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Clinical Research

Postcardiotomy Extracorporeal Membrane Oxygenation Support in Patients with Congenital Heart Disease

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Background: This study investigated mortality and morbidity in patients requiring postcardiotomy extracorporeal membrane oxygenation (ECMO) support after operations for congenital heart disease (CHD).
Methods: CHD patients requiring postoperative ECMO support between May 2011 and May 2021 were retrospectively reviewed. Patients were divided into non-survivors and survivors to hospital discharge. Survival outcomes and associations of various factors with in-hospital death were analyzed.
Results: Fifty patients required postoperative ECMO support. Patients' median age and weight at the time of ECMO insertion were 1.85 months (interquartile range [IQR], 0.23–14.5 months) and 3.84 kg (IQR, 3.08–7.88 kg), respectively. Twenty-nine patients (58%) were male. The median duration of ECMO support was 6 days (IQR, 3–12 days). Twenty-nine patients (58%) died on ECMO support or after ECMO weaning, and 21 (42%) survived to hospital discharge. Postoperative complications included renal failure (n=33, 66%), bleeding (n=11, 22%), and sepsis (n=15, 30%). Prolonged ECMO support (p=0.017), renal failure (p=0.005), continuous renal replacement therapy (CRRT) application (p=0.001), sepsis (p=0.012), bleeding (p=0.032), and high serum lactate (p=0.002) and total bilirubin (p=0.017) levels during ECMO support were associated with higher mortality risk in a univariate analysis. A multivariable analysis identified CRRT application (p=0.013) and a high serum total bilirubin level (p=0.001) as independent risk factors for death.
Conclusion: Postcardiotomy ECMO should be considered as an important therapeutic modality for patients unresponsive to conventional management. ECMO implementation strategies and management in appropriate patients without severe complications, particularly renal failure and/or liver failure, are crucial for achieving positive outcomes.

Keywords: Extracorporeal membrane oxygenation, Congenital heart disease, Thoracic surgery, Postcardiotomy

Introduction

Extracorporeal membrane oxygenation (ECMO) is the most common form of mechanical circulatory support (MCS) used in pediatric patients with severe cardiopulmonary failure [1-4]. In January 2020, the Extracorporeal Life Support Organization reported 21,368 cases of cardiac ECMO in pediatric patients, including 8,830 cases in neonatal patients. This was more than a 50% increase compared to the number of cardiac ECMO cases reported in 2015 [5].

Postcardiotomy ECMO support following an operation for congenital heart disease (CHD) has become steadily more widespread over the past 30 years [6-8]. This increased use of ECMO after open heart surgery can be attributed to the increased rate of repair and/or palliative surgery for complex CHD, increased access to ECMO equipment, accumulated experience of ECMO deployment and management, and technological advances in ECMO equipment, such as circuit tubing with reduced blood-prosthetic surface interactions and better-designed pumps and oxygenators [6-11].

ECMO is a vital tool used in postoperative management. For patients with medically refractory cardiorespiratory failure unresponsive to fluid resuscitation, inotropic drugs, and vasoactive therapies after CHD surgery, veno-arterial (VA) ECMO is used to augment cardiac output and facilitate respiratory gas exchange. VA ECMO can be inserted in patients experiencing cardiopulmonary bypass (CPB) weaning failure, systemic-to-pulmonary artery shunt thrombosis after a palliated circulation, intractable arrhythmias, postoperative low cardiac output syndrome, and cardiac arrest. Postcardiotomy VA ECMO may provide a bridge to myocardial recovery by decreasing the cardiac workload, enabling the recovery of cardiac function after an injury [1,4,6-10].

Various outcomes and risk factors have been reported for successful weaning from ECMO support and hospital survival. Although the reversibility and recovery of cardiac function is the key determinant for successful weaning from ECMO support, factors such as age, body weight, ventricle morphology, continuous renal replacement therapy (CRRT), prolonged ECMO support time, time of initiation, and volume status during ECMO support have been identified as factors associated with survival after ECMO support [4,8,11-15]. However, despite the identification of factors related to successful weaning from ECMO support, it still remains difficult to determine when to discontinue ECMO support and when further ECMO therapy no longer may provide medical benefits [4,11-15].

Cardiac failure, multisystem organ failure (MOF), and sepsis are common reasons for death. As a result, clinical features suggesting progressive failure of the heart and other organs may aid in predicting outcomes [11,12,15,16]. Nonetheless, independent risk factors for hospital survival after successful weaning from ECMO support remain unclear. In fact, despite the accumulated experience, improvements in ECMO technology and management, and the identification of risk factors associated with hospital deaths, mortality in patients requiring ECMO support after surgical intervention for CHD remains high and unchanged, with an average rate of survival to hospital discharge between 24% and 61% [4,6,8-10,13,17,18].

Therefore, in this study we reported our results of postcardiotomy ECMO support after operations for CHD and investigated independent risk factors associated with successful ECMO weaning and hospital survival.

Methods

A retrospective institutional review of 50 consecutive patients, who required ECMO support following surgery for CHD at Seoul National University Children's Hospital between May 2011 and May 2021, was performed. With approval from the Institutional Review Board of Seoul National University Hospital (IRB approval no., 2110-135-1264), all medical records of the patients were reviewed. Patients requiring ECMO support prior to surgical intervention for CHD and those who required veno-venous ECMO after surgical correction were excluded. The requirement for informed consent from individual patients was omitted because of the retrospective design of this study.

Extracorporeal membrane oxygenation indications

ECMO indications included failure to wean from CPB in the operating room (OR), severe postoperative hemodynamic instability with refractory hypoxemia, progressive decline of cardiac function despite the maximum inotropic support, or cardiopulmonary arrest.

Extracorporeal membrane oxygenation circuit

A standard ECMO circuit (PLS System; Maquet, Rastatt, Germany) coated with Bioline heparin was used. The ECMO circuit consisted of a centrifugal pump-based console (Maquet's Rotalow PLS) with an ECMO membrane oxygenator (Maquet Quadrox PLS for patients 10 kg or above, Sorin Kids D101 for patients below 10 kg). A water heat exchange system (Maquet HU35 heater unit) and electronic gas blender (Maquet EGB 40) was used to maintain a constant temperature of the blood within the circuit and to control an adequate arterial oxygen tension and carbon dioxide tension, respectively.

Extracorporeal membrane oxygenation priming

The ECMO systems were primed with a total volume of 250 mL for patients below 10 kg and 550 mL for patients 10 kg or above. Plasmalyte solution and packed red blood cells (RBCs) was used for priming: 150 mL of plasmalyte solution with 100 mL of packed RBCs for patients below 10 kg and 200 mL of plasmalyte solution with 1 pack of packed RBCs for patients 10 kg or above.

Cannulation

Cannulation was performed intraoperatively in the OR or postoperatively in the intensive care unit (ICU). Central

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ECMO implantation via transthoracic cannulation (right atrium, ascending aorta) was most commonly performed. After the initiation of central ECMO, closure of the chest was preferred. For peripheral ECMO placement, the right internal jugular vein and the right common carotid artery were more frequently used. However, femoral vessels were used for cannulation in patients with acceptable-sized femoral vessels on sonography. Appropriate vessels with acceptable sizes and without signs of stenosis or occlusion were carefully selected because the vessels were at risk of underdevelopment or occlusion from being accessed for cardiac catheterizations, especially in patients with complex CHD with histories of multiple cardiac catheterizations.

Anticoagulation

Heparin was usually administered with a bolus dose of 25–50 U/kg at the time of ECMO placement in patients requiring ECMO support in the ICU. For patients requiring ECMO support due to failure to wean from CPB, no reversal of heparin was attempted. Heparin infusion were typically started within the first 24 hours after ECMO initiation as a routine strategy. For patients in whom bleeding was a concern, however, heparin infusion was postponed until the bleeding tendency had improved. Anticoagulation was measured every 4–6 hours using the activated partial thromboplastin time (aPTT). An aPTT range of 50 to 80 seconds was tolerated, but usually a strict range of 40 to 60 seconds was maintained to prevent complications of bleeding.

Extracorporeal membrane oxygenation management

The main goal of ECMO support was to provide adequate ECMO flow necessary for maintaining satisfactory oxygenation and optimal tissue perfusion during myocardial recovery. ECMO flow was adjusted based on patient-specific variables such as systemic blood pressure, urine output, arterial blood gas analysis, and serial lactate measurements. After the initiation of ECMO support, ventilator support was reduced to a minimum to provide a lung rest mode and inotropic support was weaned to minimum levels required to maintain an optimal mean arterial blood pressure. During ECMO support, packed RBCs and blood products were provided to maintain a hemoglobin level above 12 g/dL, hematocrit above 35%–40%, and the platelet count above 100,000/μL. All patients were put under deep sedation using remifentanil, midazolam, and neuromuscular blocking agents. Neurological monitoring included weekly neurological imaging using ultrasonography or, in some cases, brain computed tomography. Vancomycin was used as a prophylactic antibiotic, and the dosage was adjusted as necessary. Antimicrobial treatment was modified according to the sensitivity of positive cultures. Regular mediastinal irrigation and debridement were carried out every 3 days for patients with central ECMO. Strict infection surveillance was conducted. Bleeding was managed by providing the necessary packed RBCs and blood products. The fibrinogen and prothrombin time was maintained within the normal range, and antifibrinolytic agents were used to enhance hemostasis. However, surgical exploration was performed to manage continued bleeding.

Extracorporeal membrane oxygenation weaning

The decision to wean patients from ECMO support was made based on tolerable hemodynamic parameters and improved cardiac contractility evaluated through echocardiography and direct inspection. ECMO flow was gradually reduced while optimizing ventilator and inotropic support. Once the patient was stable on minimal ECMO flow, the arterial and venous cannulae were subsequently removed. Immediately before removing the ECMO cannulae, intravenous heparin with a bolus dose of 20–50 U/kg was administered, and the ECMO flow was turned off to check vital signs and ensure that the patient could tolerate the absence of ECMO support. For those with a central ECMO, the chest was kept open for at least 1 day before closure. For patients presenting with severe neurological damage and/or multiple organ failure, in whom further ECMO support was considered futile, ECMO support was terminated by mutual agreement of the patient's guardian and physician.

Statistical analysis

Data were analyzed with SPSS software ver. 12.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were reported in percentages and frequencies; continuous variables were expressed as mean±standard deviation or medians with interquartile ranges (IQRs) as appropriate. Categorical variables were compared between patients who survived ECMO support and those who did not using the chi-square test or Fisher exact test, while continuous variables were compared using the 2-sample t-test or Wilcoxon rank sum test as appropriate. Logistic regression analysis was

used for univariate and multivariate prognostic risk analyses for successful weaning from ECMO or survival to hospital discharge. A multivariable logistic model for the analysis of independent prognostic risk factors was performed on variables associated with decreased survival at p-values of ≤0.05 in the univariate logistic regression analysis due to the small sample size. All statistical tests were 2-sided, with type I error set at 0.05 for statistical significance.

Results

Between May 2011 and May 2021, 50 patients with CHD required ECMO support after surgical repair for CHD. Twenty-four patients (48%) were successfully weaned from ECMO support, and 21 patients (42%) survived to hospital discharge.

Baseline clinical characteristics

At the time of cannulation, 23 patients (46%) were neonates, 14 (28%) were infants, and the remaining 13 (26%) were over 1 year old. The median age at cannulation was 1.85 months (IQR, 0.23–14.5 months). The median weight was 3.84 kg (IQR, 3.08–7.88 kg). Twenty-nine patients (58%) were male. Nine patients (18%) were syndromic or had other congenital anomalies. Sixteen patients (32%) had single-ventricular physiology, while 34 (68%) had biventricular physiology. The Aristotle Basic Complexity (ABC) score was 8.3±2.3 for non-survivors and 7.9±2.1 for survivors (p=0.16). There were no statistically significant differences between the survivors to hospital discharge and non-survivors, except for aortic cross-clamping (ACC) time (Table 1). Thirty-one patients (62%) underwent definitive surgery for total correction and 19 patients (38%) underwent palliative surgery (Table 2).

ECMO support was instituted in 22 patients (44%) due to the inability to wean from CPB, 13 (26%) due to respiratory failure, 9 (18%) due to low cardiac output syndrome, 5 (10%) for extracorporeal cardiopulmonary resuscitation, and 1 (2%) for suspected refractory vasoplegia. There were no statistically significant differences between the survivors to hospital discharge and non-survivors in terms of ECMO indications (Table 3).

Forty patients (80%) underwent central ECMO implantation via transthoracic cannulation and 10 patients (20%) underwent peripheral ECMO insertion. Twenty-three patients (46%) were placed on ECMO in the OR due to failure to wean from CPB, while ECMO was initiated in the ICU for 27 patients (54%). Before ECMO was instituted, cardiopulmonary resuscitation was required in 19 patients (38%). No statistical significance was found suggesting a poor outcome in patients who underwent rescue ECMO. The

Table 1. Baseline clinical characteristics of the patients

Characteristic	Hospital discharge			
	Total (n=50)	Non-survivors (n=29)	Survivors (n=21)	p-value
Age (mo)	1.85 (0.23–14.5)	0.33 (0.12–4.95)	6.5 (0.65–176.9)	0.618
Age (mo)	90.4±189.1	78.9±188.9	106.3±192.8	
Sex				0.917
Male	29 (58.0)	17 (58.6)	12 (41.4)	
Female	21 (42.0)	12 (57.1)	9 (42.9)	
Body weight (kg)	3.84 (3.08–7.88)	3.37 (2.90–4.50)	6.3 (3.18–29.1)	0.809
Body weight (kg)	17.1±25.2	16.4±26.3	18.1±24.1	
Morphological diagnosis/ventricle type				0.658
Single-ventricular	16 (32.0)	10 (62.5)	6 (37.5)	
Biventricular	34 (68.0)	19 (55.9)	15 (44.1)	
Congenital anomaly	9 (18.0)	4 (44.4)	5 (55.6)	0.293
Surgical procedure				0.563
Definitive	31 (62.0)	17 (54.8)	14 (45.2)	
Palliative	19 (38.0)	12 (63.2)	7 (36.8)	
Redo cardiac surgery	15 (30.0)	7 (46.7)	8 (53.3)	0.288
Cardiopulmonary bypass time (min)	231.9±150.8	209.3±143.9	263.1±157.9	0.216
Aortic cross-clamping time (min)	106.5±91.9	80.4±71.7	140.1±105.1	0.024*
Aristotle Basic Complexity score	8.114±2.2752	8.259±2.4201	7.914±2.1001	0.160

Values are presented as median (interquartile range), mean±standard deviation, or number (%), unless otherwise stated.
*p<0.05 was considered significant.

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Table 2. Anatomical diagnoses and initial surgical procedures

Variable	Hospital discharge		
	Total (n=50)	Non-survivors (n=29)	Survivors (n=21)
Diagnosis			
L-R shunted heart	3 (6.0)	2 (66.7)	1 (33.3)
Left obstructed	3 (6.0)	3 (100.0)	0
Right obstructed	2 (4.0)	2 (100.0)	0
Hypoplastic left heart syndrome	3 (6.0)	3 (100.0)	0
Cyanotic, increased PBF	8 (16.0)	6 (75.0)	2 (25.0)
Cyanotic, decreased PBF	26 (52.0)	9 (34.6)	17 (65.4)
Cyanotic, increased pulmonary congestion	4 (8.0)	4 (100.0)	0
Others	1 (2.0)	0	1 (100.0)
Initial surgical procedure			
Definitive	31 (62.0)	17 (54.8)	14 (45.2)
Total repair	31 (62.0)	17 (54.8)	14 (45.2)
Palliative	19 (38.0)	12 (63.2)	7 (36.8)
Systemic-pulmonary shunt	8 (16.0)	5 (62.5)	3 (37.5)
Bidirectional cavopulmonary shunt	1 (2.0)	0	1 (100.0)
Norwood stage I	2 (4.0)	2 (100.0)	0
Others	8 (16.0)	5 (62.5)	3 (37.5)

Values are presented as number (%).
L-R shunted heart, left to right shunted heart; PBF, pulmonary blood flow.

median duration of ECMO support was 6 days (IQR, 3–12 days). The median duration of ECMO support for non-survivors to hospital discharge and survivors was 8 days (IQR, 4–23 days) and 4 days (IQR, 3–6 days), respectively (p=0.004). Seven patients (14%) required the reinsertion of ECMO after weaning and decannulation (Table 3).

Outcomes

Thirty-three patients (66%) had 1 or more complications while on ECMO. The most frequent complication was acute kidney injury. 33 patients (66%) required renal therapy due to acute renal failure, 11 (22%) required at least 1 surgical re-exploration for bleeding, and 15 (30%) presented sepsis with a positive blood culture. Other serious ECMO complications included central nervous system injury, defined as a change on an ultrasonography scan or computed tomography scan of the brain, disseminated intravascular coagulation (DIC), and end-organ ischemia. Intracranial hemorrhage and ischemic brain injury occurred in 4 patients (8%) and 7 patients (14%), respectively. Nine (18%) presented DIC and 3 (6%) developed gastric ischemia or limb ischemia and necrosis. Eight patients (16%) required an ECMO circuit change due to blood clots in the bridging tubes and oxygenator. None of these mechanical complications were fatal (Table 4).

Twenty-four patients (48%) were successfully weaned from ECMO support, and 21 patients (42%) survived to hospital discharge. The cause of death in most patients was multifactorial. Failed myocardial recovery accounted for 16 (55.2%) deaths, septicemia for 11 (37.9%), and neurological causes for 2 (6.9%). Multiorgan failure occurred in 19 patients (65.5%) among the 29 non-survivors.

Hematological and biochemical variables during extracorporeal membrane oxygenation

Peak total bilirubin and peak lactate levels during ECMO support were markedly different between survivors to hospital discharge and non-survivors. The mean peak total bilirubin level was 10.62±12.91 mg/dL and the mean peak lactate level was 10.99±4.72 mg/dL during ECMO support. The mean peak total bilirubin levels for survivors to hospital discharge and non-survivors were 4.12±3.53 mg/dL and 15.49±15.16 mg/dL, respectively (p=0.002). The mean peak lactate levels for survivors to hospital discharge and non-survivors were 8.44±4.73 mg/dL and 12.84±3.82 mg/dL, respectively (p=0.001). Both were significantly higher in non-survivors (Table 5).

Variables affecting hospital survival

Based on the univariate analysis, the factors associated with increased hospital mortality were prolonged duration

Table 3. ECMO indications and information

Variable	Hospital discharge			
	Total (n=50)	Non-survivors (n=29)	Survivors (n=21)	p-value
Indication				
CPB weaning failure	22 (44.0)	12 (54.5)	10 (45.5)	0.661
Low cardiac output	9 (18.0)	6 (66.7)	3 (33.3)	0.561
Cardiac arrest	5 (10.0)	3 (60.0)	2 (40.0)	0.724
Hypoxia	13 (26.0)	7 (53.8)	6 (46.2)	0.724
Others	1 (2.0)	1 (100.0)	0	0.390
CPR before ECMO	19 (38.0)	11 (57.9)	8 (42.1)	0.991
CPR time (min)	0 (0–28.5)	0 (0–33.0)	0 (0–11.0)	0.377
CPR time (min)	17.7±31.0	21.0±35.9	13.1±22.6	
ECMO initiation time (day)	4.3±12.2	6.03±15.5	1.95±4.7	0.248
ECMO cannulation site				0.615
Aorta, right atrium	40 (80.0)	22 (55.0)	18 (45.0)	
Open sternum	31 (62.0)	18 (58.1)	13 (41.9)	
Closed sternum	9 (18.0)	4 (44.4)	5 (55.6)	
Femoral artery, femoral vein	5 (10.0)	3 (60.0)	2 (40.0)	
Carotid artery, IJV	3 (6.0)	3 (100.0)	0	
Other	2 (4.0)	1 (50.0)	1 (50.0)	
ECMO insertion place				0.845
Operating room	23 (46.0)	13 (56.5)	10 (43.5)	
Intensive care unit bedside	27 (54.0)	16 (59.3)	11 (40.7)	
ECMO insertion				0.390
Intraoperative	18 (36.0)	9 (50.0)	9 (50.0)	
Postoperative	32 (64.0)	20 (62.5)	12 (37.5)	
Duration of ECMO support (day)	6.0 (3.0–12.0)	8.0 (4.0–23.0)	4.0 (3.0–6.0)	0.004*
Duration of ECMO support (day)	10.5±11.7	14.5±14.0	5.0±21.0	
Irrigation/debridement	15 (30.0)	12 (41.4)	3 (14.3)	0.039*
Reinsertion	7 (14.0)	7 (100.0)	0	0.017*

Values are presented as median (interquartile range), mean±standard deviation, or number (%), unless otherwise stated.
ECMO, extracorporeal membrane oxygenation; CPB, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; IJV, internal jugular vein.
*p<0.05 was considered significant.

Table 4. Complications during ECMO support

Variable	Hospital discharge			
	Total (n=50)	Non-survivors (n=29)	Survivors (n=21)	p-value
Acute kidney injury[a]	33 (66.0)	24 (82.8)	9 (42.9)	0.003*
Renal therapy				
Peritoneal dialysis	26 (52.0)	17 (58.6)	9 (42.9)	0.271
Continuous renal replacement therapy	22 (44.0)	19 (65.5)	3 (14.3)	<0.001*
Bleeding[b]	11 (22.0)	10 (34.5)	1 (4.8)	0.016*
Septicemia	15 (30.0)	15 (51.7)	0	<0.001*
Intracranial hemorrhage	4 (8.0)	2 (6.9)	2 (9.5)	1.000
Ischemic brain injury	7 (14.0)	6 (20.7)	1 (4.8)	0.215
Gastric ischemia or limb ischemia and necrosis	5 (10.0)	4 (13.7)	1 (4.8)	0.293
Disseminated intravascular coagulation	9 (18.0)	8 (27.6)	1 (4.8)	0.061
Circuit change	8 (16.0)	6 (20.7)	2 (9.5)	0.441

Values are presented as number (%).
ECMO, extracorporeal membrane oxygenation.
*p<0.05 was considered significant. [a]Acute kidney injury was defined as an elevation in creatinine of ≥200%, a creatinine level ≥4 mg/dL, or the receipt of dialysis due to oliguria. [b]Bleeding was defined as the requirement for at least 1 surgical re-exploration.

Table 5. Comparison of survivors and non-survivors in terms of hematological and biochemical variables during extracorporeal membrane oxygenation support

Variable	Hospital discharge						p-value
	Total		Non-survivors		Survivors		
	No.	Mean±SD	No.	Mean±SD	No.	Mean±SD	
Maximum white blood cell (×10³/μL)	49	15.71±6.76	28	17.25±7.84	21	13.65±4.32	0.065
Maximum C-reactive protein (mg/dL)	49	11.90±8.58	28	13.61±10.32	21	12.63±9.30	0.529
Maximum blood urea nitrogen (mg/dL)	49	30.29±19.11	28	34.82±20.36	21	24.24±15.82	0.054
Maximum creatinine (mg/dL)	49	1.15±0.80	28	1.31±0.79	21	0.93±0.78	0.097
Maximum total bilirubin (mg/dL)	49	10.62±12.91	28	15.49±15.16	21	4.12±3.53	0.002*
Maximum lactate (mg/dL)	50	10.99±4.72	29	12.84±3.82	21	8.44±4.73	0.001*

SD, standard deviation.
*p<0.05 was considered significant.

Table 6. Univariate and multivariate analysis of mortality predictors

Risk factors	Hospital discharge			
	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Duration of ECMO support	0.846 (0.738–0.971)	0.017*	-	-
Reinsertion	0.326 (0.042–2.502)	0.281	-	-
Acute kidney injury[a]	0.156 (0.043–0.570)	0.005*	-	-
Continuous renal replacement therapy	0.088 (0.021–0.371)	0.001*	0.731 (0.572–0.935)	0.013*
Bleeding[b]	0.095 (0.011–0.815)	0.032	-	-
Sepsis	0.022 (0.001–0.431)	0.012*	-	-
Irrigation/debridement	0.236 (0.057–0.985)	0.048	-	-
Maximum total bilirubin	0.801 (0.667–0.961)	0.017*	0.050 (0.008–0.309)	0.001*
Maximum lactate	0.799 (0.691–0.924)	0.002*	-	-

OR, odds ratio; CI, confidence interval; ECMO, extracorporeal membrane oxygenation.
*p<0.02 was considered significant due to the small sample size. [a]Acute kidney injury was defined as an elevation in creatinine of ≥200%, a creatinine level ≥4 mg/dL, or the receipt of dialysis due to oliguria. [b]Bleeding was defined as the requirement for at least 1 surgical re-exploration.

of ECMO support (p=0.017), renal failure (p=0.005), the need for CRRT application (p=0.001), sepsis (p=0.012), bleeding (p=0.032), a high serum lactate level (p=0.002), and a high total bilirubin level (p=0.017). In the multivariate analysis, the need for CRRT application (p=0.013) and a high serum total bilirubin level (p=0.001) were identified as independent risk factors associated with an increased risk of hospital mortality (Table 6).

Discussion

ECMO is a widely used and important treatment for patients after operations for CHD. However, substantial morbidity and mortality remain associated with postcardiotomy ECMO. The survival rate of postcardiotomy ECMO support is 33%–67% [3,4,9,12-14,16,19,20]. In this study, the overall survival to discharge for patients on ECMO support after surgical repair for CHD was 42%, which is comparable to findings from other institutions [8,20-24].

Several factors, such as low body weight and age, have shown associations with a higher mortality rate in neonates due to immature substrate-depleted myocardium and pulmonary vascular hypertension [3,4,9]. Although age and body weight were not statistically significant, a trend towards higher mortality was observed in patients younger than 9.9 months of age and less than 4.6 kg in body weight. Furthermore, the ABC score was higher in non-survivors than in survivors, although the difference was not statistically significant.

Currently, there are no internationally established criteria for the institution of ECMO. Furthermore, there are no objective criteria or guidelines defining when ECMO support is required after cardiotomy [25,26]. The indications for postcardiotomy ECMO in this study were based on the clinical judgment of the attending surgeon, pediatric intensivist, and/or pediatric cardiologist. The initiation of ECMO

support was determined based on evidence for isolated right or left ventricular dysfunction, pulmonary hypertension, and pulmonary dysfunction. This study revealed that different indications for ECMO support did not affect survival.

ECMO duration is a strong variable associated with ECMO weaning and survival after decannulation, since myocardial function after cardiotomy is more likely to return within 3–5 days and is less likely to recover after 8–10 days [12,16,27,28]. Previous studies have reported that patients requiring a longer duration of ECMO support showed lower survival rates [4,7,14]. This study showed a trend that patients were less likely to survive after 11 days of ECMO support.

Prolonged CPB is also a variable associated with a higher mortality risk [9-11,14,18]. However, in this study, survivors to discharge had a longer ACC time. Furthermore, CPB time tended to be longer in survivors to discharge although not statistically significant.

This counterintuitive trend may have been observed since many patients were placed on ECMO support in the OR due to failure to wean from CPB. While patients were in the OR, most patients would have undergone multiple attempts of CPB weaning before the conversion to ECMO. The longer CPB time in the survivors implied that MCS can improve survival by providing myocardial function recovery even in patients with long CPB and ACC times, suggesting significant myocardial dysfunction. In addition to leading to a shorter time until ECMO initiation, the initiation of ECMO in the OR would have also provided a more tightly controlled environment during ECMO implantation.

The time until ECMO initiation may affect survival. However, there are varying reports regarding whether early initiation of ECMO is associated with a better prognosis. It is thought that early ECMO support, especially cases in which ECMO support was started in the OR, most likely aided in reducing the probability of cardiac arrest and end-organ damage. Although not statistically significant, this study showed that survivors to discharge tended to have a shorter time until ECMO support despite ECMO being initiated in the OR or ICU.

Univariate risk analysis revealed that bleeding and sepsis were independent risk factors for survival to discharge. Studies have reported that bleeding complications requiring surgical re-exploration or massive transfusion of packed RBCs or blood products during ECMO support are associated with lower survival rates [7,16,29]. Although transfusion of packed RBCs may improve oxygen delivery and provide circulatory stability, the risks of transfusion-associated lung injury, infection due to immune modulation, and cellular hypoxia also increase, which may counteract the benefits [4]. In this study, patients with bleeding were less likely to survive. Sepsis has been shown to be a risk factor for adverse outcomes in patients on ECMO support [28,29]. Furthermore, patients with cardiac dysfunction and renal dysfunction are especially predisposed to a significant incidence of infections. Those with central ECMO requiring re-exploration of the mediastinum are further predisposed to a higher risk of infection. This study revealed that no patients with sepsis survived until hospital discharge.

Multivariate risk analysis identified that the need for CRRT application and high levels of total bilirubin were independent risk factors for survival to hospital discharge. Renal insufficiency during ECMO support is a well-known risk factor associated with higher mortality. The need for CRRT reflects severe secondary organ injury due to cardiovascular collapse. A study showed that pediatric patients requiring hemofiltration during postcardiotomy ECMO support had a 5 times higher mortality rate than their counterparts [12]. Moreover, a close association has been reported between the duration of ECMO support and the development of acute renal failure [3,12]. In addition to renal failure, hepatic failure suggesting MOF is a risk factor for mortality. Liver perfusion can be affected by changes in pump flow, lack of pulsatility, and rapid changes in vasopressor doses after ECMO initiation during ECMO therapy [29]. Hemodynamic instability is associated with hypoxic hepatitis during ECMO support, which leads to an increase in total bilirubin levels. Both the need for CRRT application and high levels of total bilirubin indicate malperfusion of critical organs. Furthermore, high lactate levels, which were identified as a risk factor in the univariate analysis, are a surrogate marker of tissue perfusion. All of these variables imply that maintaining sufficient perfusion to critical organs is vital for better survival outcomes. Secondary organ damage may be the result of cardiovascular shock prior to the initiation of ECMO, or the result of poor perfusion while on ECMO support. Therefore, any delays in the application of ECMO must be avoided to provide early ECMO support prior to end-organ damage, and ECMO management should be optimized to maximize the perfusion of critical organs.

This study was a retrospective study conducted at a single center with a small sample size. The statistical analyses could have lacked power to detect clinically significant factors associated with poor survival. Many variables that

could be potential risk factors for survival (e.g., hemodynamic variables, ventilator parameters, and other laboratory variables) were not adjusted for, introducing confounding factors. Furthermore, despite total bilirubin being a marker representing hepatic failure, an increased total bilirubin level could not be interpreted as directly representing hepatic failure from malperfusion because of the lack of indirect and direct bilirubin levels in many patients. A thorough investigation of the cause of high total bilirubin levels was limited. Additionally, the protocol-driven management of hemodynamics was not the same throughout the extended period of the study, although similar principles were used.

In conclusion, ECMO is an important therapeutic modality for patients unresponsive to conventional management after surgical correction for CHD. In-depth research to examine risk factors and predict poor outcomes is crucial. Appropriate patient selection for ECMO support, early ECMO initiation before end-organ damage, improved intervention strategies, and better ECMO management in patients without severe complications, particularly hypoperfusion of critical organs, are crucial for achieving positive outcomes.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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