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Extracorporeal Membrane Oxygenation Use in the First 24 Hours Following Pediatric Heart Transplantation: Incidence, Risk Factors, and Outcomes

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Abstract

Primary graft dysfunction following heart transplantation (HTx) is associated with significant morbidity and mortality. This study aimed to assess the incidence of, risk-factors for, and outcomes of children requiring ECMO within 24-hours of HTx. This study utilized a linked PHIS/SRTR database of pediatric HTx recipients (2002–2016). Post-HTx ECMO was identified using inpatient billing data. Logistic regression assessed risk-factors for post-HTx ECMO. Kaplan-Meier analyses assessed in-hospital mortality and post-discharge survival. A total of 2,820 patients were included with 224 (7.9%) requiring ECMO. Independent risk-factors for post-HTx ECMO include

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Author contributions:

All authors reviewed, revised, and approved the final submitted manuscript.

Drs. Godown conceptualized the project, aided in data analysis, and drafted the manuscript.

Drs. Thurm and Hall performed the data linkage, extracted data, and aided in data analysis.

Drs. Bearl, Feingold, Soslow, Mettler, Smith, Profita, Singh, and Dodd aided in the analysis plan and provided critical review of the analysis and manuscript.

Disclosures:

The data reported here have been supplied by the Hennepin Healthcare Research Institute as the contractor for the SRTR. The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy or interpretation by the SRTR or the U.S. Government. The authors have no financial relationships relevant to the presented material to disclose.

Data availability:

The data that support the findings of this study are available from the authors upon request. Restrictions may apply to the availability of these data based on current data use agreements with PHIS and SRTR.

age <1yr (aOR: 2.2, 95%CI: 1.3–3.7, p=0.006) or 1–5yrs (aOR: 2.1, 95%CI: 1.3–3.4, p=0.002), and ECMO support at HTx (aOR: 27.4, 95%CI: 15.2–49.6, p<0.001). Survival to discharge decreased with increasing duration of post-HTx ECMO support; 89% for 1–3 days, 79.1% for 4–6 days, 63.2% for 7–9 days, and 18.8% for 10 days. There was no difference in long-term survival for patients requiring post-HTx ECMO who survived to hospital discharge (p=0.434). There are identifiable risk factors associated with the need for ECMO in the post-HTx period. Length of time on ECMO post-HTx is strongly associated with the risk of in-hospital mortality. Patients who require ECMO early post-HTx and survive to discharge have comparable outcomes to patients who did not require ECMO.

1. Introduction:

Primary graft dysfunction is a significant cause of morbidity and mortality following heart transplantation (HTx), accounting for nearly 40% of deaths in the first 30 days post-transplant in children¹. While re-transplantation may be considered in this setting, patients are at high risk for death while awaiting a suitable organ and survival after re-transplantation in this context is inferior compared to re-transplantation for other indications¹. Therefore, improved understanding of the factors associated with the development of primary graft failure, including pertinent donor and recipient factors, as well as knowledge of patient outcomes are clinically relevant, may aid in listing decisions, and have implications for donor acceptance.

Until recently, prior reports evaluating risk factors for the development of primary graft dysfunction have been limited to small single center studies and one retrospective review in the infant population^{2–6}. These studies have provided valuable insight into the risk factors for primary graft dysfunction and highlighted the outcomes of patients supported with extracorporeal membrane oxygenation (ECMO) post-transplant. However, they are limited by the small number of included patients and the fact that single center studies may not be generalizable to other transplant centers with varying practice patterns.

Large clinical, research, and administrative databases are widely utilized in pediatric HTx research⁷. However, primary graft dysfunction is poorly captured in existing databases and has prompted the use of surrogate end-points including early post-transplant death or re-transplantation to assess the incidence of and risk factors for primary graft failure⁸. The aim of this project was to utilize a unique data linkage between the Scientific Registry of Transplant Recipients (SRTR, Hennepin Healthcare Research Institute, Minneapolis, MN) and the Pediatric Health Information System (PHIS, Children's Hospital Association, Lenexa, KS) administrative database to determine the incidence of, risk factors for, and outcomes of pediatric HTx recipients with severe primary graft dysfunction, defined as the need for ECMO support within one day of HTx.

2. Methods:

The SRTR and PHIS databases were linked at the patient level using indirect identifiers (hospital, date of birth, sex, and date of transplant), the results of which have been previously described⁷. The SRTR data system includes data on all donor, wait-listed

candidates, and transplant recipients in the U.S., submitted by the members of the Organ Procurement and Transplantation Network (OPTN). The Health Resources and Services Administration, U.S. Department of Health and Human Services provides oversight to the activities of the OPTN and SRTR contractors. The SRTR includes data from every organ transplant and waitlist addition since October 1987. The PHIS database is an administrative and billing database that collects clinical and resource utilization data from hospital encounters from >50 tertiary children's hospitals. Importantly, PHIS records ICD-9 and ICD-10 diagnosis and procedure codes as well as inpatient billing data, thereby increasing data granularity of the linked database. Data utilized from each dataset are provided in Supplemental Table 1.

All patients <18 years of age who underwent HTx between 2002 and 2016 were identified from the linked database for inclusion in the analysis. Severe primary graft dysfunction was defined as the need for ECMO support within one day of transplantation, in concordance with a recent consensus statement defining severe primary graft dysfunction as dependence on left or biventricular mechanical support within 24 hours of surgery⁹. The need for post-HTx ECMO is not collected by SRTR and therefore the presence of ECMO billing codes on the day of or the day following transplantation were used. For patients bridged to HTx with ECMO, post-HTx ECMO support was defined by the presence of billing codes for two days following transplantation to ensure that any billing codes present on the date of transplant did not represent pre-HTx support. The number of consecutive days that billing charges for ECMO were present was used to assess the duration of ECMO support.

Baseline demographics were compared between patients who did and did not receive post-HTx ECMO. The Chi square test was used to compare categorical variables and the Student's t-test for continuous variables. A multivariable logistic regression model was constructed to assess risk factors that were independently associated with the need for ECMO support post-HTx. Variables with bivariate $p < 0.15$ were selected for inclusion in the logistic regression model. Given prior studies suggesting that patients with congenital heart disease and cardiomyopathy may have different risk profiles^{10,11}, separate logistic regression models were subsequently generated after stratifying by diagnosis. Standard error estimates were adjusted to account for clustering within centers.

In-hospital outcomes were described for patients requiring ECMO using standard summary statistics and cumulative incidence curves were generated based on the time on ECMO support post-HTx. Outcomes assessed included successful decannulation, death on ECMO, or re-transplantation. To assess risk factors for in-hospital mortality, a logistic regression model was constructed for patients who required post-HTx ECMO support. Demographics were compared between patients who did and did not survive to hospital discharge. The Chi square test or Fisher's exact test was used to compare categorical and the Student's t-test for continuous variables. Variables were selected for inclusion in the multivariable model if $p < 0.15$ on bivariate analysis. Standard error estimates were adjusted to account for clustering within centers. The Kaplan-Meier method was used to assess early (<90 days) post-HTx survival based on the need for post-operative ECMO support and survival curves were compared using the log-rank test. Post-HTx survival was then assessed conditional on survival to hospital discharge.

All statistical analyses were performed in SAS version 9.4 (SAS Institute; Cary, NC) or STATA version 15 (StataCorp LLC; College Station, TX) with two-sided $p < 0.05$ considered statistically significant. This project was approved by the Vanderbilt University IRB (IRB #181858), PHIS, and SRTR.

3. Results:

A total of 2820 patients <18 years of age from 28 different transplant centers were included. Of this group, 224 (7.9%) required ECMO in the early post-HTx period. CPR was required in 8 (3.6%) patients prior to ECMO initiation. The median time on ECMO post-HTx was 2 days (interquartile range [IQR] 1 – 6 days) with a maximum ECMO duration of 50 days.

Patient demographics are shown in Table 1. Characteristics associated with the need for post-HTx ECMO included younger patient age, a diagnosis of congenital heart disease, ECMO support at the time of HTx, ventilator support at HTx, patients listed UNOS status 1A, lower estimated creatinine clearance, higher total bilirubin, pre-HTx inhaled nitric oxide (iNO) use, donor-to-recipient weight ratio, and an ischemic time >4 hours.

Results of the multivariable logistic regression model are shown in Table 2. Final variables included in the multivariable model were age group, diagnosis (congenital heart disease, re-transplant, or cardiomyopathy), race, ECMO support at the time of HTx, ventricular assist device (VAD) support at HTx, ventilator support at HTx, UNOS listing status, pre-HTx iNO use, estimated creatinine clearance, total bilirubin, donor-to-recipient weight ratio, and ischemic time >4 hours. Factors independently associated with the need for post-HTx ECMO were age <1 year (adjusted odds ratio (aOR) 2.2, 95% CI 1.3 – 3.7) or 1–5 years (aOR 2.1, 95% CI 1.3 – 3.4) and ECMO support at the time of HTx (aOR 27.4, 95% CI 15.2– 49.6).

Results of the logistic regression models stratified by a diagnosis of cardiomyopathy or congenital heart disease are shown in Table 3. For patients with cardiomyopathy, independent risk factors for post-HTx ECMO included age 1–5 years (aOR 2, 95% CI 1.1 – 3.8) and ECMO support at HTx (aOR 41, 95% CI 16.5 – 103). For patients with congenital heart disease, ECMO support at HTx (aOR 21.4, 95% CI 12.3 – 37.4) and VAD support at HTx (aOR 3.1, 95% CI 1.3 – 7.4) were identified as independent risk factors for post-HTx ECMO.

Outcomes for patients requiring post-HTx ECMO are shown in Figure 1. Of the 224 patients requiring ECMO in the immediate post-HTx period, 32 (14.3%) died while on ECMO and 191 (85.3%) were decannulated. Of those removed from ECMO support, 167 (87.4%) survived to hospital discharge. Two patients were re-transplanted, one from ECMO support and one following decannulation. Patient outcomes based on the length of time on ECMO support are shown in Figure 2. Of the patients who were decannulated, 90% achieved decannulation by 7 days post-HTx. As time on ECMO post-HTx increased, survival to hospital discharge decreased. Survival to hospital discharge was 89% for patients requiring 1–3 days of ECMO support. This decreased to 79.1%, 63.2%, and 18.8% for patients requiring 4–6 days, 7–9 days, and 10 days of post-HTx ECMO support, respectively. The

longest period of ECMO support in which a patient survived to discharge (excluding re-transplantation) was 16 days.

Demographics of patients who required post-HTx ECMO support stratified by survival to hospital discharge are shown in Table 4. Patients who died prior to hospital discharge had a significantly longer duration of support (11.2 days vs. 2.8 days, $p<0.001$). Patients who died also were more likely to have a diagnosis of congenital heart disease, lower estimated creatinine clearance, higher total bilirubin, require dialysis post-HTx, and have an ischemic time >4 hours. Results of the multivariable logistic regression model to assess risk factors associated with in-hospital mortality is shown in Table 5. When the duration of ECMO support was excluded from the model, independent risk factors for in-hospital mortality included a graft ischemic time >4 hours (aOR 3.2, 95% CI 1.8 – 5.5). While there were trends towards lower in-hospital survival for patients with congenital heart disease and those requiring dialysis, these did not reach statistical significance. When the duration of ECMO support was included in the multivariable model, independent risk factors for in-hospital mortality included dialysis post-HTx (aOR 2.5, 95% CI 1.02 – 5.9) and the duration of ECMO support (aOR 1.4, 95% CI 1.2 – 1.6).

The need for ECMO in the early post-transplant period was associated with inferior patient survival (Figure 3) with 75% of ECMO-supported patients surviving to hospital discharge vs. 96% in the unsupported group ($p<0.001$). However, patients requiring post-HTx ECMO support who survived to hospital discharge demonstrated survival that was no different compared to patients who did not require ECMO support (Figure 4) (log rank $p=0.434$).

4. Discussion:

This analysis provides unique insights into the risk factors for severe primary graft dysfunction following HTx in children and delineates important differences in risk between patients with cardiomyopathy and those with congenital heart disease. Additionally, we report patient outcomes based on the duration of support, which may aid in post-operative management planning for patients with evidence of severe primary graft dysfunction. Most patients supported with ECMO in the post-HTx period require a brief duration of support with 90% of patients achieving decannulation within 7 days post-HTx. Prolonged support is associated with a greater likelihood of in-hospital mortality. However, patients supported with ECMO post-HTx who survive to discharge demonstrate outcomes comparable to unsupported patients.

The incidence of severe primary graft dysfunction in our study is comparable to previous reports in adult HTx recipients. Studies by Sabatino et al. and Takeda et al. reported that severe primary graft dysfunction occurred in 6.8% and 7.4% of HTx recipients, respectively^{12,13}. Similarly, a single center analysis of pediatric HTx recipients reported an incidence of primary graft dysfunction of 8.4% (17 out of 203 patients)¹⁴. However, a recent analysis of pediatric HTx recipients by Profita et al. utilizing a linkage between the Organ Procurement and Transplantation Network (OPTN) database and the Extracorporeal Life Support Organization (ELSO) registry reported an incidence of severe primary graft dysfunction of 4.3%¹⁵. The higher incidence found in our study is likely multifactorial. While SRTR and

OPTN contain the same patient populations, ELSO and PHIS vary in hospital participation. Therefore, the patient populations studied are different. Additionally, the study by Profita and colleagues excluded HTx recipients with elevated pulmonary vascular resistance, potentially representing a population at greater risk for primary graft dysfunction¹⁶. Given that both studies utilized database linkages, there may be variation in linkage reliability that contribute to the differences seen and patients that failed to successfully link may account for the lower rate of primary graft dysfunction in the study by Profita and colleagues. However, the current analysis has additional novel features which may help to guide pre- and post-transplant management. Data regarding the impact of support duration will allow providers to better counsel families of patients with primary graft dysfunction, and also may help to guide clinical management in the event that graft function does not demonstrate recovery.

Our analysis confirmed many risk factors previously associated with primary graft dysfunction including younger age and the need for pre-HTx ECMO^{3,9,15,17}. However, the assessment of risk factors based on underlying diagnosis provides additional useful insight. While pre-HTx VAD support has been reported as a risk factor for primary graft dysfunction, our analysis suggests that this is most influential in patients with congenital heart disease. This is not surprising as mechanical support in this population is known to be challenging¹⁸. While the use of VAD support is increasing overall, these data suggest that judicious use in patients with congenital heart disease may be warranted.

Most importantly, our analysis demonstrates that the duration of ECMO support strongly influences patient outcomes. This is in contrast to a prior single center study that failed to demonstrate an association between ECMO duration and in-hospital mortality¹⁴. However, a separate analysis reported that no patients survived who required ECMO support beyond 4 days post-HTx². Our analysis suggests that successful outcomes can be achieved with support durations >4 days, but that very few patients were successfully decannulated beyond 10 days of support. These data have important implications for patients with severe primary graft dysfunction post-HTx. As the duration of ECMO support increases, this may prompt consideration of other support strategies including placement of a VAD. While ECMO support has traditionally been used in the early post-HTx period^{3,4,19–21} and has demonstrated improved outcomes compared to VAD support in the setting of primary graft dysfunction¹², VAD's facilitate a longer duration of support and may be appropriate as a bridge to recovery, a bridge to re-transplantation, or a bridge to decision⁵.

Our data demonstrate that patients who survived to hospital discharge following post-HTx ECMO support have outcomes comparable to unsupported patients. A prior single center study of pediatric HTx recipients reported similar good long-term outcomes for patients requiring ECMO in the post-operative period²². These data continue to support the use of ECMO in the early post-HTx period as good outcomes can be achieved with a significant percent of patients recovering graft function.

Limitations:

This project has inherent limitations. We utilized billing codes to determine the presence and duration of ECMO support. This does not allow identification of the indication for ECMO

support and therefore may include other etiologies aside from primary graft dysfunction. Hyperacute rejection can lead to acute graft failure in the immediate post-HTx period. This is less common in the current era given advances in virtual cross-matching technology, and therefore we believe this is unlikely to significantly impact the results. Additionally, there was no significant difference in the incidence of a positive CDC crossmatch between patients who required ECMO post-HTx and those who did not. It is also possible that patients were cannulated for ECMO in the operating room pre-emptively at the time of HTx given concerns of the transplanting team. This practice cannot be assessed from the data available and represents a limitation. Additionally, as with any large dataset, missing and/or erroneous data can be problematic. However, linkage of these databases increases data granularity and allows for cross-verification between databases, potentially increasing data reliability.

Conclusion:

Primary graft dysfunction requiring early ECMO support occurred in 7.9% of pediatric HTx recipients in our analysis. Risk factors differed between patients with cardiomyopathy and congenital heart disease, with pre-HTx ECMO support being the most prominent risk factor in each group. The duration of post-HTx ECMO support is strongly associated with the risk of in-hospital mortality, with 90% of patients being decannulated within 7 days. For patients requiring prolonged support, alternative support strategies may be beneficial as a bridge to re-transplantation or a bridge to decision. Patients supported with ECMO early post-HTx who survive to hospital discharge have long-term outcomes similar to unsupported patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

ECMO	Extracorporeal Membrane Oxygenation
ELSO	Extracorporeal Life Support Organization
HTx	Heart Transplant
OPTN	Organ Procurement and Transplantation Network
PHIS	Pediatric Health Information System
SRTR	Scientific Registry of Transplant Recipients

VAD**Ventricular Assist Device****References:**

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Figure 1.
Patient outcomes following ECMO post-transplant

Note: 12% of decannulated patients subsequently died

Figure 2.

Cumulative incidence of death, decannulation, or re-transplantation based on time on ECMO support post-transplant

Figure 3.
Early post-transplant survival based on the need for ECMO

Figure 4.
Post-transplant survival conditional on survival to hospital discharge

Table 1.

Demographics based on the need for post-transplant ECMO

	Total	No ECMO	ECMO	p-value ^a
	N=2820	N=2596 (92.1%)	N=224 (7.9%)	
Recipient Factors				
Age Group				
<1 year	896 (31.8%)	790 (30.4%)	106 (47.3%)	<0.001
1–5 years	688 (24.4%)	628 (24.2%)	60 (26.8%)	
6–10 years	407 (14.4%)	383 (14.8%)	24 (10.7%)	
11–17 years	829 (29.4%)	795 (30.6%)	34 (15.2%)	
Male Gender	1539 (54.6%)	1417 (54.6%)	122 (54.5%)	0.972
Race				
Caucasian	1652 (58.6%)	1505 (58%)	147 (65.6%)	0.077
African-American	519 (18.4%)	483 (18.6%)	36 (16.1%)	
Other	649 (23%)	608 (23.4%)	41 (18.3%)	
Diagnosis				
Cardiomyopathy	1295 (46.4%)	1217 (47.4%)	78 (35.3%)	0.001
Congenital Heart Disease	1340 (48.1%)	1207 (47%)	133 (60.2%)	
Retransplant	153 (5.5%)	143 (5.6%)	10 (4.5%)	
Blood Type				
O	1273 (45.1%)	1181 (45.5%)	92 (41.1%)	0.367
A	1059 (37.6%)	967 (37.2%)	92 (41.1%)	
B	367 (13%)	340 (13.1%)	27 (12.1%)	
AB	121 (4.3%)	108 (4.2%)	13 (5.8%)	
ECMO at Transplant	156 (5.5%)	65 (2.5%)	91 (40.6%)	<0.001
VAD at Transplant	481 (17.1%)	434 (16.7%)	47 (21%)	0.104
Ventilator at Transplant	491 (17.4%)	407 (15.7%)	84 (37.5%)	<0.001
Inotropic Support at Transplant	1403 (49.8%)	1284 (49.5%)	119 (53.1%)	0.293
Listing Status				
1A	2354 (83.5%)	2148 (82.7%)	206 (92%)	0.001
1B	290 (10.3%)	276 (10.6%)	14 (6.2%)	
2	176 (6.2%)	172 (6.6%)	4 (1.8%)	
Panel of reactive antibodies (PRA) ^b				
>10%	595 (26.6%)	547 (26.6%)	48 (26.5%)	0.974
>50%	259 (11.6%)	238 (11.6%)	21 (11.6%)	0.995
Estimated creatinine clearance (mL/min) ^c	127.8 (125.3 – 130.2)	128.9 (126.4 – 131.4)	114.5 (105.5 – 123.5)	0.002
Total bilirubin (mg/dL)	1.18 (1.09 – 1.27)	1.14 (1.05 – 1.23)	1.66 (1.23 – 2.08)	0.002
Pre-transplant iNO	96 (3.4%)	81 (3.1%)	15 (6.7%)	0.004

	Total	No ECMO	ECMO	p-value^a
	N=2820	N=2596 (92.1%)	N=224 (7.9%)	
Donor/Procedural Factors				
Positive CDC crossmatch	142 (5%)	126 (4.9%)	16 (7.1%)	0.133
Donor Inotropic Support	1403 (49.9%)	1289 (49.8%)	114 (50.9%)	0.759
Donor CPR	233 (8.3%)	209 (8.1%)	24 (10.7%)	0.168
Donor CPR Duration (minutes)	24 (22 – 27)	24 (22 – 27)	25 (17 – 34)	0.778
Donor/Recipient Weight Ratio	1.38 (1.36 – 1.39)	1.35 (1.28 – 1.42)	1.27 (1.1 – 1.44)	0.013
Ischemic Time >4 Hours	898 (32.7%)	812 (32.2%)	86 (39.4%)	0.028

Data expressed as N(%) for categorical and mean (95% confidence interval) for continuous

^a p-values from the chi square test for categorical and the Student's t test for continuous data

^b Note: PRA missing 20%

^c Creatinine clearance estimated using the Schwartz formula

Abbreviations: CDC - complement-dependent cytotoxicity, CPR - cardiopulmonary resuscitation, iNO - inhaled nitric oxide, ECMO - extracorporeal membrane oxygenation, VAD - ventricular assist device

Table 2.

Risk factors for post-transplant ECMO from logistic regression model

	Adjusted Odds Ratio (95% CI)	p-value
Recipient Factors		
Age Group		
<1 year	2.2 (1.3 – 3.7)	0.006
1–5 years	2.1 (1.3 – 3.4)	0.002
6–10 years	1.5 (0.6 – 3.7)	0.361
11–17 years	Ref.	-
Diagnosis		
Cardiomyopathy	Ref.	-
Congenital Heart Disease	1.6 (0.94 – 2.8)	0.083
Retransplant	2 (0.88 – 4.6)	0.097
Race		
Caucasian	Ref.	-
African-American	0.8 (0.53 – 1.3)	0.404
Other	0.7 (0.42 – 1.2)	0.181
ECMO at Transplant	27.4 (15.2 – 49.6)	<0.001
VAD at Transplant	2.3 (0.87 – 6)	0.092
Ventilator at Transplant	0.84 (0.4 – 1.8)	0.647
Listing Status		
1A	1.9 (0.77 – 4.6)	0.167
1B	2 (0.74 – 5.4)	0.171
2	Ref.	-
Pre-transplant iNO	1.1 (0.33 – 3.7)	0.871
Estimated creatinine clearance	1 (0.99 – 1)	0.211
Total bilirubin	1.05 (0.99 – 1.1)	0.052
Donor/Procedural Factors		
Donor/Recipient Weight Ratio	1 (0.72 – 1.4)	0.989
Ischemic Time >4 Hours	1.3 (0.9 – 1.9)	0.142

Abbreviations: ECMO - extracorporeal membrane oxygenation, iNO - inhaled nitric oxide, VAD - ventricular assist device

Table 3.

Risk factors for post-transplant ECMO from logistic regression model by diagnosis

	Cardiomyopathy		Congenital Heart Disease	
	N=1217		N=1207	
	Adjusted Odds Ratio	p-value	Adjusted Odds Ratio	p-value
Recipient Factors				
Age Group				
<1 year	1.5 (0.81 – 2.8)	0.198	2.4 (0.96 – 6.1)	0.06
1–5 years	2 (1.1 – 3.8)	0.032	1.8 (0.9 – 3.5)	0.107
6–10 years	0.7 (0.3 – 1.6)	0.383	1.9 (0.6 – 5.8)	0.287
11–17 years	Ref.	-	Ref.	-
ECMO at Transplant	41 (16.5 – 103)	<0.001	21.4 (12.3 – 37.4)	<0.001
VAD at Transplant	1.9 (0.6 – 6)	0.276	3.1 (1.3 – 7.4)	0.011
Ventilator at Transplant	1.5 (0.7 – 2.9)	0.28	0.64 (0.26 – 1.57)	0.33
Listing Status				
1A	1.5 (0.22 – 10.7)	0.671	1.36 (0.44 – 4.25)	0.592
1B	0.66 (0.05 – 9)	0.756	1.4 (0.37 – 5.2)	0.622
2	Ref.	-	Ref.	-
Pre-transplant iNO	0.68 (0.1 – 4.8)	0.698	1.4 (0.41 – 4.77)	0.583
Estimated creatinine clearance	1 (0.99 – 1)	0.28	1 (0.99 – 1)	0.137
Total bilirubin	1.1 (0.95 – 1.2)	0.256	1.04 (0.98 – 1.1)	0.178
Donor/Procedural Factors				
Donor/Recipient Weight Ratio	1.4 (0.73 – 2.6)	0.323	0.99 (0.62 – 1.58)	0.955
Ischemic Time >4 Hours	0.92 (0.49 – 1.7)	0.793	1.38 (0.88 – 2.18)	0.161

Abbreviations: ECMO - extracorporeal membrane oxygenation, iNO - inhaled nitric oxide, VAD - ventricular assist device

Table 4.

Demographics of patients requiring post-transplant ECMO based on survival to hospital discharge

	Total	Survived to discharge	In-hospital mortality	p-value ^a
	N=224	N=168 (75%)	N=56 (25%)	
Recipient Factors				
Duration of ECMO support (days)	5 (4.1 – 5.9)	2.8 (2.4 – 3.3)	11.2 (8.5 – 14)	<0.001
Age Group				
<1 year	106 (47.3%)	72 (42.9%)	34 (60.7%)	0.066
1–5 years	60 (26.8%)	50 (29.8%)	10 (17.9%)	
6–10 years	24 (10.7%)	17 (10.1%)	7 (12.5%)	
11–17 years	34 (15.2%)	29 (17.3%)	5 (8.9%)	
Male Gender	122 (54.5%)	91 (54.2%)	31 (55.4%)	0.877
Race				
Caucasian	147 (65.6%)	112 (66.7%)	35 (62.5%)	0.847
African-American	36 (16.1%)	26 (15.5%)	10 (17.9%)	
Other	41 (18.3%)	30 (17.9%)	11 (19.6%)	
Diagnosis				
Cardiomyopathy	78 (35.3%)	68 (41.2%)	10 (17.9%)	0.004
Congenital Heart Disease	133 (60.2%)	89 (53.9%)	44 (78.6%)	
Retransplant	10 (4.5%)	8 (4.8%)	2 (3.6%)	
Blood Type				
O	92 (41.1%)	68 (40.5%)	24 (42.9%)	0.862
A	92 (41.1%)	68 (40.5%)	24 (42.9%)	
B	27 (12.1%)	22 (13.1%)	5 (8.9%)	
AB	13 (5.8%)	10 (6%)	3 (5.4%)	
ECMO at Transplant	91 (40.6%)	69 (41.1%)	22 (39.3%)	0.814
VAD at Transplant	47 (21%)	37 (22%)	10 (17.9%)	0.507
Ventilator at Transplant	84 (37.5%)	60 (35.7%)	24 (42.9%)	0.339
Inotropic Support at Transplant	119 (53.1%)	89 (53%)	30 (53.6%)	0.938
Listing Status				
1A	206 (92%)	157 (93.5%)	49 (87.5%)	0.308
1B	14 (6.2%)	9 (5.4%)	5 (8.9%)	
2	4 (1.8%)	2 (1.2%)	2 (3.6%)	
Panel of reactive antibodies (PRA) ^b				
>10%	48 (26.5%)	37 (27.8%)	11 (22.9%)	0.571
>50%	21 (11.6%)	16 (12%)	5 (10.4%)	1
Estimated creatinine clearance (mL/min) ^c	114.5 (105.5 – 123.5)	121.6 (111.4 – 131.8)	91.8 (73.9 – 109.8)	0.005
Total bilirubin (mg/dL)	1.66 (1.23 – 2.08)	1.37 (1 – 1.73)	2.59 (1.24 – 3.93)	0.015

	Total	Survived to discharge	In-hospital mortality	p-value^a
	N=224	N=168 (75%)	N=56 (25%)	
Pre-transplant iNO	15 (6.7%)	10 (6%)	5 (8.9%)	0.447
Dialysis Post-Transplant	33 (14.8%)	18 (10.7%)	15 (27.3%)	0.003
Donor/Procedural Factors				
Positive CDC crossmatch	16 (7.1%)	14 (8.3%)	2 (3.6%)	0.369
Donor Inotropic Support	114 (50.9%)	87 (51.8%)	27 (48.2%)	0.643
Donor CPR	24 (10.7%)	18 (10.7%)	6 (10.7%)	1
Donor CPR Duration (minutes)	25 (17 – 34)	29 (18 – 39)	17 (5 – 28)	0.187
Donor/Recipient Weight Ratio	1.27 (1.09 – 1.45)	1.32 (1.12 – 1.52)	1.14 (0.75 – 1.52)	0.381
Ischemic Time >4 Hours	86 (39.4%)	52 (31.9%)	34 (61.8%)	<0.001

Data expressed as N(%) for categorical and mean (95% confidence interval) for continuous

^a p-values from the chi square test or Fisher exact test for categorical and the student t-test for continuous data

Abbreviations: CDC - complement-dependent cytotoxicity, CPR - cardiopulmonary resuscitation, iNO - inhaled nitric oxide, ECMO - extracorporeal membrane oxygenation, VAD - ventricular assist device

Table 5.

Risk factors for in-hospital mortality for patients requiring post-transplant ECMO from logistic regression model

A.		
	Adjusted Odds Ratio (95% CI)	p-value
Recipient Factors		
Age Group		
<1 year	1.3 (0.35 – 4.9)	0.685
1–5 years	1.1 (0.31 – 4.1)	0.853
6–10 years	1.6 (0.19 – 13.9)	0.649
11–17 years	Ref.	-
Diagnosis		
Cardiomyopathy	Ref.	-
Congenital Heart Disease	3.6 (0.96 – 13.5)	0.058
Retransplant	2.1 (0.16 – 28.3)	0.569
Estimated creatinine clearance	0.99 (0.98 – 1)	0.221
Total bilirubin	1.1 (0.96 – 1.26)	0.175
Dialysis Post-Transplant	2.3 (0.99 – 5.3)	0.053
Donor/Procedural Factors		
Ischemic Time >4 Hours	3.2 (1.8 – 5.5)	<0.001
B.		
	Adjusted Odds Ratio (95% CI)	p-value
Recipient Factors		
Days on ECMO support	1.4 (1.2 – 1.6)	<0.001
Age Group		
<1 year	0.9 (0.1 – 8.1)	0.931
1–5 years	0.8 (0.12 – 5.7)	0.848
6–10 years	0.9 (0.15 – 5.1)	0.874
11–17 years	Ref.	-
Diagnosis		
Cardiomyopathy	Ref.	-
Congenital Heart Disease	2.6 (0.68 – 9.6)	0.167
Retransplant	2.5 (0.06 – 107.2)	0.629
Estimated creatinine clearance	0.99 (0.98 – 1)	0.175
Total bilirubin	1.1 (0.91 – 1.4)	0.262
Dialysis Post-Transplant	2.5 (1.02 – 5.9)	0.044
Donor/Procedural Factors		
Ischemic Time >4 Hours	2.4 (0.67 – 8.5)	0.179

Abbreviations: ECMO - extracorporeal membrane oxygenation