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ORIGINAL RESEARCH

# Performance of Processes of Care and Outcomes in Patients With *Staphylococcus aureus* Bacteremia

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**BACKGROUND:** *Staphylococcus aureus* bacteremia (SAB) is associated with significant morbidity and mortality in hospitalized adults.

**OBJECTIVE:** We aimed to identify current practice patterns in the management of SAB, and to evaluate their association with clinical outcomes.

**DESIGN:** Retrospective cohort study.

**SETTING:** A 1558-bed tertiary care teaching hospital.

**PATIENTS:** Adult patients hospitalized between January 1, 2012 through April 30, 2013, who had at least 1 positive blood culture with *S aureus*.

**INTERVENTION:** None

**MEASUREMENTS:** Electronic medical records were reviewed and the processes of care in the management of SAB were identified. The main outcome was clinical failure, defined as a composite endpoint of in-hospital mortality and persistent bacteremia.

**RESULTS:** Two hundred fifty episodes of SAB occurred in 241 patients, and 78 (32.4%) had clinical failure. Processes of care that impacted the risk of clinical failure included: timing of follow-up blood cultures (delays of >4 days had a relative risk [RR] of 6.6; 95% confidence interval [CI]: 2.1–20.5; $P = 0.001$), consultation with infectious diseases specialist within 6 days from diagnosis of SAB (RR: 0.3; 95% CI: 0.1−0.9; $P = 0.03$), and use of β-lactams in patients with methicillin-susceptible *S aureus* bacteremia (RR: 0.1; 95% CI: 0.04−0.5; $P = 0.002$).

**CONCLUSIONS:** The processes of care identified in our study could serve as quality and patient safety indicators for the management of SAB. *Journal of Hospital Medicine* 2016;11:27–32. © 2015 Society of Hospital Medicine

*Staphylococcus aureus* is one the most common pathogens isolated in nosocomial and community-onset bloodstream infections (BSI) in the United States.[1,2] *S aureus* bacteremia (SAB) has been reported in the literature to have substantial morbidity and mortality, with rates ranging between 15% and 60% worldwide.[3–6] In the United States, patients with infections due to *S aureus* have on average 3 times the length of hospital stay than inpatients without these infections (14.3 days vs 4.5 days; $P < 0.01$).[7] Healthcare costs are negatively impacted by these infections. In a recent meta-analysis, Zimlichman et al.[8] reported that central-line BSI (CLABSI) and surgical-site infection (SSI) caused by methicillin-resistant *S aureus* (MRSA) resulted in the highest estimated costs associated with hospital-acquired infections in the United States ($58,614 [95% CI: $16,760-$174,755] for CLABSI and $42,300 [95% CI: $4,005-$82,670] for SSIs).

Appropriate management of SAB includes not only selecting the correct antimicrobial based on susceptibilities but also timely control of the source of infection, appropriate use of ancillary studies when indicated, and pharmacokinetic and pharmacodynamic therapeutic monitoring of antimicrobial therapy when vancomycin is used.[9] Consultation with an infectious diseases (ID) specialist has been associated with increased compliance with evidence-based strategies in the management of SAB,[10–14] such as appropriate antibiotic choice, optimized duration of treatment, removal of the source of infection, and better use of cardiac echocardiography, resulting in improved outcomes.[13,14]

Some, but not all, institutions have adopted bundles,[14] mandatory ID consultation[10] or daily prospective audit and feedback review[15] as part of antimicrobial stewardship program (ASP) interventions aiming to optimize the management of SABs. As part of our ASP quality improvement activities we performed the present study to determine our institutional rate of clinical failure in the treatment of SAB, to identify current practice patterns in the delivery of processes of care, and evaluate their association with clinical outcomes of hospitalized patients with SAB to identify future areas of improvement.

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## METHODS

A retrospective cohort study was performed at a 1558 licensed-bed tertiary teaching hospital in Miami, Florida. All hospitalized patients 18 years of age or older with at least 1 positive blood culture with MRSA or methicillin-susceptible *S aureus* (MSSA) between January 1, 2012 and April 30, 2013 were included. Patients were identified from the electronic microbiology laboratory database. For the purposes of this study, only the first episode of SAB was included in the analysis. Patients were excluded if aged younger than 18 years or if SAB was detected in an outpatient setting. The primary outcome was clinical failure, defined as a composite endpoint of in-hospital mortality or persistent bacteremia; persistent bacteremia was defined as bacteremia for 7 or more days after the first positive blood culture. *S aureus* isolates were identified by standard methods.[16] Species identification was performed by latex agglutination. Antimicrobial susceptibility testing was performed using an automated system (Vitek 2; bioMerieux, Durham, NC) according to standard guidelines.

Data collected included baseline demographics, comorbidities, and treating healthcare provider's service; provider's service was categorized into 1 of 5 groups: internal medicine (academic), internal medicine (hospitalist), surgery, trauma, or neurosurgery. Duration of bacteremia was recorded and defined as the time between first positive and first negative blood culture. The time of first positive culture was defined as the date in which the culture was obtained. Patients who failed to have at least 1 follow-up blood culture were not counted toward the main outcome. Additionally, presence of a foreign body (cardiac device, orthopedic prosthesis, tunneled catheter, nontunneled catheter) and presumed source of infection as documented in the electronic medical record by the treating service was also collected. Infections were considered community associated when onset of bacteremia occurred within the first 72 hours of admission, and hospital associated if onset of bacteremia occurred after 72 hours of admission.

Based on current practice guidelines,[9] the variables considered processes of care were the time to obtain the first follow-up blood culture, time from first positive blood culture to initiation of appropriate antibiotic therapy (defined as a loading dose of vancomycin of 15 mg/kg, or a β-lactam if the organism was susceptible), time to obtain the first vancomycin trough (when indicated), time from first positive blood culture to consultation with ID specialist, appropriate antibiotic de-escalation (vancomycin to β-lactam antibiotic if the organism was susceptible and the patient had no allergies or contraindications), and obtaining an echocardiographic study (transthoracic echocardiogram or transesophageal echocardiogram).

Statistical analyses were performed using SAS 9.2 (SAS Institute, Cary, NC). Differences in proportions were analyzed with $\chi^2$ or Fisher exact test, accordingly. Differences in means among continuous variables were evaluated using independent samples of paired samples *t* tests as appropriate for the analysis. Continuous variables were dichotomized using a clinically established cutoff to determine relative risk (RR). A univariate analysis of risk factors associated with clinical failure was performed. Multivariable analyses were performed using logistic regression. Models were created using the backward stepwise approach and included all variables found to be statistically significant at less than 0.05 level in the univariate model and those of clinical significance. The study was reviewed and approved by the institutional review boards at the University of Miami and Jackson Memorial Hospital.

## RESULTS

During the study period, 241 patients with a first episode of SAB were identified. MRSA and MSSA were isolated in 124 (51.4%) and 117 (48.5%) patients, respectively. Demographic and clinical characteristics of the study population based on isolate are summarized in Table 1. One hundred seventy-nine (74.3%) patients were under the care of internal medicine services. There was no association between treating service (medical vs surgical) and clinical failure.

The onset of infection occurred in the community in 77 (62.1%) patients with MRSA and in 77 (65.8%) patients with MSSA. The documented source of bacteremia was unknown in 30% of patients with MRSA and 44% of those with MSSA BSI. When ID specialists were consulted, patients were more likely to have a source of infection identified (RR: 1.5; 95% confidence interval [CI]: 1.2-1.8; $P < 0.0001$). The most commonly documented sources of infection were CLABSI, which occurred in 32 (25.8%) patients with MRSA and 21 (17.9%) patients with MSSA, followed by skin and soft tissue infections in 24 (19.3%) patients with MRSA BSI and 20 (17.1%) patients with MSSA BSI. All patients with CLABSI had documentation of catheter removal.

Clinical failure (defined as in-hospital mortality or persistent bacteremia) occurred in 78 (32.4%) patients. Of these, 50 (20.7%) represented in-hospital mortality, and 31 (12.9%) had persistent bacteremia. Table 2 summarizes the demographic and clinical characteristics associated with clinical failure. In the univariate analysis, the variables statistically significantly associated with clinical failure were: age greater than 60 years (RR: 1.4; 95% CI: 1.1-1.8; $P = 0.001$), bacteremia due to MRSA (RR: 1.7; 95% CI: 1.1-2.5; $P = 0.008$), white race (RR: 0.7; 95% CI: 0.6-1; $P = 0.03$), acute kidney injury during admission (RR: 2.2; 95% CI: 1.3-3.7; $P = 0.004$), presence of nontunneled central venous catheters at the onset of

**TABLE 1.** Demographic and Clinical Characteristics of Patients with Methicillin-Resistant *Staphylococcus aureus* and Methicillin-Susceptible *Staphylococcus aureus* Bacteremia

| Variable | MRSA, N= 124 (%) | MSSA, N= 117(%) | Overall, N=241 |
|---|---|---|---|
| Demographics | | | |
| Age, y (mean) | 53.9 ± 15.57 | 53.9 ± 15.22 | 53.9 ± 15.3 |
| Age greater than 60 years | 41 (33.1) | 39 (33.3) | 80 (33.2) |
| Male sex | 80 (64.5) | 80 (68.4) | 160 (66.4) |
| White race | 63 (50.8) | 69 (59) | 132 (54.8) |
| Comorbidities | | | |
| Diabetes mellitus | 35 (28.2) | 40 (34.2) | 75 (30.7) |
| Hypertension | 56 (45.2) | 40 (34.2) | 96 (39.8) |
| CHF | 6 (4.8) | 9 (7.7) | 15 (6.2) |
| CVD | 8 (6.4) | 6 (5.1) | 14 (5.8) |
| Chronic pulmonary disease | 14 (11.3) | 14 (12) | 28 (11.6) |
| Malignancy | 9 (7.3) | 19 (16.2) | 28 (11.6) |
| Active chemotherapy | 5 (4) | 10 (8.5) | 15 (6.2) |
| HIV | 27 (21.8) | 17 (14.5) | 44 (18.2) |
| Cirrhosis | 6 (4.8) | 8 (6.8) | 14 (5.8) |
| Hepatitis C infection | 7 (5.6) | 11 (9.4) | 18 (7.5) |
| Acute kidney injury | 88 (71) | 80 (68.4) | 168 (69.7) |
| Chronic kidney disease | 29 (23.4) | 24 (20.5) | 53 (22) |
| End-stage renal disease | 25 (20.2) | 22 (18.8) | 47 (19.5) |
| Connective tissue disease | 3 (2.4) | 3 (2.6) | 6 (2.5) |
| Alcohol abuse | 3 (2.4) | 1 (0.8) | 4 (1.7) |
| IVDU | 4 (3.2) | 5 (4.3) | 9 (3.7) |
| Hemiplegia | 4 (3.2) | 0 | 4 (1.7) |
| Chronic osteomyelitis | 4 (3.2) | 0 | 4 (1.7) |
| History of transplant | 7 (5.6) | 0 | 7 (2.9) |
| Surgery during current admission | 29 (23.4) | 46 (39.3) | 75 (31.1) |
| Surgery during the previous 30 days | 31 (25) | 36 (30.8) | 67 (25.3) |
| Treating service | | | |
| Medical service | 89 (71.8) | 90 (76.9) | 179 (74.3) |
| Surgical service | 21 (16.9) | 16 (13.7) | 37 (15.3) |
| Other | 7 (5.6) | 11 (9.4) | 18 (7.5) |
| Presence of foreign body | | | |
| PICC line | 24 (19.3) | 34 (29.1) | 58 (24.1) |
| Tunneled CVC | 24 (19.3) | 15 (12.8) | 39 (16.2) |
| Nontunneled CVC | 13 (10.5) | 28 (23.9) | 41 (17) |
| AV fistula | 3 (2.4) | 7 (6) | 10 (4.1) |
| Cardiac device | 8 (6.4) | 9 (7.7) | 17 (7) |
| Other | 4 (3.2) | 11 (9.4) | 15 (6.2) |
| Source of infection | | | |
| CLABSI | 32 (25.8) | 21 (17.9) | 53 (22) |
| SSTI | 24 (19.3) | 20 (17.1) | 44 (18.2) |
| Endocarditis | 10 (8.1) | 7 (6) | 17 (7) |
| Thrombophlebitis | 2 (1.6) | 2 (1.7) | 4 (1.7) |
| Prostatic abscess | 3 (2.4) | 1 (0.8) | 4 (1.7) |
| Paravertebral abscess | 2 (1.6) | 2 (1.7) | 4 (1.7) |
| Mediastinal abscess | 2 (1.6) | 1 (0.8) | 3 (1.2) |
| CAP | 4 (3.2) | 4 (3.4) | 8 (3.3) |
| VAP | 3 (2.4) | 2 (1.7) | 5 (2.1) |
| Surgical site infection | 2 (1.6) | 1 (0.8) | 3 (1.2) |
| Ventriculostomy | 0 | 1 (0.8) | 1 (0.4) |
| Bone or joint infection | 2 (1.6) | 3 (2.6) | 5 (2.1) |
| Unknown | 38 (30.6) | 52 (44.4) | 90 (37.3) |
| Onset | | | |
| Community onset* | 77 (62.1) | 77 (65.8) | 154 (63.9) |
| Hospital onset† | 47 (37.9) | 40 (34.2) | 87 (36.1) |

NOTE: **Abbreviations:** AV, arteriovenous; CAP, community-acquired pneumonia; CHF, congestive heart failure; CLABSI, catheter-line–associated bloodstream infection; CVC, central venous catheter; CVD, cerebrovascular disease; HIV, human immunodeficiency virus; IVDU, intravenous drug infection; PICC, peripherally inserted central catheter; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; SSTI, skin and soft tissue infection; VAP, ventilator-associated pneumonia.*Denotes onset of bacteremia within the first 72 hours of admission. †Denotes onset of bacteremia after 72 hours of admission.

bacteremia (RR: 1.9; 95% CI: 1.3-2.7; $P = 0.004$), and endocarditis (RR: 2.9; 95% CI: 2.1-3.9; $P < 0.0001$). In the multivariable analysis, age greater than 60 years and endocarditis were found to be independent risk factors for the development of clinical failure.

### Performance of Process of Care and Association With Outcomes

The analysis of the performance of the processes of care and outcomes is shown in Table 3. After adjusting for relevant clinical and demographic characteristics, and those with a level of significance of <0.05, obtaining follow-up blood cultures more than 4 days after the onset of bacteremia independently increased the risk of clinical failure (RR: 6.5; 95% CI: 2.1-20.5; $P = 0.001$). When consultation with an ID specialist was obtained within the first 6 days from onset of bacteremia, the risk of clinical failure was 0.3 (95% CI: 0.1-0.9; $P = 0.03$); however, consultation with an ID specialist overall was not associated with clinical failure (RR: 1; 95% CI: 0.7-1.4; $P = 0.98$).

A comparison of the average number of days to performance of processes of care is presented in Table 4. Patients with clinical failure had significantly greater elapsed time from the first positive blood culture to the first follow-up blood culture as compared to those who did not have clinical failure (mean 2.32 ± 1.3 days vs 3.88 ± 3.37; $P < 0.0001$). Forty-one patients (17.1%) failed to have at least 1 follow-up blood culture.

Among patients with clinical failure, an ID specialist was consulted at a mean time of 7 days from the onset of bacteremia, compared to patients with no clinical failure in whom a consult was obtained at a mean of 4 days ($P = 0.06$) (Table 4). Overall, ID specialists were only consulted in 97/241 (40.2%) episodes.

Echocardiographic studies were performed in 141/241 (58.5)% of episodes, and they were more likely to be obtained when an ID specialist was consulted (RR: 1.7; 95% CI: 1.4-2.1; $P < 0.0001$). Lack of performance of these studies was not associated with clinical failure (Table 3).

### Antibiotic Administration and De-escalation of Therapy

There were no significant differences in the average time from the first positive blood culture to the administration of antibiotics between patients who had clinical failure and those who did not (0.57 ± 1.11 vs 0.43 ± 1.05; $P = 0.63$) (Table 4).

Patients with MSSA BSI and no documented penicillin allergy were treated with β-lactam or cephalosporin antibiotics in 56/103(54.3%) episodes. Patients were 2.5 times more likely to receive β-lactam antibiotics when an ID specialist was consulted (95% CI: 1.8-3.5; $P < 0.0001$). Among patients with MSSA BSI,

**TABLE 2.** Association of Demographics, Clinical Characteristics, and Clinical Failure in Patients with *Staphylococcus aureus* Bacteremia

| Variable | Clinical Failure, N = 78 (%) | No Clinical Failure, N = 163 (%) | Unadjusted RR (CI) | *P* Value* | Adjusted OR (CI) | *P* Value* |
|---|---|---|---|---|---|---|
| Demographics | | | | | | |
| Age >60 years | 37 (47.4) | 43 (26.4) | 1.4 (1.1-1.8) | 0.001 | 2.4 (1.2-4.5) | 0.008 |
| Male | 46 (60) | 114 (69.9) | 0.7 (0.5-1.04) | 0.09 | | |
| White race | 35 (44.9) | 97 (59.5) | 0.7 (0.6-1) | 0.03 | 0.5 (0.3-1.02) | 0.058 |
| Isolate | | | | | | |
| MRSA | 50 (64.1) | 74 (45.4) | 1.7 (1.1-2.5) | 0.008 | 1.8 (0.6-5.2) | 0.3 |
| MSSA | 28 (35.9) | 89 (54.6) | 0.6 (0.4-0.9) | 0.008 | | |
| Comorbidities | | | | | | |
| Diabetes mellitus | 21 (26.9) | 54 (33.1) | 0.8 (0.5-1.2) | 0.34 | | |
| Cirrhosis | 6 (7.7) | 8 (4.9) | 1.3 (0.7-2.5) | 0.35 | | |
| Acute kidney injury | 65 (83.3) | 103 (63.2) | 2.2 (1.3-3.7) | 0.004 | 1.6 (0.5-5.4) | 0.43 |
| Chronic kidney disease | 12 (15.4) | 41 (25.1) | 0.6 (0.4-1.1) | 0.11 | | |
| End-stage renal disease | 15 (19.2) | 32 (19.6) | 1 (0.6-1.5) | 0.94 | | |
| IVDU | 3 (3.8) | 6 (3.7) | 1.03 (0.4-2.6) | 1 | | |
| Treating service | | | | | | |
| Medical | 61 (78.2) | 118 (72.4) | 1.3 (0.7-2.6) | 0.33 | | |
| Surgical | 11 (14.1) | 67 (41.1) | 1 (0.9-1.1) | 0.71 | | |
| Presence of foreign body | | | | | | |
| Cardiac device | 6 (7.7) | 11 (6.7) | 1.1 (0.6-2.1) | 0.78 | | |
| PICC line | 20 (25.6) | 38 (23.3) | 1.1 (0.7-1.6) | 0.69 | | |
| Nontunneled CVC | 22 (28.2) | 19 (11.7) | 1.9 (1.3-2.7) | 0.004 | 3.6 (0.7-17.7) | 0.11 |
| Tunneled CVC | 15 (19.2) | 24 (14.7) | 1.2 (0.8-1.9) | 0.36 | | |
| AV fistula | 0 | 10 (6.1) | 0.1 (0.09-2) | 0.15 | | |
| Other | 4 (5.1) | 11 (6.7) | 0.8 (0.3-1.9) | 0.64 | | |
| Onset | | | | | | |
| Community onset† | 46 (59) | 108 (66.3) | 0.8 (0.6-1.2) | 0.27 | | |
| Hospital onset‡ | 32 (41) | 55 (33.7) | 1.2 (0.8-1.8) | 0.27 | | |
| Source | | | | | | |
| CLABSI | 15 (19.2) | 38 (23.3) | 0.8 (0.5-1.4) | 0.48 | | |
| SSTI | 12 (15.4) | 32 (19.6) | 0.8 (0.5-1.4) | 0.44 | | |
| Endocarditis | 14 (17.9) | 3 (1.8) | 2.9 (2.1-3.9) | <0.0001 | 9.4 (2.2-1.1) | 0.003 |
| Thrombophlebitis | 0 | 4 (2.4) | 0.3 (0.02-4.2) | 0.37 | | |
| Prostatic abscess | 1 (1.3) | 3 (1.8) | 0.8 (0.1-4.2) | 0.76 | | |
| Paravertebral abscess | 0 | 4 (2.4) | 0.3 (0.02-4.2) | 0.37 | | |
| Mediastinal abscess | 1 (1.3) | 2 (1.2) | 1.03 (0.2-5.1) | 0.97 | | |
| CAP | 4 (5.1) | 4 (2.4) | 1.5 (0.8-3.2) | 0.21 | | |
| VAP | 2 (2.6) | 3 (1.8) | 1.2 (0.4-3.7) | 0.7 | | |
| Surgical site infection | 1 (1.3) | 2 (1.2) | 1.03 (0.2-5.2) | 0.97 | | |
| Ventriculostomy | 0 | 1 (0.6) | 0.8 (0.1-8.5) | 0.82 | | |
| Bone or joint infection | 1 (1.3) | 4 (2.4) | 0.6 (0.1-3.6) | 0.59 | | |
| Unknown | 27 (34.6) | 63 (38.6) | 0.9 (0.6-1.3) | 0.55 | | |

NOTE: **Abbreviations:** AV, arteriovenous; CAP, community acquired pneumonia; CI = confidence interval; CLABSI, catheter-line–associated bloodstream infection; CVC, central venous catheter; IVDU, intravenous drug infection; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; PICC, peripherally inserted central catheter; SSTI, skin and soft tissue infection; VAP, ventilator-associated pneumonia. **P* value was calculated using the $\chi^2$ test or Fisher exact text, accordingly. †Denotes onset of bacteremia within the first 72 hours of admission. ‡Denotes onset of bacteremia after 72 hours of admission.

treatment with β-lactams was an independent predictor of decreased risk of clinical failure (RR: 0.2; 95% CI: 0.07-0.9; $P = 0.005$) (Table 3).

## DISCUSSION

Our study showed a significant rate of morbidity associated with *S aureus* bacteremia and identified processes of care in the management of SAB that impact patient outcomes.

Our results show that early consultation with an ID specialist was associated with a decreased risk of developing clinical failure, increased likelihood of identification of a source of infection, and positively impacted administration of appropriate antibiotic therapy, especially in cases of MSSA BSI, with overall improvement in patient outcomes. However, consultation with an ID specialist was only obtained in 40.2% of our cases, which is consistent with published data.[10–13] Consultation with an ID specialist itself did not impact clinical failure, but rather timeliness in obtaining expert guidance was associated with better outcomes. As shown in previous studies,[10–14] compliance with the standards of care and patient prognosis are improved when ID specialists are involved in the management of SAB. Our study reiterates that early consultation with an ID specialist has a positive outcome in patient care, as opposed to delaying consultation once the patient has persistent bacteremia for more than 7 days. This association could be explained by considering that the majority of the standards of care are time sensitive, which

**TABLE 3.** Association of Performance of Processes of Care and Outcomes in Patients With *Staphylococcus aureus* Bacteremia

| Variable | Clinical Failure, n = 78 (%) | No Clinical Failure, n = 163 (%) | Unadjusted RR (CI) | *P* Value* | Adjusted OR (CI) | *P* Value* |
|---|---|---|---|---|---|---|
| Timing of follow-up blood culture, n = 200 | | | | | | |
| Less than 2 days | 30 (19.2) | 87 (53.4) | 0.7 (0.5-0.9) | 0.01 | 1.2 (0.5-2.9)† | 0.60 |
| 2–4 days (ref) | 16 (20.5) | 39 (23.9) | 0.9 (0.8-1.1) | 0.53 | | |
| More than 4 days | 19 (24.3) | 9 (5.5) | 1.3 (1.1-1.5) | <0.0001 | 6.6 (2.1-20.5)† | 0.001 |
| Early antibiotic therapy, n = 232‡ | 66 (84.6) | 132 (81) | 1.2 (0.7-2.3) | 0.45 | | |
| Monitoring of vancomycin levels, n = 156§ | 37 (20.8) | 97 (59.5) | 0.8 (0.6-1.03) | 0.09 | | |
| Therapy with β-lactam, n = 103‖ | 7 (8.8) | 49 (30.1) | 0.4 (0.2-0.8) | 0.01 | 0.1 (0.04-0.5)¶ | 0.002 |
| Consultation with ID specialist, n = 241 | 31 (39.7) | 66 (40.5) | 1 (0.7-1.4) | 0.98 | | |
| Early consultation with ID specialist, n = 97# | 19 (24.3) | 56 (34.3) | 0.5 (0.3-0.8) | 0.006 | 0.3 (0.1-0.9)† | 0.03 |
| Echocardiography, n = 241 | 45 (57.7) | 96 (58.9) | 1 (0.7-1.4) | 0.86 | | |
| Early echocardiography, n = 141** | 35 (44.9) | 91 (55.8) | 0.7 (0.5-1.07) | 0.11 | | |

NOTE: **Abbreviations:** CI = confidence interval; ID, infectious diseases. **P* value was calculated using the $\chi^2$ test or Fisher exact test, accordingly. †Model for multivariate logistic regression included methicillin resistance, race (white/nonwhite), age greater than 60 years, acute kidney injury, presence of central venous catheter, and endocarditis as source of infection. ‡Antibiotic therapy initiated within 24 hours from first blood culture positive with *Staphylococcus aureus*. §Trough obtained after 3 doses of vancomycin. ‖Patients with methicillin-susceptible *Staphylococcus aureus* bacteremia and no documentation of penicillin allergy. ¶ Model for multivariate logistic regression included race (white/nonwhite), age greater than 60 years, acute kidney injury, presence of central venous catheter, and endocarditis as source of infection. #Consultation with infectious diseases specialist within 6 days from first positive blood culture. **Performance of an echocardiographic study within 6 days from first positive blood culture.

include: obtaining surveillance blood cultures 48 to 96 hours after initial detection[10] or initiating therapy,[11,14] removal of foci of infection,[10–12,14] use of parenteral β-lactams for the treatment of MSSA,[10,11,13,14] performing echocardiography when clinically indicated,[10,11,13,14] and appropriate duration of therapy.[10,13,14] Importantly, studies have shown that when ID specialists' recommendations are followed, patients are more likely to be cured,[10,11,13] and are less likely to relapse.[10–12] Given the complexities of treating patients with SAB and high rates of clinical failures, routine guidance could be beneficial to healthcare providers as part of a multidisciplinary structured strategy that is set in motion the moment a patient with SAB is identified by the microbiology laboratory. The processes of care outlined in this this study can serve as quality of care indicators and be integrated into a structured strategy to optimize the management of SAB.

Regarding optimal timing for follow-up blood cultures, our results show that delays in obtaining follow-up blood cultures (more than 4 days from onset of bacteremia) was independently associated with increased risk of clinical failure. Timely follow-up blood cultures have been previously identified as quality of care indicators.[10,11,13,14] Compliance with obtaining follow-up blood cultures improves when this step is integrated into a bundle of care.[14]

**TABLE 4.** Comparison of Average Number of Days to the Performance of Processes of Care Based on Clinical Failure in Patients With *Staphylococcus aureus* Bacteremia

| Process of Care | Clinical Failure | No Clinical Failure | *P* Value* |
|---|---|---|---|
| First follow-up blood culture, n = 200† | 3.88 ± 3.37 | 2.32 ± 1.3 | <0.0001 |
| Consultation with infectious diseases, n = 97† | 6.9 ± 6.55 | 4.35 ± 4.34 | 0.06 |
| First antibiotic dose, n = 232† | 0.43 ± 1.05 | 0.57 ± 1.11 | 0.63 |
| First dose of β-lactam, n = 56† | 4.4 ± 1.6 | 3.5 ± 1.4 | 0.1 |
| First vancomycin trough, n = 156 | 2.63 ± 2.04 | 2.55 ± 2.02 | 0.81 |
| Echocardiography, n = 141† | 3.42 ± 1.74 | 3.31 ± 2.05 | 0.47 |

NOTE: **P* value was calculated using Student *t* test.**Days since first positive blood culture.

Antimicrobial therapy was promptly initiated in the majority of the patients in our study. However, areas for improvement were identified. Vancomycin was the empirical therapy of choice in most of the cases, but an appropriate dose was only received by 65% of the patients, and vancomycin levels after the fourth dose were obtained in 85.9% of instances when indicated. Although in our cohort these results were not significantly associated with clinical failure, previous studies have described attainment of a target therapeutic vancomycin trough (15–20 mg/dL) as a factor for treatment success.[17,18] This problem could be addressed through physician education on therapeutic drug monitoring,[19] as well as through an ASP intervention, which have successfully led efforts to improve vancomycin utilization and dosing.[20] Among patients with MSSA BSI, therapy with β-lactams was associated with improved outcomes, and was more likely to be administered when an ID specialist was consulted. This is in accordance with previous studies that have shown that higher rates of appropriate antimicrobial therapy are achieved when ID specialists are involved in management of SAB.[10,11,13,14] The use of β-lactams for treatment of MSSA BSI has been consistently associated with lower SAB-related mortality and relapse.[21–26]

Echocardiographic studies were obtained in only half of the patients in our cohort, and they were twice more likely to be obtained when an ID specialist was consulted. Although we did not evaluate the appropriateness of the echocardiographic study, the increased proportion of studies performed when ID specialists were consulted could indicate a more in-depth evaluation of the case. Moreover, in our cohort, when ID specialists where involved in direct patient care, a

source of infection was more likely to be identified. This is in accordance with previous studies proposing that because evaluation by ID specialists are more detailed, they lead to increased use in ancillary studies and recognition of complicated cases.[10,12]

Limitations of this study include its retrospective design and the fact that it was performed in a single institution. The source of infection was defined as documented by treating providers and not by independent diagnostic criteria. Antibiotic use was collected throughout duration of admission, and was not followed after patients were discharged, as these data were not available on the electronic medical record for all patients. Deaths that may have occurred after hospital discharge were not included. We did not account for elevated vancomycin minimum inhibitory concentration as a risk factor for the main outcome, and adjustment of vancomycin based on serum levels was not factored in. Acute kidney injury was accounted for anytime during hospitalization, but not in relation to antimicrobial administration. Despite the limitations, our study has strengths that make our results generalizable. Although our institution is a single medical center, it serves a large and diverse population as reflected in our cases. Even though this is a retrospective cohort study, the use of a centralized electronic medical record allowed us to identify each aspect of the management of SAB, as implemented by different treating services (medical and surgical), as continuous variables (days) rather than only in a dichotomous fashion. Moreover, by being a community teaching hospital, we were able to explore aspects of the practice of physicians in training versus practicing clinicians. These results could be extrapolated to other healthcare facilities aiming to improve the management of SAB.

## CONCLUSIONS

Our results suggest that obtaining timely follow-up blood cultures, use of β-lactams in patients with MSSA BSI, and early consultation with infectious diseases are the processes of care that could serve as quality and patient-safety indicators for the management of SAB. These results contribute to a growing body of evidence supporting the implementation of structured processes of care to optimize the management and clinical outcomes of hospitalized patients with SAB.

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