



## Pulmonary

## Creation of an empiric tool to predict ECMO deployment in pediatric respiratory or cardiac failure

Punkaj Gupta<sup>a,b,\*</sup>, Jeffrey M. Gossett<sup>b,c</sup>, Danny Kofos<sup>a</sup>, Mallikarjuna Rettiganti<sup>b</sup><sup>a</sup> Section of Cardiac Critical Care, Methodist Children's Hospital, San Antonio, TX, United States<sup>b</sup> Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, AR, United States<sup>c</sup> Department of Biostatistics, St. Jude Children's Research Hospital, Memphis, TN, United States

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## ABSTRACT

**Purpose:** To create a real-time prediction tool to predict probability of ECMO deployment in children with cardiac or pulmonary failure.

**Materials and methods:** Patients ≤18 years old admitted to an ICU that participated in the Virtual Pediatric Systems database (2009–2015) were included. Logistic regression models using adaptive lasso methodology were used to identify independent factors associated with ECMO use.

**Results:** A total of 538,202 ICU patients from 140 ICUs qualified for inclusion. ECMO was deployed in 3484 patients (0.6%) with a mortality of 1450 patients (41.6%). The factors associated with increased probability of ECMO use included: younger age, pulmonary hypertension, congenital heart disease, high-complexity cardiac surgery, cardiomyopathy, acute lung injury, shock, renal failure, cardiac arrest, use of nitric oxide, use of either conventional mechanical ventilation or high frequency oscillatory ventilation, and higher annual ECMO center volume. The area under the receiver operating curve for this model was 0.90 (95% CI: 0.85–0.93). This tool can be accessed at <https://soipredictiontool.shinyapps.io/ECMORisk/>.

**Conclusions:** Here, we present a tool to predict ECMO deployment among critically ill children; this tool will help create real-time risk stratification among critically ill children, and it will help with benchmarking, family counseling, and research.

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## 1. Introduction

Despite using extracorporeal membrane oxygenation (ECMO) for over 40 years, there is wide variability in the decision-making process to deploy ECMO in critically ill children [1]. There are guidelines published by the Extracorporeal Life Support Organization (ELSO) for ECMO deployment in children with potentially reversible cardiac or respiratory failure in whom conventional medical strategies have been exhausted [2]. However, these guidelines are based on expert opinion and serve only as a guide to deploy ECMO, thereby leaving much to the judgement of the treating physician.

Given the ambiguity in this important decision-making process, it becomes logical to test the validity of ELSO guidelines by empiric research and to possibly create a tool to help physicians make this important decision. As clinical judgement alone can be imperfect, it is suggested that prediction tools might be used as adjuncts to the clinical decision-making process [3,4]. Recently, severity-of-illness scores were developed to predict mortality among patients receiving ECMO (using

data from the ELSO registry) [5–7]. However, none of these tools can predict the probability of ECMO deployment in critically ill children. To address this gap in knowledge, we used multi-institutional data to identify factors associated with ECMO deployment and to create a real-time prediction tool to predict the probability of ECMO deployment in children with cardiac or pulmonary failure.

## 2. Materials and methods

## 2.1. Data source

Virtual Pediatric Systems (VPS, LLC, Los Angeles, CA) is an online pediatric critical care network formed by the NACHRI (National Association of Children's Hospitals and Related Institutions, now part of the Children's Hospital Association), Children's Hospital Los Angeles, and Children's Hospital of Wisconsin to develop a database with prospective data collection using standardized clinical data definitions, data quality control, and data analysis [8]. The VPS database is a prospective observational cohort of consecutive PICU admissions from a diverse set of hospitals caring for children in the United States. Data are collected and entered by trained individuals. VPS staff perform initial and quarterly inter-rater reliability (IRR) testing. IRR testing in the VPS database is

\* Corresponding author at: Section of Cardiac Critical Care, Methodist Children's Hospital, 7700 Floyd Curl Drive, San Antonio, Texas 78229.  
 E-mail address: [punkaj.gupta@hotmail.com](mailto:punkaj.gupta@hotmail.com) (P. Gupta).

consistently above 0.95. In addition, VPS staff perform extensive quality control checks on data before it is released for analysis; thus, the data have high fidelity.

## 2.2. Patient population

Patients  $\leq 18$  years of age admitted to an ICU at a VPS-participating hospital (2009–2015) qualified for inclusion in the study; no specific exclusion criteria were applied. Patients with both cardiac (cardiac-medical and cardiac-surgical) and non-cardiac (trauma, respiratory, hematologic, neurologic oncologic, genetic, endocrinologic, gastrointestinal, infectious, injury, poisoning, metabolic, and transplant) diagnoses were included. The University of Arkansas for Medical Sciences Institutional Review Board for the protection of human subjects reviewed the study protocol and determined that querying de-identified patient data did not require Institutional Review Board oversight.

Data were collected on demographics, patient diagnoses, mechanical ventilation, and severity of illness. Specific data collected for demographics and severity of illness included age, gender, pediatric index of mortality-2 (PIM-2) score, presence of a developmental or genetic disorder, and failure to thrive. Resource utilization data were collected, including ECMO deployment, cardiac surgery (and complexity of cardiac surgery), the use of nitric oxide, conventional mechanical ventilation (CMV), high-frequency oscillatory ventilation (HFOV), and duration of mechanical ventilation. Center characteristics were also collected, including average annual ECMO cases per center, training programs (residency and fellowship), and presence of 24/7 ICU attending coverage.

## 2.3. Statistical analysis

### 2.3.1. Model development

The aim of this study was to create a reliable tool for predicting the deployment of ECMO among critically ill children. We used a logistic regression model using adaptive lasso methodology with Akaike Information Criteria validation to perform variable selection and penalization [9]. The following variables were considered for variable selection: age (0 to <1 year, 1 to <8 years, and 8 to 18 years); gender (female or male); weight (kg); race (white, black, Hispanic, or other); PIM 2 score; specific diagnosis indicators (respiratory, cardiovascular, endocrinologic, gastrointestinal, infectious, metabolic/genetic, hematologic/oncologic, renal/genitourinary, transplant, neurologic, and injury/poisoning/adverse effects); cardiomyopathy/myocarditis (yes/no); shock/hypotension (yes/no); pulmonary hypotension (yes/no); renal failure (yes/no); failure to thrive (yes/no); chromosomal anomaly (yes/no); congenital heart disease (yes/no); acute respiratory failure (yes/no); sepsis (yes/no); ICU visit after trauma (yes/no); cardiac arrest (yes/no); common ventricle (yes/no); cardiac surgery (yes/no); STAT (Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery) category of index heart operation; use of nitric oxide (yes/no); mechanical ventilation (none, conventional, or high frequency); average annual ECMO volume; training hospital (yes/no); and 24/7 attending coverage (yes/no). None of the variables completely dropped out in the lasso model; consequently, all of the variables were included in the final model to create the tool. A logistic regression model with random effects at the center level to account for clustering of patients within centers was used to create the final prediction model. Two separate models were also created to predict the chance of ECMO among cardiac surgery patients and non-cardiac patients.

### 2.3.2. Model validation

A 10-fold internal cross-validation approach was used to validate each of the predictive models. The data were split randomly into 10 groups. In each iteration, 9 of the 10 groups were combined and used as the sample to create the score (training sample). The model thus created was assessed for accuracy on the remaining subset. This process

was repeated 10 times so that each of the 10 subsets of data were used for validation. The discriminative ability of the model was assessed by averaging the area under the receiver operating characteristic curve over the 10 validation samples.

### 2.3.3. General considerations

Patient and center variables were summarized using median and quartiles for continuous variables and frequency and percentage for categorical variables. A Wilcoxon rank sum test was used to compare continuous variables between two groups, whereas a chi-squared test was used for categorical variables. We created an online tool with R Shiny to allow users to compute the probability of ECMO deployment in an individual patient [10]. We also provided an integer score for each variable for ease of computation. This was done by scaling the absolute value of the regression coefficient from the final prediction model and rounding up to the nearest integer. All statistical tests were two-sided, assuming a significance level of 5%. All analyses were done using the software package R (R Core Team, Vienna, Austria), SAS/STAT® (SAS Institute Inc., Cary, NC), or JMP® Pro 13 (SAS Institute Inc.).

## 3. Results

Of the 538,202 ICU patients from 140 VPS-participating ICUs, ECMO was deployed in 3484 patients (0.6%) with a mortality of 1450 patients (41.6%). Among the ECMO patients, veno-arterial ECMO was deployed in 2629 patients (75.4%), with a mortality of 1162 patients (44.2%), and veno-venous ECMO was deployed in 727 patients (20.8%), with a mortality of 219 patients (30.1%). The majority of patients receiving ECMO were children with heart disease (2313 patients, 66.4%) and children <1 year of age (2181 patients, 62.6%). Patient and center characteristics are presented in Supplemental Table 1.

We performed logistic regression analysis using adaptive lasso methodology with Akaike Information Criteria validation to select independent factors associated with ECMO deployment in critically ill children (Table 1). The independent factors associated with the increased probability of ECMO use included: younger age, pulmonary hypertension, high PIM-2 score at ICU admission, congenital heart disease, cardiac surgery during hospital admission, cardiomyopathy or myocarditis, acute lung injury, shock, renal failure, cardiac arrest, use of nitric oxide, and use of either CMV or HFOV. We noted that higher center volume (that is, more ECMO cases per year) was associated with the increased use of ECMO. Conversely, factors associated with the decreased probability of ECMO use included: failure to thrive; chromosomal anomaly; trauma; and certain diagnoses such as gastrointestinal diagnosis, injury or poisoning, and neurological diagnosis. The area under the receiver operating curve was 0.90 (95% CI: 0.85–0.93) (calculated for this model using a 10-fold internal cross-validation approach), suggesting excellent discriminative ability for this novel tool (Supplemental Fig. 1).

We then used a variable selection model to select independent factors associated with ECMO use in children undergoing cardiac surgery (Table 2). The factors associated with increased probability of ECMO deployment included: younger age, lower weight, increased complexity of heart operation (as demonstrated by higher STAT category [Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery]), high PIM-2 score after heart operation, cardiomyopathy, acute lung injury, shock, renal failure, cardiac arrest, use of nitric oxide, and use of either CMV or HFOV. We noted that higher center volume (more ECMO cases per year) and the presence of 24/7 ICU attending-physician coverage were also associated with the increased use of ECMO. We also used a variable selection model to select independent factors associated with ECMO use among non-cardiac patients (Table 3). The majority of the factors associated with ECMO use in this model were similar to the previous models.

**Table 1**  
Lasso variable selection model predicting use of ECMO Among All Patients (Cardiac and Non-Cardiac).

Variable	Comparison	Coefficient	Odds Ratio (95% CI)	P	Score
Intercept		−9.2202			
Male gender	vs. Female	−0.07378	0.92 (0.85, 1.01)	0.06	−1
Age					
1–8 years	vs. < 1 year	−0.5032	0.60 (0.54, 0.66)	<0.0001	−9
9–18 years	vs. < 1 year	−0.4422	0.64 (0.57, 0.72)	<0.0001	−8
Race/Ethnicity					
African American	vs. White	−0.03032	0.97 (0.86, 1.08)	0.58	−1
Other race	vs. White	−0.02087	0.97 (0.87, 1.09)	0.72	0
Hispanic	Yes vs. No	−0.0569	0.94 (0.83, 1.07)	0.38	−1
Developmental delay	Yes vs. No	−0.4213	0.65 (0.57, 0.75)	<0.0001	−7
Chromosomal anomaly	Yes vs. No	−0.4367	0.64 (0.52, 0.79)	<0.0001	−8
Pulmonary hypertension	Yes vs. No	0.5504	1.73 (1.54, 1.94)	<0.0001	10
Congenital heart disease	Yes vs. No	0.2997	1.34 (1.19, 1.52)	<0.0001	5
PIM-2 score	1 unit increase	0.1427	1.15 (1.12, 1.17)	<0.0001	3
Diagnosis category					
Cardiovascular	vs. Respiratory	0.182	1.19 (1.03, 1.38)	0.01	3
Endocrinologic	vs. Respiratory	−0.7046	0.49 (0.18, 1.34)	0.1673	−12
Gastrointestinal	vs. Respiratory	−1.2773	0.27 (0.17, 0.44)	<0.0001	−22
Infectious	vs. Respiratory	0.1619	1.17 (0.98, 1.39)	0.06	3
Metabolic/Genetic	vs. Respiratory	−0.9791	0.37 (0.18, 0.76)	0.007	−17
Hematologic/Oncologic	vs. Respiratory	−0.01178	0.98 (0.54, 1.81)	0.96	0
Renal/Genitourinary	vs. Respiratory	−1.087	0.33 (0.17, 0.65)	0.001	−19
Transplant	vs. Respiratory	0.2299	1.25 (0.72, 2.18)	0.41	4
Neurologic	vs. Respiratory	−1.9381	0.14 (0.09, 0.21)	<0.0001	−34
Injury/Poisoning	vs. Respiratory	−0.6819	0.50 (0.37, 0.67)	<0.0001	−12
Other	vs. Respiratory	0.1699	1.18 (1.01, 1.37)	0.02	3
Trauma	Yes vs. No	−1.0756	0.34 (0.24, 0.47)	<0.0001	−19
Cardiac surgery	Yes vs. No	0.4628	1.58 (1.39, 1.80)	<0.0001	8
Cardiomyopathy	Yes vs. No	1.14	3.12 (2.68, 3.64)	<0.0001	20
Acute lung injury	Yes vs. No	0.2071	1.23 (1.11, 1.35)	<0.0001	4
Sepsis	Yes vs. No	0.1386	1.14 (0.99, 1.32)	0.06	2
Shock	Yes vs. No	0.6812	1.97 (1.76, 2.21)	<0.0001	12
Renal failure	Yes vs. No	1.2758	3.58 (3.21, 3.98)	<0.0001	22
Cardiac arrest	Yes vs. No	1.6876	5.41 (4.93, 5.92)	<0.0001	30
Use of nitric oxide	Yes vs. No	1.4562	4.28 (3.88, 4.74)	<0.0001	26
Mechanical ventilation					
CMV	vs. None	3.1408	23.13 (17.54, 30.47)	<0.0001	55
HFOV	vs. None	4.9326	138.74 (103.51, 185.97)	<0.0001	87
Annual ECMO cases	5 case increase	0.6735	1.96 (1.69, 2.27)	<0.0001	12

Abbreviations: PIM-2: Pediatric Index of Mortality; ECMO: extracorporeal membrane oxygenation; CMV: conventional mechanical ventilation; HFOV: high frequency oscillatory ventilation. An online calculator for the tool can be accessed at: <https://soipredictiontool.shinyapps.io/ECMORisk/>

#### 4. Discussion

Here, we used multi-institutional data and advanced statistical tools to develop a real-time prediction tool to predict the probability of ECMO deployment in children with cardiac or pulmonary failure. This tool, composed of patient demographics and baseline characteristics, patient diagnoses, and data related to resource utilization, has a high degree of discrimination for predicting ECMO deployment during a hospital stay. All of the variables used in our tool are easily accessible and are consistent with prior analyses of predictors associated with ECMO deployment in critically ill children. In an ICU setting, these patients' cases evolve quickly with the addition of new diagnoses and procedures. Some of these diagnoses (shock, head trauma, stroke, etc.) and/or procedures (cardiopulmonary resuscitation, ECMO, HFOV, cardiac surgery, etc.) can have a significant impact on the patient's clinical status and often require families and care-providers to make stressful critical decisions about further interventions (such as the need for ECMO). Our real-time prediction tool, which is derived from real-life observational data, allows physicians and families to understand the impact of specific diagnoses or interventions on the need for ECMO deployment and to form realistic goals and expectations for a child in the ICU. This tool also allows physicians to deploy ECMO in a timely manner, ensuring the best possible outcome.

Recently, Barbaro et al. and Bailly et al. used data from the ELSO registry to develop risk adjustment tools to predict mortality among patients receiving ECMO [5–7]. Barbaro et al. proposed the Neonatal Risk Estimate Score for Children using Extracorporeal Respiratory Support (Neo-RESCUERS) to predict the risk of in-hospital death for neonates prior to receiving ECMO support (5). In another study, Barbaro et al. proposed the Pediatric Risk Estimation Score for Children Using Extracorporeal Respiratory Support (Ped-RESCUERS) to estimate the risk of in-hospital death for children prior to receiving ECMO support [6]. Bailly et al. proposed Pediatric Pulmonary Rescue with Extracorporeal Membrane Oxygenation Prediction Score (P-PREP) to predict mortality at the time of ECMO initiation for children with respiratory failure [7]. However, none of these tools could predict if someone should receive ECMO; this is because they were developed with data on ELSO patients who all received ECMO. To our knowledge, our tool is the first to predict the probability of ECMO deployment in critically ill children, as it contains all critically ill patients (ECMO and non-ECMO) admitted to 140 pediatric ICUs over a period of 6 consecutive years.

Most of the factors associated with ECMO deployment in critically ill children included indications mentioned in the ELSO guidelines (such as younger age, pulmonary hypertension, congenital heart disease, high complexity cardiac surgery, cardiomyopathy, acute lung injury, shock, renal failure, cardiac arrest, use of nitric oxide, and use of either CMV

**Table 2**  
Lasso Variable Selection Model Predicting Use of ECMO Among Patients Undergoing Cardiac Surgery.

Variable	Comparison	Coefficient	Odds Ratio (95% CI)	P	Score
Intercept		−6.965			
Age					
1–8 years	vs. < 1 year	−0.2246	0.79 (0.61, 1.03)	0.08	−3
9–18 years	vs. < 1 year	0.3086	1.36 (0.71, 2.59)	0.34	4
Weight	1 kg increase	−0.01536	0.98 (0.97, 0.99)	0.02	0
Race/Ethnicity					
African American	vs. White	0.06318	1.06 (0.86, 1.31)	0.55	1
Other race	vs. White	0.0846	1.08 (0.89, 1.32)	0.87	1
Hispanic	Yes vs. No	0.01764	1.01 (0.81, 1.27)	0.39	0
Pulmonary hypertension	Yes vs. No	−0.2759	0.75 (0.59, 0.96)	0.02	−3
Congenital heart disease	Yes vs. No	0.1578	1.17 (0.76, 1.78)	0.46	2
Single ventricle anatomy	Yes vs. No	0.03617	1.03 (0.81, 1.31)	0.76	0
PIM-2 score	1 unit increase	0.1562	1.16 (1.11, 1.22)	<0.0001	2
Diagnosis category					
Cardiovascular	vs. Respiratory	−0.3221	0.72 (0.44, 1.19)	0.21	−4
Infectious	vs. Respiratory	−0.1458	0.86 (0.28, 2.63)	0.79	−2
Metabolic/Genetic	vs. Respiratory	0.1277	1.13 (0.11, 12.1)	0.91	2
Renal/Genitourinary	vs. Respiratory	−1.0367	0.35 (0.02, 6.23)	0.47	−12
Transplant	vs. Respiratory	−0.8588	0.42 (0.03, 5.03)	0.49	−10
Injury/Poisoning	vs. Respiratory	−0.5487	0.57 (0.06, 5.23)	0.62	−6
Other	vs. Respiratory	−0.459	0.63 (0.31, 1.31)	0.21	−5
Trauma	Yes vs. No	−0.4982	0.61 (0.17, 2.08)	0.42	−6
Cardiomyopathy	Yes vs. No	0.4282	1.53 (1.03, 2.26)	0.03	5
Acute lung injury	Yes vs. No	0.2302	1.25 (1.06, 1.48)	0.006	3
Sepsis	Yes vs. No	0.158	1.17 (0.86, 1.58)	0.31	2
Shock	Yes vs. No	0.8436	2.32 (1.89, 2.85)	<0.0001	10
Renal failure	Yes vs. No	1.5817	4.86 (3.99, 5.91)	<0.0001	19
Cardiac arrest	Yes vs. No	2.5082	12.28 (10.52, 14.32)	<0.0001	30
Use of nitric oxide	Yes vs. No	1.3068	3.69 (3.14, 4.33)	<0.0001	15
STAT category					
STAT category 2	vs. STAT Category 1	0.6527	1.92 (1.43, 2.56)	<0.0001	8
STAT category 3	vs. STAT Category 1	0.892	2.43 (1.81, 3.30)	<0.0001	11
STAT category 4	vs. STAT Category 1	1.223	3.39 (2.58, 4.46)	<0.0001	14
STAT category 5	vs. STAT Category 1	1.9853	7.28 (5.38, 9.85)	<0.0001	23
Mechanical ventilation					
CMV	vs. None	1.4901	4.43 (2.66, 7.38)	<0.0001	18
HFOV	vs. None	3.0048	20.18 (10.84, 37.56)	<0.0001	36
Center characteristics					
Annual ECMO cases	1 case increase	0.06359	1.06 (1.03, 1.10)	0.0002	1
24/7 coverage	Yes vs. No	0.098	1.10 (0.69, 1.74)	0.67	1

Abbreviations: PIM-2: Pediatric Index of Mortality; ECMO: Extracorporeal Membrane Oxygenation; CMV: Conventional Mechanical Ventilation; HFOV: High Frequency Oscillatory Ventilation; STAT: Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery. An online calculator for the tool can be accessed at: <https://soipredictiontool.shinyapps.io/ECMORisk/>

or HFOV) [2]. We also noted that center-level factors were important predictors of ECMO deployment. In our study, higher center volume (more ECMO cases per year) and the presence of residency or fellowship training were associated with higher odds of ECMO deployment. It is known that center-level factors play an important role in predicting outcomes for critically ill children [13,14].

Surprisingly, patients with development delays or chromosomal anomalies experienced lower odds of ECMO deployment, and the exact reasons for this are not known. It is possible that these pre-existing conditions dissuaded some physicians and/or families from placing these patients on ECMO. However, recent studies have shown that ECMO can be used in children with genetic syndromes with good results [11,12]. In the recent times, life expectancy and treatment for non-cardiovascular morbidities in patients with various syndromes have improved. Outcomes for patients undergoing congenital heart disease surgery in these patients have also improved, because of refinements in surgical techniques and because of improvements in perioperative care. Given the fact that treatment options for the underlying cardiovascular and non-cardiovascular abnormalities in these patients are improving, ECMO should not be a contraindication for this patient population.

Our study has several limitations. Its retrospective nature renders it susceptible to study design flaws and bias. Although we attempted to adjust for important risk factors, our dataset may have lacked important variables that could have improved our prediction model. Because our data represent retrospective evaluations from a multicenter database, our analysis may have been limited by site compliance and validation across multiple sites. However, the VPS database uses consistent definitions, electronic automated data feedback, and a rigorous centralized abstractor certification process for data abstractors that may have potentially mitigated these shortcomings. Despite these shortcomings, we used multicenter data from 140 ICUs from the most recent years (2009–2015) to create this tool, increasing its generalizability.

Our tool was derived using a dataset that did not include patients from neonatal ICUs. Even though the data used to create the prediction tool included neonates, it is possible that this tool might not be specific and sensitive enough to predict deployment of ECMO for cases that are common in neonatal ICUs (meconium aspiration, diaphragmatic hernia, etc.). Moreover, our study did not address creation of separate tools in patients receiving veno-arterial ECMO and veno-venous ECMO. Another potential shortcoming of our study is that the dataset used to develop our tool was also used to validate it. We, therefore, recommend validating

**Table 3**  
Lasso Variable Selection Model Predicting Use of ECMO Among Non-Cardiac Patients Only.

Variable	Comparison	Coefficient	Odds Ratio (95% CI)	P	Score
Intercept		−11.1165			
Male gender	vs. Female	−0.07011	0.93 (0.81, 1.06)	0.31	−1
Age					
1–8 years	vs. < 1 year	−0.4672	0.62 (0.52, 0.74)	<0.0001	−7
9–18 years	vs. < 1 year	−0.3878	0.67 (0.50, 0.91)	0.01	−6
Weight	1 kg increase	0.00492	1.01 (1.00, 1.02)	0.04	0
Race/Ethnicity					
African American	vs. White	−0.03649	0.96 (0.80, 1.15)	0.69	−1
Other race	vs. White	0.09324	1.09 (0.89, 1.33)	0.35	1
Hispanic	Yes vs. No	−0.2314	0.79 (0.63, 0.99)	0.04	−3
Developmental delay	Yes vs. No	−0.5673	0.56 (0.43, 0.73)	<0.0001	−8
Chromosomal anomaly	Yes vs. No	−1.2361	0.29 (0.15, 0.54)	0.0001	−18
Pulmonary hypertension	Yes vs. No	1.5864	4.88 (3.97, 6.01)	<0.0001	23
PIM-2 score	1 unit increase	0.1471	1.15 (1.11, 1.20)	<0.0001	2
Diagnosis category					
Endocrinologic	vs. Respiratory	−0.346	0.70 (0.24, 2.01)	0.51	−5
Gastrointestinal	vs. Respiratory	−1.2835	0.27 (0.15, 0.48)	<0.0001	−18
Infectious	vs. Respiratory	0.2941	1.34 (1.09, 1.65)	0.0056	4
Metabolic/Genetic	vs. Respiratory	−0.8043	0.44 (0.16, 1.24)	0.12	−11
Hematologic/Oncologic	vs. Respiratory	0.2132	1.23 (0.63, 2.39)	0.52	3
Renal/Genitourinary	vs. Respiratory	−1.2637	0.28 (0.11, 0.72)	0.008	−18
Transplant	vs. Respiratory	−1.2529	0.28 (0.09, 0.86)	0.02	−18
Neurologic	vs. Respiratory	−1.7892	0.16 (0.11, 0.25)	<0.0001	−26
Injury/Poisoning	vs. Respiratory	−0.6339	0.53 (0.38, 0.74)	0.0002	−9
Other	vs. Respiratory	−0.0918	0.91 (0.75, 1.10)	0.35	−1
Trauma	Yes vs. No	−0.8568	0.42 (0.28, 0.62)	<0.0001	−12
Acute lung injury	Yes vs. No	0.2571	1.29 (1.06, 1.56)	0.009	4
Sepsis	Yes vs. No	0.3456	1.41 (1.11, 1.78)	0.004	5
Shock	Yes vs. No	0.376	1.45 (1.16, 1.81)	0.0008	5
Renal failure	Yes vs. No	0.9086	2.48 (2.06, 2.98)	<0.0001	13
Cardiac arrest	Yes vs. No	0.9945	2.71 (2.27, 3.21)	<0.0001	14
Use of nitric oxide	Yes vs. No	1.7013	5.48 (4.52, 6.64)	<0.0001	24
Mechanical ventilation					
CMV	vs. None	3.9912	54.11 (31.79, 92.12)	<0.0001	57
HFOV	vs. None	6.0828	438.26 (252.79, 759.81)	<0.0001	87
Center characteristics					
Training program	Yes vs. No	0.8988	2.45 (1.09, 5.52)	0.03	13
24/7 coverage	Yes vs. No	−0.07136	0.93 (0.56, 1.53)	0.78	−1
Annual ECMO cases	5 case increase	0.8367	2.30 (1.87, 2.84)	<0.0001	12

Abbreviations: PIM-2: Pediatric Index of Mortality; ECMO: extracorporeal membrane oxygenation; CMV: conventional mechanical ventilation; HFOV: high frequency oscillatory ventilation; STAT: Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery. An online calculator for the tool can be accessed at: <https://soipredictiontool.shinyapps.io/ECMORisk/>

this tool in a different multi-institutional dataset. We believe that there is an opportunity to improve the model discrimination with additional clinical data. We further recommend that this proposed tool be validated over time for continued reproducibility. Like other prediction models, our tool could be subject to drift and require frequent modifications.

## 5. Conclusions

To our knowledge, this prognostic tool is the first to predict, in real-time, ECMO deployment in children with acute severe cardiac or pulmonary failure that is potentially reversible and unresponsive to conventional management. The newly proposed prediction tool, composed of patient demographics and baseline characteristics, patient diagnoses, and data related to resource utilization, has a high degree of discrimination for predicting ECMO deployment during a hospital stay. Like other prediction models, our tool may require frequent modifications because of drift. Future studies should seek external validation and improved discrimination of this prediction tool.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jccr.2018.10.007>.

## References

- [1] Kuo KW, Barbaro RP, Gadepalli SK, Davis MM, Bartlett RH, Odetola FO. Should Extracorporeal Membrane Oxygenation be Offered? An International Survey. *J Pediatr* 2017;182:107–13.
- [2] ELSO General Guidelines. Patient care practice guidelines. Ann Arbor, Michigan: extracorporeal life support organization; 2013. Link: <https://www.elseo.org/resources/guidelines.aspx>. Accessed: April 30, 2018.
- [3] Gupta P, Chakraborty A, Gossett JM, Rettiganti M. A Prognostic Tool to Predict Outcomes in Children Undergoing the Norwood Operations. *J Thorac Cardiovasc Surg* 2017;154(6):2030–7.
- [4] Gupta P, Rettiganti M, Gossett JM, Daufeldt J, Rice TB, Wetzel RC. Development and Validation of an Empiric Tool to Predict favorable Neurologic Outcomes among Pediatric ICU patients. *Crit Care Med* 2018;46(1):108–15.
- [5] Barbaro RP, Bartlett RH, Chapman RL, Paden ML, Roberts LA, Gebremariam A, et al. Development and validation of the neonatal risk estimate score for children using extracorporeal respiratory support. *J Pediatr* 2016;173:56–61.
- [6] Barbaro RP, Boonstra PS, Paden ML, Roberts LA, Annich GM, Bartlett RH, et al. Development and validation of the pediatric risk estimate score for children using extracorporeal respiratory support (Ped-RESCUERS). *Intensive Care Med* 2016;42:879–88.
- [7] Bailly DK, Reeder RW, Zabrocki LA, Hubbard AM, Wilkes J, Bratton SL, et al. Extracorporeal Life support Organization Member Centers. Development and Validation of a score to Predict Mortality in Children Undergoing Extracorporeal Membrane Oxygenation for respiratory failure: Pediatric Pulmonary rescue with Extracorporeal Membrane Oxygenation Prediction score. *Crit Care Med* 2017;45(1):e58–66.
- [8] VPS, LLC Database. Available at <http://www.myvps.org>. Accessed date: 30 April 2018.
- [9] Zou H. The adaptive lasso and its oracle properties. *J Am Stat Assoc* 2006;101:1418–29.
- [10] Chang W, Cheng J, Allaire JJ, Shiny: Web application Framework for R. R package version 0.14.1. Available at <https://CRAN.R-project.org/package=shiny>; Accessed: January 31, 2018.
- [11] Gupta P, Gossett JM, Rycus PT, Prodhon P. Extracorporeal Membrane Oxygenation in Children with Heart Disease and down Syndrome: a Multicenter Analysis. *Pediatr Cardiol* 2014;35(8):1421–8.
- [12] Prodhon P, Gossett JM, Rycus PT, Gupta P. Extracorporeal Membrane Oxygenation in Children with Heart Disease and del22q11 Syndrome: a Review of the Extracorporeal Life support Organization Registry. *Perfusion* 2015;30(8):660–5.
- [13] Gupta P, Rettiganti M. Association between Extracorporeal Membrane Oxygenation Center volume and Mortality among Children with Heart Disease: Propensity and Risk Modeling. *Pediatr Crit Care Med* 2015;16(9):868–74.
- [14] Freeman CL, Bennett TD, Casper TC, Freeman CL, Bennett TD, Casper TC. Pediatric and neonatal extracorporeal membrane oxygenation: does center volume impact mortality? *Crit Care Med* 2014;42(3):512–9.