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Major Article

Hospital-acquired *Staphylococcus aureus* primary bloodstream infection: A comparison of events that do and do not meet the central line–associated bloodstream infection definition

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Background: This study was done to describe the incidence and outcomes of primary hospital-acquired bloodstream infection (HABSI) secondary to *Staphylococcus aureus* (SA) that did and did not meet the National Healthcare Safety Network's (NHSN's) definition for central line–associated bloodstream infection (CLABSI).

Methods: Consecutive hospitalized patients during a 48-month study period with an SA HABSI were categorized according to those who did and did not meet the NHSN's definitions for CLABSI and non-CLABSI. Primary outcomes were mortality at 30 days and 1 year. Secondary outcomes were the incidence of complicated bacteremia and the need for operative intervention secondary to the HABSI event.

Results: A total of 122 episodes of primary SA HABSIs were identified: 78 (64%) were CLABSIs, and 44 (36%) were non-CLABSIs. Overall 30-day and 1-year mortality in the cohort was 21.3% and 38.5%, respectively, and did not differ significantly between the 2 groups. Complicated SA HABSI was significantly more common in the non-CLABSI group (15.9% [n = 7] vs 0% [n = 0], $P \leq .001$).

Conclusions: Primary SA HABSI was associated with significant 30-day and 1-year mortality. Complications from SA non-CLABSI requiring surgical intervention were significantly more common than in those with a CLABSI event. Our findings affirm the significance of non–device-related hospital-acquired infections.

Staphylococcus aureus (SA) is a common cause of hospital-acquired bloodstream infection (HABSI) in the United States and is associated with significant morbidity, mortality, and health care costs.[1] The presence of a central venous catheter (CVC) is the single greatest risk factor for developing a bloodstream infection with SA.[2,3] However, SA HABSIs do occur in the absence of a CVC. Characterization of the etiologies, complications, and outcomes of primary SA HABSI not attributable to a CVC remain an area of interest, especially in the era of health care outcome reporting, reimbursement, and emphasis on catheter-associated bloodstream infection (CLABSI) reduction. Although the risk of infection is higher with the usage of CVCs,[4] the vast number of peripheral intravenous catheters (PIVs) may make these infections an important contributor to primary SA HABSI rates. A recent report estimates that there may be as many as 10,028 SA bloodstream infections per year related to PIV usage.[5] Because progress has been made in preventing device-related infections, non–device-related hospital-acquired infections (HAIs), such as those associated with PIVs, should be included in efforts to decrease HAI.

A series of significant clinical events were noted among patients at our institution with SA HABSI that occurred in the absence of a central line. We sought to better understand the epidemiology of primary SA HABSI to improve the delivery of care and outcomes. As such, our objective was to determine the incidence, clinical complications, and outcomes of primary SA HABSI that meet and do not meet the National Healthcare Safety Network's CLABSI definition.[6]

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METHODS

Case ascertainment

We performed a retrospective analysis of all patients diagnosed with SA HABSI at Cleveland Clinic from January 1, 2010-December 31, 2013. Cases were obtained from the Cleveland Clinic Infection Prevention Registry as a part of ongoing prospective HABSI surveillance. Charts were reviewed to ensure the primary nature of each infection and extraction of key demographic and clinical information was performed.

Definitions

An HABSI was classified as being either primary or secondary as per the National Healthcare Safety Network's definitions.[6] Primary HABSI was further evaluated to determine if the definition for CLABSI was met. All primary SA HABSIs that did not meet the definition of CLABSI were considered non-CLABSI. For the non-CLABSIs, the potential portal of entry was determined by chart review. A PIV or midline catheter was considered the portal of entry if the treating clinician documented signs of infection or if purulent material from the insertion site was culture positive. Demographics, microbiologic data, and outcomes of infection were collected and a comparison of events meeting and not meeting the definition of CLABSI were compared. The Charlson Comorbidity Index scores were calculated for each patient based on the degree of medical comorbidity and compared for each group as proxies for overall illness.

The primary outcomes for this study were 30-day all-cause mortality, mortality at 1 year from time of infection, and presence of complicated bacteremia, including operative interventions during the index hospitalization as a consequence of the bloodstream infection. Dates of death were ascertained by review of hospital expiration summaries and use of a social security death index. Bacteremia was considered complicated if it was associated with cardiac implantable electrophysiologic device infection, vertebral osteomyelitis, or infective endocarditis as noted in the patient electronic medical record. Septic thrombophlebitis was defined as PIV or midline catheter infection accompanied by concurrent ultrasound documentation of superficial thrombophlebitis.

Statistical analyses

Differences between CLABSI and non-CLABSI distributions of categorical and continuous measures were examined for significance using either the χ^2 or Fisher exact test as appropriate. Univariate Cox proportional hazard models were constructed to look for significant univariate correlations between categorical and continuous measures and survival to 30 and 365 days.

RESULTS

During the study period there were 346 SA HABSIs with an incidence density of 0.24 per 1,000 patient days. A total of 122 primary SA HABSIs were identified: 78 (64%) were CLABSIs, and 44 (36%) were non-CLABSIs (Table 1). Thirty-eight (48.7%) CLABSIs and 19 non-CLABSIs (43.2%) were methicillin resistant ($P = .60$). Twenty-six non-CLABSIs had documented evidence of either an infected PIV (n = 16) or a midline catheter (n = 10). The remaining 18 non-CLABSIs occurred in the presence of a PIV. In 19 of the non-CLABSI events (43.2%), the positive SA blood culture was obtained in the intensive care unit, and 27 non-CLABSI events required admission to the intensive care unit during the course of their hospitalization. The mean time from admission to first positive blood culture was significantly shorter for non-CLABSIs compared with CLABSI events (6 vs 16.3 days, $P = .001$). Patients in the non-CLABSI group were older, with a mean age of 64.5 years compared with the CLABSI group (95% confidence interval [CI], 45.9-83.1 years). The mean Charlson Comorbidity Index scores were similar between the non-CLABSI (95% CI; 1.1-9.1) and CLABSI groups (95% CI, 1.8-8.4). The patient was a transfer from an outside hospital in 66.4% of events, but there was no difference between non-CLABSI and CLABSI according to this variable. The rate of an infectious disease consultation was similar in both groups (82.1% CLABSI compared with 86.4% non-CLABSI, $P = .54$). Use of echocardiography (including both transthoracic and transesophageal approaches) was not significantly different for CLABSI and non-CLABSI patients.

Table 1
Characteristics of primary *Staphylococcus aureus* HABSI associated with a CLABSI and non-CLABSI

Characteristic	CLABSI (n = 78)	Non-CLABSI (n = 44)	*P* value
Male	44 (56.4)	25 (56.8)	.97
MRSA	38 (48.7)	19 (43.2)	.56
Evidence of PIV infection	0 (0)	16 (20.4)	<.001
Evidence of midline infection	0 (0)	10 (22.7)	.002
Positive culture obtained in ICU	30 (38.5)	19 (43.2)	.61
Vancomycin MIC ≥2	4 (5.1)	0 (0)	.30
Infectious disease consultation	64 (82.1)	38 (86.4)	.54

NOTE. Values are n (%) or as otherwise indicated.
CLABSI, central line–associated bloodstream infection; *ICU*, intensive care unit; *MIC*, minimum inhibitory concentration; *MRSA*, methicillin-resistant *S aureus*; *PIV*, peripheral intravenous catheter.

Table 2
Comparison of CLABSI versus non-CLABSI outcomes using contingency tables to test for association

Outcome	CLABSI (n = 78)	Non-CLABSI (n = 44)	*P* value
Complicated bacteremia	0 (0)	7 (15.9)*	<.001
Septic thrombophlebitis	17 (21.8)	18 (40.9)	.025
Vertebral osteomyelitis	0 (0)	2 (4.6)	.13
Infective endocarditis	0 (0)	3 (6.8)	.046
Cardiac device infections	0 (0)	3 (2.3)	.045
Operative intervention required†	0 (0)	4 (9.1)	.016
30-day all-cause mortality	17 (21.8)	9 (20.4)	.86
365-day all-cause mortality	14 (39.7)	7 (36.4)	.71

NOTE. Values are n (%) or as otherwise indicated.
CLABSI, central line–associated bloodstream infection.
*Seven total patients with complicated bacteremia.
†One operation for infective endocarditis and 3 operations for cardiac implantable electrophysiologic device removal.

Outcomes associated with primary SA HABSI are shown in Table 2. Overall, 30-day and 1-year mortality in the cohort were 21.3% and 38.5%, respectively. Thirty-day mortality was 21.8% in those with a CLABSI and 20.4% in those with a non-CLABSI ($P = .90$), and 1-year mortality was 39.7% in those with a CLABSI and 36.4% in those with a non-CLABSI ($P = .70$).

Complicated SA HABSI was significantly more common in the non-CLABSI group (15.9% vs 0%, $P \leq .001$). Septic thrombophlebitis was the most common complication for both groups. However, only the non-CLABSI group had associated extravascular complications, including vertebral osteomyelitis (n = 2), cardiac implantable electrophysiologic device infection (n = 3), and infective endocarditis (n = 3). Four patients with non-CLABSI required operation for complications of their bacteremia, including 3 cardiac device extractions and 1 aortic valve replacement for infective endocarditis. There were no operative interventions in those with a CLABSI sec-