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ORIGINAL ARTICLE

Single center utilization and post-transplant outcomes of thoracoabdominal normothermic regional perfusion deceased cardiac donor organs

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Abstract

Introduction: Thoracoabdominal normothermic regional perfusion (TA-NRP) following cardiac death is an emerging multivisceral organ procurement technique. Recent national studies on outcomes of presumptive TA-NRP-procured organs are limited by potential misclassification since TA-NRP is not differentiated from donation after cardiac death (DCD) in registry data.

Methods: We studied 22 donors whose designees consented to TA-NRP and organ procurement performed at our institution between January 20, 2020 and July 3, 2022. We identified these donors in SRTR to describe organ utilization and recipient outcomes and compared them to recipients of traditional DCD (tDCD) and donation after brain death (DBD) organs during the same timeframe.

Results: All 22 donors progressed to cardiac arrest and underwent TA-NRP followed by heart, lung, kidney, and/or liver procurement. Median donor age was 41 years, 55% had anoxic brain injury, 45% were hypertensive, 0% were diabetic, and median kidney donor profile index was 40%. TA-NRP utilization was high across all organ types (88%–100%), with a higher percentage of kidneys procured via TA-NRP compared to tDCD (88% vs. 72%, $p = .02$). Recipient and graft survival ranged from 89% to 100% and were comparable to tDCD and DBD recipients ($p \geq .2$). Delayed graft function was lower for kidneys procured from TA-NRP compared to tDCD donors (27% vs. 44%, $p = .045$).

Conclusion: Procurement from TA-NRP donors yielded high organ utilization, with outcomes comparable to tDCD and DBD recipients across organ types. Further large-scale study of TA-NRP donors, facilitated by its capture in the national registry, will be critical to fully understand its impact as an organ procurement technique.

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1 | INTRODUCTION

Transplantation is the optimal treatment for end-stage organ failure, but access to this lifesaving therapy is limited by the ongoing organ shortage. This imbalance between organ supply and demand has prompted increasing pursuit of potential donors after cardiac death (DCD). In the United States, the number of these donors, hereafter referred to as traditional DCD (tDCD), has been increasing for nearly 15 years, and accounted for 30.2% of all organs procured for transplantation in 2021.[1] However, warm ischemia associated with tDCD procurement can result in allograft injury that can be more severe than that incurred in the setting of donation after brain death (DBD), and generally yields increased rates of post-transplant complications and greater risks of graft dysfunction.[2–6] As a result, tDCD organs are less likely to be transplanted compared to DBD organs.

For donors who do not meet criteria for brain death, thoracoabdominal normothermic regional perfusion (TA-NRP) following withdrawal of support and subsequent cardiac arrest has emerged as a procurement technique that may be an alternative to tDCD. Upon cardiac arrest and declaration of death, donors are cannulated onto extracorporeal membrane oxygenation (ECMO) with their cerebral vessels clamped or ligated prior to initiation, allowing for in situ regional perfusion of the thoracoabdominal compartment.[7] This novel procurement strategy has several putative advantages over tDCD including reduction of warm ischemia, the potential protective effects of preconditioning, and the ability to assess organ function in situ prior to recovery.[8,9]

Several, mostly single-center studies have reported encouraging outcomes following TA-NRP for both thoracic and abdominal organs. Among thoracic transplant recipients, reported 3-month patient survival has ranged from 98.3% to 100%.[10,11] Given that procurement via tDCD has historically been rare, favorable outcomes of TA-NRP heart procurement is especially impactful since it is estimated that broader adoption of TA-NRP could increase the number of hearts available for transplantation by 15%–30%, and reduce waitlist mortality by an estimated 40%.[12,13] For abdominal transplantation, reported 12-month recipient and graft survival has ranged from 94% to 97% and 93% to 97%, respectively.[2,14–16] In studies conducted at European centers exploring abdominal-only NRP procurement, biliary complications after liver transplantation and delayed graft function after kidney transplantation were less likely compared to tDCD-procured organs.[16,17]

TA-NRP is new and not yet broadly adopted in the United States. Our center implemented this practice early and has accrued a high-volume experience.[18] Since TA-NRP as a distinct procurement technique is not captured in the national registry, recently published analyses using these data are subject to misclassification.[19–22] To explore the potential value of broader national adoption, we characterized the utilization and outcomes of thoracic and abdominal organs known with certainty to have been procured by TA-NRP technique and compared them to those procured after tDCD and DBD.

2 | MATERIALS AND METHODS

2.1 | Data sources

This study leveraged data from a pilot study (ClinicalTrials.gov number, NCT04284319) of patients who received heart transplants from TA-NRP donors at New York University Langone Health between January 2020 and July 2022.[18] This study was approved by the NYU Grossman School of Medicine Institutional Review Board (S19-01664), with oversight from an independent Data Safety Monitoring Board.

Donor Organ Procurement and Transplantation Network (OPTN) identification numbers for known TA-NRP donors were linked to the Scientific Registry of Transplant Recipients (SRTR) to evaluate utilization and recipient outcome data. The SRTR data system includes data on all donor, wait-listed candidates, and transplant recipients in the US, submitted by the members of the Organ Procurement and Transplantation Network (OPTN). The Health Resources and Services Administration (HRSA), U.S. Department of Health and Human Services provides oversight to the activities of the OPTN and SRTR contractors. The SRTR dataset has previously been described elsewhere.[23]

2.2 | Study population

We studied 22 donors aged 20–51 years with no known history of cardiac disease or cardiovascular risk factors, who underwent organ procurement using TA-NRP technique at New York University Langone Health from January 20, 2020 to July 3, 2022.[18]

Potential donor candidates were identified from the local organ procurement organization, who subsequently obtained authorization for organ donation and research from the donor next-of-kin or consent designee. Following authorization, each donor candidate was transported to our center's intensive care unit for continued supportive medical care. Once confirmed to be a candidate for donation, donors were transported to the operating room for planned withdrawal of support followed by TA-NRP and organ procurement if they progressed to circulatory death. Our center's TA-NRP protocol is described elsewhere.[7,18] For a comparator cohort, we identified from the national data registry all adult (≥18 years) controlled tDCD and DBD donors during the same timeframe.

Donor demographics and clinical characteristics except for pertinent intraoperative times specific to TA-NRP recoveries (e.g., time/duration of ECMO initiation) were ascertained from the national registry. Warm ischemia time for TA-NRP donors was defined as the interval between the start of the donor agonal phase as captured by the OPTN and the time of ECMO initiation as captured in our pilot study. For tDCD donors, warm ischemia time was defined as the interval between the start of the donor agonal phase and time of cross clamp, both captured by the OPTN. Notably, definitions of what clinical parameters constitute the onset of agonal phase in donors are not specified in the national registry.

2.3 | Utilization of TA-NRP organs

We defined utilization as the number of organs used for transplant divided by the number of organs procured for transplantation. We counted double, split, and en bloc procedures as one transplant. To characterize the impact of TA-NRP utilization as a source of transplantable organs, we calculated the proportion of utilized TA-NRP organs and compared them to their tDCD and/or DBD counterparts.

2.4 | Recipients of TA-NRP organs

We identified all adult recipients of TA-NRP, tDCD, and DBD hearts, lungs, kidneys, and/or livers. For fair comparison, we excluded tDCD and DBD recipients who received multiorgan transplants or underwent a different transplant procedure as compared to TA-NRP recipients.

2.5 | Outcomes

2.5.1 | Patient and graft survival

Recipients were followed from date of transplant until death (and/or graft failure), or date of administrative censorship on March 31, 2023, whichever came first. All-cause graft survival was defined as the proportion of recipients who did not experience death, graft loss, retransplant, or return to maintenance dialysis (for kidney recipients). Death-censored graft survival was defined as the proportion of recipients who did not experience graft loss, retransplant, or return to maintenance dialysis (for kidney recipients). We estimated recipient and all-cause graft survival using the Kaplan-Meier method for each procurement technique, and compared them using the log-rank test. We did not use Cox regression to calculate measures of association, given the small number of events among TA-NRP recipients.

2.5.2 | Primary graft dysfunction, delayed graft function, renal allograft function, and length of stay

Primary graft dysfunction (hearts) was defined as left ventricular, right ventricular, or biventricular dysfunction that occurs within 24 h following surgery and was ascertained for TA-NRP heart transplant recipients from our center's electronic health record. Delayed graft function (kidneys) was defined as the need for postoperative dialysis within seven days of kidney transplantation, as reported to the OPTN. Renal allograft function was measured using estimated glomerular filtration rate (eGFR; CKD-EPI Creatinine Equation 2021) at 6 months following transplantation. Hospital length of stay was defined as days from transplant until hospital discharge following the index admission. We used descriptive statistics to compare the incidence of these outcomes for TA-NRP, tDCD, and DBD recipients, given the small number of events among those who received TA-NRP organs.

2.6 | Statistical analysis

To analyze donor characteristics, we used descriptive statistics. To compare utilization and recipient characteristics across groups, we used two sample *t*-tests or Wilcoxon rank-sum tests for continuous variables, and Pearson's $\chi 2$ tests or Fisher exact tests for categorical variables. Column percentages in recipient tables may slightly be below or above 100% due to rounding. Missing data were excluded. All analyses were performed using Stata 17.0/MP for Linux (College Station, Texas).

3 | RESULTS

3.1 | TA-NRP donors

Between January 2020 and July 2022, all 22 donors whose designees consented to TA-NRP progressed to cardiac arrest following planned terminal extubation and underwent TA-NRP followed by organ procurement (Table 1). Although our TA-NRP protocol allows for up to 180 min from extubation to cardiac arrest, median progression from extubation to cardiac arrest was 19 min (IQR: 14, 23) and required more than 30 min for only one individual (Supplementary Table). The median time from cardiac arrest to cross clamp and initiation of cold flush was 130 min (IQR: 110, 158) and median warm ischemia time was 28 min (IQR: 26, 32).

Overall, median donor age was 41 years (IQR: 34, 44), 77% were male, and 68% were White. The most common cause of death indicated was anoxia (55%), 45% had a history of hypertension, 0% had a history of diabetes, 5% were seropositive for hepatitis C virus. The median kidney donor profile index (KDPI) was 40% (IQR: 34, 55). Biopsies were performed on 95% of procured kidneys and 9% of livers.

3.2 | Heart: TA-NRP utilization and recipient outcomes

Of 22 TA-NRP hearts available, 1 was not procured (deemed unacceptable for transplantation based on predonation clinical data), 2 were procured with intent for research use only. Nineteen were procured with intention to transplant, and all were transplanted. This 100%

TABLE 1 Characteristics of thoracoabdominal normothermic regional perfusion donors.

	TA-NRP ($N = 22$)
Characteristic	
Age (years), median (IQR)	41 (34, 44)
Male gender, %	77
Race/ethnicity, %	
Asian	5
Black	5
Hispanic/Latino	23
White	68
Blood type, %	
A	18
B	14
O	68
Left ventricular ejection fraction (%), median (IQR)	65 (60, 70)
Hypertensive, %	45
Diabetic, %	0
BMI (kg/m^2), median (IQR)	27 (23, 34)
ALT (U/L, median (IQR)	40 (25, 68)
AST (U/L), median (IQR)	46 (34, 73)
Serum creatinine (mg/dL), median (IQR)	.8 (.7, 1.5)
HCV IgG antibody positive, %	5
HCV NAT positive, %	0
Cause of death, %	
Anoxia	55
Cerebrovascular/stroke	23
Head trauma	23
Kidney donor profile index (%), median (IQR)	40 (34, 55)
Biopsy	
Liver, %	9
Kidney, %	95
Glomerulosclerosis	
0%–5%	90
6%–10%	5
≥20%	5
Kidney machine perfusion, %	95
Pertinent intra-operative times (min)	
Extubation to cardiac arrest, median (IQR)	19 (14, 23)
Cardiac arrest to ECMO initiation, median (IQR)	10 (8, 17)
Total time from extubation to ECMO initiation, median (IQR)	29 (27, 34)
ECMO initiation to cross clamp, median (IQR)	130 (110, 158)
Extubation to cross clamp, median (IQR)	160 (141, 177)
Warm ischemia time, median (IQR)	28 (26, 32)

Abbreviations: ALT, alanine transaminase; AST, aspartate transaminase; ECMO, extracorporeal membrane oxygenation; HCV, hepatitis C virus, IQR, interquartile range; NAT, nucleic acid test.

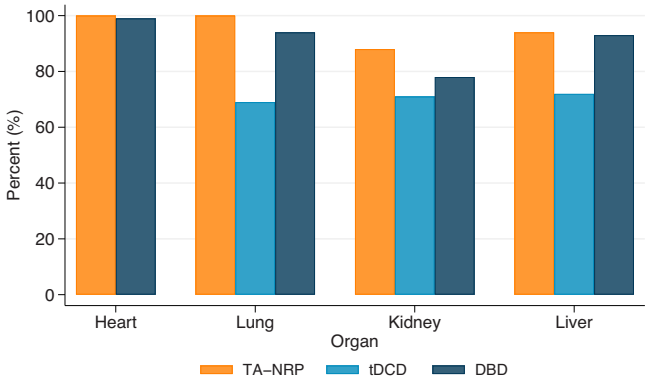

FIGURE 1 Percentage of organs utilized for transplantation, by recovery protocol and organ type. TA-NRP utilization was high, ranging from 88% to 100%, across organ types. Although utilization across procurement protocols were similar for hearts, lungs, and livers ($p \geq .054$), the percentage of kidneys procured via TA-NRP was statistically significantly higher than those procured via tDCD ($p = .02$). TA-NRP; thoracoabdominal normothermic regional perfusion; tDCD, traditional donation after cardiac death; DBD, donation after brain death.

utilization was comparable to that of DBD (99%, $n = 7692/7746$; $p > .9$) donors (Figure 1).

Among TA-NRP heart recipients, median age was 56 years (IQR: 50, 60), 81% were male, and 50% were White (Table 2). The most common indication for heart transplantation was nonischemic cardiomyopathy (81%), 50% had a ventricular assist device, 31% were on inotropic support, 6% had an intra-aortic balloon pump, 62% were status 4 at time of transplantation, and median cold ischemia time was 72 min (IQR: 68, 79). TA-NRP recipients had statistically significantly lower listing status priority (19% transplanted with listing status 4, $p = .003$) and shorter cold ischemia time (median [IQR] minutes: 206 [174, 238], $p < .001$) compared to their DBD counterparts.

Overall, patient and graft survival for TA-NRP recipients was 100% at 38 months following transplantation (Figure 2A,B) (Table 2). Median hospital length of stay was 15 days (IQR: 11, 21). Outcomes of TA-NRP recipients were similar to their DBD counterparts ($p \geq .2$).

3.3 | Lung: TA-NRP utilization and recipient outcomes

Of 44 TA-NRP lungs available, 30 were intentionally not procured (based on predonation clinical data), 2 were procured with intent for research use only, and 12 lungs were used for bilateral transplantation. This translated into a utilization of 100%, which was comparable to that of tDCD (69%, $n = 446/650$, $p = .2$) and DBD (94%, $n = 5502/5861$, $p > .9$) donors (Figure 1).

Among TA-NRP bilateral lung recipients, median age was 63 years (IQR: 61, 64), 100% were male, and 67% were White (Table 3). The indication for lung transplantation was restrictive lung disease (100%), median percentage of predicted forced expiratory volume (FEV1) was 74% (IQR: 68, 81), median lung allocation score was 38 (IQR: 35, 39), and median cold ischemia time was 2 h (IQR: 2, 3). TA-NRP recipients

TABLE 2 Characteristics of thoracoabdominal normothermic regional perfusion donor heart recipients.

	TA-NRP ($n = 16$)	DBD ($n = 7095$)
Characteristics		
Age (years), median (IQR)	56 (50, 60)	57 (47, 64)
Male gender, %	81	74
Race/ethnicity, %		
Black	19	26
Hispanic/Latino	31	10
Multiracial or other	0	5
White	50	59
Blood type, %		
A	19	39
B	19	16
AB	0	5
O	62	40
Cause of end-stage heart disease, %		
Ischemic cardiomyopathy	19	26
Non-ischemic cardiomyopathy	81	63
Transplant	0	3
Congenital	0	3
Other	0	5
Height (cm), median (IQR)	174 (169, 178)	175 (168, 180)
Weight (kg), median (IQR)	77 (69, 89)	84 (71, 97)
Status at time of transplant, %		
1	0	**10**
2	19	**51**
3	12	**15**
4	62	**19**
5	0	**1**
6	6	**5**
Ventricular assist, %	50	36
ECMO, %	0	6
Intra-aortic balloon pump, %	6	29
IV inotropes, %	31	41
Previous transplant, %	0	3
Multiorgan transplant, %		
Heart	94	90
Simultaneous heart kidney	6	10
Warm ischemia time (min), median (IQR)	28 (25, 34)	–
Cold ischemia time (min), median (IQR)	72 (68, 79)	**206 (174, 238)**
Outcomes		
Survival, %	100	88
All-cause graft survival, %	100	88
Primary graft dysfunction, %	6	N/A[a]
Hospital length of stay (days), median (IQR)	15 (11, 21)	17 (12, 26)

Bold denotes $p < .05$ as compared to TA-NRP.

Abbreviations: DBD, donation after brain death; ECMO, extracorporeal membrane oxygenation; IQR, interquartile range; IV, intravenous; LVAD, left ventricular assist device; RVAD, right ventricular assist device; TAH, total artificial heart; TA-NRP, thoracoabdominal normothermic regional perfusion.

[a]Primary graft dysfunction is unable to be evaluated due to incomplete capture in national registry.

had higher median FEV1 compared to their tDCD (median: 36%, $p = .01$) and DBD (median: 42%, $p = .02$) counterparts. However, TA-NRP recipients had shorter median cold ischemia time compared to their tDCD (median: 6 h, $p = .004$) and DBD counterparts (median: 4 h, $p = .007$).

Overall, patient and graft survival for TA-NRP lung recipients was 100% at 14 months following transplantation (Figure 2C,D) (Table 3). Median hospital length of stay was 15 days (IQR: 9, 19). Outcomes of TA-NRP recipients were similar to their tDCD and DBD counterparts ($p \geq .07$).

3.4 | Kidney: Utilization and recipient outcomes

Of 44 TA-NRP kidneys available, 2 were intentionally not procured (based on predonation clinical data), 5 were procured but not accepted for transplantation, and 37 were used for transplantation. This translated into a utilization of 88%, which was statistically significantly higher than that of tDCD (71%, $n = 12\,384/17\,471$; $p = .02$), but comparable to that of DBD (78%, $n = 31\,066/40\,033$; $p = .1$) donors (Figure 1).

Among TA-NRP recipients, median age was 55 years (IQR: 47, 63), 57% were male, and 35% were Black (Table 4). The most common indication for kidney transplantation was hypertension (41%), 70% were blood type O, 30% had a calculated panel reactive antibody (cPRA) ≥80%, and median time on dialysis was 6 years (IQR: 2, 8). Nearly all recipients received a kidney-only transplant (95%). Altogether 65% of transplanted kidneys were placed locally. Compared to both tDCD and DBD, TA-NRP recipients were more likely to have blood type O (70% vs. 46% vs. 46%; $p \leq .01$) and have a cPRA ≥80% (30% vs. 15% vs. 16%; $p = .03$).

Overall, patient and all-cause graft survival for TA-NRP kidney recipients was 97% at 3 months, 95% at 12 months, 89% at 24 months, and 89% at 36 months following transplantation (Figure 2E,F)

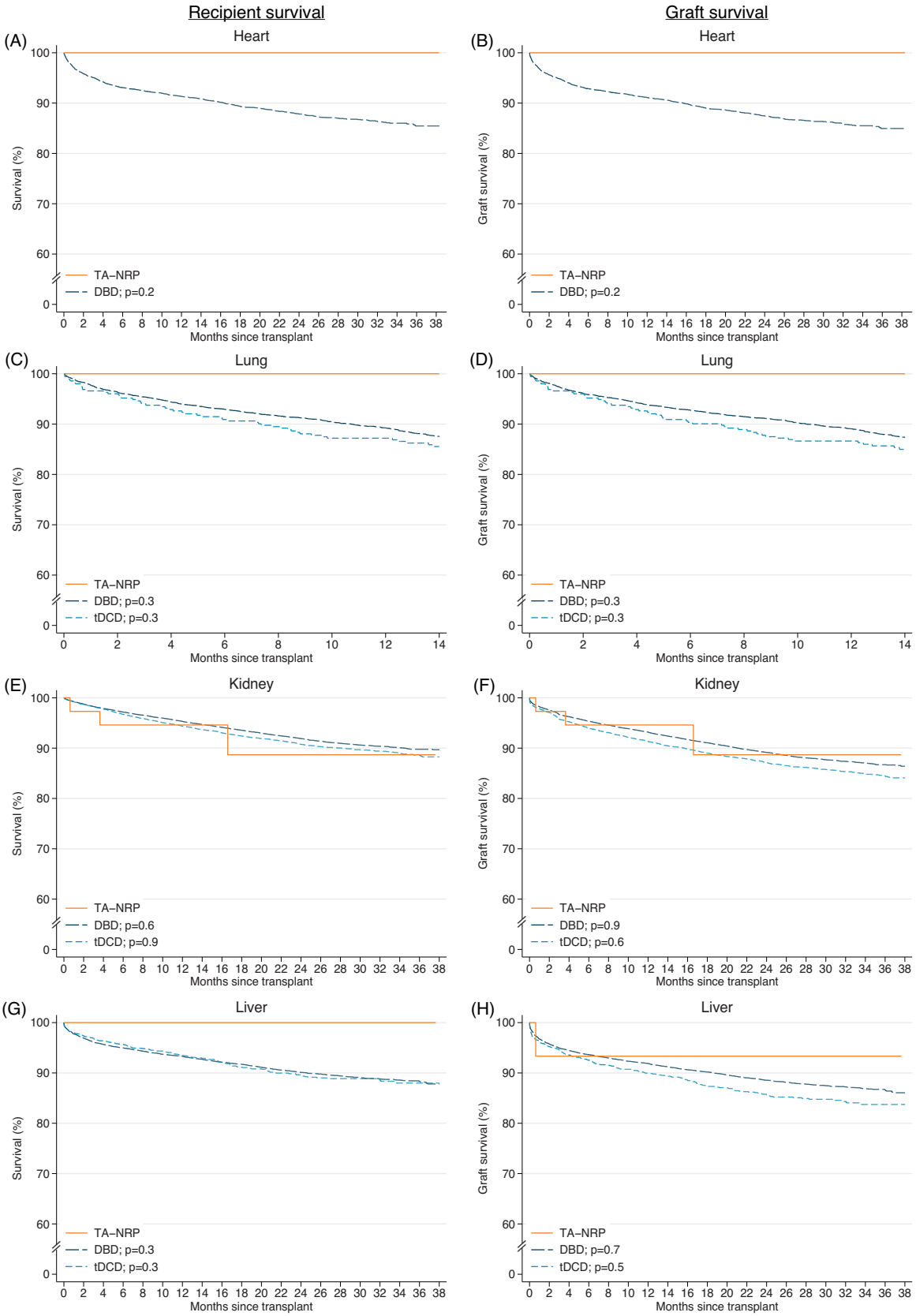

FIGURE 2 Cumulative patient and all-cause graft survival following receipt of thoracoabdominal normothermic regional perfusion donor hearts, lungs, kidneys, and livers. *p*-values represent comparisons between TA-NRP and other procurement protocols (i.e., tDCD and DBD). Each graph illustrates the crude patient and all-cause graft survival (columns) at the end follow-up by to organ types (rows; hearts: [A, B], dual lungs [C, D], kidneys [E, F], and livers [G, H]). Across all organ types, TA-NRP recipient and all-cause survival ranged from 89% to 100%. Outcomes were comparable to other procurement protocols ($p \geq .2$ for all comparisons). TA-NRP; thoracoabdominal normothermic regional perfusion; tDCD, traditional donation after cardiac death; DBD, donation after brain death.

TABLE 3 Characteristics of thoracoabdominal normothermic regional perfusion donor lung recipients.

	TA-NRP ($n = 3$)	tDCD ($n = 352$)	DBD ($n = 4087$)
Characteristic			
Age (years), median (IQR)	63 (61, 64)	61 (54, 65)	60 (52, 66)
Male gender, %	100	57	62
Race/ethnicity, %			
Black	0	11	11
Hispanic/Latino	33	9	13
Multiracial or other	0	3	5
White	67	77	71
Blood type, %			
A	0	32	38
B	0	9	12
AB	0	4	4
O	100	55	47
Cause of end-stage lung disease, %			
Obstructive lung disease	0	32	21
Pulmonary vascular disease	0	3	6
Cystic fibrosis or immunodeficiency disorder	0	2	2
Restrictive lung disease	100	64	71
BMI (kg/m^2), median (IQR)	27 (24, 28)	26 (22, 29)	26 (23, 29)
LAS at allocation, median (IQR)	38 (35, 39)	39 (34, 51)	44 (36, 67)
FEV1 predicted (%), median (IQR)	74 (68, 81)	**36 (22, 55)**	**42 (26, 59)**
ECMO, %	0	8	11
Ventilator support, %	0	7	8
Abnormal bronchoscopy, %	0	11	15
Warm ischemia time (minutes), median (IQR)	31 (20, 35)	24 (19, 32)	–
Cold ischemia time (h), median (IQR)	2 (2, 3)	**6 (4, 8)**	**4 (4, 5)**
Outcomes			
Survival, %	100	79	82
All-cause graft survival, %	100	77	82
Hospital length of stay (days), median (IQR)	15 (9, 19)	24 (16, 45)	20 (14, 35)

Bold denotes $p < .05$ as compared to TA-NRP.

Abbreviations: DBD, donation after brain death; ECMO, Extracorporeal membrane oxygenation; FEV1, forced expiratory volume; IQR, interquartile range; NRP, normothermic regional perfusion; TA-NRP, thoracoabdominal normothermic regional perfusion; tDCD, traditional donation after circulatory death.

(Table 4). Median hospital length of stay was 5 days (IQR: 4, 8) and 27% experienced delayed graft function. TA-NRP recipients had a statistically significant lower incidence of DGF compared to their tDCD counterparts (27% vs. 44%, $p = .045$), but a slightly longer length of stay compared to their DBD counterparts (median [IQR]: 5 [4,7], $p = .04$).

3.5 | Liver: Utilization and recipient outcomes

Of 22 TA-NRP livers available, 3 were intentionally not procured (based on predonation clinical data), 2 were procured with intention for research only, 1 was procured but not used for transplantation, and 16 were used for transplantation. This translated into a utilization of 94%, which was comparable to tDCD (72%, $n = 2063/2861$; $p = .054$) and DBD (93%, $n = 17\ 278/18\ 615$; $p \geq .9$) donors (Figure 1).

Among TA-NRP recipients, median age was 61 years (IQR: 57, 66), 62% were male, 62% were White (Table 5). The most common indication for liver transplantation was hepatocellular carcinoma (44%) and 12% were seropositive for hepatitis C virus. Median biologic and allocation MELD scores were 18 (IQR: 12, 19) and 25 (IQR: 20, 28). Most (75%) TA-NRP transplanted livers were placed locally. Median cold ischemia time was 5 h (IQR: 4, 6) for TA-NRP livers, slightly shorter than

TABLE 4 Characteristics of thoracoabdominal normothermic regional perfusion donor kidney recipients.

	TA-NRP ($n = 37$)	tDCD ($n = 12\,158$)	DBD ($n = 28\,225$)
Characteristic			
Age (years), median (IQR)	55 (47, 63)	57 (47, 65)	55 (44, 64)
Male gender, %	57	61	61
Race/ethnicity, %			
Black	35	33	34
Hispanic/Latino	27	18	20
Multiracial or other	11	10	10
White	27	39	36
Blood type, %			
A	14	**36**	**34**
B	16	**13**	**15**
AB	0	**5**	**5**
O	70	**46**	**46**
BMI (kg/m^2), median (IQR)	27 (24, 30)	28 (25, 32)	28 (25, 33)
Cause of end-stage renal disease, %			
Glomerular diseases	19	23	26
Diabetes	22	35	30
Hypertension	41	24	24
Polycystic kidney disease	3	8	7
Other	16	11	14
cPRA ≥80%, %	30	**15**	**16**
Previous history of transplant, %	11	12	13
Preemptive transplant, %	11	11	14
Years on dialysis, %	6 (2,8)	4 (2,6)	4 (2,7)
EPTS, median (IQR)	53 (27, 69)	54 (30, 77)	48 (23, 74)
Multiorgan, %			
Kidney only	95	98	92
Simultaneous kidney heart	3	<1	3
Simultaneous liver kidney	3	2	6
Local sharing, %	65	55	53
Warm ischemia time (min), median (IQR)	28 (26, 31)	**23 (18, 31)**	–
Cold ischemia time (h), median (IQR)	18 (15, 24)	20 (16, 24)	18 (12, 23)
Outcomes			
Survival, %	92	92	92
All-cause graft survival, %	92	88	90
Death-censored graft survival, %	100	95	96
eGFR at 6 months (mL/min/1.73 m^2), median (IQR)	59 (46, 70)	52 (39, 67)	57 (44, 73)
Delayed graft function, %	27	**44**	27
Hospital length of stay (days), median (IQR)	5 (4, 8)	5 (4, 7)	**5 (4, 7)**

Bold denotes $p < .05$ as compared to TA-NRP.

Abbreviations: CIT, cold ischemia time; DBD, donation after brain death; DCD, donation after circulatory death; eGFR, estimated glomerular filtration rate; EPTS, Estimated Post Transplant Survival; ESRD, end stage renal disease; IQR, interquartile range, TA-NRP, thoracoabdominal normothermic regional perfusion.

TABLE 5 Characteristics of thoracoabdominal normothermic regional perfusion donor liver recipients.

	TA-NRP ($n = 16$)	tDCD ($n = 2057$)	DBD ($n = 16\,827$)
Characteristic			
Age (years), median (IQR)	61 (57, 66)	59 (52, 65)	57 (47, 64)
Male gender, %	62	68	63
Race/ethnicity, %			
Black	0	5	7
Hispanic/Latino	38	15	17
Multiracial or other	0	4	6
White	62	76	70
Blood type, %			
A	19	39	36
B	19	8	14
AB	0	2	5
O	62	51	45
Height (cm), median (IQR)	170 (160, 175)	173 (165, 180)	173 (165, 180)
Weight (kg), median (IQR)	88 (70, 104)	86 (73, 100)	85 (72, 100)
Cause of end-stage liver disease, %			
Hepatitis C	6	7	5
Alcoholic liver disease	19	31	38
Non-alcoholic steatohepatitis	19	21	19
Autoimmune hepatitis	0	2	3
Primary sclerosing cholangitis	0	3	4
Hepatocellular carcinoma	44	26	18
Other	12	10	13
Biologic MELD, median (IQR)	18 (12, 19)	17 (13, 21)	**25 (17, 33)**
Allocation MELD, median (IQR)	25 (20, 28)	23 (19, 26)	**30 (24, 36)**
Hepatitis C virus antibody positive, %	12	18	13
Previous history of transplant, %	0	1	5
Multiorgan, %			
Liver only	94	90	91
Simultaneous liver kidney	6	10	9
Local sharing, %	75	52	35
Warm ischemia time (min), median (IQR)	28 (26, 32)	**20 (16, 24)**	–
Cold ischemia time (h), median (IQR)	5 (4, 6)	**5 (4, 7)**	**6 (5, 7)**
Outcomes			
Survival, %	100	90	90
All-cause graft survival, %	94	86	89
Hospital length of stay (days), median (IQR)	10 (8, 16)	**8 (6, 13)**	11 (7, 18)

Bold denotes $p < .05$ as compared to TA-NRP.

Abbreviations: CIT, cold ischemia time; DBD, donation after brain death; ESLD, end stage liver disease; HCV, hepatitis C virus; MELD, model for end stage liver disease, TA-NRP, thoracoabdominal normothermic regional perfusion; NRP, normothermic regional perfusion; tDCD, traditional donation after circulatory death.

that of their DBD counterparts (6 h [IQR: 5,7], $p = .008$). Compared to DBD recipients, TA-NRP recipients had lower biologic and allocation MELD scores (25 and 30, $p < .003$).

Overall, patient and graft survival for TA-NRP liver recipients was 100% and 93% at 38 months following transplantation, respectively (Figure 2G,H) (Table 5). Median hospital length of stay was 10 days (IQR: 8, 16) (Table 5). Compared to tDCD recipients, TA-NRP recipients had a longer length of stay (median: 8 days, IQR: 6–13, $p = .03$). TA-NRP recipients had comparable outcomes to their DBD counterparts ($p \geq .3$).

4 | DISCUSSION

In this single-center study, we observed that TA-NRP can facilitate the procurement of thoracic and abdominal organs with overall high utilization (88%–100%). Although utilization across procurement techniques was similar for hearts, lungs, and livers, the percentage of transplanted kidneys procured via TA-NRP was higher than that of kidneys procured via tDCD (88% vs. 72%). Moreover, we found that TA-NRP recipient and all-cause graft survival was high (89%–100%), and comparable to other procurement techniques. Recipients of TA-NRP kidneys had lower incidence of delayed graft function compared to their tDCD counterparts (27% vs. 44%). Overall, these findings are encouraging and suggest TA-NRP's potential value as an alternative procurement strategy.

Our results are consistent with other single- and multicenter reports demonstrating that NRP yields comparable outcomes to hearts and lungs procured via tDCD and/or DBD techniques.[10,11,24,25] However, for heart transplantation, we add to the existing literature as only short-term recipient and graft survival, and hospital length of stay have been described. Our center's initial experience with TA-NRP found that 4 recipients had 100% 1-year recipient and graft survival.[18] Here, we report that the 100% survival has held through 3 years post-transplant and for an additional 12 recipients. These outcomes are comparable to those of recipients who received DBD hearts. Although we observed higher recipient and graft survival at 3 years as compared to the lung transplant literature, which has ranged from 66.4% to 68.7%,[10,24] it is likely that differences in sample size and procurement protocols are responsible for this discrepancy.

Likewise, they may account for the comparable findings observed across organ types between NRP and tDCD techniques in single-center studies.[14,25,26] For example, in two multicenter studies of abdominal-only NRP procured organs—including 545 liver recipients and 865 NRP kidney recipients—found differences in patient and graft survival, with better outcomes for NRP as compared to tDCD recipients.[16,17] Additionally, we observed that TA-NRP kidney recipients had a lower incidence of delayed graft function than tDCD recipients (27% vs. 44%), but a comparable incidence to DBD recipients. This is mirrored in the literature, including the reported incidence of delayed graft function among NRP recipients (20.7%–48.4%).[2,14,16,27,28]

It is important to acknowledge that the high rates of recipient and graft survival observed in the present study may be in part driven by the overall lower clinical acuity of the TA-NRP organ recipients, in particular for heart, lung, and liver recipients. TA-NRP heart recipients had lower listing status priority and less intra-aortic balloon pump usage; lung recipients had higher FEV1 and a trend toward lower lung allocation score; liver recipients had lower biologic and allocation MELD compared to tDBD and/or DBD recipients. This may be reflective of the novelty of TA-NRP in the United States and may indicate reticence to use these organs for the highest clinical acuity patients until their outcomes are better understood. We also recognize that having both the donor and recipient in the same hospital reduced the total ischemia time for the thoracic transplant cases, which may have contributed to the heart and lung outcomes observed for TA-NRP recipients. Nonetheless, the findings of overall favorable outcomes are in alignment with studies conducted in the United Kingdom and Europe where NRP has been used since 1989.[11,24,26,29–32]

Certain limitations of this single-center study must be acknowledged. While our study may be limited in terms of generalizability due to its design, our center was among the first to perform TA-NRP in the United States, and thus may have informed TA-NRP procurement protocols at other centers nationwide. Moreover, all TA-NRP donors were managed at our center with dedicated intensive care and anesthesia teams under broadly consistent conditions, which may not represent the experience of teams who travel to remote hospitals for procurement. Although we leveraged national registry data to obtain reliable post-transplant outcome ascertainment, the small sample size and infrequency of death and graft loss events precluded us from quantifying estimates of risk. Similarly, given our small sample size, it is possible that we were underpowered to detect smaller effect sizes that are clinically important. Given the relative homogeneity of intraoperative donor ischemic times in our cohort, we were unable to evaluate the potential impacts of TA-NRP duration on organ utilization. Nevertheless, the major strength of our study is the longer-term follow-up of recipients known with certainty to have received TA-NRP organs[18,29]; and the comparison to organs procured by the alternative techniques, tDCD, and DBD. Until TA-NRP donor technique is differentiated from tDCD in the national registry, analyses using these data will continue to rely on speculation and may result in misclassification.[19–22]

Further large-scale study of TA-NRP as a procurement strategy is still needed but will not likely be feasible until this procurement technique is specifically captured in national registry data. Until then, our experience with TA-NRP, which reveals high utilization of thoracic and abdominal organs, and post-transplant outcomes comparable to tDCD and/or DBD donors in the United States, lends support for the broader adoption of this emerging donation modality.

AUTHOR CONTRIBUTIONS

Jennifer D. Motter, Allan B. Massie., Dorry L. Segev, and Bonnie E. Lonze participated in the concept and research design. Jennifer D. Motter performed the statistical analysis. Jennifer D. Motter, Ian S. Jaffe, and Imad Aljabban performed data interpretation. Nader Moazami, Deane E. Smith, Zachary N. Kon, Greta L. Piper, Alex Reyentovich, Philip M. Sommer, Stephanie H. Chang, Robert A. Montgomery, and Bonnie E. Lonze participated in recovery and transplant of thoracoabdominal normothermic regional perfusion donor organs and data collection. Jennifer D. Motter and Bonnie E. Lonze wrote the manuscript. All authors reviewed, revised, and approve of the manuscript.

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CONFLICT OF INTEREST STATEMENT

Dr. Kon is the CEO of ProCure On-Demand, Inc., and a member of EConnect-1, LLC. The remaining authors of this manuscript have no conflicts of interest to disclose as described by Clinical Transplantation.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the Scientific Registry of Transplant Recipients (SRTR). Restrictions apply to the availability of these data, which were used under license for this study. Data are available with the permission of the corresponding author and that of the SRTR. The internal NYU Langone data that support the findings of this study will be shared upon reasonable request to the corresponding author.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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