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Assessing Kidney Transplantation Using ECMO-Supported Donors Within a KDPI-Based Allocation System

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Background. Organ donors supported by extracorporeal membrane oxygenation (ECMO) have historically been considered high-risk and are judiciously utilized. This study examines transplant outcomes using renal allografts from donors supported on ECMO for nondonation purposes. **Methods.** Retrospective review of the Gift of Life (Pennsylvania, New Jersey, Delaware) organ procurement organization database, cross-referenced to the Organ Procurement and Transplantation Network database, assessed kidney transplants using donors supported on venoarterial (VA) and venovenous (VV) ECMO for nondonation purposes. Transplants using VA- and VV-ECMO donors were compared with Kidney Donor Profile Index (KDPI)-stratified non-ECMO donors. Regression modeling of the entire ECMO and non-ECMO populations assessed ECMO as predictive of graft survival. Additional regression of the ECMO population alone assessed for donor features associated with graft survival. **Results.** Seventy-eight ECMO donors yielded 128 kidney transplants (VA: 80, VV: 48). Comparing outcomes using these donors to kidney transplants using organs from KDPI-stratified non-ECMO donors, VA- and VV-ECMO donor grafts conferred similar rates of delayed graft function and posttransplant renal function to KDPI-matched non-ECMO counterparts. VA-ECMO kidneys demonstrated superior graft survival compared with the lowest-quality (KDPI 86%–100%) non-ECMO kidneys and similar graft survival to KDPI <85% non-ECMO kidneys. VV-ECMO showed inferior graft survival to all but the lowest-quality (KDPI 86%–100%) non-ECMO kidneys. VV-ECMO, but not VA-ECMO, was associated with increased risk of graft loss on multivariable regression (hazard ratios—VA: 1.02, VV: 2.18). Higher KDPI, advanced age, increased body mass index, hypertension, and diabetes were identified as high-risk features of ECMO donors. **Conclusions.** Kidney transplantation using appropriately selected ECMO donors can safely expand the donor pool. Ongoing studies are necessary to determine best practice patterns using kidneys from these donors.
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Solid organ transplantation remains limited by a persistent organ shortage. Despite the coronavirus 2019 pandemic, data from the Organ Procurement and Transplantation Network (OPTN) have shown a progressive increase in deceased-donor transplantation in each successive year since 2014.[1] As transplant waitlists continue to grow, expanding the donor pool is vital to increase organ availability. One area of focus remains increasing the use of the "marginal" donor population to better access and utilizes organs previously considered unsuitable for donation.

A population of marginal donors that have been judiciously utilized are those requiring extracorporeal membrane

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oxygenation (ECMO) as a means of cardiopulmonary support. ECMO, a variant of the cardiopulmonary bypass system first utilized by John Gibbon Jr in 1953,[2] can provide full pulmonary support through venovenous (VV) bypass or both cardiac and pulmonary support using venoarterial (VA) bypass. Pulmonary support via VV bypass is achieved by effectively bypassing pulmonary circulation through venous cannulae that pull deoxygenated blood into a circuit containing an oxygenator and subsequently redistribute the oxygenated blood back into systemic venous circulation. As the name implies, VA-ECMO utilizes a venous cannula to pull blood into the ECMO circuit, after which it distributes it back into an arterial cannula. This can serve the purpose of both bypassing a failing heart and offloading pulmonary circulation by providing oxygenated blood into the systemic arterial system. Ultimately, ECMO has been increasingly and more effectively applied as a rescue strategy to stabilize patients with refractory cardiopulmonary compromise over the past 2 decades.[3,4]

Donors supported by ECMO represent a unique and intriguing population because they suffer from acute refractory cardiopulmonary collapse but are otherwise healthy enough to be considered suitable candidates for initiation of therapy. There exists a growing body of literature assessing the use of organs from ECMO-supported donors, although these have largely been published in the context of ECMO used as a bridge to donation.[5-11] Although machine perfusion and normothermic regional perfusion are a growing means to expanding the donor pool, few studies have examined the safety and feasibility of utilizing organs from donors supported by ECMO for nondonation purposes.[12-15] Using the largest cohort of ECMO-supported donors available in the literature to date, this study intended to assess safety and utility of using allografts from this unique, but increasingly prevalent, population by evaluating their outcomes in kidney transplantation.

MATERIALS AND METHODS

Patient Population

A retrospective review of the Gift of Life (Pennsylvania, New Jersey, Delaware) Donor Program database from April 14, 2008, to April 18, 2021, assessed all donors supported by ECMO before donation who contributed at least 1 kidney or pancreas for transplant. No donor was supported on ECMO for donation purposes alone. Donors were stratified by ECMO support—VA or VV. Those on both VA and VV support were classified as VA-supported donors. ECMO-supported donors were then cross-referenced to their transplant recipients within the United Network for Organ Sharing OPTN database to assess for postoperative outcomes (Figure 1). Approval to conduct this analysis was obtained from the Thomas Jefferson University Institutional Review Board.

Analysis of Kidney Transplants Using VA- and VV-ECMO Donors Compared With Non-ECMO Donors

ECMO donors supplying at least 1 kidney for transplantation (n = 78) were stratified by VA and VV support. Transplants using kidneys from these donors were compared with isolated kidney transplants using allografts from non-ECMO donors within the same organ procuring organization over the same time period derived from the OPTN database. Kidney Donor Profile Index (KDPI) is currently utilized as a means to assess graft quality.[16] To better understand where these ECMO-supported donors may be considered in an allocation scheme dictated in part by KDPI, kidney transplants using VA- and VV-ECMO donors were compared with transplants from non-ECMO donors across 4 strata of KDPI: 0%–20%, 21%–34%, 35%–85%, and 86%–100%. Baseline characteristics of donor, recipient, and the transplant procedure were compared between groups. Outcomes assessed were rates of delayed graft function (DGF), posttransplant creatinine at 1 y in functioning kidneys, and graft and patient survival up to 5 y.

Assessing ECMO as Predictive of Kidney Graft Survival

To better understand the impact of donor ECMO support on posttransplant kidney graft survival, VA- and VV-ECMO support were assessed as covariates predictive of graft survival in both univariate and adjusted multivariable Cox proportional hazard regression models. Additional factors included in the multivariable model were recipient, donor, and transplant factors predictive of graft failure at $P < 0.20$. Recipient factors included age, Black race, male gender, log body mass index (BMI), disabled functional status, diabetes, hypertension, previous kidney transplant, and history of malignancy. KDPI was incorporated as a donor factor (composed of the following covariates: age >51, age <18, inverse log height, weight <80 kg, ethnicity, hypertension, diabetes, cerebrovascular accident as cause of death, log creatinine at donation, hepatitis C virus status, and donation after cardiac death). Finally, use of machine perfusion and cold ischemia time (CIT) were utilized as transplant-specific covariates.

Factors Predictive of Kidney Graft Survival in Organs From ECMO-Supported Donors

Transplants using kidneys from ECMO-supported donors were then isolated to further assess for factors predictive of graft survival. These analyses were performed for all ECMO donors, as well as individually for both VA- and VV-ECMO cohorts. Given the utility of the KDPI as a marker of donor quality to estimate posttransplant graft survival, we assessed its potential utility in the ECMO donor population. Here, logistic regression was used to assess the concordance between KDPI and kidney graft survival specifically in ECMO-supported donors while receiver operating characteristic curves assessed sensitivity versus specificity of KDPI predicting graft survival in ECMO-supported donors. Additional Cox proportional hazard modeling was again utilized to assess for additional donor factors predictive of graft survival. Further analysis of transplant outcomes using ECMO-supported donors stratified by KDPI category were performed as outlined in the analysis of kidney transplants from ECMO compared with non-ECMO donors and can be found in **Supplementary Material** (**SDC**, http://links.lww.com/TXD/A572).

Statistical Analysis

Continuous variables were evaluated for normality using the Shapiro-Wilk test. Nonparametrically distributed variables were compared with a Wilcoxon rank-sum test and were represented as median (interquartile range). Categorical variables were compared using a chi-square test and were represented as number (percentage of population). Posttransplant

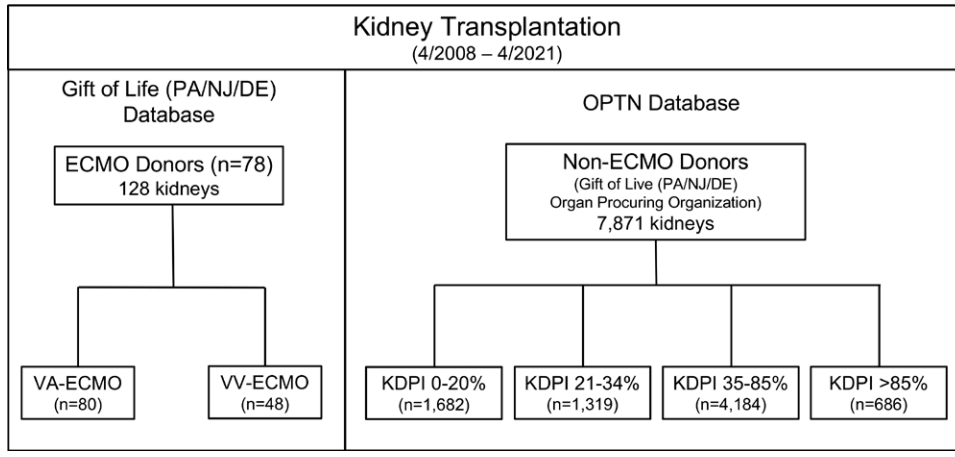

FIGURE 1. Flow diagram of data sources and study populations. DE, Delaware; ECMO, extracorporeal membrane oxygenation; KDPI, Kidney Donor Profile Index; NJ, New Jersey; OPTN, Organ Procurement and Transplantation Network; PA, Pennsylvania; VA, venoarterial; VV, venovenous.

patient and graft survival were reported graphically with Kaplan-Meier curves and numerically by time-varying Cox proportional hazard ratios (HRs) and 95% confidence intervals (95% CIs). Two-sided statistical significance was set a priori at $P < 0.05$. All statistical analyses were performed using Stata/MP 16.1 (StataCorp, College Station, TX).

RESULTS

Analysis of Kidney Transplants Using VA- and VV-ECMO Compared With Non-ECMO Donors

We first assessed baseline recipient characteristics in renal transplantation using ECMO-supported donor kidneys (VA: 80; VV: 48) and compared them to a KDPI-stratified non-ECMO-supported donor population (Table 1). Assessing recipient profiles, we found that VA-ECMO (56 y old) and VV-ECMO (55) kidney recipients were, on average, significantly older than non-ECMO KDPI 0%–20% recipients (43; $P < 0.01$ [VA/VV]), similar in age to non-ECMO KDPI 21%–34% recipients (55; $P = 0.35/0.62$ [VA/VV]), and significantly younger than recipients of higher-KDPI (35%–100%) non-ECMO kidneys. BMI of VA-ECMO recipients (26.37) tended to be lower than non-ECMO kidney recipients across KDPI strata, whereas VV-ECMO recipients (30.47) were generally significantly higher. No differences were seen in rates of pretransplant dialysis dependence when comparing both recipients of VA- and VV-ECMO kidneys to non-ECMO kidneys of any KDPI group. Duration of pretransplant dialysis was also largely similar between groups, with the exception of VA-ECMO kidney recipients being dialysis-dependent for longer periods than non-ECMO KDPI 86%–100% kidney recipients (1745 versus 1348 d; $P = 0.03$). Recipients of VA- and VV-ECMO kidneys had prior kidney transplants in 8.50% and 10.42% of cases, comparable to all non-ECMO kidney recipients apart from those receiving the highest KDPI (86%–100%) non-ECMO kidneys (3.50%; $P = 0.03/0.04$ [VA/VV]). Etiology of renal failure was significantly different between VA- and VV-ECMO kidney transplants and those using non-ECMO kidneys of the lowest KDPI (0%–20%) but was similar to non-ECMO kidneys with KDPI >20%. No significant differences were seen in recipient gender, ethnicity, or functional status when comparing VA- and VV-ECMO transplants to non-ECMO transplants of any KDPI group.

We then compared donor characteristics between groups (Table 1). Overall, the median KDPI was 44% for VA-ECMO and 48% for VV-ECMO donors, whereas median terminal creatinine was 1.10 (VA) and 1.03 mg/dL (VV). Average age was 31 for VA- and 29 for VV-ECMO donors, older than non-ECMO KDPI 0-20% donors (24; $P < 0.01$ [VA/VV]) and younger than non-ECMO donors of all KDPI categories >35%. Incidence of both diabetes and hypertension for VA- and VV-ECMO donors were comparable to non-ECMO KDPI 35%–85% donors, whereas inotropic support was less common in VA-ECMO (36.25%) and VV-ECMO (25.00%) donors than non-ECMO donors of all KDPI strata. Donor death from cerebrovascular accidents was comparable between ECMO (VA: 7.50%, VV: 8.33%) and lower-KDPI (0-34%) non-ECMO donors but less frequent than the KDPI 35%–85% (28.70%) and KDPI 86%–100% (65.45%) non-ECMO donors (all $P < 0.01$). Assessing donor kidney biopsies, >10% glomerulosclerosis was present in 9.10% and 11.11% of VA- and VV-ECMO donor kidneys, respectively; this was higher than non-ECMO kidneys from KDPI 0%–20% donors (2.38%), but comparable to kidneys from non-ECMO donors with KDPI >20%.

Finally, transplant characteristics were compared. HLA mismatch profiles were comparable between VA-ECMO and non-ECMO transplants of with KDPI ≤85%, whereas KDPI 85%–100% non-ECMO kidney transplants more HLA mismatches than the VA-ECMO group (median 5 versus 4.5; $P = 0.03$). No differences were seen in HLA mismatches between VV-ECMO and non-ECMO kidney transplants. Median CIT of VA-ECMO kidneys (16.60 h) was statistically significantly higher than kidneys from KDPI 0%–34% non-ECMO donors but comparable to donors with KDPI ≥35%. Transplants using VV-ECMO kidneys, conversely, had longer CITs on average (20.78 h) than all categories of non-ECMO kidneys regardless of KDPI (0%–20%: 12.11 h; 21%–34%: 14.57 h; 35%–85%: 15.47 h; 86%–100%: 17.00 h; all $P < 0.01$). Kidneys from both VA-ECMO donors and VV-ECMO donors were more likely to be placed on a perfusion pump (VA: 51.25%, VV: 68.75%) than non-ECMO kidneys of all KDPI groups. This correlated to VA- and VV-ECMO donors being statistically more likely to share kidneys with transplant centers of greater distance than lower KDPI (0%–34%) non-ECMO donors, with 41.25% and 56.25% of VA- and VV-ECMO kidneys, respectively, being regional or national shares.

TABLE 1.

Kidney transplant baseline recipient, donor, and transplant characteristics

			Non-ECMO			
Outcomes	**VA-ECMO**	**VV-ECMO**	**KDPI 0%–20%**	**KDPI 21%–34%**	**KDPI 35%–85%**	**KDPI 86%–100%**
Number	80	48	1682	1319	4184	686
Recipient characteristics						
Age	56 (47–64)	55 (49–61)	45 (33–57)	55 (45–63)	59 (50–66)	66 (60–70)
Female sex	25 (31.25%)	20 (41.67%)	692 (40.55%)	526 (39.88%)	1604 (38.34%)	256 (37.32%)
Race						
White	29 (36.25%)	17 (35.42%)	725 (43.10%)	533 (40.41%)	1718 (41.06%)	288 (41.98%)
Black	35 (43.75%)	21 (43.75%)	653 (38.82%)	543 (41.17%)	1623 (38.79%)	263 (38.34%)
Hispanic	7 (8.75%)	8 (16.67%)	186 (11.06%)	142 (10.77%)	503 (12.02%)	77 (11.22%)
Asian	9 (11.25%)	2 (4.17%)	99 (5.89%)	85 (6.44%)	294 (7.03%)	49 (7.14%)
Other	0 (0.00%)	0 (0.00%)	19 (1.13%)	16 (1.21%)	46 (1.10%)	9 (1.31%)
BMI	26.37 (22.97–32.43)	30.47 (25.59–34.37)	27.17 (22.78–31.95)	28.01 (24.55–32.38)	27.99 (24.43–31.93)	27.46 (24.48–31.18)
Days on waitlist	609 (276–1295)	1079 (507–1524)	818 (282–1523)	880 (280–1626)	807 (278–1503)	698 (240–1286)
Disabled functional status	2 (2.50%)	0 (0.00%)	25 (1.49%)	18 (1.36%)	42 (1.00%)	10 (1.46%)
Hemodialysis	72 (90.00%)	44 (91.67%)	1487 (88.41%)	1193 (90.45%)	3820 (91.30%)	625 (91.11%)
Dialysis duration (d)	1745 (890–2419)	1508 (787–2006)	1542 (881–2332)	1699 (1010–2542)	1616 (953–2300)	1348 (735–1990)
Previous kidney transplant	7 (8.75%)	5 (10.42%)	268 (15.93%)	188 (14.15%)	410 (9.80%)	24 (3.50%)
Etiology of renal failure						
Diabetes	24 (30.00%)	16 (33.33%)	262 (15.58%)	377 (28.58%)	1360 (32.50%)	271 (39.50%)
Hypertension	24 (30.00%)	11 (22.92%)	402 (23.90%)	345 (26.16%)	1165 (27.84%)	205 (29.88%)
Other	32 (40.00%)	21 (43.75%)	1018 (60.53%)	597 (45.26%)	1659 (39.65%)	210 (30.62%)
Donor characteristics						
Age	31 (22–46)	29 (21–53)	24 (20–29)	31 (25–38)	47 (37–53)	61 (57–67)
Female sex	35 (43.75%)	25 (52.08%)	416 (24.73%)	432 (32.75%)	1822 (43.55%)	354 (51.60%)
BMI	27.78 (22.78–34.13)	28.04 (23.78–36.05)	26.02 (23.05–30.10)	26.50 (23.11–30.93)	27.82 (23.72–33.27)	28.40 (24.51–33.66)
Creatinine (mg/dL)	1.10 (0.78–1.70)	1.03 (0.70–1.63)	0.90 (0.70–1.20)	1.08 (0.73–1.68)	1.00 (0.70–1.60)	1.10 (0.80–1.50)
Diabetes	9 (11.25%)	4 (8.33%)	16 (0.95%)	24 (1.82%)	411 (9.83%)	227 (33.24%)
Hypertension	27 (33.75%)	17 (35.42%)	180 (10.70%)	157 (11.92%)	1713 (41.01%)	548 (80.35%)
Inotropic support	29 (36.25%)	12 (25.00%)	923 (54.88%)	677 (51.33%)	2164 (51.72%)	447 (65.16%)
KDPI (%)	44 (23–62)	48 (24–70)	11 (6–16)	28 (24–31)	57 (46–70)	92 (89–95)
Cause of death—CVA	6 (7.50%)	4 (8.33%)	59 (3.51%)	122 (9.25%)	1201 (28.70%)	449 (65.45%)
Glomerulosclerosis on biopsy						
0%–10%	40 (90.91%)	24 (88.89%)	205 (97.62%)	360 (95.24%)	1893 (84.21%)	494 (76.95%)
11%–20%	2 (4.55%)	3 (11.11%)	4 (1.90%)	14 (3.70%)	257 (11.43%)	103 (16.04%)
>20%	2 (4.55%)	0 (0.00%)	1 (0.48%)	4 (1.06%)	98 (4.36%)	45 (7.01%)
Transplant details						
CIT (h)	16.60 (12.00–21.69)	20.78 (15.85–27.99)	12.11 (8.69–17.16)	14.57 (10.00–19.90)	15.47 (10.82–21.00)	17.00 (12.40–21.90)
Kidney perfusion	41 (51.25%)	33 (68.75%)	298 (17.72%)	463 (35.10%)	1465 (35.01%)	230 (33.53%)
HLA mismatch	4.5 (4–5)	5 (4–5)	4 (3–5)	4 (3–5)	4.5 (4–5)	5 (4–5)
Share						
Local	47 (58.75%)	21 (43.75%)	1368 (81.33%)	993 (75.28%)	2826 (67.54%)	333 (48.54%)
Regional/national	33 (41.25%)	27 (56.25%)	314 (18.67%)	326 (24.72%)	1358 (32.46%)	353 (51.46%)

Values are listed as median ± interquartile range or n (%).
BMI, body mass index; CIT, cold ischemia time; CVA, cerebrovascular accident; ECMO, extracorporeal membrane oxygenation; KDPI, Kidney Donor Profile Index; VA, venoarterial; VV, venovenous.

After characterizing donor, recipient, and transplant details, we set out to assess posttransplant outcomes in a similar fashion. Kidney transplants from VA-ECMO-supported donors were first compared with the non-ECMO population (Table 2). Here, VA-ECMO donors conferred higher rates of DGF (46.25%) than non-ECMO-supported donors of KDPI 0%–20% (16.45%; $P < 0.01$) but had comparable rates to non-ECMO kidneys of KDPI >20%. A similar trend was observed in assessing kidney function at 1-y follow-up, where median creatinine in VA-ECMO kidneys (1.24 mg/dL) was higher than non-ECMO KDPI 0%–20% (1.10 mg/dL; $P < 0.01$) but comparable non-ECMO KDPI >20% groups. Graft and patient survival at 1, 3, and 5 y were comparable between VA-ECMO kidneys and non-ECMO kidneys in the KDPI 0%–20%, 21%–34%, and 35%–85% groups, whereas VA-ECMO kidney transplants had higher 3- and 5-y graft and patient survival than the non-ECMO KDPI 86%–100% group (Table 2; Figure 2).

Kidney transplants from donors supported on VV-ECMO were then similarly compared with the KDPI-stratified non-ECMO groups. Here, rates of DGF were higher in the VV-ECMO population (54.17%) than non-ECMO-supported kidneys of KDPI 0%–20% (23.01%; $P < 0.01$) and KDPI 21%–34% (36.54%; $P = 0.01$) but comparable to those with KDPI 35%–85% (40.97%; $P = 0.08$) and KDPI 86%–100% (44.31%; $P = 0.23$; Table 2). In the VV-ECMO

TABLE 2.

ECMO transplant outcomes

		Non-ECMO										
Outcomes	**VA-ECMO**	**KDPI 0%–20%**	**HR (95% CI)**	***P***	**KDPI 21%–34%**	**HR (95% CI)**	***P***	**KDPI 35%–85%**	**HR (95% CI)**	***P***	**KDPI 86%–100%**	**HR (95% CI)**	***P***
Number	80	1682			1319			4184			686		
DGF	37 (46.25%)	387 (23.01%)		<0.01	482 (36.54%)		0.10	1714 (40.97%)		0.36	304 (44.31%)		0.81
Creatinine at 1-y follow-up (mg/dL)	1.24 (1.07–1.64)	1.10 (0.90–1.36)		<0.01	1.20 (1.00–1.50)		0.16	1.38 (1.10–1.71)		0.32	1.56 (1.25–2.00)		0.08
Graft survival													
1 y	93.50%	96.26%	1.83 (0.74-4.56)	0.19	94.86%	1.33 (0.53-3.30)	0.54	92.50%	0.89 (0.37-2.17)	0.81	36.19%	0.47 (0.19-1.16)	0.10
3 y	91.85%	90.65%	1.01 (0.45-2.30)	0.97	87.73%	0.76 (0.33-1.71)	0.51	83.30%	0.54 (0.24-1.21)	0.13	74.06%	0.32 (0.14-0.73)	0.01
5 y	70.76%	83.23%	1.64 (0.95-2.82)	0.07	79.03%	1.24 (0.72-2.13)	0.44	72.79%	0.90 (0.53-1.53)	0.70	60.37%	0.56 (0.33-0.97)	0.04
Patient survival													
1 y	96.01%	98.40%	2.59 (0.78-8.56)	0.12	96.88%	1.32 (0.41-4.29)	0.64	95.73%	0.96 (0.31-3.00)	0.94	91.99%	0.50 (0.16-1.61)	0.25
3 y	96.01%	95.35%	1.04 (0.33-3.28)	0.94	91.95%	0.58 (0.18-1.85)	0.36	89.13%	0.43 (0.14-1.33)	0.14	81.08%	0.23 (0.07-0.74)	0.01
5 y	86.22%	90.01%	1.49 (0.69-3.20)	0.30	85.44%	0.93 (0.43-1.99)	0.86	80.13%	0.65 (0.26-1.37)	0.26	68.92%	0.38 (0.18-0.82)	0.01
		Non-ECMO											
	VV-ECMO	**KDPI 0%–20%**	**HR (95% CI)**	*P*	**KDPI 21%–34%**	**HR (95% CI)**	*P*	**KDPI 35%–85%**	**HR (95% CI)**	*P*	**KDPI 86%–100%**	**HR (95% CI)**	*P*
Number	48	1682			1319			4184			686		
DGF	26 (54.17%)	387 (23.01%)		<0.01	482 (36.54%)		0.01	1714 (40.97%)		0.08	304 (44.31%)		0.23
Creatinine at 1-y follow-up (mg/dL)	1.45 (1.20–1.78)	1.10 (0.90–1.36)		<0.01	1.20 (1.00–1.50)		0.02	1.38 (1.10–1.71)		0.56	1.56 (1.25–2.00)		0.47
Graft survival													
1 y	77.23%	96.26%	2.62 (1.87-3.66)	<0.01	94.86%	2.23 (1.60-3.12)	<0.01	92.50%	1.83 (1.34-2.52)	<0.01	36.19%	1.33 (0.96-1.84)	0.09
3 y	69.03%	90.65%	2.07 (1.56-2.75)	<0.01	87.73%	1.79 (1.35-2.38)	<0.01	83.30%	1.51 (1.14-1.99)	<0.01	74.06%	1.16 (0.87-1.54)	0.29
5 y	55.76%	83.23%	1.93 (1.51-2.47)	<0.01	79.03%	1.68 (1.31-2.16)	<0.01	72.79%	1.44 (1.13-1.83)	<0.01	60.37%	1.13 (0.88-1.45)	0.32
Patient survival													
1 y	81.81%	98.40%	3.55 (2.38-5.27)	<0.01	96.88%	2.53 (1.73-3.71)	<0.01	95.73%	2.15 (1.51-3.07)	<0.01	91.99%	1.56 (1.08-2.27)	0.02
3 y	81.81%	95.35%	2.27 (1.57-3.28)	<0.01	91.95%	1.70 (1.18-2.45)	<0.01	89.13%	1.46 (1.02-2.07)	0.03	81.08%	1.08 (0.75-1.54)	0.67
5 y	78.54%	90.01%	1.82 (1.29-2.56)	<0.01	85.44%	1.45 (1.03-2.04)	0.03	80.13%	1.22 (0.88-1.69)	0.23	68.92%	0.94 (0.67-1.31)	0.73

CI, confidence interval; DGF, delayed graft function; ECMO, extracorporeal membrane oxygenation; HR, hazard ratio; KDPI, Kidney Donor Profile Index; VA, venoarterial.

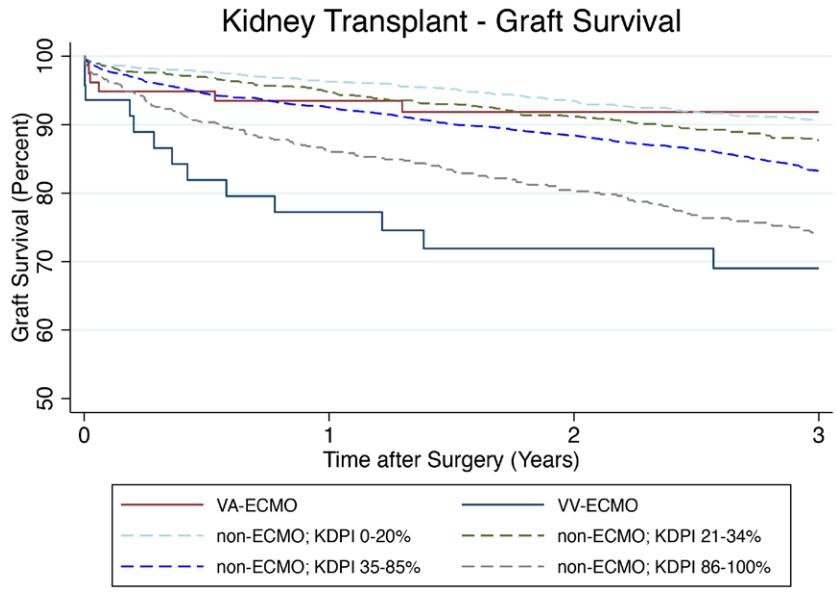

FIGURE 2. Posttransplant kidney graft survival. ECMO, extracorporeal membrane oxygenation; KDPI, Kidney Donor Profile Index; VA, venoarterial; VV, venovenous.

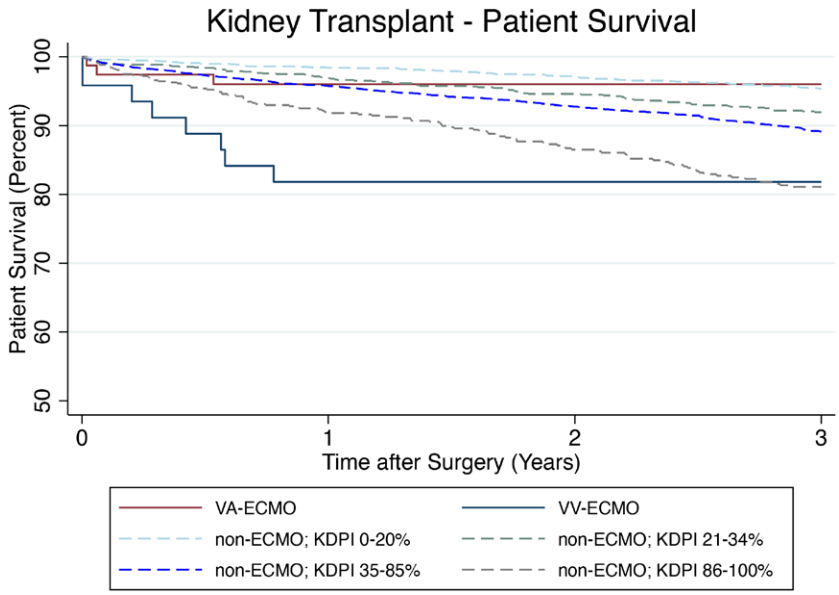

FIGURE 3. Posttransplant patient survival. ECMO, extracorporeal membrane oxygenation; KDPI, Kidney Donor Profile Index; VA, venoarterial; VV, venovenous.

group, creatinine at 1 y (1.45 mg/dL) was higher than non-ECMO KDPI <35% kidneys (KDPI 0%–20%: 1.10 mg/dL; $P < 0.01$ and KDPI 21%–35%: 1.20 mg/dL; $P = 0.02$) and comparable to KDPI ≥35% non-ECMO transplants. Graft survival at 1, 3, and 5 y in the VV-ECMO group was inferior to non-ECMO kidneys with KDPI ≤85% and comparable to non-ECMO KDPI 86%–100% kidney transplants (Figure 2). Again, patient survival in VV-ECMO versus non-ECMO transplants largely followed similar trends observed in graft survival (Figure 3).

Assessing ECMO As Predictive of Kidney Graft Survival

We then set out to determine the impact ECMO itself had on kidney graft survival. To do this, we again separately assessed VA- and VV-ECMO supported kidneys. As demonstrated in Table 3, VV-ECMO was associated with graft failure on both univariate (HR, 2.17; 95% CI, 1.41-3.33) and multivariable analysis that adjusted for recipient, donor, and transplant factors similarly predictive of graft failure (HR, 2.18; 95% CI, 1.41-3.35). VA-ECMO, however, was not associated with graft failure on univariate (HR, 1.03; 95% CI, 0.65-1.61) or adjusted multivariable analysis (HR, 1.02; 95% CI, 0.65-1.61).

Factors Predictive of Kidney Graft Survival in Organs From ECMO-Supported Donors

To better understand which kidneys from ECMO-supported donors may be suitable for transplant, and which may be high risk, we performed regression analyses assessing donor and transplant-specific factors associated with graft survival. As shown in Table 4, univariate analysis revealed higher KDPI

TABLE 3.

ECMO as predictive of graft failure in kidney transplant recipients

	Univariate		Adjusted multivariable[a]	
Covariates	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
VA-ECMO	1.03 (0.65-1.61)	0.91	1.02 (0.65-1.61)	0.92
VV-ECMO	2.17 (1.41-3.33)	<0.01	2.18 (1.41-3.35)	<0.01

[a] Recipient factors predictive of graft failure included in adjusted multivariable regression: age, Black race, male gender, log BMI, disabled functional status, diabetes, hypertension, previous kidney transplant, and history of malignancy. Donor factors included KDPI (age >51, age <18, inverse log height, weight <80 kg, ethnicity, hypertension, diabetes, cause of death as CVA, log creatinine at donation, HCV status, DCD). Transplant factors included in multivariable model: cold ischemia time and kidney perfusion.

BMI, body mass index; CI, confidence interval; CVA, cerebrovascular accident; DCD, donation after cardiac death; ECMO, extracorporeal membrane oxygenation; HCV, hepatitis C virus; HR, hazard ratio; KDPI, Kidney Donor Profile Index; VA, venoarterial; VV, venovenous.

TABLE 4.

Univariate regression analyses of donor factors predictive of graft failure in kidney transplant recipients of ECMO organs

	All ECMO	VA-ECMO	VV-ECMO
Outcomes	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
KDPI	7.34 (2.04-26.34)	4.46 (0.57-35.19)	5.75 (1.17-27.87)
Age	1.02 (1.00-1.04)	0.98 (0.96-1.01)	1.03 (1.00-1.06)
BMI	1.04 (1.01-1.07)	1.03 (0.99-1.08)	1.06 (1.01-1.11)
Hypertension	2.46 (1.30-4.64)	1.06 (0.37-2.98)	4.56 (1.84-11.30)
Diabetes	3.89 (1.43-10.59)	5.83 (1.43-23.87)	3.73 (0.80-17.41)
Kidney biopsy—acute inflammation	2.69 (0.79-9.18)	1.16 (0.15-9.18)	35.40 (3.14-399.21)

BMI, body mass index; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; HR, hazard ratio; KDPI, Kidney Donor Profile Index; VA, venoarterial; VV, venovenous.

as being significantly associated with graft failure for ECMO-supported donor kidneys (HR, 7.34; 95% CI, 2.04-26.34). When separating by ECMO type, VA-ECMO was associated with a HR of 4.46 (95% CI, 0.57-35.19), whereas KDPI was more strongly correlated to graft survival in VV-ECMO kidneys (HR, 5.75; 95% CI, 1.17-27.87). Outcomes of transplants from ECMO donors when stratified by KDPI category were also assessed, with data available in Tables S1 and S2 (**SDC**, http://links.lww.com/TXD/A572) and **Figure S1** (**SDC**, http://links.lww.com/TXD/A572). Here, ECMO-supported donors with KDPI 0%–20% had superior overall graft survival to ECMO donors with KDPI 35%–85% (HR, 2.21; 95% CI, 1.21-4.04) and KDPI 86%–100% (HR, 1.88; 95% CI, 1.13-3.13). Similarly, ECMO donors with lower KDPI performed better than higher KDPI kidneys with respect to renal function at 1-y posttransplant. Sensitivity analyses demonstrated that the KDPI score C-statistic of the area under the receiver operating characteristic curve was 0.61 for the entire ECMO donor cohort; for VA-ECMO, the C-statistic was 0.57, and for VV-ECMO the C-statistic was 0.68. As a reference, the C-statistic for the non-ECMO cohort was 0.61.

We then assessed additional donor factors predictive of graft survival in the overall ECMO group. Here, advanced age (HR, 1.02; 95% CI, 1.00-1.04), BMI (HR, 1.04; 95% CI, 1.01-1.07), hypertension (HR, 2.46; 95% CI, 1.30-4.64), and diabetes (HR, 3.89; 95% CI, 1.43-10.59) were all associated with graft failure. Similar to KDPI analyses above, these factors largely failed to reach statistical significance in the VA-ECMO group, whereas for VV-ECMO transplants these factors' association with graft survival largely reached statistical significance.

DISCUSSION

This study assessed kidney transplantation using allografts from donors with cardiopulmonary collapse requiring ECMO for nondonation purposes. Using data from the Gift of Life, Philadelphia, organ procurement organization, and cross-referencing these data with the United Network for Organ Sharing OPTN database, our study represents the largest series available assessing kidney transplantation using this unique marginal donor population. Here, we identified 78 total donors in the Gift of Life, Philadelphia, Donor Program database on ECMO from 2008 to 2021 who contributed at least 1 kidney or pancreas for transplant. Here, the median KDPI for VA- and VV-ECMO donors was 44% and 48%, respectively. Compared with non-ECMO donors of similar KDPI strata, ECMO donors were younger and less likely to have died from a cerebrovascular event. They were also more likely to be placed on perfusion pumps and transplanted across greater distances with longer CITs. Comparing outcomes using these donors to kidney transplants using organs from KDPI-stratified non-ECMO donors, we found that grafts from VA-ECMO supported donors conferred similar rates of DGF and posttransplant renal function to their KDPI-matched non-ECMO counterparts. Assessing graft survival, we found that VA-ECMO kidneys had similar graft survival to non-ECMO kidneys of KDPI <85% and had superior graft survival when compared with the lowest-quality (KDPI 86%–100%) non-ECMO kidneys. These outcomes surpassed those of VV-ECMO kidneys, whose DGF incidence and renal function was also comparable to KDPI-matched non-ECMO donor transplants, but whose graft survival was inferior to all but the lowest-quality (KDPI 86%–100%) non-ECMO kidneys. Univariate and adjusted multivariable regression models assessing the association between VA- and VV-ECMO and graft failure reinforced these findings, with VV-ECMO, but not VA-ECMO, being associated with increased risk of graft loss. To determine high-risk features of donors on ECMO support, we again used regression modeling as well as sensitivity analyses to discover that KDPI was generally predictive of graft survival and graft outcomes in ECMO donors. We also identified donor age, BMI, presence of hypertension, diabetes, and acute inflammation on biopsy as factors associated greater risk of graft loss in either the overall ECMO group or in one of the VA-ECMO or VV-ECMO subgroups. Finally, in the one simultaneous pancreas-kidney transplant, both kidney and pancreas remained functioning at the time of censorship (7.4 y).

ECMO has been increasingly utilized in the past several decades to support patients with refractory cardiac, pulmonary, or cardiopulmonary compromise.[1,2] Patients on ECMO support who ultimately succumb to their underlying disease represent an intriguing population from a potential donor standpoint, as their being considered candidates for ECMO signifies a favorable underlying physiologic state. As a costly and resource-intensive treatment, ECMO is only used for patients with potentially recoverable illness, and contraindications for its use (such as malignancy, chronic organ

dysfunction, vascular disease preventing cannulation)[17] makes it so that ECMO itself selects a more favorable potential donor population. Reluctance to use of organs supported by ECMO, however, is related to the significant physiologic alterations generated by the extracorporeal circuitry in addition to the initial cardiopulmonary decompensation. ECMO generates a state of systemic coagulopathy,[18] inflammation[19] and oxidative stress[20] that begins early following cannulation. The kidney, in particular, is susceptible to this type of insult. With many patients already in a globally hypoperfused state, acute kidney injury is a frequent finding in patients supported by ECMO.[21] The cause for this is multifactorial because the nonpulsatile nature of ECMO induces dysregulation of the renin-angiotensin-aldosterone axis[22] and downregulation of atrial natriuretic peptide,[23] in addition to generating the previously mentioned inflammatory and oxidative injuries. The donor population in our study carried a median donation creatinine of 1.10 mg/dL for VA-ECMO patients, and 1.03 mg/dL for VV-ECMO, comparable to all but the highest quality, lowest KDPI, non-ECMO-supported donors. Considering these data suggest no difference in renal function at donation, the superior graft function and survival of VA- over VV-ECMO kidneys seen in our study may highlight an important physiologic distinction between the 2 classes of extracorporeal support. Although VV-ECMO patients in theory have sufficient cardiac reserve to maintain systemic perfusion, there may exist a state of systemic hypoperfusion that VA-ECMO patients do not incur with cardiac and pulmonary support.

Studies investigating renal function in ECMO have shown that patients on VA support at lower flow rates are more likely to have kidney injury, whereas renal function is maintained in VA-ECMO patients at higher flow rates and VV-ECMO patients who have preserved cardiac function.[24-26] Our study cohort was comprised of patients unable to be salvaged by ECMO support, and it is possible that the differences in outcomes we observed between the VA- and VV-ECMO populations were related to the ability for the VA-ECMO circuit to mitigate renal hypoperfusion.

Much of the current literature assessing ECMO use in transplant relates to stabilization of patients to facilitate organ donation in a controlled setting. Few studies thus far have assessed use of organs from patients who have been cannulated for ECMO support with therapeutic, nondonation intent. Previously, Bronchard et al[14] had described the largest cohort of organ transplants from this specific type of ECMO-supported donor population. Assessing the French national registry from 2007 to 2013, 64 ECMO-supported donors contributed 109 kidneys, 37 livers, 7 hearts, and 1 lung. Concordant with our findings, 1-y kidney graft survival was similar between kidneys from ECMO-supported donors matched non-ECMO kidneys.[14] In a similar study, Carter et al[13] analyzed 41 donors supported on ECMO from 1995 to 2012 from the same Gift of Life organ procuring organization from which our data were derived. Here, 1-y graft survival was 93% in 51 kidney transplants from ECMO-supported donors,[13] comparable to the 93.50% survival we observed in kidney transplants from VA-ECMO donors but higher than the 77.23% survival seen in VV-ECMO kidney transplants. Additional case reports describe successful kidney transplantation from VA-ECMO supported donors with acceptable outcomes at 3 mo and 1 y.[12,15] Although data regarding use of kidneys from ECMO-supported donors who were cannulated with therapeutic intent are limited, it certainly appears that our data, in conjunction with the previously published literature, consistently suggest safe outcomes, especially in the VA-ECMO supported population.

Another underlying trend observed in our study is related to geographic utilization of kidneys from ECMO-supported donors. In the non-ECMO cohort, we observed that higher KDPI kidneys were more likely to be declined by local transplant centers and ultimately require regional or national sharing, which similarly correlated to increased rates of machine perfusion use and higher CIT in these transplants. Transplants using kidneys from ECMO-supported donors, and, in particular, VV-ECMO donors, were also less likely to be utilized by a local transplant center which resulted in higher rates of kidney pumping and increased CIT. Because increased CIT is associated with higher rates of DGF and is inversely related to graft survival, the reticence in using kidneys from ECMO-supported donors we observed may be negatively impacting outcomes in the ECMO populations, increased local utilization may be more reflective of the true utility of these kidneys.

Our study did suffer from several notable limitations. Although this study utilizes a study population that encompasses the largest population of ECMO-supported donors to date from a single organ procurement organization, demographic data as well as outcomes were supplemented with a federally maintained, large national database in which certain granularity is lacking. Additionally, it is important to note an inherent selection bias in our patient population—as marginal donors who are only utilized under intense scrutiny, the patients who contributed organs for donation after being supported on ECMO represent only the most suitable candidates. This study also intended to analyze where along the KDPI-based kidney allocation spectrum allografts from ECMO-supported donors may be allocated, which must be considered in the context that many factors which are impacted by the need for and sequelae of ECMO. Finally, although we were able to provide data regarding VA or VV cannulation and the indication for each, important procedural and periprocedural details certainly exist that impact patient status and the health of the kidneys.

Organ shortages remain one of the most pressing issues facing the field of transplantation today. In the past 5 y, >65 000 patients in North America have been initiated on ECMO (~40 000 VA, ~26 000 VV), and overall survival has been 52% (VA: 48%, VV: 58%).[27] Extrapolating these numbers there have been almost 21 000 patients supported by VA-ECMO and 11 000 on VV-ECMO who have ultimately succumbed to their illness. Although many of these patients may ultimately not be suitable candidates for organ donation, the ECMO population represents a significant and growing population of patients with refractory cardiopulmonary compromise. Understanding when, and how, to best utilize organs from these patients for transplant can continue to help expand the marginal donor population and perhaps continue to increase organ utilization.

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