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Clinical outcomes of pediatric extracorporeal life support: Single center experience

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Ethics Committee Approval
This study was approved by Ege University Faculty of Medicine clinical research ethics committee (number: 21-2T/18, 19.02.2021). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: The use of extracorporeal life support (ECLS) in children has notably increased over the last two decades, the indications for its use are expanding. According to the Extracorporeal Life Support Organization (ELSO) 2016 report, the rate of pediatric extracorporeal membrane oxygenation (ECMO) runs was 24% among all ECMO patients. A relationship between higher ECMO volume and mortality for neonates and adult patients supported with ECLS was reported. Different mortality rates were reported for different diagnostic and age groups for ECMO patients. The objective of this study was to describe our experience with pediatric ECMO.

Methods: A retrospective cohort study was conducted on patients between 1 month and 18 years who underwent ECMO treatment in a pediatric intensive care unit from January 2015 to June 2022. Patients' characteristics, outcomes, and complications were recorded.

Results: A total of 22 children underwent ECMO during the study period. The median age of the patients was 4.5 years (ranging from 2 months to 18 years). Eight (36.4%) patients required venoarterial (VA) ECMO, and 14 patients (63.6%) required venovenous (VV) ECMO. Among the eight children who underwent VA ECMO, central cannulation was performed in 62.5% of cases. Seven children who required VV ECMO were cannulated with a double lumen catheter (42.8%). Thirteen (59.1%) patients were successfully weaned from ECMO. Weaning rates were 25% and 78.5% for VA and VV ECMO, respectively. Among 22 patients, overall hospital mortality was 72.7%. Mortality rates were 87.5% and 64.2% for VA and VV ECMO. Five patients (22.7%) survived to hospital discharge.

Conclusion: Extracorporeal life support is one of the life-saving treatment modalities. This study found that the children requiring VA ECMO had a higher mortality rate than children requiring VV ECMO, a result that is consistent with the ELSO registry report. In our study, children requiring VV ECMO had a higher weaning rate than the ELSO registry data. However, they had a lower survival to discharge rate than the ELSO registry data. We feel that by describing this case series, the spread of ECMO practice may be supported in Turkey.

Keywords: extracorporeal life support, children, heart failure, respiratory failure, intensive care

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Introduction

Extracorporeal membrane oxygenation (ECMO) or extracorporeal life support (ECLS) is a treatment modality used in patients with severe respiratory and/or heart failure [1,2]. The first successful case of neonatal ECMO support was implemented in 1976 [3]. According to the Extracorporeal Life Support Organization (ELSO) 2016 report, the rate of pediatric ECMO runs was 24% among all ECMO patients (9.6% respiratory, 10.6% cardiac, and 3.8% ECLS to support cardiopulmonary resuscitation) [4].

ECMO is basically implemented in two different ways: (1) venovenous ECMO (VV-ECMO) or (2) venoarterial ECMO (VA-ECMO). While the main purpose in VV-ECMO is to support lung function, the main purpose in VA-ECMO is to provide both respiratory and cardiac support. Both VA and VV ECMO can be applied to pediatric patients who are experiencing respiratory failure, but VV ECMO is preferred primarily to avoid systemic thromboembolic complications. While an increase in the frequency of VV ECMO has been observed in this patient population in recent years, it is thought that increasing availability for double lumen cannula is associated with this condition.

Survival rates for ECMO patients have been reported with a variety of ranges among different patient age groups and different indications. Neonatal respiratory patients have the highest survival rates, while extracorporeal cardiopulmonary resuscitation (ECPR) patients have the lowest [5]. In children with severe multi-organ failure, survival is 43%–47% [6,7]. The rate of survival to discharge is 61% for pediatric respiratory ECMO cases and 44%–54% for neonatal and pediatric congenital heart disease patients [8,9].

In this study, we aimed to describe the patient demographics, indications, complications and outcomes in children requiring VV or VA ECMO.

Materials and methods

A retrospective cohort study was conducted on patients between one month and 18 years supported with ECMO in a 17-bed tertiary pediatric intensive care unit (PICU) at Ege University Children's Hospital from January 2015 to June 2022. The study was approved by the Ethics Committee of Ege University Faculty of Medicine (2021-2T/18). We retrospectively analyzed the medical records from 22 children. Incomplete medical records were excluded. Patient's demographics, primary diagnosis, comorbidities, pre-ECMO/post-ECMO laboratory analysis, ECMO variables, cannula size, duration of ECMO support, vasoactive inotropic score (VIS), weaning from ECMO, and complications were evaluated. The Pediatric Risk of Mortality (PRISM) score, Pediatric Logistics Organ Dysfunction (PELOD) score, length of PICU stay, and in-hospital mortality was recorded.

Cannulation is performed at the bedside for VV ECMO and both peripheral and central VA ECMO by the cardiovascular surgeon. Unfractionated heparin infusion was given with the goal of reaching an activated clotting time within 180 to 220 s. The ECMO flow was set to maintain adequate tissue perfusion pressure; for VA ECMO, 80–150 ml/kg/min and for VV ECMO, 60–120 ml/kg/min. A central venous oxygen saturation > 70%, normal arterial lactate, adequate mean arterial blood pressure indicated adequate tissue perfusion.

ECMO indications included a reversible cause of respiratory and/or circulatory failure with persistent inadequate gas exchange and/or high need for vasoactive inotropic medications [10,11].

Statistical analysis

We performed descriptive analysis on the data using SPSS 22 for statistical calculations. Continuous values are presented as medians with interquartile range (IQR). The Mann–Whitney U test was used for continuous data. Chi-squared analysis and Fisher's exact test were used for categorical data. *P*-value <0.05 was considered significant.

Results

A total of 22 children underwent ECLS during the study period. The median age of the patients was 4.5 years (ranging from 2 months to18 years), and 54.5% of participants were female. Eight (36.4%) patients required VA ECMO, and 14 patients (63.6%) required VV ECMO. Among the eight children who underwent VA ECMO, central cannulation was performed in 62.5% of cases. Six children who required VV ECMO were cannulated using a double lumen catheter. Nine children (40.9%) had an underlying medical condition, of which acquired immune deficiencies (5/22, 22.7%), and congenital immune deficiencies (2/22, 9%) were the most common. Among VV ECMO patients, one child was diagnosed with pediatric acute respiratory distress syndrome due to coronavirus 2019 (COVID-19)-associated pneumonia. The demographic data of the patients are given in Table 1.

The median PRISM score was 20, and the median PELOD score was 21. Inotropic support was needed in 78.2% of cases. The median vasoactive inotrope score was 62.1 (range, 0–440). The median oxygenation index was 33 (range 7.8–100.1) in VV ECMO patients and 24 (range 2.7–29.5) in VA ECMO patients. The median duration of ECMO support was 15.2 days (ranging from 4 h to 53 days). The median length of stay in the PICU was 30 days (range 1–139 days). Oxygenators were changed in 26% of patients without adverse effects.

A comparison of VV and VA ECMO patients is shown in Table 2. VVECMO patients had a longer duration of mechanical ventilation days (36.5 [30.7–70.7] versus 13.5 [4.5–24.2]; P=0.004), longer ECMO duration (16 [11.7–36] versus 7.5 [3.5–14.5] day; P=0.035), longer PICU length of stay (43.5 [30.7–71.7] versus 17 [7–24] days; P=0.006), and longer hospital stays (64 [30.7–83] versus 17 [7 –24] days; P=0.002). The other variables showed no significant differences between the two groups.

Anticoagulation-related complications were diagnosed in 68.1% of children (15/22). Among patients, four children had major bleeding (three patients with intracranial hemorrhage and one patient with a gastrointestinal system hemorrhage). The lower gastrointestinal system hemorrhage, which developed in a double lumen VV ECMO patient, was managed by correction of coagulopathy, intestinal resection, and a jejunostomy procedure. Limb ischemia developed in a patient with peripheral VA ECMO managed by perfusion cannulation.

Table 1: Patients demographics and outcomes

Patient	Age (year)	Weight (kg)	Pre-existing condition	Comorbidities	ECMO modality	Decanulated from ECMO	Alive at discharge
1	9	52	Posterior mediastinal mass	B Cell ALL	VV	Yes	Yes
2	14	40	Heart failure		VA	No	No
3	2.5	10	Trauma, PARDS		VV	Yes	No
4	12	50	Pneumonia, air leak	Langerhans cell histiocytosis	VV	Yes	No
5	14	47	Dilated cardiomyopathy		VA	No	No
6	2	10	Fulminant hepatitis	Liver transplantation atypical HUS	VV	No	No
7	4	12	Myocarditis		VA	Yes	No
8	11	36	PARDS	Cystic fibrosis	VV	No	No
9	18	70	Postpartum cardiomyopathy		VA	No	No
10	15	47	Calcium channel blocker intoxication		VA	Yes	Yes
11	0.5	6	Cardiopulmonary arrest		VA	Yes	No
12	1.5	12	PARDS		VV	Yes	No
13	4.5	15	PARDS		VV	Yes	Yes
14	12	78	Septic shock	AML M2	VV	Yes	No
15	16	30	Dilated cardiomyopathy		VA	No	No
16	2.5	4.5	Myocarditis		VA	No	No
17	0	3.7	Bacterial pneumonia, PARDS	LAD	VV	No	No
18	2	12	Viral Pneumonia, PARDS	Common B ALL	VV	Yes	Yes
19	3	19	Viral Pneumonia, PARDS	B Cell ALL	VV	No	No
20	3	15	COVID-19 pneumonia, PARDS	SCID	VV	No	No
21	11	47	Hydrocarbon inhalation, PARDS		VV	Yes	Yes
22	1.3	10	Viral pneumonia, PARDS		VV	Yes	Yes

ECMO: Extracorporeal membrane oxygenation, ALL: Acute lymphoblastic leukemia, PARDS: Pediatric acute respiratory distress syndrome, HUS: Hemolytic uremic syndrome, AML: Acute myeloid leukemia, LAD: Leukocyte adhesion deficiency, COVID-19: Coronavirus disease-2019, SCID: Severe combined immunodeficiency

Table 2: Clinical characteristics of patients with VV-ECMO and VA-ECMO

	VV-ECMO (n = 14)	VA-ECMO (n = 8)	*P*-value
Gender; Male, n (%)	7 (50)	3 (37.5)	
Age (years), median (IQR)	4.2 (1.4–11.2)	8.5 (2.1–14.7)	0.402
Weight (kg), median (IQR)	15 (11.5–46.2)	29.5 (10–47)	0.868
PRISM score, median (IQR)	16 (13.5–21)	23 (15.7–30.7)	0.095
PELOD score, median (IQR)	16.5 (11.7–22.2)	22 (13.5–23)	0.365
Peak VIS in first 24h of sepsis, median (IQR)	40 (5.0–86)	75 (50–130)	0.067
Duration of MV (days), median (IQR)	36.5 (30.7–70.7)	13.5 (4.5–24.2)	0.004
Hospital days prior ECMO, median (IQR)	3.5 (2–4.2)	2.5 (1–8.5)	0.616
ECMO duration, median (IQR)	16 (11.7–36)	7.5 (3.5–14.5)	0.035
PICU length of stay (days), median (IQR)	43.5 (30.7–71.7)	17 (7–24)	0.006
Hospital length of stay (days), median (IQR)	64 (30.7–83)	17 (7–24)	0.002
Mortality, n (%)	9 (64.2)	7 (87.5)	0.613

VV-ECMO: Venovenous extracorporeal membrane oxygenation, VA-ECMO: Venoarterial extracorporeal membrane oxygenation, IQR: Interquartile range, PRISM: Pediatric risk of mortality, PELOD: Pediatric Logistic Organ Dysfunction, VIS: Vasoactive inotropic score, MV: mechanical ventilation, PICU: Pediatric intensive care unit

Table 3: Comparison between survivors and non-survivors

	Survivors (n = 6)	Non-survivors (n = 16)	*P*-value
Gender; Male, n (%)	2 (33.3)	8 (50)	0.646
Age (years), median (IQR)	6 (1.8–12)	4.2 (1.6–13.5)	1.000
Weight (kg), median (IQR)	29.5(11.5–56.5)	17.5 (10–45.2)	0.449
ECMO modality **VV ECMO, n (%)** **VA ECMO, n (%)**	 5 (35.7) 1 (12.5)	 9 (64.3) 7 (87.5)	
PRISM score, median (IQR)	19 (14–24)	18.5 (12.5–24.2)	0.747
PELOD score, median (IQR)	16.5 (11.7 - 22.2)	21.5 (11–23)	0.858
Pre-ECMO lactate (mmol/L)	6.5 (2.9–18)	2.2 (0.8–7.6)	0.083
Requirement of CRRT, *n* (%)	2 (33.3)	8 (50)	0.646
Peak VIS in first 24h of sepsis, median (IQR)	20 (5.0–88.7)	50 (15–90)	0.381
Duration of MV (days), median (IQR)	36.5 (26.5–57.5)	28 (14.2–60.2)	0.367
Hospital days prior ECMO, median (IQR)	2.5 (1.7–4)	3.5 (1.2–5.7)	0.494
ECMO duration, median (IQR)	11.5 (8–44.5)	15 (5.2–27.2)	1.000
PICU length of stay (days), median (IQR)	43.5 (29.5–61.2)	28 (15.5–60.2)	0.407
Hospital length of stay (days), median (IQR)	75.5 (49–83)	28 (15.5–60.2)	0.098

IQR: Interquartile range, ECMO; extracorporeal membrane oxygenation, VV: venovenous, VA: venoarterial, PRISM: Pediatric risk of mortality, PELOD: Pediatric Logistic Organ Dysfunction, CRRT: continuous renal replacement therapy, VIS: Vasoactive inotropic score, MV: mechanical ventilation, PICU: Pediatric intensive care unit

All patients required mechanical ventilation support. Ten patients required continuous renal replacement treatment (CRRT) during ECMO support, and pre-existing acute kidney injury was present in five patients. Three patients underwent plasmapheresis due to coagulopathy and multiple organ failure. All central cannulations were performed bedside in the intensive care unit, and no patient developed mediastinitis.

Thirteen (59.1%) patients were successfully weaned from ECMO. The weaning rate was 25% for VA ECMO and 78.5% for VV ECMO. Among 22 patients, overall hospital mortality was 72.7%. Five patients (21.7%) survived to hospital discharge. The mortality rates of VA ECMO and VV ECMO were 87.5% and 64.2%, respectively. No differences in terms of disease severity scores, peak VIS, pre-ECMO lactate levels, ECMO duration, and lengths of PICU and hospital stays between the survivors and non-survivors were found (Table 3). The mortality rate attributed to ECMO was 27.2% (6/22 patients). The two non-survivors who underwent bronchoscopy were considered to have developed irreversible lung damage on the basis of progressive pulmonary fibrosis.

Discussion

The use of ECMO in patients with cardiac and pulmonary failure has increased over the last three decades despite optimal medical treatment [1]. VV ECMO indications in children, especially, cover a broad range of lung diseases. In our case series of 22 patients, ECMO was applied to cases with different diagnoses due to respiratory and cardiac failure.

According to the ELSO report, pediatric respiratory ECLS has a 58% rate of for survival to discharge. Among pediatric cardiac ECLS patients, cardiogenic shock has a rate of 42% survival to discharge [3,4]. In our patient population, we found a lower survival to discharge rate, especially for the VA ECMO group. Among eight patients who underwent cardiac ECLS, five had dilated cardiomyopathy, two had myocarditis, and one had cardiogenic shock due to intoxication. Our patients with end-stage heart failure, whose only chance was a heart transplant, could not survive because they could not be bridged to transplantation.

Our patient population did not include the children with congenital heart disease who underwent VA ECMO to wean them from cardiopulmonary bypass following cardiac surgery. In our hospital, PICU is located in a different building from the cardiovascular and pediatric surgery departments. This situation results in ECMO runs for patients with congenital heart disease

and congenital diaphragmatic hernia to be performed outside the PICU.

Previous studies have reported that higher annual ECMO patient volume is associated with a lower mortality rate [12,13]. It has also been speculated that higher ECMO volume is associated with better patient outcomes. ELSO registry reported that higher age group specific ECMO volume was associated with lower mortality rates for neonates and adults. They reported no relationship in the pediatric population [4]. Pediatric specific analysis revealed that the relationship between mortality and higher patient volume is present only in pediatric patients requiring cardiac ECMO [12]. We think that the high mortality rates in our study, especially for VA ECMO patients, may be related to the fact that our patient population did not include congenital heart surgery patients.

In developing countries, such as ours, with limited human and financial resources, it is important to identify new ECMO centers, establish ECMO teams, and organize their training. ECMO education and training should be provided for all healthcare professionals who are responsible for caring for ECMO patients. Providing the best outcome for ECMO patients depends on a multidisciplinary team of well-educated and experienced surgeons, intensivists, nurses, and perfusionists.

Limitations

Our study has several limitations, mainly as a result of retrospective study design. Our patient cohort has a small population similar to those in previously reported single center studies. In our study, children requiring ECMO after congenital heart surgery were not included in the cohort. For this reason, we think that the mortality rates of VA ECMO patients are higher than the previously reported rates.

Conclusion

Extracorporeal life support is one of several lifesaving treatment modalities. This study found that the children requiring VA ECMO had higher mortality rates than children requiring VV ECMO, a finding that is consistent with the ELSO registry report. In our study, children requiring VV ECMO had higher weaning rates than the ELSO registry data. However, they had a lower survival to discharge rates than the ELSO registry data. We feel that by describing this case series, the spread of ECMO practice may be supported in Turkey.

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