

# Outcomes of protocol-based management for venoarterial extracorporeal membrane oxygenation in congenital heart surgery – A 2-decade experience

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## ABSTRACT

**Background** : Extracorporeal membrane oxygenation (ECMO) is a vital mechanical circulatory support used with increasing frequency in complex congenital cardiac surgeries. This study evaluated the outcomes of a protocol-based venoarterial (VA) ECMO program following congenital heart surgeries.

**Methods and Results** : This was a retrospective review of 198 patients who underwent VA-ECMO after congenital cardiac surgeries at our institute between 2004 and 2023. Patients were divided into pre-ECMO protocol (2004–2017) and post-ECMO protocol (2018–2023) implementation. There were 107 patients in the preprotocol era and 91 in the postprotocol era. We compared weaning from ECMO and survival to hospital discharge between the two eras. An analysis of the factors influencing survival to hospital discharge was also done. ECMO was initiated through the central cannulation technique through median sternotomy in all patients. The median age and weight at initiation were 4 months (interquartile range [IQR] 1–33.5 months) and 4.4 kg (IQR 3.3–10.1 kg), respectively. The successful weaning of the ECMO ( $n = 67/91$ , 73.6%) and survival to discharge ( $n = 43/91$ , 47.3%) were higher in patients of the postprotocol era. However, it was not statistically significant. Higher risk adjustment for congenital heart surgery-1 >3 and acute kidney injury were independent predictors of poorer survival to hospital discharge.

**Conclusions** : A protocol-based ECMO program may improve outcomes of successful weaning and survival to discharge in patients undergoing congenital cardiac surgeries.

**Keywords** : Congenital heart disease, mechanical circulatory support, pediatric cardiac surgery, survival

## INTRODUCTION

Extracorporeal membrane oxygenation (ECMO) is a major form of mechanical circulatory support, being used to

support the failing heart, refractory to conventional medical management in children undergoing congenital

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cardiac surgeries. The ECMO provides organ perfusion while allowing the heart to recover completely.<sup>[1]</sup>

Among the different indications for venoarterial (VA) ECMO in the pediatric population, congenital heart disease remains the most common indication (81% neonatal and 52% pediatric). The reported survival to discharge for patients receiving VA ECMO for cardiac disease is 43% and 53% in neonates and other pediatric patients, respectively.<sup>[2,3]</sup> According to the Society of Thoracic Surgeons, 2.8% of pediatric patients require ECMO in the perioperative setting, and risk factors for ECMO in this population include young age (average age 13 days), perioperative factors (mechanical ventilation, arrhythmia, or shock), higher complexity operation (STAT category 4 or 5), and prolonged cardiopulmonary bypass (CPB) time.<sup>[4]</sup> With time, the development of consensus guidelines for using ECMO in various populations and the improved ECMO technology have significantly enhanced ECMO utilization, morbidity, and mortality.<sup>[5,6]</sup> With the growing number of complex congenital surgeries performed at our institution, the ECMO has become an integral part of the perioperative management of these patients. At inception, the ECMO usage was surgeon-driven, and a protocol-based approach was introduced in 2018. This protocol-based approach was established to ensure structured management of patients on ECMO and improve patient outcomes. This study aimed to assess the impact of a structured ECMO protocol on successful weaning of ECMO and survival to hospital discharge.

## MATERIALS AND METHODS

This was a single-center retrospective observational study conducted in the tertiary national pediatric cardiac referral center. The study was approved by the hospital's Ethics Committee. All patients requiring VA ECMO after corrective or palliative surgery for congenital heart disease were included. Data collection included the period from the commencement of ECMO services in 2004 until December 2023. Electronic and hospital records were used to obtain information. Data collected included demographic parameters such as age, weight, gender, cardiac diagnosis, previous intervention, type of surgery with risk adjustment for congenital heart surgery (RACHS-1) grouping, CPB time, and aortic cross-clamp time. Outcome parameters such as the reason for ECMO initiation, site of ECMO initiation, duration of ECMO, need for cardiopulmonary resuscitation, and complications were also collected. The primary outcomes of the study were successful ECMO termination and survival to hospital discharge.

### Definitions

Successful ECMO termination was defined as the patients who survived beyond 48 h after ECMO decannulation.<sup>[7]</sup>

Survival to discharge was defined as the patients who survived until discharge from the hospital or transferred to other hospitals. Acute kidney injury (AKI) was defined as an increase of creatinine level of more than 50% from baseline within 7 days and requiring renal replacement therapy.<sup>[8]</sup> The record was only included if dialysis was required during ECMO. Neurological complications depended on whether there was a computed tomography or ultrasound report of neurological injury, regardless of severity. Bleeding was determined to be significant if it necessitated chest exploration while on ECMO.

### Extracorporeal membrane oxygenation protocol

ECMO can be initiated in the operating theater (OT) or intensive care unit (ICU). Initiation in OT would occur after failed attempts at weaning from CPB and fulfilling indications for ECMO. Aortic cannula and venous cannulas were connected to the ECMO machine. Heparinization was not reversed. Flows were adjusted according to the patient's age group. The patient was then transferred to the ICU. If ECMO initiation occurred in the ICU, the chest would be reopened. Central ECMO was then initiated through aortic and right atrial cannulation. In those with severe left ventricular dysfunction, a left atrial vent was placed either through the left atrial appendage or the right superior pulmonary vein. Depending on the case, an additional drainage cannula was used to improve myocardial decompression. Following heparinization, central cannulation was performed by the attending cardiothoracic surgeon. ECMO flows were optimized to achieve flows appropriate for age. The sweep gas flow rate equals the pump flow rate on initiation but was titrated based on carbon dioxide in blood gas afterward. Titration of ECMO flows would be done to achieve adequate systemic perfusion (normalized lactate levels, normalized cerebral oximetry readings, and urine output >1 mL/kg/h) and hemodynamic stability (mean arterial pressure between the 5<sup>th</sup> and 50<sup>th</sup> percentile of 50<sup>th</sup> height centile).<sup>[9]</sup> Electrolyte abnormalities, blood sugar derangement, and metabolic acidosis were aggressively corrected from the hourly blood gas collected within the initial 6–12 h of ECMO initiation. Once this was achieved, the frequency of blood sampling was reduced to every 2–4 h. Inotropes would be removed except for low-dose milrinone 0.3 µg/kg/min, used for its lusitropy effect, once ECMO was successfully initiated. Ventilation would be kept on rest ventilator settings. Anticoagulation was maintained with unfractionated heparin and monitored with activated clotting time (ACT). Antibiotic prophylaxis was prescribed based on institutional policy. All ICU care bundles (chest open/ventilator/central line/urinary/pressure sores) were vigilantly performed for patients on ECMO. Peritoneal dialysis was used to correct any AKI or fluid overload. Integration with a dialysis machine may be used if peritoneal dialysis is not adequate or unavailable. Bronchoscopy may be used to toilet the airways in the

event of airway obstruction with blood clots or mucus. During the ECMO run, clots and fibrin observation were carried out vigilantly by the perfusionist and nursing team. If any signs of circuit thrombosis were identified, an urgent discussion was carried out on the possibility of ECMO termination.

Once improvement in the clinical course (improving pulse pressure beyond 10 mm Hg) and recovery of end-organ function (such as normalization or near normalization of biochemical blood parameters for kidney-creatinine and liver-alkaline transaminase levels) were achieved, weaning from ECMO was then planned during daily discussion. Inotropes and ventilation were optimized several hours earlier, along with weaning of ECMO flows (full to  $\frac{2}{3}$ , then  $\frac{1}{3}$ ). An echocardiography assessment (at  $\frac{1}{3}$  flows) was performed before the decision for ECMO termination was finalized. Echocardiography should show improving left and right ventricular function with no gross residual structural lesion. Heparin must be continued while waiting for ECMO termination. The anesthesiologist and surgeon would then proceed with ECMO termination. Weaning targets: blood gases during the weaning process should achieve normal pH with no raised

lactate or metabolic acidosis, such as partial pressure of carbon dioxide 35–45 mmHg and partial pressure of oxygen >80 mmHg for biventricular hearts and 40–60 mmHg in univentricular heart based on its physiology. Ventilator settings in pressure control mode should not exceed FIO<sub>2</sub> 80%, peak inspiratory pressure of 25 cmH<sub>2</sub>O, and rate 40 breaths/min. Hemodynamic (age-appropriate heart rate and blood pressure) should remain stable on adrenaline <0.1 µg/kg/min, with or without noradrenaline <0.1 µg/kg/min, before termination and decannulation. If the patient shows signs of inability to cope with ECMO weaning (poor blood gases, hemodynamic, and echocardiographic findings), a decision to either abort the ECMO weaning and reassess again in 24–48h, arrange for investigation (diagnosis cardiac catheterization) or one-way ECMO termination will be carried out. More information on targets during the ECMO run and differences between the previous and current protocol are presented in Table 1.

### Statistical analysis

Descriptive statistics were reported as median and interquartile range (IQR) for continuous variables and as frequencies and percentages for categorical variables.

**Table 1: Differences between previous and current extracorporeal membrane oxygenation protocol**

| Targets                             | 2004–2017  | 2018–2023   |
|-------------------------------------|--|---|
| Decision for ECMO                   | Decided by the attending surgeon, assisted by perfusionist and ECMO nurses, with <i>ad-hoc</i> input from anesthesiologists, cardiologists, and intensivists | Decision during multidisciplinary discussion. In emergency ECMO, decision by two consultants – a surgeon and either cardiologist, anesthesiologist, or intensivist  |
| Approach and cannulation strategies | Central approach through aortic and right atrial cannulation   | Central approach through aortic and right atrial cannulation. Left atrial venting frequently performed  |
| ECMO flows                          | 100 mL/kg/min with adjustment by surgeon   | 100–150 mL/kg/min in infants, 80–120 mL/kg/min in children, and 60–80 mL/kg/min in adolescents and beyond, titrated based on end-organ perfusion; sweep gas flow equals pump flow rate at initiation and titrated based on blood gases thereafter |
| Ventilator settings                 | Pressure control FIO <sub>2</sub> 30%, PEEP 6–8 cmH <sub>2</sub> O, PIP 20 cmH <sub>2</sub> O, iT 0.5–1 s, rate 10–15, adjusted by intensivist               | Pressure control FIO <sub>2</sub> 30%, PEEP 10 cmH <sub>2</sub> O, PIP 20 cmH <sub>2</sub> O achieving tidal volume 4–6 mL/kg, iT 1 s, rate 10, chest radiograph daily  |
| Blood gas targets                   | Parameters decided by an intensivist   | Works on achieving clearance of lactate within 6–12 h of ECMO, parameters targeted on anatomy and physiology of lesion  |
| Transfusion thresholds              | Hemoglobin 13–15 g/dL; platelet >100,000×10 <sup>9</sup> /L, fibrinogen >200 mg/dL, fresh frozen plasma transfusion if bleeding as ordered by the surgeon    | Hemoglobin 12–14 g/dL, 10–12 g/dL if stable; platelet >50,000×10 <sup>9</sup> /L, >100,000×10 <sup>9</sup> /L if bleeding; fibrinogen >100 mg/dL, >150 mg/dL if bleeding; fresh frozen plasma transfusion if bleeding and INR >1.5                |
| Anticoagulation                     | Maintained on unfractionated heparin with daily coagulation profile, hourly ACT targets 180–220 s, titration according to a sliding scale                    | Maintained on unfractionated heparin with daily coagulation profile, 1–4 hourly ACT target 180–200 s or 160–180 s if bleeding, titration according to the sliding scale   |
| Monitoring                          | Ultrasound of the brain based on an order by the intensivist   | Regular ultrasound of the brain, cerebral oximetry part of monitoring, CT brain after ECMO termination in the presence of neurological signs  |
| Hemodynamic targets                 | Age-appropriate targets set by an intensivist, low-dose milrinone 0.3 µg/kg/min and adrenaline 0.03 µg/kg/min used   | MAP (5 <sup>th</sup> percentile at 50 <sup>th</sup> height percentile)=1.5 × age in years + 40, and MAP (50 <sup>th</sup> percentile at 50 <sup>th</sup> height percentile)=1.5 × age in years + 55), low-dose milrinone 0.3 µg/kg/min used       |
| Renal replacement therapy           | The only option of peritoneal dialysis   | Uses peritoneal dialysis as the primary modality. Integration with a dialysis machine may be used if peritoneal dialysis is not effective/unavailable   |
| Weaning and termination             | Suitability is determined by a surgeon with assistance from the anesthesiologist   | Daily review with discussion between surgeon and intensivist. ECMO flow reduction with initiation of ventilation and inotropes occurring 1–4 h before ECMO termination. Echocardiography at 1/3 flow showing satisfactory results                 |

ECMO: Extracorporeal membrane oxygenation, IQR: Interquartile range, CT: Computed tomography, ACT: Activated clotting time, INR: International normalized ratio, MAP: Mean arterial pressure, PIP: Peak inspiratory pressure, PEEP: Positive end-expiratory pressure, iT: Inspiratory time

Continuous variables were analyzed using the Mann-Whitney *U* test, while the categorical variables were analyzed using the Pearson Chi-square test or Fisher's exact test. Logistic regression was used to measure the association between the clinical variables and survival to hospital discharge. All statistical analysis was performed using IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp. Significance was determined as  $P < 0.05$ .

## RESULTS

### Patient demographics

Table 2 shows the demographic of patients divided into survivor and nonsurvivor groups. During the 20-year period, there were a total of 198 patients who required VA ECMO postcardiac surgery. The overall survival to discharge was 41.4% ( $n = 81/198$ ). The median age at operation was 4 months (IQR 1–33.5 months), median weight of 4.4 kg (IQR 3.3–10.1 kg), and comprised

61.6% ( $n = 122/198$ ) of males. The nonsurvivor group was smaller and younger than the survivor group but was not statistically significant. Transposition of great arteries (TGA) was the most common diagnosis in 29.3% (39-simple TGA and 19-complex TGA), followed by tetralogy of Fallot at 17.2% ( $n = 34/198$ ). There were five patients with single-ventricle physiology put on ECMO, with only one survivor among them. The nonsurvivor group had significantly more patients with RACHS-1  $>3$  among the groups. Patients with previous interventions did not differ among both groups.

### Extracorporeal membrane oxygenation outcomes

Outcome parameters are illustrated in Table 3. The most common indication for ECMO was the inability to wean off bypass (54.5%,  $n = 108/198$ ), followed by cardiac arrest (21.7%,  $n = 43/198$ ), low cardiac output syndrome (21.2%,  $n = 42/198$ ), and other causes. In the group with different causes, four had arrhythmias and one had a tracheal anastomotic leak. Indications for ECMO, along with bypass time, cross-clamp time,

**Table 2: Patient demographics**

| Variables  | Total patients<br>( $n=198$ ), $n$ (%) | Survivor<br>( $n=82$ ), $n$ (%) | Nonsurvivor<br>( $n=116$ ), $n$ (%) | <i>P</i> |
|--|--|---------------------------------|-------------------------------------|----------|
| Age at operation (month), median (IQR)                   | 4.0 (1.0–33.5)                         | 5.0 (1.0–31.4)                  | 2.9 (1.0–37.5)                      | 0.665    |
| Weight (kg), median (IQR)                                | 4.4 (3.3–10.1)                         | 4.8 (3.4–10.0)                  | 4.1 (3.2–10.7)                      | 0.569    |
| Gender   |  |                                 |                                     |          |
| Male   | 122 (61.6)                             | 54 (65.9)                       | 68 (58.6)                           | 0.303    |
| Female   | 76 (38.4)                              | 28 (34.1)                       | 48 (41.4)                           |          |
| Diagnosis  |  |                                 |                                     |          |
| Simple TGA   | 39 (19.7)                              | 19 (23.2)                       | 20 (17.2)                           | 0.407    |
| TGA with associated lesions                              | 19 (9.6)                               | 6 (7.3)                         | 13 (11.2)                           |          |
| Tetralogy of Fallot                                      | 34 (17.2)                              | 15 (18.3)                       | 19 (16.4)                           |          |
| Anomalous left coronary artery from the pulmonary artery | 11 (5.6)                               | 7 (8.5)                         | 4 (3.4)                             |          |
| Ventricular septal defect                                | 11 (5.6)                               | 6 (7.3)                         | 5 (4.3)                             |          |
| Ventricular septal defect with coarctation of the aorta  | 4 (2.0)                                | 2 (2.4)                         | 2 (1.7)                             |          |
| Single-ventricle physiology                              | 5 (2.5)                                | 1 (1.2)                         | 4 (3.4)                             |          |
| Other lesions  | 75 (37.9)                              | 26 (31.7)                       | 49 (42.2)                           |          |
| RACHS-1 score  |  |                                 |                                     |          |
| $\leq 3$   | 145 (73.2)                             | 68 (82.9)                       | 77 (66.4)                           | 0.010*   |
| $>3$   | 53 (26.8)                              | 14 (17.1)                       | 39 (33.6)                           |          |
| Previous reintervention                                  | 36 (18.2)                              | 16 (19.5)                       | 20 (17.2)                           | 0.683    |

\* $P < 0.05$  considered significant. IQR: Interquartile range, RACHS-1: Risk adjustment for congenital heart surgery, TGA: Transposition of great arteries

**Table 3: Extracorporeal membrane oxygenation outcomes**

| Variables                             | Total patients ( $n=198$ ) | Survivor ( $n=82$ ) | Nonsurvivor ( $n=116$ ) | <i>P</i>   |
|---------------------------------------|----------------------------|---------------------|-------------------------|------------|
| Indication for ECMO, $n$ (%)          |                            |                     |                         |            |
| Unable to wean off bypass             | 108 (54.5)                 | 45 (54.9)           | 63 (54.3)               | 0.786      |
| Cardiac arrest                        | 43 (21.7)                  | 16 (19.5)           | 27 (23.3)               |            |
| Low cardiac output syndrome           | 42 (21.2)                  | 18 (22.0)           | 24 (20.7)               |            |
| Other causes                          | 5 (2.5)                    | 3 (3.7)             | 2 (1.7)                 |            |
| Bypass time (min), median (IQR)       | 245.0 (177.0–314.0)        | 265.0 (185.0–320.3) | 235.0 (169.0–304.0)     | 0.258      |
| Cross-clamp time (min), median (IQR)  | 120.0 (81.0–166.5)         | 131.0 (84.0–174.0)  | 115.0 (79.8–162.0)      | 0.261      |
| Duration of ECMO (days), median (IQR) | 4.0 (3.0–5.0)              | 4.0 (3.0–5.0)       | 4.0 (3.0–5.0)           | 0.742      |
| Site of deployment, $n$ (%)           |                            |                     |                         |            |
| ICU                                   | 84 (42.4)                  | 37 (45.1)           | 47 (40.5)               | 0.518      |
| Operation theater                     | 114 (57.6)                 | 45 (54.9)           | 69 (59.5)               |            |
| AKI, $n$ (%)                          | 143 (72.2)                 | 48 (58.5)           | 95 (81.9)               | $<0.001^*$ |
| Neurological complications, $n$ (%)   | 28 (14.1)                  | 17 (20.7)           | 11 (9.5)                | 0.025*     |
| Bleeding, $n$ (%)                     | 77 (38.9)                  | 26 (31.7)           | 51 (44.0)               | 0.081      |

\* $P < 0.05$  considered significant. ECMO: Extracorporeal membrane oxygenation, IQR: Interquartile range, AKI: Acute kidney injury, ICU: Intensive care unit



and duration of ECMO, were not different between survivor and nonsurvivor groups. Similarly, the site of deployment, whether in the ICU or OT, did not influence survival to discharge. Among the three complications studied, the nonsurvivor group had significantly more patients with AKI ( $P < 0.05$ ), while the survivor group had higher neurological complications ( $P < 0.05$ ). Bleeding outcomes were not different between both groups.

**Factors influencing survival to hospital discharge**

Logistic regression analysis was used to determine factors associated with survival to hospital discharge, as shown in Table 4. Multivariate analysis after adjusting for confounding factors showed that RACHS-1  $>3$  (odds ratio [OR] = 0.287, confidence interval [CI] = 0.133–0.620) and AKI (OR = 0.299, CI = 0.095–0.940) were significant risk factors associated with poorer survival to hospital discharge. Neurological complications with an OR = 2.859 (CI = 1.142–7.161) were more common in the survivor group compared to the nonsurvivor.

**Comparison between outcomes of the two eras**

ECMO outcomes after the introduction of protocol-based management in 2018 are shown in Table 5. The median duration of ECMO was 4 days in the preprotocol era and 5 days in the postprotocol era ( $P = 0.018$ ). There were significantly more patients with AKI in the preprotocol era (80.4% vs. 62.6%,  $P = 0.005$ ). There was a higher proportion of patients with neurological complications and bleeding in the postprotocol era, but it was not statistically significant. Outcomes of successful ECMO termination improved from 60.7% to 73.6% after the introduction of protocol-based management but were not statistically significant. Similarly, survival to hospital discharge went up from 36.4% in the preprotocol era to 47.3% in the postprotocol era, although this was not statistically significant too.

**DISCUSSION**

**Extracorporeal membrane oxygenation program**

This study investigated pediatric cardiac patients who received postsurgical VA-ECMO support at a single center in Malaysia over a 20-year period (2004–2023). Initially, ECMO was primarily used for refractory cardiac failure, with no formal protocol for initiation or management. The pediatric cardiac surgeon led the process, assisted by perfusionists and ECMO nurses, with *ad hoc* input from anesthesiologists, cardiologists, and intensivists. The decision to commence ECMO, ECMO flows and targets, and termination of ECMO were managed primarily by the surgeon. The only written protocols were transfusion and ACT targets for the bedside nurses to follow. In 2018, intensivist involvement increased, and a standardized written protocol was implemented for ECMO indications, consultations, targets, maintenance, and weaning. ECMO could be initiated in the OT or ICU. After assessing indications and contraindications, agreement from at least two consultants was required, especially for cases after a cardiopulmonary resuscitation. Our center, serving a large geographic area, saw an increase in VA-ECMO use for pediatric cardiac surgery over the past decade, ranging from 8 to 22 cases per year, likely due to the rising complexity of procedures.<sup>[10]</sup> This aligns with Extracorporeal Life Support Organization (ELSO) guidelines for maintaining an ECMO program. While no international consensus exists for initiating postcardiotomy VA-ECMO for cardiorespiratory failure, our multidisciplinary team makes case-by-case decisions based on empirical judgment, with a strong emphasis on reversible cardiac pathology as an indication.<sup>[11]</sup> Recognizing that ECMO is costly and carries significant complication risks, clear indications and potential benefits are crucial before initiation.<sup>[12]</sup> Consequently, in 2018, we introduced an ECMO protocol specifically tailored to our institution's needs.

**Table 4: Logistic regression analysis for factors influencing the survival to hospital discharge**

| Variables                  | Univariate analysis |            | Multivariate analysis |        |
|----------------------------|---------------------|------------|-----------------------|--------|
|                            | OR (95% CI)         | P          | OR (95% CI)           | P      |
| Age at operation (months)  | 0.996 (0.991–1.002) | 0.213      | 0.999 (0.984–1.014)   | 0.906  |
| Weight (kg)                | 0.978 (0.945–1.011) | 0.187      | 0.977 (0.892–1.071)   | 0.620  |
| RACHS-1 score ( $>3$ )     | 0.406 (0.203–0.812) | 0.011*     | 0.287 (0.133–0.620)   | 0.002* |
| AKI                        | 0.312 (0.164–0.595) | $<0.001^*$ | 0.299 (0.095–0.940)   | 0.039* |
| Neurological complications | 2.497 (1.101–5.663) | 0.029*     | 2.859 (1.142–7.161)   | 0.025* |

\* $P < 0.05$  considered significant. OR: Odd ratio, CI: Confidence interval, RACHS-1: Risk adjustment for congenital heart surgery, AKI: Acute kidney injury

**Table 5: Comparison between the outcomes of the two eras**

| Variables                             | 2004–2017 ( $n=107$ ), $n$ (%) | 2018–2023 ( $n=91$ ), $n$ (%) | P      |
|---------------------------------------|--------------------------------|-------------------------------|--------|
| Duration of ECMO (days), median (IQR) | 4.0 (3.0–5.0)                  | 5.0 (3.0–6.0)                 | 0.018* |
| AKI                                   | 86 (80.4)                      | 57 (62.6)                     | 0.005* |
| Neurological complications            | 11 (10.3)                      | 17 (18.7)                     | 0.091  |
| Bleeding                              | 39 (36.4)                      | 38 (41.8)                     | 0.445  |
| Successful ECMO termination           | 65 (60.7)                      | 67 (73.6)                     | 0.055  |
| Survival to hospital discharge        | 39 (36.4)                      | 43 (47.3)                     | 0.124  |

\* $P < 0.05$  considered significant. IQR: Interquartile range, ECMO: Extracorporeal membrane oxygenation, AKI: Acute kidney injury

### Benefits of a structured extracorporeal membrane oxygenation program

A structured ECMO program presumably helps streamline care for patients with possible maximal benefit. Our study examined weaning success and survival to discharge as outcomes, achieving a 66.7% weaning rate comparable to experienced centers.<sup>[13]</sup> Notably, successful weaning increased from 60.7% preprotocol to 73.6% postprotocol, although not statistically significant. Hospital discharge survival varied in published studies ranging from 39% to 85%.<sup>[14-16]</sup> Our 41.4% survival to hospital discharge rate falls within this range but lower than the 54% reported for Asia Pacific reported in the ELSO registry.<sup>[17]</sup> Importantly, our preprotocol period saw a 36.4% survival rate, improving to 47.3% survival postprotocol. This could be attributed to better ECMO management with the institution of ECMO protocol and improved surgical skills and CPB management.

### Indications for extracorporeal membrane oxygenation

Postcardiac surgical ECMO use in pediatric patients varies in indications and frequency. Common triggers include failure to wean from CPB, cardiac arrest, and low cardiac output syndrome due to conditions like biventricular, right ventricular, or left ventricular failure or pulmonary hypertensive crisis.<sup>[18,19]</sup> Notably, preprotocol period decisions relied on individual clinical judgment, while the postprotocol period followed a structured ECMO protocol. Our study showed a 25.3% cardiac arrest rate, exceeding the 22% reported in a UK study by Balasubramanian *et al.*<sup>[11]</sup> This higher rate, however, did not impact the survival and remained stable across both periods. This may suggest that the benefit of early ECMO initiation may potentially reduce cardiac arrest and organ damage. A study supports this notion, linking precardiac arrest ECMO with better outcomes.<sup>[19]</sup> However, caution is necessary to avoid unnecessary ECMO use in potentially nonneedy patients. Failure to wean from CPB was the most common indication, aligning with established literature. In addition, survival outcomes remained unaffected by specific initiation triggers.

### Factors associated with extracorporeal membrane oxygenation weaning and survival to hospital discharge

Numerous studies have identified factors that negatively impact successful weaning of ECMO and survival to hospital discharge after receiving ECMO support postcardiac surgery, which includes AKI, uncorrected residual lesions, longer CPB time, single ventricle physiology, ECMO beyond 7 days, and ECMO-related complications to mention a few.<sup>[20-22]</sup> Our study reaffirms some of these findings while illuminating crucial areas for improvement in patient care.

Our study demonstrated a promising reduction in overall complications, particularly AKI requiring dialysis, after implementing a specific ECMO protocol (80.4%–62.6%), which was statistically significant. Although there were reductions in AKI, it remains a significant risk factor affecting survival to discharge. This finding was similar to the regional ECMO study by Iamwat in Thailand.<sup>[18]</sup> A retrospective six-center kidney intervention during an extracorporeal membrane oxygenation database study reported an association of increased mortality when fluid overload occurred with AKI in ECMO patients.<sup>[23]</sup> Unfortunately, this study was unable to obtain data on fluid overload. With this robust finding, all clinicians caring for patients on ECMO will need to exercise greater effort to prevent fluid overload and AKI.

The presence of neurological complications was associated with reduced survival to hospital discharge.<sup>[24,25]</sup> However, this study had a higher prevalence of neurological insult among survivors compared to nonsurvivors. This was attributed to the increased neurological screening among survivors of ECMO, as defined in the protocol. Hence, the prevalence of neurological insults in the nonsurvivors was likely underrepresented. Improving neurologic monitoring at our institution during the peri-ECMO period is vital for early detection of acute neurologic injury and may potentially improve ECMO outcomes.<sup>[26]</sup>

Most patients with RACHS-1 >3 did not survive hospital discharge, accounting for about 73.6% (39/53) of all patients with RACHS-1 >3. Mortality in this group of patients was high, with a statistically significant  $P = 0.01$ . This was in line with another study that showed that the higher the RACHS-1, the lower the chance of survival to hospital discharge.<sup>[4]</sup>

Whether in the OT or ICU, the site of ECMO initiation did not significantly impact survival in this study, challenging the expectation of shorter initiation times and tighter control within the OT, thus improving chances of survival to hospital discharge. It is thought that early ECMO support, especially in cases in which ECMO support was started in the OT, would likely aid in reducing the probability of cardiac arrest and end-organ damage, which would impact survival. Available literature shows there is no difference in survival to hospital discharge for OT or ICU ECMO-initiated patients, and this is likely because ECMO was initiated promptly when needed, irrespective of the site of initiation.<sup>[27,28]</sup> More research is required to isolate the specific effect of the site of initiation and time to initiation of ECMO on survival to hospital discharge.

This study possesses certain limitations inherent to its retrospective design. Missing data were present for some variables, potentially introducing bias and limiting the comprehensiveness of the analysis. In addition, the single-center nature restricts the generalizability of the

findings to other institutions with potentially different patient populations, protocols, and resource availability. While our center is a large referral center representing the region to some extent, broader validation across diverse settings would strengthen the generalizability of the conclusions. Furthermore, the analysis did not incorporate other potentially influential variables on survival to discharge, such as pre-ECMO AKI, lactate levels, bilirubin levels, specific details of cardiovascular support, and ventilation parameters. While these data might not have been readily available, their inclusion could have provided a more comprehensive understanding of the factors associated with survival after ECMO weaning.

## CONCLUSIONS

Our study findings reinforce the importance of having ECMO protocols in optimizing patient outcomes. The implemented protocol showed promising initial effects in reducing complications, especially AKI, suggesting its potential to improve survival rates further. Structuring ECMO management protocols as a crucial life-saving intervention requires ongoing refinement and institutional adaptation to improve further survival rates of children undergoing surgery for congenital heart disease.

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## Conflicts of interest

There are no conflicts of interest.

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