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Pediatric Risk to Orthotopic Heart Transplant (PRO) score: Insights from United Network for Organ Sharing (UNOS) waitlist mortality findings

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Abstract

Background: Pediatric heart transplant candidates on the waitlist have the highest mortality rate amongst all solid organ transplants. A risk score incorporating a candidate's individual risk factors may better predict mortality on the waitlist and optimize organ allocation to the sickest of those awaiting transplant.

Methods: Using the United Network for Organ Sharing (UNOS) database, we evaluated a total of 5542 patients aged 0–18 years old on the waitlist for a single, first time, heart transplant from January 2010-June 2019. We performed a univariate analysis on two-thirds (N=3705) of these patients to derive the factors most associated with waitlist mortality or delisting secondary to deterioration within 1 year. Those with a p-value<0.2 underwent a multivariate analysis and the resulting factors were used to build a prediction model using the Fine-Grey model analysis. This predictive scoring model was then validated on the remaining one-third of the patients (N=1852).

Results: The Pediatric Risk to OHT (PRO) scoring model utilizes the following unique patient variables: blood type, diagnosis of congenital heart disease, weight, presence of ventilator support, presence of inotropic support, extracorporeal membrane oxygenation (ecmo) status, creatinine level, and region. A higher score indicates an increased risk of mortality. The PRO score had a predictive strength of 0.762 as measured by Area Under the ROC curve at 1 year.

Conclusion: The PRO score is an improved predictive model with the potential to better assess mortality for patients awaiting heart transplant.

Relevant social media pages: None

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Author Contributions: Dr. Stephanie Raymundo, Dr. Juan Alejos, and Dr. Neeraj Srivastava conceptualized the study. Dr. Stephanie Raymundo and Holly Wilhalme designed the study. Dr. Stephanie Raymundo, Dr. Anila Chaudhary and Krystal Karunungan drafted the initial manuscript. All authors critically reviewed the manuscript for important intellectual context and revised the manuscript. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

pediatric heart transplant; pediatric transplantation; risk factors; solid organ transplantation

INTRODUCTION

Waitlist mortality remains highest for pediatric orthotopic heart transplant (OHT) among all solid-organ transplants in the United States. Once patients are listed for OHT, they are sub-classified based on medical urgency (Status 1A, Status 1B, Status 2), with Status 1A denoting the greatest acuity. The criteria for Status 1A listing has been modified several times in attempt to assure that available organs are allocated to the most critical patients. However, there remains significant heterogeneity in the ability of listing status to accurately predict waitlist mortality, particularly among children^{1,2}. Mortality has also been found to vary considerably within Status 1A with up to a tenfold difference between patients within the group³. Collectively, these findings suggest that improvements in risk assessment of pediatric OHT candidates may assist in improving wait list mortality and optimizing organ allocation.

Clinical variations in mortality risk have been observed with various factors associated with greater waitlist mortality: younger age at listing⁴, ventilator support¹, presence of congenital heart disease^{1,3,4}, extracorporeal membrane oxygenation (ecmo) support^{1,3,5}, and racial and ethnic disparities^{1,3}. There are currently scoring systems to help predict post- transplant mortality in high risk patients, with risk of death increasing when a patient has more than one high risk criteria prior to transplantation⁶. No studies to date, however, have investigated the development of a pre-transplant risk calculator to predict mortality in children while awaiting heart transplant.

METHODS

This was a retrospective study of the Organ Procurement and Transplantation Network (OPTN) database which is a registry of organ transplants performed in the United States of America. The OPTN database was queried for demographic and clinical variables in 0–18 year old patients on the waitlist for a single organ heart transplant from January 2010 to June 2019. Patients who were repeat transplants or who were undergoing multiple organ transplants were excluded. A total of 5542 patients were included in the analysis.

The patients were randomly divided into a "derivation cohort" and a "validation cohort." The "derivation cohort" was used to develop the prediction model and the "validation cohort" was used to validate the model. The "derivation cohort" comprised two-thirds of the total number of patients (N=3695). A Fine and Grey survival analysis of time to death or delisting secondary to deterioration within one year of listing was used to conduct a univariate analysis of the patient factors. Fine and Grey was chosen in order to account for competing risks ⁷. Patients who were transplanted were considered a competing event and censored. Factors with a p-value of <0.2 were considered for inclusion in a multivariate predictive model and a combination of backwards selection and clinical expertise were used to build a prediction model using the Fine-Grey model survival model. We excluded patients

with a creatinine greater than 5 (n=14) as these were outliers. Only patients with complete case data for all variables chosen for the model were used. Missing data not considered for bivariate analysis. Status category at listing was used. The rms packing in R was used to construct a nomogram with the weight to each factor derived from the coefficient in the model. This predictive scoring model was validated on the "validation cohort" (N=1852) by comparing descriptive statistics of the clinical risk score with the "derivation cohort" as well as calculating the area under the ROC curve within the "derivation cohort". All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC) and Stata IC 16 (StataCorp LP, College Station, TX). This study was submitted to the institutional review board at the University of California-Los Angeles and determined that review was not required.

RESULTS

Of the 5,557 patients included in the study analysis, the majority were male (56.2%), white (53.3), and publicly insured (53.9%) (Table 1). Among age and weight categories, the greatest proportion of patients were <1 year old (35.2%) and <10 kg (40.8%), respectively. Patients were most commonly listed as Status 1A (65.2%) and with a diagnosis of congenital heart disease (50.8%) or dilated cardiomyopathy (32.6%). At the time of listing for transplant, some patients required significant cardio-respiratory support: 45.7% on vasopressors and inotropes, 20.1% on a mechanical ventilator, 11.6% with a ventricular assist device (VAD), 7.1% were on ecmo (extracorporeal membrane oxygenation), and 3.1% on renal replacement therapy.

Of the demographic and clinical factors evaluated, after a univariate analysis the following were found to have a significant (p-value <0.2) association with death or delisting: age, gender, insurance, race, blood type, diagnosis, weight, VAD use, inotrope use, ventilator use, defibrillator use, ecmo use, dialysis use, comorbid cancer, creatinine, and UNOS region (Table 2). These factors then underwent application of the multivariate predictive model (significance p-value <0.2), backwards selection, and clinical prioritization, the resulting factors together most associated with death or delisting were blood type, diagnosis (congenital heart disease vs other), weight, ventilator status, inotrope use, ecmo use, creatinine, and UNOS region (Table 3) and thus used to create the Pediatric Risk to OHT (PRO) scoring model (Figure 1). Each clinical factor within the scoring model is a scaled version of the proportion of that factor's contribution to the outcome (death or delisting while on the waitlist). The total points are mapped to the one-year mortality probability while on the waitlist with a higher score indicating an increased risk of mortality.

The PRO score had a predictive strength of 0.762 as measured by Area Under the ROC curve at 1 year (Figure 2). Applying the prediction model from the test data to the validation cohort resulted in an area under the ROC curve of 78.8 (95% CI 75.9, 81.8) and Brier score of 9.9 (95% CI 7.3–12.6) which resulted in an Index of Prediction of 12.5% indicating a moderate discrimination and an improvement relative to the null model ⁸. The derivation group had a PRO score mean of 0.65 (standard deviation 0.91) and median of 0.62, while the validation group had a PRO score mean of 0.65 (standard deviation of 0.92) and median of

DISCUSSION

Though each listing status for pediatric heart transplant has criteria, the population remains heterogeneous, especially within those listed as 1A. As a result, there is still a wide range of clinical acuity without a method by which to differentiate them. When the PRO score is applied to each listing status, the previously homogenous listing status becomes differentiated with a wide range of resulting scores (Figure 4). This study is unique as it utilizes a combination of clinical factors to provide the best estimate of the risk of mortality among patients awaiting heart transplant and provides a clinical tool for providers to utilize in risk assessment of their patients, such as when applying for exemptions when listing. For example, a 15 kg patient with congenital heart disease listed for heart transplant in Region 5 with AB blood type on ventilator support but no ecmo support and a most recent creatinine of 1.77 would result in a PRO score of 125 which corresponds to a waitlist mortality of approximately 0.25 (Figure 1). Prior studies have shown that weight, specifically less than 3 kg, ecmo and ventilation support, and inotropic support, are independently associated with increased risk of death in patients listed for heart transplant^{1,3,9,10}. Nonwhite race/minority ethnicity has been shown to be a risk factor for mortality in prior studies ^{1,3}; however, the current analysis did not find a statistically significant association of nonwhite race/minority ethnicity, inotropic support, and VAD support with mortality and thus was not included in the final calculation. This could be secondary to a change in the capture of patients within the cohort or a confounded association with other factors that we have now parsed out.

Multiple regions exist across the United States and are overseen by UNOS and there exist differences in mortality between regions which require further evaluation. There was a notable difference in mortality for patients awaiting heart transplant in patients located in region 10 and 11 compared to other regions. The cause for this difference was not apparent, but potential contributing factors may be multifactorial, including access, offer acceptance ratios, and center volume. It has been previously shown that there are differences in rates of heart transplantation at low volume centers, defined as less than 3 transplants a year, compared to high volume centers, defined as 10 transplants a year (36% vs 89% between 2002 to 2014)¹¹. Children at low volume centers had >400% risk of death while awaiting heart transplant when compared to those at high volume centers, though the exact cause for this is unknown and likely multifactorial¹¹. Thus, further elucidation of the factors within regions associated with patient mortality while awaiting heart transplant is needed.

There were limitations to the current study which are inherent to database studies such as errors in the database itself and lack of patient level clinical data (i.e. specific congenital heart disease diagnosis, bilirubin level, estimated GFR) which may affect the mortality risk awaiting transplant. Missing data (0.6%) was not considered for bivariate analysis as only patients with complete case data for all variables chosen for the model were used for the training set. The same patient population was used for both the derivation and validation of the scoring model, though the cohorts had similar characteristics (Table 4). Patients listed as ABO incompatible candidates are a unique situation as those listed may have a

risk profile more similar to an AB candidate. This is not inherently accounted for in our model. Finally, pediatric heart transplant listing criteria was changed in 2016 with the goal to more appropriately stratify patients and likely impact mortality while on the waitlist. As our cohort encompasses this change, it may have impacted the criteria we found associated with waitlist mortality.

The application of a standardized scoring system with individualized variables may allow for transplant of those most ill sooner, improving waitlist mortality as children who are sicker have the highest benefit from heart transplantation¹². Studies in adults have looked at using a more personalized approach to predict pre- and post-transplant death using algorithms and machine learning to address the heterogeneity in clinical status that is present amongst adults awaiting heart transplant¹³. This novel idea, if applied to pediatric patients, can potentially address the heterogeneity of pediatric patients and their varying risk of mortality while awaiting transplantation. In addition to guidance during listing, regularly scoring patients on the waitlist could assist with guidance regarding listing exemptions or considering offers, particularly in light of new program metrics such as pre-transplant mortality and offer acceptance rates. Future directions include completing prospective analysis to determine the effectiveness of a risk calculator in predicting mortality, external validation, scoring trend and impact on waitlist time, and impact on post-transplant outcomes.

CONCLUSION

In conclusion, the PRO score has the potential to predict mortality among pediatric patients awaiting heart transplant. These findings demonstrate that a higher score indicates an increased risk of mortality. With prospective application, this study aims to improve allocation of a limited resource and improve the mortality rate in pediatric patients awaiting heart transplant.

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Data Availability Statement:

Raw data were generated at the Organ Procurement and Transplant Network (OPTN) database. Derived data that support the findings of this study are available from the corresponding author upon reasonable request.

ABBREVIATIONS

ecmo	extracorporeal membrane oxygenation
ОНТ	orthotopic heart transplant
PRO	Pediatric Risk to Orthotopic Heart Transplant
UNOS	United Network for Organ Sharing

VAD

ventricular assist device

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Figure 1:

Nomogram incorporating the variables of the final PRO score- a higher score indicates an increased 1 year waitlist mortality probability (Diagnosis: C= congenital, O= other, H= hypertrophic cardiomyopathy, R= restrictive cardiomyopathy, M= myocarditis, D= dilated cardiomyopathy). The ruler length for each clinical factor is a scaled version of the proportion of that factor's contribution (range of possible values times coefficient) divided by the maximum predictor contribution. The total points are mapped to the one-year mortality probably while on the waitlist. For example, a 15 kg patient with congenital heart disease listed for heart transplant in Region 5 with AB blood type on ventilator support but no ecmo support and a most recent creatinine of 1.77 would result in a PRO score of 125 which corresponds to a waitlist mortality of approximately 0.25





Area under the curve for derivation (training) cohort and validation cohort showing the PRO score with a predictive strength of 0.762.



Figure 3:

PRO score distribution of the derivation (training) group and the validation group demonstrating a similar bell curve characteristic.



Figure 4:

PRO Score distribution within each listing status: 1A, 1B, and 2. Variation of scores within each status conveys the heterogeneity of the patients within that group. As expected, there is a greater distribution of higher scores within Status 1A compared to Status 1B and Status 2.

Table 1

Demographics of pediatric patients listed for heart transplant from January 2010 to June 2019.

Variable	N (%)
Age, years	
<1	1958 (35.2)
1-4	1089 (19.6)
5–12	1155 (20.8)
13–18	1355 (24.4)
Female	2436 (43.8)
Race	
White	2960 (53.3)
Black	1125 (20.2)
Hispanic	1061 (19.1)
Asian	198 (3.6)
Other	213 (3.8)
Weight, kg	
<10	2268 (40.8)
10–19	1051 (18.9)
20–39	797 (14.3)
40–59	760 (13.7)
60	681 (12.3)
Insurance	
Private	2437 (43.9)
Public	2995 (53.9)
Other	124 (2.2)
Blood Type	
А	1945 (35.0)
AB	200 (3.6)
В	734 (13.2)
0	2678 (48.2)
UNOS Region	
Region 1	171 (3.1)
Region 2	459 (8.3)
Region 3	907 (163)
Region 4	496 (8.9)
Region 5	846 (15.2)
Region 6	179 (3.2)
Region 7	546 (9.8)
Region 8	526 (9.5)
Region 9	344 (6.2)
Region 10	452 (8.1)
Region 11	631 (11.4)

Variable
Initial status
Status 1A
Status 1B
Status 2
Inactive
Diagnosis
Coronary artery dis

Status 1A	3618 (65.2)
Status 1B	885 (16.0)
Status 2	944 (17.0)
Inactive	101 (1.8)
Diagnosis	
Coronary artery disease	19 (0.3)
Congenital	2822 (50 8)
Dilated cardiomyopathy	1810 (32.6)
Hypertrophic cardiomyopathy	175 (3.1)
Restrictive cardiomyopathy	286 (5.1)
Myocarditis	202 (3.6)
Valvular disease	9 (0.2)
Other	234 (4.2)
Any cancer	78 (1.4)
VAD at listing	
LVAD	511 (9.2)
Other	136 (2.4)
None	4910 (88.4)
Inotropes	2539 (45.7)
Ventilator	1115 (20.1)
Defibrillator	475 (8.5)
ECMO	396 (7.1)
Dialysis	170 (3.1)
Creatinine, mean (SD)	0.54 (0.74)
Albumin, mean (SD)	3.53 (0.79)

N (%)

VAD: ventricular assist device; LVAD: left ventricular assist device; ECMO: extracorporeal membrane oxygenation

Table 2

Variables after a univariate analysis of predictors of 1 year waitlist mortality or delisting for worsening medical condition. Those with a p-value of <0.2 were then considered for inclusion in a multivariate predictive model, then a combination of backwards selection and clinical expertise were used to build a prediction model using the Fine-Grey model survival model.

Variable/Category	Hazard Radio	95% CI	P Value
Age 1–4 (vs <1)	0.57	0.45 - 0.71	<.0001
Age 5–12 (vs <1)	0.35	027 - 0.46	
Age 13–18 (vs <1)	0.22	0.16 - 0.29	
Female (vs Male)	1.02	0.86 – 1 22	0.7858
Insurance - Other (vs Private)	0.95	0.49 – 1.86	0.3858
Insurance - Public (vs Private)	1.13	0.94 - 1.35	
Rare - Asian (vs White)	0.83	0.48 - 1.43	0.4809
Race - Black (vs White)	1.16	0.93 - 1.45	
Race - Hispanic (vs White)	0.98	0.77 - 1.24	•
Race - Other (vs White)	1.24	0.82 - 1.87	
Blood Type - A (vs O)	0.78	0.64 - 0.95	0.0211
Blood Type - AB (vs O)	0.56	0.3 - 1.02	•
Blood Type - B (vs O)	0.8	0.6 - 1.05	
Status - Inactive (vs 2)	2.34	1.13 - 4.84	< 0001
Status - 1A (vs 2)	3.49	2.48 - 4.91	•
Status - 1B (vs 2)	1.54	1 - 2.37	
Diagnosis dilated (vs congenital)	0.38	0.3 - 0.47	<.0001
Diagnosis - hypertrophic (vs congenital)	0.37	0.19 - 0.72	•
Diagnosis - myocarditis (vs congenital)	0.67	0.41 - 1.12	•
Diagnosis - other (vs congenital)	0.86	0.58 - 1.28	•
Diagnosis - restrictive (vs congenital)	0.31	0.17 - 0.55	
Weight - <10kg (vs >=60)	4.63	3.06 - 6.99	<.0001
Weight - 10–19kg (vs >=60)	2.4	1.53 - 3.76	•
Weight - 20–39kg (vs >=60)	1.51	0.91 - 2.5	
Weight - 40–59kg (vs >=60)	0.97	0.56 - 1.68	
VAD at list - LVAD (vs none)	0.68	0.48 - 0.97	0.0529
VAD at list - Other (vs none)	1.29	0.8 - 2.09	
Inotropes (1-unit increase)	1.4	1.18–1.67	0.0001
Ventilator (Vent vs None)	3.15	2.63 - 3.76	<.0001
Defib (Defib vs None)	0.49	0.32 - 0.74	0.0006
ECMO (Yes vs No)	3.99	3.16 - 5.03	<.0001
Dialysis (Yes vs No)	1.73	1.14 - 2.62	0.0105
Any Cancer (Yes vs No)	0.99	0.5 - 1.94	0.9707
Creatinine (1-unit increase)	1.08	0.82 - 1.42	0.5715
Albumin (1-unit increase)	0.64	0.58 - 0.71	<.0001
Region 1 (vs 3)	0.68	0.38 - 1.25	0.0003

Variable/Category	Hazard Radio	95% CI	P Value
Region 2 (vs 3)	0.93	0.64 - 1.35	
Region 4 (vs 3)	0.75	0.51 - 1.11	
Region 5 (vs 3)	0.79	0.57 - 1.09	
Region 6 (vs 3)	0.75	0.43 - 1.3	
Region 7 (vs 3)	0.72	0.49 - 1.04	
Region 8 (vs 3)	1.03	0.73 - 1.45	
Region 9 (vs 3)	0.6	0.37 - 0.97	
Region 10 (vs 3)	1.46	1.06 - 2.03	
Region 11 (vs 3)	1.3	0.96 - 1.77	

Table 3

Fine and Grey Survival model with the final factors- Blood type, diagnosis, weight, ventilator, ecmo, creatinine, region- predicting 1 year waitlist mortality (delisting for worsening medical condition as a competing event).

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Variable/Category	Hazard Ratio	95% CI	P Value
Blood Type - A (vs O)	0.72	0.59 – 0.89	0.0020
Blood Type - AB (vs O)	0.47	0.25 - 0.9	0.0216
Blood Type - B (vs O)	0.86	0.65 - 1.14	0.2835
Diagnosis - dilated (vs congenital)	0.43	0.34 - 0.55	<.0001
Diagnosis - hypertrophic (vs congenital)	0.52	0.27 – 1.03	0.0600
Diagnosis - myocarditis (vs congenital)	0.53	0.31 – 0.91	0.0204
Diagnosis - other (vs congenital)	0.93	0.61 – 1.4	0.7177
Diagnosis - restrictive (vs congenital)	0.55	0.3 – 1.01	0.0526
Weight - 10–19kg (vs >=60)	2.4	1.47 – 3.91	0.0004
Weight - 20–39kg (vs >=60)	1.53	0.9 - 2.61	0.1156
Weight - 40–59kg (vs >=60)	0.96	0.54 – 1.69	0.8810
Weight - <10kg (vs >=60)	3.86	2.41 - 6.19	<.0001
Ventilator (Vent vs None)	1.77	1.43 - 2.2	<.0001
ECMO (Yes vs No)	2.73	2.09 - 3.55	<.0001
Creatinine (1-unit increase)	1.83	1.41 – 2.39	<.0001
Region - 1 (vs 3)	0.78	0.43 - 1.4	0.4004
Region - 2 (vs 3)	0.93	0.64 - 1.36	0.7238
Region - 4 (vs 3)	0.77	0.52 - 1.15	0.2072
Region - 5 (vs 3)	0.84	0.6 - 1.17	0.2904
Region - 6 (vs 3)	0.58	0.33 - 1.02	0.0599
Region - 7 (vs 3)	0.67	0.46 - 0.99	0.0417
Region - 8 (vs 3)	0.88	0.62 - 1.24	0.4611
Region - 9 (vs 3)	0.72	0.43 - 1.18	0.1894
Region - 10 (vs 3)	1.47	1.04 - 2.08	0.0275
Region - 11 (vs 3)	1.09	0.79 – 1.5	0.6150

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Table 4:

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Comparison

Variable	Overall (N=5542)	Training (N=3695)	Validation (N=1847)
Age			
1-4	1088 (19.6%)	732 (19.8%)	356 (19.3%)
13–18	1348 (24.3%)	918 (24.8%)	430 (23.3%)
5-12	1150 (20.8%)	750 (20.3%)	400 (21.7%)
<1	1956 (35.3%)	1295 (35.0%)	661 (35.8%)
Sex			
ц	2433 (43.9%)	1644 (44.5%)	789 (42.7%)
W	3109 (56.1%)	2051 (55.5%)	1058 (57.3%)
Race			
Asian	197 (3.6%)	128 (3.5%)	69 (3.7%)
Black	1121 (20.2%)	710 (19.2%)	411 (22.3%)
Hispanic	1057 (19.1%)	711 (19.2%)	346 (18.7%)
Other	212 (3.8%)	156 (4.2%)	56 (3.0%)
White	2955 (53.3%)	1990 (53.9%)	965 (52.2%)
Insurance			
other	123 (2.2%)	73 (2.0%)	50 (2.7%)
private	2432 (43.9%)	1640 (44.4%)	792 (42.9%)
public	2986 (53.9%)	1981 (53.6%)	1005 (54.4%)
Missing	1	1	
ABO			
Υ	1941 (35.0%)	1276 (34.5%)	665 (36.0%)
AB	199 (3.6%)	124 (3.4%)	75 (4.1%)
B	733 (13.2%)	489 (13.2%)	244 (13.2%)
0	2669 (48.2%)	1806 (48.9%)	863 (46.7%)
Init Stat			
Inactive	100 (1.8%)	76 (2.1%)	24 (1.3%)

Variable	Overall (N=5542)	Training (N=3695)	Validation (N=1847)
Status 1A	3611 (65.3%)	2385 (64.6%)	1226 (66.5%)
Status 1B	881 (15.9%)	586 (15.9%)	295 (16.0%)
Status 2	941 (17.0%)	643 (17.4%)	298 (16.2%)
Missing	6	5	4
Diagnosis (categorized)			
congenital	2816 (50.8%)	1884 (51.0%)	932 (50.5%)
dilated	1802 (32.5%)	1222 (33.1%)	580 (31.4%)
hypertrophic	175 (3.2%)	120 (3.2%)	55 (3.0%)
myocarditis	202 (3.6%)	128 (3.5%)	74 (4.0%)
other	262 (4.7%)	164 (4.4%)	98 (5.3%)
restrictive	285 (5.1%)	177 (4.8%)	108 (5.8%)
Weight			
10–19	1050 (18.9%)	719 (19.5%)	331 (17.9%)
20–39	791 (14.3%)	511 (13.8%)	280 (15.2%)
40–59	756 (13.6%)	510 (13.8%)	246 (13.3%)
<10	2266 (40.9%)	1498~(40.5%)	768 (41.6%)
>=60	679 (12.3%)	457 (12.4%)	222 (12.0%)
VAD List			
LVAD	510 (9.2%)	339 (9.2%)	171 (9.3%)
Other	135 (2.4%)	96 (2.6%)	39 (2.1%)
none	4897 (88.4%)	3260 (88.2%)	1637 (88.6%)
Inotropes			
No	3005 (54.2%)	2012 (54.5%)	993 (53.8%)
Yes	2537 (45.8%)	1683 (45.5%)	854 (46.2%)
Ventilator			
No	4428 (79.9%)	2939 (79.5%)	1489~(80.6%)
Yes	1114 (20.1%)	756 (20.5%)	358 (19.4%)
Defib			
defib	473 (8.5%)	327 (8.9%)	146 (7.9%)

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Variable	Overall (N=5542)	Training (N=3695)	Validation (N=1847)
none	5068 (91.5%)	3367 (91.1%)	1701 (92.1%)
Missing	1	1	
ECMO			
No	5146 (92.9%)	3435 (93.0%)	1711 (92.6%)
Yes	396 (7.1%)	260 (7.0%)	136 (7.4%)
Dialysis			
No	5380 (97.1%)	3584 (97.0%)	1796 (97.2%)
Yes	162 (2.9%)	111 (3.0%)	51 (2.8%)
Any Cancer			
No	5465 (98.6%)	3638 (98.5%)	1827 (98.9%)
Yes	77 (1.4%)	57 (1.5%)	20 (1.1%)
Creatnine			
u	5521	3681	1840
Mean (SD)	0.513 (0.3402)	0.516 (0.3445)	0.509 (0.3317)
Median	$0.410\ (0.300,\ 0.610)$	$0.410\ (0.3000,\ 0.6300)$	$0.410\ (0.3000,\ 0.6000)$
Min, Max	0.03, 5.00	0.03, 5.00	0.10, 4.00
Serum Albumin			
u	5274	3520	1754
Mean (SD)	3.53 (0.786)	3.54 (0.795)	3.52 (0.769)
Median	3.60 (3.00, 4.00)	3.60 (3.000, 4.000)	3.50 (3.000, 4.000)
Min, Max	0.5, 9.7	0.5, 9.7	0.5, 8.0
Region			
1	169 (3.0%)	116 (3.1%)	53 (2.9%)
10	452 (8.2%)	307 (8.3%)	145 (7.9%)
11	631 (11.4%)	412 (11.2%)	219 (11.9%)
2	457 (8.2%)	305 (8.3%)	152 (8.2%)
3	902 (16.3%)	602 (16.3%)	300 (16.2%)
4	492 (8.9%)	322 (8.7%)	170 (9.2%)
5	844 (15.2%)	550 (14.9%)	294 (15.9%)

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Training (N=3695)

Variable

137 (3.7%)

Overall (N=5542) 179 (3.2%)

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546 (9.9%) 526 (9.5%) 344 (6.2%)

179 (9.7%) 170 (9.2%)

356 (9.6%)

221 (6.0%)

6

367 (9.9%)

123 (6.7%)