

1 **Identification of Early Risk Factors for Mortality in Pediatric Venous-Arterial Extra Corporeal**

2 **Membrane Oxygenation: The Patient Matters**

3 Bennett Weirnerman, MD^{1,2}, Soon Bin Kwon, PhD^{1,3*}, Tammam Alalqum, BS^{1,3}, Daniel Nametz, BS^{1,3},
4 Murad Megjhani, PhD^{1,3}, Eunice Clark, MSN, RN, FNP-C⁴, Caleb Varner⁵, Eva W. Cheung, MD¹, Soojin
5 Park, MD^{1,3,6,7}

6

7 ¹ Program for Hospital and Intensive Care Informatics, Department of Neurology, Columbia University
8 Vagelos College of Physicians and Surgeons, New York, USA

9 ² Department of Pediatrics, Division of Critical Care & Hospital Medicine, Columbia University Vagelos
10 College of Physicians and Surgeons and New York-Presbyterian Morgan Stanley Children's Hospital,
11 New York, USA

12 ³ Department of Neurology, Columbia University Vagelos College of Physicians and Surgeons, New York,
13 USA

14 ⁴ Department of Nursing, New York-Presbyterian Morgan Stanley Children's Hospital, New York, USA

15 ⁵ Department of Perfusion, New York-Presbyterian Morgan Stanley Children's Hospital, New York, USA

16 ⁶ New York-Presbyterian Hospital, Columbia University Irving Medical Center, New York, USA

17 ⁷ Department of Biomedical Informatics, Columbia University, New York, USA

18

19 * Co-First Authors

20

21 **Corresponding Author:**

22 Soojin Park MD

23 sp3291@cumc.columbia.edu

24 710 West 168th Street

25 New York, NY 10032

26 (212) 305-7236 phone

27 (212) 305-2792 fax

28

29 Soon Bin Kwon: Sk4984@cumc.columbia.edu

30 Tammam Alalqum: Ta2767@cumc.columbia.edu

31 Daniel Nametz: Dcn2123@cumc.columbia.edu

32 Murad Megjhani: Mm5025@cumc.columbia.edu

33 Eunice Clark: Euc9002@nyp.org

34 Caleb Varner: cv2541@cumc.columbia.edu

35 Eva Cheung: Ec2335@cumc.columbia.edu

36 Soojin Park: Sp3291@cumc.columbia.edu

37

38 Word Count: 2,739

39

40 **Disclosures:**

41 Soojin Park is supported by the National Institutes of Health (1R01NS131606, 1R01NS129760). Murad

42 Megjhani is supported by the America Heart Association (20Post35210653).

43

44 **ABSTRACT:**

45 **Objective:** Pediatric Venous-Arterial Extra Corporeal Membrane Oxygenation (VA ECMO) is a life saving
46 technology associated with high mortality. A successful VA ECMO course requires attention to multiple
47 aspects of patient care, including ECMO and patient parameters. Early, potentially modifiable, risk factors
48 associated with patient mortality should be analyzed and adjusted for when assessing VA ECMO risk
49 profiles.

50 **Method:** Retrospective single center experience of pediatric patients requiring VA ECMO from January
51 2021 to October 2023. Laboratory and ECMO flow parameters were extracted from the patients record
52 and analyzed. Risk factors were analyzed using a Cox proportion hazard regression

53 **Main Results:** There were 45 patients studied. Overall survival was 51%. Upon uncorrected analysis
54 there were no significant differences between the patients who survived and those who died. Utilizing a
55 Cox proportion hazard regression, platelet count, fibrinogen level and creatine level were significant risk
56 factors within the first twenty-four hours of a patient's ECMO course.

57 **Significance:** Although we did not find a significant difference among ECMO flow parameters in this
58 study, this work highlights that granular ECMO flow data can be incorporated to risk analysis profiles and
59 potential modeling in pediatric VA ECMO. This study demonstrated, that when controlling for ECMO
60 flow parameters, kidney dysfunction and clotting regulation remain key risk factors for pediatric VA
61 ECMO mortality.

62
63 **Introduction**

64 Extra Corporeal Membrane Oxygenation (ECMO) was first introduced as a viable medical therapy in the
65 1970s in the setting of severe acute respiratory distress syndrome (ARDS) (1). Since that time, ECMO
66 has undergone major refinement, leading to increased utilization and improved outcomes. Venous-Arterial
67 ECMO (VA-ECMO) treats patients who are often on the brink of viable physiology, and thus are at
68 extremely high risk of mortality. VA ECMO is increasingly implemented in pediatric patients, with
69 mortality improving over the past decades with current literature citing a mortality around 40-60% (2-7).

70
71 Decisions regarding goals of care are often clouded by the inability of the clinical team to provide
72 accurate prognostic information. Accurate risk factors for poor outcomes allow the clinical team to have
73 more informed conversations with care givers. Studies have tried to predict which patients will have
74 better outcomes after implementation of ECMO support. Several adult studies have leveraged machine
75 learning algorithms (8-10); however, these models largely rely on registry data(11). Many pediatric
76 ECMO research studies have found that age, gender, the development of renal or hepatic dysfunction
77 were associated with mortality. Other groups who have included more diverse pediatric patient

78 populations have found that lactate, pH (both before and after cannulation), as well as, renal dysfunction,
79 including use of continuous renal replacement, and active cannulation during cardiopulmonary
80 resuscitation (eCPR) are associated with mortality(4-6, 12, 13). Other variables, such as single-ventricle
81 physiology, location of patient cannulation and length of ECMO run are often, but not always, cited as
82 significant risk factors(6, 12). Novel non-invasive metrics, like echocardiographic studies have also been
83 associated with pediatric ECMO survival (3). Notably, these studies do not rigorously analyze the ECMO
84 derived flow parameters for each patient.

85
86 A successful VA-ECMO run requires attention to detail from multifaceted team members. There are
87 multiple technical as well as patient and ECMO physiologic variables that must be continuously adjusted
88 for optimal outcomes. This retrospective observational cohort study investigated routinely collected
89 laboratory data, as well as ECMO flow data within the first 24 hours of the ECMO run to determine
90 whether to elucidate early risk factors for patient mortality once on VA ECMO. Our aim was to focus on
91 early metrics with a goal of minimizing confounding variables.

92

93 **Methods**

94 *Study Population*

95 This is a retrospective observational cohort study at a single academic institution with both a neonatal and
96 pediatric cardiac intensive care unit. Pediatric patients who were treated with VA ECMO between January
97 2021 and October 2023 were included. Location of cannulation included operating room, PICU, Neonatal
98 Intensive Care Unit (NICU) and in other hospital locations (i.e. cardiac catheterization lab) were
99 recorded. The underlying indication for the patient's decompensation, necessitating the need for VA
100 ECMO, was extracted from their medical records based on progress notes. Patients were excluded from
101 analysis based on the following criteria: (1) ECMO run lasting less than 24 hours; (2) multiple ECMO
102 runs; (3) single-ventricle anatomy; (4) missing data due to cannulation location or incomplete data. The
103 Columbia University IRB committee approved this research study (Protocol # AAAU5398). Research
104 was conducted in accordance with the principles embodied in the Declaration of Helsinki and in
105 accordance with local statutory requirements. This study was a non-treatment, retrospective, observational
106 review of physiologic and ECMO data that was obtained as part of routine standard of care, and the IRB
107 approved a waiver of informed consent.

108 *ECMO Circuit*

109 Our institution performs 40-50 VA ECMO runs per year. ECMO cannulation was performed by a member
110 of the Pediatric Cardiothoracic Surgery or Pediatric General Surgery Team. Central or peripheral
111 cannulation was at the discretion of the surgical team based on the timing of the most recent sternotomy.

112 ECMO support was provided by the Cardiohelp ECMO system from Getinge (Göteborg, Sweden), with
113 either a 5.0 oxygenator for patients <19kg or the 7.0 oxygenator for children >19kg. A perfusionist
114 adjusted the ECMO settings in consultation with the clinical team. Our hospital does not have a protocol
115 or pathway for weaning ECMO support. Anti-coagulation was adjusted per institution protocol based on
116 bleeding and non-bleeding conditions.

117 Data Collection

118 Physiologic data was collected by the bedside monitor as part of routine standard of care. ECMO flow
119 data was retrospectively extracted from the Spectrum module (Gloucester, UK) at a sampling frequency
120 of 0.016Hz or 1 sample per minute. The first 24-hours of data after ECMO cannulation were included for
121 analysis. The start of the ECMO run was defined as the time that ECMO parameters were output from the
122 Spectrum data file. This date and time stamp was corroborated with our internal ECMO database to
123 ensure validity. ECMO Flow data consisted of Arterial Flow, Delta Pressure, Fractional Delivery of
124 Oxygen (FDO₂), Arterial Pressure, Venous Pressure, Cardiac Index (CI), Revolutions Per Minute (RPM),
125 SaO₂, SpO₂, SvO₂, and Sweep. Laboratory data included Hemoglobin, Hematocrit, Platelet Count,
126 Arterial pH, Arterial partial pressure of carbon dioxide (paCO₂), arterial bicarbonate (HCO₃), Creatinine,
127 Fibrinogen, Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), and plasma free
128 hemoglobin.

129 Statistical Analysis

130 All data analyses were performed using MATLAB 2020a (MathWorks, Massachusetts). For each patient,
131 the average value was calculated over the 24-hour period of the ECMO run for each variable. For each
132 group (i.e. Deceased or Survived), an average was calculated. Students' *t*-test with a significance level of
133 ≤ 0.05 was performed to compare the difference between the two groups. For demographic and baseline
134 characteristics between the two groups, continuous variables were compared using a non-paired Student's
135 *t*-test, assuming heterogenous variance. Categorical variables were compared using Fisher's exact test, or
136 Chi-squared test when appropriate with a significance level of ≤ 0.05 . Cox proportion hazard regression
137 was performed to identify risk factors for 180-day mortality. Among the variables with high correlation,
138 only one variable was included to reduce bias introduced to the analysis. For example, for AST and ALT,
139 only AST was used. Similarly, only hematocrit was incorporated into the model from the choice of
140 hemoglobin or hematocrit. While it is recognized that pH, pCO₂ and sweep are all interconnected, given
141 their clinical significance, all three variables were included in the model. Similarly, RPM and CI were
142 both included in the regression given their clinical implications.

143 **Results**

144 There were 106 patients who were cannulated to VA-ECMO between January 2021 and October 2023.
145 Nine patients had multiple ECMO runs, and the 22 patients who had single ventricle anatomy were

146 removed from analysis. Seven, nine and fourteen patients had an ECMO run <24 hours, were cannulated
147 at an outside hospital and subsequently transferred to our institution or had missing data respectively, and
148 were removed from analysis. Of the remaining 45 patients 23 (51%) survived and 22 (49%) died. Twelve
149 (27%) patients were cannulated in the setting of respiratory indications, twenty-three (51%) were
150 cannulated for primarily cardiac indications and ten (22%) were cannulated in the setting of eCPR (**Table**
151 **1**).

152 The study included 23 (51%) females. The patients' ages ranged from birth (0 days) to 22 years old with
153 an average of 4.5 years old (54 months). The average patient's weight prior to cannulation was 16.9kg.
154 The average ECMO run was 182.78 hours. There was no significant difference in patient demographic
155 data comparing those who survived, versus those who died (**Table 1**).

156 Twenty-three patients were cannulated while in the PICU (51.1%). Fourteen patients were cannulated in
157 the NICU (31.1%). Six patients (13.3%) were cannulated in the operating room and two patients (4.4%)
158 were cannulated in the cardiac catheterization lab.

159 The most common diagnoses were pulmonary hypertension (8 patients), Valvular disease (5 patients),
160 Heart transplant complications (4 patients), congenital diaphragmatic hernia (4 patients), dilated
161 cardiomyopathy (3 patients), restrictive cardiomyopathy (3 patients), infection (2 patients), Tetralogy of
162 Fallot (2 patients) and Hypoplastic Left Heart (2 patients). For a complete breakdown of the entire cohort
163 please see *supplementary table 1*.

164 Lab values and ECMO flow data were averaged over the first 24-hour period of the ECMO run per
165 patient and then averaged for each cohort (survived or deceased). For the laboratory values within the first
166 24 hours of the ECMO run, the average ALT (Units/Liter) was 543.7 in those who survived compared to
167 455.9 in those who died ($p = 0.77$). The average fibrinogen (mg/dL) was 192.1 versus 151.11 ($p = 0.053$)
168 between the survivors and the deceased respectively. The average hematocrit (%) among the survivors
169 was 32.0 versus 31.2 in the deceased patients ($p=0.56$). The average platelet count ($\times 10^3/\mu\text{L}$) was 111.5
170 and 104.4 ($p = 0.68$) in the patients who survived versus those who died. Among survivors the average
171 creatinine (mg/dL) was 0.67 versus 1.01 ($p = 0.067$) in those who died. The average pH and paCO_2
172 (mmHg) was 7.34 and 41.7 in the survivors compared to 7.36 and 42.5 in those who died respectively,
173 with corresponding p - values of 0.56 and 0.64. The average lactate level (mmol/L) was 3.68 in survivors
174 and 4.16 ($p = 0.66$) in those patients who died (**Table 2**)

175 For the ECMO flow values the average CI ($\text{L}/\text{min}/\text{m}^2$) was 1.94 in survivors versus 2.13 in those who
176 died ($p = 0.073$). The corresponding average RPMs were 2708.2 compared to 2854.1 ($p = 0.21$) in those
177 patients who survived and those who died. The average ECMO sweep was 0.96 in the patients who
178 survived compared to 1.0 ($p = 0.87$) in those who lived. The FDO₂ of the ECMO circuit averaged 59.7
179 for patients who survived compared to 60.6 ($p = 0.88$) for patients who died. (**Figure 1**).

180 A Cox regression was run using the same variables above. The 180-day survival analysis is shown in
181 **Table 3**. After running the Cox survival analysis only three values were significant. For fibrinogen, the
182 Cox coefficient was -0.015, with a hazard ratio of 0.99 and a p value of 0.004. The corresponding 95th
183 percentile hazard ratio confidence interval ranged from 0.98 to 1.00. For creatinine the Cox coefficient
184 was 1.14 with a hazard ratio of 3.12 and a p value of 0.022. The 95th percentile hazard ratio confidence
185 interval ranged from 1.18 to 8.27 for Creatinine. The Cox coefficient for Platelet count was 0.011, with a
186 hazard ratio of 1.01 and a p value of 0.04. The 95th percentile hazard ratio confidence interval ranged from
187 1.00 to 1.02.

188 **Discussion**

189 Among patients requiring a singular run of VA ECMO we found a survival rate of 51%. This survival rate
190 is consistent with previously cited pediatric studies and congruent with data published by the ELSO
191 network (14-17). Our analysis was comprised of pediatric patients recovering after cardiac surgery as well
192 as patients admitted for other medical indications who subsequently required VA ECMO, including those
193 patients who required eCPR.

194 Within the first 24 hours of VA ECMO cannulation, we did not find any laboratory or ECMO parameter
195 that were significantly different among those patients who survived versus those who died. Upon using a
196 180-day Cox regression, we found that fibrinogen ($p = 0.004$), creatinine ($p = 0.02$) and platelet count (p
197 $= 0.04$) were significant risk factors associated with mortality within the first 24 hours of a patients
198 ECMO run.

199 Renal dysfunction and/or requiring continuous renal replacement therapy (CRRT) while on ECMO has
200 been reported as a significant risk factor for mortality (16, 18). Additionally, decreased urine output,
201 likely a measure of both end organ perfusion and ongoing nephrogenic insult has been cited as a risk
202 factor for pediatric VA ECMO mortality (15). Authors have gone on to stratify the degree of renal
203 dysfunction, based on the Kidney Disease Improving Global Outcome (KDIGO) definition, and its impact
204 on in-hospital mortality for patients requiring VA ECMO (17). Our findings suggest that the risk
205 associated with kidney disease is evident within the first 24 hours of a patients ECMO course; even while
206 controlling for the impact of other ECMO parameters.

207 Additionally, a patient's hematologic risk profile has been associated with mortality (19). We found that
208 platelet and fibrinogen levels are risk factors for patient survival. Interestingly, our data suggests that
209 higher fibrinogen levels may be slightly protective, evident by a hazard ratio less than 1. Conversely, a
210 higher platelet count was associated with a marginal increased risk of mortality. It is important to note the
211 complexity of the clotting cascade, and how both fibrinogen and platelet are impacted by systemic
212 inflammation, bleeding and the ECMO circuit itself. Our findings further highlight how critical
213 appropriate anti-coagulation is when managing pediatric VA ECMO (20-22).

214 We hoped to eliminate some confounding factors by focusing on the first 24 hours of a patient's ECMO
215 course, where ideally the ECMO oxygenator and tubing is relatively devoid of significant fibrin
216 deposition (19). However, we cannot account for the microscopic changes that occur at the blood-
217 oxygenator membrane(23-25), or the inflammatory changes that occur due to the presence of the ECMO
218 cannulations themselves (26). Unfortunately, within the first 24 hours of a patients ECMO run, we did not
219 have enough data to comment on the role of plasma free hemoglobin, or other clotting factors.
220 Additionally, our institution only uses centrifugal ECMO circuits, and the implication on roller versus
221 centrifugal systems is not addressed in our study.

222 Laboratory evidence of poor organ perfusion is frequently cited as being risk factors for patient mortality
223 while on ECMO. In our regression, we did not find hepatic enzymes (ALT), lactate or pH to be significant
224 (15, 17, 27). As we only looked at data within the first 24 hours, it is likely that some of these markers
225 would have become significant given a longer sampling window. We were unable to include the partial
226 pressure of oxygen (paO₂) as a laboratory parameter, given the uncertainty surrounding this lab value.
227 Given the retrospective nature of this study we were not able to determine if the paO₂ values were taken
228 from the patient or the ECMO circuit, and thus were not analyzed.

229 To our knowledge this is the first pediatric study to examine relatively high frequency ECMO variables in
230 conjunction with patient laboratory markers. Given the complexity of ECMO, we believe it is imperative
231 for retrospective studies to incorporate the impact that the ECMO circuit and ECMO parameters have on
232 the patient's survival; however, in our study, ECMO circuit parameters were not significant risk factors
233 within the first 24 hours. It seems clear to the practicing clinician, that the odds of survival are much
234 different for a child requiring a CI of 3.5 L/min/m² versus 1.5 L/min/m², or a sweep of 10 L/min versus a
235 sweep of 0.3 L/min, yet these variables were not significant during the first 24 hours of a patient's ECMO
236 course. This study further demonstrates that ECMO flow parameters can be captured and should be
237 controlled for, in any risk analysis. Additionally, we selected laboratory and ECMO parameters that are
238 frequently cited as being risk factors for patient outcomes. We decided to focus on the first 24 hours of a
239 patient's ECMO run, hoping to elucidate early modifiable risk factors that may change a patients'
240 outcome, while limiting other confounding variables.

241 This was a retrospective study of pediatric patients requiring VA ECMO and thus has limitations. We
242 included patients who were cannulated both centrally and peripherally, thus this study includes a
243 heterogeneous population. Furthermore, our institution does not have strict criteria as to which patients
244 get cannulated onto ECMO, thus there is even more heterogeneity based on the
245 anesthesiologist/intensivist and the surgeon involved in the cannulation. Our sample size is relatively
246 large for a single center; however, more patients would better elucidate the significance of each risk

247 factor. Additionally, we did not incorporate physiologic parameters in this analysis (i.e. heart rate, mean
248 arterial pressure etc.), which we hope to do in subsequent studies.

249 **Conclusion**

250 Over a 3-year period we analyzed 45 pediatric patients who were cannulated onto VA-ECMO with a 51%
251 survival rate. While there were no overt significant differences between the two groups, using a Cox
252 regression including key ECMO parameters, we found that creatinine, fibrinogen and platelet count are
253 key risk factors for patient mortality within the first 24 hours of a patient's ECMO run. Our data provide
254 evidence that maximal effort should be spent optimizing the patient, as none of the ECMO parameters
255 were significant risk factors for patient mortality.

256 The use of mechanical circulatory support is a complex and nuanced science that has provided lifesaving
257 therapy to a heterogenous population. For accurate and impactful prediction, it is necessary to capture as
258 many aspects of these patients' care as possible, including ECMO support parameters. We hope that with
259 more multifaceted, granular clinical data, we will be better able to arm the clinical team with accurate and
260 predictive information.

261

262

263

264

265

266

267

268

269

270

271

272

273

274

275

276

277

278

279

280

281 **Tables and Figures**

282 **Table 1:**

| | Total (45) | Survived (23) | Deceased (22) | p - value |
|-----------------------------|-----------------------|--------------------------|--------------------------|----------------------|
| Age at cannulation (months) | 54.0 | 48.81 | 59.47 | 0.66 |
| Gender (F:M) | 23:22 | 11:12 | 12:10 | 0.77 |
| Weight (kg) | 16.9 | 15.2 | 18.8 | 0.57 |
| Cannulation | | | | 0.75 |
| Central | 13 | 6 | 7 | |
| Peripheral | 32 | 17 | 15 | |
| Cannulation Location | | | | 1.00 |
| PICU | 23 | 12 | 11 | |
| NICU | 14 | 7 | 7 | |
| OR | 6 | 3 | 3 | |
| Cath Lab | 2 | 1 | 1 | |
| Indication | | | | 0.41 |
| Cardiac | 23 | 14 | 9 | |
| Respiratory | 12 | 5 | 7 | |
| eCPR | 10 | 4 | 6 | |
| Length of ECMO run (hours) | 182.79 | 178.18 | 187.60 | 0.85 |
| Diagnosis (Top 10) | | | | |
| pHTN | 8 | 6 | 2 | |
| Valvular Disease | 5 | 3 | 2 | |
| OHT Complication | 4 | 1 | 3 | |
| CDH | 4 | 3 | 1 | |
| DCM | 3 | 3 | 0 | |
| RCM | 3 | 2 | 1 | |
| Infection | 2 | 0 | 2 | |
| Tetralogy of Fallot | 2 | 2 | 0 | |
| HLH | 2 | 2 | 0 | |

283 **Table 1:** Demographic information for patients analyzed on Veno-Arterial Extracorporeal Membrane
284 Oxygenation. (PICU = Pediatric Intensive Care Unit, NICU = Neonatal Intensive Care Unit, OR =
285 Operating Room, Cath Lab = Cardiac Catheterization Laboratory, ECMO = Extracorporeal Membrane
286 Oxygenation, pHTN = Pulmonary Hypertension, OHT = Orthotopic Heart Transplant, CDH = Congenital
287 Diaphragmatic Hernia, DCM = Dilated Cardiomyopathy, RCM = Restrictive Cardiomyopathy, HLH =
288 Hemophagocytic Lymphohistiocytosis)

289

290

291

292

293

294 **Table 2:**

| Laboratory and ECMO flow Data Mean and Standard Deviation | | | |
|--|--------------------|--------------------|---------|
| | Survived (n=23) | Deceased (n=22) | p-value |
| Arterial pH | 7.34 (0.09) | 7.36 (0.06) | 0.56 |
| paCO ₂ (mmHg) | 41.73 (5.86) | 42.53 (5.42) | 0.64 |
| Lactate (mmoL/L) | 3.68 (3.5) | 4.16 (3.8) | 0.66 |
| Hematocrit (%) | 32.01 (4.9) | 31.22 (4.2) | 0.56 |
| Platelet (×10 ³ μL) | 111.5 (60.5) | 104.4 (55.3) | 0.68 |
| Fibrinogen (mg/dL) | 192.08 (79.8) | 151.11 (55.2) | 0.053 |
| Creatinine (mg/dL) | 0.67 (0.4) | 1.01 (0.8) | 0.067 |
| ALT (U/L) | 543.7 (1210.4) | 455.9 (659.0) | 0.77 |
| CI (L/min/m ²) | 1.94 (0.4) | 2.13 (0.3) | 0.073 |
| RPM | 2708.18 (317.2) | 2854.12 (443.6) | 0.21 |
| Sweep (L/min) | 0.96 (1.7) | 1.04 (1.7) | 0.87 |
| FDO ₂ | 59.69 (21.1) | 60.62 (19.8) | 0.88 |

295 **Table 2:** Averaged values and standard deviation for each patient cohort, survived versus deceased.
296 (paCO₂ = arterial partial pressure of carbon dioxide, ALT = alanine aminotransferase, CI = Cardiac Index,
297 RPM = Revolutions per Minute, FDO₂ = Fraction of Delivered Oxygen)
298

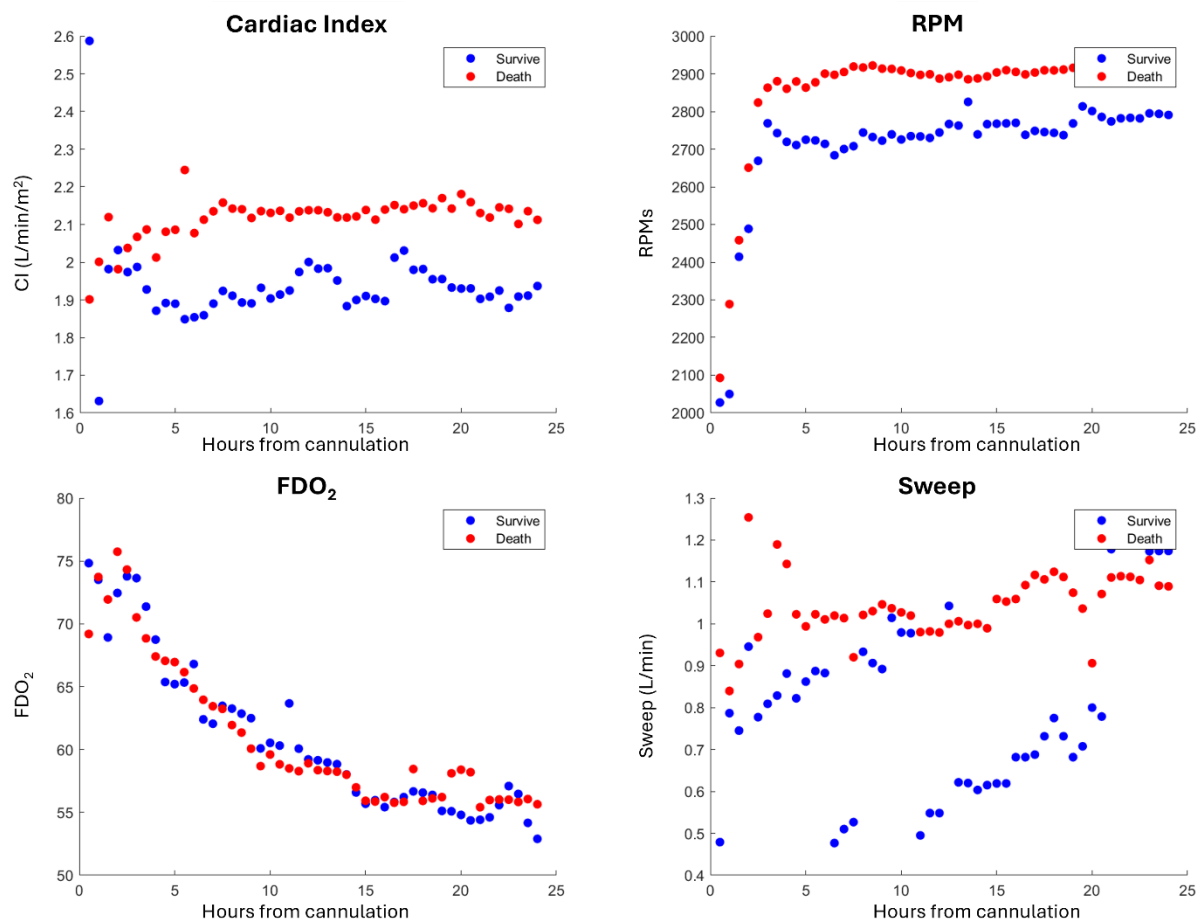
299
300
301
302
303
304
305
306
307
308
309
310
311
312
313
314

315 **Table 3:**

| | Coefficient | Hazard Ratio | p-value | Hazard Ratio 95% CI | |
|--------------------------------|-------------|--------------|---------|------------------------|--------|
| pH | 4.31 | 74.1 | 0.33 | 0.013 | 430761 |
| paCO ₂ (mmHg) | 0.027 | 1.03 | 0.50 | 0.95 | 1.11 |
| Lactate (mmol/L) | 0.14 | 1.14 | 0.15 | 0.95 | 1.38 |
| Hematocrit (%) | - 0.044 | 0.96 | 0.49 | 0.85 | 1.08 |
| Platelet (×10 ³ μL) | 0.011 | 1.01 | 0.04 | 1.00 | 1.02 |
| Fibrinogen (mg/dL) | - 0.015 | 0.99 | 0.004 | 0.98 | 1.00 |
| Creatinine (mg/dL) | 1.14 | 3.12 | 0.02 | 1.18 | 8.27 |
| ALT (U/L) | -0.0005 | 1.00 | 0.073 | 1.00 | 1.00 |
| CI (L/min/m ²) | 0.44 | 1.55 | 0.60 | 0.30 | 8.01 |
| RPM | 0.0007 | 1.00 | 0.47 | 1.00 | 1.00 |
| Sweep (L/min) | 0.017 | 1.02 | 0.95 | 0.58 | 1.79 |
| FDO ₂ | - 0.012 | 0.99 | 0.49 | 0.96 | 1.02 |

316 **Table 3:** Cox Hazard Coefficient and Hazard ratio for each variable analyzed between the two cohorts,
 317 survived versus deceased. (paCO₂ = arterial partial pressure of carbon dioxide, ALT = alanine
 318 aminotransferase, CI = Cardiac Index, RPM = Revolutions per Minute, FDO₂ = Fraction of Delivered
 319 Oxygen)

320 **Figure 1**



321

322 **Figure 1:** Averaged ECMO parameters every hour from time of ECMO cannulation, grouped on those
323 who survived versus those who died. CI = Cardiac Index, RPM = Revolutions per Minute, FDO₂ =
324 Fraction of Delivered Oxygen.

325

326

327

328

329

330

331

332

333

334

335

336

337 **Supplemental Table:**

| Diagnosis associated with ECMO Cannulation | Total Count | Survived | Deceased |
|--|-------------|----------|----------|
| Pulmonary Hypertension | 8 | 2 | 6 |
| Valvular Disease | 5 | 3 | 2 |
| Congenital Diaphragmatic Hernia | 4 | 3 | 1 |
| Heart Transplant Complication | 4 | 1 | 3 |
| Dilated Cardiomyopathy | 3 | 3 | 0 |
| Restrictive Cardiomyopathy | 3 | 2 | 1 |
| Tetralogy of Fallot | 2 | 2 | 0 |
| Infection | 2 | 0 | 2 |
| Hemophagocytic lymphohistiocytosis | 2 | 2 | 0 |
| Cardiac Mass | 1 | 1 | 0 |
| Heart Failure | 1 | 0 | 1 |
| Alveolar Capillary Dysplasia | 1 | 0 | 1 |
| Double Aortic Arch | 1 | 1 | 0 |
| Double Outlet Right Ventricle with Transposition of the Great Arteries | 1 | 1 | 0 |
| d-Transposition of the Great Arteries | 1 | 1 | 0 |
| Hypertrophic Cardiomyopathy | 1 | 1 | 0 |
| Atrio-Ventricular Canal | 1 | 0 | 1 |
| Partial Anomalous Pulmonary Venous Return | 1 | 0 | 1 |
| Asthma | 1 | 1 | 0 |

338 **Supplemental Table 1:** Diagnoses of patients included in the analysis.

- 339 1. Trembl B, Breitkopf R, Bukumirić Z, Bachler M, Boesch J, Rajsic S. ECMO Predictors of
340 Mortality: A 10-Year Referral Centre Experience. *J Clin Med*. 2022 Feb 24;11(5). PubMed PMID:
341 35268314. PMCID: PMC8911127. Epub 20220224. eng.
- 342 2. Djordjevic I, Sabashnikov A, Deppe AC, Kuhn E, Eghbalzadeh K, Merkle J, et al. Risk
343 factors associated with 30-day mortality for out-of-center ECMO support: experience from the
344 newly launched ECMO retrieval service. *J Artif Organs*. 2019 Jun;22(2):110-7. PubMed PMID:
345 30673894. Epub 20190123. eng.
- 346 3. Punn R, Axelrod DM, Sherman-Levine S, Roth SJ, Tacy TA. Predictors of mortality in
347 pediatric patients on venoarterial extracorporeal membrane oxygenation. *Pediatr Crit Care Med*.
348 2014 Nov;15(9):870-7. PubMed PMID: 25230312. PMCID: PMC4221423. eng.
- 349 4. Kolovos NS, Bratton SL, Moler FW, Bove EL, Ohye RG, Bartlett RH, et al. Outcome of
350 pediatric patients treated with extracorporeal life support after cardiac surgery. *Ann Thorac Surg*.
351 2003 Nov;76(5):1435-41; discussion 41-2. PubMed PMID: 14602263. eng.
- 352 5. Morris MC, Ittenbach RF, Godinez RI, Portnoy JD, Tabbutt S, Hanna BD, et al. Risk
353 factors for mortality in 137 pediatric cardiac intensive care unit patients managed with

- 354 extracorporeal membrane oxygenation. *Crit Care Med.* 2004 Apr;32(4):1061-9. PubMed PMID:
355 15071402. eng.
- 356 6. Derby CD, Kolcz J, Kerins PJ, Duncan DR, Quezada E, Pizarro C. Aristotle score
357 predicts outcome in patients requiring extracorporeal circulatory support following repair of
358 congenital heart disease. *ASAIO J.* 2007;53(1):82-6. PubMed PMID: 17237653. eng.
- 359 7. Delmo Walter EM, Alexi-Meskishvili V, Huebler M, Loforte A, Stiller B, Weng Y, et al.
360 Extracorporeal membrane oxygenation for intraoperative cardiac support in children with
361 congenital heart disease. *Interact Cardiovasc Thorac Surg.* 2010 May;10(5):753-8. PubMed
362 PMID: 20139198. Epub 20100205. eng.
- 363 8. Stephens AF, Šeman M, Diehl A, Pilcher D, Barbaro RP, Brodie D, et al. ECMO PAL:
364 using deep neural networks for survival prediction in venoarterial extracorporeal membrane
365 oxygenation. *Intensive Care Med.* 2023 Sep;49(9):1090-9. PubMed PMID: 37548758. PMCID:
366 PMC10499722. Epub 20230807. eng.
- 367 9. Pappalardo F, Pieri M, Greco T, Patroniti N, Pesenti A, Arcadipane A, et al. Predicting
368 mortality risk in patients undergoing venovenous ECMO for ARDS due to influenza A (H1N1)
369 pneumonia: the ECMOnet score. *Intensive Care Med.* 2013 Feb;39(2):275-81. PubMed PMID:
370 23160769. PMCID: PMC7095375. Epub 20121116. eng.
- 371 10. Schmidt M, Burrell A, Roberts L, Bailey M, Sheldrake J, Rycus PT, et al. Predicting
372 survival after ECMO for refractory cardiogenic shock: the survival after veno-arterial-ECMO
373 (SAVE)-score. *Eur Heart J.* 2015 Sep 01;36(33):2246-56. PubMed PMID: 26033984. Epub
374 20150601. eng.
- 375 11. Shah N, Said AS. Extracorporeal Support Prognostication-Time to Move the Goal Posts?
376 *Membranes (Basel).* 2021 Jul 15;11(7). PubMed PMID: 34357187. PMCID: PMC8304743. Epub
377 20210715. eng.
- 378 12. Mehta NM, Turner D, Walsh B, Zurakowski D, Betit P, Wilson J, et al. Factors associated
379 with survival in pediatric extracorporeal membrane oxygenation--a single-center experience. *J*
380 *Pediatr Surg.* 2010 Oct;45(10):1995-2003. PubMed PMID: 20920718. eng.
- 381 13. Barbaro RP, Boonstra PS, Paden ML, Roberts LA, Annich GM, Bartlett RH, et al.
382 Development and validation of the pediatric risk estimate score for children using extracorporeal
383 respiratory support (Ped-RESCUERS). *Intensive Care Med.* 2016 May;42(5):879-88. PubMed
384 PMID: 27007109. PMCID: PMC6379065. Epub 20160323. eng.
- 385 14. Barbaro RP, Paden ML, Guner YS, Raman L, Ryerson LM, Alexander P, et al. Pediatric
386 Extracorporeal Life Support Organization Registry International Report 2016. *ASAIO J.*
387 2017;63(4):456-63. PubMed PMID: 28557863. PMCID: PMC5626007. eng.
- 388 15. Taka H, Kotani Y, Kuroko Y, Iwadou S, Iwasaki T, Kasahara S. Risk factors and
389 outcomes of pediatric extracorporeal membrane oxygenation. *Asian Cardiovasc Thorac Ann.*
390 2021 Nov;29(9):916-21. PubMed PMID: 33611945. Epub 20210220. eng.
- 391 16. Aharon AS, Drinkwater DC, Churchwell KB, Quisling SV, Reddy VS, Taylor M, et al.
392 Extracorporeal membrane oxygenation in children after repair of congenital cardiac lesions. *Ann*
393 *Thorac Surg.* 2001 Dec;72(6):2095-101; discussion 101-2. PubMed PMID: 11789800. eng.
- 394 17. Liao MT, Tsai IJ, Lin FH, Tseng LJ, Huang SC, Chen YS, et al. Risk factors for in-hospital
395 mortality and acute kidney injury in neonatal-pediatric patients receiving extracorporeal
396 membrane oxygenation. *J Formos Med Assoc.* 2021 Sep;120(9):1758-67. PubMed PMID:
397 33810928. Epub 20210331. eng.
- 398 18. Betrus C, Remenapp R, Charpie J, Kudelka T, Brophy P, Smoyer WE, et al. Enhanced
399 hemolysis in pediatric patients requiring extracorporeal membrane oxygenation and continuous
400 renal replacement therapy. *Ann Thorac Cardiovasc Surg.* 2007 Dec;13(6):378-83. PubMed
401 PMID: 18292719. eng.
- 402 19. Chu JH, Sarathy S, Ramesh S, Rudolph K, Raghavan ML, Badheka A. Risk factors for
403 hemolysis with centrifugal pumps in pediatric extracorporeal membrane oxygenation: Is pump

- 404 replacement an answer? *Perfusion*. 2023 May;38(4):771-80. PubMed PMID: 35354417. Epub
405 20220330. eng.
- 406 20. Jenks CL, Zia A, Venkataraman R, Raman L. High Hemoglobin Is an Independent Risk
407 Factor for the Development of Hemolysis During Pediatric Extracorporeal Life Support. *J*
408 *Intensive Care Med*. 2019 Mar;34(3):259-64. PubMed PMID: 28486865. Epub 20170510. eng.
- 409 21. Annich GM. Extracorporeal life support: the precarious balance of hemostasis. *J Thromb*
410 *Haemost*. 2015 Jun;13 Suppl 1:S336-42. PubMed PMID: 26149045. eng.
- 411 22. Dalton HJ, Reeder R, Garcia-Filion P, Holubkov R, Berg RA, Zuppa A, et al. Factors
412 Associated with Bleeding and Thrombosis in Children Receiving Extracorporeal Membrane
413 Oxygenation. *Am J Respir Crit Care Med*. 2017 Sep 15;196(6):762-71. PubMed PMID:
414 28328243. PMCID: PMC5620676. eng.
- 415 23. Williams DC, Turi JL, Hornik CP, Bonadonna DK, Williford WL, Walczak RJ, et al. Circuit
416 oxygenator contributes to extracorporeal membrane oxygenation-induced hemolysis. *ASAIO J*.
417 2015;61(2):190-5. PubMed PMID: 25419829. PMCID: PMC4537148. eng.
- 418 24. Lequier L, Horton SB, McMullan DM, Bartlett RH. Extracorporeal membrane oxygenation
419 circuitry. *Pediatr Crit Care Med*. 2013 Jun;14(5 Suppl 1):S7-12. PubMed PMID: 23735989.
420 PMCID: PMC3742331. eng.
- 421 25. Kozlova E, Chernysh A, Moroz V, Sergunova V, Gudkova O, Kuzovlev A. Nanodefects of
422 membranes cause destruction of packed red blood cells during long-term storage. *Exp Cell Res*.
423 2015 Oct 01;337(2):192-201. PubMed PMID: 26169694. Epub 20150710. eng.
- 424 26. Mulholland JW, Massey W, Shelton JC. Investigation and quantification of the blood
425 trauma caused by the combined dynamic forces experienced during cardiopulmonary bypass.
426 *Perfusion*. 2000 Nov;15(6):485-94. PubMed PMID: 11131211. eng.
- 427 27. Baslaim G, Bashore J, Al-Malki F, Jamjoom A. Can the outcome of pediatric
428 extracorporeal membrane oxygenation after cardiac surgery be predicted? *Ann Thorac*
429 *Cardiovasc Surg*. 2006 Feb;12(1):21-7. PubMed PMID: 16572070. eng.

430

431

432

433

434