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Outcomes of lung and heart-lung transplants utilizing donor after circulatory death with thoracoabdominal normothermic regional perfusion

Stephanie H. Chang, MD,[a,*] Travis C. Geraci, MD,[a] Greta L. Piper, MD,[b] Justin Chan, MD,[a] Les James, MD,[a] Darien Paone, MD,[a] Philip M. Sommer,[c] Jake Natalini, MD,[d] Darya Rudym, MD,[d] Melissa Lesko, MD,[d] Syed T. Hussain, MD,[a] Alex Reyentovich, MD,[e] Nader Moazami, MD,[a] Deane E. Smith, MD,[a] and Luis Angel, MD[d]

[a]*Department of Cardiothoracic Surgery, New York University Langone Health, New York, New York*
[b]*Department of Cardiothoracic Surgery, North Shore University Hospital, Northwell Health, Manhasset, New York*
[c]*Department of Anesthesiology, Perioperative Care and Pain Medicine, NYU Langone Health, New York, New York*
[d]*Department of Medicine, NYU Langone Health, New York, New York*
[e]*Leon H. Charney Division of Cardiology, NYU Langone Health, New York, New York*

KEYWORDS:
lung transplant;
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thoracoabdominal normothermic regional perfusion;
primary graft dysfunction

BACKGROUND: Donation after circulatory death with thoracoabdominal normothermic regional perfusion (DCD-NRP) for cardiac transplant has promising results, though data for lung transplant is lacking. This study evaluates lung transplant outcomes using DCD-NRP allografts.

METHODS: All patients who underwent lung transplantation (LT) from June 1, 2020, to July 5, 2023, at a single institution were evaluated. Recipients received organs from DCD-NRP or brain dead (control) donors (donation after brain death (DBD)). All DCD-NRP were adult, primary bilateral LT (BLT) without preoperative extracorporeal membrane oxygenation (ECMO). Inclusion criteria for controls were age > 18 years, BLT, no preoperative ECMO, and primary transplantation. Comparison was separated by LT or heart-lung transplant (HLT). The primary outcome was primary graft dysfunction (PGD) grade 3 at 72 hours.

RESULTS: There were 8 LT and 3 HLT in the DCD-NRP cohort, and 138 BLT and 7 HL DBD controls. PGD grade 3 at 72 hours was 0% in the entire DCD-NRP cohort (vs control: 9.4% LT and 0% HLT). There were no statistically significant differences in donor and recipient characteristics, though DCD-NRP HLT had significantly shorter ischemic time (85 vs 200 minutes, $p < 0.02$). Thirty-day and 90-day mortality and 1-year survival are similar in both cohorts for LT and HLT. To date, DCD-NRP recipients are all on room air, with 0% acute cellular rejection rate and 91% (10/11) without chronic rejection. The lung utilization rate of evaluated DCD-NRP donors was 100%.

CONCLUSIONS: Initial results of LT using DCD-NRP organs demonstrate similar PGD grade 3 at 72 hours and similar survival to standard donors.

*Corresponding author: Stephanie H. Chang, MD, New York University Langone Health, Department of Cardiothoracic Surgery, 530 First Avenue, Suite 9V, New York, NY 10016.
E-mail address: stephanie.chang@nyulangone.org.

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Background

The recovery of lung allografts from donation after circulatory death (DCD) has expanded the donor pool for lung transplantation,[1-3] thereby reducing waitlist time, delisting, and waitlist mortality.[4] However, utilization of this strategy has been limited, accounting for approximately 5% of all lung transplants in the United States, likely due to concerns over organ quality, clinical outcomes, and procurement logistics.[5] Equally, the utilization of lung allografts from donation after circulatory death donors with direct procurement (DCD-DP) is low; a reported 13.8% of DCD lungs between 2019 and 2022.[6]

The use of in situ thoracoabdominal normothermic regional perfusion (TA-NRP) has evolved as a method for DCD in which extracorporeal membrane oxygenation (ECMO) or cardiopulmonary bypass (CPB) is rapidly employed for the expedient restoration of donor organ perfusion.[7-9] In doing so, DCD with TA-NRP (Donation after circulatory death with thoracoabdominal normothermic regional perfusion (DCD-NRP)) limits ischemic time, allows for the correction of metabolic abnormalities that may accompany circulatory death, and creates a controlled procurement process. Reports analyzing outcomes from the United Network for Organ Sharing (UNOS) database have revealed that lung recovery after DCD-NRP is safe and effective, achieving similar short-term outcomes compared DCD-DP.[6,10]

The impact of DCD-NRP on clinical outcomes in lung transplantation when compared to donation after brain death (DBD) is unknown. To evaluate clinical outcomes, specifically primary graft dysfunction (PGD), after DCD-NRP for lung transplantation, we performed a retrospective analysis of patients who received lung allografts after DCD-NRP at our institution. To address this question, we compared our cohort of DCD-NRP patients to patients who received lung allografts from DBD.

Material and methods

Study design

We performed a retrospective analysis of all lung transplant recipients who were transplanted at New York University Langone Health (NYULH) between June 1, 2020, and July 5, 2023. At NYULH, the first DCD-NRP heart lung transplant was performed in June 2020 and the first DCD-NRP lung transplant was performed in December 2021. Patients were separated into those who received DBD, DCD-DP, and donation after circulatory death with normothermic regional perfusion (DCD-NRP). Patients were also separated by lung transplant vs heart-lung transplant. DCD-NRP lung transplant recipients all received bilateral lung transplants. All DCD-NRP lung and heart-lung recipients were adults, primary transplants with no redo transplantation, and no preoperative ECMO support. Due to the DCD-NRP group characteristics, inclusion criteria for controls included bilateral lung transplants, no preoperative ECMO, primary transplantation, and recipient age >18 years old. After applying the inclusion criteria, the control group was limited to DBD for comparison, as the DCD-DP group was too small for meaningful comparison with $n = 2$ (Figure 1). The NYULH institutional review board approved this human subjects study and data were collected from direct chart review (IRB # i23-01133). This study is in compliance with the International Society for Heart and Lung Transplantation (ISHLT) ethics statement.

Donor selection and NRP protocol

All DCD-NRP lung and heart-lung donors were from Maastricht category III donors, defined as patients with controlled circulatory arrest and expectant death after withdrawal of life-sustaining therapy (WLST). All donors underwent chest computed tomography, chest radiography, and bronchoscopy prior to acceptance for lung transplantation. If the DCD donor was a candidate heart donor, TA-NRP was utilized as the procurement strategy. The DCD donors were age 18 to 49. All donors from the local organ procurement organization (LiveOn New York) were transferred to NYULH for donor management and procurement. All DCD-NRP donors outside of the local organ procurement organization were procured at the donor facility. All organs were placed in standard cold storage on ice and transported back to the recipient hospital for implantation.

TA-NRP was initially performed as described by Smith et al, with donor transfer to the cardiac recipient hospital and use of CPB,[7,11] though has since evolved to using a mobile ECMO circuit with a reservoir to allow for left atrial venting. For all DCD-NRP procurements, the donor is brought into the operating room, a femoral arterial line is placed, the donor is draped, and 50,000 units of heparin is administered 3 minutes prior to WLST. After cardiopulmonary arrest and pronouncement of death, a 5-minute standoff period is observed prior to the procurement team entering the operating room. A median sternotomy is performed, and the pericardium is opened. The innominate vein is ligated and divided. The innominate artery, carotid artery, and subclavian artery are all clamped. Cerebral perfusion was monitored using cerebral oximetry measurements. An aortic cannula is placed in the ascending aorta, and the right atrium is cannulated. At this point, reperfusion is established via CPB or ECMO with a reservoir

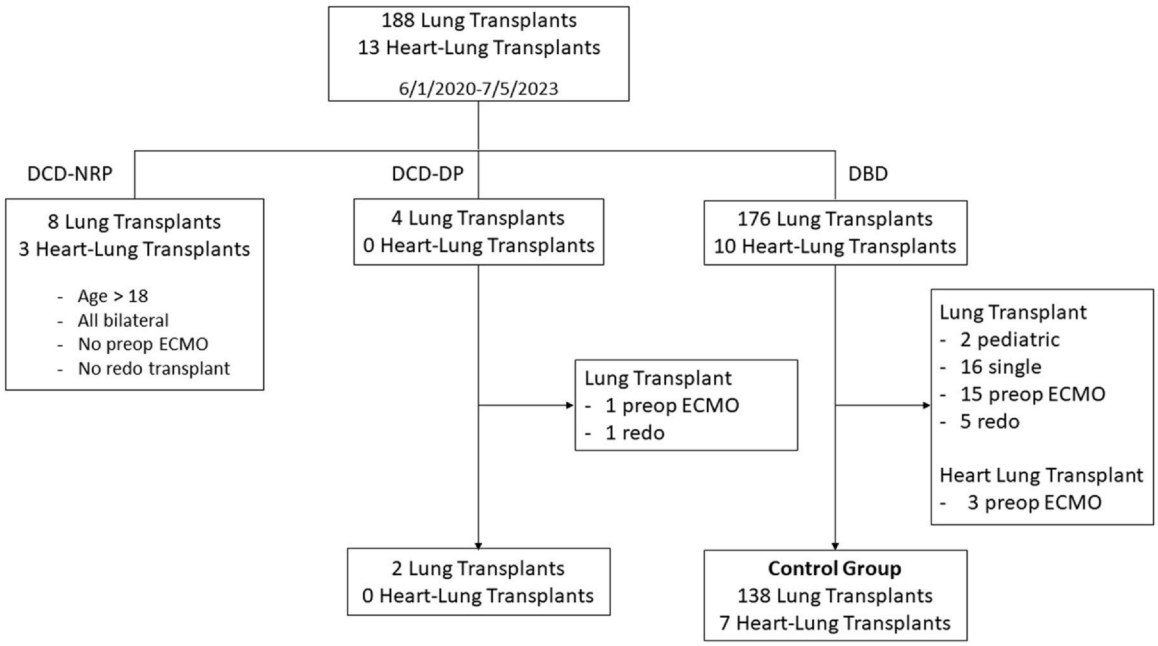

Figure 1 Cohort flowchart. DBD, donation after brain death; DCD, donation after circulatory death; DCD-NRP, donation after circulatory death with normothermic regional perfusion; ECMO, extracorporeal membrane oxygenation.

in the circuit. A left atrial vent is placed via the left atrial appendage. The patient is reintubated, and a bronchoscopy is performed to clear all secretions. After initiation of NRP at 37°C, 3 sodium chloride zero-balance ultrafiltration bags with 50 mEq sodium bicarbonate and 0.5 g calcium carbonate are used to reduce circulating inflammatory cytokines and alleviate electrolyte imbalances. Blood transfusions were given as needed to maintain a hemoglobin of 8 mg/dl for the cardiac allograft. After 30 minutes of reperfusion, the lungs are recruited, and CPB or ECMO support is weaned off. After the cardiac allograft is assessed, the fraction of inspired oxygen is increased to 100% and the positive end-expiratory pressure is kept at 5 mm Hg. An arterial blood gas is taken from the femoral arterial line or from the ascending aorta if no femoral arterial line is present. A PaO_2:FiO_2 (P/F) ratio of 300 or greater was used for allograft acceptance. After evaluation, CPB or ECMO is resumed until all teams are ready to proceed with cross clamp. After recovery, all organs were directly implanted in the recipient without use of ex-vivo lung perfusion (EVLP).

Outcomes

The primary outcome was PGD grade 3 (P/F < 200 mm Hg) at 72 hours after transplantation, as defined by the ISHLT.[12] Patients on ECMO support at 72 hours were also classified as PGD grade 3 as per the ISHLT definition. Secondary end points were P/F ratio at 24 hours after transplant, duration of mechanical ventilation, ECMO requirement, airway complication rate, hospital length of stay, 30-day mortality, 90-day mortality, and 1 year survival. Total warm ischemic time (defined as time from WLST to initiation of CPB) and total CPB time are reported when available. Most recent DCD-NRP recipient pulmonary function tests, oxygen requirement, rate of acute cellular rejection (ACR) and chronic lung allograft dysfunction (CLAD) are also reported. Organ utilization rate is reported as number of organs transplanted divided by the number of organs available for any DCD donor where the organ was evaluated intraoperatively for DCD-NRP lung transplantation.

Statistical analysis

Data analysis and statistics were performed with GraphPad Prism version 10.0. Nonparametric variables were evaluated with Mann-Whitney tests. Fisher's exact test and chi-square were used for categorical data. Results were considered statistically significant at $p < 0.05$.

Results

Patients

From June 1, 2020, to July 5, 2023, 188 lung transplants and 13 heart-lung transplants were performed at NYULH. Of these, 8 lung transplants and 3 heart-lung transplants were performed utilizing DCD-NRP. In the DBD control group, 138 lung transplants and 7 heart lung transplants met inclusion criteria.

Donor and recipient characteristics

Donors utilized for lung transplant DCD-NRP trended toward being slightly older, but the difference was not statistically significant. The remainder of donor characteristics are similar, as shown in Table 1. No characteristics of the recipients were statistically different, though recipients of DCD-NRP lung transplants were more likely to have a

Table 1 Lung Transplant Cohort Characteristics

	DCD-NRP lungs $n = 8$	Control lungs $n = 138$	p-value
Donor			
Age, median (IQR), year	38.5 (33-44.8)	32 (25-43)	0.14
Male sex	64% (5)	54% (74)	0.73
Best PaO_2:FiO_2, median (IQR), mm Hg[a]	469 (324-489)	457 (393-503)	0.68
PaO2:FiO2 ratio < 300 mm Hg	13% (1)	6.5% (9)	0.44
Abnormal CXR (n)	64% (5)	67% (93)	0.72
Smoking > 20 pack year (n)	13% (1)	5.8% (8)	0.41
Positive respiratory culture			
Positive sputum (n)	38% (3)	40% (55)	> 0.99
Positive BAL (n)	13% (1)	6.5% (9)	0.44
Hep C positive (n)	13% (1)	22% (30)	> 0.99
Recipient			
Age, median (IQR), year	64 (60-65)	63 (56-68)	0.88
Male sex	75% (6)	63% (87)	0.71
Transplant diagnosis group			0.29
A	38% (3)	16% (22)	
B	0% (0)	1.4% (2)	
C	12.5% (1)	5% (7)	
D	50% (4)	77.5% (107)	
UNOS LAS, median (IQR)	34.7 (34-36.3)	38.4 (34.4-49.3)	0.06
Hospitalized at time of transplant (n)	25% (2)	21% (29)	0.42
Mechanical ventilation at time of transplant (n)	0% (0)	1.4% (2)	
Time to transplant, median (IQR), days	32 (18-42)	21 (6-64)	0.69
Transplant			
Cold ischemic time, median (IQR), minutes	247 (197-309)	298 (262-360)	0.11
Multiorgan transplant (n)			
Transplant + liver	0% (0)	2.2% (3)	> 0.99
Transplant + kidney	0% (0)	1.4% (2)	> 0.99

BAL, bronchoalveolar lavage; CXR, chest X ray; DCD-NRP, donation after circulatory death with thoracoabdominal normothermic regional perfusion; IQR, interquartile range; LAS, lung allocation score.

[a]Obtained prior to withdrawal of life sustaining therapy.

lower lung allocation score, increased time to transplant, and slightly lower ischemic time, while control lung transplant recipients had a higher percentage of category D diagnosis.

In heart-lung DCD-NRP transplants, donors and recipients were not statistically different from those utilized for DBD heart-lung transplants. However, DCD-NRP donors trended toward being older with a lower best P/F ratio. In terms of transplant characteristics, DCD-NRP heart-lung transplants had significantly shorter ischemic time (85 vs 200 minutes, $p < 0.02$), likely secondary to all DCD-NRP heart transplants having the donors transferred to the recipient hospital for procurement.

Procurement data

None of the 11 donors required inotropes when CPB or ECMO was weaned, which was consistent with the 100% utilization of cardiac allografts from these donors (Table 2). Data regarding warm ischemic time, CPB time, and intraoperative P/F ratio were available for 10 of 11 (91%) procurements (Table 3). The range of total warm ischemic time was 21 to 91 minutes, with a median of 33 minutes. The total CPB time ranged from 19 to 199 minutes, with a median of 70 minutes. The intraoperative P/F ratio at time of weaning from CPB/ECMO ranged from 283 to 506 with a median of 424.

Clinical outcomes with DCD-NRP vs control

The incidence of PGD grade 3 at 72 hours was 0% in the DCD-NRP lung transplant group, compared to 9.4% in the control lung transplant group. No DCD-NRP lung transplant recipients required postoperative ECMO utilization, while 5% of control lung transplant recipients were placed on postoperative ECMO support. There was no significant difference in P/F ratio at 24 hours, length of mechanical ventilation, hospital length of stay, airway complication rate, 30-day mortality, 90-day mortality, or 1-year survival (Table 4), though the control group trended toward a higher P/F ratio at 24 hours.

On evaluation of the primary endpoint in heart-lung transplants, both the DCD-NRP heart-lung and control heart-lung recipients had a 0% rate of PGD grade 3 at 72 hours. However, the first DCD-NRP heart-lung recipient was placed on postoperative venoarterial (VA)-ECMO support for initial heart and lung graft dysfunction. The patient was decannulated on postoperative day 2, with a P/F

Table 2 Heart Lung Transplant Cohort Characteristics

	DCD-NRP heart lungs $n = 3$	Control heart lungs $n = 7$	p-value
Donor			
Age, median (IQR), year	44 (43-47.5)	35 (29-39.5)	0.10
Male sex	67% (2)	86% (6)	> 0.99
Best PaO_2:FiO_2, median (IQR), mm Hg[a]	450 (435-476)	510 (502-530)	0.10
PaO_2:FiO_2 ratio < 300 mm Hg	0% (0)	0% (0)	> 0.99
Abnormal CXR (n)	67% (2)	71% (5)	> 0.99
Smoking > 20 pack year (n)	0% (0)	14% (1)	> 0.99
Positive respiratory culture			
Positive sputum (n)	0% (0)	29% (2)	> 0.99
Positive BAL (n)	0% (0)	14% (1)	> 0.99
Hep C positive (n)	0% (0)	14% (1)	> 0.99
Recipient			
Age, median (IQR), year	53 (49-58)	50 (44-57)	0.67
Male sex	67% (2)	43% (3)	> 0.99
UNOS LAS, median (IQR)	39 (37-42)	46 (41-55)	0.38
Hospitalized at time of transplant (n)	33% (1)	71% (5)	0.26
Mechanical ventilation at time of transplant (n)	0% (0)	0% (0)	> 0.99
Time to transplant, median (IQR), days	35 (24-73)	39 (21-96)	0.83
Transplant			
Cold ischemic time, median (IQR), minutes	**85 (84.5-85.5)**	**200 (157-228)**	**< 0.02**
Multiorgan transplant (n)			
Transplant + liver	0% (0)	0% (0)	> 0.99
Transplant + kidney	0% (0)	14% (1)	> 0.99

BAL, bronchoalveolar lavage; CXR, chest X ray; DCD-NRP, donation after circulatory death with thoracoabdominal normothermic regional perfusion; IQR, interquartile range; LAS, lung allocation score.

Bold indicates statistically significant differences with p value < 0.05.

[a]Obtained prior to withdrawal of life sustaining therapy.

ratio of 283 mm Hg at 72 hours after transplant. The rate of VA-ECMO use was 33% (1/3) in the DCD-NRP heart-lung cohort and 0% (0/7) in the control heart lung cohort. Similar to the lung transplant cohort, there was no significant difference in the P/F ratio at 24 hours, hospital length of stay, airway complication rate, 30-day mortality, 90-day mortality, or 1-year survival between DCD-NRP and controls in the heart-lung transplant group (Table 5).

Clinical status of DCD-NRP transplants

All 8 recipients of DCD-NRP lung allografts and 3 heart-lung allografts are currently alive on room air (Table 6). The lung transplant recipients have a percent predicted forced expiratory volume over 1 second (FEV1) ranging from 71% to 121%, with 1 (9%) patient having CLAD. The rate of ACR was 0%. Of the 8 recipients, 4 are over 1 year

Table 3 DCD-NRP Intraoperative Procurement Data

	Warm ischemic time (minutes)	Total cardiopulmonary bypass time (minutes)	Intraoperative P/F ratio
Lung transplant patients			
1	91	199	467
2	33	140	461
3	28	109	366
4	n/a	n/a	n/a
5	33	45	506
6	65	19	424
7	59	87	335
8	40	71	308
Heart lung transplant patients			
1	32	68	423
2	29	64	283
3	21	38	452

n/a, not available; P/F, partial pressure of oxygen in arterial blood to fraction of inspired oxygen ratio.

Table 4 Lung Transplant Outcomes

	DCD NRP lungs $n = 8$	Control lungs $n = 138$	p-value
Primary end point			
PGD grade 3 at 72 hours (n)	0% (0)	9.4% (13)	> 0.99
Secondary end point			
Postoperative ECMO use (n)			
Veno-venous ECMO	0% (0)	3.6% (5)	> 0.99
Veno-arterial ECMO	0% (0)	1.4% (2)	> 0.99
PaO_2:FiO_2 at 24 hours, median (IQR), mm Hg	323 (317-411)	404 (345-463)	0.25
Mechanical ventilation, median (IQR), days	1.5 (1-3.5)	2 (1-3)	0.70
Hospital stay, median (IQR), days	15 (11-16.5)	14 (10-18)	0.58
Airway complications (n)	0% (0)	0.7% (1)	> 0.99
Mortality at 30 days (n)	0% (0)	1.4% (2)	> 0.99
Mortality at 90 days (n)	0% (0)	1.4% (2)	> 0.99
1-year survival (n)	100% (8)	96.4% (134)	> 0.99

DCD-NRP, donation after circulatory death with thoracoabdominal normothermic regional perfusion; ECMO, extracorporeal membrane oxygenation; IQR, interquartile range; PGD, primary graft dysfunction.

Table 5 Heart Lung Transplant Outcomes

	DCD-NRP heart lungs $n = 3$	Control heart lungs $n = 7$	p-value
Primary end point			
PGD grade 3 at 72 hours (n)	0% (0)	0% (0)	> 0.99
Secondary end point			
Postoperative ECMO use (n)			
Veno-venous ECMO	0% (0)	0% (0)	> 0.99
Veno-arterial ECMO	33% (1)	0% (0)	0.30
PaO_2:FiO_2 at 24 hours, median (IQR), mm Hg	356 (337-375)	380 (309-432)	0.89
Mechanical ventilation, median (IQR), days	4 (3.5-4.5)	5 (3.5-6.5)	0.48
Hospital stay, median (IQR), days	33 (24.5-33.5)	43 (21-87.5)	0.52
Airway complications (n)	0% (0)	0% (0)	> 0.99
Mortality at 30 days (n)	0% (0)	0% (0)	> 0.99
Mortality at 90 days (n)	0% (0)	0% (0)	> 0.99
1-year survival (n)	100% (3)	86% (6)	> 0.99

DCD-NRP, donation after circulatory death with thoracoabdominal normothermic regional perfusion; ECMO, extracorporeal membrane oxygenation; IQR, interquartile range; PGD, primary graft dysfunction.

out from their transplant, with median follow-up time of 336 days for the DCD-NRP lung transplant cohort.

For the 3 recipients of the DCD-NRP heart-lung allografts, the first patient developed a significant decrease in lung function, with an FEV 1 of 0.89 liter (34% predicted), though remains functional over 3 years post-transplant. The 2 other patients do not have any evidence of CLAD. All 3 patients are alive on room air, with 0% rate of ACR, with a median follow-up time of 741 days.

Organ utilization

During the study period, a total of 11 donors utilizing DCD-NRP for heart transplant were evaluated: 8 for lung transplant and 3 for heart-lung transplant. In all 11 cases, the donor had cardiac arrest within the allotted 180-minute time frame after WLST. The lung allografts were accepted and implanted with a 100% utilization rate. For the 8 DCD-NRP lung allografts utilized, all 8 heart allografts were utilized.

Discussion

To our knowledge, this retrospective case-control study is the first reported data evaluating the rate of PGD after lung transplantation using thoracoabdominal DCD-NRP. Additionally, DCD-NRP lung transplant and heart-lung transplant outcomes are compared to clinically similar patients who received allografts from DBD. Our comparative data support the notion that DCD-NRP is an acceptable method for lung and heart-lung transplantation, with similar initial and intermediate outcomes to DBD. Patients who received lung allografts via DCD-NRP had similar P/F ratios at 24 hours, no significant difference in grade 3 PGD at 72 hours, and no postoperative ECMO utilization compared to those who received lungs via DBD. Importantly, there was no difference in 1-year survival between the groups. Additionally, our DCD-NRP lung transplant cohort has acceptable long-term functional results with a postoperative FEV1 range from 71% to 121%. These data support the

Table 6 DCD-NRP Recipient Clinical Status.

	1-year survival	Time to follow up (days)	Status	Most recent FEV1 (liter)	Most recent FEV1% predicted	ACR episodes	Treated for ACR	CLAD status	Current oxygen requirement
Lung transplant patients									
1	Yes	657	Alive	4.03	121	0	No	0	Room air
2	Yes	594	Alive	2.46	75	0	No	0	Room air
3	Yes	573	Alive	1.98	82	0	No	0	Room air
4	Yes	370	Alive	2.05	100	0	No	0	Room air
5	n/a	302	Alive	3.52	119	0	No	0	Room air
6	n/a	243	Alive	2.36	111	0	No	0	Room air
7	n/a	216	Alive	2.31	71	0	No	0	Room air
8	n/a	105	Alive	2.6	89	0	No	0	Room air
Heart lung transplant patients									
1	Yes	1,211	Alive	0.89	34	0	No	3	Room air
2	Yes	741	Alive	2.69	76	0	No	0	Room air
3	Yes	540	Alive	2.34	87	0	No	0	Room air

ACR, acute cellular rejection; CLAD, chronic lung allograft dysfunction; DCD-NRP, donation after circulatory death with thoracoabdominal normothermic regional perfusion; FEV1, forced expiratory volume over 1 second.

safety and efficacy of DCD-NRP for lung transplantation, and reinforce the concept that lung recovery from DCD-NRP is an acceptable method for lung allograft recovery.

Analysis of the UNOS database has revealed that lung recovery after DCD-NRP has comparable short-term outcomes to DCD-DP donors.[6,8] Reviewing 17 patients who underwent DCD-NRP for lung transplantation, Zhou et al reported that recipients of DCD-NRP lungs had similar rates of intubation, use of ECMO at 72 hours, and acute rejection, when compared to DCD-DP.[10] Importantly, 30-, 60-, and 90-day survival (92.9% vs 93.6%; $p > 0.9$) were similar. These results were reiterated by Malas et al in an overlapping UNOS database cohort of 63 lung transplant patients utilizing DCD-NRP. In this analysis, DCD-NRP lung transplant recipients had similar rates of treatment for acute rejection, use of ECMO and inhaled nitric oxide, and similar 6-month survival (85.7% vs 89.1%; $p = 0.67$).[6] These studies are limited by utilization of a database where there is no classification of NRP so the reported data may be misclassified due to stratification based on time between asystole and cross clamp. Notably, the studies used different cut-off times to determine which patients "likely" underwent DCD-NRP (≥50 vs > 20 minutes), which may explain the significant difference of patients included in the cohorts over a similar time period.

Furthermore, the comparison data are to DCD-DP with ex-situ perfusion of cardiac allografts, not to DBD outcomes. Among our 4 DCD-DP lung transplants that were performed during this time point, 2 of the DCD-DPs were performed when the heart was procured using ex-situ perfusion. Due to the small number of patients, as well as 1 of our recipients being a bridge to transplant utilizing VA-ECMO, the outcomes were not evaluated in our study. However, the patient on preoperative ECMO had severe PGD from the directly implanted DCD lung. The other patient did well with no postoperative graft dysfunction or ECMO requirement.

Another interesting finding is the rate of postoperative ECMO utilization in the DCD-NRP lung transplants. The reported rates were 6% (1/17) or 7% (2/26) in the 2 database studies. Our reported ECMO rate was 0% in this cohort, though that is limited secondary to the small number of patients. However, there are 2 notable differences between our cohort and the 2 reported studies. First, none of our allografts were evaluated using EVLP, compared to 6% (1/17) and 19% (5/26) of those in the database. No published data have evaluated the effect of EVLP on DCD-NRP allografts, though there is the potential that EVLP may adversely affect allografts obtained from DCD-NRP. Second, the method of DCD-NRP procurement is not elucidated in this study. For our patients, all patients had a left atrial vent utilized during reperfusion. A porcine study suggested NRP resulted in higher pulmonary artery pressure and lactate when evaluated using EVLP, but the model did not include venting the left atrium.[13] Further standardization of technique for procurement is likely necessary for reliable procurement of lung allografts from DCD-NRP.

Our 100% utilization rate of lung and heart-lung allografts is a significant departure from previously reported lung acceptance rates after directly procured DCD (13.8%) and DCD-NRP (14.9%).[6] One explanation is that our data represent a single-center experience, which allows for selection of suitable donors, colocation of donor and recipients when feasible, and control of perioperative management. Due the requisite resources and expertise, DCD-NRP may benefit from regionalization to specialized centers in a given donor service area.

Though DCD-NRP procurement is increased in complexity compared to DCD-DP, it should be noted that one limitation to cardiac DCD-DP and ex-situ perfusion is the inability to perform en-bloc heart-lung transplant. It is currently not feasible to concomitantly evaluate both allografts from a DCD donor in an ex-situ setting. Our results demonstrate that heart-lung transplant utilizing DCD-NRP is feasible with good short- and long-term outcomes.

Regarding the technique of DCD-NRP management of the supra-aortic vessels, patients in this series had their supra-aortic vessels clamped without venting. This technique

is how our center and many centers in the United States perform DCD-NRP. While there are concerns regarding the need to vent these vessels in order to preclude brain perfusion,[14-16] we monitored cerebral perfusion using cerebral oximetry. However, cerebral oximetry may not be the best surrogate to monitor cerebral perfusion. Further guidance of DCD-NRP technique is still warranted with either standardization of venting the supra-aortic vessels or improved monitoring to assure no cerebral perfusion during NRP.

Limitations of this study include a limited cohort size, which is underpowered for meaningful statistical analysis. Equally, this is a single-center experience of DCD-NRP, which may have inherent selection bias when accepting donors and recipients. While there are no significant differences of our reported variables between DCD-NRP and the control DBD cohorts, our comparative data should be interpreted with caution as we did not perform propensity-matching given the limited sample size. Additionally, our records did not contain functional warm ischemic time (time when blood pressure drops below 50-60 mm Hg to initiation of CPB/ECMO), so only total warm ischemic times were reported in this study.

In conclusion, the use of DCD-NRP appears to be a promising method to obtain lung and heart-lung allografts. Given the inability to utilize DCD-DP donors for heart-lung transplant, DCD-NRP can expand the donor pool for heart-lung allografts. Our institutional experience demonstrates that patients who receive lung allografts via DCD-NRP have good short-term perioperative clinical outcomes, including low rates of PGD, and excellent intermediate survival with acceptable pulmonary function. These outcomes are comparable to DBD lung transplantation at our institution. Given these results, DCD-NRP may be an underutilized method for lung procurement, especially given the increasing use of DCD-NRP for cardiac transplantation. Further efforts to research and optimize DCD-NRP for procurement of lung and heart-lung allografts are warranted.

Author contributions

S.H.C., T.C.G., L.F.A. were involved in the study conceptualization, study design, and drafted the manuscript. S.H.C., T.C.G., L.J., D.P., L.F.A. conducted the data analysis. All authors were involved in data interpretation, manuscript review, critical revisions, and final approval of the manuscript.

Disclosure statement

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