Predictors of 6-Month Mortality in *Staphylococcus aureus* Bacteremia: A Population-Based Study in Olmsted County, Minnesota, from 2006 to 2020

Joya-Rita Hindy, M.D.[1], Juan A. Quintero-Martinez, M.D.[1], Brian D. Lahr, M.S.[1], Daniel C. DeSimone, M.D.[1], Larry M. Baddour, M.D.[1]
[1]Mayo Clinic, Rochester, Minnesota, United States of America

Address: 200 First Street SW, Rochester, Minnesota, USA 55905

E-mail addresses: hindy.joya-rita@mayo.edu; quintero-Martinez.juan@mayo.edu; lahr.brian@mayo.edu; desimone.Daniel@mayo.edu; baddour.larry@mayo.edu

ABSTRACT

- **Background:** *Staphylococcus aureus* bacteremia (SAB) has high mortality, which is influenced by several factors related to the host-pathogen interaction. The current study aims to provide a contemporary evaluation of predictors of the 6-month mortality rate in a population-based cohort of incident SAB.
- **Methods:** We performed a retrospective population-based study of 541 adult residents of Olmsted County, MN with monomicrobial SAB from January 1, 2006, through December 31, 2020. The study's primary outcome was the 6-month mortality rate; a survival analysis was prepared by the Kaplan-Meier method. Multivariable Cox regression was used to investigate risk factors associated with 6-month mortality.
- **Results:** The median (interquartile range [IQR]) age of 541 patients with SAB was 66.8 (54.4-78.5) years and 39.6% were female. The median (IQR) Charlson Comorbidity Index was 6 (3-9). Overall, 144 patients died during the six-month period following their initial episode (30-day and 6-month mortality = 16.5% and 26.7%, respectively). In a multivariable analysis, older age, ICU admission, and unknown source of infection were significant predictors of increased 6-month mortality. In contrast, having an infectious diseases (ID) consultation was associated with reduced mortality in the first 2 weeks of follow-up. Secondary analyses revealed the early benefit of ID consultation extended to the first 30 days, and that infective endocarditis as a source of infection was an additional predictor of 6-month mortality.
- **Conclusions:** To our knowledge, this investigation represents the only US population-based study evaluating predictors of mortality in SAB patients. The finding of a short-term survival benefit associated with ID consultation may relate to increased diagnostic evaluation.

INTRODUCTION

- Incidence of *Staphylococcus aureus* bacteremia (SAB) varies between geographical regions, reflecting differences in infection control practices, health care delivery, and data surveillance in different countries.
- 30-day mortality in SAB patients remains as high as 30% despite good adherence to quality indicators for the clinical management of SAB.

METHODS

- The Rochester Epidemiological Project is a large unified information system linking the medical records of Olmsted County MN residents since 1966, allowing a unique resource for population-based research.
- Electronic health records of all patients with SAB were manually reviewed for abstraction of demographic, clinical and outcome data.
- Primary outcome: 6-month all-cause mortality.
- Secondary outcomes: hospital length of stay, in-hospital and 30-day mortality, and re-infection (relapse within 12 weeks or recurrence after 12 weeks.
- Survival analysis was by Kaplan-Meier and Cox regression methods.
- A multivariable Cox model was used to investigate risk factors associated with 6-month mortality.
  - 11 candidate risk factors chosen according to clinical relevance and published research.
  - Hazard ratios (HRs) describe the magnitude and direction of association for each factor.

RESULTS

- 541 incident cases of monomicrobial SAB identified from January 1, 2006, and December 31, 2020, from Mayo Clinic and Olmsted Medical Center (Tables 1-2).
- An age- and sex-adjusted incidence rate of SAB of 33.9 (95% CI, 31.0-36.8) cases per 100,000 person-years.
- Six-month mortality rate was 26.7% (Figure 1).
- Older age, ICU admission, and unknown source of infection were significant predictors of increased 6-month mortality (Table 3).

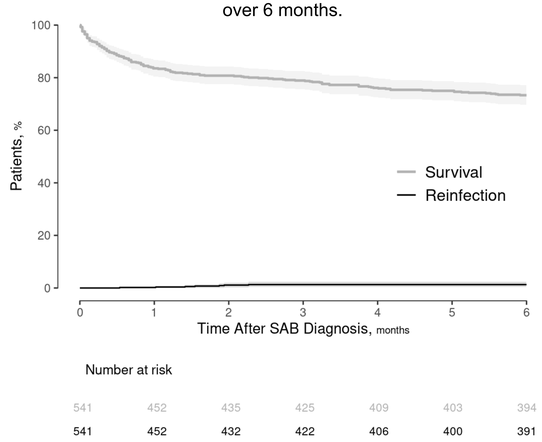
RESULTS

Table 1. Baseline characteristics of SAB patients.

Characteristic	Overall (N=541)
Age (Years)	66.8 (54.4-78.5)
Sex: Female	214 (39.6%)
Diabetes Mellitus	249 (46.0%)
Liver Disease	156 (28.8%)
Chronic Kidney Disease	
No	322 (59.5%)
Yes, Without HD	168 (31.1%)
Yes, With HD	51 (9.4%)
Charlson Comorbidity Index	6 (3-9)
Source Of SAB	
Unknown	108 (20.0%)
SSTI	203 (37.5%)
Pneumonia	70 (12.9%)
Catheter Related	67 (12.4%)
Septic Arthritis	52 (9.6%)
Foley Catheter Associated UTI	43 (7.9%)
Osteomyelitis	42 (7.8%)
Endocarditis	27 (5.0%)
Site of Infection Onset	
Healthcare-associated	265 (49.2%)
Community-acquired	217 (40.3%)
Nosocomial	57 (10.6%)
MRSA	232 (43.8%)
Hospitalization	532 (98.3%)
ICU Admission	144 (26.7%)
ID Consult	424 (78.5%)

Values are median and interquartile range for continuous variables.

Figure 1. Survival and reinfection rates of patients with SAB over 6 months.



RESULTS

Table 2. Outcomes in SAB patients.

Outcome	Overall (N=541)
Complicated Bacteremia	202 (37.4%)
Deep-seated Abscess	49 (9.1%)
Septic Arthritis	47 (8.7%)
Non-vertebral Osteomyelitis	40 (7.4%)
Infective Endocarditis	39 (7.2%)
Pneumonitis	30 (5.6%)
Vertebral Osteomyelitis	30 (5.6%)
Septic Emboli	16 (3.0%)
Altered Mental Status	11 (2.0%)
Epidural Abscess	9 (1.7%)
Cerebral Abscess	5 (0.9%)
Psoas Abscess	4 (0.7%)
Stroke	4 (0.7%)
Splenic Abscess	3 (0.6%)
Meningitis	2 (0.4%)
Renal Abscess	2 (0.4%)
Liver Abscess	0 (0.0%)
Cerebral Hemorrhage	0 (0.0%)
Hospital Length of Stay (Days)	10 (6-19)
In-hospital Mortality	59 (11.2%)
6-month Mortality	144 (26.7%)

Values are median and interquartile range for continuous variables.

Table 3. Predictors of 6-month mortality in SAB patients.

Predictor	Comparison	HR (95% CI)	P
Age	78.5 Years vs. 54.4 Years	3.53 (2.57 - 4.85)	<0.001
Sex	Female vs. Male	0.77 (0.55 - 1.08)	0.125
Diabetes Mellitus	Yes vs. No	0.71 (0.49 - 1.04)	0.083
Liver Disease	Yes vs. No	1.13 (0.75 - 1.70)	0.569
Chronic Kidney Disease			0.237
	Yes, Without HD vs. No	1.36 (0.91 - 2.03)	
	Yes, With HD vs. No	1.53 (0.79 - 2.97)	
Charlson Comorbidity Index	9 vs. 3	1.21 (0.89 - 1.64)	0.392
Source of SAB	Unknown vs. Known	1.58 (1.09 - 2.29)	0.015
Site of Infection Onset			0.610
	HA vs. Nosocomial	1.29 (0.78 - 2.14)	
	CA vs. Nosocomial	1.08 (0.74 - 1.57)	
Type of SAB	MRSA vs. MSSA	0.79 (0.56 - 1.12)	0.189
ICU Admission	Yes vs. No	2.38 (1.69 - 3.36)	<0.001
ID Consult	Yes vs. No; Phase = Early	0.30 (0.17 - 0.50)	<0.001
	Yes vs. No; Phase = Late	0.90 (0.51 - 1.59)	0.715

CONCLUSIONS

- The current contemporary investigation is the only US population-based study evaluating predictors of mortality in SAB patients.
- Older age, ICU admission, and unknown source of infection were significant predictors of increased 6-month mortality.
- Short-term survival benefit was associated with early ID consultation reflecting potential improvement due to diagnostic efforts.