Original articles

# Prognostic value of the ICU-SEPSA score for mortality in patients with multidrug - resistant infections

***Nguyen Van Vien[1], Tran Thai Anh[2], Nguyen Tat Dung[3], Le Thi Thuy Vy[4], Phan Thang[4*]***

*[1]Department of Critical Care - Toxicology, Tay Nguyen Regional General Hospital, Daklak, Vietnam*
*[2]Department of Nephrolory, Vietnam -Cuba Dong Hoi Friendship Hospital, Quang Tri, Vietnam*
*[3]Intensive Care Unit, Hue central hospital, Hue, Vietnam*
*[4]Department of Anesthesiology, Intensive Care and Emergency Medicine, University of Medicine and Pharmacy, Hue University, Hue, Vietnam*

***Corresponding author:** Phan Thang; Email: pthang@huemed-univ.edu.vn
**Received:** 25/03/2026; **Accepted:** 21/08/2026; **Published:** 25/08/2026
DOI: 10.34071/jmp.2026.4.1021

**Abstract**

**Background:** Multidrug-resistant (MDR) bacterial infection is a serious global health problem, especially in Intensive Care Units (ICUs). The ICU-SEPSA score was developed to predict mortality in patients with MDR infections.

**Objective**: To evaluate the prognostic value of the ICU-SEPSA score for predicting mortality among ICU patients with MDR bacterial infections at Hue Central Hospital.

**Methods**: We conducted a prospective observational study of 108 patients with MDR bacterial infections admitted to the ICU from June 2024 to June 2025. ICU-SEPSA was recorded at the time the index culture was identified. Univariate logistic regression examined the association between ICU-SEPSA and mortality. Discrimination was evaluated using receiver operating characteristic (ROC) analysis to determine the optimal cut-off, area under the curve (AUC), sensitivity, and specificity. An exploratory combined model with the Sequential Organ Failure Assessment (SOFA) score was derived using logistic regression, yielding a linear predictor SOFA + 1.104 × ICU-SEPSA.

**Results**: The overall mortality was 77.8%. The mean ICU-SEPSA score at the time of culture isolation was 7.0 ± 1.9. On univariate analysis, ICU-SEPSA predicted mortality (OR = 1.420; $p < 0.001$). At a cut-off value of 7.3, ICU-SEPSA demonstrated moderate discrimination (AUC = 0.686), with 56.0% sensitivity and 83.3% specificity. The exploratory combined model (SOFA + 1.104 × ICU-SEPSA) demonstrated better discrimination (AUC = 0.773); at a cut-off of 10.2, sensitivity was 95.2% and specificity 50.0%.

**Conclusions**: The ICU-SEPSA score has prognostic value for mortality in ICU patients with MDR bacterial infections, and combining ICU-SEPSA with SOFA further improves predictive performance.

**Keywords:** *ICU-SEPSA score; multidrug-resistant bacteria; mortality prediction; intensive care unit.*

## 1. INTRODUCTION

Antimicrobial resistance (AMR) is currently recognized as one of the most critical challenges in 21st-century medicine, with profound and long-term consequences for global public health [1]. A 2019 report by the World Health Organization estimated that multidrug-resistant (MDR) bacterial infections are responsible for at least 700,000 deaths annually, with projections rising to 10 million deaths per year by 2050, potentially surpassing many non-communicable diseases as a leading cause of mortality [2,3]. Intensive Care Units (ICUs) represent high-risk settings, where critically ill patients—often characterized by immunosuppression, multiple comorbidities, invasive interventions, and advanced age—are particularly vulnerable to severe infections and increased mortality, especially in the context of MDR pathogens. Early identification of patients at high risk of poor outcomes is therefore essential to guide individualized treatment strategies and optimize resource allocation. Various prognostic models have been developed, including widely used scoring systems such as Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation II (APACHE II). However, these conventional scores primarily focus on physiological derangements and organ dysfunction and do not specifically incorporate clinical characteristics associated with multidrug-resistant (MDR) infections, such as host factors, infection sources, and antimicrobial resistance-related challenges. Furthermore, previous studies have often focused on specific resistant pathogens, limiting the generalizability of their findings to the

broader population of patients with MDR bacterial infections [4-7]. The ICU-SEPSA score, developed specifically to assess mortality risk in patients with MDR infections, has demonstrated promising predictive performance across different risk groups [8]. Nevertheless, its applicability has not yet been evaluated in Vietnam.

Therefore, this study aims to evaluate the prognostic value of the ICU-SEPSA score in predicting mortality among ICU patients with MDR bacterial infections.

## 2. METHODS

### 2.1. Study design

This single-center, prospective observational study was conducted in the Intensive Care Unit of Hue Central Hospital, a tertiary referral center in Vietnam, between June 2024 and June 2025. Adult patients (aged ≥18 years) with a confirmed diagnosis of multidrug-resistant (MDR) bacterial infection, defined according to antimicrobial susceptibility testing based on the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) criteria, were eligible for inclusion. Patients were excluded if essential clinical or laboratory data required to calculate the Sequential Organ Failure Assessment (SOFA) score or the Acute Physiology and Chronic Health Evaluation II (APACHE II) score were unavailable. The study aimed to evaluate the prognostic performance of the ICU-SEPSA score in predicting mortality among ICU patients with MDR infections..

### 2.2. Sample size estimation

The required sample size was calculated using the formula for estimating a single proportion with a predefined relative precision:

$$n = \frac{Z^2_{1-\alpha/2} \times (1-p)}{\varepsilon^2}$$

where $n$ represents the minimum sample size, $Z_{1-\alpha/2}$ corresponds to the standard normal deviate at a two-sided significance level of 5% (Z = 1·96), $p$ is the expected proportion, and $\varepsilon$ denotes the acceptable relative error·

Based on prior research by Sirichayanugul et al. (2022), the expected predictive accuracy was set at $p$ = 0·8054 [8], with a relative error of ε = 0·1· The calculated minimum sample size was 93 patients· Ultimately, 108 patients were enrolled using a convenience sampling approach·

### 2.3. Definitions and Study variables

Multidrug-resistant (MDR) infection was defined as resistance to at least one agent in three or more antimicrobial classes [8]. Immunosuppression was defined by the presence of immunosuppressive therapy, chemotherapy, prolonged corticosteroid use, acquired immunodeficiency syndrome (AIDS), chronic alcohol abuse, hemodialysis, or uncontrolled diabetes mellitus [10]. Comorbidities included major chronic conditions such as cardiovascular, respiratory, renal, hepatic, metabolic, neurological, and psychiatric diseases. Prior antibiotic exposure was defined as use within the preceding three months. Infection severity was classified according to Sepsis-3 criteria: sepsis was defined as suspected or confirmed infection with an increase in SOFA score ≥ 2 points, and septic shock as sepsis requiring vasopressors to maintain mean arterial pressure ≥65 mmHg with lactate > 2 mmol/L despite adequate fluid resuscitation. The SOFA score assesses six organ systems (respiratory, coagulation, hepatic, cardiovascular, neurological, and renal).

The primary variables were components of the ICU-SEPSA score recorded at the time of positive culture, including immunosuppression, chronic obstructive pulmonary disease, urinary tract infection, sepsis, mechanical ventilation, pneumonia, septic shock, and prior antibiotic exposure. The detailed components and scoring system of the ICU-SEPSA score are provided in Appendix 1. The SOFA score, APACHE II score, and the presence of multiple organ dysfunction were also assessed at the time of MDR pathogen identification. Secondary variables included demographic characteristics, comorbidities, clinical parameters, laboratory findings, use of invasive devices, infection severity, causative pathogens, and 28-day mortality.

### 2.4. Statistical analysis

Statistical analyses were performed using SPSS software version 27.0 (IBM Corp., Armonk, NY, USA).

### 2.5. Research ethics

The study protocol was approved by the Biomedical Research Ethics Committee of University of Medicine and Pharmacy, Hue University (Approval No. H2024/224, approved on June 10, 2024).

## 3. RESULTS

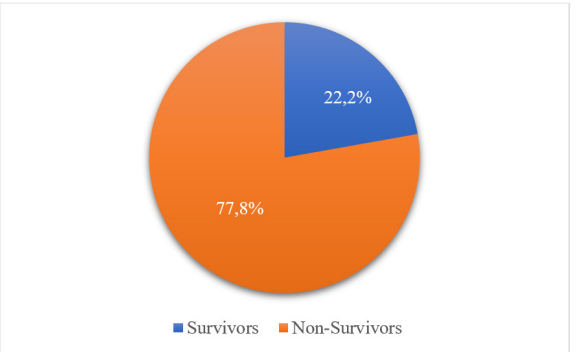



**Figure 1.** Patient outcomes

The study cohort demonstrated a high mortality rate of 77.8% among patients with multidrug-resistant infections.

**Table 1**. Baseline characteristics of patients stratified by treatment outcomes

| Facto | | Survivors (n = 24) | Non-survivors (n = 84) | P-value |
|---|---|---|---|---|
| Age (years) | | 64.5 ± 17.9 | 69 ± 15.5 | > 0.05 |
| Male sex | | 18 (75%) | 55 (65.5%) | > 0.05 |
| Comorbidities | | 21 (87.5%) | 77 (91.7%) | > 0.05 |
| Invasive procedures | | 23 (95.8%) | 74 (88.1%) | > 0.05 |
| Immunosupression | | 2 (8.3%) | 23 (27.4%) | > 0.05 |
| White blood cell count ($\times 10^9$/L)* | | 14.9 [11.9 - 18.5] | 13.7 [9.4 - 19.5] | > 0.05 |
| Total bilirubin (µmol/L)* | | 13.4 [9.7 - 16.3] | 11.6 [7.1 - 16.4] | > 0.05 |
| Creatinine (µmol/L)* | | 61.2 [43.6 - 108.0] | 104.8 [58.7 - 199.3] | < 0.05 |
| $PaO_2/FiO_2$ ratio* | | 249.0 [196.0 - 317.0] | 210.0 [147.3 - 294.8] | > 0.05 |
| Procalcitonin (ng/mL)* | | 0.5 [0.2 - 1.3] | 1.9 [0.3 - 6.0] | < 0.05 |
| Lactate (mmol/L)* | | 2.1 [1.5 - 3.4] | 2.6 [1.6 - 4.0] | > 0.05 |
| Antimicrobial resistance level | MDR | 11 (45.8%) | 8 (9.5%) | < 0.05 |
| | XDR | 6 (25.0%) | 14 (16.7%) | |
| | PDR | 7 (29.2%) | 62 (73.8%) | |
| Multiple organ dysfunction | | 4 (16.7%) | 37 (44.0%) | < 0.05 |
| Infection severity | Mild infection | 5 (20.8%) | 0 (0%) | < 0.05 |
| | Sepsis | 13 (54.2%) | 40 (47.6%) | |
| | Septic shock | 6 (25.0%) | 44 (52.4%) | |
| SOFA score* | | 3.0 [2.0 - 7.6] | 8.0 [5.0 - 11.0] | < 0.05 |
| APACHE II score* | | 11.5 [9.0 - 16.8] | 24.0 [20.3 - 27.0] | < 0.05 |
| ICU-SEPSA score* | | 6.0 [5.0 - 6.5] | 8.0 [6.0 - 8.5] | < 0.05 |

*Abbreviations: MDR, multidrug-resistant; XDR, extensively drug-resistant; PDR, pandrug-resistant; SOFA, Sequential Organ Failure Assessment; APACHE II, Acute Physiology and Chronic Health Evaluation II; $PaO_2/FiO_2$, ratio of arterial oxygen partial pressure to fractional inspired oxygen.*

*Values are presented as mean ± standard deviation, median (IQR) or number (%), (a) t-test, (b) Mann-Whitney U test, (c) $\chi^2$ test.*

The non-survivor group had higher procalcitonin and creatinine levels, along with a greater incidence of multiple organ dysfunction compared to the survivor group ($p < 0.05$). Mortality increased with the degree of antimicrobial resistance, with rates of 9.5% in MDR, 16.7% in XDR, and 73.8% in PDR ($p < 0.05$). Greater infection severity was also associated with higher mortality: septic shock was observed in 52.4% of non-survivors versus 25.0% of survivors. Additionally, prognostic scores for mortality, including SOFA, APACHE II, and ICU-SEPSA, were significantly higher in the non-survivor group compared to the survivor group ($p < 0.05$).

**Table 2**. Predictive performance of ICU-SEPSA, SOFA, and APACHE II for mortality

| | AUC | Cut-off | Sensitivity (%) | Specificity (%) | 95% CI | p-value |
|---|---|---|---|---|---|---|
| **ICU-SEPSA** | 0.686 | 7.3 | 56.0 | 83.3 | 0.56 - 0.81 | **< 0.001** |
| **SOFA** | 0.763 | 3.5 | 89.3 | 54.2 | 0.65 - 0.88 | **< 0.001** |
| **APACHE II** | 0.960 | 17.5 | 94.0 | 87.5 | 0.92 - 1.00 | **< 0.001** |

*Abbreviations: AUC, area under the curve; CI, confidence interval.*

The optimal cut-off values of ICU-SEPSA, SOFA, and APACHE II for predicting mortality in patients with multidrug-resistant infections were 7.3, 3.5, and 17.5, respectively. ICU-SEPSA demonstrated an AUC of 0.686, with a sensitivity of 56.0% and specificity of 83.3%; SOFA showed an AUC of 0.763, with a sensitivity of 89.3% and specificity of 54.2%; while APACHE II exhibited the highest discriminative performance, with an AUC of 0.960, sensitivity of 94.0%, and specificity of 87.5% ($p < 0.001$).

**Table 3**. Multivariable logistic regression analysis of ICU-SEPSA and SOFA

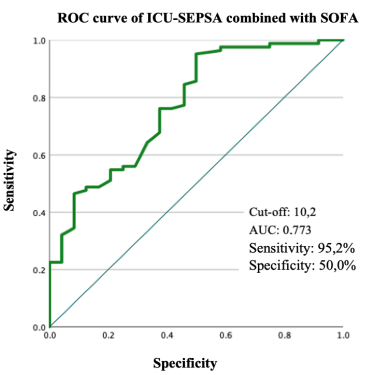
| | Regression coefficient (B) | 95% CI | p-value |
|---|---|---|---|
| **ICU-SEPSA** | 0,27 | 1,11 - 1,54 | **0,001** |
| **SOFA** | 0,29 | 1,03 - 1,76 | **0,030** |

Based on the regression coefficients, with ICU-SEPSA (B = 0.297) and SOFA (B = 0.269), a combined variable was derived as follows: SOFA + 1.104 × ICU-SEPSA, where 1.104 represents the ratio of the regression coefficients (0.297/0.269).

**Table 4.** Univariate logistic regression analysis of ICU-SEPSA, SOFA and APACHE II

| Variable | Odds ratio (OR) | 95% CI | p-value |
|---|---|---|---|
| **ICU-SEPSA** | 1.42 | 1.15 - 1.83 | **0.006** |
| **SOFA** | 1.33 | 1.13 - 1.57 | **< 0.001** |
| **APACHE II** | 1.88 | 1.38 - 2.58 | **< 0.001** |
| **ICU-SEPSA + SOFA** | 1.31 | 1.14 - 1.50 | **< 0.001** |

Univariate analysis demonstrated that ICU-SEPSA, SOFA, APACHE II, and the combined ICU-SEPSA + SOFA model were significant predictors of mortality in patients with multidrug-resistant infections (all $p < 0.05$).




*Abbreviations:ROC, receiver operating characteristic.*

**Figure 2.** ROC curve of ICU-SEPSA combined with SOFA for mortality prediction in patients with multidrug-resistant infections

The combined ICU-SEPSA and SOFA model showed acceptable discriminative performance for mortality prediction (AUC = 0.773, $p < 0.05$). At a cut-off value of 10.2, it provided high sensitivity (95.2%) but moderate specificity (50.0%).

**Table 6**. Comparison of the predictive performance of different scoring systems for mortality

| Comparision | Z | p-value |
|---|---|---|
| SOFA vs APACHE II | -3.20 | **0.001** |
| SOFA vs ICU-SEPSA | 0.19 | 0.85 |
| SOFA vs SOFA + ICU-SEPSA | -0.45 | 0.65 |
| ICU-SEPSA vs SOFA + ICU-SEPSA | -0.61 | 0.54 |
| APACHE II vs ICU-SEPSA | 3.14 | **0.002** |
| APACHE II vs SOFA + ICU-SEPSA | 2.82 | **0.005** |

Following Holm–Bonferroni adjustment, DeLong test results demonstrated that the AUC of APACHE II had significantly discriminative performance compared with SOFA ($Z = 3.41$, $p = 0.003$), ICU-SEPSA ($Z = 4.23$, $p < 0.001$), and the combined SOFA–ICU-SEPSA model ($Z = 3.45$, $p = 0.003$).

## 4. DISCUSSION

This study included 108 patients with multidrug-resistant infections admitted to the Intensive Care Unit and aimed to assess the prognostic performance of the ICU-SEPSA score in predicting mortality. The overall mortality rate observed in our cohort was 77.8%, which is markedly higher than previously reported rates, including 34.1% in the study by Sirichayanugul et al (2022) [8], 43.6% by Ahmed et al (2025) [11], and 22.6% by Dinh Phung Tran et al (2016) [12]. This high mortality rate may be explained by the severity of illness among critically ill patients admitted to a tertiary ICU, together with the high proportion of PDR infections among non-survivors (73.8%) and the high prevalence of septic shock and multiple organ dysfunction in this cohort. In this context, many patients in both survivor and non-survivor groups presented with multiple MDR-related risk factors, resulting in overlapping ICU-SEPSA score distributions. Mortality was significantly associated with elevated serum creatinine, increased procalcitonin levels, the presence of multiple organ dysfunction, higher levels of antimicrobial resistance, greater infection severity, and increased SOFA, APACHE II, and ICU-SEPSA scores ($p < 0.05$).

The ICU-SEPSA score was found to be an independent predictor of mortality, with an odds ratio (OR) of 1.420 ($p = 0.006$). At a cut-off value of 7.3, it demonstrated moderate discriminative ability (AUC = 0.686), with a sensitivity of 56.0% and specificity of 83.3%. Both SOFA and APACHE II also showed significant prognostic value. SOFA was associated with mortality (OR = 1.33), yielding a sensitivity of 83.3% and specificity of 62.5% at a threshold of 3.5. In comparison, APACHE II exhibited a stronger association (OR = 1.88) and excellent discriminative performance (AUC = 0.96), with a sensitivity of 94.0% and specificity of 87.5% at a cut-off of 17.5. These results are consistent with prior studies. For instance, Wei et al. (2022) reported optimal cut-off values of SOFA > 7 and APACHE II > 21 ($p < 0.001$) in patients with *Acinetobacter baumannii* infection, with SOFA (AUC = 0.909) slightly outperforming APACHE II (AUC = 0.895) and a strong correlation between the two scores ($r^2 = 0.441$) [13]. Similarly, Maia et al. (2020) identified both APACHE II (OR = 1.07; 95% CI: 1.01–1.13) and SOFA (OR = 1.28; 95% CI: 1.09–1.50) as independent predictors of in-hospital mortality [14]. Importantly, the combination of ICU-SEPSA with SOFA was explored based on the complementary characteristics of these two scores. ICU-SEPSA incorporates clinical and background factors related to multidrug-resistant infections, whereas SOFA reflects the degree of organ dysfunction, which is a major determinant of mortality in critically ill patients. The combined model (SOFA + 1.104 × ICU-SEPSA) demonstrated an AUC of 0.773, with a sensitivity of 95.2% and a specificity of 50.0% at a cut-off value of 10.2. Although this model showed higher sensitivity, its overall discriminative performance was not significantly superior to SOFA alone based on comparative ROC analysis. APACHE II demonstrated the highest discriminative performance in this cohort and remained significantly superior to ICU-SEPSA, SOFA, and the combined model ($p = 0.001$, 0.002, and 0.005, respectively). However, APACHE II is a comprehensive severity score requiring multiple physiological and laboratory parameters, whereas ICU-SEPSA was specifically developed to incorporate MDR-related clinical characteristics using a simpler

scoring approach. Therefore, ICU-SEPSA should not be considered a replacement for established severity scores but rather a potential complementary tool for risk assessment in patients with multidrug-resistant infections.

This study has some limitations, including a short study duration, small sample size, and single-center design at Hue Central Hospital, which may limit statistical power and generalizability. In addition, the predominance of PDR infections among non-survivors may represent a potential confounding factor, and further studies with larger cohorts are needed to determine whether ICU-SEPSA provides independent prognostic information after adjustment for antimicrobial resistance patterns.

## 5. CONCLUSION

The ICU-SEPSA score demonstrated prognostic value for mortality assessment in critically ill patients with multidrug-resistant infections; however, its performance was inferior to established severity scores. ICU-SEPSA may serve as a complementary MDR-specific risk assessment tool, particularly when combined with conventional severity evaluation.

## REFERENCES


1. Murray CJL, Ikuta KS, Sharara F, Swetschinski L, Robles Aguilar G, Gray A, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. The Lancet. 2022;399(10325):629-55.

2. World Health Organization: New report calls for urgent action to avert antimicrobial resistance crisis. https://www.who.int/news/item/29-04-2019-new-report-calls-for-urgent-action-to-avert-antimicrobial-resistance-crisis (2019).

3. O'Neill J. Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations. The Review on Antimicrobial Resistance; 2014.

4. Oh Y, Roh J, Lee J, Chung HS, Lee K, Lee MK. Sequential Organ Failure Assessment score as a predictor of mortality in ventilated patients with multidrug-resistant bacteremia. Acute and Critical Care. 2020;35(3):169-78.

5. Hariyanto H, Yahya CQ, Cucunawangsih C, Pertiwi CLP. Antimicrobial resistance and mortality. Afr J Infect Dis. 2022;16(2):13-20.

6. Chen Y-P, Tasi X-W, Chang K, Cao X-D, Chen J-R, Liao C-S. Multi-Drug Resistant Organisms Infection Impact on Patients Length of Stay in Respiratory Care Ward. Antibiotics. 2021;10(5):608.

7. Al-Hasan MN, Lahr BD, Eckel-Passow JE, Baddour LM. Predictive scoring model of mortality in Gram-negative bloodstream infection. Clinical Microbiology and Infection. 2013;19(10):948-54.

8. Taranee Sirichayanugul, Srisawat Chansinee, Thummakomut C, Prawang Abhisit, Huynh Nina S., Saokaew Surasak, et al. Development and internal validation of simplified predictive scoring (ICU-SEPSA score) for mortality in patients with multidrug resistant infection. Frontiers in Pharmacology. 2022;13.

9. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clinical Microbiology and Infection. 2012;18(3):268-81.

10. Delves PJ, Roitt IM. The Immune System. New England Journal of Medicine. 2000;343(1):37-49.

11. Ahmed Yassin, Eid RA, Mohammad MF, Elgendy MO, Mohammed Z, Abdelrahim MEA, et al. Microbial Multidrug-Resistant Organism (MDRO) Mapping of Intensive Care Unit Infections. Medicina. 2025;61(7):1220.

12. Dinh Phung Tran, Quang Dai Huynh, Thi Ngoc Thao Pham. Ventilator-associated pneumonia at Cho Ray Hospital. Ho Chi Minh City Journal of Medicine (Supplement). 2016;20(1):91–95.

13. Wei Z, Zhou S, Zhang Y, Zheng L, Zhao L, Cui Y, et al. Microbiological characteristics and risk factors on prognosis associated with Acinetobacter baumannii bacteremia in general hospital: A single-center retrospective study. Frontiers in Microbiology. 2022;13.

14. Maia Marcelo De Oliveira, Da Silveira CDG, Gomes M, Fernandes SES, Bezerra De Santana R, De Oliveira DQ, et al. Multidrug-Resistant Bacteria on Critically Ill Patients with Sepsis at Hospital Admission: Risk Factors and Effects on Hospital Mortality. Infection and Drug Resistance. 2023;Volume 16:1693-704.