



# Infections Acquired During Venoarterial Extracorporeal Membrane Oxygenation Postcardiac Surgery in Children: A Retrospective Observational Study

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## Abstract

**Introduction** Extracorporeal membrane oxygenation (ECMO) is increasingly being used in refractory cardiac and pulmonary dysfunction as a rescue modality. The common indications for establishing venoarterial ECMO (VA-ECMO) support in children postcardiac surgery are failure to wean from cardiopulmonary bypass (CPB), postcardiotomy cardiogenic shock (PCCS), refractory pulmonary arterial hypertension, and as a bridge to recovery or transplant. The survival rate of children on VA-ECMO support is 45%. The most frequently encountered complications during VA-ECMO are bleeding, thrombosis, acute kidney injury, and infections. Among those, infections acquired during VA-ECMO lead to high morbidity and mortality. Hence, this study aimed to determine infection rates, causal microorganisms, and mortality risk factors in children developing an infection during VA-ECMO therapy.

**Methods** This retrospective observational study was conducted on 106 children under 14 years of age who underwent elective or emergent cardiac surgery (between 2016 and 2020) and required VA-ECMO support. Medical records were reviewed to collect the targeted variables and analyzed.

**Results** Out of 106 children, 49 (46.23%) acquired infections representing a prevalence of 46.23% and an infection rate of 186.4 episodes per 1,000 ECMO days. Prevalence and acquired infection rate/1,000 ECMO days were higher in the non-survivor group than in the survivor group (26.42 vs. 19.81%) and (215.07 vs. 157.49), respectively. The bloodstream infection (BSI) and catheter-associated urinary tract infection (CAUTI) episodes were 53.04 and 68.19 per 1,000 ECMO days, and the ventilator-associated pneumonia (VAP) rate was 44.50 per 1,000 ventilator days. The

## Keywords

- ▶ acquired infections
- ▶ postcardiac surgery
- ▶ VA-ECMO

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mean preoperative admission duration, aortic cross-clamping duration, CPB duration (minutes), and vasoactive-inotropic score were higher in the nonsurviving children ( $p < 0.001$ ). Similarly, prolonged mean ECMO duration was also found in the nonsurvivor group compared with the survivor group ( $p = 0.03$ ).

**Conclusion** In our study, the prevalence of acquired infection during VA-ECMO was 46.23%. The incidence of BSI, CAUTI, and VAP per 1,000 ECMO days was higher in the nonsurvivor group than in survivors. *Acinetobacter baumannii* was the most common cultured gram-negative organism in VAP and BSI, with 67.65% *Acinetobacter* spp. resistant to carbapenems. CAUTI was predominately due to *Candida* species during VA-ECMO.

## Introduction

Extracorporeal membrane oxygenation (ECMO) is increasingly being used in refractory cardiac and pulmonary dysfunction as a rescue modality.<sup>1</sup> It provides reliable and sustained circulatory support in children who have undergone cardiac surgery. The common indications for establishing venoarterial ECMO (VA-ECMO) support in children postcardiac surgery are failure to wean from cardiopulmonary bypass (CPB), postcardiotomy cardiogenic shock (PCCS), refractory pulmonary arterial hypertension, and as a bridge to recovery or transplant.<sup>2,3</sup> PCCS is a significant concern in children, particularly neonates. Occasionally, PCCS is refractory to inotropic support and, in the absence of mechanical circulatory support, may prove fatal.<sup>4</sup> For nearly five decades, the VA-ECMO has been the first-line mechanical circulatory support in patient's refractory to conventional therapies after cardiac surgery.<sup>5,6</sup> VA-ECMO allows blood to be drained from a central vein and returned to the arterial system. Therefore, VA-ECMO provides both respiratory and circulatory support. The survival rate of children on VA-ECMO support is 45%.<sup>7</sup> Timely initiation of VA-ECMO in selected candidates is essential to achieve maximum survival benefits. VA-ECMO has evolved and undergone improvements over the decades, but it still carries significant complications. The most frequently encountered complications during VA-ECMO are bleeding, thrombosis, acute kidney injury, and infections.<sup>8,9</sup> Among those, infections acquired during VA-ECMO lead to high morbidity and mortality.<sup>10–12</sup>

Hence, this study aimed to determine infection rates, causal microorganisms, and mortality risk factors in children developing infections on VA-ECMO support after cardiac surgery. The primary objective of our study was to determine infection rates, causal microorganisms, and mortality risk factors in children developing an infection during VA-ECMO. Our secondary objectives were to compare infection rates among survivor and nonsurvivor groups and to understand the pattern of change in infectious agents and their antibiotic resistance over the study period.

## Methods

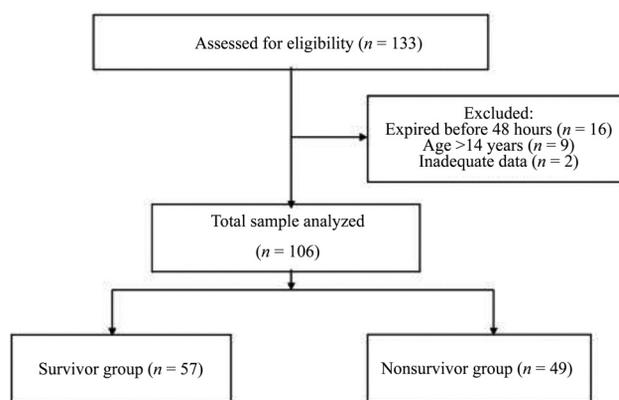
This retrospective, observational study was conducted between January 2016 and December 2020 in All India Institute

of Medical Sciences, New Delhi, India. The study protocol was approved by the Institute Ethics Committee (IECPG-278/3/2021). The study included children <14 years of age who underwent elective or emergency cardiac surgery and required VA-ECMO. We excluded children who expired within 48 hours of initiation of VA-ECMO, and preoperative positive cultures were excluded from the study.

### Study Protocol

After institutional ethics committee approval, the medical records of all children who underwent VA-ECMO following cardiac surgery from January 2016 to December 2020 were reviewed and collected the following variables—demographic data; aortic cross-clamp (AXC), CPB, and ECMO duration; vasoactive-inotropic score; complications during ECMO; and microorganisms isolated from different samples (blood, endotracheal or tracheal, urine, pleural fluid, and wound swab) of patients. VA-ECMO protocol and management at our institute has been published earlier by Singh et al.<sup>13</sup> Vasoactive-inotropic scores were calculated from a website (<https://peds.ufl.edu/apps/nsafa/default.aspx>), and VISmax score quantified the amount of inotropic agent infused to maintain hemodynamic stability.<sup>14</sup> Antibiotics were changed as per our intensive care unit (ICU) protocol, antibiotics after cardiac surgery protocol, which has been published earlier as well.<sup>15</sup>

An infection acquired during ECMO was recognized as infection only when a causal organism could be isolated from the sample (e.g., blood, endotracheal or tracheal, urine, pleural fluid, and wound swab) after initiation of ECMO to 48 hours after ECMO discontinuation. Bloodstream infection (BSI) was defined as the presence of viable bacterial or fungal microorganism in the bloodstream (later demonstrated by the positivity of one or more blood cultures) that elicit or have elicited an inflammatory response characterized by the alteration of clinical, laboratory, and hemodynamic parameters.<sup>16</sup> Ventilator-associated pneumonia (VAP) was defined by infection of the pulmonary parenchyma in the patients exposed to invasive mechanical ventilation for at least 48 hours.<sup>17</sup> Catheter-associated urinary tract infection (CAUTI) was defined as the infection of the urinary tract caused by a urinary catheter after second day of placement.<sup>18</sup>



**Fig. 1** Algorithm for patient distribution of VA ECMO for this study.

### Statistical Analysis

All the statistical analyses were performed with SPSS 20.0; IBM, Chicago, IL, United States). All data were presented in mean, standard deviation (SD), and number with percentage. Differences between survivor and nonsurvivor were tested with the Mann–Whitney test for continuous variables and Fisher's exact test for categorical variables. To evaluate the risk for mortality, a stepwise logistic regression analysis was performed, and results were presented as the odds ratio (OR) and 95% confidence interval. A  $p$ -value  $<0.05$  was considered significant for all the statistical tests.

### Results

In total, 133 children who underwent VA-ECMO between 2016 and 2020 were analyzed for this study. Among them, 27 were excluded (16 expired before 48 hours, 9 children were more than 14 years old, and 2 had inadequate data). The remaining 106 children were included in the study (► **Fig. 1**).

#### Cardiac Surgeries Requiring VA-ECMO Support

The most common surgery that required VA-ECMO support in the immediate postoperative period was arterial switch operation 87.73% (93 of 106) followed by anomalous left coronary artery from the pulmonary artery repair 3.77% (4 of 106) and total anomalous pulmonary venous connection (TAPVC) repair 3.77% (3 of 106). Three children who underwent repair for TAPVC required VA-ECMO support but none of them survived. Other children requiring ECMO support underwent tetralogy of Fallot repair (one), mitral valve replacement plus tricuspid valve repair (one), hemitruncus repair (two), repair for congenital aortic stenosis (one), and right pulmonary artery reimplantation (one). In total, 77 children could not be weaned off CPB after undergoing surgery and 29 developed refractory PCCS, for which they required VA-ECMO support. Out of these 106 children, 32 were  $<1$  month, 66 children were 1 to 12 months, and 8 were  $>12$  months. Based on survival, these children were divided into survivor ( $n = 57$ ) and nonsurvivor groups ( $n = 49$ ).

#### Prevalence and Infection Rates on ECMO

In our cohort, 49 children had acquired infections out of total 106 ECMO patients from January 2015 to December 2020,

representing a prevalence of 46.23% and an infection rate of 186.4 episodes per 1,000 ECMO days. The prevalence of infection was highest in 1 to 12 months group followed by  $<1$  month group and  $>12$  months group that were 27.36%, 16.98 and 1.89%, respectively. The children aged between 1 and 12 months had a higher incidence of BSI and CAUTI than children less than 1 month of age. The incidence of VAP was higher in children less than 1 month of age compared with 1 to 12 months old. No BSI and CAUTI were found in  $>12$  months group (► **Table 1**). Prevalence and acquired infection rate/1,000 ECMO days were higher in the nonsurvivor group than in the survivor group (26.42 vs. 19.81%) and (215.07 vs. 157.49) respectively. The BSI and CAUTI episodes were 53.04 and 68.19 per 1,000 ECMO days, and the VAP rate was 44.50 per 1,000 ventilator days. The incidence of BSI, CAUTI, and VAP was higher in nonsurvivor group than in the survivor group (► **Table 2**).

#### Cultured Microorganisms During VA-ECMO Support

The most frequently cultured organism in children with culture-positive samples during VA-ECMO was *Acinetobacter baumannii* (34.78%). Of these, 67.5% of samples were carbapenem-resistant, but all samples were susceptible to colistin. Other gram-negative isolates were *Klebsiella pneumoniae* (10.43%), *Escherichia coli* (6.08%), *Pseudomonas aeruginosa* (4.34%), *Stenotrophomonas maltophilia* (3.47%), and *Burkholderia cepacia* (2.61%). In our study, VAP, CAUTI, and BSI were the predominant infections (► **Table 3**). Isolated microorganisms from cultures and their antibiotic sensitivity and resistance patterns are depicted in ► **Table 4**. All bacterial isolates showed some degree of resistance to commonly used antibiotics in the ICU. There was no resistance to colistin. Carbapenem resistance for *P. aeruginosa*, *A. baumannii*, *K. pneumoniae*, and *E. coli* was 100, 67.5, 66.66, and 57.14% respectively. *B. cepacia* was found to be 100% sensitive to carbapenems (► **Table 5**).

#### Survivors and Nonsurvivors After VA-ECMO Support

The mean age and SD of survivor and nonsurvivor group were  $7.87 \pm 17.76$  and  $8.04 \pm 22.28$  months, respectively. Similarly,  $4.23 \pm 2.35$  and  $4.88 \pm 4.37$  were body weights recorded in the survivor and nonsurvivor groups. The mean preoperative admission duration (hours) was higher in nonsurvivor children ( $302.55 \pm 249.28$  vs.  $128.03 \pm 99.55$ ;  $p < 0.001$ ). Similarly, the mean AXC duration, CPB duration (minutes), and vasoactive-inotropic score were higher in the nonsurvivor group ( $101.19 \pm 27.09$  vs.  $72.86 \pm 27.66$ ;  $p < 0.001$ ), ( $158.59 \pm 39.77$  vs.  $120.27 \pm 44.22$ ;  $p < 0.001$ ), and ( $29.91 \pm 10.51$  vs.  $18.05 \pm 5.68$ ;  $p < 0.001$ ), respectively.

Prolonged mean ECMO duration was also found in the nonsurvivor group compared with the survivor group ( $54.28 \pm 29.67$  vs.  $66.53 \pm 27.07$ ;  $p = 0.03$ ). Interestingly, the survivor group had longer mean ventilator assistance (hours) than the nonsurvivor group ( $191 \pm 145.56$  vs.  $173.09 \pm 159.49$ ;  $p = 0.26$ ). Similarly, the survivor group had longer ICU stay ( $351.49 \pm 245.26$  vs.  $198.45 \pm 197.75$ ;  $p < 0.001$ ) that was clinically significant. Reexploration for bleeding was three times (74.08 vs. 25.92%;  $p < 0.001$ ) and

**Table 1** Various infection rate during ECMO and VAP rate during VA-ECMO support in different categories of pediatric population

Infection rate	<1 mo (n = 32)	1–12 mo (n = 66)	>12 mo (n = 8)
Prevalence rate	16.98%	27.36%	1.89%
Infection rate /1,000 ECMO days	198.39	194.5	9.38
BSI rate/1,000 ECMO days	53.69	60.21	0
CAUTI rate/1,000 ECMO days	64.43	86.96	0
VAP rate/1,000 ventilator days	48.65	40.77	26.76

Abbreviations: BSI, bloodstream infection; CAUTI, catheter-associated urinary tract infection; ECMO, extracorporeal membrane oxygenation; VA, venoarterial; VAP, ventilator-associated pneumonia.

**Table 2** Various infection rate during VA-ECMO support among survivor and nonsurvivor groups

Infection rate	Total (n = 106)	Survived (n = 59)	Nonsurvived (n = 47)
Prevalence	46.23%	19.81%	26.42%
Infection rate /1,000 ECMO days	186.4	157.49	215.07
BSI rate/1,000 ECMO Days	53.04	29.99	76.81
CAUTI rate/1,000 ECMO days	68.19	59.99	69.13
VAP rate/1,000 ventilator days	44.50	52.31	67.59

Abbreviations: BSI, bloodstream infection; CAUTI, catheter-associated urinary tract infection; ECMO, extracorporeal membrane oxygenation; VA, venoarterial; VAP, ventilator-associated pneumonia.

**Table 3** Microorganisms associated with various acquired infection during VA-ECMO in children

BSI, n = 18 (15.65%)		VAP, n = 62 (53.91%)		Drain fluid, n = 11 (9.5%)		CAUTI, n = 23 (20%)		PD fluid, n = 1 (0.86)	
Organism	n (%)	Organism	n (%)	Organism	n (%)	Organism	n (%)	Organism	n (%)
<i>Acinetobacter baumannii</i>	5 (27.77)	<i>A.baumannii</i>	32 (51.61)	<i>A.baumannii</i>	3 (27.27)	<i>Klebsiella pneumoniae</i>	1 (4.34)	<i>K.pneumoniae</i>	1 (100)
<i>K. pneumoniae</i>	4 (22.22)	<i>Escherichia coli</i>	7 (11.29)	<i>K.pneumoniae</i>	1 (9.09)	<i>Candida spp</i>	20 (86.95)		
<i>Pseudomonas aeruginosa</i>	2 (11.11)	<i>K.pneumoniae</i>	5 (8.06)	<i>Enterococcus faecium</i>	1 (9.09)	Polymicrobial	2 (8.69)		
<i>Stenotrophomonas maltophilia</i>	2 (11.11)	<i>P.aeruginosa</i>	3 (4.83)	Polymicrobial	6 (54.54)				
<i>Staphylococcus aureus</i>	1 (5.55)	<i>Burkholderia cepacia</i>	3 (4.83)						
<i>Candida spp</i>	1 (5.55)	<i>S.maltophilia</i>	2 (3.22)						
Polymicrobial	3 (16.66)	<i>S.aureus</i>	1(1.61)						
		Polymicrobial	9 (14.52)						

Abbreviations: BSI, bloodstream infection; CAUTI, catheter-associated urinary tract infection; ECMO, extracorporeal membrane oxygenation; PD, peritoneal dialysis; VA, venoarterial; VAP, ventilator-associated pneumonia.

blood transfusion >100 mL/kg four times (80.77 vs.19.23%;  $p = 0.001$ ) higher in the nonsurvivor group. Acute kidney injury (AKI) and peritoneal dialysis (PD) were slightly higher in the nonsurvivor group than in the survivor group (11 [52.38%] vs. 10 [47.62%];  $p = 0.017$ ) and (8 [61.54%] vs. 5 [38.46%];  $p = 0.037$ ), respectively (–Table 6). A stepwise logistic regression analysis was conducted to determine the independent risk factors for mortality. The analysis determined that weight <4 kg ( $p < 0.05$ ), CBP time >120

minutes ( $p < 0.001$ ), surgical exploration ( $p < 0.001$ ), packed red blood cells (PRBC) transfusion >100 mL/kg ( $p < 0.001$ ), and culture positive samples ( $p < 0.05$ ) were significant independent predictors of mortality in VA-ECMO.

## Discussion

A total of 49 infections were reported in 106 VA-ECMO patients from 2015 to 2020, representing a prevalence of

**Table 4** Antibiotic resistance patterns on commonly isolated gram-negative bacteria during VA-ECMO in our study

Microorganism and antibiotic resistance	<i>Acinetobacter baumannii</i> n = 40 (%)	<i>Klebsiella pneumoniae</i> n = 12 (%)	<i>Escherichia coli</i> n = 7 (%)	<i>Pseudomonas aeruginosa</i> n = 5 (%)	<i>Burkholderia cepacia</i> n = 3 (%)
Amikacin	37 (92.5)	12 (100)	6 (85.71)	2 (40)	3 (100)
Ciprofloxacin	38 (95)	10 (83.33)	7 (100)	1 (20)	3 (100)
Ceftazidime	40 (100)	12 (100)	7 (100)	0	1 (33.33)
Piperacillin/Tazobactam	40 (100)	12 (100)	5 (71.43)	5 (100)	3 (100)
Cefoperazone/tazobactam	26 (100)	12 (100)	5 (71.43)	5 (100)	3 (100)
Meropenem	30 (75)	9 (75)	4 (57.14)	5 (100)	0
Imipenem	29 (72.5)	8 (66.66)	4 (57.14)	5 (100)	3 (100)
Colistin	0	0	0	0	0

Abbreviations: ECMO, extracorporeal membrane oxygenation; VA, venoarterial.

**Table 5** Isolated gram-negative bacteria and carbapenem sensitivity patterns during VA-ECMO support

Cultured organism on ECMO	Total cultures positive n = 115 (%)	Carbapenem sensitive n (%)	Carbapenem resistant n (%)
<i>Acinetobacter baumannii</i>	40 (34.78)	13 (32.5)	27 (67.5)
<i>Klebsiella pneumoniae</i>	12 (10.43)	4 (33.33)	8 (66.66)
<i>Escherichia coli</i>	7 (6.08)	3 (42.85)	4 (57.14)
<i>Pseudomonas aeruginosa</i>	5 (4.34)	0	5 (100)
<i>Burkholderia cepacia</i>	3 (2.60)	3 (100)	0

Abbreviations: ECMO, extracorporeal membrane oxygenation; VA, venoarterial.

46.23% and an infection rate of 186.4 per 1,000 ECMO days. We also found a higher prevalence of approximately 26.42% and an acquired infection rate of 215.07/1,000 ECMO days in the nonsurvivor group. We also found a higher prevalence of approximately 26.42% and an acquired infection rate of 215.07/1,000 ECMO days in the nonsurvivor group. Austin et al reported fewer VA-ECMO infections as 7.2 to 18%, with an estimated incidence between 4.82 and 17.2 episodes per 1,000 ECMO days.<sup>19</sup> Furthermore, Bizzarro et al and Kutleša et al, in their studies, also found similar ECMO infection rates of 20.9 and 35%, respectively.<sup>20,21</sup>

Our study showed that BSI and CAUTI episodes were 53.04 and 68.19 per 1,000 ECMO days and VAP rate 44.50 per 1,000 ventilator days, and all were higher in the nonsurvivor group than in the survivor group. Another study showed that 64% (142 out of 220) patients had developed hospital-acquired infections (mostly VAP and BSI) with VA-ECMO >48 hours duration. This study also found higher septic shock episodes with BSI followed by VAP and mediastinitis.<sup>8</sup> Aubron et al proved that the adult population had a higher risk of nosocomial infection than the pediatric population during ECMO support (20.5 vs. 6.1%;  $p < 0.001$ ).<sup>9</sup> In our study, children aged between 1 and 12 months had a higher incidence of BSI and CAUTI than children less than 1 month of age. The incidence of VAP was higher in children less than 1 month of age compared with 1 to 12 months old.

The most frequently isolated organism was *A. baumannii* for both VAP and BSI in our study. The other organisms

isolated were *K. pneumoniae*, *E. coli*, *P. aeruginosa*, and *S. maltophilia*, and *B. cepacia*. A recent study by Kim et al also reported gram-negative bacteria as common isolates from VAP and BSI in unison with our findings.<sup>22</sup> In contrast to our study, the Extracorporeal Life Support Organization Registry reported coagulase-negative staphylococcus as the most frequently isolated organism from ECMO patients. Other infectious agents reported were *Candida* species, *P. aeruginosa*, Enterobacteriaceae, *Staphylococcus aureus*, and Enterococcus species.<sup>2</sup> The reason for different infection rates and microorganisms in our study may be distinct microbial flora and customized antimicrobial stewardship programs of our ICU. The incidence of polymicrobial growth (more than three organisms reported in samples) was VAP, 9 out of 62; drain fluid, 6 out of 11; BSI, 3 out of 18; and CAUTI, 2 out of 23. Schmidt et al also reported a similar result in their study.<sup>8</sup> The occurrence of progressive antimicrobial resistance in gram-negative bacteria is a sign of concern.

*Candida* species is a commonly isolated organism from patients during ECMO support.<sup>23</sup> *Candida* species were isolated in 95.23% (20 out of 21) of urine samples in our study. Sun et al reported that *Candida* species were isolated in two-third of the urine cultures, whereas *E. coli* was isolated in one-third of the samples.<sup>24</sup> Children requiring ECMO support are critically ill and undergo immunomodulation due to blood contact with a nonbiological foreign surface and the use of steroids. They also receive broad-spectrum antibiotics, multiple invasive devices, and

**Table 6** The demographics and baseline characteristics of VA-ECMO children's data in combined, survivor, and nonsurvivor groups

Variables	Total <i>n</i> = 106 Mean ± SD	Survivor <i>n</i> = 57 Mean ± SD	Nonsurvivors <i>n</i> = 49 Mean ± SD	<i>p</i> -Value
Age, months	7.95 ± 19.79	7.87 ± 17.76	8.04 ± 22.28	0.0084
Weight, kilograms	4.52 ± 3.39	4.23 ± 2.35	4.88 ± 4.37	0.1654
Male, gender	106	47 (44.33%)	45 (42.45%)	0.930
Preoperative admission, hours	205.42 ± 200.72	128.03 ± 99.55	302.55 ± 249.28	<0.001
AXC duration, minutes	85.42 ± 30.73	72.86 ± 27.66	101.19 ± 27.09	<0.001
CPB duration, minutes	137.26 ± 46.25	120.27 ± 44.22	158.59 ± 39.77	<0.001
ECMO duration, hours	59.72 ± 29.06	54.28 ± 29.67	66.53 ± 27.07	0.0305
Vasoactive-inotropic score, VIS	23.32 ± 10.06	18.05 ± 5.68	29.91 ± 10.51	<0.001
Ventilation duration, hours	83.05 ± 151.42	191 ± 145.56	173.09 ± 159.49	0.2670
ICU duration, hours	283.63 ± 237.06	351.49 ± 245.26	198.45 ± 197.75	<0.001
Surgical exploration (more than three times)	27 (25.47%)	7 (25.92%)	22 (74.08%)	<0.001
PRBC transfusion (>100 mL/kg)	26 (26.53%)	5 (19.23%)	21 (80.77%)	0.001
Acute kidney injury	21 (19.81%)	10 (47.62%)	11 (52.38%)	0.017
Peritoneal dialysis	13 (12.26%)	5 (38.46%)	8 (61.54%)	0.037
Tracheostomy	10 (9.43%)	7 (70.00%)	3 (30.00%)	0.403
Limb ischemia	12 (11.32%)	7 (58.34%)	5 (41.66%)	0.9
Cerebral hemorrhage	2 (1.88%)	0	2 (100%)	0.1

Abbreviations: AXC, aortic cross-clamping; CPB, cardiopulmonary bypass; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; PRBC, packed red blood cells; SD, standard deviation; VA, venoarterial.

frequent blood transfusions, all risk factors for *Candida* infection.

Central VA-ECMO is a complex, invasive procedure that requires open sternum, skin, and the prolonged use of invasive devices that makes children vulnerable to infections. A prolonged ECMO support leads to dysregulated immune response and an incessant inflammatory reaction. The reexploration surgeries for bleeding, multiple blood transfusions during ECMO, and hypoperfusion state aggravate this inflammatory cascade.<sup>25,26</sup> Immunomodulation occurring during ECMO serves as a risk factor for infection. A recent study done by Burket et al reported that the rate of BSI increased proportionately from 9.5 to 64.5 per 1,000 ECMO days with an increased duration of ECMO.<sup>27</sup> Another study reported that the only predictor for acquired nosocomial BSI during VA-ECMO was a duration of support >10 days.<sup>28</sup> Meyer et al concluded that sepsis in ECMO patients is an independent negative predictor of survival for the neonates.<sup>29</sup> A logical conclusion is that prolonged duration of ECMO leads to BSI and sepsis, especially in neonates, thus increasing mortality. In our study, the duration of ECMO therapy also significantly correlated with adverse outcomes ( $p = 0.0305$ ).

In our cohort, male children predominate in both survivor and nonsurvivor groups. Younger children had more survival benefits in the survivor group ( $p = 0.008$ ). The survivor's group had fewer preoperative admission hours than nonsurvivors, which was statistically significant ( $p < 0.001$ ). A

prolonged preoperative stay in nonsurviving children may indicate sicker children requiring medical optimization or intensive care therapy before surgery.

In our study, VA-ECMO was instituted for children with hemodynamic instability and poor ventricular function while weaning from CPB in the operating room. The mean AXC, CPB time, and VIS were significantly more in the nonsurvivor group than in the survivor group ( $p < 0.001$ ). Because not all the children were operated on by the same surgeon, prolonged AXC and CPB time may reflect the complexity of the surgery and the surgeon's experience.

In total, 93 (87.73%) out of 106 children were weaned successfully from VA-ECMO support, of which 59 (55.66%) were subsequently discharged from ICU. However, the remaining 34 weaned from ECMO support died in the ICU. These patients' primary cause of death was sepsis and consecutive multiorgan failure. In 13 (12.26%) out of 106 children who required ECMO support, cardiac function did not improve, weaning was not possible, VA-ECMO support had to be withdrawn, and they died subsequently. The leading cause of death in patients with failed weaning was persistent low cardiac output (10 out of 13). Other causes of mortality were coagulopathy (8 out of 13), culture-proven infections (4 out of 13), and cerebral hemorrhagic stroke (2 out of 13). Rastan et al and Hsu et al reported a better weaning rate with VA-ECMO following PCCS patients ranging from 31 to 60%, despite high "in-hospital" mortality of 59 to 84%.<sup>30,31</sup> In this study, we could not establish the percentage

of children discharged from the hospital due to the study's retrospective nature. An earlier prospective study of our group showed a 45% survival at discharge and at 4 months follow-up.<sup>13</sup>

In our study, 21 (19.81%) children had AKI, in which 13 (12.26%) received PD, the incidence of which was statistically significant between survivor and nonsurvivor groups (► **Table 6**). The AKI could be due to systemic hypotension, systemic inflammatory response, nephrotoxic drugs, and microembolization to renal vasculature during ECMO. Lee et al in their study reported a higher incidence (55.6%) of AKI in VA-ECMO patients and associated it with increased mortality.<sup>32</sup> Another study in children by Selewski et al showed continuous renal replacement therapy reduced fluid overload during ECMO in survivors compared with nonsurvivors (24.5 vs. 38%,  $p = 0.006$ ).<sup>33</sup>

Two children (1.88%) in our cohort had a cerebral bleed after 48 hours of ECMO initiation, and they were declared dead on ECMO. These two children had thrombocytopenia and required >100 mL/kg PRBC transfusion. Seven children in the survivor group and five in the nonsurvivor group developed arterial thrombus due to arterial lines during and after weaning VA-ECMO. A logistic regression analysis model identified weight <4 kg, CBP time >120 minutes, surgical exploration, PRBC transfusion >100 mL/kg, and culture-positive children as independent predictors of ECMO mortality.

They are certain limitations of the study. Ours is a retrospective study. We did not consider culture-negative sepsis and biochemical markers of infections. The number of children more than 1 year of age was less.

In conclusion, the prevalence of acquired infection during VA-ECMO was 46.23% in our study. The prevalence was highest in 1 to 12 months group followed by <1 month group and >12 months group which were 27.36, 16.98, and 1.89%, respectively. The incidence rates of BSI, CAUTI, and VAP per 1,000 ECMO days were higher in nonsurvivor group compared with survivors. *A. baumannii* was the most common cultured gram-negative organism in VAP and BSI during VA-ECMO with 67.65% Acinetobacter samples resistant to carbapenems and CAUTI was predominately due to Candida species during VA-ECMO.

#### Disclosures

None.

#### Financial Disclosure

None.

#### Conflict of Interest

None declared.

#### References

- Shekar K, Mullany DV, Thomson B, Ziegenfuss M, Platts DG, Fraser JF. Extracorporeal life support devices and strategies for management of acute cardiorespiratory failure in adult patients: a comprehensive review. *Crit Care* 2014;18(03):219–223
- Thiagarajan RR, Barbaro RP, Rycus PT, et al; ELSO Member Centers. Extracorporeal Life Support Organization Registry International Report 2016. *ASAIO J* 2017;63(01):60–67
- Golding LA. Postcardiotomy mechanical support. *Semin Thorac Cardiovasc Surg* 1991;3(01):29–32
- Guihaire J, Dang Van S, Rouze S, et al. Clinical outcomes in patients after extracorporeal membrane oxygenation support for postcardiotomy cardiogenic shock: a single-centre experience of 92 cases. *Interact Cardiovasc Thorac Surg* 2017;25(03):363–369
- Baffes TG, Fridman JL, Bicoff JP, Whitehill JL. Extracorporeal circulation for support of palliative cardiac surgery in infants. *Ann Thorac Surg* 1970;10(04):354–363
- Soeter JR, Mamiya RT, Sprague AY, McNamara JJ. Prolonged extracorporeal oxygenation for cardiorespiratory failure after tetralogy correction. *J Thorac Cardiovasc Surg* 1973;66(02):214–218
- Xie A, Phan K, Tsai Y-C, Yan TD, Forrest P. Venoarterial extracorporeal membrane oxygenation for cardiogenic shock and cardiac arrest: a meta-analysis. *J Cardiothorac Vasc Anesth* 2015;29(03):637–645
- Schmidt M, Bréchet N, Hariri S, et al. Nosocomial infections in adult cardiogenic shock patients supported by venoarterial extracorporeal membrane oxygenation. *Clin Infect Dis* 2012;55(12):1633–1641
- Aubron C, Cheng AC, Pilcher D, et al. Infections acquired by adults who receive extracorporeal membrane oxygenation: risk factors and outcome. *Infect Control Hosp Epidemiol* 2013;34(01):24–30
- Peitz G, Brown T, Murry DJ. Incidence and characterization of sepsis in an ECMO population. *Crit Care Med* 2018;46:325
- Allyn J, Ferdynus C, Lo Pinto H, et al. Complication patterns in patients undergoing venoarterial extracorporeal membrane oxygenation in intensive care unit: multiple correspondence analysis and hierarchical ascendant classification. *PLoS One* 2018;13(09):e0203643
- Gopalakrishnan R, Vashisht R. Sepsis and ECMO. *Indian J Thorac Cardiovasc Surg* 2021;37(Suppl 2):267–274
- Singh SP, Sengupta S, Sahu MK, et al. Outcome of cardiac ECMO in children less than 1 year age undergoing corrective cardiac surgery. *J Card Crit Care* 2020;4:25–32
- Aziz KB, Lavilla OC, Wynn JL, Lure AC, Gipson D, de la Cruz D. Maximum vasoactive-inotropic score and mortality in extremely premature, extremely low birth weight infants. *J Perinatol* 2021;41(09):2337–2344
- Singh SP, Yagani S, Shamsiya TPP, Pandey S, Sahu MK, Dhatteval US. Impact of an evidence-based antibiotic protocol on common gram-negative bacteria's antibiotic resistance in a cardiac surgical intensive care unit. *J Card Crit Care* 2021;5:12–17
- Viscoli C. Bloodstream infections: the peak of the iceberg. *Virulence* 2016;7(03):248–251
- Papazian L, Klompas M, Luyt CE. Ventilator-associated pneumonia in adults: a narrative review. *Intensive Care Med* 2020;46(05):888–906
- Gould CV, Umscheid CA, Agarwal RK, Kuntz G, Pegues DA. Health-care Infection Control Practices Advisory Committee. Guideline for prevention of catheter-associated urinary tract infections 2009. *Infect Control Hosp Epidemiol* 2010;31(04):319–326
- Austin DE, Kerr SJ, Al-Soufi S, et al. Nosocomial infections acquired by patients treated with extracorporeal membrane oxygenation. *Crit Care Resusc* 2017;19(Suppl 1):68–75
- Bizzarro MJ, Conrad SA, Kaufman DA, Rycus P. Extracorporeal Life Support Organization Task Force on Infections, Extracorporeal Membrane Oxygenation. Infections acquired during extracorporeal membrane oxygenation in neonates, children, and adults. *Pediatr Crit Care Med* 2011;12(03):277–281
- Kutleša M, Santini M, Krajinović V, et al. Nosocomial blood stream infections in patients treated with venovenous extracorporeal membrane oxygenation for acute respiratory distress syndrome. *Minerva Anestesiol* 2017;83(05):493–501
- Kim GS, Lee KS, Park CK, et al. Nosocomial infection in adult patients undergoing veno-arterial extracorporeal membrane oxygenation. *J Korean Med Sci* 2017;32(04):593–598

- 23 Coffin SE, Bell LM, Manning M, Polin R. Nosocomial infections in neonates receiving extracorporeal membrane oxygenation. *Infect Control Hosp Epidemiol* 1997;18(02):93–96
- 24 Sun HY, Ko WJ, Tsai PR, et al. Infections occurring during extracorporeal membrane oxygenation use in adult patients. *J Thorac Cardiovasc Surg* 2010;140(05):1125–32.e2
- 25 O'Neill JM, Schutze GE, Heulitt MJ, Simpson PM, Taylor BJ. Nosocomial infections during extracorporeal membrane oxygenation. *Intensive Care Med* 2001;27(08):1247–1253
- 26 Millar JE, Fanning JP, McDonald CI, McAuley DF, Fraser JF. The inflammatory response to extracorporeal membrane oxygenation (ECMO): a review of the pathophysiology. *Crit Care* 2016;20(01):387–392
- 27 Burket JS, Bartlett RH, Vander Hyde K, Chenoweth CE. Nosocomial infections in adult patients undergoing extracorporeal membrane oxygenation. *Clin Infect Dis* 1999;28(04):828–833
- 28 Steiner CK, Stewart DL, Bond SJ, Hornung CA, McKay VJ. Predictors of acquiring a nosocomial bloodstream infection on extracorporeal membrane oxygenation. *J Pediatr Surg* 2001;36(03):487–492
- 29 Meyer DM, Jessen ME, Eberhart RC. Extracorporeal Life Support Organization. Neonatal extracorporeal membrane oxygenation complicated by sepsis. *Ann Thorac Surg* 1995;59(04):975–980
- 30 Rastan AJ, Dege A, Mohr M, et al. Early and late outcomes of 517 consecutive adult patients treated with extracorporeal membrane oxygenation for refractory postcardiotomy cardiogenic shock. *J Thorac Cardiovasc Surg* 2010;139(02):302–311, 311.e1
- 31 Hsu PS, Chen JL, Hong GJ, et al. Extracorporeal membrane oxygenation for refractory cardiogenic shock after cardiac surgery: predictors of early mortality and outcome from 51 adult patients. *Eur J Cardiothorac Surg* 2010;37(02):328–333
- 32 Lee SW, Yu M-Y, Lee H, et al. Risk factors for acute kidney injury and in-Hospital mortality in patients receiving extracorporeal membrane oxygenation. *PLoS One* 2015;10(10):e0140674
- 33 Selewski DT, Cornell TT, Blatt NB, et al. Fluid overload and fluid removal in pediatric patients on extracorporeal membrane oxygenation requiring continuous renal replacement therapy. *Crit Care Med* 2012;40(09):2694–2699