Prophylactic antibiotic treatment for preventing nosocomial infection in extracorporeal membrane oxygenation–resuscitated circulatory arrest patients

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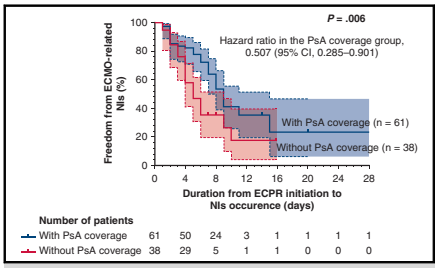
ABSTRACT

Objective: We aimed to investigate the characteristics of nosocomial infections (NIs) and the impact of prophylactic antibiotic administration on NI outcomes in patients who underwent extracorporeal cardiopulmonary resuscitation (ECPR).

Methods: This retrospective study analyzed the rate, type, pathogens, outcomes, and risk factors of NIs that developed in adult patients who underwent ECPR at our institution between January 2002 and January 2022.

Results: Among 105 patients (median age, 58.59 [interquartile range, 46.53-67.32] years), 57 (54.29%) patients developed NIs during their extracorporeal membrane oxygenation courses. The incidence rates per 1000 extracorporeal membrane oxygenation days were 135.91 for overall infections and 40.06 for multidrug-resistant (MDR) infections. Ventilator-associated pneumonia was the most common type of NI (73.68%), followed by bloodstream infections (17.89%). Prophylactic antibiotics with *Pseudomonas aeruginosa* coverage were protective factors against NI (hazard ratio [HR], 0.518; 95% confidence interval [CI], 0.281-0.953; $P = .034$). High dynamic driving pressure of the ventilator (cmH_2O) was a prognostic factor for hospital mortality (HR, 1.096; 95% CI, 1.008-1.192; $P = .032$). An Acute Physiology and Chronic Health Evaluation II score of ≥24 (HR, 6.443; 95% CI, 1.380-30.088; $P = .018$) was a risk factor for developing MDR infections.

Conclusions: In patients who undergo ECPR, prophylactic antibiotic treatment with *P aeruginosa* coverage is associated with a lower incidence of NIs, whereas an Aeruginosa Acute Physiology and Chronic Health Evaluation II score of ≥24 is a risk factor for MDR infections. In the modern era of antibiotic therapy, the development of NIs does not increase hospital mortality among patients undergoing ECPR. (JTCVS Open 2023;16:582-601)



ECPRs with prophylactic antibiotics against *P aeruginosa* have lower NI prevalence.

CENTRAL MESSAGE

Prophylactic antibiotic treatment against *P aeruginosa* might be associated with a lower incidence of NIs in ECPR patients.

PERSPECTIVE

In patients undergoing ECPR, prophylactic antibiotic treatment with *P aeruginosa* coverage may decrease the incidence of nosocomial infections. The impact of prophylactic antibiotic treatment on ECPR mortality requires further investigation.

Extracorporeal cardiopulmonary resuscitation (ECPR) is an advanced rescue therapy with venoarterial (VA) extracorporeal membrane oxygenation (ECMO) support. It aims to restore circulation in select patients, especially those refractory to conventional cardiopulmonary resuscitation.[1] Still, hospital mortality in patients who receive ECPR, including in patients who experience out-of-hospital cardiac arrest (OHCA) and in-hospital cardiac arrest (IHCA),

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Abbreviations and Acronyms

APACHE = acute physiology and chronic health evaluation
BSI = bloodstream infection
CI = confidence interval
ECMO = extracorporeal membrane oxygenation
ECPR = extracorporeal cardiopulmonary resuscitation
HR = hazard ratio
ICU = intensive care unit
IHCA = in-hospital cardiac arrest
IQR = interquartile range
MDR = multidrug-resistant
NI = nosocomial infection
OHCA = out-of-hospital cardiac arrest
VA = venoarterial
VAP = ventilator-associated pneumonia

remains high, with survival rates of only 24.1% to 35.4%. Nosocomial infections (NIs) remain a major cause of morbidity and mortality in ECMO support.[2-4] Some studies have demonstrated that patients who experience cardiac arrest may have impaired immune responses to pathogens and are thus susceptible to infection after arrest.[5,6] In addition, immunocompromised conditions, additional medical devices such as renal-replacement therapy, and invasive mechanical ventilation increase the risk of NIs in patients who receive VA-ECMO.[7]

However, it remains unknown whether patients who receive ECPR have a greater risk of NIs than patients who receive VA-ECMO support without cardiac arrest. Further, data on the clinical features and outcomes of NIs in ECPR patients are scarce,[8] and the role and efficacy of antimicrobial prophylaxis or prophylactic antibiotic treatment in patients receiving ECMO and ECPR remain unclear.[9-11] Thus, this study aimed to analyze the incidence, microbial etiology, resistance patterns, risk factors, and clinical outcomes of NI and the relationship between prophylactic antibiotic treatment and NI outcomes in patients undergoing ECPR. We hypothesized that among patients undergoing ECPR, those who develop NI may have worse clinical outcome than those who do not develop NI. In addition, prophylactic antibiotic treatment might be beneficial in patients who receive ECPR.

METHODS

Study Design and Ethics

This retrospective study was approved by the institutional review board of National Cheng Kung University Hospital (no. B-ER-110-430; date of approval: January 10, 2023) and was conducted according to the tenets of the Declaration of Helsinki. The requirement for informed consent was waived by the review board owing to the retrospective nature of the study.

Patients

Consecutive adult patients (aged ≥18 years) who developed NI after resuscitative ECMO support (ECPR) at the National Cheng Kung University Hospital between January 2002 and January 2022 were included in the chart review. Patients were excluded if the ECMO duration was <24 hours, if an NI developed >72 hours after weaning off ECMO, or if any infection developed ≤7 days before ECMO. We retrospectively evaluated the microbiological cultures obtained from 24 hours after the initiation of ECMO support to 72 hours after decannulation. The microbiological cultures were performed at the discretion of the medical care staff. Clinicodemographic data included age, sex, medical history (diabetes mellitus, hypertension, coronary artery disease, chronic obstructive pulmonary disease, and immunosuppression), and ECMO management variables (indication, total ECMO days, and allogeneic blood transfusion).

ECMO Implantation for Resuscitation

The ECPR protocol was initiated for patients who received cardiopulmonary resuscitation as previously described.[12,13] ECMO was not performed in a controlled environment owing to the emergency condition of the patients, but it was only performed by 1 of 4 cardiovascular surgeons on duty in our medical center. The choice of central or peripheral ECMO (Medos; Maquet; Sorin; and Terumo) cannulation was determined at the discretion of the surgeons.[12,14] The detailed cannulation procedures, adjunctive care for organ functions, ECMO management, and weaning protocols have been reported previously.[12-14]

Infection Prevention and Control During ECMO Support

The following protocols were implemented during ECMO: (1) ventilator-associated pneumonia (VAP) prevention bundles included elevation of the head of the bed, stress ulcer prevention, and pain assessment and sedation scale evaluation every 8 hours; (2) early enteral feeding when feasible; (3) prophylactic or selective decontamination antibiotic regimens administered within 2 days after ECMO run based on intensivist preference[9,15,16]; (4) daily monitoring of catheters and cannulas insertion sites; (5) needle-free closed systems for drug infusion and blood withdrawal; and (6) alcohol-based hand hygiene.

Definition of NI

NI was identified and evaluated by 2 independent investigators following the current definitions of the Centers for Disease Control and Prevention National Nosocomial Infections Surveillance System.[17] ECMO-associated NIs were defined as infections occurring ≥24 hours after ECMO initiation and ≤72 hours after ECMO discontinuation.[18] Criteria for the diagnosis and classification of infection were based on the study by Ko and colleagues.[8] Multidrug-resistant (MDR) pathogens were identified based on the definition from the Centers for Disease Control and Prevention.[19] Identification of the pathogens from serum, sputum, or urine samples were performed as described previously.[20]

VAP was suspected when patients presented with fever ≥38.3 °C, a new and persistent radiographic with infiltrate purulent secretions, and leukocyte count $>10^3/\mu L$. VAP was determined by standard culture (endotracheal aspirate $\geq 10^6$ colony-forming units per milliliter or bronchoalveolar lavage specimen $\geq 10^4$ colony-forming units per milliliter).[21] Bloodstream infection (BSI) was defined as 2 separate positive blood cultures with a pathogenic organism and signs of infection including leukocytosis, leukopenia, fever, and hypothermia.[22] Such infections were defined as early if they occurred ≤7 days after ECPR.[21] Antibiotics with *Pseudomonas aeruginosa* coverage in our hospital include ceftazidime,

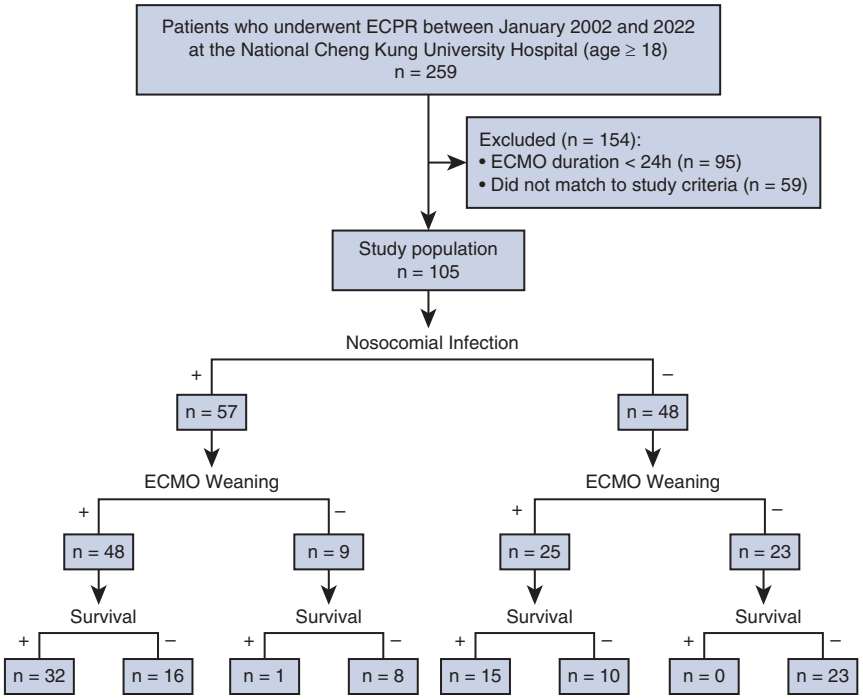

FIGURE 1. Flow chart for patient enrollment, allocation, follow-up, and analysis. *ECPR*, Extracorporeal membrane oxygenation resuscitation; *ECMO*, extracorporeal membrane oxygenation.

cefepime, ciprofloxacin, levofloxacin, and meropenem. Antibiotic treatment protocols were based on the discretion of the infection specialists.

Outcomes and Follow-up

The cohort was divided into 2 groups: those with NIs and those without NIs during ECMO support. The primary outcome variables included the rate of ECMO weaning, cerebral performance category score at discharge, and survival to hospital discharge. The cerebral performance category scores at discharge were available for all patients who survived the ECMO run. The secondary outcomes included readmission and infection-related and all-cause mortalities after discharge.

Statistical Analysis

Variables were compared between the NI and noninfection groups using χ^2 tests and Mann-Whitney *U* test. The values are presented as medians (interquartile ranges [IQRs]). Variables that were significantly correlated (ie, with *P* values < .15 in the univariate Cox regression analysis) with the primary outcome of in-hospital mortality and prognostic factors of ECPR in-hospital mortality rates reported in other studies were included in the stepwise multivariate Cox regression analysis. The inclusion and exclusion criteria were set to $P < .10$ and $P > .15$, respectively.[23,24] Survival curves were generated using the Kaplan–Meier method and were analyzed using the log-rank test. All statistical analyses were performed using SPSS (version 25.0; IBM Corp) for Windows.

RESULTS

Patient Characteristics

A total of 259 adult patients received ECPR during the study period between January 2002 and January 2022, and 105 patients who met the inclusion criteria were included in the analysis. All patients received peripheral cannulation. Among them, 57 (54.29%) and 48 (45.71%) patients did and did not develop NI during the ECMO course, respectively (Figure 1). Compared with the non-NI group, the NI group was older (median age, 60.08 [IQR, 47.91-69.60] years vs 55.47 [IQR, 41.88-65.36] years; $P = .137$) and included more male patients (89.47% vs 70.83%, $P = .024$). The patient characteristics are shown in Table 1. Other clinicodemographic characteristics were comparable between the NI and non-NI groups, except for greater incidences of chronic obstructive pulmonary disease and coronary artery disease in the NI group ($P = .001$ and .047, respectively). Laboratory examination within 24 to 48 hours after ECPR also revealed lower lymphocyte counts ($P = .007$) but greater granulocyte counts ($P = .012$) and blood urea nitrogen levels ($P = .003$) in the NI group (Table 1).

With respect to the respiratory and hemodynamic ECMO data, the 24-hour post-ECMO serum lactate levels and inotropic equivalent numbers were significantly greater the non-NI group ($P = .004$ and .040, respectively; Table E1). Regarding ventilator settings, FiO_2 and peak inspiratory pressures were significantly lower in the NI group ($P = .035$ and .003, respectively; Table E1).

Infection Sites and Pathogens

A total of 95 episodes of NI developed in the 57 patients (Table E2). The incidence rate of NI was 135.91 infection episodes per 1000 ECMO days. There were 73, 16, and 6 patient events of Gram-negative bacteria, Gram-positive

TABLE 1. Clinicodemographic patient characteristics

Variable	NI group (n = 57)	Non-NI group (n = 48)	*P* value
Age, y	60.08 [47.91-69.60]	55.47 [41.88-65.36]	.137
Male sex	51 (89.47)	34 (70.83)	.024
Body mass index, kg/m^2	26.24 [23.44-28.09]	26.23 [23.44-28.09]	.736
Hypertension	25 (43.86)	13 (27.08)	.103
Diabetes mellitus	19 (33.33)	12 (25)	.396
End-stage renal disease	8 (14.04)	5 (10.42)	.768
Dyslipidemia	14 (24.56)	6 (12.5)	.140
Chronic obstructive pulmonary disease	17 (29.82)	2 (4.17)	.001
Coronary artery disease	38 (66.67)	22 (45.83)	.047
Immunosuppression*	7 (12.28)	6 (12.5)	1.000
Pulmonary hypertension	1 (1.75)	2 (4.17)	.591
Cause of cardiac arrest			
AMI	31 (54.39)	17 (35.42)	.076
Non-AMI			
Postcardiotomy shock	4 (7.02)	1 (2.08)	.372
Cardiogenic shock	8 (14.04)	11 (22.92)	.456
Myocarditis	1 (1.75)	1 (2.08)	.499
Pulmonary embolism	4† (7.02)	7 (14.58)	.338
Hemorrhagic shock	3 (5.26)	7 (14.58)	
Trauma	0 (0)	5‡ (10.42)	.018
Postoperation	2 (3.51)	1 (2.08)	>.999
Massive right hemopneumothorax	1 (1.75)	0 (0)	>.999
Postpartum hemorrhage	0 (0)	1 (2.08)	.457
Hyperkalemia	2 (3.51)	1 (2.08)	>.999
Others	2§ (3.51)	5‖ (10.42)	.242
Procedure or operation during ECMO run	32 (56.14)	21 (43.75)	.237
Mechanical ventilation ≥24 h before ECPR	3 (5.26)	4 (8.33)	.700
Transferred from an outside hospital	3 (5.26)	2 (4.17)	.372
Low-flow time, min	45.50 [29.25-55.00] (n = 56)	41.00 [32.00-52.00] (n = 43)	.544
Cardiac rhythm before ECMO support			
VT/VF noticed	36 (63.16)	26 (54.17)	.427
Previous IABP	2 (3.51)	3 (6.25)	.658
OHCA	22 (38.60)	12 (25)	.150
Receiving targeted temperature management (TTM)	20 (35.09)	11 (22.92)	.202
Targeted temperature, °C	36.0 [35.0-36.0]	36.0 [33.0-36.0]	.602
The duration of TTM, h	24.0 [24.0-24.0]	24.0 [24.0-24.0]	>.999
APACHE II score	25.0 [20.0-29.0]	24.0 [21.0-28.75]	.937
APACHE IV score	98.00 [83.00-111.50]	104.00 [93.50-118.00]	.080
APACHE II score ≥24	34 (59.65)	24 (50)	.686
APACHE IV score >100	25 (43.86)	27 (56.25)	.116
Laboratory examination within 24-48 h after ECPR (peak)			
White blood count, $10^3/\mu$L	12.2 [9.4-17.2]	10.6 [5.7-14.3]	.067
Monocytes, %	4.8 [3.4-6.3]	4.4 [2.9-6.5]	.266
Lymphocytes, %	6.0 [4.1-8.8]	8.5 [5.9-13.7]	.007
Granulocytes, %	87.0 [80.7-91.0]	84.5 [75.2-87.5]	.012
Hemoglobin, g/dL	10.5 [9.7-11.8]	10.9 [10.0-12.4]	.499
Platelet, $10^3/\mu$L	108.0 [79.5-139.0]	98.7 [69.2-121.5]	.286

(Continued)

TABLE 1. Continued

Variable	NI group (n = 57)	Non-NI group (n = 48)	*P* value
Blood urea nitrogen, mg/dL	33.0 [25.5-50.1]	25.0 [19.6-34.5]	.003
Creatinine, mg/dL	2.0 [1.4-3.2]	1.9 [1.1-2.9]	.554
eGFR, mL/min/1.73 m^2	37.0 [20.9-55.4]	34.5 [22.2-57.5]	.789
Aspartate aminotransferase, U/L	520.0 [156.7-1074.2]	673.7 [323.0-1543.0]	.145
Alanine aminotransferase, U/L	133.5 [68.0-411.5]	229.0 [95.5-385.5]	.255
Bilirubin, total, mg/dL	1.5 [1.1-2.9]	1.5 [0.9-2.3]	.596
Bilirubin, direct, mg/dL	1.1 [0.6-2.0]	0.8 [0.4-1.5]	.285
C-reactive protein, mg/L	56.8 [16.8-163.3]	36.7 [25.5-63.3]	.594
CK, U/L	2064.6 [384.1-5228.2]	1827.2 [394.8-7567.2]	.820
CK-MB, ng/mL	98.2 [16.2-415.7]	142.3 [13.1-358.3]	.781
hscTroponin-T, ng/L	0.7 [0.3-14.7]	3.0 [0.4-6.8]	.972

Data are presented as n (%) or as the median [interquartile range]. *NI*, Nosocomial infection; *AMI*, acute myocardial infarction; *ECMO*, extracorporeal membrane oxygenation; *ECPR*, extracorporeal cardiopulmonary resuscitation; *VT/VF*, ventricular tachycardia/ventricular fibrillation; *IABP*, intra-aortic balloon pump; *OHCA*, out-of-hospital cardiac arrest; *APACHE*, Acute Physiology and Chronic Health Evaluation; *eGFR*, estimated glomerular filtration rate; *CK-MB*, creatine phosphokinase-MB. *Includes patients with acquired immune deficiency syndrome, solid-organ transplantation, and hematologic malignancy and those who received chemotherapy, immunosuppressive agents, or long-term corticosteroid therapy. †One patient received surgical removal of a pulmonary embolism during ECMO run. ‡One clamshell incision and right lower lobe (RLL) lobectomy; 1 right upper lobe lobectomy (posterolateral thoracotomy); 1 above-the-knee amputation and transcatheter arterial embolization; 1 thoracic endovascular aortic repair and RLL wedge resection (posterolateral thoracotomy); 1 patient did not receive operation. §One thyrotoxic crisis; 1 asthma attack. ‖One anaphylactic shock (sevoflurane related); 1 transfusion related acute lung injury; 1 cancer-related hypovolemic shock; 2 airway obstruction.

bacteria, and fungal infections, respectively (Table E2). The pathogen distribution among patients who received ECPR, stratified by the duration from ECPR to NI, is summarized in Figure E1. More than 50% of the episodes of Gram-negative infections occurred 4 to 7 days after ECPR, whereas there was a similar distribution of patient events in Gram-positive infections at different time periods after ECPR.

The most frequent type of infection was VAP, occurring in 70 patients (73.68%; Table E2). The prevalence of VAP was 100.14 episodes per 1000 ECMO days. The second-most common type of infection was BSI, followed by wound infection (1 micro-organism from femoral ECMO wound and 4 micro-organisms from surgical-site wound), with a prevalence of 24.32 and 7.15 episodes per 1000 ECMO days, respectively (Table E2). The number of NIs, stratified by ECMO support duration, showed a predominant case distribution at 4 to 14 days after ECPR for BSI, whereas VAP mostly occurred within the initial 7 days after ECPR (Figure E2).

Of the 70 VAP episodes, 21.43% (15/70) were caused by *P aeruginosa*, 17.14% (12/70) by *Acinetobacter spp*., and 15.71% (11/70) by *Klebsiella spp*. (Table E2). The major micro-organism in BSIs was coagulase-negative *Staphylococcus* (4/17, 23.53%). There were 28 events of MDR bacterial infection in the NI group, with an incidence rate of 40.06 infection episodes per 1000 ECMO days (Table E2).

Regarding prophylactic antibiotics, third-generation cephalosporins combined with vancomycin were among the most commonly used (26.09%, 24/92), with ceftazidime being the most commonly used third-generation cephalosporin (22.83%, 21/92, Table E3). In addition, third-generation cephalosporins were the most commonly used single prophylactic antimicrobial agents (16.30%, 15/92), followed by piperacillin–tazobactam (13.04%, 12/92), first-generation cephalosporins (8.70%, 8/92), and cefepime (7.61%, 7/92) (Table E3). There was a trend for increased *Pseudomonas* spp. coverage with antibiotic treatment in the non-NI group (74.42%, $P = .098$). The median duration of prophylactic antibiotic treatment was 3 [IQR, 3.00-5.00] days. Comparison of the prophylactic antibiotic regimen (antibiogram) and major microorganisms between the first decade (2002-2012) and the second decade (2013-2022) within the 20-year study period (Figure E3) showed no significant differences between the first and second decades.

Follow-up Outcomes

The intensive care unit (ICU) and hospital survival rates were 47.61% and 45.71%, respectively. Hospital outcome analysis showed lower rates of ICU mortality (38.60% [22/57] vs 68.75% [33/48], $P = .006$) and in-hospital mortality (42.11 [24/57] vs 68.75% [33/48], $P = .010$) in the NI group than in the non-NI group (Table E4). The NI group had significantly longer durations of ECMO support (7 days vs 3 days, $P < .001$), ventilator use (17 days vs 7 days, $P < .001$), ICU stay (19 days vs 8 days, $P < .001$), and hospital stay (32 days vs 13.50 days, $P < .001$) (Table E4).

Patients who received prophylactic antibiotics with *P aeruginosa* coverage within 72 hours after ECPR had a significantly lower prevalence of NI (hazard ratio [HR], 0.507; 95% confidence interval [CI], 0.285-0.901; $P = .006$; Figure 2, *A*) and early VAP (HR, 0.485; 95% CI, 0.263-0.893; $P = .007$; Figure 2, *B*). Multivariate Cox regression analysis revealed that prophylactic antibiotics with *P aeruginosa* coverage were protective against NI

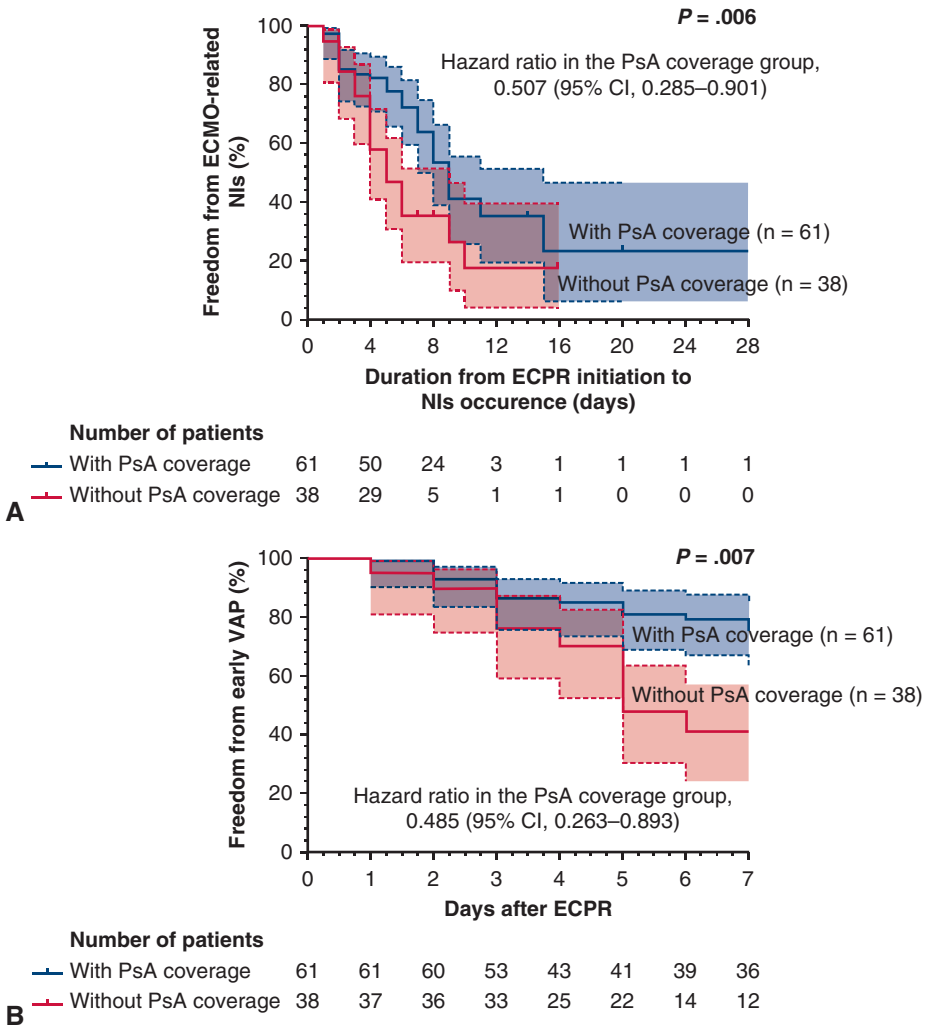

FIGURE 2. Analysis of (A) freedom from NIs and (B) freedom from early ventilator-associated pneumonia (*VAP*) in patients treated with prophylactic antibiotics with *P aeruginosa* (PsA) coverage within 72 h after ECPR. *NIs*, Nosocomial infections; *ECPR*, extracorporeal membrane oxygenation resuscitation; *CI*, confidence interval.

(HR, 0.518; 95% CI, 0.281-0.953, $P = .034$; Table 2). In addition, greater dynamic driving pressure (per cmH_2O) in the ventilator within the first 24 hours after ECPR and longer low-flow time were predictive of hospital mortality (HR, 1.096; 95% CI, 1.008-1.192; $P = .032$, and HR, 1.020; 95% CI, 1.001-1.039; $P = .039$, respectively; Table 3).[25] Subgroup analysis also showed that an Acute Physiology and Chronic Health Evaluation (APACHE) II score of ≥24 was a risk factor for MDR in patients who received ECPR (HR, 6.433; 95% CI, 1.380-30.088; $P = .018$; Table E5). Follow-up analysis after discharge showed no significant differences in readmission due to recurrent or all-cause infections between the NI and non-NI groups ($P = .175$ and .800, respectively; Figure E4, *A* and *B*).

DISCUSSION

This retrospective study shows that NIs presents as a comorbidity associated with an increased duration of ECMO support and hospital stay among patients with circulatory arrest who are resuscitated with ECMO. Prophylactic antibiotic treatment with *P aeruginosa* coverage reduces the incidence of NIs in patients with ECPR (Figure 3). In the modern era of antibiotics, the presence of NIs does not influence hospital mortality following adequate antimicrobial management. We propose that the mortality outcome should be associated with multiple morbidities developed after ECPR. Furthermore, the development of MDR is influenced by the underlying conditions resulting in an APACHE II score of ≥24. In addition, increased dynamic driving pressure of the

TABLE 2. Multivariate Cox regression for influencing factors of nosocomial infection among patients who received ECPR

Factor	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	*P* value	Hazard ratio (95% CI)	*P* value
Prophylactic antibiotics with *Pseudomonas* spp. coverage	0.515 (0.297-0.892)	.018	0.512 (0.278-0.944)	.032
Out-of-hospital cardiac arrest	1.551 (0.902-2.668)	.112	1.346 (0.754-2.402)	.314
Diabetes mellitus	1.008 (0.577-1.762)	.977	0.808 (0.439-1.488)	.494
Prophylactic antibiotics with MRSA coverage	0.845 (0.477-1.498)	.565		
Duration of ECMO, d	0.998 (0.966-1.032)	.920		
Immunosuppression*	0.899 (0.406-1.991)	.793	0.877 (0.366-2.102)	.768
APACHE II score ≥24	1.648 (0.943-2.883)	.080	1.538 (0.811-2.915)	.187
Blood transfusion within 24 h after ECPR	1.728 (0.622-4.798)	.294		
Total steroid use in 24 h after ECPR (hydrocortisone, mg/d)	1.000 (0.999-1.001)	.629		
Procedure or operation during ECMO run	1.381 (0.814-2.344)	.231	1.122 (0.617-2.038)	.707

ECPR, Extracorporeal membrane oxygenation resuscitation; *CI*, confidence interval; *MRSA*, methicillin-resistant *Staphylococcus aureus*; *ECMO*, extracorporeal membrane oxygenation; *APACHE*, Acute Physiology and Chronic Health Evaluation. *Includes patients with acquired immune deficiency syndrome, solid-organ transplantation, and hematologic malignancy and those receiving chemotherapy, immunosuppressive agents, or long-term corticosteroid therapy.

ventilator may lead to significant in-hospital mortality in patients undergoing ECPR. The underlying comorbidities and complications secondary to NIs negatively impact the outcomes, but not the mortality, of ECPR during hospitalization. The identification of common pathogens, followed by adequate prophylactic antibiotic treatment, might reduce the incidence of NIs in ECPR cases.

NIs increase the risk of morbidity and mortality in critically ill patients, and patients who receive ECPR are at greater risk of infection.[8] The NI rate in our study was 54.29%, within the range of 20.5% to 64% in previous studies of IHCA with ECPR and VA-ECMO patient populations.[8,18,26] Among the infection types, VAP was the most common NI, with a rate of 47.62% (50/105), still within the range of 20.3% to 56% in other VA-ECMO patient studies.[18,27,28] A total of 73.68% (70/95) of the infection episodes were VAP. This is comparable with the VAP rate of 74% (163/220) in adult patients with cardiogenic shock receiving VA-ECMO support evaluated by Schmidt and colleagues,[18] despite their study population being different, with only approximately 10% experiencing cardiac arrest. The incidence rate of NI in our study was greater than that in other studies of VA-ECMO and IHCA with ECPR patients (40.8-75.5 episodes per 1000 ECMO days).[8,18,28] More than 30% of our study population had OHCA before ECPR, and these patients receiving ECPR had longer low-flow times than IHCA patients with ECPR in the study by Ko and colleagues[8]

Shiba and colleagues[29] demonstrated that cardiac arrest and ECPR were significantly associated with the development of early-onset pneumonia owing to unprotected upper airways and longer low-flow times. Roumy an d colleagues[30] reported that VA-ECMO could adversely affect lung function through various

TABLE 3. Multivariate Cox regression for influencing factors of hospital mortality in patients who received ECPR

Factors	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	*P* value	Hazard ratio (95% CI)	*P* value
APACHE II score ≥24	1.953 (1.087-3.510)	.025	1.778 (0.862-3.670)	.119
Dynamic DP at the first 24 h after ECPR, cmH_2O*	1.085 (1.049-1.123)	<.001	1.096 (1.008-1.192)	.032
Lactate level within 24 h after ECPR, mmol/L	1.066 (1.016-1.119)	.010	1.045 (0.992-1.100)	.096
Prophylactic antibiotics with *Pseudomonas* spp. coverage	0.995 (0.574-1.726)	.987		
Prophylactic antibiotics with MRSA coverage	0.719 (0.401-1.290)	.269		
Immunosuppression†	1.979 (0.716-5.471)	.188		
VT/VF before ECMO support	0.552 (0.329-0.924)	.024	0.608 (0.319-1.158)	.130
Low-flow time (min)	1.015 (1.000-1.029)	.045	1.020 (1.001-1.039)	.039
Out-of-hospital cardiac arrest	1.051 (0.607-1.820)	.858		

ECPR, Extracorporeal membrane oxygenation resuscitation; *CI*, confidence interval; *APACHE*, Acute Physiology and Chronic Health Evaluation; *DP*, driving pressure; *MRSA*, methicillin-resistant *Staphylococcus aureus*; *VT/VF*, ventricular tachycardia/ventricular fibrillation; *ECMO*, extracorporeal membrane oxygenation. *Dynamic driving pressure is defined as the difference between the peak inspiratory pressure and positive end expiratory pressure.[25] †Includes patients with acquired immune deficiency syndrome, solid-organ transplantation, or hematologic malignancy and those receiving chemotherapy, immunosuppressive agents, or long-term corticosteroid therapy.

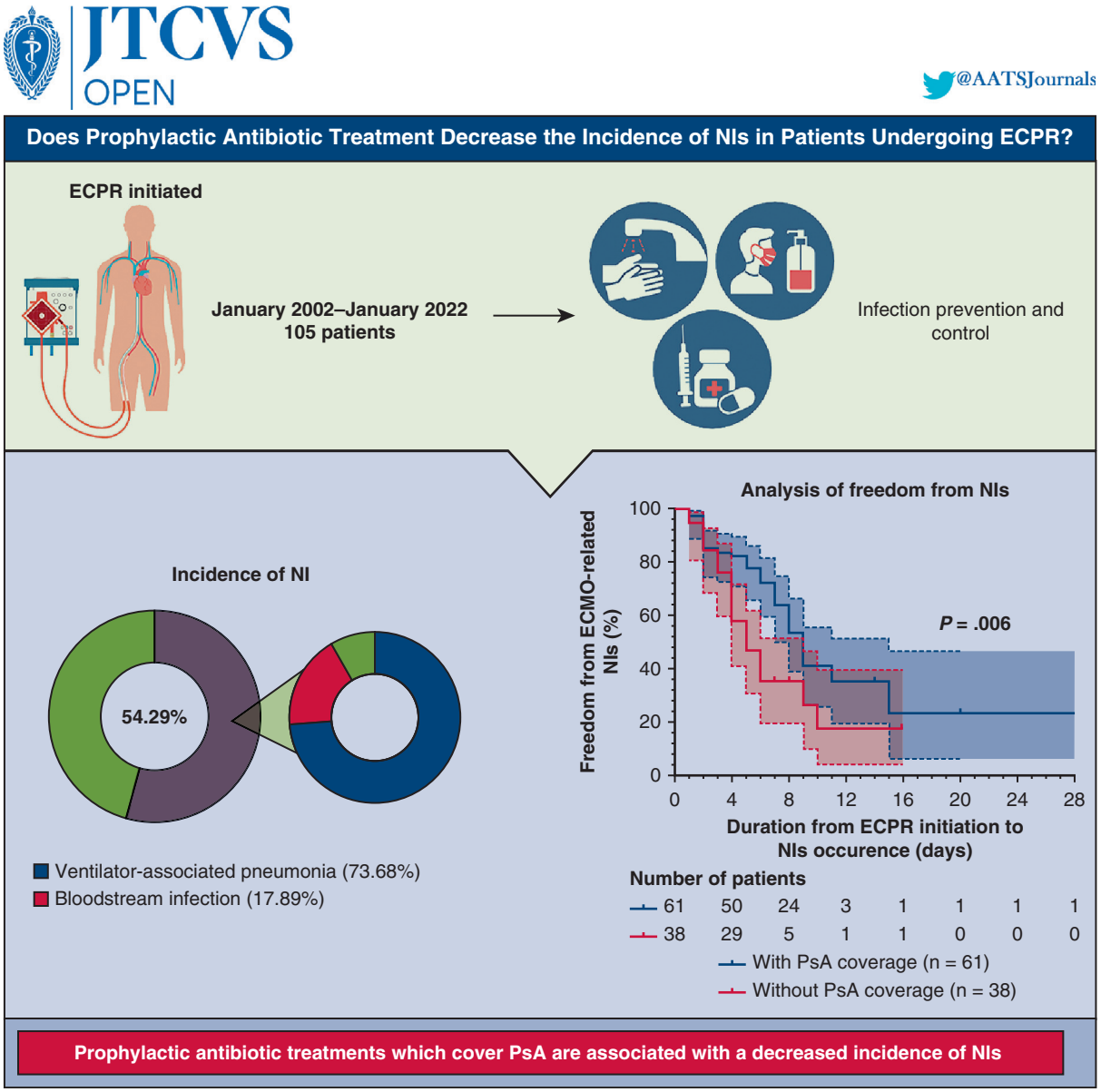

FIGURE 3. Results of a single-center, retrospective study analyzing the impact of prophylactic antibiotic administration on nosocomial infection (*NI*) outcomes in patients undergoing extracorporeal cardiopulmonary resuscitation (*ECPR*). This image summarizes the incidence of different types of NIs in patients who receive ECPR. This study indicates that ventilator-associated pneumonia is the most common type of NI, and patients who receive prophylactic antibiotics with *P aeruginosa* coverage within 72 hours after ECPR have a significantly lower prevalence of NI (HR, 0.507; 95% CI, 0.285-0.901; $P = .006$). *HR*, Hazard ratio; *CI*, confidence interval; *ECMO*, extracorporeal membrane oxygenation; *PsA*, *Pseudomonas aeruginosa*.

pathophysiologic mechanisms, including the development of systemic inflammatory response syndrome in the lungs by the contact of blood with biomaterial and the relative hypoperfusion of the entire pulmonary vasculature. These mechanisms lead to impaired pulmonary function that may require long-term mechanical ventilation and increase the risk of ventilator-induced lung injury and VAP.[30] These findings suggested that cardiac arrest with longer low-flow time and ECMO support may predispose patients to infectious complications, especially VAP.[29,30] Importantly, this may explain our study's greater incidence of VAP and NI in patients undergoing ECPR.

Our study revealed that treatment with prophylactic antibiotics with *P aeruginosa* coverage within 72 hours after ECPR was a protective factor against early VAP and NI. Gram-negative bacteria were involved in 80% of VAPs, in line with up to 70% of VAP in IHCA with ECPR and VA-ECMO patient populations in other

studies.[8,18,28] *P aeruginosa* was the most common Gram-negative bacteria causative of VAP in our study (21.43%), comparable with the rate of 13% to 26% in other VA-ECMO-related studies.[18,27,28] *P aeruginosa* was also a predominant blood isolate in a study of VA-ECMO or VV-ECMO support in patients without cardiac arrest.[31] Bouglé and colleagues[28] reported that infection by *P aeruginosa* in the first episode of pneumonia was associated with VAP treatment failure in patients receiving VA-ECMO by causing persistence, relapse, or superinfection.

A previous review showed that there is no robust evidence supporting routine use of prophylactic antimicrobials in patients receiving ECMO support, although the age range of the study population was very wide.[10] Schmidt and colleagues[18] reported that prophylactic antibiotic therapy was not associated with NI occurrence in patients undergoing VA-ECMO, but nearly 90% (192/220) of their study patients had no cardiac arrest,[18] different from our study population. Nevertheless, >35% of their cohort received antibiotics at the time of ECMO cannulation, whereas 88% (92/105) of our study patients received antibiotics at the time of ECMO cannulation. Kao and colleagues[32] reported that 74% of ECMO centers used prophylactic antibiotics. To date, the role of prophylactic antibiotic treatment in patients undergoing ECPR remains unclear.

For patients aged >18 years, Kondo and colleagues[9] reported that prophylactic antibiotic treatment during ECMO support is associated with reduced in-hospital mortality and nosocomial pneumonia. However, only 25% (1807/7300) of their patients underwent ECPR. The current study revealed a trend of greater rates of antibiotic treatment with *Pseudomonas* spp. coverage in the non-NI group and a significantly lower incidence of early VAP in patients treated with prophylactic antibiotics with *P aeruginosa* coverage. The greater risk of NIs in patients with ECPR and *P aeruginosa* being the most common causative bacteria of VAP indicate that it is reasonable to provide prophylactic antibiotic treatment with *P aeruginosa* coverage to decrease the incidence of NIs.[9,18,28]

In the modern era of antibiotic treatment, prophylactic or therapeutic treatments can lower infection-related complications and death. In the current study, 10.5% (11/105) of the patients who received ECPR had sepsis. Collectively, NIs appeared to have a limited impact on hospital mortality in patients who received ECPR, but we were not able to observe the incidence of NI among those patients who died shortly during the ECMO run. Although NIs did not influence hospital mortality, there were significantly longer durations of VA-ECMO, ventilator use, ICU stay, and hospital stay in patients with NIs who received ECPR. This is consistent with the report by Ko and colleagues.[8] Sun and colleagues[31] reported that the rates of NIs were greater in patients with prolonged ECMO support and those with more severe diseases. In addition, ECPR and ECMO support involve exposure of blood to the extracorporeal biomaterials, possibly lowering the immune response and causing failure of other organs. Thus, it is important to protect patients receiving ECPR from NIs.[30,31]

Although Holmberg and colleagues[33] showed inconclusive evidence for supporting the use of ECPR for patients who experience OHCA and IHCA, other studies demonstrated that ECPR was associated with more favorable outcomes in select patients.[3] The survival rates of conventional CPR are only 2% to 10% for OHCA and 22% to 34% for IHCA.[3] The hospital survival rate in the current study was 45.71%, greater than those in the studies by Lunz and colleagues[3] (24%) and Hadaya and colleagues (34.05%).[4] This can be explained, in part, by the lower proportion of OHCA patients in our study (32.4%) than those in the studies by Lunz and colleagues[3] (61%) and by Hadaya and colleagues (50.7%). ECPR survival might be improved by identifying risk factors of hospital mortality.[23,24]

The current study revealed that MDR bacterial infection is associated with an APACHE II score of ≥24 within 24 hours of ECPR initiation. Karvouniaris and colleagues[34] reported an association between a high APACHE II score on ICU admission and colistin-resistant Gram-negative associated-bloodstream infection. Ko and colleagues[8] showed that NIs with MDR occurred more frequently in IHCA with ECPR patients on prolonged ECMO duration. In the present study, patients with APACHE II scores of ≥24 had longer ECMO uses (data not shown), and nearly all (17/19) patients with MDR infection received antibiotic treatment during ECMO. A greater APACHE II score indicates more critical and severe disease, as well as a need for longer ECMO and antibiotic treatments and may aggravate the risk of MDR development. Collectively, the findings indicate a potential association between higher APACHE II scores and MDR infections in patients who receive ECPR.[8,34]

The present study has some limitations. First, the small sample size limited the strength of our findings. Second, our study might have contained confounding bias owing to its observational design. Third, our study was conducted over a long period, during which ICU management may have changed, and this could have affected patient outcomes. Fourth, there could be risks of developing MDR infection in patients using prophylactic antibiotics, although there were no significant differences in our study (Table E6). Fifth, the study spans 20 years, and the changes of antibiogram could be a bias in this study. Finally, although our study results indicated NIs have no influence on ECPR mortality, we were not able to observe the incidence of NI among those patients who died shortly

during ECMO run. Therefore, the impact of prophylactic antibiotic treatment on ECPR mortality requires further investigation.

CONCLUSIONS

In the modern era of antibiotic therapy, the development of NIs does not increase hospital mortality among patients with ECPR; however, it may influence ICU outcomes, including the length of ICU stay and duration of mechanical ventilation. Treatment with prophylactic antibiotics with *P aeruginosa* coverage is associated with a lower incidence of NIs, whereas an APACHE II score of $\geq$24 is a risk factor for MDR infections. In addition, greater dynamic driving pressure in the ventilator settings increases hospital mortality in patients with ECPR. Careful monitoring followed by adequate management of NI will help improve the outcomes of patients undergoing ECPR.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: extracorporeal cardiopulmonary resuscitation, infection, *Pseudomonas aeruginosa*, ventilator-associated pneumonia, circulatory arrest, prophylactic antibiotic treatment

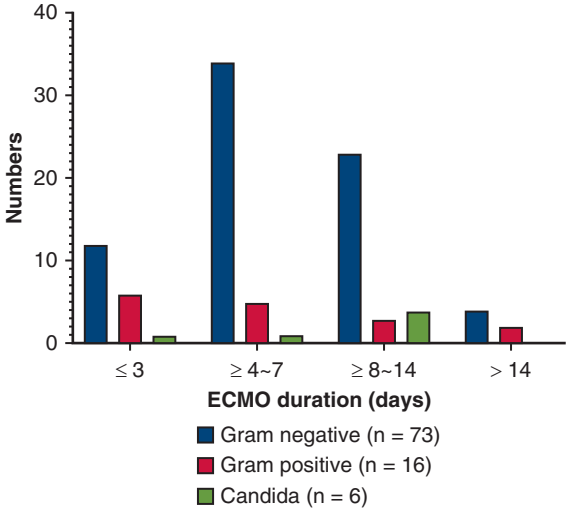


FIGURE E1. Pathogen distribution stratified by extracorporeal membrane oxygenation (*ECMO*) duration.

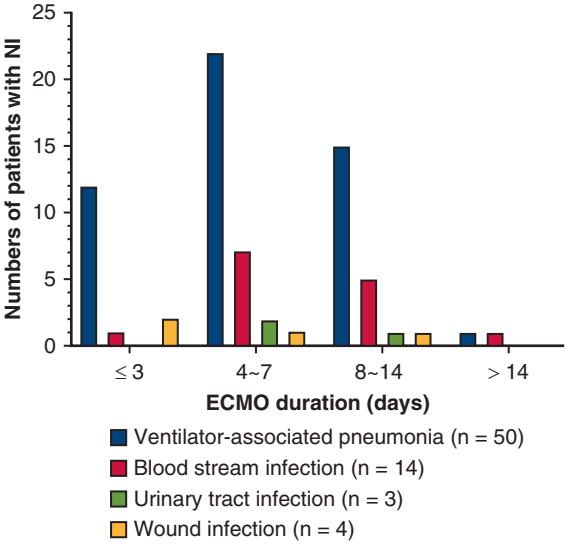


FIGURE E2. Incidence of nosocomial infection (*NI*) stratified by extracorporeal membrane oxygenation (*ECMO*) duration. A total of 10 patients with VAP also had BSI during the ECMO course, 2 patients with VAP also had UTI during the ECMO course, and 2 patients with VAP also had wound infection during the ECMO course. *VAP*, Ventilator-associated pneumonia; *BSI*, bloodstream infection; *UTI*, urinary tract infection.

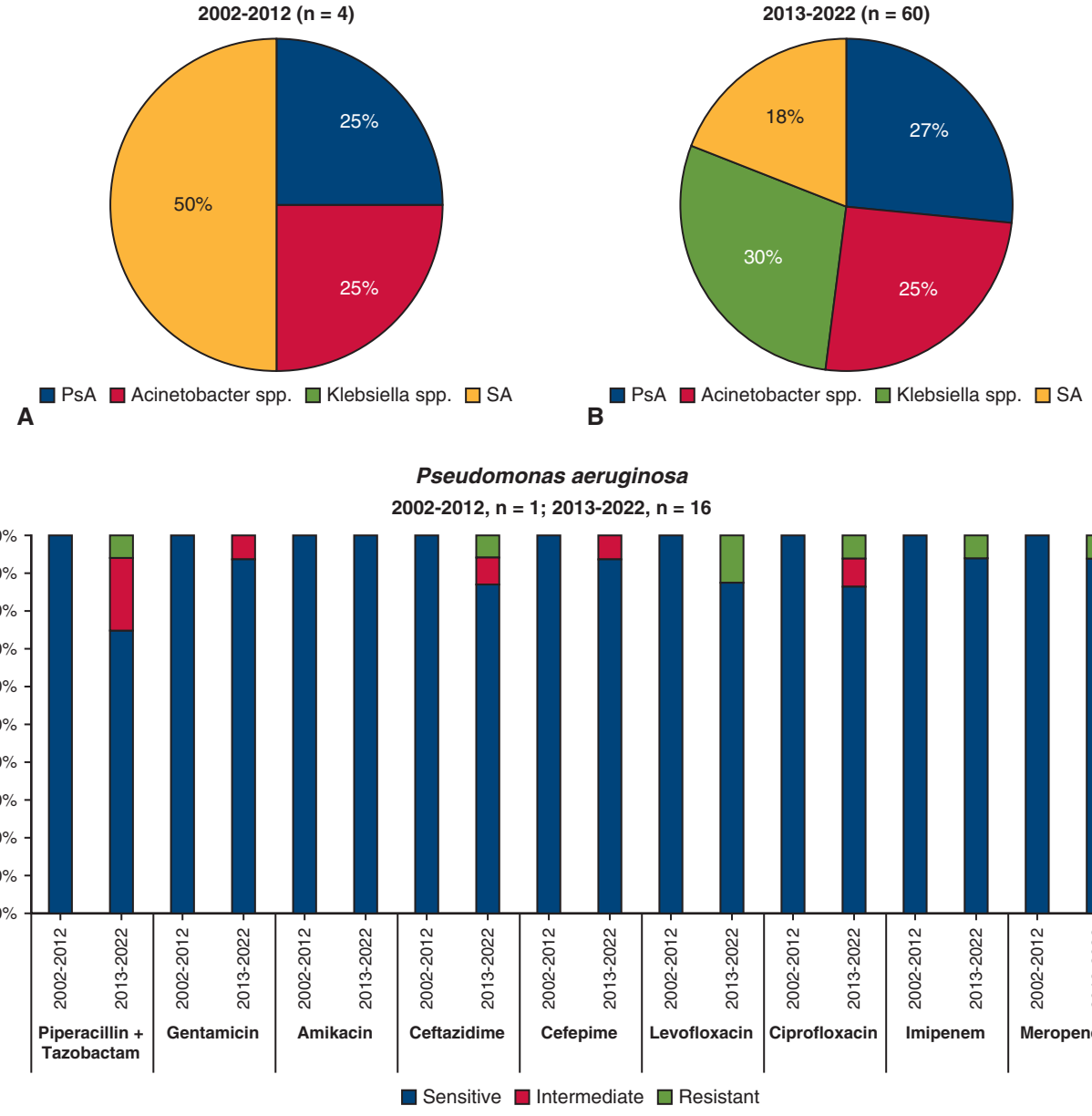
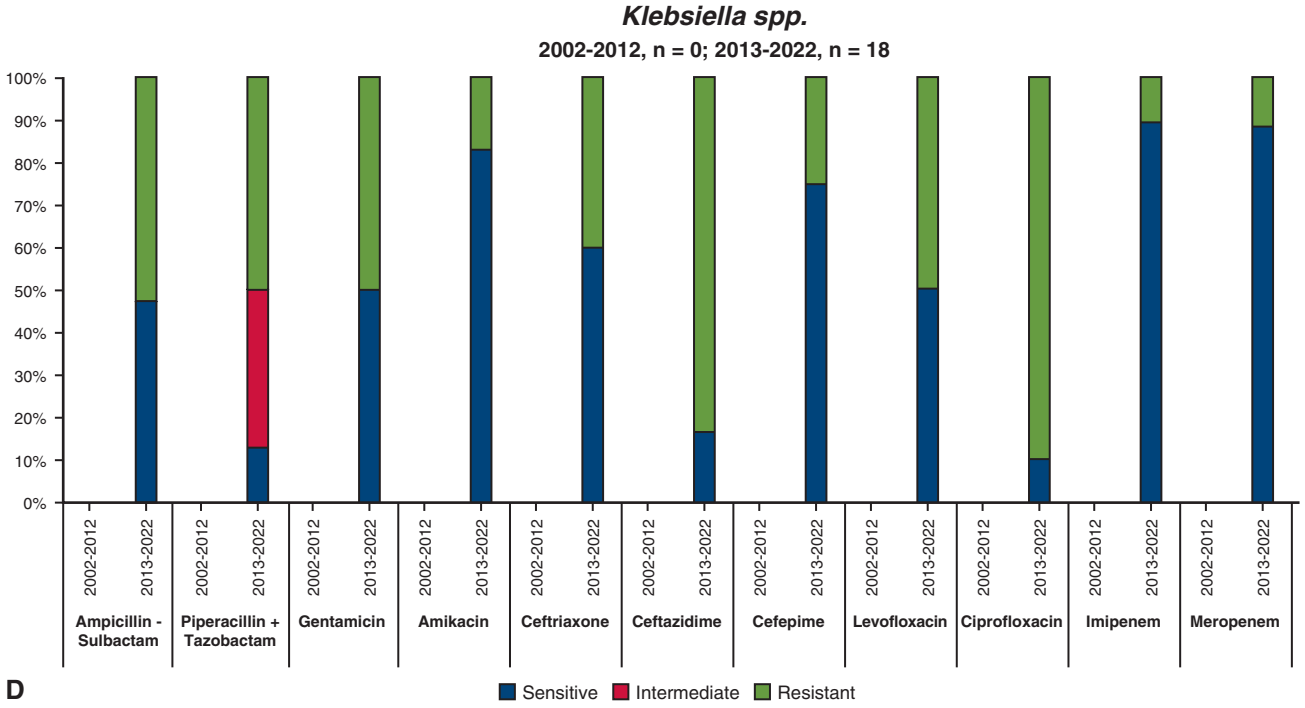


FIGURE E3. Stratification (A) from 2002 to 2012 and (B) from 2013 to 2022 of prevalent organisms and antibiotic susceptibilities of (C) *Pseudomonas aeruginosa*; (D) *Klebsiella* spp.; (E) *Acinetobacter* spp.; and (F) *Staphylococcus aureus*.



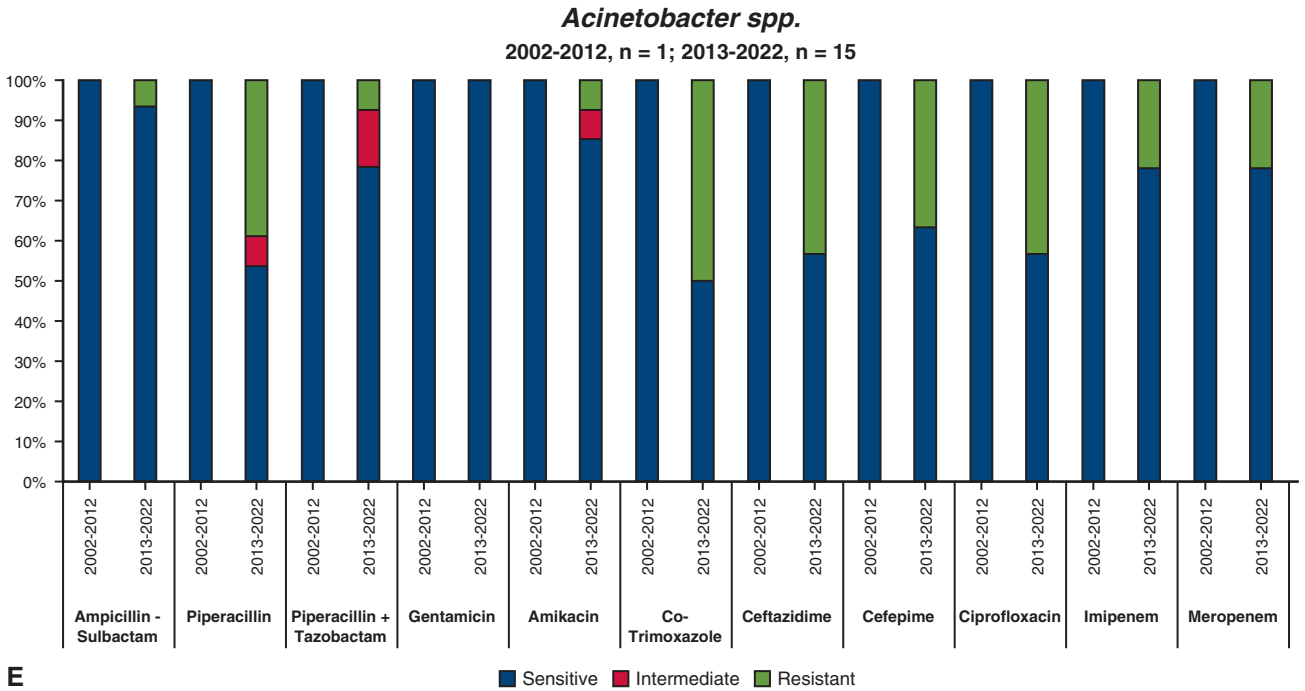


FIGURE E3. (*continued*).

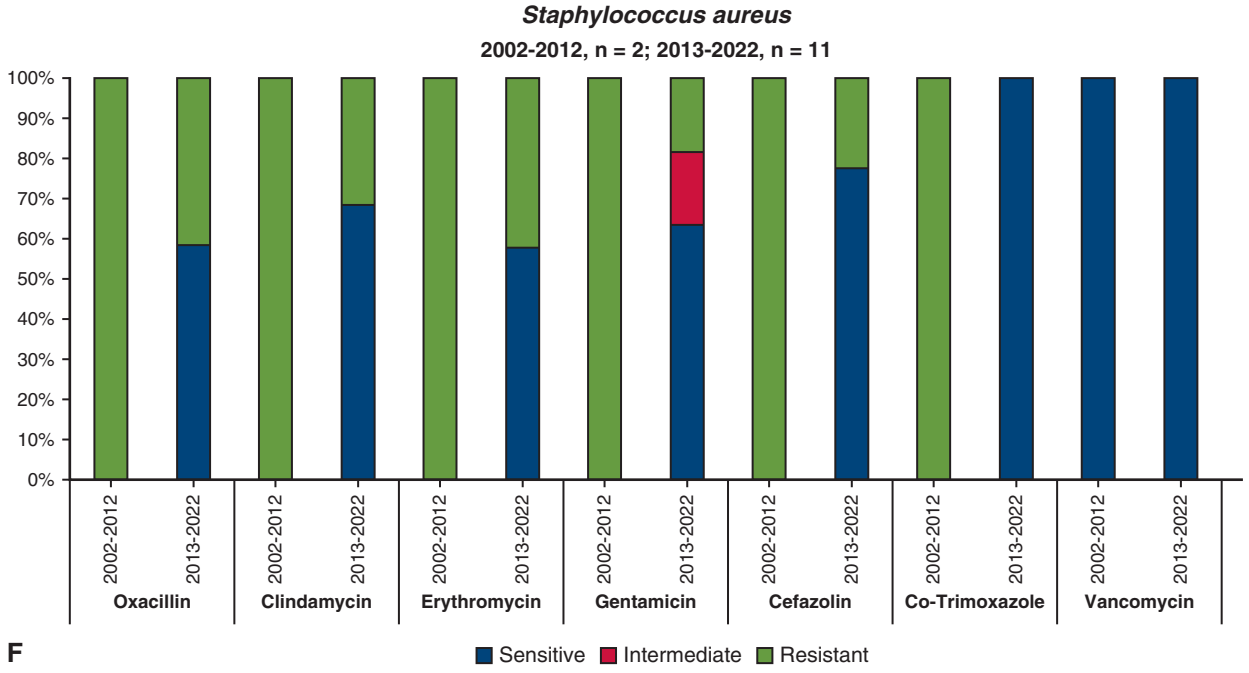


FIGURE E3. (*continued*).

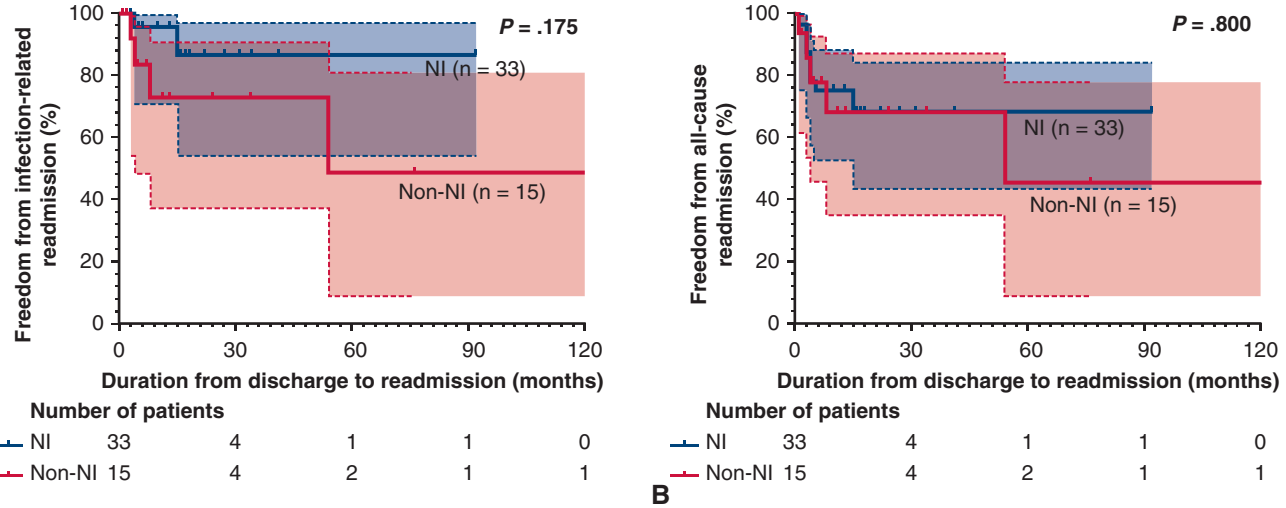


FIGURE E4. Analysis of (A) freedom from readmission due to infection (HR, 3.921; 95% CI, 0.588-18.420; $P = .175$) and (B) all-cause readmission in extracorporeal membrane oxygenation resuscitation patients (HR, 1.117; 95% CI, 0.346-3.956; $P = .800$). *HR*, Hazard ratio; *CI*, confidence interval; *NI*, nosocomial infection.

TABLE E1. Clinical data of patients with ECPR

Variable	NI group (n = 57)	Non-NI group (n = 48)	*P* value
Arterial blood gas 1 h before ECMO			
pH	7.200 [7.030-7.280]	7.165 [6.988-7.288]	.653
$PaCO_2$, mm Hg	48.00 [35.00-61.70]	46.70 [35.50-76.55]	.691
PaO_2, mm Hg	66.00 [31.00-124.00]	58.00 [37.00-107.50]	.841
BEecf, mmol/L (negative)	11.40 [4.60-16.70]	10.40 [5.75-16.25]	.934
Lactate, mmol/L	9.900 [5.900-11.925]	10.50 [7.23-12.95] (n = 24)	.266
Arterial blood gas 24 h after ECMO			
pH	7.5 [7.5-7.6]	7.5 [7.4-7.6]	.892
$PaCO_2$, mm Hg	44.1 [39.5-50.3]	45.0 [39.4-51.0]	.971
PaO_2, mm Hg	471.5 [354.2-540.8]	464.9 [371.3-535.0]	.864
Bicarbonate, mmol/L	24.8 [22.8-28.1]	24.5 [22.0-29.4]	.950
BEb, mmol/L	1.1 [−1.8 to 4.5]	0.5 [−1.9 to 6.1]	.960
BEecf, mmol/L	1.0 [−2.5 to 4.4]	−0.1 [−2.4 to 6.4]	.928
Lactate, mmol/L	10.9 [8.1-14.6]	14.9 [13.1-18.5]	.004
Inotropic equivalent (IE) (total at 24 h)	7.500 [4.850-16.645]	18.555 [5.028-41.538]	.040
ECMO blood flow, L/min at 24 h	2.980 [2.490-3.765]	2.670 [2.308-3.473]	.234
ECMO greater support at 24 h, ≥2.5 L/min	43 (75.44)	32 (66.67)	.284
Ventilator setting at 24 h after ECMO			
Rate, breaths per minute	12 [12-15]	14 [12-17.5]	.214
FiO_2	50 [50-50]	50 [50-68.75]	.035
Peak inspiratory pressure, cmH_2O	23.00 [20.00-26.00]	28.00 [22.00-32.50]	.003
PEEP, cmH_2O	8 [6-9]	8 [6-10]	.842
PaO_2/FiO_2	315.80 [187.80-717.35]	433.50 [210.45-785.00]	.516
Hydrocortisone, mg/d	0 [0-200]	0 [0-200]	.778
Blood transfusion	53 (92.98)	44 (91.67)	.729
RL, PRBC, unit	6.0 [2.5-12.0]	8.0 [4.0-23.0]	.098
Fresh-frozen plasma, U	4.0 [0-9.0]	4.0 [0-22.0]	.417
Platelet, U	0 [0-24.0]	0 [0-24.0]	.912

Data are presented as n (%) or the median [interquartile range]. *ECPR*, Extracorporeal cardiopulmonary resuscitation; *NI*, nosocomial infection; *ECMO*, extracorporeal membrane oxygenation; *$Paco_2$*, partial pressure of carbon dioxide; *Pao_2*, partial pressure of oxygen; *BEb*, base excess of blood; *BEecf*, base excess of extracellular fluid; *Fio_2*, fraction of inspired oxygen; *PEEP*, positive end-expiratory pressure; *RL*, Ringer's lactate; *PRBC*, packed red blood cells.

TABLE E2. Number of events for micro-organisms of NIs during ECMO support

Gram staining/ organism	Ventilator-associated pneumonia	Bloodstream infection	Urinary tract infection	Wound infection*	Overall	Multidrug-resistant infection
Number of infection (% of the NIs)	70 (73.68)	17 (17.89)	3 (3.16)	5 (5.26)	95 (100)	28 (100)
Incidence (numbers of NIs/1000 ECMO days)	100.14	24.32	4.29	7.15	135.91	40.06
Gram negative	56 (80)	10 (58.82)	2 (66.67)	5 (100)	73 (76.84)	21 (75)
Pseudomonas aeruginosa	15 (21.43)				15 (15.79)	2 (7.14)
Acinetobacter spp.	12 (17.14)	1 (5.88)			13 (13.68)	3 (10.71)
Klebsiella spp.	11 (15.71)	1 (5.88)		1 (20)	13 (13.68)	6† (21.43)
Escherichia coli	7 (10)		1 (33.3)	3 (60)	11 (11.58)	2 (7.14)
Burkholderia spp.	3 (4.29)	1 (5.88)		1 (20)	5 (5.26)	
Enterobacter spp.	2 (2.86)	2 (11.76)			4 (4.21)	3 (10.71)
Haemophilus influenzae	2 (2.86)				2 (2.11)	
Others	4‡ (5.71)	5§ (29.41)	1‖ (33.3)		10 (10.52)	5¶ (17.86)
Gram positive	9 (12.86)	7 (41.18)			16 (16.84)	7 (25)
Staphylococcus aureus	7 (10)	1 (5.88)			8 (8.42)	5 (17.86)
Coagulase negative *Staphylococcus*		4 (23.53)			4 (4.21)	
Streptococcus spp.	2 (2.86)	1 (5.88)			3 (3.16)	
Others		1# (5.88)			1 (1.05)	2** (7.14)
Fungal	5 (7.14)		1 (33.33)		6 (6.32)	
Candida spp.	5 (7.14)		1 (33.33)		6 (6.32)	

NIs, Nosocomial infections; *ECMO*, extracorporeal membrane oxygenation. *1 ECMO insertion-site infection and 4 operation wound infections. †Extended-spectrum β-lactamase (ESBL)-producing *Klebsiella pneumoniae* (4) and Carbapenem-resistant *Klebsiella pneumoniae* (2). ‡Aeromonas, *Cupriavidus gilardii*, *Elizabethkingia anopheles*, *Sphingomonas paucimobilis*. §*Alcaligenes xylosoxidans* (Gram negative), *Bacteroides fragilis*, *Neisseria* species, *Parabacteroides distasonis*, *Stenotrophomonas maltophilia*. ‖*Proteus mirabilis*. ¶*Chryseobacterium indologenes* (2), *Stenotrophomonas*, *Serratia*, *Sphingomonas paucimobilis*. #*Collinsella aerofaciens*. **Methicillin-resistant *Staphylococcus epidermidis*, vancomycin-resistant *Enterococcus*.

TABLE E3. Prophylactic antibiotic regimens among patients who received ECPR

Prophylactic antibiotics treatment	NI group (n = 49*)	Non-NI group (n = 43*)	*P* value
Single antibiotics treatment			
First-generation cephalosporins	6 (12.24)	2 (4.65)	.286
Second-generation cephalosporins	1 (2.04)	0 (0)	>.999
Third-generation cephalosporins	9 (18.37)	6 (13.95)	.779
Ceftazidime	1 (2.04)	3 (6.98)	.293
Cefepime	5 (10.20)	2 (4.65)	.450
Ampicillin-sulbactam	1 (2.04)	2 (4.65)	.589
Piperacillin-tazobactam	2 (4.08)	10 (23.26)	.011
Vancomycin	1 (2.04)	0 (0)	>.999
Two-antibiotic combination			
Third-generation cephalosporins + vancomycin	11 (22.45)	13 (30.23)	.480
Ceftazidime + vancomycin	9 (18.37)	12 (27.91)	.324
Third-generation cephalosporins + gentamycin	2 (4.08)	0 (0)	.499
Third-generation cephalosporins + Metronidazole	0 (0)	3 (6.98)	.090
Cefepime + vancomycin or teicoplanin	4 (8.16)	0 (0)	.124
Ampicillin-sulbactam + doxycycline	1 (2.04)	0 (0)	>.999
Piperacillin-tazobactam + vancomycin or teicoplanin	1 (2.04)	1 (2.33)	>.999
Piperacillin-tazobactam + moxifloxacin	1 (2.04)	0 (0)	>.999
Fluoroquinolones + vancomycin	1 (2.04)	0 (0)	>.999
Penicillin-derived combination	3 (6.12)	1 (2.33)	.624
Three or more antibiotic combinations			
Levofloxacin + ceftazidime + vancomycin	0 (0)	1 (2.33)	.455
Co-Trimoxazole + meropenem + vancomycin	1 (2.04)	0 (0)	>.999
Amphotericin B + clindamycin + meropenem	1 (2.04)	0 (0)	>.999
Third-generation cephalosporins + vancomycin + fluconazole + meropenem	0 (0)	1 (2.33)	.455
Prophylactic antibiotic treatment			
With *Pseudomonas* spp. coverage	29 (59.18)	32 (74.42)	.098
With MRSA coverage	19 (38.78)	17 (39.53)	.836
Duration of prophylactic antibiotic treatment, d	3.00 [3.00-5.00]	3.00 [3.00-4.50]	.571

ECPR, Extracorporeal cardiopulmonary resuscitation; *NI*, nosocomial infection; *MRSA*, methicillin-resistance *Staphylococcus aureus*. *Number of patients who received prophylactic antibiotic treatment.

TABLE E4. Hospital outcomes of patients who received ECPR

Variable	NI group (n = 57)	Non-NI group (n = 48)	*P* value
ECMO weaning	48 (84.21)	25 (52.08)	<.001
ECMO complication	28 (49.12)	18 (37.50)	.244
Intracranial hemorrhage	10 (17.54)	8 (16.67)	1.000
Gastrointestinal bleeding	11 (19.30)	4 (8.33)	.161
Hemothorax	6 (10.53)	4 (8.33)	.751
ECMO wound poor healing	3 (6.26)	4 (8.33)	.700
Peri-ECMO RRT	29 (50.88)	25 (52.08)	1.000
Duration of ECMO, d	7.00 [4.00-10.00]	3.00 [2.00-5.75]	<.001
Duration of ventilator, d	17.00 [11.00-26.00]	7.00 [3.00-14.50]	<.001
Duration of ventilator after ECPR days >7	54 (94.74)	27 (56.25)	<.001
Duration of hospital, d	32.00 [22.00-58.00]	13.50 [4.15-35.25]	<.001
Duration of ICU, d	19.00 [14.75-31.50]	8.00 [4.00-17.75]	<.001
ICU mortality	22 (38.60)	33 (68.75)	.006
In-hospital mortality	24 (42.11)	33 (68.75)	.010
Cause of death (n = 57)			
Multiorgan dysfunction	22 (91.67)	31 (93.94)	>.999
Non-sepsis-related	13 (54.17)	29 (87.88)	.006
Sepsis-related	9 (37.50)	2 (6.06)	.005
Sepsis during ECMO support	5 (20.83)	0 (0)	.205
Hypoxic ischemic brain injury	2 (8.30)	2 (6.06)	>.999
GCS score before ICU discharge	9.0 [3.0-14.0]	3.0 [3.0-14.8]	.061
CPC score at discharge	2.0 [1.0-2.5] (n = 33)	1.0 [1.0-2.0] (n = 15)	.180
1	14 (42.42%, 14/33)	10 (66.67%, 10/15)	
2	11 (33.33%, 11/33)	3 (20%, 3/15)	
3	3 (9.09%, 3/33)	0 (0)	
4	5 (15.15%, 5/33)	1 (6.67%, 1/15)	
5	0	1 (6.67%, 1/15)	

ECPR, Extracorporeal cardiopulmonary resuscitation; *NI*, nosocomial infection; *ECMO*, extracorporeal membrane oxygenation; *RRT*, renal-replacement therapy; *ICU*, intensive care unit; *GCS*, glasgow coma scale; *CPC*, cerebral performance category.

TABLE E5. Multivariate Cox regression analysis for the development of multiple drug-resistant infections among patients who received ECPR

Factor	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	*P* value	Hazard ratio (95% CI)	*P* value
APACHE II score ≥24	4.145 (1.160-14.811)	.029	6.443 (1.380-30.088)	.018
Prophylactic antibiotics with *Pseudomonas* spp. coverage	0.625 (0.231-1.692)	.355	0.881 (0.280-2.771)	.829
Prophylactic antibiotics with MRSA coverage	0.614 (0.211-1.784)	.370	0.572 (0.171-1.911)	.364
Diabetes mellitus	1.016 (0.405-2.549)	.973		
Immunosuppression*	0.611 (0.140-2.676)	.514		
Duration of prophylactic antibiotic treatment, d	0.877 (0.600-1.283)	.499		

ECPR, Extracorporeal cardiopulmonary resuscitation; *CI*, confidence interval; *APACHE*, Acute Physiology and Chronic Health Evaluation; *MRSA*, methicillin-resistant *Staphylococcus aureus*. *Includes patients with acquired immune deficiency syndrome, solid-organ transplantation, and hematologic malignancy and those receiving chemotherapy, immunosuppressive agents, or long-term corticosteroid therapy.

TABLE E6. MDR infection development in prophylactic antibiotics use from postdecannulation to discharge among patients who underwent ECPR

	Prophylactic antibiotics use from postdecannulation to discharge (n = 42%)	No prophylactic antibiotics use from postdecannulation to discharge (n = 6%)	*P* value
MDR infection	13 (30.95)	1 (16.67)	.656

MDR, Multidrug resistant; *ECPR*, extracorporeal cardiopulmonary resuscitation.