Staphylococcus aureus Bloodstream Infections: The Association Between Age and Mortality and Functional Status

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OBJECTIVES: To assess the association between *Staphylococcus aureus (S. aureus)* blood stream infections (BSIs) and morbidity and mortality in older adults.

DESIGN: Retrospective review.

SETTING: Veterans Affairs Ann Arbor Healthcare System.

PARTICIPANTS: All patients with *S. aureus* BSI during 2004/05.

MEASUREMENTS: Outcomes included in-hospital and 6-month mortality, as well as need for subacute care.

RESULTS: Sixty-eight patients with *S. aureus* BSI were identified (mean age 63.5 ± 13.0). Outcomes of interest included in-hospital mortality (19.1%), 6-month mortality (33.8%), and need for subacute care (65.4%). Univariate analysis identified several predictors of death, including older age, chronic renal insufficiency, catheter-related infection, Charlson weighted index of comorbidity score, and infection with methicillin-resistant *S. aureus* (MRSA). Multivariable analysis demonstrated that older age (odds ratio (OR) = 1.1, $P < .01$), chronic renal insufficiency (OR = 16.6, $P = .01$), and MRSA infection (OR = 5.1, $P = .03$) were independently associated with 6-month mortality. These results suggest that, for every decade increase in age, the odds of death within 6 months of *S. aureus* BSI doubles (OR = 1.1). Chronic renal insufficiency was also independently associated with in-hospital mortality. Of the previously community-dwelling patients (n = 50), 41 survived hospitalization, of whom 22 (53.7%) required subacute care after discharge.

CONCLUSION: Better understanding of the epidemiology of *S. aureus* BSI in older patients and validation of risk factors for poor functional outcomes and death should be the focus of future prospective studies. **J Am Geriatr Soc 56:1485–1489, 2008.**

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

Despite vast improvements in medical care, adjusted rates of hospitalization for bloodstream infection (BSI) continue to climb in older adults.[1,2] In recent years, death rates due to BSI have risen two to three times in persons aged 65 and older, seven times in those aged 75, and 20 times in those aged 85 and older.[2] In some series, overall BSI-associated mortality has been reported to be greater than 50% in older adults, with the highest mortality rates associated with *Staphylococcus aureus (S. aureus)* infection.[1–14]

S. aureus BSIs are among the most morbid of common infections, and the incidence continues to increase at a higher rate than BSI caused by other organisms.[15–18] The epidemiology of *S. aureus* BSI in elderly people differs from that of younger patients in that older adults are more likely to have catheter- and device-related infections and less likely to have infections related to intravenous drug use.[3,13,18] Older adults also have a higher incidence of methicillin-resistant strains, reflecting the higher rates of healthcare-associated acquisition.[3,4,18] Associated risk factors for development of *S. aureus* BSI include a higher incidence of comorbid illness, such as congestive heart failure, chronic pulmonary disease, hypertension, and diabetes mellitus. Risk factors for death include methicillin resistance, age, renal failure, length of mechanical ventilation, and presence of devices.[3,15–18]

In the general population, recent studies of *S. aureus* BSI demonstrate overall 30-day mortality rates of 30% despite appropriate antimicrobial therapy.[16] Few studies specifically assess prognosis and outcomes from infection in older adults.[19] Despite high (and increasing) incidence and substantial overall mortality, *S. aureus* BSI remains under-

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studied, especially in elderly people. Although mortality is higher in older adults with *S. aureus* BSI, the effect of infection on physical and cognitive functional status and long-term care needs is not known. It is likely that older adults not only suffer higher mortality from *S. aureus* BSI, but also experience longer recovery times and more-persistent functional impairment than younger adults, leading to prolonged hospitalization, need for subacute care, and higher healthcare costs.

To better understand the relationship between older age and clinical outcomes and to identify other variables of interest, a retrospective study was conducted of all community- and healthcare-associated *S. aureus* BSI in patients admitted to the Veterans Affairs (VA)Ann Arbor Healthcare System during 2004/05. In addition to mortality (in-hospital and 6-month), the need for subacute care was also assessed as a marker of functional status, and available Minimum Data Set (MDS) records were examined for information on activities of daily living (ADLs) and mobility. The findings are presented in this article.

METHODS

Overall Research Design

The VA Ann Arbor Healthcare System (AAVA) is a 150-bed tertiary care facility closely affiliated with the University of Michigan Health System. *S. aureus* BSI was defined as any blood culture positive for *S. aureus* with an appropriate clinical presentation. Baseline demographic data, clinical conditions, and characteristics of the BSI were recorded. In addition, comorbidity was measured using the Charlson weighted index of comorbidity (WIC).[20] Outcomes of interest included in-hospital mortality and death within 6 months of the development of the BSI. Need for subacute care after discharge in patients who survived hospitalization was also recorded as a measure of diminished functional status. The admitting service generally determined the need for subacute care in consultation with the divisions of geriatric medicine and infectious diseases. Patients requiring subacute care were admitted to the AAVA's attached extended care center (ECC) or discharged to a community nursing center. The institutional review board of the AAVA approved this study.

Data Analysis

Univariate analysis using simple logistic regression identified risk factors for death in patients with *S. aureus* BSI. A two-tailed *P*-value less than .05 was considered statistically significant. Crude odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Age was represented in a continuous fashion in the model with 1 year serving as the unit of measure. Variables that were significant at a *P*-value of .20 in univariate analysis and variables that had a priori clinical significance were then analyzed using multivariable logistic regression modeling. All statistical analysis was performed using SAS 9.1 (SAS Institute Inc., Cary, NC).

RESULTS

Patient characteristics are listed in Table 1. Sixty-eight patients with a *S. aureus* BSI with a mean age of 63.5 ± 13 (range 20–89) were identified; all but one were male (98.5%). (Figure 1) Common medical comorbidities of patients were hypertension (70.6%), diabetes mellitus (50%), and coronary artery disease (42.6%). The most common sources of *S. aureus* infection were catheter related (32.2%), wound related (26.5%), and endocarditis

Table 1. Characteristics of 68 Patients with *Staphylococcus aureus* Blood Stream Infections

Characteristic	Value
Age, mean ± SD	63.5 ± 13.2
Male, n (%)	67 (98.5)
Comorbidities, n (%)	
Hypertension	48 (70.6)
Coronary artery disease	29 (42.6)
Congestive heart failure	15 (22.1)
Peripheral vascular disease	22 (32.3)
Diabetes mellitus	34 (50)
End-stage renal disease	9 (13.2)
Chronic renal insufficiency*	8 (11.8)
Pulmonary disease	18 (26.5)
Cirrhosis	10 (14.7)
Psychiatric illness	15 (22.1)
Malignancy	15 (22.1)
Stroke	10 (14.7)
Recent hospitalization, n (%)†	22 (32.3)
Need for enteral feeding, n (%)	6 (8.8)
Charlson weighted index score, mean ± SD	5.6 ± 2.5
Source of infection, n (%)	
Catheter	22 (32.3)
Endocarditis	14 (20.6)
Wound	18 (26.5)
Respiratory tract	11 (16.2)
Unknown source	11 (16.2)
Osteoarticular	6 (8.8)
Genitourinary	2 (3.0)

* Baseline serum creatinine of 2 mg/dL.
† Hospital admission within previous 30 days.
SD = standard deviation.

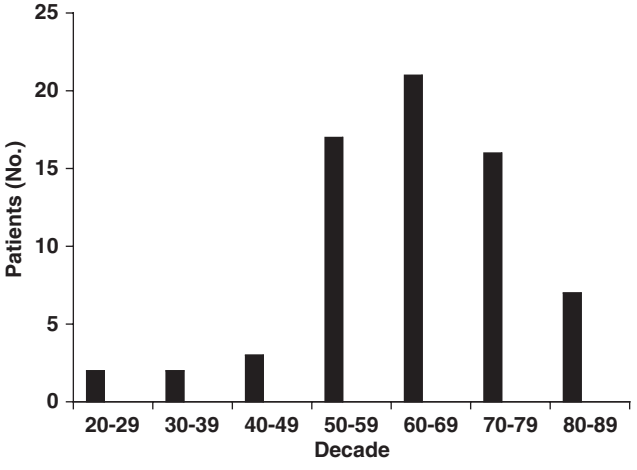

Figure 1. Age distribution of patients with *Staphylococcus aureus* bloodstream infection according to decade (N = 68).

Table 2. Univariate Analysis of the Effect of Patient Characteristics on In-Hospital and 6-Month Mortality from *Staphylococcus aureus* Bloodstream Infections

Characteristic and Source of Infection	Survived to Discharge (n = 55)	Died in Hospital (n = 13)	Unadjusted OR (95% CI)	*P*-Value	Alive at 6 Months (n = 45)	Dead at 6 Months (n = 23)	Unadjusted OR (95% CI)	*P*-Value
Patient characteristics								
Age, mean ± SD*	62.3 ± 14	68.9 ± 8	1.05 (1.0–1.1)	.10	60.6 ± 14	69.4 ± 9	1.07 (1.0–1.1)	.01
Charlson index, mean ± SD	5.2 ± 2.5	7.1 ± 2.1	1.38 (1.0–1.8)	.02	4.9 ± 2.2	6.9 ± 2.5	1.5 (1.1–1.9)	<.001
Diabetes mellitus, n (%)	26 (47.2)	8 (61.5)	1.8 (0.5–6.1)	.35	21 (46.7)	13 (56.5)	1.5 (0.5–4.1)	.44
Peripheral vascular disease, n (%)	16 (29.1)	6 (46.2)	2.1 (0.6–7.2)	.23	13 (28.9)	9 (39.1)	1.6 (0.5–4.5)	.40
Chronic renal insufficiency, n (%)	4 (7.2)	4 (30.8)	5.7 (1.2–27)	.05	2 (4.4)	6 (26.1)	7.5 (1.4–41)	.02
End-stage renal disease, n (%)	7 (12.7)	2 (15.4)	1.3 (0.2–6.8)	.64	4 (8.8)	5 (21.7)	2.8 (0.7–12)	.25
Enteral feeding, n (%)	4 (7.2)	2 (15.4)	2.3 (0.4–14)	.99	2 (4.4)	4 (17.4)	4.5 (0.7–27)	.20
Source of infection, n (%)								
Catheter related	16 (29.1)	6 (46.2)	2.1 (0.6–7.2)	.24	11(24.4)	11 (47.8)	2.8 (1.0–8.2)	.05
Wound related	15 (27.2)	3 (23.1)	0.8 (0.2–3.3)	.99	13 (28.9)	5 (21.7)	0.7 (0.2–2.2)	.74
Endocarditis	13 (23.6)	1 (7.7)	0.3 (0.03–2.3)	.38	12 (26.7)	2 (8.7)	0.3 (0.1–1.3)	.12
Unknown	7 (12.7)	4 (30.8)	3.1 (0.7–12.6)	.99	5 (11.1)	6 (26.1)	2.8 (0.8–10.5)	.22
Methicillin-resistant *Staphylococcus aureus*	27 (49.1)	9 (69.2)	2.3 (0.6–8.5)	.30	19 (42.2)	17 (73.9)	3.8 (1.3–11.7)	.01

* Odds ratio (OR) for age reported for 1-year unit.
CI = confidence interval.

(20.6%). Thirty-six episodes of BSI (52.9%) were secondary to MRSA, the remaining 32 (47.1%) were secondary to methicillin-sensitive *S. aureus* (MSSA).

Of the 68 patients, 50 lived in the community before admission, either alone (n = 11) or with family members (n = 39). Another 16 patients were admitted from an extended care setting, either chronic or subacute care. The remaining two patients were transferred from another hospital, although both lived in the community before admission to the outside hospital.

Thirteen of the 68 patients (19%) died before discharge during the initial hospitalization. An additional 10 patients died within 6 months of developing the *S. aureus* BSI (Table 2). Of the 55 patients who survived hospitalization, 36 (65.4%) required admission to an extended care facility. Twenty-six of the 36 extended care patients received subacute care at the VA's ECC. Primary reasons for subacute care included impaired mobility and nutrition, wound care, and need for parenteral antimicrobial therapy. The ECC does not offer long-term care. The AAVA has a well-established home antimicrobial program,[21] so few patients were sent to subacute care just to complete a course of therapy. Of the previously community-dwelling patients (n = 50), 41 survived hospitalization, of whom 22 (53.7%) required subacute care after discharge. Not surprisingly, older age predicted need for subacute care in previously independent patients (OR = 1.05, $P = .04$).

MDS data were available for 26 of the 68 (38%) patients. Nine of the 26 were independent or needed minimal assistance with ADLs and mobility. The remaining 17 (65.4%) patients required a minimum of assistance with two or more ADLs, bed mobility, or both from one person. Of the 17, 12 (70.5%) were initially admitted from the community, all living independently alone or with family. The other five patients were admitted from a subacute or skilled care setting.

Univariate analysis identified several factors associated with mortality (in-hospital and 6-month) including age, chronic renal insufficiency (defined as serum creatinine $\geq$2 mg/dL), catheter-related infection, Charlson WIC score, and MRSA infection (Table 2). Of these characteristics, three remained independently associated with 6-month mortality based on multivariate analysis: age (OR = 1.1, $P < .01$), chronic renal insufficiency (OR = 16.6, $P = .01$), and MRSA infection (OR = 5.1, $P = .03$) (Table 3). The adjusted OR for age suggests that, for every 10 years increase in age, the odds of dying within 6 months of *S. aureus* BSI doubles. Chronic renal insufficiency was also independently associated with in-hospital mortality (OR = 7.0, $P = .03$); age demonstrated borderline significance for in-hospital mortality (OR = 1.05, $P = .08$).

DISCUSSION

The preceding results offer further evidence that older age is an independent predictor of mortality associated with *S. aureus* BSI. These results suggest that, for every 10 years increase in age, the odds of dying within 6 months of *S. aureus* BSI doubles (OR = 1.1). In addition to significant mortality, *S. aureus* BSI is perhaps associated with a decline in functional status in older adults. Specifically, the need for subacute care after discharge was seen in two-thirds of patients who survived hospitalization. Even in those who lived independently in the community before admission, more than half required care after discharge. Age predicted the need for such care in previously independent patients (OR = 1.05, $P = .04$), as well as in the overall study population. Although there are multiple reasons why patients require subacute care posthospitalization, including antimicrobial administration and wound care, the limited MDS records available suggested significant impairments in mo-

Table 3. Multivariate Analysis of the Association of Select Patient Characteristics on In-Hospital and 6-Month Mortality from *Staphylococcus aureus* Bloodstream Infections

	In-Hospital Mortality			6-Month Mortality		
	Unadjusted	Adjusted*		Unadjusted	Adjusted*	
Characteristic	OR (95% CI)		*P*-Value	OR (95% CI)		*P*-Value
Age†	1.05 (1.0–1.1)	1.05 (1.0–1.1)	.08	1.07 (1.0–1.1)	1.1 (1.0–1.2)	<.01
Chronic renal insufficiency	5.7 (1.2–27)	7.0 (1.2–40.8)	.03	7.5 (1.4–41)	16.6 (1.8–153)	.01
Catheter-related infection	2.1 (0.6–7.2)	4.1 (8–22.3)	.10	2.8 (1.0–8.2)	4.5 (0.7–27)	.10
MRSA	2.3 (0.6–8.5)	1.8 (0.4–8.0)	.46	3.8 (1.3–11.7)	5.1 (1.1–22.9)	.03

* Odds ratios (ORs) and 95% confidence intervals (CIs) are based on a multivariable logistic regression adjusting for age, chronic renal insufficiency, end-stage renal disease, recent hospitalization, catheter-related infection, endocarditis, Charlson weighted comorbidity index, and methicillin-resistant *Staphylococcus aureus* (MRSA).

† OR for age reported for 1-year unit.

bility and cognitive function in patients who previously lived independently.

Before planned prospective studies related to functional status and *S. aureus* infection were begun, this pilot study was performed to identify potential predictors of mortality. Although its retrospective design, a small sample size, and incomplete functional assessments limited the present study, the results suggest an association between age and functional decline and between age and mortality. This study was conducted at a VA hospital, which serves a population that tends to be overwhelmingly male and relatively young, with high rates of comorbid illnesses. Although 98% of the study patients were male, these preliminary results are generalizable, given that there is no evidence in the literature that outcome for *S. aureus* BSI varies according to sex.

The difference between in-hospital and 6-month mortality and the possible effect of age is intriguing. The results suggest that, even if an older adult survives hospitalization for a *S. aureus* BSI, a significant risk of debility at discharge and death at 6 months remains. This potential difference offers further support for future studies to assess functional status and the effect of rehabilitation on outcomes from *S. aureus* BSI. Better understanding of the epidemiology of *S. aureus* BSI in older patients, as well as validation of risk factors for poor functional outcomes and death, can also help direct future studies of focused interventions such as decolonization, antimicrobial-coated devices, and even vaccines.[22–24]

Assessing who among elderly people develops *S. aureus* BSI, who is likely to survive, and what effect is seen on functional status will be important in developing prognostic indices and new treatment algorithms.[19,25]

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Conflict of Interest: Malani, Rana, Banerjee, and Bradley report no conflicts of interest related to this work.

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

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