MHA MEDIHEALTH ACADEMY

Eurasian Journal of
Anesthesiology & Intensive Care

Original Article

doi
10.51271/EAJAIC-0057

Clinical, microbiological, and biomarker profiles of mechanically ventilated ICU patients with positive tracheal aspirate cultures

Filiz Çimen*[1], Ayhanım Tümtürk[2], Akif Burak Çakmak[3]

[1]Department of Chest Diseases, VM Medical Park Ankara Hospital, Ankara, Turkiye
[2]Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, Yüksek İhtisas University, Ankara, Turkiye
[3]Department of Anesthesiology and Reanimation, VM Medical Park Ankara Hospital, Ankara, Turkiye

Cite this article: Çimen F, Tümtürk A, Çakmak AB. Clinical, microbiological, and biomarker profiles of mechanically ventilated ICU patients with positive tracheal aspirate cultures *Eur J Anesthesiol Intens Care.* 2026;3(3):68-76. doi:10.51271/EAJAIC-0057

***Corresponding Author:** Filiz Çimen, fhcimen@yahoo.com

Received: 17/06/2026 ◆ **Accepted**: 26/07/2026 ◆ **Published**: 29/08/2026

ABSTRACT

Aims: To evaluate antimicrobial resistance patterns, clinical characteristics, and inflammatory biomarker profiles in mechanically ventilated intensive care unit patients with positive tracheal aspirate (TA) cultures.

Methods: Between January 2020 and December 2024, 187 intubated ICU patients with positive TA cultures and complete biomarker data were retrospectively analyzed. Demographic characteristics, AMR patterns, clinical and microbiological findings, and exploratory biomarker profiles were recorded. Exploratory receiver operating characteristic (ROC) analyses were performed to descriptively assess potential relationships between selected biomarkers and in-hospital mortality.

Results: Gram-negative pathogens predominated (89.3%), and overall in-hospital mortality was 95.7%. Mortality was higher among patients with gram-negative microorganisms than among those with gram-positive microorganisms (97.0% vs. 83.3%, p=0.007) and increased progressively across resistance categories. APACHE II scores did not differ significantly between groups. Among the evaluated biomarkers, the Prognostic Nutritional Index, lactate, and the C-reactive protein-to-albumin ratio (CAR) demonstrated moderate-to-high discriminatory performance and were associated with in-hospital mortality in exploratory ROC analyses.

Conclusion: Gram-negative microorganisms and AMR were more frequently observed among patients with adverse outcomes in this high-risk ICU cohort. Biomarker findings should be interpreted as exploratory observations requiring validation in prospective studies.

Keywords: Mechanical ventilation, drug resistance microbial, critical illness, prognosis, nutritional status, nosocomial infection

INTRODUCTION

Antimicrobial resistance (AMR) is recognized as one of the most important global health threats. In 2019, approximately 1.3 million deaths were directly attributable to AMR, and projections suggest that this number may increase to 10 million deaths annually by 2050.[1] Intensive care unit (ICU) patients are particularly vulnerable to resistant infections because of frequent invasive procedures, prolonged hospitalization, mechanical ventilation, and extensive exposure to broad-spectrum antimicrobial agents. Gram-negative microorganisms, particularly *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, represent major challenges in ICU settings because of their virulence factors and complex resistance mechanisms. Multidrug-resistant (MDR), extensively drug-resistant (XDR), and pan-drug-resistant (PDR) strains have been associated with increased mortality, prolonged ICU stay, and higher healthcare costs.[2–4]

Although established severity scoring systems such as the Acute Physiology and Chronic Health Evaluation II (APACHE II) score are widely used to assess prognosis in critically ill patients, they may not fully reflect the clinical heterogeneity associated with antimicrobial resistance. Therefore, several inflammatory and nutritional biomarkers, including lactate, neutrophil-to-lymphocyte ratio (NLR), C-reactive protein-to-albumin ratio (CAR), blood urea nitrogen-to-albumin ratio

(BAR), and Prognostic Nutritional Index (PNI), have been investigated as potential indicators of disease severity and outcome in critically ill and septic populations. [5–10]

Recent evidence suggests that inflammatory and nutritional biomarkers may provide additional prognostic information when evaluated together with microbiological characteristics and AMR patterns. However, data regarding their clinical significance in mechanically ventilated ICU patients with positive tracheal aspirate (TA) cultures remain limited. Furthermore, although conventional inflammatory indices have been extensively studied, the potential role of newer hematological biomarkers, including pan-immune inflammation value (PIV), red cell distribution width (RDW), and mean platelet volume (MPV), has not been adequately investigated in this patient population. PIV reflects the overall immune-inflammatory burden and has been associated with mortality in inflammatory conditions such as sepsis.[11] RDW has been linked to systemic inflammation, oxidative stress, mortality, and prolonged hospitalization in critically ill patients.[12] MPV, an indirect marker of platelet activation, has also been proposed as a potential indicator of disease severity and adverse outcomes in sepsis and critical illness.[13] Nevertheless, studies simultaneously evaluating these biomarkers together with AMR profiles and microbiological characteristics in mechanically ventilated ICU patients remain scarce. Therefore, the present study aimed to evaluate the associations between microorganism type, AMR patterns, inflammatory biomarker profiles, and clinical outcomes in mechanically ventilated ICU patients with positive TA cultures.

METHODS

Ethics

This study was approved by the Health Sciences Researches Ethics Committee of Yüksek İhtisas University (Date: 30.10.2025, Decision No: 17/348). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Participants

Medical records of adult ICU patients admitted between January 1, 2020, and December 31, 2024, were retrospectively reviewed. Eligible patients were mechanically ventilated individuals with documented microbial growth in TA cultures.

TA cultures were obtained from mechanically ventilated patients with clinical suspicion of lower respiratory tract infection or ventilator-associated pneumonia (VAP). Clinical indications included new or worsening pulmonary infiltrates, fever, leukocytosis or leukopenia, purulent respiratory secretions, and/or worsening oxygenation. These findings were evaluated according to routine ICU practice and documented by the treating physicians during the study period.

Because of the retrospective design and the inherent limitations of TA cultures, differentiation between true infection, colonization, and contamination could not be standardized in all cases. Therefore, positive TA cultures were interpreted within the overall clinical context rather than being considered definitive evidence of infection alone. Patients were followed until hospital discharge or in-hospital death.

The inclusion criteria were as follows:

- Age≥18 years
- ICU stay≥48 hours
- Documented pathogen growth in TA culture
- Availability of complete clinical data, including APACHE II score, mortality status, ICU length of stay, and duration of mechanical ventilation
- Availability of laboratory parameters, including complete blood count, CRP, albumin, urea, creatinine, lactate, and inflammatory indices

The exclusion criteria were as follows:

- Polymicrobial growth in TA cultures
- Growth detected only in bronchoalveolar lavage, blood, or urine cultures without corresponding growth in TA cultures
- Missing clinical, laboratory, or microbiological data
- Confirmed COVID-19 infection

Data Collection

Data were retrospectively extracted from the Hospital Information Management System, Laboratory Information System, and institutional microbiology databases.

The following variables were recorded:

Laboratory parameters: complete blood count, C-reactive protein (CRP), albumin, urea, creatinine, and lactate levels obtained at the time of microbiological sampling.

Inflammatory and nutritional indices: NLR, PLR, LMR, SII, SIRI, CAR, BAR, PNI, and PIV.

Microbiological variables: pathogen identification, gram classification, and AMR phenotype.

AMR categories were defined according to the international expert consensus criteria proposed by Magiorakos et al. Multidrug resistance (MDR) was defined as non-susceptibility to at least one agent in three or more antimicrobial categories. XDR organisms were defined as non-susceptibility to at least one agent in all but two or fewer antimicrobial categories, whereas PDR organisms were defined as non-susceptibility to all agents in all antimicrobial categories.

Two isolates classified as “other microorganisms” were identified in the study cohort. Because of the limited sample size (n=2), these isolates were included in the overall descriptive analyses but were excluded from organism-specific subgroup analyses.

The primary outcome was in-hospital mortality. Secondary outcomes included ICU length of stay and duration of mechanical ventilation.

Biomarker and Index Definitions

In this research, a range of inflammatory and exploratory biomarkers were assessed to define immune response, nutritional status, and organ dysfunction in critically ill

patients. The NLR was determined by calculating the absolute neutrophil count in relation to the absolute lymphocyte count, while the platelet-to-lymphocyte ratio (PLR) was established as the platelet count divided by the lymphocyte count.[14,15] The Systemic Immune-Inflammation Index (SII) was derived using the formula platelet count×neutrophil count/lymphocyte count, whereas the Systemic Inflammation Response Index (SIRI) was calculated as neutrophil count×monocyte count/lymphocyte count.[16,17] All inflammatory indices were calculated using absolute cell counts expressed as/mm^3.

The CAR was calculated by dividing serum CRP levels (mg/l) by serum albumin concentration (g/dl). The blood urea nitrogen–to–albumin ratio (BAR) was defined as blood urea nitrogen (mg/dl) divided by serum albumin (g/dl).[18,19]

Additional biomarkers included RDW, which reflects erythrocyte size variability and has been associated with systemic inflammation, oxidative stress, and increased mortality risk in critically ill patients.[20] MPV, an indirect marker of platelet activation, has been linked to prothrombotic states and adverse outcomes.[21] Nutritional status and immune competence were assessed using the PNI , calculated according to the standard formula as (10×serum albumin [g/dl])+(0.005×absolute lymphocyte count [/mm^3]).[22] Finally, the PIV, defined as neutrophil×monocyte×platelet counts divided by lymphocyte count, was used as a composite indicator of overall systemic inflammatory burden.[23]

Statistical Analysis

The primary endpoint was in-hospital mortality. Associations between clinical variables, AMR patterns, gram stain results, and biomarkers were first evaluated using univariate analyses.

Comparisons between groups were performed using:

- χ^2 or Fisher's exact test for categorical variables
- Independent samples t-test or Mann–Whitney U test for continuous variables, as appropriate

Continuous variables with skewness>1 were $\log_1$p-transformed before analysis.

An exploratory receiver operating characteristic (ROC) analysis was conducted to evaluate the potential discriminatory power of the chosen biomarkers for in-hospital mortality. The area under the curve (AUC), ideal cut-off values (based on the Youden index), and sensitivity and specificity were determined. Ninety-five percent confidence intervals were estimated using bootstrap resampling with 5000 iterations. Correlation analyses were performed utilizing Pearson's correlation coefficient.

Missing data were handled using complete-case analysis. Multiple comparisons were adjusted using the Benjamini–Hochberg false discovery rate procedure. Statistical significance was defined as $p<0.05$. All analyses were performed using Python (Pandas, Statsmodels, Scikit-Learn) and. IBM SPSS Statistics version 26.0.

RESULTS

Patient Characteristics

Between January 2020 and December 2024, 1,680 patients were admitted to the intensive care unit. Fourteen patients who died on the day of ICU admission were excluded because complete clinical and laboratory data were unavailable. Among the remaining patients, 935 were intubated and had TA cultures obtained. Of these, 187 patients with documented microbial growth and complete laboratory data were included in the final analysis. The patient selection process is summarized in (Figure 1).

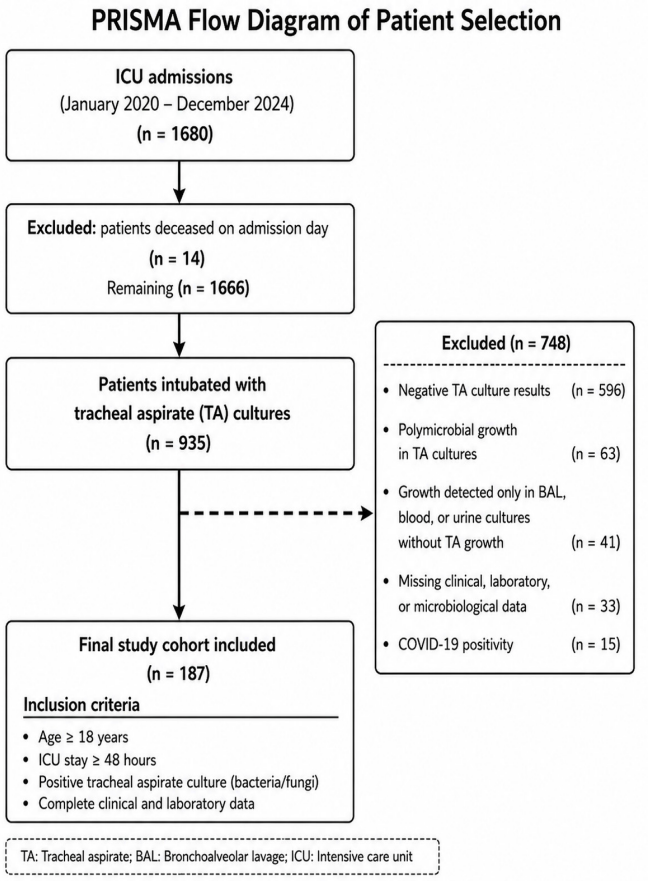

Figure 1. PRISMA flow diagram of patient selection

A total of 187 patients (93 females, 94 males; mean age 76.7±12.1 years) were included. The mean APACHE II score was 26.7±9.2, corresponding to an expected mortality of 56.3%±25.3. Hypertension (55.6%), cardiovascular disease (51.3%), and diabetes mellitus (25.7%) were the most common comorbidities. Gram-negative microorganisms predominated (89.3%). Sepsis was present in 26.2% of patients, and urosepsis in 9.6%.

Two isolates (1.1%) were classified as other microorganisms. Because of their limited number, they were not included in organism-specific subgroup analyses. The observed in-hospital mortality rate was 95.7% (Table 1).

Resistance Patterns

Only 9.6% of isolates were susceptible, while most exhibited antimicrobial resistance, including MDR: 36.4% and extensive drug resistance (XDR: 52.9%). Pandrug resistance (PDR) was identified in 1.1% of cases. Resistance to carbapenems was notably high (68.4%), and ESBL positivity was detected in 43.9% of isolates. Resistance to colistin (17.1%), oxacillin (14.4%), and methicillin (11.8%) was also observed, whereas resistance to ceftazidime–avibactam remained relatively low (8.0%).

Table 1. Socio/demographic and clinical characteristics of ICU patients

Variable	n (%) or mean±SD	95% CI
Gender		
- Male	93 (49.7%)	42.6–56.8%
- Female	94 (50.3%)	43.2–57.4%
APACHE II Score	26.7±9.2	25.4–28.0
Expected mortality (%)	56.3±25.3	52.7–59.9
Comorbidities		
- Diabetes mellitus	48 (25.7%)	19.6–31.7%
- Hypertension	104 (55.6%)	48.5–62.7%
- COPD/asthma	49 (26.2%)	20.1–32.2%
- Chronic kidney disease	31 (16.6%)	11.2–22.0%
- Cardiovascular disease	96 (51.3%)	44.2–58.4%
- Malignancy	28 (15.0%)	9.8–20.2%
- Neurological disease	73 (39.0%)	32.1–45.8%
Microorganism type		
- Gram negative	167 (89.3%)	84.7–93.9%
- Gram positive	18 (9.6%)	5.3–13.9%
- Other	2 (1.1%)	0–2.6%
Sepsis	49 (26.2%)	20.1–32.2%
Urosepsis	18 (9.6%)	5.3–13.9%
Outcome		
- Survived	8 (4.3%)	2.18–8.21 %
- Deceased	179 (95.7%)	91.79–97.82 %

Data are presented as mean±standard deviation or n (%), CI: Confidence interval, ICU: Intensive care unit, APACHE II: Acute Physiology and Chronic Health Evaluation II COPD: Chronic obstructive pulmonary disease. SD: Standard deviation.

MDR and XDR phenotypes accounted for 36.4% and 52.9% of isolates, respectively (Table 2).

Table 2. Antibiotic resistance profile

Category/resistance type	Percentage (%)	95% CI
No resistance	9.6%	6.2–14.7%
MDR	36.4%	29.8–43.5%
XDR	52.9%	45.8–60.0%
PDR	1.1%	0.3–3.8%
Colistin resistance	17.1%	12.4–23.2%
Oxacillin resistance	14.4%	10.1–20.2%
Carbapenem resistance	68.4%	61.5–74.7%
Ceftazidime–avibactam resistance	8.0%	4.9–12.8%
Methicillin resistance	11.8%	7.9–17.2%
ESBL positivity	43.9%	36.9–51.0%

CI: Confidence interval, MDR: Multi-drug resistant, XDR: Extensively drug-resistant, PDR: Pandrug-resistant, ESBL: Extended-spectrum beta-lactamase

Laboratory and Inflammatory Markers

Most patients exhibited marked leukocytosis, pronounced neutrophilia, and lymphopenia, along with relatively elevated monocyte counts and wide variability. Anemia was evident, while platelet counts were within the normal range but showed substantial interindividual variability. Inflammatory activity was prominent, as reflected by markedly elevated CRP levels (133.75±89.59 mg/L) and increased composite inflammatory indices.

Hypoalbuminemia was common (2.58±0.56 g/dl), resulting in significantly elevated inflammatory ratios, particularly the (CAR: 56.61±41.11) and blood urea nitrogen–to-albumin ratio (BAR: 20.27±13.98). The majority of patients exceeded a BAR value of 7.5, a threshold previously associated with poor prognosis. Renal dysfunction was frequently observed, with elevated urea (105.54±64.82 mg/dl), creatinine (1.81±1.43 mg/dl), and blood urea nitrogen (49.68±30.10 mg/dl) levels. Mean lactate concentration was markedly increased (5.36±5.13 mmol/l). Among hematological inflammatory indices, NLR and PLR were elevated, with mean values of 20.81±20.74 and 314.69±343.38, respectively. PLR values showed considerable variability across the study population. The lymphocyte-to-monocyte ratio (LMR) also exhibited considerable variability (2.66±3.05). The SII and SIRI reached high levels, with marked heterogeneity (4181.14±5644.45 and 11.99±16.32, respectively). BAR>7.5 was observed in 164 patients (87.7%; 95% CI 82.4–91.9). The PNI was 26.94±6.18, and the PIV was 2804.22±5878.22.

Markedly elevated CRP, lactate, CAR, BAR, NLR, SII, SIRI, and PIV values, together with low albumin and PNI levels, were observed in the study cohort (Table 3).

Table 3. Laboratory and inflammatory findings in ICU patients

Parameter (unit)	Mean±SD	95% CI
White blood cell count (K/µL)	15.04±7.75	13.93–16.15
Neutrophil count (K/µL)	13.17±7.46	12.10–14.24
Lymphocyte count (K/µL)	1.03±0.83	0.91–1.15
Monocyte count (K/µL)	0.60±0.42	0.54–0.66
Platelet count (K/µL)	210.78±124.22	192.98–228.58
Hemoglobin (g/dl)	10.35±2.44	10.00–10.70
Hematocrit (%)	31.95±7.82	30.83–33.07
RDW	16.39±2.59	16.02–16.76
MPV	11.19±1.67	10.95–11.43
CRP (mg/L)	133.75±89.59	120.91–146.59
Albumin (g/dl)	2.58±0.56	2.50–2.66
Urea (mg/dl)	105.54±64.82	96.25–114.83
Creatinine (mg/dl)	1.81±1.43	1.61–2.01
BUN (mg/dl)	49.68±30.10	45.37–53.99
BUN/creatinine ratio	32.95±16.68	30.56–35.34
BUN/albumin ratio (BAR)	20.27±13.98	18.27–22.27
Calcium (mg/dl)	8.13±0.95	7.99–8.27
Lactate (mmol/l)	5.36±5.13	4.62–6.10
NLR	20.81±20.74	17.84–23.78
PLR	314.69±343.38	265.48–363.91
LMR	2.66±3.05	2.23–3.10
SII	4181.14±5644.45	3372.12–4990.15
SIRI	11.99±16.32	9.65–14.33
CAR	56.61±41.11	50.71–62.50
PNI	26.94±6.18	26.05–27.82
PIV	2804.22±5878.22	1961.69–3646.74

Data are presented as mean±standard deviation with 95% confidence intervals.
WBC: White blood cell, RDW: Red cell distribution width, MPV: Mean platelet volume, CRP: C-reactive protein, BUN: Blood urea nitrogen, BAR: Bun-to-albumin ratio, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, LMR: Lymphocyte-to-monocyte ratio, SII: Systemic Immune-Inflammation Index, SIRI: Systemic Inflammatory Response Index, CAR: C-reactive protein-to-albumin ratio, PNI: Prognostic Nutritional Index, PIV: Pan-immune Inflammation Value.

Outcomes by Gram Status

Mortality was significantly higher in the gram-negative group than in the gram-positive group (97.0% vs. 83.3%, p=0.007), and ICU length of stay was longer among patients with gram-negative microorganisms (17.8±13.5 vs. 11.7±10.9 days, p=0.041). APACHE II scores (26.7±9.3 vs. 26.1±8.3, p>0.05) and expected mortality rates (56.4%±25.6% vs. 54.6%±24.5%, p>0.05) did not differ significantly between the groups.

Inflammatory indices, including NLR, PLR, LMR, SII, SIRI, CAR, and PIV, tended to be higher in patients with gram-negative microorganisms, whereas PNI values tended to be higher in the gram-positive group; however, none of these differences reached statistical significance (Table 4).

higher among non-survivors and correlated positively with APACHE II scores and expected mortality. Lactate showed significant associations with mortality and severity indices, including positive correlations with APACHE II scores and expected mortality and an inverse correlation with ICU length of stay.

Among inflammatory indices, NLR, SIRI, and CAR were significantly associated with mortality, whereas PLR demonstrated limited discriminatory performance. LMR was not associated with mortality but correlated with prolonged ICU stay. PNI values were significantly higher among survivors. PIV values were higher among non-survivors and were associated with both mortality and prolonged ICU stay.

Table 4. Clinical outcomes by gram status and organism group

Panel A. outcomes by gram status

Outcome	Gram-negative (n=167)	Gram-positive (n=18)	p-value
Mortality rate, n (%)	162 (97.0%)	15 (83.3%)	0.007
ICU stay (days),mean±SD	17.80±13.53	11.72±10.92	0.041
APACHE II score,mean±SD	26.72±9.32	26.06±8.32	0.799
Expected mortality (%), mean±SD	56.42±25.59	54.64±24.52	0.769

Panel B. outcomes by organism group

Organism group	Mortality rate (%)	ICU stay (days, mean±SD)	OR for mortality vs gram-positive (95% CI)	p value
Klebsiella	94.8	19.71±15.37	3.67 (0.67–20.05)	0.130
Acinetobacter	100.0	18.14±10.48	20.10 (0.98–411.42)	0.016
Pseudomonas	100.0	20.43±15.62	6.55 (0.31–138.06)	0.274
Serratia	88.9	11.17±12.97	1.60 (0.23–10.94)	0.658
Escherichia coli	100.0	12.59±10.30	10.16 (0.49–210.94)	0.074
Gram-positive	83.3	11.72±10.92	Reference	—

Note: Data are presented as mean±standard deviation (SD) or n (%). Mortality rates were compared using the χ^2 test or Fisher's exact test, as appropriate. Continuous variables were compared using the independent samples t-test or Mann–Whitney U test, as appropriate. A p-value <0.05 was considered statistically significant. Organism-specific mortality rates and odds ratios should be interpreted cautiously because small subgroup sizes, zero-event cells, and wide confidence intervals indicate substantial statistical uncertainty. Mortality rates were compared using χ^2 or Fisher's exact test, as appropriate, and continuous variables were compared using independent samples t test or Mann–Whitney U test. In Panel B, gram-positive organisms were used as the reference group for odds ratio calculations. A continuity correction was applied where necessary due to sparse data. Two isolates categorized as "other microorganisms" were included in the overall descriptive analyses but were not analyzed as a separate subgroup because of the limited sample size (n=2). OR: Odds ratio, CI: Confidence interval, ICU: Intensive care unit, SD: Standard deviation

When outcomes were further examined according to individual microorganism groups, marked heterogeneity was observed (Table 4). The highest observed mortality rates were noted in cases involving *Acinetobacter, Pseudomonas,* and *Escherichia coli* isolates, all of which reached 100% mortality in this cohort. *Klebsiella* isolates were also associated with a very high mortality rate (94.8%), whereas *Serratia* isolates demonstrated a relatively lower—but still substantial—mortality rate (88.9%). Gram-positive microorganisms demonstrated an intermediate mortality rate (83.3%).

In odds ratio analyses using gram-positive organisms as the reference, point estimates suggested a trend toward higher mortality risk for *Acinetobacter, Escherichia coli*, and *Pseudomonas* isolates. However, because of the small subgroup sizes and the presence of zero-event cells, confidence intervals were extremely wide and included unity in most comparisons, indicating substantial statistical uncertainty. Therefore, these organism-specific findings should be interpreted cautiously and should not be considered definitive evidence of increased mortality risk.

Biomarker Performance and Mortality

Associations between key biomarkers and clinical outcomes are summarized in Table 5. BAR levels were significantly

In ROC analyses with bootstrap-derived confidence intervals, PNI demonstrated discriminatory performance for in-hospital mortality (AUC=0.88, 95% CI 0.71–0.98). Lactate (AUC=0.80) and CAR (AUC=0.73) also demonstrated moderate-to-high discriminatory performance, whereas NLR, PIV, and BAR showed moderate performance. APACHE II demonstrated limited discrimination (AUC=0.61) (Table 5).

Outcomes by Resistance Category

Mortality and ICU length of stay increased progressively from susceptible isolates to MDR, XDR, and PDR categories, with the highest observed mortality in the PDR subgroup (Table 6). Interpretation of the PDR subgroup should be made with considerable caution because only two patients were included (n=2), precluding meaningful comparative analyses or generalizable conclusions. APACHE II scores and expected mortality estimates did not increase proportionally across resistance categories. The PDR subgroup demonstrated an expected mortality rate of 33% despite adverse clinical outcomes (Table 6).

Blood and Urine Culture Findings

Microbial growth was detected in blood cultures from 50 patients. *Staphylococcus* spp. were the most frequently isolated organisms (52% of positive blood cultures), followed by *Klebsiella* spp. and

Table 5. Association of key biomarkers with mortality and their prognostic performance

Parameter	Survivors (mean±SD)	Non-survivors (mean±SD)	p (mortality)	AUC (95% CI)	Cut-off	Sensitivity	Specificity
PNI	36.75± 6.50	26.66±5.98	0.003	0.88 (0.71–0.98)	≤32.78	0.87	0.88
Lactate	2.04±0.87	5.51±5.19	<0.001	0.80 (0.64–0.92)	≥1.70	0.89	0.62
BAR	8.08±4.28	20.81±14.01	<0.001	0.83 (0.72–0.93)	≥13.41	0.65	1.00
NLR	10.96±6.36	21.07±21.18	0.002	0.64 (0.48–0.79)	≥19.28	0.36	1.00
SIRI	5.81±2.72	12.27±16.62	<0.001	0.61 (0.35–0.84)	≥10.00	0.60	0.58
CAR	27.56±22.94	57.90±41.30	0.007	0.73 (0.51–0.90)	≥9.96	0.93	0.50
PIV	2150.32±1850.22	5630.41±7200.18	0.001	0.66 (0.45–0.85)	≥2500	0.72	0.65
APACHE II	—	—	—	0.61 (0.48–0.73)	≥31.00	0.37	1.00

Data are presented as mean±standard deviation. Comparisons between survivors and non-survivors were performed using the independent samples t test or the Mann–Whitney U test, as appropriate. Prognostic performance was evaluated using receiver operating characteristic (ROC) curve analysis. The AUC and 95% confidence intervals (CI) were calculated using bootstrap resampling (5,000 iterations). Optimal cut-off values were determined using the Youden index. Because only eight patients survived, the reported AUC values, optimal cut-off values, sensitivity, and specificity estimates should be considered exploratory and should not be interpreted as definitive clinical thresholds.BAR: Blood urea nitrogen-to-albumin ratio, NLR: Neutrophil-to-lymphocyte ratio, SIRI: Systemic Inflammation Response Index, CAR: C-reactive protein-to-albumin ratio, PNI: Prognostic Nutritional Index, PIV: Pan-immune inflammation value, ICU: Intensive care unit, SD: Standard deviation, CI: Confidence intervals, AUC: Area under the curve, APACHE II: Acute Physiology and Chronic Health Evaluation II.

Table 6. Clinical outcomes according to antimicrobial resistance category

Outcome	No resistance (n=18)	MDR (n=68)	XDR (n=99)	PDR (n=2)	p-value
Mortality rate, n (%)	16 (88.9%)	64 (94.1%)	97 (98.0%)	2 (100.0%)	0.256*
ICU stay (days), mean±SD	8.5±6.9	15.1±12.1	20.4±14.8	24.0±2.8	0.001
APACHE II score, mean±SD	26.6±8.1	29.1±9.9	25.2±8.6	19.0±4.2	0.053
Expected mortality (%), mean±SD	56.3±23.9	62.9±25.1	52.4±25.1	33.0±13.4	0.037

*p-values represent overall comparisons among antimicrobial resistance categories. Data are presented as number (%) or mean±standard deviation. Clinical outcomes are shown descriptively according to antimicrobial resistance categories (susceptible, MDR, XDR, and PDR). Interpretation of the PDR subgroup should be made with considerable caution because only two patients were included (n=2), which is insufficient for meaningful comparative analyses or generalizable conclusions. MDR: Multidrug-resistant, XDR: Extensively drug-resistant, PDR: Pandrug-resistant, ICU: Intensive care unit, CI: Confidence interval, APACHE II: Acute Physiology and Chronic Health Evaluation II.

Escherichia coli. *Enterobacter* spp. and *Serratia* spp. were identified less frequently.

No growth was detected in urine cultures from 169 patients (90.4%). Among the 18 patients (9.6%) with positive urine cultures, *Klebsiella* spp. were the most frequently isolated organisms (50% of positive urine cultures), followed by *Escherichia coli*. *Staphylococcus* spp. and *Acinetobacter* spp. were identified less frequently.

DISCUSSION

In this study, 187 critically ill, intubated ICU patients with positive TA cultures were evaluated with respect to clinical outcomes, antimicrobial resistance, and the performance of inflammatory biomarkers. The overall in-hospital mortality rate was remarkably high (95.7%), indicating the severely ill and highly selected nature of this cohort. Within this high-risk population, gram-negative microorganisms and antimicrobial-resistant pathogens—particularly MDR, XDR, and PDR organisms—were associated with adverse clinical outcomes.

The exceptionally high mortality likely reflects several contextual factors and is consistent with previous reports describing high mortality among mechanically ventilated ICU patients with suspected lower respiratory tract infections associated with antimicrobial resistance.[2,24] The cohort consisted exclusively of elderly, mechanically ventilated patients with positive TA cultures obtained in the setting of suspected lower respiratory tract infection, representing a highly selected subgroup of ICU admissions. As a tertiary referral center, our ICU frequently manages patients transferred at advanced stages of illness, often after initial treatment failure elsewhere. In addition, end-of-life decisions or limitations of life-sustaining therapy may have contributed to the observed mortality, although such variables were not systematically captured. Therefore, these outcomes should be interpreted within the context of a high-risk referral population rather than generalized to broader ICU settings. The inclusion of only intubated patients with positive TA cultures may have introduced selection bias toward more severe cases, which should also be considered when interpreting the exceptionally high mortality rate.

Furthermore, the exceptionally high in-hospital mortality substantially limits the external validity and generalizability of our findings. Therefore, the observed associations between antimicrobial resistance, biomarker profiles, and clinical outcomes should be interpreted within the context of this highly selected cohort and should not be extrapolated to broader ICU populations with different patient characteristics, illness severity, or case mix.

Mortality was significantly higher among patients with gram-negative microorganisms compared with those with gram-positive microorganisms (97% vs. 83%; p=0.007), and ICU length of stay was significantly longer (17.8±13.5 vs. 11.7±10.9 days; p=0.041). In contrast, APACHE II scores and predicted mortality did not differ between groups, suggesting that conventional severity scoring systems may not fully reflect the additional clinical burden associated with gram-negative pathogens and antimicrobial resistance. The results are consistent with previous reports reporting an association between gram-negative bacteremia, antimicrobial resistance, and higher mortality.[2,4] Differences in host inflammatory responses and pathogen-related factors may have contributed to the more severe clinical course observed among patients with gram-negative microorganisms.[3]

Gram-negative pathogens predominated in our cohort, consistent with previous ICU-based TA studies reporting

similar microbial distributions.[25] Similar microbiological distributions and high AMR rates have also been reported in ICU-based studies from Turkiye.[26,27] At the pathogen-specific level, mortality remained extremely high across nearly all organism groups. In this cohort, cases involving *Acinetobacter* isolates, *Pseudomonas*, and *Escherichia coli* were associated with very high observed mortality rates, reaching 100% in small subgroups. *Klebsiella* and *Serratia* isolates also demonstrated markedly elevated mortality rates. Gram-positive pathogens demonstrated comparatively lower—but still substantial—mortality. Although odds ratio analyses suggested higher mortality risk for certain gram-negative organisms, wide confidence intervals due to small subgroup sizes and zero-event cells warrant prudent interpretation.

A clear resistance gradient was observed. Mortality and ICU length of stay increased progressively from susceptible isolates to MDR, XDR, and PDR phenotypes, with the highest observed mortality in the PDR subgroup. However, APACHE II scores and predicted mortality did not increase in proportion to the severity of resistance. This difference may reflect deficiencies of traditional scoring systems, which do not incorporate pathogen-specific characteristics or resistance phenotypes. Similar limitations of APACHE II and SOFA scores in critically ill patients with AMR have been reported previously.[10]

It is noteworthy that the in-hospital mortality rate remained high (88.9%) even among patients with susceptible (non-resistant) isolates. This finding likely reflects the overall severity of illness in the study cohort rather than the antimicrobial susceptibility profile alone. All patients were critically ill, mechanically ventilated ICU patients with suspected lower respiratory tract infection, advanced age, multiple comorbidities, and high baseline disease severity. Therefore, mortality was probably influenced by multiple factors beyond antimicrobial resistance, including the underlying critical illness, organ dysfunction, and other concurrent medical conditions. Accordingly, antimicrobial susceptibility should not be interpreted as the sole determinant of clinical outcome in this highly selected population.

Biomarker analyses provided additional exploratory clinical and inflammatory insights in this high-risk ICU cohort. The cohort exhibited pronounced leukocytosis, neutrophilia, lymphopenia, hypoalbuminemia, and elevated CRP levels, consistent with marked systemic inflammatory and physiological stress responses. Among evaluated biomarkers, PNI showed relatively higher discriminatory performance for mortality and was significantly higher among survivors. This finding may suggest a possible association between preserved nutritional and immunological reserve and clinical outcomes in critically ill patients; however, further prospective validation is required.[9] Lactate also demonstrated moderate-to-high discriminatory performance and was associated with mortality, consistent with previous studies in critically ill and sepsis populations.[5,6] Similarly, CAR and BAR were associated with mortality and disease severity parameters in exploratory analyses, possibly indicating the combined effects of systemic inflammation, renal dysfunction, and nutritional compromise.[7,8,28]

Inflammatory indices, including NLR, SIRI, and CAR, were significantly associated with mortality, whereas SII and PLR showed limited discriminatory performance.[14-17,28] The PIV, integrating neutrophil, monocyte, platelet, and lymphocyte counts, was associated with both mortality and prolonged ICU stay in exploratory analyses. In contrast, RDW and MPV showed limited associations with clinical outcomes in this cohort, consistent with heterogeneous findings reported in previous studies.[12,13]

From a clinical perspective, the observed associations between AMR patterns and adverse clinical outcomes demonstrate the complexity of managing critically ill ICU patients with positive TA cultures. However, because treatment-related variables, such as the timing and appropriateness of empirical antibiotic therapy, were not systematically available, the independent contribution of AMR to mortality could not be fully determined. Although treatment-related variables were not systematically available in the present study, previous studies have highlighted the potential importance of timely empirical antimicrobial therapy and antimicrobial stewardship strategies in critically ill patients. Integration of biomarker-based assessment—particularly incorporating PNI and lactate—may reflect additional inflammatory and physiological alterations not entirely captured by conventional severity scores. Prolonged ICU stays associated with resistant microorganisms also have important consequences for resource utilization, infection control, and healthcare costs.

It should also be acknowledged that the precise causes of death were not systematically documented in this retrospective study. Critically ill ICU patients often have multiple concurrent conditions, including multiorgan failure, severe underlying comorbidities, and other life-threatening complications that may independently contribute to mortality. Therefore, the observed associations between antimicrobial resistance, biomarker profiles, and mortality should not be interpreted as evidence that the isolated microorganisms were the direct cause of death but rather as associations observed within this critically ill population.

In conclusion, mortality was exceptionally high in this elderly, mechanically ventilated ICU population with positive TA cultures. Gram-negative microorganisms and AMR patterns were more frequently observed among patients with prolonged ICU stays and adverse clinical outcomes that were not fully reflected by conventional severity scoring systems. Biomarkers—particularly PNI and lactate—showed exploratory associations with mortality and may reflect additional inflammatory and physiological alterations not completely captured by conventional severity scores. These exploratory findings may help generate hypotheses for future prospective investigations integrating AMR profiles and biomarker assessment.

Limitations

The primary limitations of this research include its retrospective design conducted at a single center, a limited number of participants in the PDR subgroup, the risk of type I error from multiple comparisons, and measurement variability. Multivariable regression analysis could not be conducted due to a significant imbalance in events (95.7% mortality), which may have led to model instability, overfitting, and unreliable parameter estimates.

In addition, only eight patients survived, resulting in an extreme imbalance between survivors and non-survivors. Consequently, the exploratory ROC analyses were based on a very small survivor

group, substantially reducing the statistical power of the calculated AUC values and increasing the risk of overfitting when estimating optimal cut-off values, sensitivity, and specificity. Therefore, these findings should be interpreted as hypothesis-generating rather than definitive clinical thresholds and require validation in larger prospective cohorts before clinical application.

Several inflammatory and hematological biomarkers evaluated in this study, including PIV, RDW, MPV, NLR, and PNI, may be affected by multiple comorbid conditions such as malignancy, hematological disorders, corticosteroid exposure, immunosuppressive therapy, and chronic systemic inflammation. Because these variables were not systematically available in the retrospective dataset, residual confounding could not be fully excluded. Therefore, the observed biomarker associations should be interpreted cautiously and considered exploratory rather than definitive indicators of clinical severity or prognosis.

In addition, primary ICU admission diagnoses and indications for ICU admission were not systematically available in a standardized format because of the retrospective design. As these factors are important determinants of disease severity and mortality, their absence limited further characterization of the study population and may have introduced residual confounding.

Furthermore, data regarding the appropriateness and timing of empirical antibiotic therapy were not systematically available, representing a potentially important unmeasured confounder that may have influenced clinical outcomes. Because TA cultures may reflect colonization rather than true infection in mechanically ventilated patients, the retrospective design limited the ability to fully differentiate infection from colonization or contamination in all cases.

Moreover, the specific causes of death were not systematically documented in a standardized format. Consequently, it was not possible to determine the extent to which mortality was directly attributable to the microorganisms isolated from TA cultures rather than to underlying critical illness or other concurrent medical conditions. Therefore, the observed associations between antimicrobial resistance, biomarker profiles, and mortality should be interpreted as associations rather than evidence of direct causality.

Although a 100% mortality rate was observed in the PDR group, this finding should be interpreted with considerable caution because only two patients were included (n=2). Therefore, the PDR subgroup is insufficient for meaningful comparative analyses or for drawing generalizable conclusions.

Therefore, these outcomes should be validated in larger, multicenter, prospective cohorts that incorporate standardized infection definitions, treatment-related variables, and more comprehensive adjustment for potential confounding factors. Future studies evaluating the resistance–outcome relationship may also benefit from advanced multivariable and competing-risk analytical approaches.

CONCLUSION

In this cohort of elderly mechanically ventilated ICU patients with positive TA cultures, overall mortality was remarkably high, indicating the critically ill and highly selected nature of the study population. Gram-negative microorganisms and increasing AMR patterns were more frequently associated with adverse clinical outcomes and prolonged ICU stay and may be associated with poorer clinical outcomes in this highly selected cohort. Observed mortality tended to increase progressively across resistant phenotypes, particularly among MDR and XDR isolates, although interpretation of the PDR subgroup should be cautious given the limited sample size.

Conventional severity scoring systems, such as APACHE II, did not fully reflect the adverse clinical outcomes observed in patients with resistant microorganisms. In contrast, several inflammatory and nutritional biomarkers, including PNI, lactate, and CAR, demonstrated associations with mortality in exploratory analyses. However, given the retrospective design, the exceptionally high mortality rate, and the inability to fully differentiate true infection from colonization in all cases, these biomarker findings should be interpreted cautiously.

Overall, this study suggests possible associations among AMR patterns, biomarker profiles, and adverse clinical outcomes in mechanically ventilated ICU patients with positive TA cultures. However, because of the retrospective design, the lack of treatment-related data, and the inability to fully distinguish colonization from true infection, these findings should not be interpreted as evidence of causality. Larger prospective multicenter studies incorporating standardized infection definitions and treatment-related variables are required to confirm these exploratory observations.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was approved by the Health Sciences Researches Ethics Committee of Yüksek İhtisas University (Date: 30.10.2025, Decision No: 17/348).

Informed Consent

This retrospective study used pre-existing anonymized patient data. No additional intervention was performed, and there was no direct patient contact. The study was approved by the Ethics Committee, and the requirement for written informed consent was waived by the ethics committee.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

The authors received no financial support for the conduct or publication of this research.

Author Contributions

Concept: FÇ, AT, ABÇ; Design: FÇ, AT, A.B.Ç; Control: AT, ABÇ; Resources: FÇ, AT; Materials: FÇ, AT; Data Collection and/or Processing: FÇ, AT; Analysis and/or Interpretation: FÇ, AT, ABÇ; Literature Review: FÇ; Writing the Article: FÇ, AT, ABÇ; Critical Review: FÇ, AT, ABÇ.

REFERENCES

1. World Health Organization. Global Antimicrobial Resistance and Use Surveillance System (GLASS) Report 2021. World Health Organization; 2021.
2. Paramythiotou E, Routsi C. Association between infections caused by multidrug-resistant gram-negative pathogens and mortality in the intensive care unit. *World J Crit Care Med*. 2016;5(2):111-120. doi: 10.5492/wjccm.v5.i2.111
3. Nelson RE, Hyun D, Jezek A, Samore MH. Mortality, length of stay, and healthcare costs associated with multidrug-resistant bacterial infections among elderly hospitalized patients in the United States. *Clin Infect Dis*. 2021 ;74(6):1070-1080. doi: 10.1093/cid/ciab696
4. Tang A, Shi Y, Dong Q, et al. Prognostic differences in sepsis caused by gram-negative bacteria and gram-positive bacteria: a systematic review and meta-analysis. *Crit Care*. 2023;27(1):467. doi: 10.1186/s13054-023-04750-w
5. Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. *Intensive Care Med*. 2021;47(11):1181-1247. doi: 10.1007/s00134-021-06506-y
6. Deulkar P, Singam A, Mudiganti VNKS, Jain A. Lactate monitoring in intensive care: a comprehensive review of its utility and interpretation. *Cureus*. 2024;16(8):e66356. doi: 10.7759/cureus.66356
7. Zhang H, Wang X, Zhang Y, et al. Blood urea nitrogen-to-albumin ratio as a predictor of mortality in patients with sepsis: a retrospective cohort study. *Front Med (Lausanne)*. 2022;9:967332. doi: 10.3389/fmed.2022.967332
8. Zhang L, Wang H, Liu X, et al. Blood urea nitrogen to albumin ratio as a prognostic factor in critically ill patients: a large cohort study. *Sci Rep*. 2024; 14:4411. doi: 10.1038/s41598-024-44110-7
9. Wu H, Zhou C, Kong W, Zhang Y, Pan D. Prognostic Nutrition Index is associated with the all-cause mortality in sepsis patients: a retrospective cohort study. *J Clin Lab Anal*. 2022;36(4):e24297. doi: 10.1002/jcla.24297
10. Raith EP, Udy AA, Bailey M, et al. Prognostic accuracy of the SOFA score, SIRS criteria, and qSOFA score for in-hospital mortality among adults with suspected infection admitted to the intensive care unit. *JAMA*. 2017; 317(3):290-300. doi:10.1001/jama.2016.20328
11. Xu HB, Xu YH, He Y, et al. Association between admission pan-immune-inflammation value and short-term mortality in septic patients: a retrospective cohort study. *Sci Rep*. 2024;14(1):15205. doi: 10.1038/s41598-024-66142-6
12. Zhang Z, Xu X, Ni H, Deng H. Red cell distribution width is associated with hospital mortality in unselected critically ill patients. *J Thorac Dis*. 2013;5(6):730-736. doi: 10.3978/j.issn.2072-1439.2013.11.14
13. Tajarernmuang P, Phrommintikul A, Limsukon A, Pothirat C, Chittawatanarat K. The role of mean platelet volume as a predictor of mortality in critically ill patients: a systematic review and meta-analysis. *Crit Care Res Pract*. 2016;2016:4370834. doi: 10.1155/2016/4370834
14. Lagunas-Rangel FA. Neutrophil-to-lymphocyte ratio and lymphocyte-to-C-reactive protein ratio in patients with severe COVID-19. *Int Immunopharmacol*. 2020;85:106507. doi: 10.1016/j.intimp.2020.106507
15. Qu R, Ling Y, Zhang YHZ, et al. Platelet-to-lymphocyte ratio is associated with prognosis in patients with coronavirus disease-19. *J Med Virol*. 2020; 92(9):1533-1541. doi: 10.1002/jmv.25767
16. Yang R, Chang Q, Meng X, Gao N, Wang W. Prognostic value of Systemic Immune-Inflammation Index in cancer: a meta-analysis. *J Cancer*. 2018; 9(18):3295-3302. doi: 10.7150/jca.25691
17. Liang L, Su Q. Systemic Immune-Inflammation Index and the short-term mortality of patients with sepsis: a meta-analysis. *Biomol Biomed*. 2025;25(4):798-809. doi: 10.17305/bb.2024.11494
18. Kinoshita A, Onoda H, Imai N, et al. The C-reactive protein/albumin ratio, a novel inflammation-based prognostic score, predicts outcomes in patients with hepatocellular carcinoma. *Ann Surg Oncol*. 2015;22(3):803-810. doi: 10.1245/s10434-014-4048-0
19. Han K, Tao Y, Wang J, Lu J. Prognostic value of blood urea nitrogen to albumin ratio in septic patients with acute kidney injury: a retrospective study based on MIMIC database. *Front Med (Lausanne)*. 2025;12:1510919. doi: 10.3389/fmed.2025.1510919
20. Salvagno GL, Sanchis-Gomar F, Picanza A, Lippi G. Red blood cell distribution width: a simple parameter with multiple clinical applications. *Crit Rev Clin Lab Sci*. 2015;52(2):86-105. doi: 10.3109/10408363.2014.992064
21. Zhang Z, Xu X, Ni H, Deng H. Platelet indices are novel predictors of hospital mortality in intensive care unit patients. *J Crit Care*. 2014;29(5):885.e1-885.e6. doi: 10.1016/j.jcrc.2014.05.008
22. Mohri Y, Inoue Y, Tanaka K, et al. Prognostic Nutritional Index predicts postoperative outcome in colorectal cancer. *World J Surg*. 2013;37(11):2688-2692. doi: 10.1007/s00268-013-2156-9
23. Fuca G, Guarini V, Antoniotti C, et al. The pan-immune-inflammation value (PIV) as a new prognostic biomarker in metastatic colorectal cancer: results from a pooled analysis of the Valentino and TRIBE first-line trials. *Ann Oncol*. 2020;31(10):1535-1541. doi: 10.1016/j.annonc.2020.06.020
24. Shi Y, Wang S, Li Q. Multidrug and extensively drug-resistant *Acinetobacter baumannii* in pediatric intensive care unit: risk factors and clinical outcomes. *BMC Infect Dis*. 2020;20:555. doi:10.1186/s12879-020-05226-0
25. Islam MS, Saha S, Jahan N, Sultana N, Rahman M. Bacterial isolates from tracheal aspirates of patients in the intensive care unit and their antimicrobial susceptibility patterns. *Arch Clin Biomed Res*. 2021;5(6):697-711. doi: 10.26502/acbr.50170205
26. Alp E, Güven M, Yıldız O, Aygen B, Voss A. Incidence, risk factors and mortality of nosocomial pneumonia in intensive care units: a prospective study. *Ann Clin Microbiol Antimicrob*. 2004;3:17. doi: 10.1186/1476-0711-3-17
27. Erbay H, Yalcin AN, Serin S, et al. Nosocomial infections in the intensive care unit in a Turkish university hospital: a 2-year survey. *Intensive Care Med*. 2003;29(9):1482-1488. doi: 10.1007/s00134-003-1903-2
28. Ranzani OT, Zampieri FG, Forte DN, et al. C-reactive protein/albumin ratio predicts 90-day mortality of septic patients. *PLoS One*. 2013;8(3):e59321.