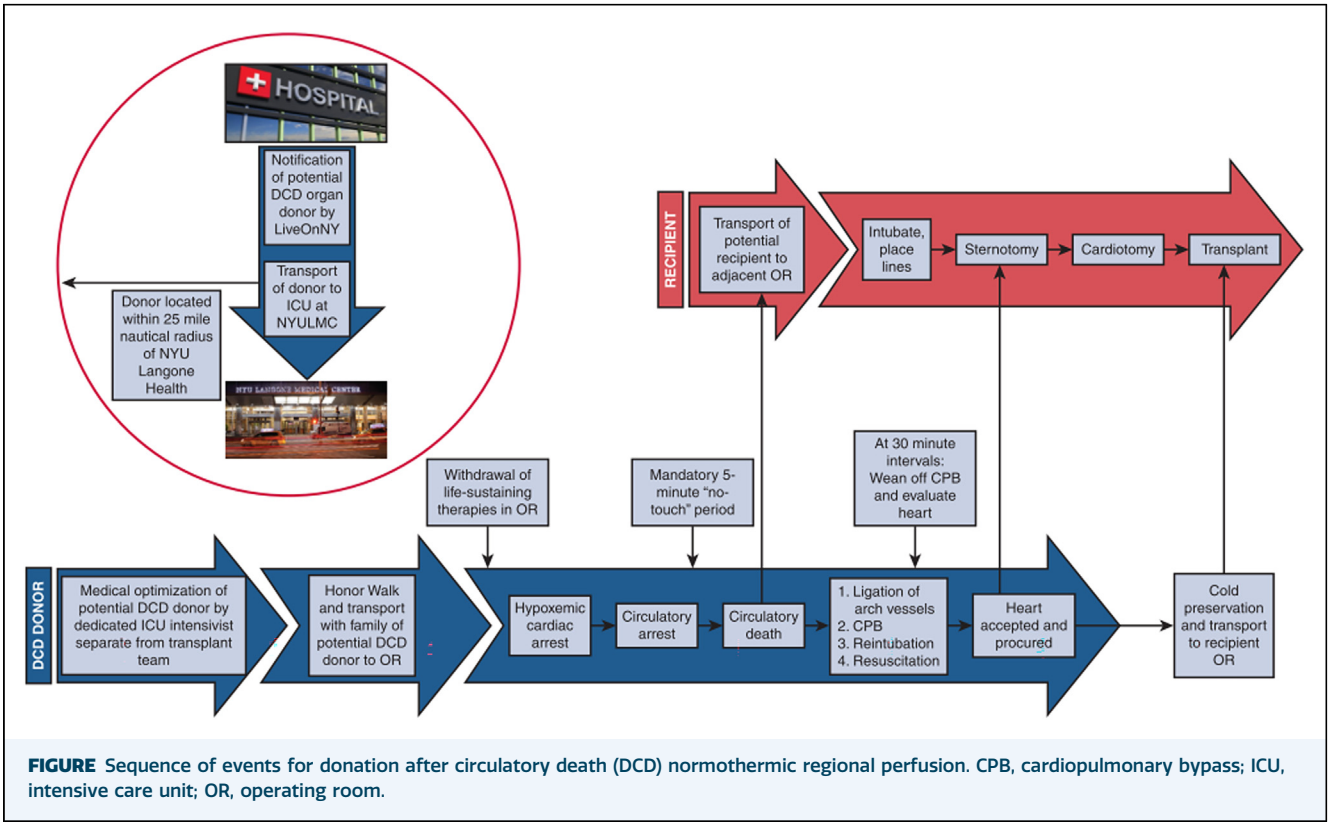

FIGURE Sequence of events for donation after circulatory death (DCD) normothermic regional perfusion. CPB, cardiopulmonary bypass; ICU, intensive care unit; OR, operating room.

donor, a 40-year-old man with uncontrolled hypertension with 20-pack-year smoking history, had aortic dissection immediately after arterial cannulation. The second donor, a 47 year-old man who previously underwent a decompressive hemicraniotomy secondary to a traumatic brain injury, had an intramural hematoma on initiation of CPB and was found to have severe right ventricular dysfunction with moderate aortic insufficiency. In both cases, the donor heart was declined. Therefore, a total of 32 patients underwent DCD heart transplantation. Baseline characteristics are provided in Table 1. Median age of the recipient cohort was 56 years, with most (66%) being male. The most common cause of heart failure was nonischemic cardiomyopathy (56%), and 41% of patients required preoperative mechanical circulatory support before transplantation. Of these, 8 (25%) patients were supported with a durable ventricular assist device, 4 (13%) were supported with an intra-aortic balloon pump, and 1 (3%) required venoarterial ECMO. Table 1 also includes donor characteristics; median age of the donor cohort was 39 years, with most (84%) being male. More commonly, donors were co-localized with the recipient at our center during procurement (n = 21 [66%]), whereas 34% (n = 11) were procured at an outside hospital.

OPERATIVE CHARACTERISTICS OF DONORS UNDERGOING TA-NRP. The operative characteristics of donors undergoing TA-NRP are provided in Table 2. In addition to isolated heart transplantation (n = 26 [81%]), 3 patients underwent simultaneous heart-kidney transplantation and another 3, heart-lung transplantation. All donor hearts were preserved and transported in cold static storage solution after procurement. The median time from WLST to TA-NRP was 31 minutes, with a median time of 9 minutes from skin incision to initiation of CPB. The median donor CPB time was 89 minutes. The median total warm ischemia time was 37 minutes, and median total cold ischemia time was 82 minutes. Finally, median LVEF both before and after TA-NRP was favorable at 55% and 50%, respectively.

SUBGROUP ANALYSIS OF CO-LOCALIZED VS DISTANT DONORS. In a subgroup analysis (Supplemental Table), co-localized donors (n = 21) were compared with distant donors (n = 11). Distant donors and recipients experienced significantly longer warm ischemia times (47 vs 30 minutes;

TABLE 1 Donor and Recipient Characteristics at Baseline

Baseline Characteristics	Total (N = 32)
Recipient	
Age, years	56 (41–72)
Sex	
Male	21 (66)
Female	11 (34)
Body mass index, kg/m^2	23.8 (21.6–34.4)
Reoperative sternotomy	8 (25)
Cause of heart failure	
Nonischemic dilated cardiomyopathy	18 (56)
Ischemic cardiomyopathy	7 (22)
Hypertrophic cardiomyopathy	4 (13)
Restrictive cardiomyopathy	3 (9)
Preoperative mechanical circulatory support	13 (41)
Durable left ventricular assist device	8 (25)
Intra-aortic balloon pump	4 (13)
Venoarterial extracorporeal membrane oxygenation	1 (3)
Donor	
Age, years	39 (26–46)
Sex	
Male	27 (84)
Female	5 (16)
Body mass index, kg/m^2	28.2 (22.2–38.3)
Tobacco use	
Former	22 (69)
Never	10 (31)
Alcohol use	24 (75)
Illicit drug use	23 (72)
Hypertension	11 (34)
Preoperative cardiac catheterization	11 (34)
Donor location	
Co-localized	21 (66)
Distant	11 (34)
Donor terminal illness	
Anoxia	16 (50)
Head trauma	9 (28)
Cerebrovascular accident	7 (22)

Categorical variables are presented as number (percentage). Continuous variables are presented as median (interquartile range).

$P < .005$) and cold ischemia times (213 vs 76 minutes; $P < .005$) compared with co-localized donors and recipients. There were, however, no differences in postoperative LVEF (64.8% vs 65.9%; $P = .62$), length of postoperative inotropic support (7.1 vs 7.1 days; $P = .45$), or postoperative length of stay (19.9 vs 28.4 days; $P = .26$) between the groups.

POSTOPERATIVE OUTCOMES. Table 3 summarizes outcomes after DCD heart transplantation. Most patients were extubated within 24 hours (63%), with median duration of postoperative inotropic support being 4 days. The median postoperative cardiac index was 3.0 L/min/m^2. One-year survival was 100%. However, there was 1 mortality in the cohort that occurred 3 years after transplantation. Severe CAV (grade 3) had developed in this patient, who was electively admitted for retransplantation workup; however, she succumbed to sepsis during her hospital stay. The PGD rate was 12.5%, wherein 1 patient with moderate PGD required postoperative intra-aortic balloon pump support and the second patient with severe PGD required central venoarterial ECMO support. The incidence of grade 2R acute cellular rejection was 13% without any evidence of biopsy-proven antibody-mediated rejection. CAV (grade 1) had developed in 5 (23%) patients at 1 year after transplantation. Six patients (19%) had postoperative acute kidney injury, during which 1 patient with severe right ventricular dysfunction required continuous renal replacement therapy.

COMMENT

Our study findings depict excellent 1-year survival and transplant rejection rates with TA-NRP for single- and dual-organ recipients. Both co-localized

TABLE 2 Operative Characteristics of Donors Undergoing TA-NRP and Number of Organs Transplanted

Operative Characteristics	Total (N = 32)
Transplanted organs	
Heart	26 (81)
Simultaneous heart-kidney	3 (9)
Combined heart-lung	3 (9)
Organ preservation strategy	
Cold static storage	32 (100)
Time from WLST to TA-NRP, minutes	31 (17–117)
Time from skin incision to initiation of cardiopulmonary bypass, minutes	9 (6–12)
Total donor cardiopulmonary bypass time, minutes	89 (32–231)
Total warm ischemia time, minutes	37 (29–44)
Total cold ischemia time, minutes	82 (71–209)
Left ventricular ejection fraction before TA-NRP, %	55 (50–60)
Left ventricular ejection fraction after TA-NRP, %	50 (45–65)
Mild right ventricular dysfunction	4 (12)
Complications	
Aortic dissection	1 (3)
Intramural hematoma	1 (3)

Categorical variables are presented as number (percentage). Continuous variables are presented as median (interquartile range). TA-NRP, thoracoabdominal normothermic regional perfusion; WLST, withdrawal of life-sustaining therapy.

TABLE 3 Recipient Outcomes After DCD Heart Transplantation by TA-NRP Protocol

Outcomes	Total (N = 32)
Extubation <24 hours	20 (63)
<6 hours	6 (19)
6–12 hours	6 (19)
12–24 hours	8 (25)
Length of postoperative inotropic support, days	4 (2–35)
Postoperative acute kidney injury	6 (19)
Continuous renal replacement therapy required	1 (3)
Cardiac index, L/min/m^2	3.0 (1.2–4.7)
Postoperative left ventricular ejection fraction, %	65 (55–70)
Primary graft dysfunction	4 (12.5)
Intra-aortic balloon pump	1 (3)
Central venoarterial extracorporeal membrane oxygenation	1 (3)
No device	2 (6)
Rejection	
Grade ACR 2R/3A	4 (13)
Cardiac allograft vasculopathy (n = 22)	
Grade 1	5 (23)
Grade >1	0 (0)
Postoperative length of stay, days	18 (8–88)
1-year survival, %	100
Overall mortality	1 (3)
Follow-up, days	395 (191–730)
Readmission rate at 1 year (n = 22)	14 (64)

Categorical variables are presented as number (percentage). Continuous variables are presented as median (interquartile range). ACR, acute cellular rejection; DCD, donation after circulatory death; TA-NRP, thoracoabdominal normothermic regional perfusion.

and distant TA-NRP groups had similar outcomes when the total cold ischemia time was limited to <4 hours. The rate of DCD heart transplantation has rapidly expanded in the United States and is currently being performed in >15% of heart transplant centers.[6] Previously, Hoffman and colleagues[7] reported a 100% 30-day survival in 15 heart transplant recipients with average total ischemia time of 183 minutes. Their average cold ischemia time in the distant donors group was 213 minutes.

In another contemporary analysis by Siddiqi and coworkers[8] comparing DCD and DBD heart-only transplantation, outcomes with respect to 1-year survival, PGD, rejection, and development of CAV were similar with no differences in outcomes (P = NS). More important, the DCD donors were younger (26 years of age) than the DBD donors (31 years of age). Despite older donors, our rates of PGD, rejection, CAV, and survival were comparable to their rates. These data further reaffirm the feasibility of use of donors who otherwise would have been declined because of older age or need for coronary angiography. Although our 1-year primary and secondary outcomes are encouraging, challenges to widespread adoption of TA-NRP still remain. For instance, we had 4 runs in which donor hearts were not recovered. For each procurement, there were 2 surgeons, 2 perfusionists, and 1 preservationist employed. The minimum cost to assess a donor heart with TA-NRP would be roughly US $4000.[9] This would necessitate cost sharing between a cooperative network of hospitals, organ procurement organizations, and perhaps the government.[10]

Finally, our study had several limitations including retrospective design, small sample size, and median follow-up of 1 year only. Also, we did not perform any direct comparison with the DBD donor cohort. Whereas the results of a single center may not be generalizable to other centers, institutional protocols with periodic optimization in both donor selection and retrieval techniques can lead to improved outcomes. In line with the American Society of Transplant Surgeons, which has established a centralized DCD registry for abdominal surgeons to collect TA-NRP donor and recipient data, a similar database of thoracic transplantations would play a pivotal role in facilitating future research and thereby improve patient outcomes.

In conclusion, our experience provides further validation for the safety and feasibility of TA-NRP with use of cold static storage for procurement of DCD hearts, with acceptable outcomes in both single- and dual-organ recipients with respect to 1-year survival, severe PGD, and CAV at 1 year. Outcomes from even older DCD donors remain excellent.

The Supplemental Table can be viewed in the online version of this article [https://doi.org/10.1016//j.atssr.2024.09.016] on http://www.annalsthoracicsurgery.org.

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