Sequential Organ Failure Assessment score as a predictor of mortality in ventilated patients with multidrug-resistant bacteremia

Yeseul Oh, Jiyeon Roh, Jaemin Lee, Hyun Sung Chung, Kwangha Lee, Min Ki Lee

Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Internal Medicine, Pusan National University School of Medicine, Busan, Korea

Background: The occurrence of multidrug-resistant (MDR) bacteremia in ventilated patients may be associated with a high mortality rate. We evaluated whether Sequential Organ Failure Assessment (SOFA) score on the day of bacteremia could predict 90-day mortality in these patients.

Methods: Data were obtained retrospectively from 202 patients (male, 60.4%; median age, 64 years) hospitalized at a single university-affiliated tertiary care hospital. All adult patients who had were ventilated and had one of the following six MDR bacteremias between March 2011 and February 2018 were enrolled: methicillin-resistant *Staphylococcus aureus*, extended-spectrum β-lactamase-producing Gram-negative bacteria (*Escherichia coli* and *Klebsiella pneumonia*), carbapenem-resistant Gram-negative rods (*Acinetobacter baumannii* and *Pseudomonas aeruginosa*), or vancomycin-resistant *Enterococcus faecium.*

Results: The overall 90-day mortality rate after the day of bacteremia was 59.9%. The areas under the receiver operating characteristic curves for the SOFA and Acute Physiology and Chronic Health Evaluation (APACHE) II scores were 0.732 (95% confidence interval [CI], 0.666 to 0.792; P<0.001) and 0.662 (95% CI, 0.593 to 0.727; P<0.001), respectively, with no difference between the two (P=0.059). Also, the cutoff value of the SOFA score was 9 (based on Youden's index). Multivariate Cox regression analysis showed that this cut-off value was significantly associated with higher mortality rate (hazard ratio, 2.886; 95% CI, 1.946 to 4.221; P<0.001).

Conclusions: SOFA score measured on the day of bacteremia may be a useful prognostic indicator of 90-day mortality in ventilated patients with MDR bacteremia.

Key Words: bacteremia; intensive care unit; prognosis

INTRODUCTION

Although clinical guidelines have recommended reductions in empirical treatment with broad-spectrum antibiotics, timely administration of more appropriate antibiotics, and development of strict infection control policies [1-5], the incidence of serious complications caused by multidrug-resistant (MDR) bacteria has been increasing in intensive care unit (ICU) patients [6]. Of these complications, the presence of MDR bacteria in the bloodstream (bacteremia) can have serious health consequences, including sepsis, septic shock, and he-

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matogenous spread to other organs. These sequelae are associated with increased need for medical resources over long periods of time and high medical costs.

Notably, occurrence of MDR bacteremia in ventilated ICU patients may result in longer ICU and hospital length of stay and higher mortality rates despite intensive resource utilization, including treatment with antibiotics. Therefore, identification of clinical factors associated with poor prognosis, including mortality, may allow future health care planning. Moreover, critical care resources and facilities, even at university hospitals, are frequently limited in developing countries [7-9]. Few studies to date, however, have assessed prognostic indicators in patients with MDR bacteremia who received mechanical ventilation.

Because bacteremia is frequently accompanied by sepsis, and sepsis is diagnosed based on Sequential Organ Failure Assessment (SOFA) score, the present study hypothesized that SOFA score on the first day of bacteremia would be useful for predicting patient prognosis [10,11]. Therefore, the aim of the present study was to investigate whether SOFA score would be useful for predicting mortality after the day of blood culture in ventilated patients with MDR bacteremia. In addition, the prognostic ability of the SOFA score was compared with that of the Acute Physiology and Chronic Health Evaluation (APACHE) II score on the day of bacteremia [12].

MATERIALS AND METHODS

Study Design and Subjects
This retrospective study included patients admitted to the ICUs of a 1,100-bed university-affiliated tertiary care hospital from March 1, 2011 to February 28, 2018. This hospital has six functionally separate ICUs with a total of 85 beds, including 12 in the medical, 10 in the surgical, 14 in the cardio-stroke, 13 in the neurosurgical, 20 in the emergency, and 16 in the trauma ICU. All of these ICUs have full cardiovascular and close airway monitoring equipment, as well as one full-time ICU specialist; the nurse-to-bed ratio is 1:3. All subjects were managed according to therapeutic recommendations, which were based on a lung-protective ventilator strategy [13].

Records of all adult patients aged ≥18 years admitted to these six ICUs were screened to determine whether they had received ventilator care and had a positive blood culture during the study period. Patients were finally enrolled if they had one of the following six MDR bacteremias: methicillin-resistant *Staphylococcus aureus*, extended-spectrum β-lactamase-producing Gram-negative bacteria (*Escherichia coli* and *Kleb-*

siella pneumoniae), carbapenem-resistant Gram-negative rods (*Acinetobacter baumannii* and *Pseudomonas aeruginosa*), or vancomycin-resistant *Enterococcus faecium*. Patients with polymicrobial bacteremia and those who experienced a subsequent episode of bacteremia within 3 days after the first (index) episode of bacteremia were excluded [14]. Organisms in all positive blood cultures were identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS; Bruker Daltonics, Bremen, Germany). Antimicrobial susceptibility was assessed using the VITEK-2 and E-tests (bioMérieux, Marcy l'Etoile, France). The primary outcome was all-cause mortality 90 days after bacteremia.

All investigators confirmed that the study objectives and procedures were disclosed honestly to all patients, and all investigators had full access to all data. Case report forms, including all relevant medical, laboratory, and radiological data, were completed for each included patient. The study protocol was approved by the Institutional Review Board of Pusan National University Hospital (IRB No. 1904-004-077), which waived the requirement for informed consent from enrolled patients or their surrogates because of the observational nature of this study. This study had no impact on the future treatment of enrolled patients.

Data Collection
Demographic and clinical data were obtained retrospectively from the electronic medical records of each subject; these included age, sex, comorbidities before ICU admission, duration of ventilator care, and length of stay in the ICU and hospital. Severity of illness was measured using the APACHE II score, and accompanying organ failure was assessed according to the SOFA score [10,12], with both scores calculated from laboratory and clinical data recorded on the day of blood culture. Diagnosis of acute respiratory distress syndrome (ARDS) on the day of bacteremia was based on the Berlin Definition [15].

The recorded clinical data included the primary sources of infection and requirements for hemodialysis (defined as any
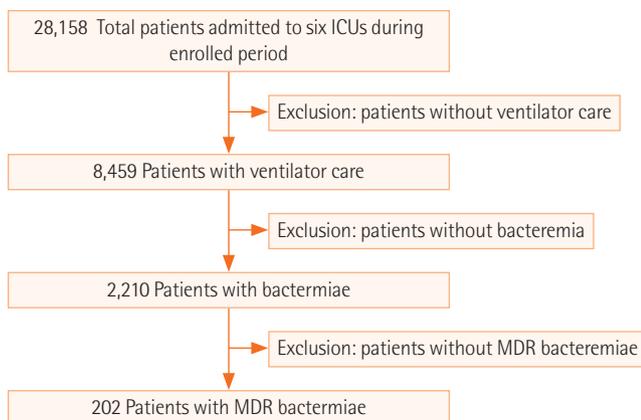
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Figure 1. Flowchart of recruited and enrolled study participants. ICU: intensive care unit; MDR: multidrug-resistant.

form of renal replacement therapy), neuromuscular blocking agents, and vasopressors on the day of blood culture. Because no standardized nationwide antimicrobial stewardship program addressing increased antimicrobial resistance has been recognized internationally [16], this study also assessed whether the choice of antimicrobial agents was based on consultations with a specialist in infectious diseases.

In-hospital mortality was defined as death prior to hospital discharge, whereas 90-day mortality was defined as mortality within 90 days of the day of blood culture. Survival status through February 28, 2019 was assessed in all patients by review of the National Health Insurance Service Database.

Statistical Analysis

Continuous variables are expressed as the median (range) and were compared using Student t-test or the Mann-Whitney U-test, as applicable. Categorical variables are expressed as numbers (percentages) and were compared using the chi-square test or Fisher's exact test (for small numbers), as appropriate. Receiver operating characteristics (ROC) curves and the areas under the ROC curves (AUCs) for SOFA scores were calculated, and an optimal cut-off value for the SOFA score was determined based on the maximum Youden's index [17]. The sensitivity (SS), specificity (SP), positive likelihood ratio (PLR), negative likelihood ratio (NLR), positive predictive value (PPV), and negative predictive value (NPV) of SOFA scores for predicting mortality were determined. Univariate Cox proportional hazard models were developed to determine the relationships between SOFA scores and other clinical variables with mortality. Variables with $P < 0.1$ on univariate models were included in multivariate Cox proportional hazard models, followed by backward elimination of any fac-

Table 1. Demographic and clinical characteristics of all enrolled patients

Characteristics	Total (n = 202)
Age (yr)	64 (18–95)
Male sex	122 (60.4)
Hospital LOS (day)	40 (2–431)
ICU LOS (day)	23 (1–430)
Duration of MV (day)	17 (1–430)
Comorbidity	
Cardiovascular disease	63 (31.2)
Diabetes mellitus	55 (27.2)
Hemato-oncological diseases	43 (21.3)
Cerebrovascular diseases	31 (15.3)
Chronic renal diseases	27 (13.4)
Chronic lung diseases	15 (7.4)
Chronic liver diseases	13 (6.4)
Neuromuscular diseases	12 (5.9)
Biliary diseases	9 (4.5)
Alimentary diseases	8 (4.0)
Main infection source	
Pneumonia	98 (48.5)
Vascular catheter-related	46 (22.8)
Intra-abdominal	25 (12.4)
Musculoskeletal and soft tissue	15 (7.4)
Urinary	9 (4.5)
Other[a]	9 (4.5)
Period from ICU admission to bacteremia (day)	9 (0–360)
APACHE II score[b]	19 (5–38)
SOFA score[b]	9 (2–20)
Microorganism identified	
Methicillin-resistant *Staphylococcus aureus*	77 (38.1)
Vancomycin-resistant *Enterococcus faecium*	25 (12.4)
Carbapenem-resistant *Acinetobacter baumannii*	63 (31.2)
ESBL(+) *Klebsiella pneumoniae*	25 (12.4)
ESBL(+) *Escherichia coli*	18 (8.9)
Carbapenem-resistant *Pseudomonas aeruginosa*	5 (2.5)
Requirement for vasopressors[b]	113 (55.9)
Requirement for hemodialysis[b]	56 (29.2)
Requirement for neuromuscular blocking agents[b]	51 (25.2)
ARDS on the day of bacteremia	153 (75.7)
ID consultations by ID specialists regarding management of bacteremia	128 (63.4)
Period from day of bacteremia to hospital discharge (day)	18 (0–373)
In-hospital mortality	115 (56.9)
90-Day mortality after bacteremia	121 (59.9)

Values are presented as median (range) or number (%).
LOS: length of stay; ICU: intensive care unit; MV: mechanical ventilation; APACHE: Acute Physiology and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment; ESBL: extended-spectrum β-lactamase-producing; ARDS: acute respiratory distress syndrome; ID: infectious diseases.
[a]Other included meningitis (n = 3), infective endocarditis (n = 3), ventriculo-peritoneal shunt infection (n = 2), and retropharyngeal abscess (n = 1); [b]All clinical data were calculated or obtained from medical records on the day of blood collection.

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tor with a P-value >0.05 in the multivariate model. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated. Kaplan-Meier estimates of mortality were stratified according to the SOFA score cutoff values developed in this study, and curves (total and subgroups) were compared using log-rank tests. The AUCs of SOFA scores and APACHE II scores for 90-day mortality were compared using DeLong's test [18]. All tests were two-tailed, and P-values <0.05 were considered statistically significant. All analyses were performed using IBM SPSS ver. 24.0 (IBM Corp., Armonk, NY, USA) and Med-Calc version 18.11.6 (MedCalc, Ostend, Belgium).

RESULTS

General Characteristics

During the study period, 28,158 patients were admitted to one of the six ICUs. Of these, 202 patients (1.1%) were eligible for participation in the study (Figure 1). Table 1 shows the baseline characteristics and clinical outcomes of these patients. The median period from ICU admission to bacteremia was 9 days (range, 0–360 days). Pneumonia was the most common source of bacteremia (n=98, 48.5%). When we further evaluated these patients to see whether the same organisms would be identified in tracheal aspirates and bronchoscopic alveolar lavage specimens, 83 patients (84.7%) had the same organism in these respiratory specimens. Of the 202 patients, 100 (49.5%) and 106 (52.5%) patients had Gram-positive and Gram-negative bacteremia, respectively, with four (2.0%) patients having both. In addition, 153 patients (75.7%) were diagnosed with ARDS on the day of bacteremia, and 128 patients (63.4%) consulted with an infectious diseases specialist for positive blood culture results. The in-hospital and 90-day mortality rates were 56.9% and 59.9%, respectively.

Predicting Mortality Using SOFA Score

ROC curve analyses were performed to determine the SOFA score cutoffs for predicting mortality, as well as the SS, SP, PLR, NLR, PPV, and NPV of each, in all patients and in those with Gram-positive or Gram-negative bacteremia. In total patients, the AUC was 0.732 (95% CI, 0.666 to 0.792; P<0.001; SS, 72.8%; SP, 65.3%; PLR, 2.1; NLR, 0.4; PPV, 58.4%; NPV, 78.2%) and the cutoff value was 9. The AUC of patients with Gram-positive bacteremia was 0.733 (95% CI, 0.666 to 0.792; P<0.001; SS, 67.4%; SP, 72.2%; PLR, 2.4; NLR, 0.5; PPV, 67.4%; NPV, 72.2%) and that of patients with Gram-negative bacteremia was 0.720 (95% CI, 0.624 to 0.803; P<0.001; SS, 72.2%; SP, 67.1%; PLR, 2.2; NLR, 0.4; PPV, 53.1%; NPV, 82.5%). In both groups, cutoff values

Table 2. Sensitivity, specificity, and positive and negative predictive values of Sequential Organ Failure Assessment score for predicting mortality

Category	AUC (95% CI)	Cutoff value[a]	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Total patients	0.732 (0.666–0.792)	9	72.8 (61.8–82.1)	65.3 (56.1–73.7)	2.1 (1.6–2.8)	0.4 (0.3–0.6)	58.4 (51.5–65.0)	78.2 (71.1–84.0)
Subgroup								
Gram-positive bacteremia	0.733 (0.636–0.817)	8	67.4 (52.0–80.5)	72.2 (58.4–83.5)	2.4 (1.5–3.9)	0.5 (0.3–0.7)	67.4 (56.2–76.9)	72.2 (62.4–80.3)
Gram-negative bacteremia	0.720 (0.624–0.803)	9	72.2 (54.8–85.8)	67.1 (54.9–77.9)	2.2 (1.5–3.3)	0.4 (0.2–0.7)	53.1 (43.3–62.6)	82.5 (73.0–89.1)

The data show the cutoff values of Sequential Organ Failure Assessment score for 90-day mortality after the day of bacteremia as determined by ROC curve analyses in total patients and in patients with Gram-positive or Gram-negative bacteremia. Also shown are the sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, positive predictive value, and negative predictive value of these cutoffs for predicting mortality.

AUC: area under the receiver operating characteristic curve; CI: confidence interval.

[a]All "optimal" cutoff levels were based on highest Youden index value.

Table 3. Comparison of clinical characteristics between survivors and non-survivors after the day of bacteremia

Characteristics	Survivor (n=81)	Non-survivor (n=121)	P-value
Comorbidity[a]			
Cardiovascular disease	26 (32.1)	37 (30.6)	0.877
Diabetes mellitus	25 (30.9)	30 (24.8)	0.420
Hemato-oncological diseases	11 (13.6)	32 (26.4)	0.035
Cerebrovascular diseases	13 (16.0)	18 (14.9)	0.844
Chronic renal diseases	11 (13.6)	16 (13.2)	>0.999
Main infection source[a]			
Respiratory	37 (45.7)	61 (50.4)	0.566
Vascular catheter-related	27 (33.3)	19 (15.7)	0.006
Intra-abdominal	3 (3.7)	22 (18.2)	0.002
Musculoskeletal and soft tissue	7 (8.6)	8 (6.6)	0.595
Urinary	5 (6.2)	4 (3.3)	0.489
Microorganism identified			
Methicillin-resistant *Staphylococcus aureus*	41 (50.6)	36 (29.8)	0.003
Vancomycin-resistant *Enterococcus faecium*	5 (6.2)	20 (16.5)	0.030
Carbapenem-resistant *Acinetobacter baumannii*	22 (27.2)	41 (33.9)	0.354
ESBL(+) *Klebsiella pneumoniae*	9 (11.1)	16 (13.2)	0.828
ESBL(+) *Escherichia coli*	7 (8.6)	11 (9.1)	>0.999
Carbapenem-resistant *Pseudomonas aeruginosa*	0	5 (4.1)	0.084
Requirement for vasopressors[b]	30 (37.0)	83 (68.6)	<0.001
Requirement for hemodialysis[b]	13 (16.0)	46 (38.0)	0.001
Requirement for neuromuscular blocking agents[b]	15 (18.5)	36 (29.8)	0.098
Consultation with an ID specialist regarding management of bacteremia	61 (75.3)	67 (55.4)	0.005
ARDS[b]	47 (58.0)	106 (87.6)	<0.001

Values are presented as number (%) and compared by chi-square tests.
ID: infectious diseases; ARDS: acute respiratory distress syndrome.
[a]Comparisons of the top five diseases; [b]All clinical data were calculated or obtained from medical records on the day of bacteremia.

were 8 and 9, respectively (Table 2).

Comparisons of the clinical characteristics of survivors and non-survivors showed that the rates of hemato-oncologic diseases as comorbidities and intra-abdominal infections as main infectious sources were significantly higher in non-survivors. In addition, the rates of identification of Vancomycin-resistant *Enterococcus faecium*, requirements for vasopressors and hemodialysis on the day of bacteremia, and ARDS on the day of bacteremia were significantly higher in non-survivors (Table 3).

To evaluate the effect of SOFA score cutoff value on mortality, univariate and multivariate Cox regression models were constructed (Table 4). Multivariate Cox regression analyses of all patients and those with Gram-positive or Gram-negative bacteremia showed that SOFA score cutoff values were significantly associated with 90-day mortality rate (total patients: HR, 2.886 [95% CI, 1.946 to 4.221; P<0.001], patients with Gram-pos-

itive bacteremia: HR, 2.458 [95% CI, 1.312 to 4.603; P<0.001], patients with Gram-negative bacteremia: HR, 2.987 [95% CI, 1.786 to 4.995]; P<0.001). Kaplan-Meier analyses of 90-day survival yielded consistent results, showing the prognostic benefits of these cut-off values in all patients and those with Gram-positive or Gram-negative bacteremia (Figure 2).

Comparison of SOFA Score with APACHE II Score on the Day of Bacteremia

The present study also compared the prognostic utility of APACHE II score on the day of bacteremia with that of SOFA score for predicting mortality. For all patients, the AUC for APACHE II score was 0.662 (95% CI, 0.593 to 0.727; P<0.001), which did not differ significantly from the AUC for SOFA score. Subgroup analyses, however, showed that the AUC for predicting mortality was significantly higher for SOFA score than for APACHE

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Table 4. Univariate and multivariate analysis of factors associated with mortality in all patients and in patients with Gram-positive or Gram-negative bacteremia

Factor	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Total patients				
SOFA score ≥9[a]	3.099 (2.123–4.523)	<0.001	2.886 (1.946–4.221)	<0.001
No infectious disease consultation	2.193 (1.528–3.146)	<0.001	2.261 (1.534–3.331)	<0.001
Intra-abdominal infections as source of infection	2.614 (1.637–4.172)	<0.001	2.023 (1.252–3.268)	0.004
Requirement for NMBAs[a]	1.629 (1.102–2.409)	0.014		
Hemato-oncologic diseases as comorbidities	1.714 (1.142–2.572)	0.009		
Gram-positive bacteremia				
SOFA score ≥8[a]	3.206 (1.763–5.831)	<0.001	2.458 (1.312–4.603)	0.005
Age ≥65 years	2.251 (1.311–3.866)	0.003	1.942 (1.116–3.379)	0.019
Hemato-oncologic malignancies as comorbidities	4.032 (2.059–7.894)	<0.001		
Requirement for NMBAs[a]	1.875 (1.053–3.341)	0.033		
Intra-abdominal infections as source of infection	5.473 (2.390–12.535)	<0.001		
No infectious disease consultation	1.767 (1.025–3.046)	0.040		
Gram-negative bacteremia				
SOFA score ≥9[a]	3.129 (1.886–5.189)	<0.001	2.987 (1.786–4.995)	<0.001
No infectious disease consultation	2.709 (1.677–4.376)	<0.001	2.671 (1.641–4.348)	<0.001
Intra-abdominal infections as source of infection	1.785 (1.005–3.171)	0.048		

Statistical significance was determined by univariate and multivariate Cox proportional hazards models. Mortality was defined as mortality 90 days after the day of blood culture.
HR: hazard ratio; CI: confidence interval; SOFA: Sequential Organ Failure Assessment; NMBA: neuromuscular blocking agent.
[a]All clinical data were calculated or obtained from medical records on the day of bacteremia.

II score in patients with Gram-negative, but not Gram-positive, bacteremia (Figure 3).

DISCUSSION

The present study found that SOFA score on the day of bacteremia can predict the risk of mortality in ventilated patients with MDR bacteremia. Based on the ROC curve, this score may be an appropriate predictor of 90-day mortality after bacteremia. To our knowledge, this is the first comprehensive study to evaluate the clinical ability of SOFA score to predict long-term mortality in ventilated patients with MDR bacteremia in our country.

Also, this study found that the SOFA score cutoff values for predicting 90-day mortality differed in the total patient population and in the subgroups with Gram-positive or Gram-negative bacteremia. Although multivariate Cox regression analyses showed different prognostic factors in these subgroups, SOFA score cut-offs were significant prognostic indicators in both subgroups. In addition, Kaplan-Meier analysis showed that 90-day mortality rates were about 2-fold higher in patients

with SOFA scores above than below these cut-offs. Taken together, these findings suggest that SOFA score on the day of bacteremia may help in future care planning for these patients.

There is literature regarding the SOFA score cutoff values for predicting mortality in patients with Gram-negative bacteremia. Chen et al. [19] evaluated patients with carbapenem-resistant *Acinetobacter baumannii* bacteremia, and calculated the effectiveness of SOFA score at the onset of bacteremia in predicting the mortality. They reported that ventilator care was performed in 63.8% patients and SOFA scores >8 and >7 were associated with significantly higher 14-day and in-hospital mortality rates, respectively [19]. Their study design and the SOFA score cutoff levels were similar to the present study. However, the enrollment criteria were different, and the SOFA cutoff value was evaluated for predicting 90-day mortality in our study.

Our study also found that ROC curves of the SOFA score were significantly higher than those of the APACHE II score for predicting 90-day mortality in patients with Gram-negative bacteremia, which was consistent with a previous report [19]. Our data suggest that SOFA score would be more useful
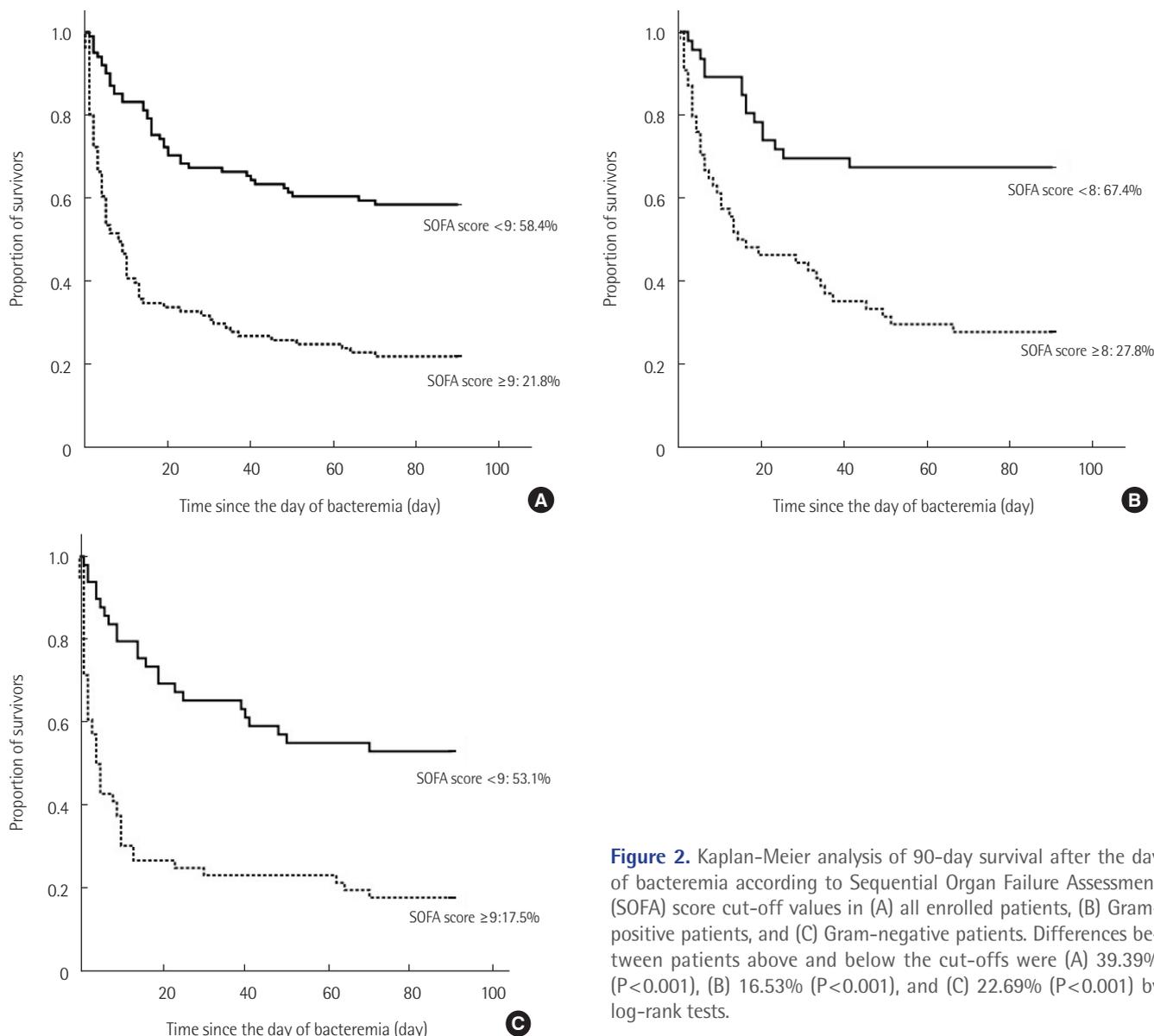
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Figure 2. Kaplan-Meier analysis of 90-day survival after the day of bacteremia according to Sequential Organ Failure Assessment (SOFA) score cut-off values in (A) all enrolled patients, (B) Gram-positive patients, and (C) Gram-negative patients. Differences between patients above and below the cut-offs were (A) 39.39% (P<0.001), (B) 16.53% (P<0.001), and (C) 22.69% (P<0.001) by log-rank tests.

for predicting mortality in ventilated patients with Gram-negative bacteremia. However, the present study was a retrospective design, and large-scale, multicenter investigations are needed to determine whether the SOFA score would be a more useful prognostic indicator than other severity-of-illness scoring systems in MDR bacteremia patients.

In addition to SOFA score, we sought to select the best subset of prognostic indicators, including baseline demographic factors, comorbidities, and clinical parameters on the day of bacteremia, and to develop models predicting short-term and/or long-term mortality. None of these factors differed significantly, however, which again may have been due to the small number of patients. SOFA score is not ideal for assessing prognosis because it does not take pre-existing comorbidities

into account. Rather, a new, expanded prognostic model, including comorbidities, sources of infection, and various clinical parameters, will be necessary to increase the ability to predict short- and long-term mortality.

The present study showed that roughly 60% of enrolled patients consulted an infectious diseases specialist for selection of optimal antibiotics. Although the percentages of patients with Gram-positive and Gram-negative bacteremia who consulted a specialist did not differ significantly (66.0% vs. 61.9%, P=0.664), consultation was especially associated with a reduced mortality rate in patients with Gram-negative bacteremia. Although several previous studies have reported that consultation was associated with reduced in-hospital mortality rates and overall hospital costs [20,21], few antimicrobial

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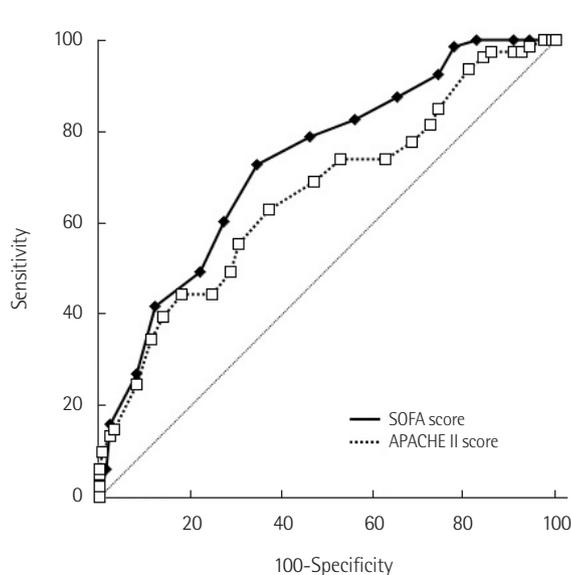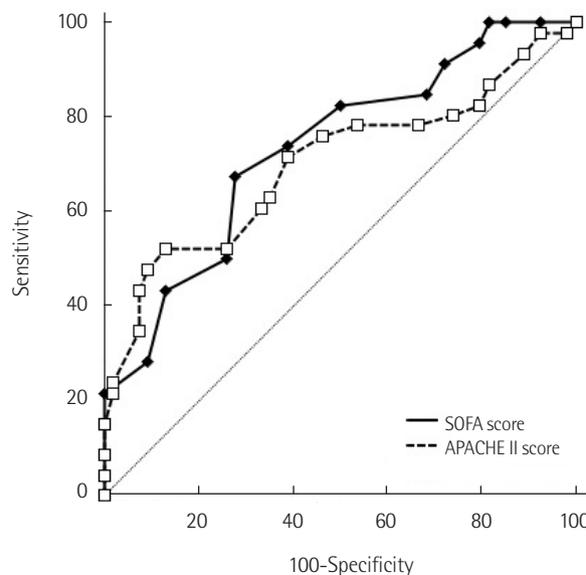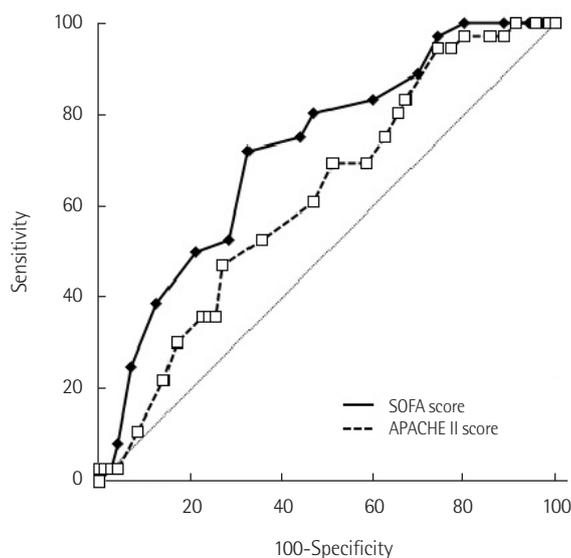
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Figure 3. Receiver operating characteristic (ROC) curves for Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation (APACHE) II scores for predicting 90-day mortality after the day of bacteremia in (A) all enrolled patients, (B) Gram-positive patients, and (C) Gram-negative patients. (A) In all patients, the area under the ROC curves for the SOFA and APACHE II scores were 0.732 (95% confidence interval [CI], 0.666–0.792; P<0.001) and 0.662 (95% CI, 0.593–0.727; P< 0.001), respectively, with no difference between the two (P=0.059). (B) In patients with Gram-positive bacteremia, the AUCs for the SOFA and APACHE II scores were 0.733 (95% CI, 0.636–0.817; P<0.001) and 0.701 (95% CI, 0.601–0.788; P<0.001), respectively, with no difference between the two (P=0.572). (C) In patients with Gram-negative bacteremia, the AUCs for the SOFA and APACHE II scores were 0.720 (95% CI, 0.624–0.803; P<0.001) and 0.622 (95% CI, 0.523–0.714; P<0.001), respectively. The AUC for SOFA score was significantly higher than the AUC for APACHE II score (P=0.037).

stewardship programs have been established at university-affiliated hospitals in Korea, despite their increasing consumption of empirical broad-spectrum antibiotics. The present findings suggest that antibiotic stewardship programs are needed to control the increasing prevalence of MDR bacteria in our country.

This study had several limitations. First, the study was single-centered and retrospective. In addition, SOFA scores were determined at a university-affiliated tertiary care. Therefore, it may not be possible to generalize our data to other settings, although most Korean patients with bacteremia are managed in tertiary care hospitals. Second, careful interpretation is necessary in clinical meanings of the SOFA score because total enrolled patients were from six functionally separate ICUs with

different patient subgroups. Third, this study was a retrospective design, and we could not accurately measure the SOFA score, especially the Glasgow Coma Scale or PaO$_2$/FiO$_2$ ratio, which may result in a selection bias. Fourth, other clinical factors (in addition to the cutoff values of SOFA score) were associated with prognosis as shown in Table 4. These factors were different in patients with Gram-positive and Gram-negative bacteremia, respectively. We could not accurately analyze these differences in prognostic factors in both groups due to the retrospective design. Fifth, we hypothesized that the SOFA score would be a more useful prognostic factor in some subgroups, including patients with ARDS, those aged ≥65 years, and those with hemato-oncologic malignancies as comorbidities. However, none of these factors differed significantly in

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survivors and non-survivors, a finding that may be attributed to the small number of enrolled patients.

In conclusion, SOFA score on the day of bacteremia may be a useful prognostic indicator for predicting 90-day mortality in ventilated patients with MDR bacteremia. Large-scale multicenter studies are needed to determine whether SOFA score is a prognostic indicator of short-term and/or long-term mortality as well as to compare SOFA score with other scoring methods for predicting prognosis.

CONFLICT OF INTEREST

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

ORCID

Yeseul Oh	https://orcid.org/0000-0002-9777-3258
Jiyeon Roh	https://orcid.org/0000-0002-1595-9535
Jaemin Lee	https://orcid.org/0000-0003-1022-0667
Hyun Sung Chung	https://orcid.org/0000-0002-8834-7302
Kwangha Lee	https://orcid.org/0000-0001-9878-201X
Min Ki Lee	https://orcid.org/0000-0002-0163-115X

AUTHOR CONTRIBUTIONS

Conceptualization: YO, KL. Data curation: YO, JR, JL, HSC. Formal analysis: YO, KL. Funding acquisition: KL, MKL. Methodology: YO, JR, JL, HSC. Project administration: KL, MKL. Visualization: YO, KL. Writing–original draft: YO, JR, JL, HSC. Writing–review & editing: YO, KL.

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