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Outcomes of extracorporeal membrane oxygenation support in pediatric hemato-oncology patients

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Background: In this study, we reviewed the outcomes of pediatric patients with malignancies who underwent hematopoietic stem cell transplantation (HSCT) and extracorporeal membrane oxygenation (ECMO).

Methods: We retrospectively analyzed the records of pediatric hemato-oncology patients treated with chemotherapy or HSCT and who received ECMO in the pediatric intensive care unit (PICU) at Seoul National University Children's Hospital from January 2012 to December 2020.

Results: Over a 9-year period, 21 patients (14 males and 7 females) received ECMO at a single pediatric institute; 10 patients (48%) received veno-arterial (VA) ECMO for septic shock (n=5), acute respiratory distress syndrome (ARDS) (n=3), stress-induced myopathy (n=1), or hepatopulmonary syndrome (n=1); and 11 patients (52%) received veno-venous (VV) ECMO for ARDS due to pneumocystis pneumonia (n=1), air leak (n=3), influenza (n=1), pulmonary hemorrhage (n=1), or unknown etiology (n=5). All patients received chemotherapy; 9 received anthracycline drugs and 14 (67%) underwent HSCT. Thirteen patients (62%) were diagnosed with malignancies and 8 (38%) were diagnosed with non-malignant disease. Among the 21 patients, 6 (29%) survived ECMO in the PICU and 5 (24%) survived to hospital discharge. Among patients treated for septic shock, 3 of 5 patients (60%) who underwent ECMO and 5 of 10 patients (50%) who underwent VA ECMO survived. However, all the patients who underwent VA ECMO or VV ECMO for ARDS died.

Conclusions: ECMO is a feasible treatment option for respiratory or heart failure in pediatric patients receiving chemotherapy or undergoing HSCT.

Key Words: extracorporeal membrane oxygenation; hematopoietic stem cell transplantation; intensive care unit, pediatrics; neoplasm

Original Article

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INTRODUCTION

Extracorporeal membrane oxygenation (ECMO) is a cornerstone intervention for the management of adult and pediatric severe cardiac or respiratory failure that is unresponsive to conventional treatment [1,2]. ECMO is used to supply oxygen, assist with clearance of CO_2, and provide circulatory support, creating an opportunity for resuscitation and reducing organ damage from treatment [3]. The use of ECMO in children with certain conditions, especially malignant disease and organ transplantation, poses a high risk of mortality [4]. In pediat-

ric oncology, application of ECMO is challenging due to the unique pathophysiological aspects and complications associated with malignancy and its treatment. The performance of ECMO in children with malignant disease is controversial, and the reported mortality rate ranges from 25%–100%, the latter in a group of children undergoing hematopoietic stem cell transplantation (HSCT) [5,6].

In one multicenter survey, 78% of doctors did not consider malignancy a contraindication for ECMO, 17% considered it a relative contraindication, and 5% an absolute contraindication [7]. Pediatric patients with cancer often present with complications, such as infection, bleeding, and organ dysfunction, which can complicate ECMO management. The type of underlying malignancy, stage of the disease, and associated complications may play significant roles in determining survival outcomes in pediatric patients. In the present study, we aimed to investigate these factors and their effects on ECMO survival outcomes, specifically in pediatric patients with malignancies and subjects undergoing HSCT.

KEY MESSAGES

- Six of 21 patients (29%) survived extracorporeal membrane oxygenation (ECMO) in the pediatric intensive care unit and 5 patients (24%) survived to hospital discharge.
- ECMO is a feasible treatment option for respiratory or heart failure in pediatric patients receiving chemotherapy or undergoing hematopoietic stem cell transplantation.

MATERIALS AND METHODS

We retrospectively analyzed the medical records of all 21 children treated with chemotherapy or HSCT and who received ECMO in the pediatric intensive care unit (PICU) at Seoul National University Children's Hospital from January 2012 to December 2020. The Institutional Review Board of Seoul National University waived the need to obtain ethics approval for the study protocol and written consent from the study participants (No. H-2108-122-1246).

Continuous variables are presented as means±standard deviations if normally distributed and as medians (ranges/interquartile ranges [IQRs]) if non-normally distributed. Categorical variables are presented as frequencies (percentages). Statistical analysis was conducted using R software (ver. 3.3.2 GUI 1.68 Mavericks build; The R Foundation for Statistical Computing). The Kaplan-Meier method was performed for analysis of event-free and overall survival, and the log-rank test was used for subgroup comparisons. A $P<0.05$ was considered statistically significant.

RESULTS

Clinical Characteristics

The mean age of the 21 patients was 4.97 years, 13 patients (62%) had an underlying malignant disease, and 9 patients (43%) previously used doxorubicin. HSCT was performed in 14 patients (67%); 7 (50%) experienced graft-versus-host disease. During treatment, 12 patients (57%) underwent continuous renal replacement therapy and 20 (95%) received ventilation; 5 (25%) received high-frequency ventilation. Five patients (24%) underwent cardiopulmonary resuscitation before EMCO, and ECMO was initiated 75 days on average after anticancer drug administration and 4 days after ventilator application. On average, ECMO was performed for 22 days. Infection was confirmed in 13 patients (62%), some testing positive for 2 or more types of bacteria. Six of 17 patients (35%) were administered 3 or more inotropic agents. The mean oxygen saturation index was 22.17, the mean partial pressure of carbon dioxide (PCO_2) was 77.62 mm Hg, mean pH was 7.18, and mean lactic acid concentration was 1.5 mmol/L. The demographic and key clinical characteristics of the 21 patients are summarized in Tables 1 and 2.

Outcomes

Among the 21 patients, two (10%) underwent veno-venous (VV) to veno-arterial (VA) ECMO conversion due to aggravation of cardiac function, one (5%) underwent VA to VV ECMO conversion to improve cardiac function, and two (10%) underwent lung transplantation (Table 3). The mean number of continuous ECMO days was 22.0, ranging from 6.0–42.0 days. Malignant relapse after ECMO occurred in four of 13 patients (31%) with malignant disease. The ICU and hospital survival rates were six of 21 (29%) and five of 21 (24%), respectively. The mean survival was 38.0 days, with a range of 11–180 days. Among the 16 patients who died during their hospital stay, five (31%) died of infection, four (25%) due to bleeding, two (13%) to heart failure, four (25%) of unknown causes, and one (6%) because the family requested ECMO be discontinued. Regarding ECMO complications, infection occurred in seven of 21

Table 1. Patients' characteristics

Demographic	Value (n=21)
Male	14 (66.7)
Age (yr)	5 (4–8)
Underlying malignant disease	13 (61.9)
Adriamycin use history	9 (42.9)
Hematopoietic stem cell transplantation history	14 (66.7)
GVHD history (n=14)	7 (50.0)
Apply continuous renal replacement therapy	12 (57.1)
Apply mechanical ventilator	20 (95.2)
Apply high frequency ventilator (n=20)	5 (25.0)
Cardiopulmonary resuscitation	5 (23.8)
ECMO from starting chemotherapy days	75.0 (19.0–129.0)
ECMO from applying ventilator care days	4.0 (0–15.5)
VV ECMO	11 (52.4)
ECMO duration (day)	22 (6–42)
Proven infection	13 (61.9)
Fungal infection	7 (33.3)
Bacterial infection	4 (19.1)
Viral infection	5 (23.8)
Ejection fraction of heart (%)	58.4±20.4
Using inotropics	17 (81.0)
More than three kinds of inotropics (n=17)	6 (35.3)
Systolic blood pressure (mm Hg)	68.9±26.1
Heart rate (bpm)	143.8±24.2
Oxygen saturation (%)	67.4±23.5
Oxygenation saturation index	22.2 (13.9–41.1)
FiO_2	0.7±0.1
Mean airway pressure (cm H_2O)	21.0±6.1
Total bilirubin (mg/dl)	1.2 (0.8–2.7)
Platelet count (x10^9/L)	51,000 (32,000–93,000)
White blood cell count (x10^6/L)	1,710 (860–5,340)
Absolute neutrophil count (x10^6/L)	730 (80–3,630)
Hemoglobin (g/dl)	10.4±1.7
pH	7.18±0.08
PCO_2 (mm Hg)	77.6±28.6
Lactic acid (mmol/L)	1.5 (0.9–8.9)

Values are presented as number (%), median (interquartile range), or mean±standard deviation.
GVHD: graft-versus-host disease; ECMO: extracorporeal membrane oxygenation support; VV: veno-venous; FiO_2: fraction of inspired oxygen; PCO_2: partial pressure of carbon dioxide.

cases (33%), bleeding in four of 21 (19%), heart failure in two of 21 (10%), and thromboembolism in four of 21 (19%).

Analyses

Between survivors (n=5) and non-survivors (n=16), significant differences were observed in the number of days ECMO was provided with a ventilator (0.8±1.5 vs. 9.9±9.4, P=0.002), percentage of patients receiving VV ECMO (0% vs. 69%, P=0.030), left ventricular ejection fraction (29% [IQR, 24%–50%] vs. 69% [IQR, 59%–76%], P=0.002), and percentage of patients administered more than three types of inotropics (80,0% vs. 12.5%, P=0.019), and PCO_2 (51.4±18.3 mm Hg vs. 85.8±26.4 mm Hg, P=0.014) (Table 4).

Among the 21 participants, 6 had heart-related morbidities (heart group) and 15 had lung-related morbidities (lung group) (Table 5). Comparison of the two groups resulted in several notable observations. The median (IQR) age of participants in the heart group was 9 years (6–16 years, whereas that in the lung group was 4 years (2–6 years, P=0.045). Regarding ECMO modes, all six participants in the heart group underwent VA ECMO, and 73% subjects in the lung group underwent VV ECMO (P=0.011). Regarding oxygenation measures, the mean oxygen saturation was significantly higher in the heart group (87.3% ±17.0% vs. 59.5%±21.2%, P=0.010) and the median oxygenation saturation index was significantly higher in the lung group (28.8 [IQR, 19.7–43.1] vs. 6.7 [IQR, 6.2–9.3], P=0.001). The mean hemoglobin concentration was lower in the heart group (9.1±1.8 g/dl) than in the lung group (11.0±1.4 g/dl, P=0.016). In blood gas analyses, the median PCO_2 level was significantly higher in the lung group (94.0 mm Hg [IQR, 70.5–114.5 mm Hg] vs. 41.0 mm Hg [IQR, 35.0–62.0 mm Hg], P=0.001). The median lactic acid level was significantly higher in the heart group (11.0 mmol/L [IQR, 6.5–15.0 mmol/L] vs. 1.1 mmol/L [IQR, 0.8–1.7 mmol/L], P=0.004) and the median survival time was significantly longer (432.0 days [IQR, 180.0–702.0 days] vs. 30.0 days [IQR, 8.0–41.5 days], P=0.004). The ICU survival rate was significantly higher in the heart group (83% vs.7%, P=0.003) and similar to the hospital discharge rate (67% vs. 7%, P=0.019).

In our analysis of survival curves (Figure 1), we observed a significant divergence between the groups undergoing VV ECMO and VA ECMO, as evidenced by the log-rank test P-value of 0.010 (Figure 1B). This indicated a statistically significant difference in survival rates between these two patient groups. Furthermore, infection type appeared to influence survival outcomes. Specifically, patients with viral infections exhibited a worse survival trajectory than subjects without viral infections (P=0.005) (Figure 1C). This difference may be because viral infections more frequently manifested as respiratory failure than non-viral infections. We also evaluated the effect of complications on patient survival. Notably, patients with bleeding complications had a significantly worse survival curve than

Table 2. Total patients' outcomes (n=21)

Patient no.	Age (yr)	Year	Underlying disease	HCST/last chemo (day)	Reason/pathogenesis	ECMO type	RRT/CPR	ECMO duration days/ related complication	Survival duration	Outcome (ICU/ward/discharged, cause of death)
1	4.4	2012	B acute lymphoblastic leukemia	NA/+27	ARDS/PCP	VA	Y/N	36/Infection (*Trichosporon asahii*)	36 day	Death (ICU, septic shock)
2	4.2	2012	Osteopetrosis	rBMT/+120	Septic shock/ mucormycosis	VA	N/Y	42/Cerebral infarction	42 day	Death (ICU, wanted)
3	4.4	2014	Acute myeloblastic leukemia	uCBT/+144	ARDS/air leak, CMV	VV	Y/N	21/NA	21 day	Death (ICU, unknown)
4	1.2	2015	Neuroblastoma	NA/+18	ARDS/air leak	VV	N/N	1/Hemothorax	1 day	Death (ICU, bleeding)
5	8.2	2016	B acute lymphoblastic leukemia	NA/+23	Myopathy/unknown	VA	N/N	6/Thromboembolism	Last follow-up, 4.6 yr	Alive
6	1.7	2017	Hemophagocytic lymphohistiocytosis	uPBSCT/+88	ARDS/unknown, CMV	VV	N/N	27/Infection (IRAB)	38 day	Death (ICU, septic shock)
7	4.7	2017	Medulloblastoma	aPBSCT/+75	ARDS/unknown	VV	N/N	4/Infection (IRAB) hemoperitoneum	4 day	Death (ICU, bleeding)
8	15.7	2018	Severe aplastic anemia	uPBSCT/+19	Septic shock/IRAB	VA	Y/N	5/Infection (IRAB)	180 day	Death (ward, septic shock)
9	0.7	2018	B acute lymphoblastic leukemia	NA/+3	ARDS/parainfluenza	VA	N/Y	0/Thromboembolism	0 day	Death (ICU, ECMO insertion failure)
10	1.2	2018	Hemophagocytic lymphohistiocytosis	NA/+12	ARDS/aspergillus, influenza	VV	Y/Y	5/Infection (IRAB)	11 day	Death (ICU, septic shock)
11	7.3	2019	Neuroblastoma	aPBSCT/+80	ARDS/pulmonary hemorrhage	VV	Y/N	45/Heart failure, air leak	45 day	Death (ICU, heart failure)
12	2.5	2019	B acute lymphoblastic leukemia	uPBSCT/+473	ARDS/air leak	VV	Y/N	30/NA	30 day	Death (ICU, unknown)
13	5.0	2019	Chronic granulomatous disease	hPBSCT/+129	ARDS/PCP	VV	N/N	38/NA	38 day	Death (ICU, Unknown)
14	21.7	2019	Chronic granulomatous disease	hPBSCT/+128	ARDS/unknown	VV	N/N	79/Infection (*Aspergillus*) Intracranial hemorrhage	79 day	Death (ICU, Bleeding)
15	6.3	2019	Pleuropulmonary blastoma	NA/+15	Septic shock/*Candida*	VA	Y/Y	22/Neuropathy	Last follow-up, 1.9 yr	Alive
16	18.0	2019	Myelodysplastic syndrome	hPBSCT/+224	Septic shock/ *Escherichia coli*	VA	Y/N	6/NA	391 day	Death (discharged, secondary AML)
17	5.4	2019	Dyskeratosis congenital	hPBSCT/+1170	Hepatopulmonary syndrome/underlying	VA	Y/N	65/NA	Last follow-up, 2.1 yr	Alive
18	8.3	2019	Renal cell carcinoma	aPBSCT/+1843	ARDS/unknown	VV	N/Y	64/Infection (IRAB)	64 day	Death (ICU, septic shock)
19	10.4	2020	Osteosarcoma	NA/+9	Septic shock/ *Klebsiella pneumoniae*	VA	Y/N	10/Embolism	Last follow-up, 1.3 yr	Alive
20	10.3	2020	Medulloblastoma	aPBSCT/+66	ARDS/pulmonary hypertension	VA	Y/N	9/Heart failure	9 day	Death (ICU, heart failure)
21	3.7	2020	Krabbe disease	hPBSCT/+61	ARDS/adenovirus	VV	Y/N	7/Hemothorax, rhabdomyolysis	7 day	Death (ICU, bleeding)

HSCT: hematopoietic stem cell transplantation; ECMO: extracorporeal membrane oxygenation; RRT: renal replacement therapy; CPR: cardiopulmonary resuscitation; ICU: intensive care unit; NA: not available; ARDS: acute respiration distress syndrome; PCP: pneumocystis carinii jirovecii; VA: veno-arterial; Y: yes; N: no; rBMT: related bone marrow transplantation; uCBT: unrelated cord blood transplantation; CMV: cytomegalovirus; VV: veno-venous; uPBSCT: unrelated peripheral blood stem cell transplantation; aPBSCT: autologous peripheral blood stem cell transplantation; IRAB: imipenem resistant *Acinetobacter baumannii*; hPBSCT: haploidentical peripheral blood stem cell transplantation; AML: acute myeloid leukemia.

Table 3. ECMO result

Variable	Value (n=21)
ECMO conversion (VV → VA)	2 (9.5)
ECMO conversion (VA → VV)	1 (4.8)
Lung transplantation	2 (9.5)
ECMO duration (day)	22.0 (6.0–42.0)
Malignant relapse after ECMO (n=13)	4 (30.8)
ICU survival	6 (28.6)
In hospital survival	5 (23.8)
Cause of death	
Infection	5 (23.8)
Bleeding	4 (19.0)
Heart failure	2 (9.5)
Unknown	4 (19.0)
Wanted	1 (4.8)
ECMO complication	
Infection	7 (33.3)
Bleeding	4 (19.0)
Thromboembolism	4 (19.0)
Air leak	1 (4.8)
Peripheral neuropathy	1 (4.8)
Rhabdomyolysis	1 (4.8)

Values are presented as number (%) or median (interquartile range).
ECMO: extracorporeal membrane oxygenation; VV: veno-venous; VA: veno-arterial; ICU: intensive care unit.

those without bleeding (P=0.048) (Figure 1D, Supplementary Figure 1).

DISCUSSION

Previous case reports have described ECMO in conjunction with various cancer-related treatments. In one study, ECMO was applied after bone marrow transplantation in patients with severe combined immunodeficiency [8], and in another study, ECMO was used in a patient with post-HSCT diffuse alveolar hemorrhaging [9]. In addition, ECMO has been used to treat tumor lysis syndrome, fungemia, and respiratory syncytial virus infection, all of which occur during the treatment of children with leukemia [10,11].

Advances in medical technology have led to improvements in the application of ECMO in pediatric patients with cancer. Recent reports have indicated an ECMO success rate in pediatric settings of 20%–40% [12,13]. In the present study, we observed ICU and hospital survival rates of 29% and 24%, respectively, similar to previously reported survival rates [14-17]. In a previous analysis conducted at a single institution in South Korea, the survival rate among 15 adult patients with

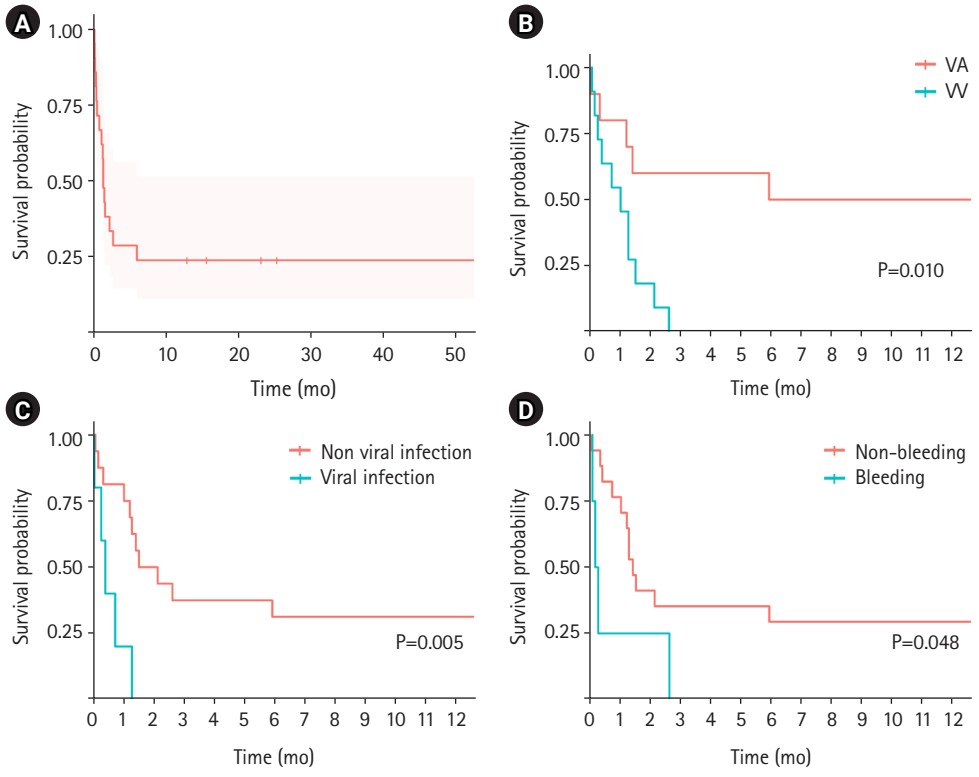

Figure 1. (A) Kaplan-Meier survival curve of extracorporeal membrane oxygenation support (ECMO). (B) Comparison between veno-arterial (VA) ECMO and veno-venous (VV) ECMO. (C) Comparison between viral infection. (D) Comparison between Bleeding event.

Table 4. Comparison between survivors and non-survivors (n=21)

Risk factor	Survivor (n=5)	Non-survivor (n=16)	P-value
Age (yr)	8 (6–10)	4 (2–8)	0.062
Male	3 (60.0)	11 (68.8)	1.000
Underlying malignant disease	4 (80.0)	9 (56.2)	0.669
Previous hematopoietic stem cell transplantation	2 (40.0)	12 (75.0)	0.365
Previous graft-versus-host disease	2 (40.0)	5 (31.2)	1.000
Previous cardiopulmonary resuscitation	1 (20.0)	4 (25.0)	1.000
ECMO from last chemotherapy (day)	23.0 (15.0–224.0)	77.5 (23.0–128.5)	0.780
ECMO from starting ventilator care (day)	0.8±1.5	9.9±9.4	0.002
VV ECMO	0	11 (68.8)	0.030
ECMO duration (day)	10.0 (6.0–22.0)	28.5 (6.0–43.5)	0.710
Therapy (high-dose steroid pulse)	1 (20.0)	6 (37.5)	0.856
Therapy (continuous renal replacement)	4 (80.0)	8 (50.0)	0.506
Fungal infection	1 (20.0)	6 (37.5)	0.856
Bacterial infection	2 (40.0)	2 (12.5)	0.475
Viral infection	0	5 (31.2)	0.406
Ejection fraction of heart (%)	29 (24–50)	69 (59–76)	0.002
FiO_2	0.7±0.2	0.7±0.1	0.906
Mean airway pressure (cm H_2O)	17.6±8.7	21.9±5.3	0.219
More than three kinds of inotropics	4 (80.0)	2 (12.5)	0.019
Systolic blood pressure (mm Hg)	56.0±18.5	72.9±27.3	0.214
Heart rate (bpm)	151.8±12.2	141.3±26.6	0.411
Saturation oxygen (%)	78.0±31.1	64.1±20.7	0.259
Oxygenation saturation index	12.8 (5.7–58.1)	26.2 (15.4–41.1)	0.335
High frequency ventilator	0	5 (31.2)	0.406
Total bilirubin (mg/dl)	1.2 (0.9–1.2)	1.8 (0.5–3.4)	0.482
Platelet count ($x10^9$/L)	51.0 (34.0–93.0)	52.0 (30.5–96.5)	0.869
White blood cell count ($x10^6$/L)	890 (210–6,050)	2,390 (1,032–4,260)	0.780
Absolute neutrophil count ($x10^6$/L)	80.0 (0–3,630.0)	925.0 (133.5–3,704.5)	0.589
Hemoglobin (g/dl)	9.2±2.2	10.8±1.4	0.066
pH	7.2±0.1	7.2±0.1	0.525
PCO_2 (mm Hg)	51.4±18.3	85.8±26.4	0.014
Lactic acid (mmol/L)	7.4 (6.5–8.9)	1.1 (0.8–5.5)	0.057

Values are presented as median (interquartile range), number (%), or mean±standard deviation.
ECMO: extracorporeal membrane oxygenation support; VV: veno-venous; FiO_2: fraction of inspired oxygen; PCO_2: partial pressure of carbon dioxide.

hematological malignancies and receiving ECMO was 0% [18]. An academic committee has recently issued guidelines on the application of ECMO for patients undergoing HSCT [19,20]. These guidelines suggest that ECMO should not be considered a contraindication for adult or children HSCT patients. Instead, a multidisciplinary approach should be adopted. The guidelines emphasize the importance of carefully considering the patient's underlying conditions and the potential for relapse when making decisions.

In the present study, the 1-year survival was 38% (95% confidence interval, 0.21–not available). Among patients treated for septic shock, three of five (60%) who underwent ECMO and five of 10 (50%) who underwent VA ECMO survived. However, all the patients who underwent VA ECMO or VV ECMO for acute respiratory distress syndrome died. ECMO for circulatory failure yielded significantly better results than ECMO for respiratory failure, which might have been due to the significantly older age and rapid application of ECMO from the time of initiation of ventilator care in the latter group. Furthermore, in VA ECMO cases, the pathogen was identified relatively quickly, and appropriate antibiotics were available. However, in VV ECMO cases, most patients were affected by viruses, rendering

Table 5. Comparison between heart group and lung group (n=21)

Variable	Heart group (n=6)	Lung group (n=15)	P-value
Age (yr)	9 (6–16)	4 (2–6)	0.045
Male	4 (66.7)	10 (66.7)	1.000
Underlying malignant disease	4 (66.7)	9 (60.0)	1.000
Previous adriamycin use	3 (50.0)	6 (40.0)	0.634
Previous hematopoietic stem cell transplantation	3 (50.0)	11 (73.3)	0.608
Previous graft-versus-host disease	2 (33.3)	5 (33.3)	1.000
Previous cardiopulmonary resuscitation	2 (33.3)	3 (20.0)	0.935
ECMO from last chemotherapy (day)	21.0 (15.0–120.0)	80.0 (44.0–136.5)	0.267
ECMO from starting ventilator care (day)	0 (0–3.0)	8.0 (1.0–16.0)	0.170
VA ECMO	6 (100.0)	4 (26.7)	0.011
VV ECMO	0	11 (73.3)	0.011
ECMO conversion (including VV → VA, VA → VV)	0	3 (20.0)	0.622
Therapy (high dose steroid pulse)	1 (16.7)	6 (40.0)	0.608
Therapy (continuous renal replacement)	4 (66.7)	8 (53.3)	0.944
Therapy (lung transplantation)	0	2 (13.3)	0.906
ECMO duration (day)	8.0 (6.0–22.0)	30.0 (8.0–54.5)	0.243
Fungal infection	3 (50.0)	4 (26.7)	0.608
Bacterial infection	3 (50.0)	1 (6.7)	0.095
Viral infection	0	5 (33.3)	0.292
Complication			
Infection	1 (16.7)	6 (40.0)	0.608
Bleeding	0	4 (26.7)	0.429
Embolism	3 (50.0)	1 (6.7)	0.095
Air leak	0	1 (6.7)	1.000
Neuropathy	1 (16.7)	0	0.627
Rhabdomyolysis	0	1 (6.7)	1.000
More than three kinds of inotropics	3 (50.0)	3 (20.0)	0.401
Systolic blood pressure (mm Hg)	55.5±16.6	74.3±27.7	0.141
Heart rate (bpm)	157.2±15.9	138.5±25.2	0.111
Saturation oxygen (%)	87.3±17.0	59.5±21.2	0.010
Oxygenation saturation index	6.7 (6.2–9.3)	28.8 (19.7–43.1)	0.001
High frequency ventilator	0	5 (33.3)	0.292
Total bilirubin (mg/dl)	1.4 (1.2–2.6)	1.1 (0.5–3.0)	0.507
Platelet count (x10^9/L)	42.5 (29.0–93.0)	63.0 (33.5–99.5)	0.640
White blood cell count (x10^6/L)	550 (180–1,505)	3,170 (1,125–7,965)	0.132
Absolute neutrophil count (x10^6/L)	105.0 (0–1,120.0)	2,287.0 (356.5–6,982.0)	0.147
Hemoglobin (g/dl)	9.1±1.8	11.0±1.4	0.016
pH	7.2±0.1	7.2±0.1	0.933
PCO_2 (mm Hg)	41.0 (35.0–62.0)	94.0 (70.5–114.5)	0.001
Lactic acid (mmol/L)	11.0 (6.5–15.0)	1.1 (0.8–1.7)	0.004
Survival (day)	432.0 (180.0–702.0)	30.0 (8.0–41.5)	0.004
ICU survival rate	5 (83.3)	1 (6.7)	0.003
Hospital discharge rate	4 (66.7)	1 (6.7)	0.019

Values are presented as median (interquartile range), number (%), or mean±standard deviation.
ECMO: extracorporeal membrane oxygenation support; VA: veno-arterial; VV: veno-venous; PCO_2: partial pressure of carbon dioxide; ICU: intensive care unit.

ineffective the use of antibiotics. Maintaining ECMO was also challenging in several conditions such as bleeding, which could explain the outcomes observed. Based on the results, lower ejection fraction, lower blood pressure, higher lactic acid concentration, and use of three or more types of inotropics may paradoxically contribute to survival, likely because VA ECMO resulted in better survival than VV ECMO. To the best of our knowledge, a direct comparison between the outcomes of VV ECMO and VA ECMO has not been reported; however, a survival rate of 44% was observed among pediatric patients with neutropenic sepsis who underwent VA ECMO [21].

In the present study, two of five patients (40%) undergoing HSCT survived ECMO, which is higher than the 20% survival rate reported in previous studies involving similar patients [22,23]. The most common complications of ECMO in the present study were infection and bleeding, and the incidence of thrombus formation was significantly higher with VA ECMO than with VV ECMO. Notably, 80% of post-infection deaths appeared attributable to imipenem-resistant *Acinetobacter baumannii*. Because patients with viral infections had worse survival trajectories than those without viral infections, the results underscore the influence of infection type on survival outcomes. Cytomegalovirus infections frequently led to respiratory failure in our study. This observation is consistent with the established understanding of the severe respiratory implications of certain viral infections. Furthermore, the presence of bleeding complications was associated with significantly worse survival rates, consistent with existing literature emphasizing the impact of bleeding complications in critical care settings, especially in patients receiving ECMO. Therefore, efforts should be made to predict, prevent, and promptly manage bleeding complications in high-risk patients. Further investigations are needed to determine the exact factors that predispose patients on ECMO to bleeding, ranging from anticoagulation management to patient-specific characteristics.

In conclusion, our results highlight the potential avenues for future research and opportunities for clinical practice improvements in ECMO management. The type of ECMO strategy used, nature of underlying infections, and management of complications, specifically bleeding, may significantly affect survival outcomes. Such insights are critical for patient-centered, evidence-based critical care in the era of ECMO. However, these results should be interpreted in consideration of the study design and context, and further studies should be performed in diverse settings and with larger patient cohorts.

CONFLICT OF INTEREST

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

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SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4266/acc.2023.01088.

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