

DOI: 10.4274/mjima.galenos.2026.26731
 Mediterr J Infect Microb Antimicrob 2026;15:26731
 Erişim: <http://dx.doi.org/10.4274/mjima.galenos.2026.26731>

Predictors of Mortality in *Staphylococcus aureus* Bacteremia: A Retrospective Cohort Study from a Tertiary-Care Center

Staphylococcus aureus Bakteriyemisinde Ölüm Oranını Belirleyen Faktörler: Üçüncü Basamak Hastaneden Retrospektif Kohort Çalışması

© Ceren Atasoy Tahtasakal¹, © Serenay Aytan¹, © Okan Derin^{1,2}, © Özlem Gül¹, © Nazife Duygu Demirbaş¹, © Hakkı Meriç Türkkan¹, © Ahsen Öncül¹, © Dilek Yıldız Sevgi¹, © Banu Bayraktar³, © İlyas Dökmetaş¹

¹University of Health Sciences Türkiye, Şişli Hamidiye Etfal Training and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, İstanbul, Türkiye

²İstanbul Medipol University, Graduate School of Health Sciences, Epidemiology PhD Program, İstanbul, Türkiye

³University of Health Sciences Türkiye, Şişli Hamidiye Etfal Training and Research Hospital, Clinic of Microbiology, İstanbul, Türkiye

Abstract

Introduction: *Staphylococcus aureus* bacteremia (SAB) remains a serious infectious condition associated with substantial early mortality despite advances in antimicrobial therapy. This study evaluated clinical, laboratory, and management-related factors associated with 28-day mortality among adults with SAB.

Materials and Methods: A total of 151 adult patients with clinically significant SAB identified by blood culture between January 1, 2023, and October 24, 2024, were retrospectively analyzed. The primary outcome was 28-day all-cause mortality. Univariable and multivariable logistic regression analyses were performed to identify independent predictors of mortality. Model discrimination was assessed using the area under the receiver operating characteristic curve (AUC).

Results: The median age of the cohort was 67 years (interquartile range, 55–78), 60% of patients were male, and 33% were managed in the intensive care unit (ICU). Overall mortality was 54.3%, and 28-day mortality was 40.7%. Compared with 28-day survivors, non-survivors were older and more frequently had ICU admission, neurological comorbidities, healthcare-associated infection, an elevated neutrophil-to-lymphocyte ratio, and higher serum lactate levels, whereas fever and chills were more frequent among survivors. Source control and infectious disease (ID) consultation within the first 24 hours were also more frequently provided to survivors. In multivariable analysis, advanced age [odds ratios (OR), 1.04; 95% confidence intervals (CI), 1.00–1.09], ICU admission (OR, 6.37; 95% CI, 1.85–24.2), and higher serum lactate levels (OR, 1.55 per mmol/L; 95% CI, 1.08–2.56) were independently associated with increased 28-day mortality. Source control and early ID consultation demonstrated protective trends after adjustment. The final model showed good discriminatory performance (AUC, 0.85; 95% CI, 0.75–0.95).

Conclusion: This study suggests that early mortality in SAB is driven primarily by host characteristics and disease severity rather than by microbiological resistance patterns alone. Advanced age, ICU admission, and elevated serum lactate were the strongest independent predictors of early mortality, whereas source control and early ID consultation demonstrated protective trends that did not reach statistical significance after adjustment. These findings support a standardized, multidisciplinary approach to SAB management that extends beyond antimicrobial therapy and emphasizes timely optimization of modifiable clinical care processes.

Keywords: *Staphylococcus aureus* bacteremia, mortality, intensive care unit, lactate, source-control, infectious disease consultation



Address for Correspondence/Yazışma Adresi: Ceren Atasoy Tahtasakal, MD, University of Health Sciences Türkiye, Şişli Hamidiye Etfal Training and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, İstanbul, Türkiye

E-mail: cerenatasoy.i@gmail.com **ORCID ID:** orcid.org/0000-0003-0392-229X

Received/Geliş Tarihi: 12.02.2026 **Accepted/Kabul Tarihi:** 05.10.2026 **Published/Yayınlanma tarihi:** 16.10.2026

Cite this article as/Atf: Atasoy Tahtasakal C, Aytan S, Derin O, Gül Ö, Demirbaş ND, Türkkan HM, Öncül A, Yıldız Sevgi D, Bayraktar B, Dökmetaş İ. Predictors of mortality in *Staphylococcus aureus* bacteremia: a retrospective cohort study from a tertiary-care center. Mediterr J Infect Microb Antimicrob. 2026;15:323-335



©Copyright 2026 The Author(s). Published by Galenos Publishing House on behalf of Infectious Diseases and Clinical Microbiology Specialty Society of Turkey. Licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License (CC BY-NC-ND 4.0)

Öz

Giriş: *Staphylococcus aureus* bakteriyemisi (SAB), antimikrobiyal tedavideki gelişmelere rağmen erken dönemde yüksek mortalite ile seyreden ciddi bir enfeksiyondur. Bu çalışmada, erişkin SAB hastalarında 28 günlük mortalite ile ilişkili klinik, laboratuvar ve yönetsel faktörler değerlendirildi.

Gereç ve Yöntem: 1 Ocak 2023 ile 24 Ekim 2024 tarihleri arasında kan kültürlerinde klinik olarak anlamlı SAB saptanan toplam 151 erişkin hasta retrospektif olarak incelendi. Birincil sonlanım noktası 28 günlük tüm nedenlere bağlı mortaliteydi. Bağımsız öngördürücüleri belirlemek amacıyla tek değişkenli ve çok değişkenli lojistik regresyon analizleri yapıldı. Modelin ayırt edici gücü, alıcı işletim karakteristiği eğrisi altında kalan alan (AUC) ile değerlendirildi.

Bulgular: Kohortun ortalama yaşı 67 yıl (çeyrekler arası açıklık: 55–78) olup hastaların %60'ı erkekti; %33'ü yoğun bakım ünitesinde izlendi. Genel mortalite %54,3, Yirmi sekiz günlük mortalite ise %40,7 idi. 28 günlük mortalite durumuna göre yapılan karşılaştırmalarda ileri yaş, yoğun bakım ünitesine yatış, nörolojik komorbidite, sağlık hizmeti ilişkili enfeksiyon, yüksek nötrofil-lenfosit oranı ve serum laktat düzeyi gruplar arasında farklılık gösterirken, ateş ve titreme 28 günlük mortalitesi olmayan hastalarda daha sık görüldü. Odak kontrolü ve ilk 24 saat içinde enfeksiyon hastalıkları konsültasyonu da 28 günlük mortalitesi olmayan hastalarda daha sıkı. Çok değişkenli analizde ileri yaş (olasılık oranı [OR] 1,04; %95 güven aralığı [GA] 1,00–1,09), yoğun bakım ünitesine yatış (OR 6,37; %95 GA 1,85–24,2) ve yüksek serum laktat düzeyi (mmol/L başına OR 1,55; %95 GA 1,08–2,56), 28 günlük mortalitenin bağımsız öngördürücüleri olarak saptandı. Odak kontrolü ve erken enfeksiyon hastalıkları konsültasyonu, düzeltme sonrasında koruyucu yönde eğilim gösterdi. Nihai model iyi ayırt edicilik gösterdi (AUC 0,85; %95 GA 0,75–0,95).

Sonuç: SAB'de erken mortalite, mikrobiyolojik direnç paternlerinden çok konakla ilişkili faktörler ve hastalık şiddeti tarafından belirlenmektedir. İleri yaş, yoğun bakım gereksinimi ve yüksek serum laktat düzeyi erken ölümün en güçlü bağımsız öngördürücüleri olarak öne çıkarken, odak kontrolü ve erken enfeksiyon hastalıkları konsültasyonu düzeltme sonrasında istatistiksel anlamlılığa ulaşmayan koruyucu eğilimler göstermiştir. Bulgular, SAB yönetiminde antibiyotik tedavisinin ötesine geçen, standartlaştırılmış ve multidisipliner bir yaklaşımı desteklemektedir.

Anahtar Kelimeler: *Staphylococcus aureus* bakteriyemisi, mortalite, yoğun bakım ünitesi, laktat, odak kontrolü, enfeksiyon hastalıkları konsültasyonu

Introduction

Staphylococcus aureus is one of the most important causative agents of both community-acquired and healthcare-associated infections, causing a broad spectrum of clinical conditions ranging from skin and soft-tissue infections to endocarditis, bacteremia, and sepsis. Despite advances in antimicrobial therapy and infection control practices, *Staphylococcus aureus* bacteremia (SAB) remains a serious clinical problem associated with substantial morbidity and mortality. Mortality rates reported in the literature generally range from 20% to 40%, depending on patients' comorbid conditions, the source of infection, and the timing and effectiveness of treatment^[1,2].

Complications such as infective endocarditis, pneumonia, and deep tissue abscesses are relatively common and can substantially increase mortality. Comorbid conditions, including advanced age, malignancy, chronic kidney disease, diabetes mellitus, and immunosuppressive therapy, are also closely associated with poor prognosis. In addition, healthcare-associated infection, inappropriate empirical antibiotic therapy, and delays in source control have been identified as modifiable risk factors associated with increased mortality in patients with SAB^[3,4].

In recent years, notable changes have been observed in the epidemiology of SAB. Although the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) has declined in many countries, methicillin-susceptible *Staphylococcus aureus* (MSSA)

bacteremia has been reported with increasing frequency, particularly among older individuals and those with multiple comorbidities. The narrowing difference in mortality between MRSA and MSSA bacteremia suggests that clinical outcomes cannot be explained solely by antimicrobial susceptibility and that early diagnosis, appropriate empirical therapy, and timely source control continue to play critical roles in patient prognosis^[5,6].

Accurate identification of clinical and laboratory indicators is essential for predicting mortality risk. Persistent bacteremia, elevated C-reactive protein (CRP) or procalcitonin levels, lymphopenia, and delays in source control have been independently associated with mortality in patients with SAB^[2]. However, data on the epidemiological characteristics, clinical course, and determinants of mortality in patients with SAB in Türkiye remain limited. Given the steadily increasing proportion of elderly patients and individuals with multiple comorbidities, generating local data is essential to inform and improve empirical treatment approaches, infection control strategies, and patient management algorithms.

In this context, the present study aimed to comprehensively evaluate the demographic, clinical, and laboratory characteristics of patients diagnosed with SAB at University of Health Sciences Türkiye, Şişli Hamidiye Etfal Training and Research Hospital and to identify factors associated with mortality.

Materials and Methods

Study Design and Setting

This single-center, retrospective cohort study included adult inpatients diagnosed with SAB at University of Health Sciences Türkiye, Şişli Hamidiye Etfal Training and Research Hospital between January 1, 2023, and October 24, 2024.

Study Population

All patients aged ≥ 18 years with at least one blood culture bottle positive for *Staphylococcus aureus* who received treatment for clinically significant bacteremia were eligible for inclusion. For patients with more than one episode of SAB, only the first episode was included in the analysis. Patients younger than 18 years, those with blood culture results considered to represent contamination, those with unavailable primary outcome data, and those with polymicrobial bacteremia in whom pathogens other than *Staphylococcus aureus* were considered to have significantly influenced the clinical course were excluded.

Definitions and Clinical Variables

The index time was defined as the time of collection of the first blood culture positive for *Staphylococcus aureus*. Antimicrobial susceptibility testing was performed using an automated system (e.g., VITEK 2, bioMérieux, France), and methicillin resistance was confirmed using cefoxitin (30 μ g) disk diffusion testing. Results were interpreted according to the European Committee on Antimicrobial Susceptibility Testing criteria, and isolates were classified as MRSA or MSSA.

Persistent bacteremia was defined as continued growth of *Staphylococcus aureus* in blood cultures obtained 48–72 hours after initiation of appropriate antimicrobial therapy. Primary bloodstream infection was defined as SAB without an identifiable infectious focus after clinical and diagnostic evaluation. Early appropriate empirical therapy was defined as initiation of at least one antimicrobial agent with in vitro activity against the isolated strain within the first 24 hours after blood culture collection. Adequate source control was defined as removal of an infected intravascular catheter and/or performance of surgical intervention or drainage procedures, when indicated, preferably within the first 72 hours.

The timing of targeted antimicrobial therapy was categorized as initiation before SAB diagnosis, on the same day as SAB diagnosis, one day after diagnosis, or two or more days after diagnosis, with the day of blood culture collection used as the reference. Whether an infectious disease (ID) and clinical microbiology consultation was obtained within the first 24 hours was also recorded.

Data Collection

Data were retrospectively collected from electronic medical records, microbiology laboratory databases, infection control surveillance records, and pharmacy and antimicrobial utilization systems. The collected variables included demographic characteristics (age and sex); comorbidities (diabetes mellitus, chronic kidney disease, chronic obstructive pulmonary disease, malignancy, and neurological diseases); clinical findings [intensive care unit (ICU) admission, fever, chills, and signs of sepsis or septic shock]; laboratory parameters [white blood cell count, neutrophil-to-lymphocyte ratio (NLR), CRP, procalcitonin, and serum lactate levels]; microbiological characteristics (MRSA or MSSA status); and management-related variables (empirical and targeted antimicrobial therapy, early ID consultation, echocardiography, and source-control interventions).

Outcomes

The primary outcome was all-cause mortality within 28 days after the index blood culture. Secondary outcomes included in-hospital mortality, ICU admission, length of hospital stays, and the development of complications, including persistent bacteremia and endocarditis. Patients who remained alive at the end of the 28-day follow-up period, including those who died subsequently after day 28, were classified as 28-day survivors. Death occurring on day 28 was considered a 28-day mortality event; thus, the 28-day follow-up period was defined as inclusive of day 28, with day 0 corresponding to the date of the index blood culture.

Ethical Approval

Ethical approval was obtained from the University of Health Sciences Türkiye, Şişli Hamidiye Etfal Training and Research Hospital Clinical Research Ethics Committee of the Health Practice and Research Center (approval number: 3305; date: January 6, 2026). Because of the retrospective nature of the study, individual informed consent was not obtained. The study protocol was reviewed and approved by the ethics committee with a waiver of the informed consent requirement.

Statistical Analysis

Data distributions were assessed to determine the appropriate statistical tests. Categorical variables were summarized as numbers and percentages, whereas continuous variables were reported as mean $\pm$ standard deviation or median [interquartile range (IQR)], as appropriate. Comparisons between 28-day survivors and non-survivors were performed using the chi-square test or Fisher's exact test for categorical variables and the Wilcoxon rank-sum test for continuous variables.

Univariable logistic regression analyses were initially performed for all candidate variables to identify potential predictors of 28-day mortality. Variables associated with mortality at $p < 0.10$ in the univariable analyses, along with clinically relevant covariates selected a priori based on previous literature, were entered into the initial multivariable model. The final model was developed through manual model reduction without using automated forward, backward, or stepwise variable-selection procedures. Model refinement was based on adjusted effect estimates, likelihood ratio tests, assessment of multicollinearity, and clinical interpretability. Multicollinearity among predictors was evaluated using variance inflation factors. Model discrimination was assessed using the area under the receiver operating characteristic curve (AUC), with 95% confidence intervals (CIs) calculated using the DeLong method. Model calibration was evaluated using the Hosmer–Lemeshow goodness-of-fit test, calibration intercept and slope, and bootstrap-corrected calibration plots based on 1,000 bootstrap resamples. Overall model performance was further assessed using Akaike's Information Criterion (AIC), pseudo- R^2 statistics, the Brier score, and mean absolute calibration error. Potential clinical utility was evaluated using decision curve analysis (DCA) across a range of threshold probabilities. Results are presented as odds ratios (ORs) with 95% CIs, and a two-sided p value < 0.05 was considered statistically significant.

Statistical Software and Reporting

All statistical analyses were performed using R version 4.5.2 (R Foundation for Statistical Computing, Vienna, Austria) through RStudio/Posit Cloud. The gtsummary package was used to generate and report summary statistics and regression tables^[7].

Results

Demographic and Clinical Characteristics of the Study Population

A total of 151 patients diagnosed with SAB were included in the study. One patient was excluded from the 28-day mortality analysis because of missing follow-up data. Among the 150 patients with available 28-day outcome data, 59.3% ($n = 89$) were male, and the median age was 67 years (IQR, 55–78). Of these patients, 66.7% ($n = 100$) were admitted to general medical wards, whereas 33.3% ($n = 50$) were managed in the ICU.

The most common comorbidities among the 150 patients with available 28-day outcome data were hypertension (52.0%, $n = 78$) and diabetes mellitus (44.0%, $n = 66$), followed by chronic kidney disease (28.0%), coronary artery disease (24.0%), malignancy (21.3%), and neurological comorbidities (18.7%). Microbiological evaluation identified MRSA in 33.3% of patients ($n = 50$) and MSSA in 66.7% ($n = 100$).

During the study period, the overall mortality rate was 54.3% ($n = 82$), whereas 28-day mortality was 40.7% ($n = 61$ among the 150 patients with complete 28-day follow-up data). One additional patient was confirmed to have died but had an unknown time of death and was therefore excluded from the 28-day mortality analysis. For the prespecified 28-day endpoint, the 20 patients who died after day 28 were classified as 28-day survivors. Accordingly, the binary 28-day outcome comprised 89 28-day survivors and 61 28-day non-survivors.

At presentation, the most frequently reported clinical symptoms were chills (30.0%) and fever (28.0%). Less frequent symptoms included nausea and vomiting (14.7%), decreased oral intake (11.3%), and rash (3.3%). With respect to risk factors, 28.7% of patients had an intravascular catheter in place, 6.0% had a history of trauma, and intravenous drug use was identified in 2.0% of cases.

Laboratory evaluation showed a median white blood cell count of 11,675 cells/ μ L (IQR, 8,600–17,350) and a median NLR of 15.0 (IQR, 7.5–22.0). Among the inflammatory markers, the median CRP level was 160.5 mg/L (IQR, 71.8–235.8), the median PCT level was 1.7 ng/mL (IQR, 0.4–8.0), and the median serum lactate level was 2.0 mmol/L (IQR, 1.3–2.8).

Evaluation of infection sources showed that catheter-related infections were the most common source (21.3%), followed by skin and soft-tissue infections (13.3%) and pneumonia (9.3%). Bone and joint infections were identified in 2.7% of patients, whereas central nervous system (CNS) infections were among the least frequent sources, occurring in 2.0% ($n = 3$) of patients. Endocarditis was detected in 10.0% ($n = 4$) of the 40 patients for whom echocardiographic data were available. No identifiable infectious focus was found in 75 patients (50%), who were therefore classified as having primary bloodstream infection (Table 1).

Comparisons Between 28-Day Survivors and Non-survivors

Comparisons of 28-day survivors and non-survivors revealed several significant differences between the two groups. ICU admission was substantially more frequent among 28-day non-survivors than among 28-day survivors (60.7% vs. 14.6%, $p < 0.001$).

A significant difference was also observed in age between the groups. The median age was higher among 28-day non-survivors than among 28-day survivors [72 (IQR, 64–81) vs. 61 (IQR, 50–73) years, $p < 0.001$].

Regarding underlying comorbidities, malignancy was more frequent among 28-day non-survivors than among 28-day survivors (26.2% vs. 18.0%), although the difference did not reach statistical significance ($p = 0.2$). In contrast, neurological comorbidities were significantly more common among 28-

Table 1. Baseline demographic, clinical, microbiological, and treatment characteristics of 28-day survivors and non-survivors.

Characteristic	n	Overall n = 150 ¹	28-day survivors n = 89	28-day non-survivors n = 61	p value ²
Admission location	150				<0.001
General ward		100 (66.7%)	76 (85.4%)	24 (39.3%)	
ICU		50 (33.3%)	13 (14.6%)	37 (60.7%)	
Sex	150				>0.9
Female		61 (40.7%)	36 (40.4%)	25 (41.0%)	
Male		89 (59.3%)	53 (59.6%)	36 (59.0%)	
Age, years	150	67 (55, 78)	61 (50, 73)	72 (64, 81)	<0.001
Comorbidities					
Diabetes mellitus	150	66 (44.0%)	40 (44.9%)	26 (42.6%)	0.8
Hypertension	150	78 (52.0%)	45 (50.6%)	33 (54.1%)	0.7
Chronic kidney disease	150	42 (28.0%)	26 (29.2%)	16 (26.2%)	0.7
Coronary artery disease	150	36 (24.0%)	17 (19.1%)	19 (31.1%)	0.090
Heart failure	150	16 (10.7%)	8 (9.0%)	8 (13.1%)	0.4
Malignancy	150	32 (21.3%)	16 (18.0%)	16 (26.2%)	0.2
Chronic obstructive pulmonary disease	150	13 (8.7%)	9 (10.1%)	4 (6.6%)	0.4
Heart valve dysfunction	150	5 (3.3%)	3 (3.4%)	2 (3.3%)	>0.9
Neurological comorbidity	150	28 (18.7%)	11 (12.4%)	17 (27.9%)	0.017
History of trauma	150	9 (6.0%)	4 (4.5%)	5 (8.2%)	0.5
Intravascular catheter	150	43 (28.7%)	29 (32.6%)	14 (23.0%)	0.2
Intravenous drug use	150	3 (2.0%)	3 (3.4%)	0 (0.0%)	0.3
Clinical symptoms					
Fever	150	42 (28.0%)	33 (37.1%)	9 (14.8%)	0.003
Chills	150	45 (30.0%)	35 (39.3%)	10 (16.4%)	0.003
Vertebral/hip pain	150	10 (6.7%)	8 (9.0%)	2 (3.3%)	0.2
Decreased oral intake	150	17 (11.3%)	7 (7.9%)	10 (16.4%)	0.11
Nausea/vomiting	150	22 (14.7%)	16 (18.0%)	6 (9.8%)	0.2
Rash	150	5 (3.3%)	3 (3.4%)	2 (3.3%)	>0.9
Laboratory parameters					
WBC, cells/ μ L	150	11,675 (8,600, 17,350)	11,220 (8,300, 16,150)	13,010 (8,710, 19,500)	0.2
Neutrophils, %	150	86.7 (80.4, 91.3)	85.5 (78.1, 91.0)	88.0 (85.0, 91.8)	0.017
Lymphocytes, %	150	6.5 (4.0, 11.1)	7.6 (4.3, 12.3)	5.4 (3.4, 8.9)	0.040
NLR	149	15.0 (7.5, 22.0)	12.0 (6.0, 21.0)	17.2 (10.0, 30.0)	0.008
Lactate, mmol/L	145	2.0 (1.3, 2.8)	1.8 (1.2, 2.5)	2.5 (1.5, 3.4)	0.005
CRP, mg/L	150	160.5 (71.8, 235.8)	146.0 (63.1, 227.3)	186.2 (86.5, 258.0)	0.10
PCT, ng/mL	132	1.7 (0.4, 8.0)	1.4 (0.3, 10.9)	2.2 (0.7, 8.0)	0.5
Microbiological characteristics					
<i>Staphylococcus aureus</i> resistance	150				0.8
MRSA		50 (33.3%)	29 (32.6%)	21 (34.4%)	
MSSA		100 (66.7%)	60 (67.4%)	40 (65.6%)	
Source of bacteremia					
Catheter-related infection	150	32 (21.3%)	22 (24.7%)	10 (16.4%)	0.2
Skin and soft-tissue infection	150	20 (13.3%)	17 (19.1%)	3 (4.9%)	0.012

Table 1. Continued.

Characteristic	n	Overall n = 150 ¹	28-day survivors n = 89	28-day non-survivors n = 61	p value ²
Pneumonia	150	14 (9.3%)	5 (5.6%)	9 (14.8%)	0.059
CNS infection	150	3 (2.0%)	1 (1.1%)	2 (3.3%)	0.6
Bone and joint infection	150	4 (2.7%)	2 (2.2%)	2 (3.3%)	>0.9
Endocarditis	40	4 (10.0%)	3 (12.5%)	1 (6.3%)	0.6
Primary bloodstream infection	150	75 (50%)	41 (46.1%)	34 (55.7%)	0.3
Infection acquisition	150				0.007
Community-associated infection		37 (24.7%)	29 (32.6%)	8 (13.1%)	
Healthcare-associated infection		113 (75.3%)	60 (67.4%)	53 (86.9%)	
Treatment and management					
Appropriate empiric therapy within 24 h	150	101 (67.3%)	63 (70.8%)	38 (62.3%)	0.3
Persistent bacteremia	84	48 (57.1%)	29 (49.2%)	19 (76.0%)	0.023
Infectious disease consultation within the first 24 h	150	112 (74.7%)	73 (82.0%)	39 (63.9%)	0.012
Targeted antibiotic therapy	146				0.3
None		4 (2.7%)	2 (2.3%)	2 (3.3%)	
Before SAB diagnosis		19 (13.0%)	15 (17.4%)	4 (6.7%)	
Same day as SAB diagnosis		77 (52.7%)	46 (53.5%)	31 (51.7%)	
1 day after SAB diagnosis		25 (17.1%)	13 (15.1%)	12 (20.0%)	
≥2 days after SAB diagnosis		21 (14.4%)	10 (11.6%)	11 (18.3%)	
Source control within 72 h	85				0.007
No		48 (56.5%)	27 (46.6%)	21 (77.8%)	
Yes		37 (43.5%)	31 (53.4%)	6 (22.2%)	
Surgical source-control procedure	90				0.009
No procedure required		43 (47.8%)	21 (35.6%)	22 (71.0%)	
Drainage/operation		14 (15.6%)	11 (18.6%)	3 (9.7%)	
Catheter removal or replacement		14 (15.6%)	13 (22.0%)	1 (3.2%)	
Procedure indicated but not performed		19 (21.1%)	14 (23.7%)	5 (16.1%)	

¹n (%); median (Q1, Q3).

²Wilcoxon rank-sum test; Pearson's chi-squared test; Fisher's exact test, as appropriate.

Percentages for variables with missing data were calculated using available-case denominators. Patients who were alive at the end of the 28-day follow-up window, including those who subsequently died after day 28, were classified as 28-day survivors.

MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; ICU, intensive care unit; NLR, neutrophil-to-lymphocyte ratio; CRP, C-reactive protein; PCT, procalcitonin; IQR, interquartile range; COPD, chronic obstructive pulmonary disease; CNS, central nervous system; ID, infectious diseases.

day non-survivors than among survivors (27.9% vs. 12.4%, $p = 0.017$).

Analysis of clinical presentation showed that fever and chills were significantly more frequent among 28-day survivors. Fever was reported in 14.8% of 28-day non-survivors compared with 37.1% of 28-day survivors ($p = 0.003$). Similarly, chills were reported in 16.4% and 39.3% of the two groups, respectively ($p = 0.003$).

Comparison of laboratory parameters demonstrated a significantly higher NLR among 28-day non-survivors than among 28-day survivors [median, 17.2 (IQR, 10.0–30.0) vs. 12.0 (IQR, 6.0–21.0), $p = 0.008$]. Serum lactate levels were also

significantly higher among 28-day non-survivors [median, 2.5 (IQR, 1.5–3.4) vs. 1.8 (IQR, 1.2–2.5) mmol/L, $p = 0.005$].

When the mode of infection acquisition was examined, healthcare-associated SAB was significantly more frequent among 28-day non-survivors than among 28-day survivors (86.9% vs. 67.4%, $p = 0.007$). However, the mode of infection acquisition was not independently associated with mortality after multivariable adjustment.

Regarding treatment and management, receipt of appropriate empirical antibiotic therapy within the first 24 hours was not significantly associated with 28-day mortality (70.8% among 28-day survivors vs. 62.3% among 28-day non-survivors, p

= 0.3). In contrast, ID consultation within the first 24 hours was significantly more frequent among 28-day survivors than among non-survivors (82.0% vs. 63.9%, $p = 0.012$).

Source control was achieved more frequently among 28-day survivors than among 28-day non-survivors (53.4% vs. 22.2% among patients with available source-control data, $p = 0.007$). Persistent bacteremia, in contrast, was more common among 28-day non-survivors than among survivors (76.0% vs. 49.2% among patients with available follow-up blood culture data, $p = 0.023$).

Variables with $p < 0.10$ in the univariable analyses, together with clinically relevant variables identified a priori, were entered into the initial candidate multivariable model. The final model was subsequently developed through clinically guided manual model reduction, without using automated forward, backward, or stepwise variable-selection procedures.

Multivariable Logistic Regression Analysis for 28-Day Mortality

Among the 150 patients with available 28-day follow-up data, 61 (40.7%) died within 28 days. In the multivariable logistic regression analysis, increasing age (OR, 1.04; 95% CI, 1.00–1.09; $p = 0.050$), ICU admission (OR, 6.37; 95% CI, 1.85–24.2; $p = 0.004$), and higher serum lactate levels (OR, 1.55 per mmol/L increase; 95% CI, 1.08–2.56; $p = 0.044$) were independently associated with increased odds of 28-day mortality. Source control (OR, 0.38; 95% CI, 0.10–1.31; $p = 0.13$) and ID consultation within the first 24 hours (OR, 0.26; 95% CI, 0.05–1.10; $p = 0.071$) yielded protective effect estimates but did not reach conventional statistical significance (Table 2).

No evidence of problematic multicollinearity was identified, with all VIF values <1.1 . The final multivariable model

demonstrated good discrimination, with an AUC of 0.85 (95% CI, 0.75–0.95). Model fit was satisfactory (AIC, 82.1; McFadden pseudo- R^2 , 0.30; Nagelkerke R^2 , 0.44), while calibration analyses indicated excellent agreement between predicted and observed risks (Hosmer–Lemeshow $\chi^2 = 4.21$, $p = 0.84$; calibration intercept ≈ 0 ; calibration slope = 1.00). Bootstrap-corrected calibration curves demonstrated minimal optimism, with a mean absolute calibration error of 0.044. Furthermore, DCA demonstrated a positive net clinical benefit across a broad range of clinically relevant threshold probabilities, supporting the potential clinical utility of the model for risk stratification in patients with SAB (Figure 1).

Discussion

In the present study, the mortality burden among adults with SAB was higher than that reported in much of the contemporary literature. The overall mortality rate was 82/151 (54%), whereas 28-day mortality was 61/150 (41%). In contrast, a large meta-analysis by Bai et al., which evaluated approximately 500,000 patients across 341 studies and examined 30-year mortality trends in SAB, demonstrated a substantial decline in 28-day mortality during the post-2011 period (18%) compared with the pre-2001 era (31%). However, despite this improvement in early mortality, the same analysis found that reductions in longer-term outcomes, including 3-month and 1-year mortality, had not yet reached clinically meaningful levels. Compared with the post-2011 data, mortality in our cohort remained notably higher^[8]. Conversely, although the literature indicates that 30-day mortality in SAB generally ranges from approximately 15% to 31% across most series and has remained largely stable in recent years, mortality consistently increases with a greater proportion of critically ill patients and a higher comorbidity burden^[9]. In our cohort, the relatively high

Table 2. Univariable and multivariable analyses of factors associated with 28-day mortality.

Characteristic	Univariable				Multivariable		
	n	OR	95% CI	p value	OR	95% CI	p value
Age	150	1.04	1.02, 1.07	<0.001	1.04	1.00, 1.09	0.050
Lactate	145	1.42	1.14, 1.88	0.006	1.55	1.08, 2.56	0.044
Source control	85						
No		1.00	—		—	—	
Yes		0.25	0.08, 0.67	0.009	0.38	0.10, 1.31	0.13
ID consultation within the first 24 h	150						
No		1.00	—		—	—	
Yes		0.39	0.18, 0.82	0.014	0.26	0.05, 1.10	0.071
ICU admission	150	9.01	4.23, 20.3	<0.001	6.37	1.85, 24.2	0.004

Reference category: No. Odds ratios represent the odds of 28-day mortality. Candidate variables initially evaluated for multivariable modeling included age, malignancy, neurological comorbidity, ICU admission, infection acquisition, source control, NLR, lactate, and early infectious disease consultation. CI, confidence interval; OR, odds ratio; ICU, intensive care unit; NLR, neutrophil-to-lymphocyte ratio; ID, infectious disease.

Performance of the final 28-day mortality model

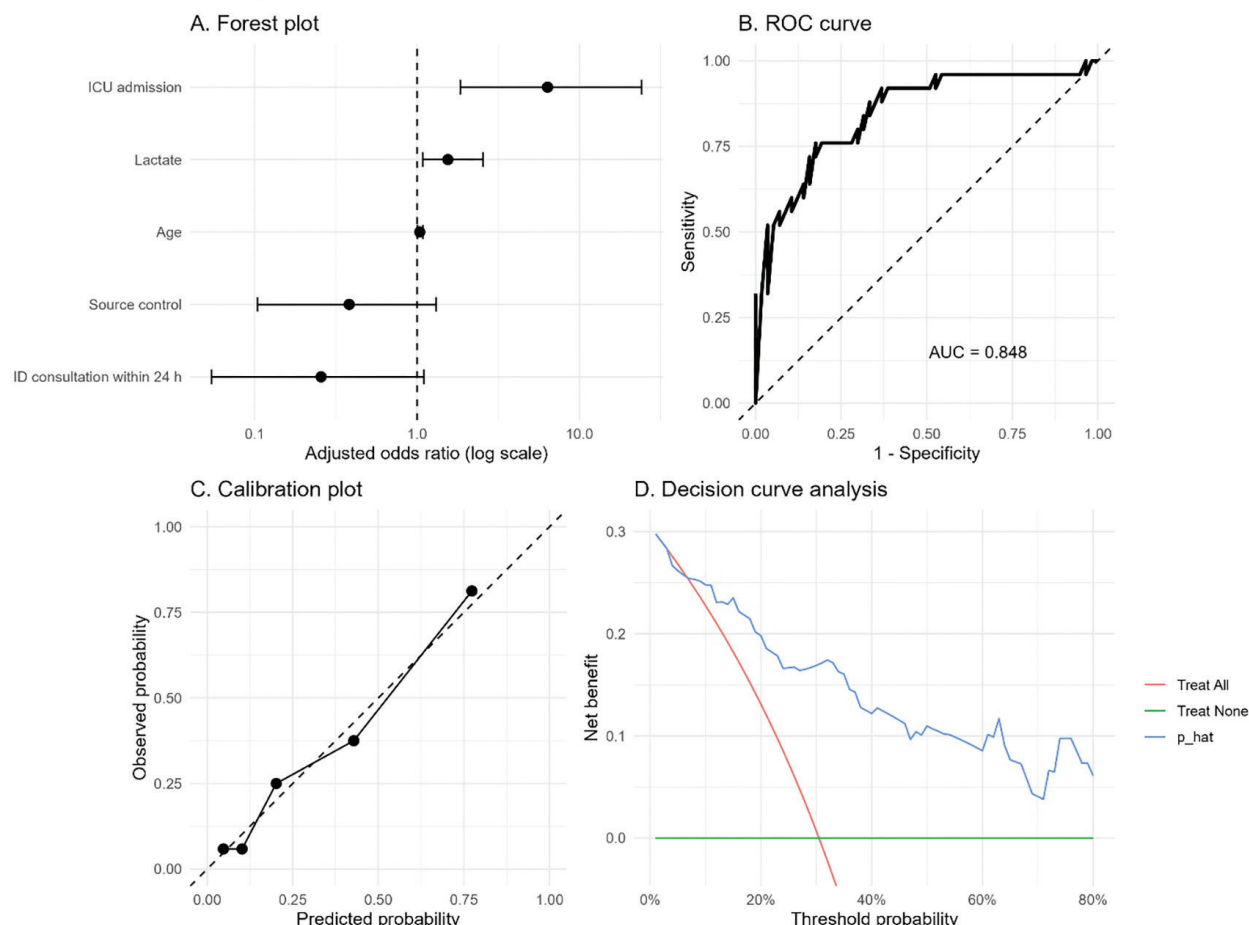


Figure 1. Performance of the final 28-day mortality model. (A) Forest plot of adjusted odds ratios from the multivariable model; (B) receiver operating characteristic (ROC) curve demonstrating an area under the curve (AUC) of 0.85; (C) calibration plot showing agreement between predicted and observed risks; and (D) decision curve analysis (DCA) demonstrating net clinical benefit across a range of threshold probabilities.

proportion of patients requiring ICU admission, together with the notable prevalence of conditions associated with increased vulnerability, such as malignancy, may help explain why the observed mortality rate approached the upper range reported in the literature. Regional differences may also contribute to variation in reported mortality rates. Despite recent improvements, when North America is used as a reference, the higher risk estimates reported from regions such as Europe and Asia suggest that mortality rates in these settings may remain above the global average^[9]. These findings underscore the continued need for research and structured programs aimed at improving the quality of care for SAB, which remains associated with substantial mortality.

In our study, age emerged as an important determinant of mortality, consistent with previous literature. Increasing age was associated with mortality in the univariable analyses, and this association remained independent in the 28-day mortality

model, with each additional year of age associated with an approximately 4% increase in the odds of mortality. Similarly, previous studies and meta-analyses have consistently identified increasing age as an important predictor of mortality in SAB^[10]. Advanced age increases the risk of mortality through several mechanisms, including immune system decline, reduced physiological reserve, and the accumulation of comorbid conditions^[10,11]. However, in a case-control study conducted by Tacconelli et al.^[12], mortality was higher among older patients despite otherwise comparable characteristics, including comorbid conditions, suggesting that advanced age may independently predict mortality irrespective of comorbidity burden.

The requirement for ICU admission, one of the strongest indicators of clinical severity, emerged as one of the strongest independent predictors of mortality in the final multivariable model among patients with SAB. ICU admission occurred in

60.7% of patients who died within 28 days compared with 14.6% of those who survived beyond 28 days, underscoring the important role of disease severity in determining early outcomes. This finding was also supported by the univariable analysis, in which ICU admission was associated with markedly increased odds of 28-day mortality, and by the multivariable analysis, in which it remained the strongest independent predictor. ICU admission has consistently been identified as one of the most robust predictors of mortality in SAB^[9]. In particular, among patients with SAB presenting with a septic clinical picture, the early development of hemodynamic instability and organ dysfunction contributes substantially to early mortality^[1].

In patients admitted to the ICU, infection is often at an advanced stage by the time of diagnosis, with delayed source control and an increased risk of persistent bacteremia, all of which are major contributors to adverse outcomes. Consistent with these findings, previous studies have demonstrated that sepsis and septic shock associated with SAB independently increase mortality and that survival is substantially reduced among patients requiring ICU admission^[4,13].

In light of these findings, the need for ICU admission in patients with SAB may serve as an early marker of increased mortality risk^[11].

In contrast to NLR, serum lactate remained independently associated with 28-day mortality in the final multivariable model, consistent with its established role as a marker of tissue hypoperfusion and sepsis severity. Elevated lactate reflects impaired tissue perfusion and mitochondrial dysfunction associated with sepsis-related organ dysfunction, and persistent lactate elevation is a well-established predictor of poor outcomes across diverse infectious etiologies. These findings support incorporating lactate, together with ICU admission and age, into early risk-stratification strategies for patients with SAB^[14].

In our cohort, source control was achieved more frequently among 28-day survivors than among 28-day non-survivors, supporting the concept that prognosis may depend less on the presence of an infectious source itself than on its early recognition and effective control^[15-17]. In the final multivariable model for 28-day mortality, source control showed a similarly protective point estimate but did not reach conventional statistical significance after adjustment for the other variables included in the model. Although statistical significance was not retained after adjustment, the consistent direction of the association suggests that source control may remain clinically relevant. This attenuation may reflect the reduced statistical power of the analytic sample ($n = 82$) because of missing source-control data, as well as residual confounding by disease

severity; patients who are too unstable to undergo source-control procedures may inherently have a higher risk of death regardless of the intervention.

ID consultation within the first 24 hours was more frequent among 28-day survivors than among 28-day non-survivors. In the final multivariable model, early ID consultation retained a protective effect estimate that approached but did not reach conventional statistical significance. Given the wide CI, this finding should be interpreted cautiously, particularly in the context of the reduced complete-case analytic sample. Nevertheless, the direction of the association is consistent with previous evidence indicating that ID consultation improves several components of SAB management^[18,19].

In our study, fever and chills were significantly more frequent among 28-day survivors than among 28-day non-survivors. These findings should not be interpreted as independent protective effects because fever and chills were not included as candidate variables in the multivariable model. Instead, their association with survival may reflect earlier recognition of infection, more prompt presentation for medical care, and timely initiation of diagnostic and therapeutic interventions.

Conversely, in vulnerable populations—particularly older patients, those with malignancy, and those requiring intensive care—SAB may present with attenuated or atypical symptoms, potentially resulting in diagnostic delays and poorer outcomes. Consistent with previous reports, the absence or blunted expression of fever has been associated with poorer prognosis in SAB, underscoring that the absence of fever or chills should not be considered a reassuring clinical feature in this setting^[1,4,9].

Although both the NLR and serum lactate levels were significantly higher among 28-day non-survivors than among 28-day survivors, these biomarkers diverged in the multivariable analysis. This finding may reflect their shared roles as early indicators of systemic inflammation and tissue hypoperfusion in SAB. Both NLR and lactate were evaluated as candidate variables; however, lactate was retained in the final model, whereas NLR was not. CRP and procalcitonin were not significantly different between 28-day survivors and non-survivors in the unadjusted analyses. Collectively, these biomarkers may function as intermediate indicators associated with the dominant clinical determinants of outcome, particularly disease severity and the need for intensive care.

Several variables, including neurological comorbidity, healthcare-associated acquisition, fever, chills, and NLR, differed significantly between 28-day survivors and non-survivors. Neurological comorbidity, healthcare-associated acquisition, and NLR were evaluated as candidate variables but were not retained in the final model, whereas fever

and chills were not entered as candidate variables. These findings suggest that their unadjusted associations may have been partly explained by stronger determinants, including advanced age, ICU admission, serum lactate levels, and overall disease severity. Accordingly, these variables may remain clinically relevant for initial risk assessment but should not be interpreted as independent predictors of early mortality after adjustment.

Malignancy was numerically more frequent among 28-day non-survivors than among 28-day survivors (26.2% vs. 18.0%), although this difference was not statistically significant. Although malignancy is a recognized marker of host vulnerability in SAB, our findings suggest that its association with early mortality was weaker than those of age, ICU requirement, and serum lactate in this cohort^[8,10].

Although male sex predominated in our cohort, sex was not associated with mortality. This finding is consistent with evidence suggesting that outcomes in SAB are driven primarily by disease severity, comorbidity burden, and modifiable processes of care rather than by biological sex alone. However, in an observational study of 1,293 patients with SAB conducted between 1988 and 2007, mortality was higher among women than among men; notably, this excess mortality could not be explained by differences in demographic characteristics, underlying conditions, infection severity, management strategies, or septic complications^[10]. Therefore, a definitive association between biological sex and mortality could not be established in our study.

Although MRSA accounted for 33% of cases in our cohort, MRSA status was not associated with mortality. Although several meta-analyses have reported a higher risk of mortality in MRSA bacteremia than in MSSA bacteremia, these findings are characterized by substantial heterogeneity^[20,21]. Our findings support the concept that antimicrobial resistance phenotype alone does not determine mortality; rather, outcomes appear to be driven primarily by host vulnerability, particularly advanced age, and by markers of severe disease and tissue hypoperfusion, including ICU admission and elevated serum lactate^[1].

In our study, healthcare-associated SAB was more frequent among 28-day non-survivors than among 28-day survivors. This finding is consistent with previous reports indicating that healthcare-associated SAB occurs more frequently among older patients and those with a greater burden of comorbidities and more severe clinical illness^[22]. Accordingly, infection acquisition was not retained as an independent predictor in the multivariable analysis after adjustment for age, ICU admission, lactate, and other clinically relevant variables. The close association of healthcare-associated infections with invasive

procedures, central venous catheters, and ICU admission may contribute to a more complex clinical context and poorer early outcomes. However, the lack of independent significance of infection origin in the multivariable analysis suggests that the adverse prognosis associated with healthcare-associated SAB may be driven less by the acquisition setting itself than by underlying host vulnerability and disease severity. These findings underscore the importance of interpreting infection origin in conjunction with clinical severity and management processes.

Risk factors such as the presence of intravascular catheters, a history of trauma, and intravenous drug use were observed in our cohort; however, catheter presence alone was not associated with mortality. The critical distinction lies not in the mere presence of a catheter but in whether the catheter represents the actual source of infection and whether timely removal and adequate source control are achieved^[17]. In our study, although catheter-related infections constituted a substantial proportion of cases, mortality appeared to be driven not by any single risk factor but by the overall severity of illness and the quality and timeliness of clinical management.

The distribution of infectious foci differed between the outcome groups. Skin and soft-tissue infections were more frequent among 28-day survivors, whereas pneumonia showed a non-significant trend toward greater frequency among 28-day non-survivors. Catheter-related infection and endocarditis were not significantly associated with 28-day mortality in the present cohort. Nevertheless, previous studies have demonstrated that endovascular and deep-seated infectious foci are clinically important because of their association with persistent bacteremia, metastatic complications, and adverse outcomes^[17,23].

Appropriate empirical antibiotic therapy within the first 24 hours was not significantly associated with 28-day mortality in our cohort. This finding should not be interpreted as evidence against the importance of timely, appropriate antimicrobial therapy^[24]. Rather, it suggests that early outcomes in SAB are influenced by multiple interacting factors, including disease severity, source control, and other components of clinical management.

Persistent bacteremia was significantly more frequent among 28-day non-survivors than among 28-day survivors (76.0% vs. 49.2%, $p = 0.023$). However, because follow-up blood culture data were unavailable for a substantial proportion of patients and persistent bacteremia is closely interrelated with source control and disease severity, it was not included in the final multivariable model. Previous studies have consistently demonstrated that persistent SAB is associated with complications, metastatic foci, and increased mortality^[3,25].

In this study, pathogen-directed antibiotic therapy did not emerge as an independent predictor of mortality. Its potential effect may have been attenuated in patients with inadequate source control, persistent bacteremia, or ICU requirement^[15,16].

From a clinical utility perspective, the final model demonstrated good discrimination (AUC, 0.85; 95% CI, 0.75–0.95) and excellent calibration, indicating close agreement between predicted and observed risks. DCA further demonstrated potential net clinical benefit across a broad range of threshold probabilities, supporting the potential applicability of the model for risk stratification in patients with SAB. The independently associated predictors—age, ICU admission, and serum lactate—are routinely available in clinical practice, while the model also incorporates source control and early ID consultation as clinically meaningful management-related variables. This combination supports pragmatic bedside interpretation while acknowledging the reduced complete-case sample used for the multivariable analysis.

Strengths of the Study

A major strength of this study is the comprehensive evaluation of clinical, laboratory, and management-related variables among patients with SAB. The use of 28-day mortality as the primary outcome enabled a focused assessment of early deaths, which represent a particularly critical period in the clinical course of SAB. The final multivariable model demonstrated good discrimination and calibration, while DCA indicated potential clinical utility across a broad range of threshold probabilities using variables that are routinely available in clinical practice.

In addition, the inclusion of directly modifiable process-of-care factors, such as ID consultation, source control, and the appropriateness of empirical therapy, enhances the practical relevance of the findings. Thus, the study extends beyond prognostic description by providing potentially actionable insights for improving clinical management. Although conducted at a single center, the study reflects real-world data from a University of Health Sciences Türkiye, Şişli Hamidiye Etfal Training and Research Hospital with a high proportion of critically ill patients, making the findings particularly relevant to similar high-acuity settings. Collectively, these strengths position the study as a meaningful contribution to the existing literature on SAB, particularly regarding the early identification of high-risk patients and the implementation of targeted intervention strategies.

Study Limitations

Several limitations of this study should be acknowledged. First, the retrospective design inherently limits causal inference and is susceptible to missing data arising from routine clinical documentation. In particular, the relatively high proportion

of missing data for source control, persistent bacteremia, and endocarditis limited the precision of analyses involving these variables. Source control was included in the final multivariable model, whereas persistent bacteremia and endocarditis were not included. Furthermore, the limited number of patients with documented endocarditis restricted our ability to fully assess the impact of this important complication on mortality. Because source control and other variables included in the model had missing observations, the final multivariable model for 28-day mortality was based on 82 patients with complete data for all variables included in the final model. This reduction in sample size limited statistical power and widened the CI around several estimates, particularly those for source control and ID consultation, and should be considered when interpreting the magnitude and precision of these associations.

Additionally, empirical and targeted antibiotic variables had to be simplified because of small sample sizes within certain subgroups, limiting a more detailed assessment of individual antimicrobial regimens. Finally, the single-center nature of the study may limit the generalizability of the findings. However, the advanced age and high comorbidity burden of the cohort may preserve their clinical relevance to tertiary-care and intensive care-oriented institutions.

Conclusion

Overall, these findings underscore that mortality in SAB reflects a complex interplay of host vulnerability, disease severity, and management-related factors rather than microbiological determinants alone. Advanced age, ICU admission, and elevated serum lactate emerged as the strongest independent predictors of 28-day mortality, whereas modifiable process-of-care factors, including timely source control and early ID consultation, demonstrated consistent protective trends. The fact that most deaths occurred within the first 28 days further underscores that SAB is a clinical condition requiring early, aggressive, and comprehensive management. In this context, implementing a standardized SAB management bundle that extends beyond antimicrobial therapy to incorporate early risk stratification, systematic source evaluation, and multidisciplinary follow-up may represent a rational strategy for reducing mortality.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the University of Health Sciences Türkiye, Şişli Hamidiye Etfal Training and Research Hospital Clinical Research Ethics Committee of the Health Practice and Research Center (approval number: 3305; date: January 6, 2026).

Informed Consent: Because of the retrospective nature of the study, individual informed consent was not obtained. The study protocol was reviewed and approved by the ethics committee with a waiver of the informed consent requirement.

Footnotes

Authorship Contributions

Surgical and Medical Practices: C.A.T., S.A., O.D., Ö.G., N.D.D., H.M.T., A.Ö., D.Y.S., İ.D., Concept: C.A.T., S.A., O.D., Ö.G., A.Ö., D.Y.S., B.B., İ.D., Design: C.A.T., Ö.G., N.D.D., H.M.T., A.Ö., D.Y.S., B.B., İ.D., Data Collection or Processing: C.A.T., S.A., H.M.T., B.B., Analysis or Interpretation: O.D., Literature Search: C.A.T., Ö.G., H.M.T., Writing: C.A.T., N.D.D.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

- Lam JC, Stokes W. The golden grapes of wrath - *Staphylococcus aureus* bacteremia: a clinical review. Am J Med. 2023;136(1):19-26
- Papadimitriou-Oliveris M, Caruana G, Senn L, Guery B. Predictors of mortality of *Staphylococcus aureus* bacteremia among patients hospitalized in a Swiss University Hospital and the role of early source control; a retrospective cohort study. Eur J Clin Microbiol Infect Dis. 2023;42(3):347-57.
- Minejima E, Mai N, Bui N, Mert M, Mack WJ, She RC, Nieberg P, Spellberg B, Wong-Beringer A. Defining the breakpoint duration of *Staphylococcus aureus* bacteremia predictive of poor outcomes. Clin Infect Dis. 2020;70(4):566-73.
- Kaasch AJ, Barlow G, Edgeworth JD, Fowler VG Jr, Hellmich M, Hopkins S, Kern WV, Llewelyn MJ, Rieg S, Rodriguez-Baño J, Scarborough M, Seifert H, Soriano A, Tilley R, Török ME, Weiß V, Wilson AP, Thwaites GE; ISAC, INSTINCT, SABG, UKCIRG, and Colleagues. *Staphylococcus aureus* bloodstream infection: a pooled analysis of five prospective, observational studies. J Infect. 2014;68(3):242-51. Erratum in: J Infect. 2014;69(3):306-7.
- Turner NA, Sharma-Kuinkel BK, Maskarinec SA, Eichenberger EM, Shah PP, Carugati M, Holland TL, Fowler VG Jr. Methicillin-resistant *Staphylococcus aureus*: an overview of basic and clinical research. Nat Rev Microbiol. 2019;17:203-18.
- Laupland KB, Lyytikäinen O, Søgaard M, Kennedy KJ, Knudsen JD, Ostergaard C, Galbraith JC, Valiquette L, Jacobsson G, Collignon P, Schønheyder HC; International Bacteremia Surveillance Collaborative. The changing epidemiology of *Staphylococcus aureus* bloodstream infection: a multinational population-based surveillance study. Clin Microbiol Infect. 2013;19(5):465-71.
- R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria | CiNii Research [Internet]. [cited 2026 Jan 22].
- Bai AD, Lo CKL, Komorowski AS, Suresh M, Guo K, Garg A, Tandon P, Senecal J, Del Corpo O, Stefanova I, Fogarty C, Butler-Laporte G, McDonald EG, Cheng MP, Morris AM, Loeb M, Lee TC. *Staphylococcus aureus* bacteraemia mortality: a systematic review and meta-analysis. Clin Microbiol Infect. 2022;28(8):1076-84.
- Willekens R, Puig-Asensio M, Suanzes P, Fernández-Hidalgo N, Larrosa MN, González-López JJ, Rodríguez-Pardo D, Pigrau C, Almirante B. Mortality in *Staphylococcus aureus* bacteraemia remains high despite adherence to quality indicators: secondary analysis of a prospective cohort study. J Infect. 2021;83(6):656-63.
- van Hal SJ, Jensen SO, Vaska VL, Espedido BA, Paterson DL, Gosbell IB. Predictors of mortality in *Staphylococcus aureus* Bacteremia. Clin Microbiol Rev. 2012;25(2):362-86.
- Yılmaz M, Elaldi N, Balkan İİ, Arslan F, Batirel AA, Bakıcı MZ, Gözel MG, Alkan S, Çelik AD, Yetkin MA, Bodur H, Sınırtaş M, Akalın H, Altay FA, Şencan İ, Azak E, Gündes S, Ceylan B, Öztürk R, Leblebicioglu H, Vahaboglu H, Mert A. Mortality predictors of *Staphylococcus aureus* bacteremia: a prospective multicenter study. Ann Clin Microbiol Antimicrob. 2016;15:7.
- Tacconelli E, Pop-Vicas AE, D'Agata EM. Increased mortality among elderly patients with methicillin-resistant *Staphylococcus aureus* bacteraemia. J Hosp Infect. 2006;64(3):251-6.
- Bai AD, Lo CKL, Komorowski AS, Suresh M, Guo K, Garg A, Tandon P, Senecal J, Del Corpo O, Stefanova I, Fogarty C, Butler-Laporte G, McDonald EG, Cheng MP, Morris AM, Loeb M, Lee TC. What Is the optimal follow-up length for mortality in *Staphylococcus aureus* bacteremia? observations from a systematic review of attributable mortality. Open Forum Infect Dis. 2022;9(5):ofac096.
- Özdemir Y, Aşkın Yılmaz İ, Serin Senger S, Çalık Ş. Clinical and laboratory predictors of mortality in *Staphylococcus aureus* bacteremia in a high-risk setting: a single-center retrospective analysis of Pitt score, SOFA, neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio. Ann Med. 2025;57(1):2573984.
- Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, Kaplan SL, Karchmer AW, Levine DP, Murray BE, J Rybak M, Talan DA, Chambers HF; Infectious Diseases Society of America. Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. Clin Infect Dis. 2011;52(3):e18-55. Erratum in: Clin Infect Dis. 2011;53(3):319.
- Holland TL, Arnold C, Fowler VG Jr. Clinical management of *Staphylococcus aureus* bacteremia: a review. JAMA. 2014;312(13):1330-41.
- Tong SYC, Fowler VG Jr, Skalla L, Holland TL. Management of *Staphylococcus aureus* Bacteremia: A Review. JAMA. 2025;334(9):798-808.
- Pragman AA, Kuskowski MA, Abraham JM, Filice GA. Infectious Disease consultation for *Staphylococcus aureus* bacteremia improves patient management and outcomes. Infect Dis Clin Pract (Baltim Md). 2012;20(4):261-7.
- Vogel M, Schmitz RP, Hagel S, Pletz MW, Gagelmann N, Scherag A, Schlattmann P, Brunkhorst FM. Infectious disease consultation for *Staphylococcus aureus* bacteremia - a systematic review and meta-analysis. J Infect. 2016;72:19-28.
- Adeiza SS, Aminul I. Meta-meta-analysis of the mortality risk associated with MRSA compared to MSSA bacteraemia. Infez Med. 2024;32(2):131-7.
- Cosgrove SE, Sakoulas G, Perencevich EN, Schwaber MJ, Karchmer AW, Carmeli Y. Comparison of mortality associated with methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* bacteremia: a meta-analysis. Clin Infect Dis. 2003;36(1):53-9.
- Lyytikäinen O, Ruotsalainen E, Järvinen A, Valttonen V, Ruutu P. Trends and outcome of nosocomial and community-acquired bloodstream infections due to *Staphylococcus aureus* in Finland, 1995-2001. Eur J Clin Microbiol Infect Dis. 2005;24(6):399-404.
- Asgeirsson H, Thalme A, Weiland O. *Staphylococcus aureus* bacteraemia and endocarditis - epidemiology and outcome: a review. Infect Dis (Lond). 2018;50(3):175-92.

24. Paul M, Kariv G, Goldberg E, Raskin M, Shaked H, Hazzan R, Samra Z, Paghis D, Bishara J, Leibovici L. Importance of appropriate empirical antibiotic therapy for methicillin-resistant *Staphylococcus aureus* bacteraemia. J Antimicrob Chemother. 2010;65(12):2658-65.
25. Kuehl R, Morata L, Boeing C, Subirana I, Seifert H, Rieg S, Kern WV, Kim HB, Kim ES, Liao CH, Tilley R, Lopez-Cortés LE, Llewelyn MJ, Fowler VG, Thwaites G, Cisneros JM, Scarborough M, Nsutebu E, Gurgui Ferrer M, Pérez JL, Barlow G, Hopkins S, Ternavasio-de la Vega HG, Török ME, Wilson P, Kaasch AJ, Soriano A; International *Staphylococcus aureus* collaboration study group and the ESCMID Study Group for Bloodstream Infections, Endocarditis and Sepsis. Defining persistent *Staphylococcus aureus* bacteraemia: secondary analysis of a prospective cohort study. Lancet Infect Dis. 2020;20(12):1409-17.