Community *versus* hospital-acquired pneumonia in patients requiring extracorporeal membrane oxygenation

Chul Park, Soo Jin Na, Chi Ryang Chung, Yang Hyun Cho, Gee Young Suh and Kyeongman Jeon (ID)

Abstract

Background: Bacterial pneumonia is a major cause of acute respiratory distress syndrome (ARDS) requiring extracorporeal membrane oxygenation (ECMO) support. However, it is unknown whether the type of pneumonia, community-acquired pneumonia (CAP) *versus* hospital-acquired pneumonia (HAP), should be considered when predicting outcomes for ARDS patients treated with ECMO.

Methods: We divided a sample of adult patients receiving ECMO for acute respiratory distress syndrome caused by bacterial pneumonia between January 2012 and December 2016 into CAP ($n = 21$) and HAP ($n = 35$) groups and compared clinical and bacteriological characteristics and outcomes.

Results: The median acute physiology and chronic health evaluation II and sequential organ failure assessment scores were 22 and 8, respectively, in the CAP and HAP groups. The most commonly identified organism in the CAP group was *Streptococcus pneumonia* ($n = 12$, 57.1%), while *Acinectobacter baumanii* was the most commonly identified in the HAP group ($n = 13$, 37.1%). However, the incidence of multidrug resistant bacteria was not different between groups (57.1% *versus* 74.3%, $p = 0.125$). Of the 56 patients in the study, 26 were successfully weaned from ECMO, and 20 were discharged from the hospital. There were no significant differences in ECMO weaning rate (47.6% *versus* 45.7%, $p > 0.999$) or survival to discharge rate (33.3% *versus* 37.1%, $p > 0.999$) between the two groups. The 30-day and 90-day mortality rates were also similar.

Conclusion: Patients with CAP and HAP who received ECMO for respiratory support had similar characteristics and clinical outcomes.

Keywords: acute respiratory distress syndrome, extracorporeal membrane oxygenation, pneumonia

Correspondence to:
Kyeongman Jeon
Department of Critical Care Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea Division of Pulmonary and Critical Care Medicine, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea
kjeon@skku.edu

Chul Park
Soo Jin Na
Chi Ryang Chung
Department of Critical Care Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Yang Hyun Cho
Department of Thoracic and Cardiovascular Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Gee Young Suh
Department of Critical Care Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea Division of Pulmonary and Critical Care Medicine, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Introduction

Acute respiratory distress syndrome (ARDS) is a life-threatening form of respiratory failure associated with a mortality rate of approximately 40–45%.[1,2] As several studies have demonstrated the benefits of extracorporeal membrane oxygenation (ECMO) in patients with ARDS who are unresponsive to conventional management, ECMO is emerging as a potential therapeutic modality, and its use in clinical practice is increasing.[3–5] However, ECMO is still a complex and costly treatment that can be exposed to several significant complications. Therefore, efforts have been made to identify patients who are more likely to survive after ECMO support.

Bacterial pneumonia is a predominant etiology of acute respiratory failure requiring ECMO.[5] Pneumonia is classified as community-acquired

pneumonia (CAP) or hospital-acquired pneumonia (HAP). CAP and HAP require different therapeutic approaches, because different causative pathogens are involved.[6,7] Some studies suggest that CAP and HAP should be regarded as distinct clinical entities since they have different clinical courses.[8,9]

Although bacterial pneumonia is regarded as a favorable factor for survival after ECMO support,[10] it is unknown whether type of pneumonia (CAP or HAP) should be considered when predicting outcomes for ARDS patients treated with ECMO. The objective of this study was to identify clinical, bacteriological, and treatment characteristics in pneumonia patients who received ECMO for respiratory support according to type of pneumonia and to compare clinical outcomes between groups.

Methods

Study design and sample
This observational study was conducted at Samsung Medical Center (a 1989-bed, university-affiliated, tertiary referral hospital in Seoul, South Korea) between January 2012 and December 2016. We included adult patients over 18 years of age who were diagnosed with ARDS caused by bacterial pneumonia and received ECMO for respiratory support during the study period. Patients under 18 years of age, in whom other pathogens (e.g. virus or fungus) were identified, who lacked microbial identification, or who were transferred from other hospitals after ECMO initiation were excluded from this study. Eligible patients were divided into two groups according to type of pneumonia, CAP or HAP. The study was approved by the Institutional Review Board of Samsung Medical Center (approval no: 2017-07-075), which waived the need for informed consent because of the retrospective observational nature of the study. All patient data were anonymized and de-identified before analysis.

Diagnosis and management of pneumonia ARDS
Pneumonia was diagnosed when we detected new radiographic infiltrates with at least two of the following clinical criteria: fever or hypothermia, new cough with or without sputum production, pleuritic chest pain, dyspnea, and altered breath sounds on auscultation.[11] If a patient was clinically suspected or diagnosed with pneumonia, empirical antibiotic therapy was initiated according to standard guidelines.[6,7] We classified pneumonia cases into two categories: CAP for pneumonia that occurred or developed outside of the hospital setting and HAP for pneumonia that occurred ≥ 2 days after hospitalization and was not incubating at the time of hospital admission.[6] According to the Berlin definition, ARDS was defined as follows: onset within 1 week of a known clinical insult or new or worsening respiratory symptoms; bilateral opacities not fully explained by effusions, lobar/lung collapse, or nodules; respiratory failure not fully explained by cardiac failure or fluid overload and requiring objective assessment to exclude hydrostatic edema if no risk factor is present; and partial arterial oxygen concentration/inspired oxygen faction (PaO_2/FiO_2) ratio $\leqslant 300\,mmHg$ with positive end-expiratory pressure or continuous positive airway pressure $\geqslant 5\,cmH_2O$.[1]

Management of mechanical ventilation (MV) was performed according to the protocol proposed by the ARDS Network as much as possible.[12,13] When patients could not maintain adequate oxygenation or carbon dioxide removal with MV, adjunctive therapies such as inhaled nitric oxide, prone positioning, and glucocorticosteroid therapy were also used at the discretion of the physician.

Initiation and management of ECMO
Patient selection, medical management, and settings of the MV and ECMO circuits followed institutional protocols that have been described previously.[14] Patients with deteriorating hypoxemia (PaO_2/FiO_2 ratio < 80 on $FiO_2 > 90\%$) or uncompensated hypercapnia (CO_2 retention with pH < 7.20 despite plateau pressure $> 30\,cmH_2O$) under advanced mechanical ventilator support with or without adjunctive therapies were considered for ECMO support. The final decisions regarding ECMO initiation were made after consultation with a multidisciplinary ECMO team consisting of intensivists, pulmonologists, and cardiothoracic surgeons.

Pump blood flow and sweep gas flow rates were adjusted to maintain target oxygen saturation and carbon dioxide removal rate at all times.

During ECMO support, pressure controlled ventilation mode was used for patients with FiO_2 lower than 30%, respiratory rate lower than 10–12 per minute, positive end-expiratory airway pressure of $10\,cmH_2O$, and peak inspiratory pressure of $20–25\,cmH_2O$ to achieve low tidal ventilation ($< 5\,ml/kg$ of predicted body weight) and prevent ventilator-induced lung injury. If patients were stable and tolerant of treatment, we changed the mode of MV to pressure support ventilation and subsequently adjusted ventilator settings for weaning. The possibility of weaning from ECMO was assessed daily, and trial off was performed to determine decannulation when arterial blood gas was maintained within the target range with a sweep gas flow of 1 l/min or less regardless of pump blood flow at acceptable ventilator settings. Patients who maintained adequate gas exchange without sweep gas flow (sweep gas off trial) were closely monitored for at least 2 h and decannulation was considered for patients who were stable during this period. The decision about total duration of weaning trial and decannulation were made by treating intensivists and an ECMO team.

Data collection and clinical outcomes

We retrospectively reviewed and obtained clinical and laboratory data from our institution`s ECMO database, which prospectively registered all patients who were treated with ECMO since 2012. Acute physiology and chronic health evaluation (APACHE) II score, sequential organ failure assessment (SOFA) score, and lung injury score were estimated by the worst value within the first 24 h in the intensive care unit (ICU) admission. For prediction of survival after ECMO support, the respiratory extracorporeal membrane oxygenation survival prediction (RESP) score[10] and predicting death for severe ARDS on VV ECMO (PRESERVE) score[15] were calculated on the first day of ECMO support. Driving pressure was calculated as peak inspiratory pressure minus positive end-expiratory pressure because all patients underwent ventilation with pressure-control mode in which the peak pressure can be used as a surrogate for plateau pressure.[16]

An etiological diagnosis was considered when a respiratory pathogen was isolated from a usually sterile specimen, pneumococcal antigen was detected in urine, or a predominant microorganism was isolated from adequate sputum or bronchial washing fluids with compatible Gram staining, as previously reported.[17] Multidrug resistant (MDR) pathogens were identified by an international expert proposal for interim standard definitions for acquired resistance,[18] which is nonsusceptible to at least one agent in three antimicrobial categories. The appropriateness of antibiotic therapy was analyzed for all cases with etiological diagnoses according to susceptibility test criteria for lower respiratory tract pathogens. Antibiotic therapy was classified as inappropriate if the initially prescribed antibiotics were not active against the identified pathogens based on *in vitro* susceptibility testing.[19] The antibiotic treatments for pneumonia were in line with the clinical practice guidelines by the Infectious Diseases Society of America/American Thoracic Society,[6,7] and the adequacy of antibiotics therapy, including the appropriateness of antibiotics selection, dosing, and duration were routinely assessed by infectious disease specialists in our hospital. We usually administered antibiotics active against the identified pathogens for 7–10 days, but sometimes longer duration of antibiotics might be indicated, depending upon the rate of improvement of clinical, radiologic, and laboratory parameters.

The primary outcome in this study was survival to discharge from hospital. Secondary outcomes were success of weaning from MV and ECMO, duration of ECMO support, appropriateness of antibiotic therapy, ECMO-related complications, and 30-day and 90-day mortality after ECMO initiation. We identified data related to clinical outcomes by review of hospital medical records.

Statistical analyses

The data are presented as median and interquartile range for continuous variables and as number (percent) for categorical variables. The data were analyzed using Kolmogorov–Smirnov tests for normal distribution. The Mann–Whitney U test was used to compare continuous variables, and the Chi-squared and Fisher's exact tests were used to compare categorical variables. A p value <0.05 was considered statistically significant. To estimate whether type of pneumonia was associated with survival to discharge, we performed multivariable logistic regression analysis to adjust for age, sex, type of pneumonia, and factors with $p < 0.2$ on univariate analysis. All data were analyzed using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA).

Results

Patient baseline characteristics

During the study period, a total of 136 patients were identified as having bacterial pneumonia-induced ARDS and receiving VV ECMO support. We excluded 50 patients lacked microbial identification, 13 patients transferred from other hospitals after ECMO initiation, 12 patients with nonbacterial pathogens, and 5 patients under 18 years of age (Figure 1). Thus, 56 bacterial pneumonia patients with ARDS receiving VV ECMO were included in this study. The baseline characteristics and clinical features of the two groups are presented in Table 1. There were 21 patients (37.5%) with CAP and 35 patients (62.5%) with HAP. The patients with HAP were older, more likely to be male, and had higher body mass index. However, these differences were not significant. Comorbidities, such as malignancy, chronic lung disease, diabetes, neurologic disease, cardiovascular disease, and chronic kidney disease, were not significantly different between the two groups. APACHE II (22.0 *versus* 22.5, $p = 0.382$) and SOFA scores (8 *versus* 8, $p = 0.893$) were not different between the two groups. In addition, vasoactive-inotropic (4 *versus* 3, $p = 0.417$) and lung injury scores (2.84 *versus* 2.67, $p = 0.107$) were not different between the two groups at the time of ICU admission.

Medical management prior to ECMO

Treatment modalities for patients in severe respiratory failure with pneumonia prior to ECMO initiation are presented in Table 2. The duration of MV prior to initiation of ECMO was similar in the CAP and HAP groups. Measurements performed during MV prior to ECMO, including positive end-expiratory pressure, peak inspiratory pressure, driving pressure, tidal volume per predicted body weight, and worst values of arterial blood gases, were not different between the two groups. Adjunctive or rescue therapies for severe respiratory failure including steroids, neuromuscular blocking agents, prone positioning, and inhaled nitric oxide were similar between the two groups. Finally, RESP and PRESERVE scores were similar between the two groups.

Laboratory and microbiologic characteristics

As shown in Table 3, laboratory findings were not different between the two groups. The distributions of pathogens are shown in Table 3. The most common pathogens were *Streptococcus pneumonia* in the CAP group ($n = 12$, 57.1%) and *Acinectobacter baumanii* in the HAP group ($n = 13$, 37.1%). The presence of MDR pathogens was more common in patients with HAP than in those with CAP; however, these findings were not significantly different between the two groups (57.1% *versus* 74.3%, $p = 0.125$). In addition, the appropriateness of initial antibiotic therapy was not different (66.7% *versus* 60.0%, $p = 0.843$).

Medical management after ECMO initiation

Treatment modalities during the first 72 h after ECMO initiation are presented in Table 4. The post-ECMO MV setting was similar in the CAP and HAP groups. In addition, the need for organ supports such as vasopressors and renal replacement therapy were not different. Finally, SOFA scores during the first 72 h after ECMO initiation were not different between the two groups.

Clinical outcomes

Clinical outcomes of patients with bacterial pneumonia-induced ARDS who received VV ECMO support are given in Table 5. Of 56 patients, 2 patients (3.6%) required conversion to venoarterial ECMO because of hemodynamic instability due to right ventricular failure and 36 patients (64.3%) died during the hospitalization. Multi-organ failure related with severe pneumonia was the leading cause of death in both CAP and HAP groups (57.1% *versus* 54.5%, $p = 0.780$). In addition, death due to an ECMO-related complication occurred in eight patients (21.4% *versus* 22.7%, $p = 0.342$). However, survival to hospital discharge, the primary endpoint in this study, was not different between the two groups (38.1% *versus* 37.1%, $p > 0.999$). In addition, other clinical outcomes including weaning from MV and ECMO, ECMO-related complications, 30-day mortality, and 90-day mortality were similar in the CAP and HAP groups. Duration of MV and ECMO and lengths of ICU and hospital stays were not different between the two groups. Univariable analysis and multivariable logistic regression analysis were used to identify variables for survival to discharge that had significant prognostic value in Table 6. There were
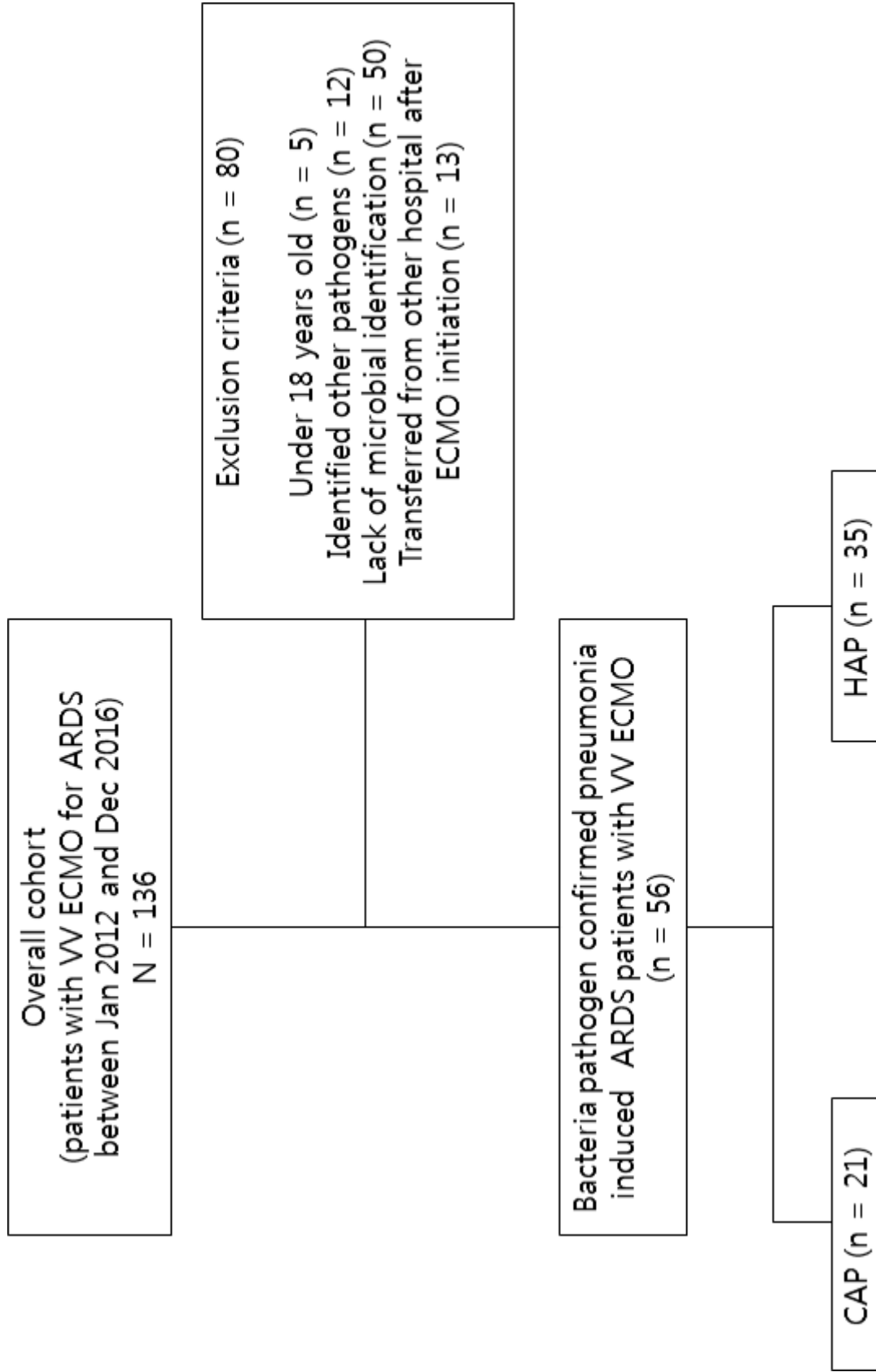
Figure 1. Study flow diagram.

ARDS, acute respiratory distress syndrome; CAP, community-acquired pneumonia; ECMO, extracorporeal membrane oxygenation; HAP, hospital-acquired pneumonia; VV, venovenous.

Table 1. Baseline characteristics of patients with pneumonia receiving venovenous extracorporeal membrane oxygenation.

Characteristics	Total (*N* = 56)	CAP (*n* = 21)	HAP (*n* = 35)	*p* value
Age, years	58.50 (50.50–67.00)	55 (49–71)	62 (50–67)	0.850
Sex, male	42 (75.0)	15 (71.4)	27 (77.1)	0.752
BMI, kg/m^2	23.45 (20.55–25.4)	23.3 (19.3–25.35)	23.5 (22.1–25.4)	0.340
Transferred from other hospital	15 (26.8)	6 (28.6)	9 (25.7)	0.336
Co-morbidity				
Malignancy	16 (28.6)	6 (28.6)	10 (28.6)	>0.999
Chronic lung disease	22 (39.3)	5 (23.8)	17 (48.6)	0.092
Diabetes	14 (25.0)	6 (10.7)	8 (22.9)	0.752
Neurologic disease	2 (3.6)	1 (4.8)	1 (2.9)	>0.999
Cardiovascular disease	3 (5.4)	1 (4.8)	2 (5.7)	0.740
Chronic kidney disease	7 (12.5)	1 (4.8)	6 (17.1)	0.237
APACHE II score	22.0 (16.6–28.8)	22.0 (19.0–28.5)	22.5 (15.0–29.5)	0.382
SOFA score	8 (5–13)	8 (5–15)	8 (4–13)	0.893
Renal replacement therapy	13 (23.2)	5 (23.8)	8 (22.9)	0.790
Vasoactive-inotropic score	3 (1–4)	4 (3–4)	3 (0–4)	0.417
Lung injury score	2.67 (2.44–3.50)	2.84 (2.00–3.33)	2.67 (2.33–3.50)	0.107

Values are given as median (interquartile range) or number (%).
APACHE, Acute Physiology and Chronic Health Evaluation; BMI, body mass index; CAP, community-acquired pneumonia; HAP, hospital-acquired pneumonia; SOFA, sequential organ failure assessment.

no significantly and independently variables associated with survival to discharge.

Discussion

In this study, we investigated whether clinical outcomes differed between CAP and HAP in ARDS patients treated with ECMO. Our results demonstrate that patients with bacterial pneumonia requiring ECMO for respiratory support have high mortality regardless of pneumonia category. Furthermore, lengths of ICU and hospital stays, as well as weaning rates from MV and ECMO, were not different between patients with CAP and HAP.

Patients with advanced age, malnutrition, immunosuppression, and severe acute or chronic illness have increased risks of developing HAP.[20,21] These factors are also associated with increased mortality, regardless of the category of pneumonia.[22] Therefore, patients with HAP are expected to have worse prognoses than patients with CAP. This view is supported by the findings of a previous study, in which the incidence of complications and the need for intensive care were higher in patients with HAP compared with patients with CAP.[8] Venditti and colleagues also reported that patients with HAP had higher pneumonia severity index and SOFA scores, longer hospital stays, and higher hospital mortality than patients with CAP.[9] However, they excluded ICU patients from their analysis; therefore, their cohort was characterized by significantly less severe disease than the patients included in our study.

Table 2. Medical management prior to venovenous extracorporeal membrane oxygenation.

Medical management	Total (N = 56)	CAP (n = 21)	HAP (n = 35)	p value
Duration of MV before ECMO, days	7.58 (5.35–12.14)	7.11 (5.25–9.33)	7.85 (5.92–13.22)	0.542
< 2 days	22 (39.3)	9 (42.9)	13 (37.1)	0.780
2–7 days	18 (32.1)	6 (28.3)	12 (34.3)	0.551
> 7 days	16 (28.6)	6 (28.6)	10 (28.6)	>0.999
Pre-ECMO treatment				
NMBA	30 (53.6)	11 (52.4)	19 (54.3)	0.511
Nitric oxide	10 (17.9)	6 (28.6)	4 (7.1)	0.152
Prone position	6 (10.7)	3 (14.3)	3 (8.6)	0.661
Steroid	7 (12.5)	3 (14.3)	4 (7.1)	0.734
Pre-ECMO MV setting				
PaO_2/FiO_2	74.4 (54.6–92.0)	71.05 (53.15–88.99)	76.45 (55.53–96.87)	0.287
PEEP, cmH_2O	10.00 (5.00–12.00)	10.00 (5.75–12.25)	9.00 (5.00–11.50)	0.246
Minute volume, l/min	9.00 (7.40–10.73)	10.45 (7.30–13.03)	8.80 (7.48–9.28)	0.114
Tidal volume/PBW, ml/kg	7.2 (5.2–9.2)	7.2 (5.4–9.0)	7.1 (5.0–9.3)	0.125
Peak inspiratory pressure, cmH_2O	30.00 (24.75–32.00)	30.00 (24.75–33.25)	28.50 (22.75– 30.00)	0.454
Respiratory rate, breaths/min	24.00 (20.00–27.75)	25.00 (21.50–32.00)	22.00 (20.00– 25.75)	0.080
Driving pressure, cmH_2O	16.00 (14.00–20.00)	16.00 (14.00–20.00)	15.00 (14.00–20.00)	0.544
Pre-ECMO blood gas				
pH	7.259 (7.127–7.362)	7.259 (7.127–7.362)	7.264 (7.127– 7.422)	0.334
$PaCO_2$, mmHg	59.9 (49.8–73.5)	59.9 (49.8–73.5)	58.6 (47.9–73.5)	0.768
PaO_2, mmHg	59.1 (53.4–70.0)	59.1 (53.4–70.0)	58.7 (52.8–70.0)	0.008
HCO_3^-, mmol/l	26.0 (22.7–30.5)	26.0 (22.7–30.5)	26.5 (23.0–30.5)	0.084
SaO_2, %	86.8 (82.6–91.3)	86.9 (82.6–91.3)	86.7 (82.1–91.3)	>0.999
RESP score	0.00 (−1.00–2.00)	0.00 (−1.50–2.00)	1.00 (−1.00–3.00)	0.179
PRESERVE score	4.50 (3.00–6.75)	4.00 (2.50–6.00)	5.00 (4.00–7.00)	0.107

Values are given as median (interquartile range) or number (%).
ARDS, acute respiratory distress syndrome; CAP, community-acquired pneumonia; ECMO, extracorporeal membrane oxygenation; FiO2, fraction of inspired oxygen; HAP, hospital-acquired pneumonia; MV, mechanical ventilation; NMBA, neuromuscular blocking agents; PaCO2, partial pressure of carbon dioxide in arterial blood; PaO2, partial pressure of oxygen in arterial blood; PBW, predictive body weight; PEEP, positive end-expiratory pressure; PRESERVE, predicting death for severe ARDS on venovenous ECMO; RESP, respiratory extracorporeal membrane oxygenation survival prediction; SaO2, arterial oxygen saturation.

In other studies including patients admitted to ICUs, severity of illness did not differ between CAP and HAP.[22–24] Furthermore, there were no differences in mortality rates according to the category of pneumonia, consistent with our results. Although the risk of organ failure

Table 3. Laboratory and microbiologic characteristics in the patients with pneumonia receiving venovenous extracorporeal membrane oxygenation.

Characteristics	Total (*N* = 56)	CAP (*n* = 21)	HAP (*n* = 35)	*p* value
Laboratory parameters				
Lactic acid, mmol/l				
Pre-ECMO	3.07 (1.67–4.49)	3.91 (1.78–6.74)	2.83 (1.42–3.26)	0.119
Post-ECMO 6 h	3.18 (1.95–5.86)	3.32 (2.42–11.37)	2.84 (1.70–4.59)	0.174
Post-ECMO 24 h	2.13 (1.56–2.95)	2.23 (1.71–6.24)	1.99 (1.26–2.68)	0.111
Post-ECMO 48 h	1.93 (1.38– 2.78)	2.14 (1.73–4.59)	1.69 (1.17–2.67)	0.068
WBC, 10^3/ml	14.49 (8.73–20.13)	13.22 (7.16–19.22)	15.45 (10.88–20.04)	0.273
Platelet, 10^3/ml	151.04 (52.00–210.25)	134.61 (41.75–183.75)	192.28 (90.75– 204.75)	0.089
Total bilirubin, mg/dl	1.60 (0.50–1.75)	1.50 (0.50–1.82)	1.73 (0.40–1.80)	0.865
Creatinine, mg/dl	1.59 (0.68–1.86)	1.71 (0.75–1.94)	1.22 (0.61–1.64)	0.391
CRP, mg/dl	5.55 (2.69–13.74)	4.17 (1.32–10.25)	6.73 (2.25–15.64)	0.643
Procalcitonin, ng/ml	2.35 (0.45–7.35)	2.05 (0.15–6.25)	2.55 (0.50–8.94)	0.873
Microbiologic parameters				
Culture positive specimen				
Trans-tracheal aspirate	44 (78.6)	17 (81.0)	27 (77.1)	0.932
Blood	16 (28.6)	9 (42.9)	7 (20.0)	0.104
Broncho-alveolar lavage fluid	8 (14.3)	3 (14.3)	5 (14.3)	>0.999
Pleural fluid	5 (8.9)	2 (9.5)	3 (8.8)	0.765
Microbiologic results				
Gram-positive pathogens				
CN Staphylococcus	3 (5.4)	1 (4.8)	2 (5.7)	
Enterococcus faecium	1 (1.8)	1 (4.8)	0 (0)	
Kocuria kristinae	2 (3.6)	0 (0)	2 (5.7)	
MRSA	7 (12.5)	2 (9.5)	5 (14.3)	
Staphylococcus aureus	1 (1.8)	0 (0)	1 (2.9)	
Streptococcus mitis	1 (1.8)	0 (0)	1 (2.9)	
Streptococcus pneumonia	17 (30.4)	12 (57.1)	5 (14.3)	
Gram-negative pathogens				
Acinetobacter baumanii	18 (32.1)	5 (23.8)	13 (37.1)	
Escherichia coli	2 (3.6)	1 (4.8)	1 (2.9)	

Table 3. (Continued)

Characteristics	Total (*N* = 56)	CAP (*n* = 21)	HAP (*n* = 35)	*p* value
Enterobacter aerogenes	2 (3.6)	1 (4.8)	1 (2.9)	
Klebsiella pneumonia	3 (5.4)	2 (9.5)	1 (2.9)	
Mycoplasma pneumonia	1 (1.8)	1 (4.8)	0 (0)	
Prevotella bivia	1 (1.8)	0 (0)	1 (2.9)	
Pseudomonas aeruginosa	6 (10.7)	4 (19.0)	2 (5.7)	
Serratia marcescens	1 (1.8)	1 (4.8)	0 (0)	
Stenotrophomonas maltophilia	3 (5.4)	2 (9.5)	1 (2.9)	
Occurrence of MDR pathogen	38 (67.9)	12 (57.1)	26 (74.3)	0.125
Inappropriate initial antibiotic treatment	21 (37.5)	7 (33.3)	14 (40.0)	0.843

Values are given as median (interquartile range) or number (%).
CAP, community-acquired pneumonia; CN, coagulase negative; CRP, C-reactive protein; ECMO, extracorporeal membrane oxygenation; HAP, hospital-acquired pneumonia; MDR, multidrug resistance; MRSA, methicillin-resistant *S. aureus*; WBC, white blood cell.

Table 4. Managements during the first 72 hours after initiation of venovenous extracorporeal membrane oxygenation.

Medical management	Total (*N* = 56)	CAP (*n* = 21)	HAP (*n* = 35)	*p* value
Post-ECMO MV setting				
PaO_2/FiO_2	81 (61–99)	79 (59–99)	81 (62–99)	0.455
PEEP, cmH_2O	9 (6–12)	9 (6–12)	9 (5–12)	0.358
Tidal volume/ PBW, ml/kg	7.2 (5.2–9.2)	7.2 (5.4–9.0)	7.1 (5.0–9.3)	0.125
Peak inspiratory pressure, cmH_2O	25 (17–28)	25 (17–28)	25 (18–29)	0.367
Respiratory rate, breaths/min	22 (18–26)	22 (19–26)	21 (18–25)	0.175
Driving pressure, cmH_2O	15 (13–17)	16 (13–17)	15 (13–17)	0.322
Acute kidney injury	5 (8.9)	2 (9.5)	3 (8.6)	0.765
Renal replacement therapy	2 (3.6)	1 (4.8)	1 (2.9)	0.190
Vasopressors	6 (10.7)	3 (14.3)	3 (8.6)	0.661
SOFA score	10 (5–17)	11 (4–17)	10 (5–18)	0.623

CAP, community-acquired pneumonia; ECMO, extracorporeal membrane oxygenation; FiO2, fraction of inspired oxygen; HAP, hospital-acquired pneumonia; PaCO2, partial pressure of carbon dioxide in arterial blood; PaO2, partial pressure of oxygen in arterial blood; PBW, predictive body weight; PEEP, positive end-expiratory pressure; SOFA, sequential organ failure assessment.

including ARDS is high in patients with HAP, the category of pneumonia does not affect prognosis in critically ill patients with bacterial pneumonia, in whom organ failure requiring mechanical support has already developed. Therefore, type of pneumonia should not be considered when making treatment decisions for patients with ARDS caused by bacterial pneumonia who are to be placed on ECMO.

In critically ill patients with pneumonia, inappropriate antibiotic treatment is related to higher

Table 5. Clinical outcomes of the patients with pneumonia receiving venovenous extracorporeal membrane oxygenation.

Clinical outcomes	Total (N = 56)	CAP (n = 21)	HAP (n = 35)	p value
Survival to hospital discharge	20 (35.7)	7 (33.3)	13 (37.1)	>0.999
MV duration after ECMO initiation, days	3.0 (1.0–4.5)	3.5 (1.0–5.0)	3.0 (1.0–4.5)	0.454
Conversion to VA ECMO	2 (3.6)	1 (4.8)	1 (2.9)	0.190
MV weaning success	23 (41.1)	7 (33.3)	16 (45.7)	0.152
ECMO weaning success	26 (46.4)	10 (47.6)	16 (45.7)	>0.999
ECMO duration, days	13.75 (5.55–29.40)	14.00 (4.50–39.50)	13.00 (6.00–25.00)	0.582
ECMO-related complication	15 (26.8)	6 (28.6)	9 (25.7)	0.355
Oxygenator failure	5 (8.9)	2 (9.5)	3 (8.6)	
Cannula site bleeding	3 (5.4)	1 (4.8)	2 (5.7)	
Limb ischemia	2 (3.6)	1 (4.8)	1 (2.9)	
Hemolysis	3 (5.4)	1 (4.8)	2 (2.9)	
Stroke	2 (3.6)	1 (4.8)	1 (2.9)	
ICU LOS, days	26.00 (15.75–35.50)	26.00 (15.75–35.50)	26.00 (14.75–35.50)	0.733
Hospital LOS, days	39.50 (19.75–56.00)	39.50 (19.75–56.00)	40.50 (19.50–56.00)	0.828
30-day mortality	22 (39.3)	9 (42.9)	13 (23.2)	0.780
90-day mortality	35 (62.5)	14 (66.7)	21 (60)	>0.999

Values are given as median (interquartile range) or number (%).
CAP, community-acquired pneumonia; ECMO, extracorporeal membrane oxygenation; HAP, hospital-acquired pneumonia; LOS, length of stay; MV, mechanical ventilation; VA, venoarterial.

mortality.[25–27] Patients with HAP are more likely to be exposed to antibiotic-resistant bacteria than patients with CAP and therefore are at risk of inappropriate initial empiric antibiotic treatment based on microbiological characteristics.[6] In the present study, however, the rates of MDR pathogen occurrence were similar between CAP and HAP groups. In addition, the appropriateness of initial antibiotic therapy did not differ. These findings could help explain why we observed no differences in clinical outcomes between the two groups.

Although this study provides new information regarding outcome prediction in pneumonia patients with ARDS receiving ECMO support, it also has some limitations that should be considered. First, because it was conducted as a retrospective cohort study, there is always the possibility that selection bias influenced the significance of our findings. However, the data were prospectively collected from all patients who consecutively received ECMO support for ARDS caused by bacterial pneumonia at our institution. Nonetheless, limited number of patients enrolled might not be sufficiently powered to detect a significant difference between the groups. Second, our study was based at a single institution with a multidisciplinary ECMO team,[14] which could limit the generalizability of our findings to other hospitals. Finally, patients with culture-negative results were excluded from the study. Thus, the true incidence of MDR pathogens and their effects on outcomes may be underestimated.

In summary, patients with severe acute respiratory failure requiring ECMO for respiratory support suffered severe disease regardless of whether they were diagnosed with CAP or HAP, and there

Table 6. Univariable and multivariable logistic regression analysis for clinical variables associated with survival to discharge in study patients.

Variable	Univariable			Multivariable		
	p value	OR	95% CI	*p* value	OR	95% CI
Age	0.1608	0.97	0.93–1.01	0.5797	0.12	0.00–222.87
SOFA score	0.1420	0.90	0.78–1.04	0.6577	1.08	0.78–1.48
Pre-ECMO nitric oxide	0.1903	0.33	0.06–1.73	0.4389	0.36	0.03–4.81
Pre-ECMO respiratory rate	0.1037	1.11	0.98–1.26	0.0523	1.31	1.00–1.72
RESP score	0.0604	1.25	0.99–1.59	0.9278	0.98	0.63–1.51
PRESERVE score	0.0608	0.77	0.58–1.01	0.5237	0.84	0.50–1.42

ARDS, acute respiratory distress syndrome; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; OR, odds ratio; PRESERVE, predicting death for severe ARDS on venovenous ECMO; RESP, respiratory ECMO survival prediction; SOFA, sequential organ failure assessment.

were no significant differences in weaning rates from ECMO and survival according to the category of pneumonia.

Conflict of interest statement
The authors declare that there is no conflict of interest.

ORCID iD
Kyeongman Jeon https://orcid.org/0000-0002 -4822-1772

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