Infection and Drug Resistance

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ORIGINAL RESEARCH

Nosocomial Infections in Nonsurgical Patients Undergoing Extracorporeal Membrane Oxygenation: A Retrospective Analysis in a Chinese Hospital

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Background: The effect of nosocomial infections (NIs) in adult patients undergoing ECMO has been rarely reported in China. Moreover, the effect of NIs on ECMO patients' mortality is still unclear and inconclusive according to literature data. In this study, we examined the prevalence, risk factors, causative organisms, and effects on outcomes of NIs in ECMO patients.

Methods: A total of 79 nonsurgical patients (mean age 53.3±15.2 year (yr); 66% male) who underwent ECMO between January 2011 and September 2020 were enrolled in this retrospective study. Patients' demographic and clinical data and ECMO parameters were collected from all patients.

Results: Among 79 patients who underwent ECMO for a total of 1253 ECMO days (mean time 15.9±14.1 d), 42 developed NIs. We observed 30 ventilator-associated pneumonia (VAP), 19 bloodstream infections (BSIs), and 4 urinary tract infections, corresponding to 23.9/1000 ECMO days, 15.2/1000 ECMO days, and 3.2/1000 ECMO days, respectively. ECMO duration (22.0±16.5 VS 8.9±5.3 d, $P < 0.001$), invasive mechanical ventilation (IMV) duration (27.4±20.5 VS 11.4±10.1 d, $P < 0001$), and ICU length of stay (35.9±22.9 VS 15.7±9.2 d, $P < 0.001$) were longer in patients with NIs. The independent risk factors for NIs were ECMO duration (Odds Ratio [OR], 1.414; 95% Confidence Interval [CI], (1.051–1.238); $P = 0.002$) and viral pneumonia (OR, 5.788; 95% CI, (1.551–21.596); $P = 0.009$). Gram-negative bacteria were the most common causative organisms of NIs; *Acinetobacter baumannii (A. baumannii), Klebsiella pneumoniae (K. pneumoniae*), and *Pseudomonas aeruginosa (P. aeruginosa)* were the most common bacteria. BSI (OR, 8.106; 95% CI, (1.384–47.474); $P = 0.02$) was an independent predictor for mortality.

Conclusion: NIs are common complications in patients during ECMO treatment, especially VAP, followed by BSI. Also, BSI can negatively affect the survival rate.

Keywords: extracorporeal membrane oxygenation, healthcare-associated infections, bloodstream infections, risk factors, mortality

Introduction

Extracorporeal membrane oxygenation (ECMO), also known as extracorporeal life support, has a life-sustaining role in critically ill patients with cardiorespiratory dysfunction.[1] ECMO contains a membrane oxygenator that directly oxygenates and absorbs carbon dioxide from the blood. Blood is drained from the venous side by an external pump, after which it returns to the venous side (venovenous ECMO) or the arterial side (venoarterial ECMO).[2,3] After its successful application during the 2009 influenza A(H1N1) pandemic, ECMO treatment became widely used worldwide, including in China.[1,4,5] However, this also led to a higher prevalence of hospital-acquired infections during ECMO, especially in critically ill patients. Previous studies have suggested that nosocomial infections (NIs) during ECMO are related to some predisposing factors, including invasiveness of ECMO and mechanical ventilation, patients' underlying condition, the severity of illness, and immunocompromised states.[6,7] Yet, the effect of NIs on adult patients undergoing ECMO has been rarely reported in China.[4,8] Moreover, the effect of NIs on ECMO patients' mortality is still unclear and inconclusive according to literature data.

Received: 30 April 2022
Accepted: 26 July 2022
Published: 29 July 2022

Therefore, the aim of this study was to analyze the prevalence, risk factors, causative organisms, and impact on mortality of NIs in nonsurgical patients receiving ECMO treatment for cardiac or respiratory failure in China.

Materials and Methods

Patients and Setting

Nonsurgical patients who received ECMO treatment in the First Affiliated Hospital, Zhejiang University School of Medicine between January 2011 and September 2020 were enrolled in the present study. A patient who did not undergo surgery during hospitalization in our hospital before ECMO initiation and during hospitalization in the previous hospital, if the patient was transferred to our hospital, was considered a nonsurgical ECMO patient. This hospital is a teaching hospital in Zhejiang Province and a regional referral center. Only nonsurgical patients were included in our study, for the patient population and underlying diseases differed between surgical and nonsurgical patients. Exclusion criteria were the following: 1) <18 years old; 2) NI occurs before ECMO initiation; 3) ECMO usage less than 48 hours.

The decision to initiate ECMO treatment was made by senior intensivists. The indications for VV ECMO were mostly acute respiratory distress syndrome and hypercapnic respiratory failure, while for VA ECMO were mainly cardiogenic shock, fulminant myocarditis, and pulmonary hypertension. VV ECMO cannula (Maquet, Rastatt, Germany; or Medos, Beijing, China) was placed in the internal jugular vein and femoral vein, whereas VA ECMO cannula (Maquet, Rastatt, Germany; or Medos, Beijing, China) was placed in the femoral vein and femoral artery. Blood was pumped by Rotaflow pumps (Maquet, Hirrlingen, Germany) and oxygenated by PLS membranes (Maquet, Hirrlingen, Germany). The procedure was performed by intensivists or emergency physicians in the intensive care unit and emergency room. Anticoagulant therapy was regularly performed targeted to an activated partial thromboplastin time (APTT) of 40 to 60s, if this patient had no active bleeding. In addition, no prophylactic antimicrobial therapy was given after the ECMO connection. Routine surveillance for NIs was not conducted unless there was clinical suspicion for NIs. All patients received urethral catheters.

This retrospective study was performed in compliance with the Declaration of Helsinki and was approved by the medical ethics committee of the First Affiliated Hospital Zhejiang University School of Medicine (Ethics approval No. IIT20220353A). The requirement for informed consent was waived by the Ethics Commission due to the retrospective and anonymous characteristics of the study.

Definitions

ECMO-associated infections were defined as infections that occurred more than 48 hours after ECMO connection and within 48 hours since ECMO disconnection. Bloodstream infection[9] (BSI) was determined by at least one positive blood culture for an identified pathogen or two positive blood cultures from two blood cultures collected within 48 hours for a common skin contaminant. In the case of a common skin contaminant, a positive sign of symptoms (at least one of fever (>38°C), hypertension, or chill) was also required. Ventilator-associated pneumonia[10] (VAP) was suspected when a new or progressive radiographic infiltrate occurred, combined with purulent secretions, worsening oxygenation, and at least one of fever, leukopenia, or leukocytosis. When the criteria of imaging test and signs/symptoms were met, VAP could be diagnosed by positive semi-quantitative culture result from bronchoalveolar lavage or endotracheal aspirate. Urinary tract infection[9] (UTI) was defined by at least one positive culture of urine (>10^5 microorganisms/mL) with one or two species of microorganisms and at least one of these symptoms (fever (>38°C), dysuria, frequency, urgency, or suprapubic tenderness) without other recognized causes. Skin and soft tissue infection (SSTI) was not included because the signs and symptoms of SSTI, such as tenderness, redness, and localized swelling, were not properly recorded. Thus, the diagnosis of SSTI was difficult. Besides, SSTI was rare in our patient population for all the patients were nonsurgical. Clostridium difficile infection was not found in these patients.

Data Collection

Patients' demographic and clinical data and ECMO parameters, including age, gender, smoking habits, Charlson Comorbidity Index,[11] diagnosis at admission, acute physiology and chronic health evaluation score II (APACHE II),[12] underlying medical condition, infection at admission, sequential organ failure assessment (SOFA)[13] at ICU admission, PaO_2/FiO_2 at ECMO

initiation, ECMO configuration, length of invasive mechanical ventilation (IMV) before and after ECMO connection, renal replacement therapy (RRT), NIs, transfusion, laboratory tests at ECMO initiation, and drug resistance patterns were collected. The recorded outcomes were NIs events, duration of ECMO, mortality in ICU, and ICU length of stay. Multidrug resistance (MDR) was defined as acquired resistance to one or more agents in at least three antimicrobial categories.[14]

Statistical Analysis

Continuous variables were described as means with standard deviations, while categorical variables were expressed as frequencies. The Mann–Whitney *U*-test or Student's *t*-test for continuous variables was conducted to compare infected with non-infected groups and survival with non-survival groups, while the χ^2 or Fisher's exact test was used for categorical variables. The probability of staying free of NI was evaluated by Kaplan–Meier survival analysis. Logistic regression models were established to identify risk factors of NIs and mortality. Variables with P value <0.05 in the univariate analysis were entered into the multivariate models (forward, stepwise logistic regression models). However, variables associated with each other were excluded from the multivariate models. All tests were 2-tailed; P value <0.05 was considered statistically significant. SPSS 26.0 (IBM Inc.) software was used for analysis.

Results

Clinical Data and Treatment Characteristics

Among 98 patients who underwent ECMO treatment between January 2011 and September 2020, 79 (66% male; mean age 53.3±15.2 yr) were included in our study. A total of 19 patients were excluded due to the following reasons: 15 received ECMO for less than 48 hours, 3 were younger than 18 years old, and 1 suffered from VAP before ECMO cannulation. Sixty-one patients received VV ECMO treatment, and 18 patients were connected to VA ECMO. At admission to ICU, viral pneumonia (28, 35%; 26/28 93%), avian influenza A/H7N9) and bacterial pneumonia (24, 30%) were the most frequent diagnosis. Included patients underwent a total of 1253 ECMO days (15.9±14.1 d), 1573 days of IMV (19.9±18.3 d), and 2086 days of ICU (26.4±20.4 d).

Clinical data and treatment characteristics, as well as comparisons between infected and non-infected patients, are summarized in Table 1. During the ECMO course, 42 (53%) patients developed 53 episodes of NIs, corresponding to 42.3/1000 ECMO days. The mean time to first NI was 6.3±3.5d, and a total of 607 infection-free days (7.7±4.7 d) were recorded. Most of the patients experienced IMV during ECMO treatment, except 5 (including one who developed BSI and UTI) who did not receive mechanical ventilation. Seventy-three patients used central venous catheters. Sixty-six patients received transfusions (at least one of red blood cells, platelets, and plasma).

Nosocomial Infections and Organisms

Among 42 infected patients, 30 VAP episodes, 19 BSI episodes, and 4 UTI episodes were observed, corresponding to 23.9/1000 ECMO days, 15.2/1000 ECMO days, and 3.2/1000 ECMO days, respectively (Figure 1). Of the 19 bloodstream infections, 15 episodes were primary BSI, and 4 were secondary to VAP. At the admission of ICU, infected patients (Table 1) were older (57.3±13.9 VS 48.8±15.5 yr, P = 0.014), had higher Charlson Comorbidity Index (2.2±1.6 VS 1.6±1.9, P = 0.037), higher rate of viral pneumonia (24 57% VS 4 11%, P < 0.001), less cardiac disease (2 5% VS 10 27%, P = 0.006), and a higher rate of community-acquired infection at admission (38 90% VS 18 49%, P < 0.001) compared with non-infected patients.

The causative organisms of NIs are listed in Table 2. *A. baumannii* was the most frequently isolated bacterium from pulmonary samples (16, 53%) and the second most common in blood samples (4, 21%). Also, *A. baumannii* was observed in all polymicrobial pulmonary samples (4, 13%). *K. pneumoniae* (4, 13%) and *P. aeruginosa* (3, 10%) were also common in patients with VAP, while *K. pneumoniae* (7, 37%) was the most involved bacterium in BSI. *Candida* was recorded in 2 UTI episodes (50%), 2 VAP episodes (6%), and 1 BSI episode (5%). Out of a total of 54 bacterial strains, only eight strains were not MDR, corresponding to an MDR rate of 85%. Moreover, all (24/24) *A. baumannii* strains, 93% (14/15) *K. pneumoniae* strains, and 75% (3/4) *P. aeruginosa* strains were MDR.

Table 1 Demographic and Clinical Characteristics of Patients Receiving Extracorporeal Membrane Oxygenation with and without Nosocomial Infections

Patients' and Treatment Characteristics	Total, n=79	Non-Infected Patients, n=37	Infected Patients, n=42	P value
Age(yr)	53.3 (15.2)	48.8 (15.5)	57.3 (13.9)	0.014
Gender (male), n (%)	52 (66)	24 (65)	28 (67)	0.87
Smoking habits, n (%)	26 (33)	13 (35)	13 (31)	0.69
Charlson Comorbidity Index	1.9 (1.7)	1.6 (1.9)	2.2 (1.6)	0.037
Diagnosis at admission, n (%)				
Respiratory disease	60 (76)	20 (54)	40 (95)	<0.001
Viral pneumonia	28 (35)	4 (11)	24 (57)	<0.001
Bacterial pneumonia	24 (30)	11 (30)	13 (31)	0.91
Other [a]	8 (10)	5 (14)	3 (7)	0.57
Cardiac disease	12 (15)	10 (27)	2 (5)	0.006
Poisoning	4 (5)	4 (11)	0 (0)	0.09
Septic shock	1 (1)	1 (3)	0 (0)	0.47
Other [b]	2 (3)	2 (5)	0 (0)	0.22
Underlying condition, n (%)				
Malignancy	6 (8)	3 (8)	3 (7)	1.0
Hypertension	25 (32)	8 (22)	17 (40)	0.07
Diabetes mellitus	12 (15)	3 (8)	9 (21)	0.10
Renal insufficiency	5 (6)	2 (5)	3 (7)	1.0
Hepatic insufficiency	4 (5)	2 (5)	2 (5)	1.0
Coronary artery disease	4 (5)	3 (8)	1 (2)	0.52
Cerebrovascular accident	2 (3)	0 (0)	2 (5)	0.5
Immunocompromised states	9 (11)	2 (5)	7 (17)	0.22
Transplantation	3 (4)	0 (0)	3 (7)	0.29
Infection at admission, n (%)	56 (71)	18 (49)	38 (90)	<0.001
APACHE II score [c]	14.2 (5.7)	15.4 (6.5)	13.1 (4.8)	0.08
SOFA score [c]	5.3 (2.4)	5.4 (2.6)	5.3 (2.3)	0.95
PaO2/FiO2 < 100 mmHg, n (%)	19 (24)	9 (24)	10 (24)	0.96
ECMO duration, (d)	15.9 (14.1)	8.9 (5.3)	22 (16.5)	<0.001
Veno-venous ECMO, n (%)	61 (77)	23 (62)	38 (90)	0.003
IMV duration, (d)	19.9 (18.3)	11.4 (10.1)	27.4 (20.5)	<0.001
IMV duration before ECMO connection, (d)	2.5 (3.9)	2.4 (4.7)	2.5 (3.2)	0.15
IMV duration after ECMO connection, (d)	17.5 (17.7)	9.0 (8.3)	24.9 (20.5)	<0.001
Central venous catheter, n (%)	73 (92.4)	34 (91.9)	39 (92.9)	1.0
RRT before ECMO connection, n (%)	13 (17)	6 (16)	7 (17)	0.96
RRT during ECMO course, n (%)	44 (56)	18 (49)	26 (62)	0.24
WBC [d], (*10^9/L)	12.5 (7.2)	13.9 (7.3)	11.3 (6.9)	0.08
Hemoglobin [d], (g/L)	110 (30)	111 (28)	110 (31)	0.84
PLT [d], (*10^9/L)	145 (96)	153 (89)	137 (102)	0.31
Transfusion, n (%)	66 (84)	29 (78)	37 (88)	0.25

Notes: Data are No. (%) of patients or mean value (± standard deviation). [a]Including interstitial pneumonia, pulmonary embolism, and lung cancer. [b]Including multiple trauma and hepatic failure. [c]Calculated at ICU admission. [d]Recorded at ECMO initiation.

Abbreviations: APACHE, acute physiology and chronic health evaluation; SOFA, sequential organ failure assessment; ECMO, extracorporeal membrane oxygenation; IMV, invasive mechanical ventilation; RRT, renal replacement therapy; WBC, white blood count; PLT, platelets.

Outcomes

Compared to the non-infected group, infected patients had more VV ECMO use (38 90% VS 23 62%, P = 0.003), significantly longer ECMO duration (22.0±16.5 VS 8.9±5.3 d, P < 0.001), IMV duration (27.4±20.5 VS 11.4±10.1 d, P < 0001), and ICU length of stay (35.9±22.9 VS 15.7±9.2 d, P < 0.001). In addition, more patients in the infected group received plasma transfusions (30 71% VS 18 47%, P = 0.039). The cumulative probability of staying free of NI was 21%

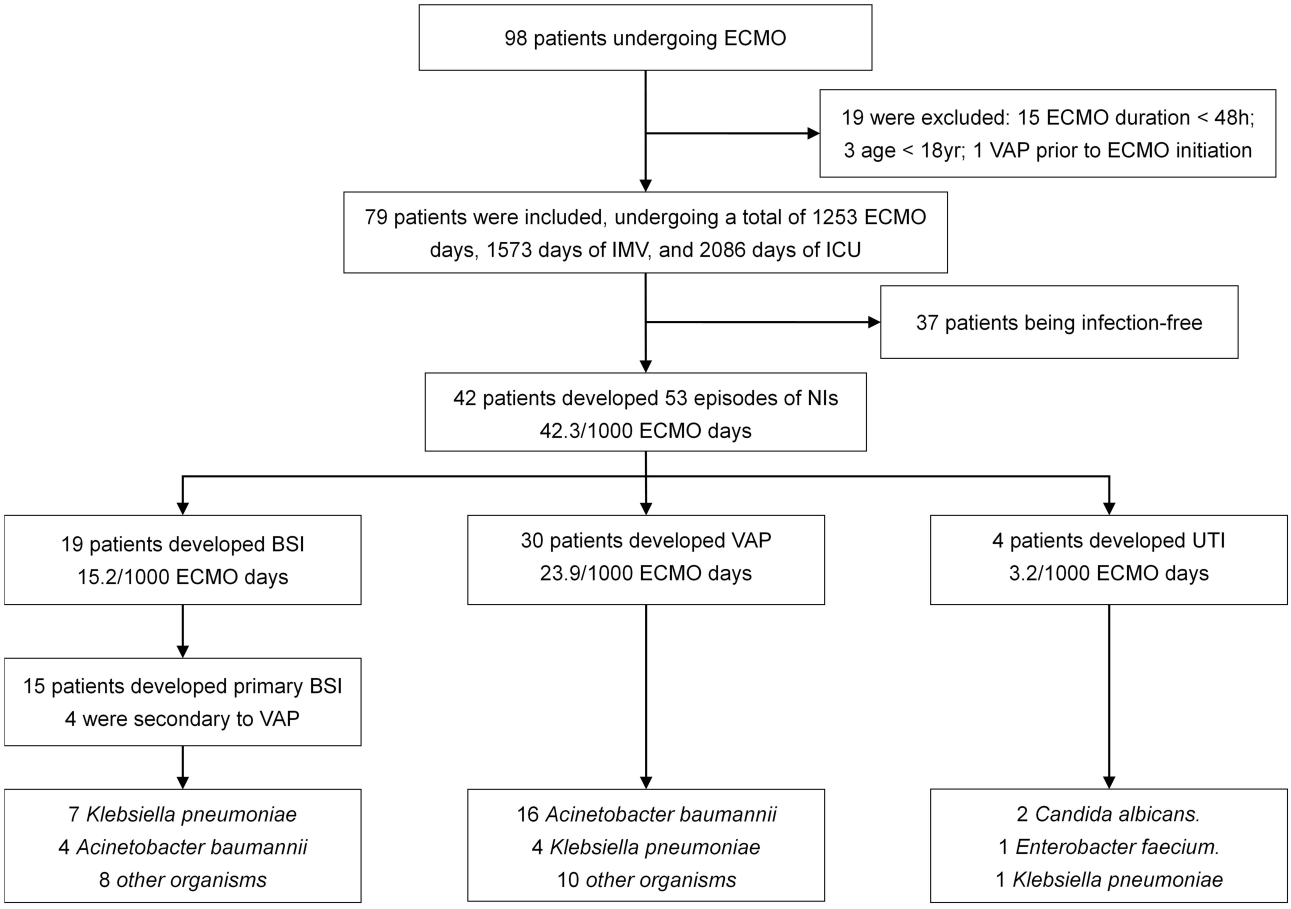

Figure 1 Study flow chart.
Abbreviations: ECMO, extracorporeal membrane oxygenation; VAP, ventilator-associated pneumonia; IMV, invasive mechanical ventilation; ICU, intensive care unit; Nis, nosocomial infections; BSI, bloodstream infection; UTI, urinary tract infection.

after 16 days of ECMO connection (Figure 2). The independent risk factors associated with nosocomial infections under ECMO by logistic regression analysis were ECMO duration and viral pneumonia (Table 3). Patients on VV ECMO had higher infection rate (62% VS 22%, P = 0.003). ECMO mode was also included in multivariate analysis. But the difference of ECMO mode in multivariate analysis was not significant. Besides, with or without ECMO mode in multivariate analysis, the final results were not affected. VV ECMO use between patients died and alive was also comparable (81% VS 68%, P = 0.18). ECMO mode had no significant impact on both NIs and mortality.

Table 2 Microorganisms of Nosocomial Infections in 42 Patients Receiving Extracorporeal Membrane Oxygenation

VAP, n=30		**BSI, n=19**		**UTI, n=4**	
Organism	**No. (%)**	**Organism**	**No. (%)**	**Organism**	**No. (%)**
Acinetobacter baumannii	16 (53)	*Klebsiella pneumoniae*	7 (37)	*Candida albicans.*	2 (50)
Klebsiella pneumoniae	4 (13)	*Acinetobacter baumannii*	4 (21)	*Enterobacter faecium.*	1 (25)
Polymicrobial [a]	4 (13)	*S. aureus*	2 (11)	*Klebsiella pneumoniae*	1 (25)
Pseudomonas aeruginosa	3 (10)	*S. epidermidis*	2 (11)		
Burkholderia cepacia	2 (7)	*Burkholderia cepacia*	2 (11)		
Stenotrophomonas maltophilia	1 (3)	*Enterococcus faecium.*	1 (5)		
		Candida albicans.	1 (5)		

Notes: [a]Including ≥ 2 pathogens; 2 *Acinetobacter baumannii* + *Klebsiella pneumoniae*, 1 *Acinetobacter baumannii* + *Klebsiella pneumoniae* + *Aspergillus*, 1 *Acinetobacter baumannii* + *Pseudomonas aeruginosa*.
Abbreviations: VAP, ventilator-associated pneumonia; BSI bloodstream infection; UTI urinary tract infection.

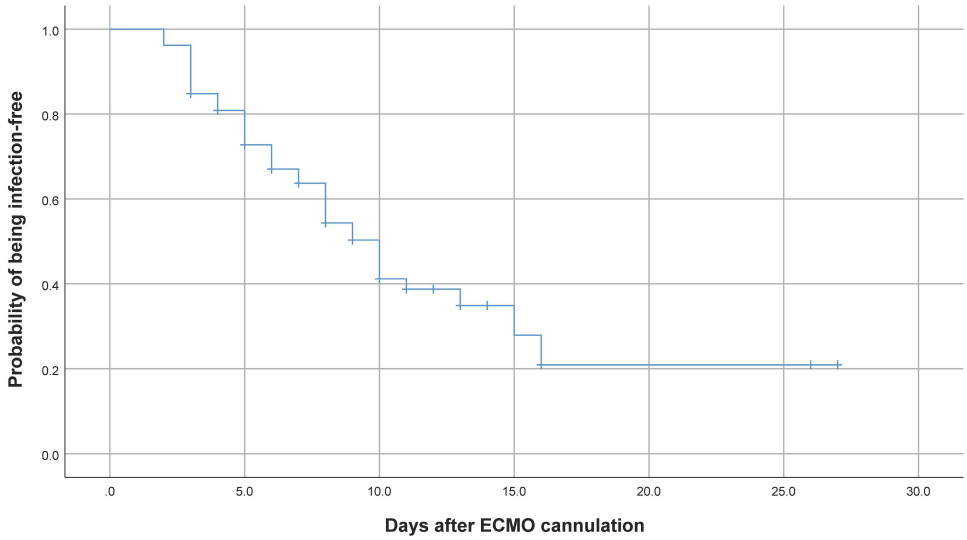

Figure 2 Kaplan-Meier estimates of the unadjusted cumulative probability of staying free of NI.
Abbreviation: ECMO, extracorporeal membrane oxygenation.

The total mortality rate in the ICU was 68% (54/79), 71% (30/42) in the infected group, and 65% (24/37) in the non-infected group, with no significant difference between the two groups (P = 0.53). The mortality rates of patients with VAP, BSI, and UTI were 65% (20/31), 89% (17/19), and 100% (4/4), respectively. The independent risk factors of mortality in the ICU were BSI and platelet transfusion, while a higher hemoglobin amount at ECMO initiation was an independent protective factor for mortality (Table 4).

Table 3 Stepwise Logistic Regression Analysis of Factors Associated with Nosocomial Infections in Patients Receiving Extracorporeal Membrane Oxygenation

Factor	Univariate Analysis		Multivariate Analysis	
	Odds Ratio (CI 95%)	P value	Odds Ratio (CI 95%)	P value
Age	1.040 (1.007–1.074)	0.017	–	–
Viral pnuemonia	11.000 (3.299–36.677)	<0.001	5.788 (1.551–21.596)	0.009
Cardiac disease	0.135 (0.027–0.665)	0.014	–	–
Infection at admission	10.028 (2.974–33.808)	<0.001	–	–
Veno-venous ECMO	5.783 (1.697–19.703)	0.005	–	–
ECMO duration	1.173 (1.078–1.275)	<0.001	1.141 (1.051–1.238)	0.002
IMV duration	1.090 (1.039–1.143)	<0.001	–	–

Abbreviations: ECMO, extracorporeal membrane oxygenation; IMV, invasive mechanical ventilation; CI, confidence interval.

Table 4 Stepwise Logistic Regression Analysis of Factors Associated with Mortality in the Intensive Care Unit

Factor	Univariate Analysis		Multivariate Analysis	
	Odds Ratio (CI 95%)	P value	Odds Ratio (CI 95%)	P value
Charlson Comorbidity Index	1.579 (1.092–2.281)	0.015	–	–
PaO2/FiO2 < 100 mmHg	0.189 (0.040–0.896)	0.036	–	–
Hemoglobin amount [a]	0.976 (0.959–0.994)	0.009	0.968 (0.946–0.990)	0.005
PLT transfusion	8.532 (1.825–39.891)	0.006	10.433 (1.924–56.587)	0.007
BSI	5.284 (1.116–25.015)	0.036	8.106 (1.384–47.474)	0.020

Notes: [a]Recorded at ECMO initiation.
Abbreviations: PLT, platelet; BSI, bloodstream infection; CI, confidence interval.

Discussion

In this study, more than half of the patients (53%) developed NIs during the ECMO course, which confirmed that NIs are still common in nonsurgical patients undergoing ECMO. VAP, BSI, and UTI were the most common type of infections. In 2017, the Extracorporeal Life Support Organization reported[1] infection rates of 17.5% and 13.0% in adult patients undergoing ECMO treatment for respiratory and cardiac failure, respectively. In this study, the infection rate (53%) was significantly higher. However, the rate (53%) and the incidence (42.3/1000 ECMO days) were consistent with previous reports (14–64% and 11.9–75.7/1000 ECMO days).[6,15–22] Our study also suggested that ECMO duration was an independent risk factor of NIs, which is consistent with other studies.[15,18,22]

According to previous studies, NIs incidence is positively correlated with the mean or median ECMO, ie, the higher incidence is seen when the duration is longer.[6,15–22] The above might partially explain the high NIs incidence in our hospital, as the mean ECMO duration in our study was 15.9 days. Another independent risk factor of NIs was viral pneumonia. Avian influenza A (H7N9) virus was the primary pathogen in hospital patients with viral pneumonia. A previous study at our hospital[23] reported a secondary bacterial infection rate of 40.3% in H7N9 patients, while the CDC estimated the NIs rate in hospitalized adult patients of 4.0%.[24] Another study reported a secondary infection rate of 44.0% of H7N9 patients.[25] This suggests that H7N9 patients are vulnerable to NIs, which could be explained by the prolonged use of IMV and central venous catheters. Besides, the mean ECMO duration of viral pneumonia patients was twice that of non-viral pneumonia patients (24.4±3.5 d VS 11.2±1.1 d). Therefore, we speculate that their vulnerability to NIs and prolonged ECMO usage contribute to the high NIs rate in patients with viral pneumonia.

Apart from the above-mentioned risk factors, there were still many factors that might affect NIs rate. In our center, antimicrobial prophylaxis was not prescribed after ECMO initiation. Compared with other centers[18,19] whose prophylactic antimicrobial therapy was regularly administrated, their NIs rates were much lower (53% VS 21%; 53% VS 13%). However, there are still no existing strategies for prophylactic antimicrobial treatment in patients on ECMO. A study[26] focused on antimicrobial prophylaxis during ECMO reported that reduction in antimicrobial usage and replacement with narrower-spectrum agents did not lead to significant changes in NIs rate. The result was encouraging, and we hope that a standard antimicrobial prophylaxis regimen will be proposed in the near future. In our study, 61 (77%) patients underwent VV ECMO and the infected group had more VV ECMO use (38 90% VS 23 62%, P = 0.003). A previous study[16] with a lower VV ECMO rate (34%) had a lower NIs rate (25% vs 53%) compared with ours. Patients on VV ECMO seemed vulnerable to NIs. However, the difference of ECMO mode was not significant in multivariate analysis in our study. In our center, the cannulas used in ECMO were provided by two companies, Maquet (Rastatt, Germany) and Medos (Beijing, China). Cannulas used in other centers were mostly provided by only one company. If the mixed use of two kind of cannulas might improve NIs rate, it needs further investigation. Age was another risk factor for NIs, which had been proved before.[6] In comparison with previous studies[16,19] with lower NIs rates, mean age of our patients was higher (53yr VS 46yr, 53yr VS 48yr).

In our study, the mean time to first NI was 6.3 days after ECMO initiation, and approximately 80% of the patients undergoing ECMO developed NIs after 16 days by Kaplan–Meier survival analysis. Grasselli et al[6] reported that the median time to first NI was 9 days after ECMO connection, and 51% of the patients had NIs within two weeks. Another study by Schmidt[21] showed that the meantime to first NI was 8 days.

Many previous studies[17,27–30] reported that *coagulase-negative staphylococci* are the primary causative organisms in patients undergoing ECMO. However, in recent years, Gram-negative bacteria have become dominant species,[6,15,19,31] owing to the extensive use of glycopeptides and vancomycin.[7] Consistent with recent studies, *non-fermenting bacilli* and *Enterobacteriaceae* were the most frequent organisms of NIs in our research, especially *A. baumannii*, while *coagulase-negative staphylococci* accounted for less than 10% of all identified pathogens.

We also observed a very high rate (85%) of multidrug resistance (MDR) in patients with bacterial infections. Grasselli et al[6] found an MDR rate of 46% in ECMO patients from a general ICU in Italy, which is significantly lower compared to our MDR rate. According to the CHINET surveillance of bacterial resistance,[32] the problem of bacterial resistance is severe and is still growing in China. Yuan et al[33] reported an MDR rate of 78.3% in a Chinese ICU. Although MDR had no significant impact on mortality in our study, urgent measures need to be applied, especially in the ICU.

BSI and platelet transfusions were associated with worse outcomes in our patient population. However, the impact of BSI on mortality remains controversial. Some studies[30,34] found a significantly higher mortality rate in patients with BSI, while others[8,35] reported no differences in mortality between BSI and no-BSI patients. Based on our results, the odds ratio of BSI was 8.1 in multivariate analysis, indicating that BSI was a strong factor in mortality. As previously reported,[36] the volume of transfused platelets significantly elevated the mortality rate in patients with VV ECMO. Almost one-third (24/79) of the patients received platelet transfusions in our study, and only two survived. According to Jiritano et al,[37] thrombocytopenia is common in patients with ECMO, which could be partially explained by contact with foreign surfaces, inflammation, platelet activation, and coagulative cascade activation, leading to increased PLT transfusions. Early studies have confirmed that thrombocytopenia is often associated with a higher chance of death in hospitalized patients, especially in ICU.[38,39]

We also noticed a high mortality rate (54/79, 68%) in our patient population and seldom reported such a high mortality rate.[18,22] It might be related to ECMO management and serious complications such as BSI, pump malfunction, oxygenator failure, bleeding events, and renal failure.[1] Yet, further investigation is required to confirm this data.

NIs caused significant damage not only to patients' health but also to the economy of patients and hospitals. More antimicrobial drugs would be administered if a patient was diagnosed with NIs, adding to hospitalization expenses. Besides, many of these drugs had side effects on the kidney, liver, and other organs. According to many previous studies,[6,40–43] NIs were associated with worse prognoses in these patients. In our study, BSI was an independent risk factor for mortality. A study[44] also demonstrated that NIs increased radiate, operational, and anesthetic expenses. Therefore, it was vital to prevent and reduce NIs. Preventive measures, such as antimicrobial prophylaxis, reeducation for the ICU team, shortening in ECMO duration, and reduction of central ECMO use, should be appropriately applied.[4]

This study has a few limitations. First, this was a retrospective and single-center study with a relatively small sample size. Second, we included only nonsurgical patients, limiting the extrapolation of our results to other ICUs with case mixed. Third, residual confounding factors that could bias the results of the multivariate analysis cannot be excluded. Finally, we did not analyze the effect of antimicrobial therapy and other severe complications of ECMO on outcomes.

Conclusions

Our results indicated that NIs are still common in nonsurgical patients undergoing ECMO treatment, especially VAP, followed by BSI and UTI. ECMO duration and viral pneumonia were the independent risk factors of NIs. *A. baumannii* was the most frequent pathogen causing NIs, and BSI significantly increased the mortality rate in ICU.

Acknowledgments

We thanked all participants for their contributions to this study.

Funding

This study was supported by Zhejiang Provincial Health and Health Commission (WKJ-ZJ-2109) and Zhejiang Natural Science Foundation (LQ20H010006).

Disclosure

All authors report no conflict of interest relevant to this article.

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