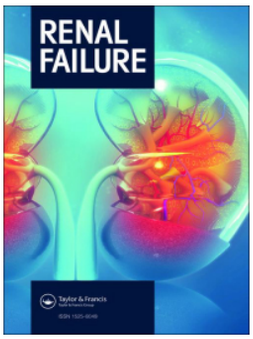

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CLINICAL STUDY

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Risk factors for mortality in patients receiving extracorporeal membrane oxygenation

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ABSTRACT

Objective: Patients on extracorporeal membrane oxygenation (ECMO) are often complex and have a high mortality rate. Currently, risk assessment and treatment decisions for patients receiving ECMO are controversial. Therefore, we sought to identify risk factors for mortality in patients receiving ECMO and provide a reference for patient management.

Methods: We retrospectively analyzed the clinical data of 199 patients who received ECMO support from December 2013 to April 2023. Univariate and multivariable logistic regression analyses were used to identify risk factors. The cutoff value was determined by receiver operating characteristic (ROC) curve analysis.

Results: A total of 199 patients were selected for this study, and the mortality rate was 76.38%. More than half of the patients underwent surgery during hospitalization. Multivariable logistic regression analysis revealed that continuous renal replacement therapy (CRRT) implantation (OR = 2.994; 95% CI, 1.405–6.167; $p=0.004$) and age (OR = 1.021; 95% CI, 1.002–1.040; $p=0.032$) were the independent risk factors for mortality. In the ROC curve analysis, age had the best predictive effect (AUC 0.646, 95% CI 0.559–0.732, $p=0.003$) for death when the cutoff value was 48.5 years. Furthermore, in patients receiving combined CRRT and ECMO, lack of congenital heart disease and previous surgical history were the independent risk factors for mortality.

Conclusions: CRRT implantation and age were independent risk factors for patients with ECMO implantation in a predominantly surgical cohort. In patients receiving a combination of CRRT and ECMO, lack of congenital heart disease and previous surgical history were independent risk factors for mortality.

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Extracorporeal membrane oxygenation; continuous renal replacement therapy; acute renal injury; risk factors; mortality

Introduction

Extracorporeal membrane oxygenation (ECMO) is a life-saving technology for critically ill patients. In the early stages, ECMO was mainly used in neonates and pediatric patients, but with the advancement of technology, ECMO has been widely used in patients with critical conditions such as reversible respiratory failure, refractory cardiogenic shock, and cardiac arrest [1]. The use of ECMO is also accompanied by some problems, including high mortality, high incidence of complications, and high occupation of medical resources. In-hospital mortality ranged from 21 to 37% and 40 to 60% in patients receiving veno-venous ECMO (V-V ECMO) and veno-arterial (V-A) ECMO, respectively [2–4]. Bleeding and nosocomial infections are the most common adverse events associated with ECMO [5].

In the extracorporeal life support in shock (ECLS-SHOCK) trial, the use of ECMO in patients with infarct-related cardiogenic shock did not increase the risk of short-term mortality compared with medical therapy alone, but it was associated with a higher risk of bleeding [6]. At the same time, the ECMO CS study confirmed that immediate implementation of V-A ECMO in patients with severe cardiogenic shock did not improve clinical outcomes compared with an early conservative strategy [7]. For patients with cardiogenic shock, the effect of ECMO needs to be further studied. However, the

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role of ECMO in maintaining hemodynamic stability and temporary replacement therapy after heart–lung transplantation has been recognized. Deciding whether to use ECMO therapy for patients requires a comprehensive assessment, but medical decisions in critical situations must be made quickly. Currently, risk assessment for patients receiving ECMO is controversial. In some previous studies, age, acute kidney injury (AKI), continuous renal replacement therapy (CRRT), ECMO mode, duration of ECMO, and blood product transfusion were considered risk factors for mortality in patients receiving ECMO [8–10].

Considering the altered disease spectrum of patients, previous studies may not be applicable to the current situation. Therefore, in this study, we performed a retrospective analysis of patients who received ECMO treatment in our center during the past 9 years. Our main objective was to evaluate the independent risk factors for mortality in ECMO patients, to identify high-risk patients early, and to provide a reference for medical decision making.

Patients and methods

Study participants and data collection

We reviewed the clinical database of consecutive critically ill patients hospitalized in the First Affiliated Hospital of Sun Yat-sen University from December 2013 to April 2023, and selected 199 patients for subsequent statistical analysis. Exclusion criteria were as follows: 1) patients who did not receive ECMO, 2) age <18 years, 3) missing data, and 4) pregnancy. The flowchart of the study is shown in Figure 1. All patients received appropriate treatment according to ECMO-related guidelines [11, 12]. Data on demographic characteristics, medical history, clinical characteristics, surgical details, and ancillary tests of the patients were collected from the medical records. The study was reviewed and approved by the Institutional Review Board of the First Affiliated Hospital of Sun Yat-sen University (approval number: 2011 [13]) and adhered to the tenets of the Declaration of Helsinki of 1975.

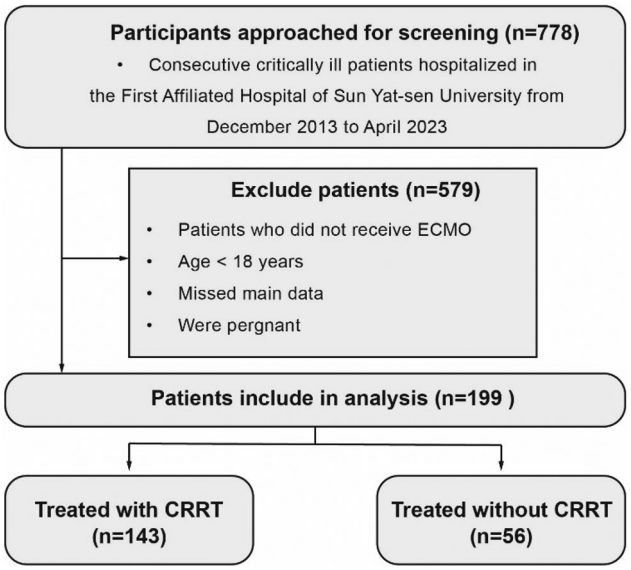

Figure 1. Flowchart for inclusion and exclusion of patients with ECMO implantation. ECMO: extracorporeal membrane oxygenation; CRRT: continuous renal replacement therapy.

Study definitions and outcome

Death was the primary outcome of our study, defined as death in the hospital or within 30 days of discharge. Heart failure was defined according to the Framingham criteria [14]. Mechanical ventilation and using vasopressor drugs represent the patient's status before ECMO implantation. Laboratory data were obtained from the first blood test after enrollment. Renal insufficiency or failure was defined as acute kidney injury (AKI) or CKD stage 3–5 according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria [15]. Previous cardiac surgery was defined as open heart surgery, excluding interventional procedures. Other variables and cutoffs were defined using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes, unless otherwise noted.

Statistical analysis

Normally distributed continuous variables are presented as means and standard deviations, and non-normally distributed continuous variables are presented as medians and ranges between the first and third quartiles. Categorical variables are presented as frequencies and percentages. Continuous variables were compared using unpaired Student's t test or Mann-Whitney U test, as appropriate. Receiver operating characteristic (ROC) curve analysis was used to assess predictive ability and determine cutoff values. Chi-squared or Fisher's exact test was used to compare categorical variables. Forward, stepwise, multivariable logistic regression analysis was performed to identify risk factors associated with mortality. All tests were two-tailed, and $p < 0.05$ was considered statistically significant. All statistical analyses were performed with SPSS (version 26.0) software (SPSS Inc., Chicago, IL) and the R statistical package (The R Foundation; http://www.r-project.org; version 4.1.3).

Results

Patient characteristics

A total of 199 patients who underwent ECMO implantation between December 2013 and April 2023 were selected for this study. In the study population, 152 patients (76.38%) died in the hospital or within 30 days of discharge. Only nearly a quarter of the patients recovered satisfactorily ($n = 47$, 23.62%). Demographic and medical characteristics of the study population are summarized in Table 1. The median age of the entire population was 54 years (39–63 years), and 141 (63.82%) patients were male. Heart failure was present in

Table 1. Demographic characteristics and clinical characteristics of patients receiving ECMO support.

Variables	Total ($N=199$)	Survival ($N=47$)	Death ($N=152$)	P-value
Age, years	54 (39–63)	47 (31–58)	57 (41–65)	0.003*
Age > 48.5 years	127 (63.82)	20 (42.55)	107 (70.39)	0.001*
Sex, male	141 (70.85)	36 (76.60)	105 (69.08)	0.322
ICU period	10 (4–19)	18 (10–23)	8 (3–17)	< 0.001*
CRRT	143 (71.86)	24 (51.6)	119 (78.29)	< 0.001*
ECMO mode				
V-A ECMO	150 (75.38)	37 (78.72)	113 (74.34)	0.542
V-V ECMO	49 (24.62)	10 (21.28)	39 (25.66)	
ECMO indication				
Severe heart failure	141 (70.85)	36 (76.6)	105 (69.08)	0.322
Myocarditis	4 (2.01)	3 (6.38)	1 (0.66)	0.015*
Pneumonia	53 (26.63)	11 (23.40)	42 (27.63)	0.567
Interstitial lung disease	9 (4.52)	0	9 (5.92)	0.088
ECMO duration	8 (5–10)	8 (5–10)	8 (6–10)	0.893
Mechanical ventilation	78 (39.20)	16 (34.04)	62 (40.79)	0.408
Using vasoactive agents	80 (40.20)	15 (31.91)	65 (42.76)	0.185
Medical history				
Smoking	41 (20.60)	11 (23.40)	30 (19.74)	0.587
Diabetes mellitus	31 (15.58)	5 (10.64)	26 (17.11)	0.285
Hypertension	69 (34.67)	12 (25.53)	57 (37.50)	0.132
Coronary heart disease	38 (19.10)	7 (14.89)	31 (20.39)	0.402
Previous PCI	10 (5.03)	1 (2.13)	9 (5.92)	0.298
Previous myocardial infarction	11 (5.53)	3 (6.38)	8 (5.26)	0.769
Congenital heart disease	16 (8.04)	7 (14.89)	9 (5.92)	0.048*
Previous cerebrovascular disease	17 (8.54)	2 (4.26)	15 (9.87)	0.229
COPD	4 (2.01)	0	4 (2.63)	0.261
Renal insufficiency or failure	22 (11.06)	3 (6.38)	19 (12.50)	0.242
Hyperlipidemia	7 (3.52)	1 (2.13)	6 (3.95)	0.554
Previous tumor history	25 (12.56)	4 (8.51)	21 (13.82)	0.338
Previous surgery history	74 (37.19)	11 (23.40)	63 (41.45)	0.025*
Previous cardiac surgery	19 (9.55)	3 (6.38)	16 (10.53)	0.398
Clinical characteristics				
Heart failure	155 (77.89)	41 (87.23)	114 (75.00)	0.077
NYHA class > 3	107 (53.77)	28 (59.57)	79 (51.97)	0.361
SOFA score	8 (6–10)	7 (5–9)	8 (6–11)	0.103
Arrhythmia				
Atrial fibrillation / flutter	32 (16.08)	6 (12.77)	26 (17.11)	0.479
Premature ventricular beats	9 (4.52)	3 (6.38)	6 (3.95)	0.483
Ventricular fibrillation and ventricular tachycardia	17 (8.54)	8 (17.02)	9 (5.92)	0.017*
Laboratory data				
White blood cell (x10^9/L)	7.91 (5.86–11.70)	8.13 (6.20–10.97)	7.85 (5.70–12.25)	0.969
Hemoglobin (g/L)	128 (101–145)	132 (108–150)	126 (97.5–143.75)	0.141
Platelets (x10^9/L)	187 (117–235)	206 (153–269)	179 (114.75–227.50)	0.102
Neutrophils (x10^9/L)	5.57 (3.57–8.88)	5.94 (3.79–7.98)	5.28 (3.52–10.48)	0.679
Lymphocytes(x10^9/L)	1.36 (0.90–2.01)	1.55 (0.90–2.17)	1.35 (0.89–1.99)	0.273
Monocyte (x10^9/L)	0.51 (0.33–0.74)	0.60 (0.37–0.70)	0.49 (0.32–0.76)	0.684
Neutrophil to lymphocyte ratio	4.14 (2.10–9.94)	3.92 (1.99–5.30)	4.26 (2.25–10.05)	0.271
lymphocyte to Monocyte ratio	2.68 (1.54–4.13)	3.14 (1.88–4.77)	2.52 (1.46–4.04)	0.198
Platelets to lymphocyte ratio	127.01 (84.86–190.43)	140.87 (81.30–202.14)	123.88 (85.74–189.53)	0.645
CK-MB (ng/mL)	2.63 (1.33–7.50)	2.20 (1.20–4.73)	2.97 (1.35–7.80)	0.315
NT-proBNP (pg/mL)	1523 (375–5997)	1634 (339–9100)	1519 (392–5943)	0.964
Log BNP	3.18 (2.57–3.78)	3.21 (2.53–3.96)	3.18 (2.59–3.77)	0.964
cTNT (ng/mL)	0.048 (0.016–0.241)	0.041 (0.020–0.254)	0.049 (0.015–0.228)	0.939
ALT (U/L)	33 (19–64)	36 (22–79)	32.50 (18.00–61.50)	0.219
AST (U/L)	39 (26–94)	40 (28–102)	39 (25–85.5)	0.208
Serum albumin (g/L)	36.09 ± 6.64	36.90 ± 7	35.84 ± 6.27	0.325
Total bilirubin (umol/L)	17.60 (11.60–31.20)	16.30 (11.10–21.70)	18.10 (11.68–33.80)	0.145
Serum creatinine (umol/L)	84 (70–122)	82 (62–102)	70 (85–136)	0.094
Urea nitrogen (mmol/L)	6.50 (4.90–10.20)	6.10 (4.10–8.30)	6.90 (5–11.08)	0.052
Surgery	113 (56.78)	26 (55.32)	87 (57.24)	0.817
Cardiovascular Surgery	94 (47.24)	24 (51.06)	70 (46.05)	0.548
CABG	14 (7.04)	2 (4.26)	12 (7.89)	0.394
Valve surgery	52 (26.13)	13 (27.66)	39 (25.66)	0.785
Heart transplantation	10 (5.03)	2 (4.26)	8 (5.26)	0.782
Aortic replacement	19 (9.55)	5 (10.64)	14 (9.21)	0.771
Congenital heart surgery	11 (5.53)	4 (8.51)	7 (4.61)	0.306
Lung surgery	3 (1.51)	0	3 (1.97)	0.322

Continuous variables are expressed as the mean ± standard deviation (SD) or as the median with the interquartile range according to normality. Categorical variables are expressed as frequency (percentages).

CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; NYHA, New York Heart Association; ALT, alanine transaminase; AST, aspartate transaminase; CABG, coronary artery bypass graft. SOFA, sequential Organ Failure Assessment.

*Statistically significant.

Table 2. Univariate and multivariable analysis of risk factors for death in patients undergoing ECMO implantation.

	Univariable		Multivariable	
Variables	OR (95% CI)	P-value	OR (95% CI)	P-value
CRRT	3.456 (1.734–6.888)	<0.001*	2.944 (1.405–6.167)	0.004*
Age (y)	1.023 (1.006–1.040)	0.009*	1.021 (1.002–1.040)	0.032*
Heart failure	0.439 (0.173–1.115)	0.083	–	–
Congenital heart disease	0.360 (0.126–1.026)	0.056	–	–
Previous surgical history	2.317 (1.096–4.896)	0.028*	1.888 (0.818–4.355)	0.136
Ventricular fibrillation and ventricular tachycardia	0.307 (0.111–0.848)	0.023*	0.419 (0.137–1.279)	0.126
Urea nitrogen (mmol/L)	1.074 (0.998–1.156)	0.055	–	–
The indication for ECMO is myocarditis	0.097 (0.010–0.957)	0.046*	0.137 (0.012–1.550)	0.108

OR, odds ratio; CI, confidence interval; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation.
*Statistically significant.

155 (77.89%) patients, including 141 (70.85%) with severe heart failure, which was the main indication for ECMO. A total of 73 (37.19%) patients had a history of previous surgery, of which 19 (9.55%) had a history of previous cardiac surgery. Hypertension was present in 31 patients (15.58%), and the incidence of coronary artery disease was 19.10% ($n = 38$). In addition, more than half of the patients ($n = 113$, 56.78%) underwent surgery during hospitalization, most commonly cardiovascular surgery ($n = 94$, 47.24%). The predominant mode of ECMO was veno-arterial ECMO ($n = 150$, 75.38%), and the remainder was veno-venous ECMO ($n = 49$, 24.62%). CRRT was performed in 143 (71.86%) patients, with incidences of 69.33% ($n = 104$) and 79.59% ($n = 39$) in the V-A ECMO and V-V ECMO groups, respectively. Compared with surviving patients, those who died were older, had more CRRT implantations, and had a lower incidence of congenital heart disease (all $p < 0.05$), but the difference in laboratory indicators was not statistically significant.

Risk factors for mortality in patients undergoing ECMO implantation

A total of 59 variables were screened. Univariate logistic regression analysis was performed to identify the potential risk factors for mortality in patients undergoing ECMO implantation. CRRT implantation, age, previous surgical history, ventricular fibrillation, ventricular tachycardia, and myocarditis were the potential risk factors for death (Table 2). Multivariable logistic regression analysis using the forward stepwise method revealed that two variables were independently and significantly associated with mortality in patients undergoing ECMO implantation, including CRRT implantation (OR = 2.994; 95% CI, 1.405–6.167; $p = 0.004$) and age (OR = 1.021; 95% CI, 1.002–1.040; $p = 0.032$) (Table 2). Furthermore, the ROC curve analysis showed that age had the highest Youden index at a cutoff value of 48.5 years, with a specificity of 57.4% and a sensitivity of 70.4% for predicting death in patients undergoing ECMO implantation (AUC 0.646, 95% CI 0.559–0.732, $p = 0.003$; Figure 2). When age > 48.5 years was used as a risk factor, the OR of univariate logistic regression analysis was 3.210 (95% CI 1.634–4.305, $p = 0.001$) and that of multivariable logistic regression analysis was 3.865 (95% CI 1.865–8.009, $p < 0.001$).

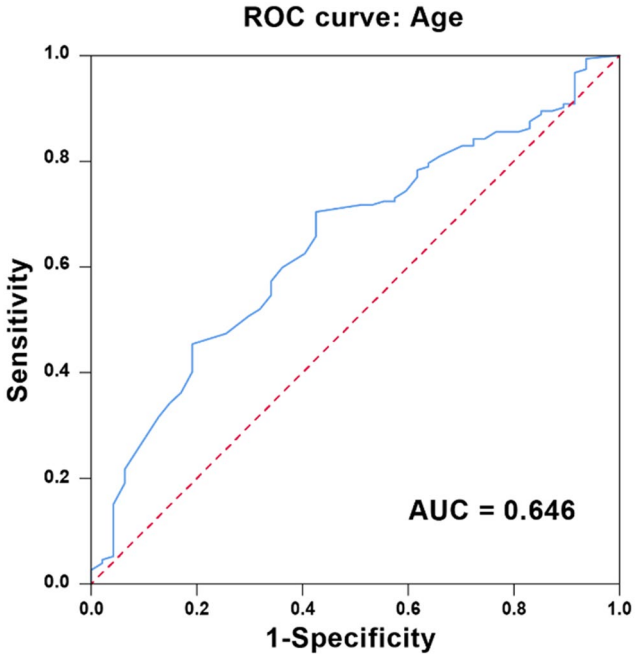

Figure 2. ROC curve analysis of age for predicting death in patients undergoing ECMO implantation. ROC: receiver operating characteristic; ECMO: extracorporeal membrane oxygenation.

Risk factors for mortality in patients with combined ECMO and CRRT

The rate of CRRT implantation was significantly higher in patients who died than in those who survived (78.29% vs. 51.06%, $p < 0.001$). This may indicate that CRRT implantation has a significant impact on the prognosis of patients on ECMO. For patients with combined CRRT and ECMO implantation, we further analyzed the independent risk factors for this category. Univariate logistic regression analysis showed that age, congenital heart disease, and previous surgical history were potential risk factors. Multivariable logistic regression analysis showed that congenital heart disease (OR = 0.216; 95% CI, 0.052–0.895; $p = 0.035$) and previous surgical history (OR = 3.104; 95% CI, 1.045–9.215; $p = 0.041$) were the independent risk factors for patients with ECMO implantation treated with CRRT (Table 3).

Table 3. Univariate and multivariable analysis of risk factors for death in patients with combined CRRT and ECMO.

	Univariable		Multivariable	
Variables	OR (95% CI)	P-value	OR (95% CI)	P-value
Age	1.019 (0.997–1.042)	0.092	–	–
Congenital heart disease	0.265 (0.069–1.026)	0.054	0.216(0.052-0.895)	0.035*
Previous surgical history	2.754 (0.963–7.871)	0.059	3.104(1.045-9.215)	0.041*

OR, odds ratio; CI, confidence interval; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation.
*Statistically significant.

Discussion

Extracorporeal membrane oxygenation (ECMO) is a life-saving technique for acute respiratory failure, cardiac arrest, cardiogenic shock, septic shock, and other acute and critical illnesses. It is commonly used in intensive care units and emergency departments to maintain hemodynamic stability and improve oxygenation index [1, 16]. Although with the advancement of technology, the application of ECMO has become more and more widespread and has brought satisfactory results, the accompanying serious complications and high mortality also deserve our attention. More than half of the patients will experience at least one serious complication, mainly including bleeding, thrombosis, infection from the indwelling lines/tubes, stroke, acute kidney injury (AKI), and so on [1, 5]. Given the seriousness of the underlying disease, the high mortality, and the high utilization of medical resources, the use of ECMO in patients requires clinicians to carefully weigh the risks and benefits. Therefore, it is particularly important to identify patients at high risk of death. In our study, we found that CRRT implantation and age were the independent risk factors for mortality in patients undergoing ECMO implantation. In patients with combined CRRT and ECMO, lack of congenital heart disease and previous surgery history were independent risk factors for prognosis.

In previous studies, the mortality of ECMO was approximately 40%–75.6% [17–21]. The results of different studies vary greatly, which may be related to different research populations. In this study, the mortality was relatively high, but it was also within the reasonable interval of previous research results. In a study of acute kidney injury in patients receiving ECMO, the in-hospital mortality of ECMO patients who developed AKI was 61.7%, while the in-hospital mortality of patients with AKI requiring dialysis was as high as 70.8% [17]. In the study by Pankaj Saxena et al., the in-hospital mortality of patients receiving ECMO was 75.6% [21], which is similar to that in our study. We speculate that there are several reasons for the high mortality. First, most of patients in our study underwent cardiac surgery, accounting for 47.24%. Cardiopulmonary bypass and ischemia–reperfusion injury can cause multi-organ dysfunction and severe heart failure, which increases the incidence of AKI. AKI, especially AKI requiring dialysis, will significantly increase the risk of mortality compared with patients receiving ECMO only [22]. Secondly, some studies found that the mortality of V-A ECMO mode is higher than that of V-V ECMO [23, 24]. In this study, most of the ECMO modes were V-A ECMO, which may be one of the reasons. Finally, the small sample size is one of the limitations, which may introduce potential bias.

In the management of ECMO in critically ill patients, CRRT is an important treatment modality, often used to manage or prevent fluid overload, AKI, and electrolyte disturbances [25]. AKI is an extremely common complication in patients receiving with ECMO and is associated with higher mortality, especially in patients requiring CRRT [26, 27]. The underlying mechanisms of AKI in ECMO-treated patients are complex and multifactorial, mainly including patient factors, critical illness, mechanical ventilation, and ECMO-related factors [27]. The most common indication for ECMO in our study was severe heart failure. Almost half of the patients had undergone cardiac surgery. In addition to destabilizing the circulation and reducing renal perfusion, severe heart failure and cardiopulmonary bypass surgery may destroy a large number of blood cells and produce inflammatory proteins or other nephrotoxic agents, increasing the risk of AKI and the frequency of CRRT implantation. The overall mortality rate for ECMO patients in this study was 76.38%, and the mortality rates for patients with and without CRRT were 83.22% and 58.93%, respectively ($p < 0.001$). Although there are no large randomized controlled trials on this outcome, CRRT implantation has often been recognized as an independent risk factor for mortality in patients on ECMO [9, 19, 28, 29]. In a retrospective study of 200 patients on ECMO, Jan et al. reported that 60% of patients required renal replacement therapy for AKI, and the 3-month survival rate of patients on renal replacement therapy (RRT) was one-third that of patients without RRT (17% vs. 53%, $p = 0.001$) [28]. Although the incidence of AKI in the above study was lower than our results, mortality was similar. This may be due to the larger proportion of patients receiving V-A ECMO in our study. Previous studies have shown that the incidence of AKI in V-A ECMO is higher than in V-V ECMO and most often occurs on the day of ECMO cannulation [26, 27]. In a report by Liao et al., the presence of AKI at 24 h after ECMO, performed in 68 of the neonatal (64.8%) and 105 of the pediatric (61.4%) patients, was a significant risk factor for in-hospital mortality, and the greater the severity of AKI, the higher the mortality rate, especially when receiving CRRT [9]. This suggests that our conclusions are still valid in children and that AKI or CRRT deserves our vigilance in all age groups.

Previously, ECMO was mainly used in neonatal and pediatric patients, and only a small number of centers pursuing ECMO in adult patients [30]. With the improvement of technology, the use of ECMO in adults has increased significantly

and shows promising prospects [1]. However, with more complications and less net benefit, current studies are controversial about the use of ECMO in elderly patients [10, 31]. The results of this study indicate that age is an independent risk factor for mortality in patients on ECMO. In a retrospective study of 355 patients on V-A ECMO, Michael et al. found that age was associated with mortality only after 63 years and increased dramatically after 72 years and was an independent predictor of in-hospital mortality [10]. Compared with this study, the patients in our study were relatively younger, but the mortality rate was higher (76.38% vs. 54%). This may be related to the difference in the study population. In our study, a majority of patients underwent cardiovascular surgery and had a higher probability of postcardiotomy shock, which may increase the mortality of elderly patients [21]. Furthermore, in some recently published pre-ECMO survival prediction scores, age was an independent risk factor for mortality and was a crucial variable in the scores [5, 13]. As the field of ECMO continues to develop, an increasing number of elderly patients may benefit from ECMO in the future. However, we should consider the risks and benefits very carefully. Because older patients may have more severe underlying disease and less tolerance for critical illness. They may have difficulty tolerating the complications of ECMO, such as bleeding, thrombosis, nosocomial infections, and neurological events [5]. Advanced age should not be a contraindication for ECMO, but individual assessment is necessary. In this study, we found that age had the best ability to predict the risk of death when the cutoff value was 48.5 years. Although this value is lower than in previous studies, it can still provide some reference for clinicians to make decisions. The upper age limit for the use of ECMO in different populations needs further research. Early identification of high-risk patients may play a potential role in improving survival.

In our study, age and CRRT were independent risk factors for mortality in ECMO patients, but whether age affects the relationship between CRRT and mortality remains unclear. Therefore, we analyzed the risk factors of patients treated with CRRT and ECMO, but we did not find that age had an effect on mortality in this category. At present, there are few relevant studies and the views are controversial [17, 32, 33]. In a study by Ankit et al., AKI requiring dialysis was observed in 14% of 17,942 ECMO hospitalizations. The authors showed that age and AKI were independent predictors of mortality, but the authors did not find that age was a risk factor for AKI, and age may modify the effect of AKI on mortality [17]. On the contrary, Jonh et al. demonstrated that younger age was associated with improved survival in patients treated with combined ECMO and CRRT [33]. The discrepancy between this conclusion and the results of our study may be due to their inadequate sample size ($N = 40$) and differences in the study populations. Interestingly, in our study, we found that congenital heart disease was a protective factor for poor prognosis. No studies have reflected this point. This may be because our study population was mostly associated with cardiac surgery, and the condition of patients with congenital heart disease is better than that of patients with coronary artery bypass grafting, aortic and great vessel surgery, or heart transplantation. Further studies are needed to elucidate the underlying mechanisms.

Our study has several limitations. First, this is a single-center retrospective study; all study data were not collected prospectively, which has inherent limitations, and the generalizability of the conclusions needs further validation. Second, analyzing patients who received V-A ECMO together with patients who received V-V ECMO is another limitation of this study. The two types of patients are not completely isolated, and their underlying pathological mechanisms are connected to a certain extent. In previous studies, it is not absolutely prohibited to analyze both types of patients at the same time [34–36], and we did not find any association between ECMO configuration and mortality. Since the majority of patients in this study underwent V-A ECMO, the findings may not apply to patients requiring V-V ECMO. Moreover, the majority of patients included in this study were cardiac surgery patients, and the conditions of other non-surgical patients varied, which may bring potential bias. Finally, we did not differentiate between the options of combining ECMO and CRRT circuits, which may have a potential influence on the results. The objective of our study is to estimate the risk and provide some guidance for treatment. Further expansion of the sample size of patients is needed to further verify the main findings of this study.

In conclusion, we found that CRRT implantation and age were independent risk factors for patients with ECMO implantation in a predominantly surgical cohort. In the subgroup analysis of patients receiving concomitant CRRT and ECMO, lack of congenital heart disease and previous surgical history were independent risk factors for mortality.

Author contributions statement

All authors have made substantial and intellectual contributions to this study. ZW, JH, and GC contributed to the conception and design of the study. JW, SH, KF, HW, LS, and ZZ contributed to the acquisition of data. JW, SH, QL, and ML contributed to the analysis and interpretation of data. JW, SH, and JH drafted the article and ZW revised it critically for important intellectual content. All authors have approved the version to be submitted.

Disclosure statement

No potential conflict of interest was reported by the authors.

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Data availability statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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