Staphylococcus aureus Bloodstream Infections in Older Adults: Clinical Outcomes and Risk Factors for In-Hospital Mortality

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OBJECTIVES: To assess clinical outcomes and identify risk factors for mortality in older adults with *Staphylococcus aureus* bloodstream infection (SAB).

DESIGN: Retrospective review.

SETTING: University of Michigan Health System, Ann Arbor.

PARTICIPANTS: All patients aged 80 and older with SAB between January 2004 and July 2008.

MEASUREMENTS: Clinical data, including comorbid conditions, SAB source, echocardiography results, Charlson Comorbidity Index, mortality (in-hospital and 6-month), and need for rehospitalization or chronic care after discharge.

RESULTS: Seventy-six patients aged 80 and older (mean 85.5 ± 4.2) with SAB were identified. Infection sources included 14 (18.4%) vascular catheter associated, 16 (21.1%) wound related, seven (9.2%) endocarditis, five (6.6%) intravascular, and 19 (25%) with unknown source; 46 (60.5%) patients had methicillin-resistant strains. Twenty-two (28.9%) patients underwent surgery or device placement within 30 days of developing SAB; 10 of these 22 had SAB associated with surgical site infection (SSI). Twenty two (28.9%) patients died in the hospital or were discharged to hospice care; at least 43 (56.6%) patients died within 6 months of presentation, and eight were lost to follow-up. Unknown source of bacteremia (odds ratio = 5.2, $P = .008$) was independently associated with in-hospital death. Echocardiography was not pursued in 45% of patients. Of surviving patients, 40 (74.1%) required skilled care after discharge; eight (20%) required rehospitalization.

CONCLUSION: SAB was associated with high mortality rates in patients aged 80 and older. The observed association between SAB and SSI may direct preventive strategies such as perioperative decolonization or antimicrobial prophylaxis. Interventions to optimize clinical care practices in elderly patients with SAB are essential given the associated morbidity and mortality. **J Am Geriatr Soc 58:300–305, 2010.**

Key words: *S. aureus*; **aging; bloodstream infections**

The continued expansion of the geriatric population has been associated with an increase in the number of serious infections in older adults, including bloodstream infections.[1–4] *Staphylococcus aureus* bloodstream infection (SAB) represents a significant burden in terms of morbidity and mortality for older adults. Major risk factors associated with the development of SAB includes the presence of comorbid illnesses, such as congestive heart failure, chronic kidney disease, and diabetes mellitus, and the use of medical devices.[5–10] The overall rates of SAB also increase with age, as does mortality and attributable mortality, which is twice as high in patients aged 65 and older as in younger patients.[5,8,9]

Recent work has suggested that the odds of death within 6 months of SAB doubles for every decade increase in age, and four of seven (57%) patients aged 80 older died within 6 months.[5] Based on these observations, it was decided to specifically review the records of a different and larger cohort of older patients (≥80) to better define risk factors for mortality and identify potential areas for intervention. The clinical course of SAB in the oldest old (≥80) and risk factors for in-hospital mortality were examined.

METHODS

Overall Research Design

A retrospective study was conducted of all patients aged 80 and older with SAB who were admitted to the University of Michigan Health System (UMHS) from January 2004 to July 2008. Patients were identified by review of a database maintained by the UMHS Microbiology Laboratory. SAB

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was defined as any blood culture positive for *S. aureus* with an appropriate clinical presentation. Source of SAB infection was determined through review of the medical record by an attending infectious diseases physician. Review of infectious diseases consultation reports corroborated this determination when applicable.

Baseline demographic information, clinical conditions, and the source of infection were recorded. Physical and occupational therapy reports were also reviewed to gather limited information on mobility and level of independence with activities of daily living (ADLs). In addition, comorbidity was measured using the Charlson weighted index of comorbidity (WIC).[11] In-hospital mortality included patients who died during their initial admission and those who were discharged to hospice care and died within 1 to 2 days. The institutional review board of the University of Michigan Healthcare System approved this study.

Data Analysis

Univariate and bivariate analysis using *t*-tests for continuous variables and chi-square or Fisher exact tests for categorical variables identified risk factors for death in patients with SAB. A two-tailed *P*-value of .05 or less was considered statistically significant. Crude odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for categorical variables. Crude ORs for continuous variables were obtained using simple logistic regression. Variables that were significant to a *P*-value of .20 and variables that had a priori clinical significance were then analyzed using multivariate logistic regression modeling. All statistical analysis was performed using SAS 9.1 (SAS Institute, Inc., Cary, NC).

RESULTS

Patient Characteristics and Sources of Infection

Characteristics of patients with SAB are listed in Table 1. Seventy-six patients aged 80 and older (mean 85.5 ± 4.2, range 80–99) were identified; 48 patients were male (63.2%). Common medical comorbidities included hypertension (71.1%), coronary artery disease (65.8%), and diabetes mellitus (34.2%).

The most common sources of SAB were wound related (21.1%), osteomyelitis (21.1%), vascular catheter associated (18.4%), and endocarditis (9.2%); 25.0% of patients had no clear source identified. Forty-six episodes of SAB (60.5%) were secondary to methicillin-resistant *S. aureus* (MRSA); the remaining 30 (39.5%) were secondary to methicillin-sensitive *S. aureus* (MSSA). Six patients (8.6%) developed *Clostridium difficile* infection during treatment for SAB. Eight patients required rehospitalization after initial discharge; in four cases, the reason for rehospitalization was recurrent SAB. Recurrent or relapsed SAB was observed in five (6.6%) patients overall.

Of the 76 patients, 56 (73.7%) had SAB at the time of admission. The remaining 20 (26.3%) patients acquired SAB during hospitalization for another medical or surgical issue. Mortality did not differ between these groups, ($P = .49$). Sixty-nine patients (90.8%) received an initial antimicrobial course that appropriately covered the infecting organism: MSSA or MRSA. Of the portion who received treatment with vancomycin, all achieved trough levels that measured 10 μg/mL or greater within three to four doses. Incorrect antimicrobial selection was not associated with mortality in this cohort; only one of the seven patients who did not receive appropriate initial therapy died in the hospital ($P = .42$).

Table 1. Underlying Conditions and Clinical Characteristics for 76 Patients Aged ≥80 with *Staphylococcus aureus* Bloodstream

Characteristic	Value
Age, mean ± SD	85.5 ± 4
Male, n (%)	48 (63.2)
Comorbidities, n (%)	
Hypertension	54 (71.1)
Coronary artery disease	50 (65.8)
Congestive heart failure	27 (35.6)
Diabetes mellitus	26 (34.2)
Chronic renal insufficiency	21 (27.6)
Hemodialysis	12 (15.8)
Malignancy	17 (22.4)
Stroke	16 (21.1)
Hospitalization within past month, n (%)	37 (48.7)
Surgery or device placement within past 30 days, n (%)	22 (31.4)
Enteral feeding, n (%)	13 (17.1)
Charlson weighted index score, mean ± SD	3.2 ± 2.3
Methicillin-resistant *Staphylococcus aureus*, n (%)	46 (60.5)
Methicillin-sensitive *Staphylococcus aureus*, n (%)	30 (39.5)
Clostridium difficile infection, n (%)	6 (8.6)
No echocardiogram obtained, n (%)*	34 (44.7)
Source of infection, n (%)	
Vascular catheter associated	14 (18.4)
Wound related	16 (21.1)
Osteomyelitis (bone or joint)	16 (21.1)
Endocarditis	7 (9.2)
Intravascular infection	5 (6.6)
Respiratory tract	6 (7.9)
Genitourinary tract	3 (3.9)
Source unknown	19 (25)
Other	4 (5.3)

* Neither transesophageal or transthoracic echo.
SD = standard deviation.

Association with Devices and Recent Surgery

Twenty patients had central vascular catheters (n = 14) or cardiac devices (n = 6) in place at the time SAB developed. All 14 central catheters were removed or changed within 1 to 3 days from the initial identification of positive blood cultures. Four patients with cardiac devices did not have the devices removed. Two patients with pacemakers were transitioned to hospice care because of a poor overall prognosis. Two others with automatic implantable cardioverter defibrillators received intravenous antibiotic therapy in an attempt to suppress infection. Both experienced relapse of SAB; one died during his second episode of infection, and the other was lost to follow-up at 6 months.

Twenty-two patients (31.4%) underwent surgery or placement of permanent medical devices during the 30 days before SAB; in 10 (45.4%) of the 22, the source of SAB appeared to be associated with the surgical procedure.[12] Specific procedures included coronary artery bypass grafting (n = 2), lumbar laminectomy (n = 3), hip arthroplasty (n = 1), prostatectomy (n = 1), and upper extremity dialysis graft placement (n = 1) (Table 2). Seven of the 10 (70.0%) patients with SSI associated SAB died within 6 months of presentation.

Pre- and Posthospitalization Living Situation

Of the 76 patients, 46 (60.5%) lived in the community and eight (10.5%) in an assisted living facility before admission. The remaining 22 (28.9%) were admitted from an extended care setting, where they were receiving chronic or subacute care. Of the 46 patients who lived in the community before developing SAB, 35 survived to discharge; 21 of the 35 (60.0%) were discharged to an extended care facility for subacute rehabilitation. For all patients, the need for subacute rehabilitation was slightly higher, with 40 (74.1%) of 54 patients who survived hospitalization requiring such care after discharge. Primary reasons for subacute care included impaired mobility, poor nutrition, wound care, and the need for extended courses of parenteral antimicrobial therapy.

Limited information on patients' mobility was collected through review of inpatient physical and occupational therapy assessments. Of the 54 survivors, 41 (75.9%) had a level of independence with ADLs at discharge similar to that at their pre-illness baseline. The other 13 (24.1%) had a decline in functional status and mobility. At baseline, all 13 of these patients were independent with ADLs and able to ambulate unassisted before admission, but upon discharge, these individuals were bedbound or required maximal assistance to transfer from bed to wheelchair. No association was observed between baseline functional status (independent vs need for assistance with ADLs) and in-hospital mortality ($P = .45$).

Table 2. Patients with *Staphylococcus aureus* Bacteremia (SAB) Associated with Surgical Site Infections (N = 10)

Age/Sex	Surgery or Procedure	SAB Source and Infecting Organism*	Time from Procedure to Detection of SAB	Treatment and Outcome
83/F	Revision of arteriovenous graft	Graft infection MSSA	4 weeks	Died of sepsis before completing planned 6-week course of IV vancomycin
87/M	Prostatectomy	Paraspinal abscess L4-L5, psoas abscess MRSA	2 weeks	Successfully treated with 8 weeks of IV vancomycin
86/M	Suprapubic urinary catheter placement	Catheter-associated abscess/wound MRSA	4 weeks	Catheter retained, patient treated with 2-week course of IV vancomycin followed by oral trimethoprim and sulfamethoxazole for chronic suppression; patient transitioned to hospice care because of advanced dementia and died soon afterward
85/F	Left hip arthroplasty	Prosthetic joint infection MRSA	4 weeks	Incision and drainage of hip, removal of prosthesis, placement of spacer along with IV vancomycin; mechanical fall and development of hemarthrosis complicated course; patient died of MRSA sepsis before completing planned 6-week course of IV therapy
85/M	Coronary artery bypass grafting	Mediastinitis, sternal osteomyelitis MRSA	1 week	Patient treated with 8-week course of vancomycin and quinupristin/dalfopristin along with operative debridement and flap coverage of sternal wound; remained on chronic suppression with oral trimethoprim/sulfamethoxazole
80/M	Redo coronary artery bypass grafting	Infected thoracotomy wound MSSA	3 weeks	Patient treated with 4 weeks of IV cefazolin, local wound care; lost to follow-up
80/M	T11-S1 posterior spinal fusion	Infected spinal wound MSSA	2 weeks	Infection successfully treated after multiple operative debridements and 6 weeks of IV cefazolin
83/M	Lumbar laminectomy L3-L4, L4-L5	Lumbar wound MRSA	2 weeks	Developed postoperative sepsis associated with lumbar wound; died within 24 hours of the infection being identified, before operative drainage
84/F	Hepatic lobectomy for resection of intrahepatic cholangiocarcinoma	Abdominal wall abscess MRSA	3 weeks	Infection treated with IV vancomycin; died from complications associated with cholangiocarcinoma
83/M	Lumbar laminectomy, L4-S1	Spinal abscess associated with laminectomy wound; SAB resulted in prosthetic aortic valve endocarditis MRSA	2 weeks	Laminectomy wound treated with multiple operative debridements to drain spinal abscess along with IV vancomycin; died with home hospice care secondary to congestive heart failure related to destruction of prosthetic aortic value

* MSSA = methicillin-sensitive *Staphylococcus aureus*; IV = intravenous; MRSA = methicillin-resistant *Staphylococcus aureus*.

Risk Factors for Mortality

Twenty-two of the 76 patients (28.9%) died in the hospital or were discharged home to hospice care and died within a few days. Bivariate analysis identified several patient characteristics associated with in-hospital mortality, including unknown source of bacteremia, lack of echocardiography evaluation, acute renal insufficiency, and high Charlson WIC (Table 3). By 6 months after initial presentation, an additional 21 patients died, so least 43 of 76 patients (56.6%) died; eight patients were lost to follow-up.

Unknown cause of infection remained independently associated with in-hospital mortality based on multivariate analysis, (adjusted OR = 3.7, $P = .05$) (Table 3). Patients with unknown cause of infection had a shorter duration of bacteremia than patients with an identifiable source (1.4 ± 0.8 days vs 4.1 ± 6.0 days, $P = .05$). Of the 19 patients with unknown cause of BSI, 11 died in the hospital or within a few days of being discharged to hospice care. Another three patients died between discharge and 6 months; only five (26.3%) remained alive at 6 months.

DISCUSSION

The preceding results provide further evidence that SAB results in substantial mortality in older adults. This patient population experienced 28.9% in-hospital and at least 56.6% 6-month mortality. Risk factors for death included unknown source of bacteremia, lack of echocardiography evaluation, acute renal insufficiency, and high Charlson WIC (Table 3). Unknown source of infection remained independently associated with in-hospital mortality on multivariable analysis (Table 4).

The reasons for the association between unknown cause of bacteremia and in-hospital mortality remains unclear. One possible explanation is that extensive diagnostic efforts to identify a source were not pursued, and therefore a source was not identified. Review of patient records suggests that this was the case for some of the patients with unknown source because clinicians caring for these individuals documented that the overall prognosis was poor. Several patients with unknown source of infection died soon after admission or were quickly discharged to hospice care. Review of the medical chart suggests that aggressive medical examination was not pursued in part because of a presumed poor prognosis. The duration of bacteremia was shorter in patients with unknown source than in patients with an identifiable source (1.4 ± 0.8 days vs 4.1 ± 6.0 days, $P = .05$). This finding probably reflects that several patients with unknown source died soon after admission or were discharged to hospice care—so these patients did not have an opportunity to have extended bacteremia.

Of the 19 patients with unknown source, 14 did not have echocardiography evaluation. The lack of echocardiography may have confounded these results, because several patients with unknown source could have had occult endocarditis, an infection associated with higher mortality than simple SAB, particularly in older adults.[13,14] Ten (52.6%) of the 19 patients with unknown source were community

Table 3. Bivariate Analysis of the Effect of Patient Characteristics on In-Hospital Mortality from *Staphylococcus aureus* Bloodstream Infections in Patients Aged ≥80 (N = 76)

Characteristic	Survived to Discharge (n = 54)	Died in Hospital (n = 22)	Unadjusted Odds Ratio (95% Confidence Interval)	*P*-Value
Age, mean ± SD	85.7 ± 4.2	85.1 ± 4.1	1.0 (0.85–1.1)	.58
Charlson index, mean ± SD	2.8 ± 1.9	4.1 ± 2.7	1.3 (1.03–1.6)	**.03**
Number of blood culture days positive, mean ± SD	3.7 ± 5.9	2.7 ± 3.3	1.0 (0.85–1.1)	.48
Methicillin-resistant *Staphylococcus aureus*, n (%)	30 (55.6)	16 (72.7)	2.1 (0.7–6.3)	.16
Echocardiogram not done, n (%)*	19 (35.2)	15 (68.2)	3.9 (1.4–11.4)	**.008**
Coronary Artery Disease, n (%)	36 (66.7)	14 (63.6)	0.9 (0.3–2.5)	.80
Congestive heart failure, n (%)	16 (29.6)	11 (50)	2.4 (0.9–6.6)	.09
Stroke, n (%)	9 (16.7)	7 (31.8)	2.3 (0.7–7.3)	.14
Diabetes mellitus, n (%)	18 (33.3)	8 (36.4)	1.1 (0.4–3.2)	.80
Acute renal insufficiency, n (%)	20 (37.0)	14 (63.6)	2.9 (1.1–8.3)	**.03**
Chronic renal insufficiency, n (%)	13 (24.1)	8 (36.4)	1.8 (0.6–5.3)	.28
Hemodialysis, n (%)	9 (16.7)	3 (13.6)	0.8 (0.2–3.2)	0.99
Enteral feeding, n (%)	8 (14.8)	5 (22.7)	1.7 (0.5–5.9)	.50
Prior hospitalization, n (%)	24 (44.4)	13 (59.1)	1.8 (0.7–4.9)	.25
Prior surgery, n (%)	15 (27.8)	7 (31.8)	1.2 (0.4–3.6)	0.72
Catheter associated, n (%)	11 (20.4)	3 (13.6)	0.6 (0.2–2.5)	.75
Endocarditis, n (%)	5 (9.3)	2 (9.1)	0.9 (0.2–5.5)	0.99
Intravascular infection, n (%)	4 (7.4)	1(4.5)	0.6 (0.1–5.6)	0.99
Wound related, n (%)	11 (20.4)	5 (22.7)	1.1 (0.3–3.8)	0.99
Unknown source, n (%)	8 (14.8)	11 (50)	5.8 (1.9–17.7)	**.001**
Respiratory tract, n (%)	6 (11.1)	0 (0.0)	0.7 (0.6–0.8)	.17

* Neither transesophageal nor transthoracic echocardiogram obtained.

SD = standard deviation.

Table 4. Multivariate Analysis of the Association Between Select Patient Characteristics and In-Hospital Mortality in Patients Aged ≥80 with *Staphylococcus aureus* Bloodstream Infections

Characteristic	OR (95% CI) *P*-Value	
	Unadjusted	Adjusted
MRSA	2.1 (0.7–6.3) .16	2.1 (0.6–7.2) .22
Unknown cause infection	5.8 (1.9–17.7) .001	5.2 (1.5–18.0) .008
Acute renal insufficiency	2.9 (1.1–8.3) .03	1.7 (0.5–5.7) .37
Charlson weighted index	1.3 (1.03–1.6) .03	1.2 (1.0–1.6) .10

Odds ratios (ORs) and 95% confidence intervals (CIs) are based on a multivariable logistic regression adjusting for methicillin-resistant *S. aureus* (MRSA), infection from unknown cause, acute renal insufficiency, and Charlson weighted index of comorbidity.

dwelling before admission, which probably increases the possibility of occult endocarditis.[13,14] The microbiology in patients with unknown source did not differ from the overall cohort; 12 (63.2%) of the 19 had MRSA (vs 60.5% overall). Regardless of possible misclassification bias, the observed association between unknown source of SAB and greater mortality warrants further investigation in larger, prospective studies.

Perhaps more importantly, the diagnostic approach to older adults with SAB should be examined critically. Forty-five percent of patients did not undergo any type of echocardiography in the setting of SAB. In general, transesophageal echocardiography (TEE) is recommended for patients with any blood culture positive for *S. aureus* to excluded occult endocarditis,[15] but TEE is an invasive procedure that requires sedation, anesthesia, or both, and some clinicians may have perceived this testing as too aggressive in this older cohort, particularly for patients who were felt to have a poor prognosis overall. Alternatively, clinicians may have had similar feelings in patients with short durations of SAB with a clearly identifiable source. Both of these scenarios were noted in the patients who did not receive TEEs. Low rates of transthoracic echo testing, which unlike TEE, is a noninvasive test, were also observed.

Prospective evaluation should consider clinicians' reasons for ordering or not ordering TEE for older adults in the setting of SAB. It remains unclear whether confirmation of a diagnosis of endocarditis would affect clinical outcomes, because definitive treatment with valve replacement surgery also has significant operative risk.[16] Elderly patients with infective endocarditis have been noted to have lower rates of surgical treatment and higher mortality than younger patients.[13] Alternatively, by excluding endocarditis, TEE results might help clinicians select shorter durations of parenteral antimicrobial therapy with confidence, thus decreasing the risk of adverse events related to extended courses of antistaphylococcal therapy and the extended need for intravenous access. Although the reasons for not obtaining echocardiography remains unclear, the results may offer important prognostic information and thus help establish overall goals of care in a population with a high incidence of adverse events (including mortality).

The association of SAB with prior surgery or other invasive procedures before SAB is another important observation. In these patients, the surgical intervention was the source of SAB almost half of the time. Interventions to decrease *S. aureus*–related surgical site infections (SSIs) include preoperative screening and decolonization efforts.[17,18] Although larger studies have failed to show consistent benefits of this strategy, older patients may benefit with a modified version of this approach. Recent work has demonstrated a strong association between ADL impairment and MRSA SSIs.[19] Although functional status is generally not considered an absolute contraindication for surgery, the observation that even modest impairment in ADLs can result in significant risk of MRSA SSI (and consequently SAB) is notable.[19] The association between SSI and SAB presents another important area for future investigation, particularly with regard to preventative strategies.[20,21]

Although MRSA is well recognized as an important risk factor for death in patients with SAB,[6,7,22,23] the results of the current study failed to show such an association. The lack of association probably reflects the large portion of patients who had MRSA, the high rates of overall mortality, or simply a Type II error due to a relatively small sample size. Although no association was observed between baseline functional status (independent vs requiring assistance with ADLs) and mortality, earlier studies have clearly demonstrated the relationship between poor functional status and infection-related mortality.[24,25] Detailed measures of functional status should be recorded in future studies of SAB to help further define the relationship between debility and infection outcomes.

Although its retrospective design and small sample size limited the present study, the results show significant in-hospital and 6-month mortality in elderly patients with SAB. There is also a possible association with recent surgeries or implantation of medical devices. The reasons why clinicians did not pursue echocardiography evaluation in this patient cohort are unclear but may reflect a belief that the risks of TEE are perceived as too high in older adults. Future investigation of SAB in older adults should focus on preventative strategies, as well as diagnostic and treatment paradigms, given the high morbidity and mortality associated with this infection.

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Author Contributions: Big: study design, data collection, manuscript preparation. Malani: study design, analysis and interpretation of data, manuscript preparation.

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