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Major article

Epidemiology of bloodstream infections caused by methicillin-resistant *Staphylococcus aureus* at a tertiary care hospital in New York

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Background: In the United States, bloodstream infections (BSIs) are predominated by *Staphylococcus aureus*. The proportion of community-acquired methicillin-resistant *S aureus* (MRSA) BSI is on the rise. The goal of this study is to explore the epidemiology of BSI caused by *S aureus* within Staten Island, New York.

Methods: This is a case-case-control study from April 2012-October 2014. Cases were comprised of patients with BSI secondary to MRSA and methicillin-sensitive *S aureus* (MSSA). The control group contained patients who were hospitalized during the same time period as cases but did not develop infections during their stay. Two multivariable models compared each group of cases with the uninfected controls.

Results: A total of 354 patients were analyzed. Infections were community acquired in 76% of cases. The major source of BSI was skin-related infections (n = 76). The first multivariable model showed that recent central venous catheter placement was an independent infection risk factor (odds ratio [OR] = 80.7; 95% confidence interval [CI], 2.2-3,014.1). In the second model, prior hospital stay >3 days (OR = 4.1; 95% CI, 1.5-5.7) and chronic kidney disease (OR = 3.0; 95% CI, 1.01-9.2) were uniquely associated with MSSA. Persistent bacteremia, recurrence, and other hospital-acquired infections were more likely with MRSA BSI than MSSA BSI.

Conclusion: Most infections were community acquired. The presence of a central venous catheter constituted a robust independent risk factor for MRSA BSI. Patients with MRSA BSI suffered worse outcomes than those with MSSA BSI.

Despite significant strides in antimicrobial therapy, *Staphylococcus aureus* continues to be implicated in a variety of infections ranging from superficial skin to deep-rooted life-threatening systemic infections.[1] In particular, morbidity and mortality rates remain elevated with *S aureus*—related bloodstream infections (BSIs) and infective endocarditis.[2-4] Methicillin-resistant *S aureus* (MRSA)—related bacteremia is associated with higher mortality, morbidity, and health care costs compared with that of methicillin-sensitive *S aureus* (MSSA).[5-7] Furthermore, the emergence of community-acquired MRSA in patients without the typically recognized risk factors has considerably altered therapeutic strategies and infection control practices in the hospital setting.[8,9] Although many infections secondary to *S aureus* have become manageable in recent times, the re-emergence of antibiotic resistance and community-acquired strains has maintained this pathogen's significance as a threat to public health.[10] This brings forth an array of obstacles that makes *S aureus* ever more difficult to treat. Some of these challenges include the decrease in glycopeptide susceptibility of MRSA and the looming threat of vancomycin-resistant *S aureus*.[8,10,11]

MRSA-related infections are considered to be a major public health concern around the world.[9] Based on data from the National Nosocomial Infections Surveillance System, the prevalence of invasive MRSA infections had all but doubled from 1996-2004.[12-16] In 2005, the Centers for Disease Control and Prevention (CDC)

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underwent active monitoring of invasive MRSA infections through the Active Bacterial Core surveillance system within 9 U.S. cities.[17] During this 6-year surveillance, the CDC observed an increase in the overall proportion of invasive community-acquired and community-onset infections despite a decrease in the total number of invasive MRSA infections.[18] Multiple studies around the world have examined *S aureus* and MRSA bacteremia, albeit with significant variations in the reported incidence rates and described epidemiology. For instance, MRSA rates in Portugal and Italy had elevated to reach 54% and 58%, respectively.[19] In Japan around the same period in time, a staggering 70% of *S aureus* bloodstream cultures were resistant to methicillin in 2001.[20] In the United States, the incidence of *S aureus* bacteremia varies across ethnicities, age groups, and specific vulnerable populations. Some of these include hemodialysis patients, injection drug users, and individuals infected with HIV.[21]

The purpose of this study is to explore the epidemiology and complications of MRSA BSIs at Staten Island University Hospital (SIUH) in New York. Specifically, the study seeks to ascertain the unique risk factors that predispose to MRSA BSI and to determine whether those infections resulted in worse outcomes than MSSA.

METHODS

Study location

The study was conducted at SIUH, a specialized 714-bed tertiary care center located in New York City. It is a major referral center for the city of Staten Island serving a population of approximately 500,000 people with surgical, medical, pediatric, and obstetric care. SIUH contains specialized burn, cardiothoracic, and ventilator units along with 4 intensive care units (ICUs) and a dialysis center. The hospital serves a wide population of different socioeconomic classes from Brooklyn and Staten Island. According to published census results in 2010, the white population, including Italian ancestry, constitutes approximately 64% of Staten Island's inhabitants. The second largest group in Staten Island was of Hispanic origin, comprising 17% of the population as determined by the same census. Asian and black individuals formed the remaining major demographic breakdown in 7.4% and 9.5%, respectively.

Study design: cases and controls

This is a case-case-control study designed to determine the risk factors and complications that are associated with MRSA BSI in patients admitted to SIUH from April 2012-October 2014. Patients included in the final analysis were distributed across 3 major groups. The first group of cases consisted of patients with MRSA BSI, whereas the second group were patients with MSSA BSI. The control group included patients hospitalized during the same time frame as cases but who did not contract infection during their hospital stay. A list of all positive blood cultures growing *S aureus* was provided by the microbiology laboratory. Adults >18 years of age who had a positive blood culture with *S aureus* on admission or during their hospitalization could be included in the final analysis. Patients with recurrent *S aureus* infections were encountered but could only be enrolled in the study once. The control group was made up entirely of uninfected patients who were also identified in a retrospective manner. Using a random integer generating software, controls were selected from a comprehensive list of patients provided by the medical records department. This group contained admitted patients who were hospitalized during the same time frame as cases but did not contract infection during their hospital stay. Two physicians reviewed the medical chart of each admission pertaining to a potential control to ensure eligibility into this category. Controls could therefore fall under any hospital service as long as it was determined that they remained free of infection during their stay.

Data collection

Clinical data were collected from every patient's electronic medical chart using a comprehensive case report form. Laboratory and radiology software were also made available to ensure completion of data. The same case report form was used for patients with MRSA- and MSSA-related BSIs. The collected information consisted of basic demographics, comorbid medical conditions, treatment, and complications (including readmission and recurrence). Specifically, the data obtained included the following: age, sex, length of hospitalization, comorbid illnesses (malignancy, chronic obstructive pulmonary disease, chronic kidney disease [CKD], diabetes mellitus, etc), recent immune suppression, hemodialysis, HIV status, history of endocarditis, and intravenous drug abuse. Other potential risk factors pertaining to recent hospitalizations were also documented. These included central venous catheters (CVCs), urinary catheters, nasogastric tube insertion, mechanical ventilation, antibiotic use, surgery, prior hospitalization, and ICU stay. The Charlson Comorbidity Index was calculated for every patient to estimate illness severity and correlate with observed complications.

The study looked at complications that arose as a result of MRSA and MSSA BSIs. The following sequelae were analyzed for both case groups: sepsis, septic shock, acute kidney injury, cardiovascular event, cerebrovascular event, persistent bacteremia, prolonged hospital stay, ICU admission, other hospital-acquired infections, respiratory failure, and recurrent infection. These outcomes were considered present if they occurred after documentation of *S aureus* BSI and before discharge from the hospital. The assessment of recurrent MRSA or MSSA BSI was performed in the same manner consistent with the case-control study design. Patients' medical records and laboratory data were retrospectively inspected for *S aureus* BSI recurrence that occurred 6 months after their initial discharge date. All records of infection complications or recurrences were collected retrospectively, and patients were neither contacted by person nor phone for data collection beyond the study initiation date.

Definitions

Variables were defined before the study was initiated. Bacteremia was considered hospital acquired when cultures were drawn >48 hours after admission.[22] In contrast, infection was designated as health care associated when it involved nursing home residents or patients receiving home or outpatient intravenous therapy, chemotherapy, wound care, or hemodialysis.[22] An absolute neutrophil count of <1,000 cells/mm^3 rendered patients as immune suppressed. Furthermore, an immune compromised state was also considered present if patients had received any immunesuppressive medication, radiation, or corticosteroids (analogous to 20 mg prednisone for at least 7 days) within 30 days of *S aureus* BSI. Patients were defined as having CKD if their glomerular filtration rate was <50 mL/min. Variables for infection acquisition, such as recent ICU stay, surgery, and prior hospital stay, were all considered to be risk factors within a time frame of 1 month from the occurrence of *S aureus* BSI. The placement of a nasogastric tube, urinary catheter, CVC, or mechanical ventilation was similarly documented when present within 1 month before infection. Information pertaining to antibiotic intake before a BSI caused by *S aureus* was collected in 2 separate variables. The first variable noted any exposure to antimicrobials for >48 hours within 30 days of infection while the second variable involved antibiotic use specifically

Table 1
Baseline demographics and clinical characteristics among cases and controls

Characteristic	MRSA	MSSA	Controls	MRSA versus controls		MSSA versus controls	
				OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age, mean (range)	66.75 (18-99)	65.86 (28-95)	69.82 (28-95)	—	.15	—	.05
Male sex, n (%)	69 (58.5)	75 (63.6)	52 (44.1)	1.79 (1.07-2.99)	.02	2.21 (1.31-3.73)	.004
Comorbidity, n (%)							
Diabetes mellitus	61 (51.7)	48 (40.7)	30 (25.4)	3.14 (1.81-5.44)	<.01	2.01 (1.16-3.50)	.02
Renal insufficiency	48 (41.0)	53 (44.9)	16 (13.6)	4.44 (2.33-8.44)	<.01	5.20 (2.74-9.86)	<.001
COPD	31 (26.3)	22 (18.6)	14 (11.9)	2.65 (1.32-5.29)	.008	—	.20
Malignancy	35 (19.7)	28 (23.7)	31 (26.3)	—	.33	—	.38
Hemodialysis	30 (25.4)	26 (22.0)	1 (0.8)	39.89 (5.34-298.12)	<.001	33.06 (4.40-248.23)	<.001

CI, confidence interval; *COPD*, chronic obstructive pulmonary disease; *MRSA*, methicillin-resistant *Staphylococcus aureus*; *MSSA*, methicillin-sensitive *S aureus*; *OR*, odds ratio.

within 24 hours of infection. The source of the bacteremia was determined to the best of our ability by reviewing the medical chart. This was performed by a physician who reviewed the daily progress notes, radiology studies, and other culture data from the microbiology department databases. The definition for persistent bacteremia adopted from Fowler et al was defined as a documented bacteremia of at least 1 week while the patient was receiving antimicrobial therapy to which the isolate is susceptible.[23]

Statistical analysis

Statistical analysis was conducted using SPSS 22.0 (IBM, Armonk, NY). Categorical variables were analyzed using χ^2 and Fisher exact tests, whereas continuous normally distributed variables were analyzed via the independent samples *t* test. Non-normally distributed continuous variables were categorized. All variables were initially examined through bivariable analysis to determine associations between potential risk factors and MRSA BSI. Associations with a $P \leq .10$ were chosen to be further analyzed in the multivariable model using backward stepwise logistic regression. Therefore, it was possible to identify independent risk factors for MRSA BSI and to control for confounding variables. An odds ratio (OR) and 95% confidence interval (CI) were calculated to ascertain the strength of associations. All tests were 2 tailed, and $P < .05$ was regarded as significant. Moreover, the predictive accuracy of the multivariable model was assessed by calculating its capability to differentiate controls from cases. This was accomplished by analyzing the receiver operating characteristic curve and defining an adequate discriminatory capability as an area under the receiver operating characteristic curve of $\geq$0.5.

A separate model was used to analyze the sequelae of *S aureus* BSI. Because variables within this section were all categorical in nature, the χ^2 test was used to compare the outcomes of MRSA and MSSA infections. Associations with $P \leq .10$ were considered sufficient for further analysis via multivariable logistic regression. Using this model, complications unique to MRSA BSI were determined. All variables were 2 tailed, and $P < .50$ was considered significant.

Ethics

The protocol was submitted to the Institutional Review Board of the North-Shore Long Island Jewish Health Care System. Approval and waiver of consent were obtained before the collection of any data.

RESULTS

Demographics and infection characteristics

A total of 354 patients were analyzed in the final dataset. During the study time frame, 121 patients with MRSA BSI were identified by the microbiology laboratory. Three of these cultures simultaneously contained other organisms and were discarded from the final analysis. Therefore, the first category of patients (MRSA BSI) was comprised of 118 cases in total. The laboratory identified 145 MSSA blood cultures during the same period, of which 118 were randomly selected to represent the second group of cases. Infections were ascertained to be community onset in 76% of cases without significant differences between MRSA (n = 89) and MSSA (n = 92). Health care–associated and nosocomial infections were encountered in 14% and 10%, respectively. Skin- and skin structure–related infections comprised most cases (n = 76), followed by pulmonary infections (n = 46), and catheter-related infections (n = 24). The baseline demographics and underlying medical conditions among all study groups are illustrated in Table 1. ORs and CIs are only displayed for those variables that were significant compared with uninfected controls. Of all of the patients, 55% were men; however, the differences in sex were not found to be significant across the 3 groups. Patients with MRSA BSI had a mean age of 66.7 years, whereas patients with MSSA infections had a mean age of 65.9 years. As shown in Table 1, the uninfected control group (group 3) patients were older than both groups of cases; however, the differences were only significant when compared with MSSA-infected patients. Overall, the MRSA group was seen to have more comorbid illnesses than patients infected with MSSA. Furthermore, both case groups were found to be sicker than the uninfected control group as demonstrated by a significantly higher Charlson Comorbidity Index (MRSA vs controls: $t_{234} = 4.29$, $P < .001$; MSSA vs controls: $t_{234} = 3.01$, $P = .003$). In particular, patients with MRSA bacteremia were observed to have more chronic obstructive pulmonary disease, diabetes mellitus, and malignancy than the MSSA and uninfected control groups.

Clinical and risk factor analysis

Bivariable analysis was conducted for all collected risk factors and comorbid medical conditions. Table 2 displays the results that were significantly different among the MRSA and MSSA groups when compared with uninfected controls. Within 30 days, patients infected with *S aureus* were more likely to have had hemodialysis, hospitalization, surgery, antibiotic use, immune-suppressive therapy, central line insertion, urinary catheter placement, ICU stay, mechanical ventilation, and nasogastric tube insertion than uninfected controls. MRSA and MSSA BSIs shared numerous predisposing factors when compared with the uninfected control group. These included the following: hemodialysis, antibiotic use within 30 days, immune suppression, recent urinary catheter for $\geq$3 days, recent mechanical ventilation for $\geq$3 days, recent hospital stay for $\geq$3 days, and recent ICU stay for $\geq$3 days. In contrast, recent surgery ($P < .001$), antibiotic use within 24 hours ($P < .001$), recent CVC insertion $\geq$3 days ($P < .001$), and recent nasogastric tube placement

Table 2
Bivariable analysis of significant risk factors for MRSA, MSSA, and uninfected controls

Characteristic	MRSA	MSSA	Controls	MRSA versus controls		MSSA versus controls	
				OR (95% CI)	*P* value	OR (95% CI)	*P* value
Risk factors							
Surgery within 30 d	20 (16.9)	5 (4.2)	3 (2.5)	7.82 (2.25-27.12)	<.001	—	.36
Antibiotic use within 24 h	13 (11.0)	6 (5.1)	1 (0.8)	14.49 (1.86-112.63)	<.001	—	.06
Antibiotic use within 30 d	26 (22.0)	11 (9.3)	4 (3.4)	8.05 (2.71-23.91)	<.001	—	.05
Steroid-immune suppressive use	17 (14.4)	15 (12.7)	2 (1.7)	9.76 (2.20-43.28)	<.001	8.44 (1.89-37.82)	<.001
Urinary catheter for ≥3 d	25 (21.2)	11 (9.3)	0 (0)	—	<.001	—	<.001
Central line for ≥3 d	15 (12.7)	4 (3.4)	1 (0.8)	17.2 (2.2-132.5)	<.001	—	.37
Mechanical ventilation for ≥3 d	11 (9.3)	2 (1.7)	0 (0)	—	<.001	—	0.50
Nasogastric tube for ≥3 d	13 (11.0)	5 (4.2)	0 (0)	—	<.001	—	.06
Hospital stay for ≥3 d	46 (39.0)	33 (28.0)	14 (11.9)	4.75 (2.43-9.27)	<.001	2.88 (1.45-5.74)	.002
ICU stay for ≥3 d	17 (14.4)	7 (5.9)	0 (0)	—	<.001	—	.01
Alive at discharge	92 (78.0)	90 (80.5)	116 (98.3)	0.06 (0.02-0.28)	<.001	0.07 (0.02-0.31)	<.001

NOTE. Values are n (%) or as otherwise indicated.
CI, confidence interval; *ICU*, intensive care unit; *MRSA*, methicillin-resistant *Staphylococcus aureus*; *MSSA*, methicillin-sensitive *S aureus*; *OR*, odds ratio.

≥3 days were found to be significantly associated with patients infected with MRSA BSI but not MSSA BSI. Furthermore, analysis of outcomes revealed that patients with MRSA BSI were more likely to develop recurrent infection ($P < .05$), persistent bacteremia ($P < .001$), and other hospital infections ($P < .05$) than patients with MSSA BSI. Mortality was evenly distributed across both case groups. In total, 48 patients had a fatal outcome. Mortality was attributable to *S aureus* bacteremia in 38 cases (23 MRSA vs 15 MSSA).

Multivariate analysis of risk factors

All variables with $P < .10$ from the bivariable analysis were included in the multivariate model. The results are displayed in Table 3. Stepwise backward logistic regression showed that retaining a CVC for ≥3 days represented a unique risk factor for MRSA BSI (OR = 80.7; 95% CI, 2.2-3,014.1). In the second multivariable model (MSSA vs uninfected controls), recent prior hospitalization for ≥3 days (OR = 4.1; 95% CI, 1.04-15.8) and CKD (OR = 3.0; 95% CI, 1.01-9.2) constituted independent predictors of infection.

Table 3
Results of multivariate analysis to identify unique risk factors for MRSA and MSSA bloodstream infections

Characteristic/risk factor	Adjusted OR	95% CI	*P* value
MRSA versus controls			
CVC for ≥3 d within 30 d	80.7	2.2-3,014.1	.02
MSSA versus controls			
Chronic kidney disease	3.0	1.01-9.2	.04
Prior hospitalization for ≥3 d within 30 d	4.1	1.04-15.8	.04

CI, confidence interval; *CVC*, central venous catheter; *MRSA*, methicillin-resistant *Staphylococcus aureus*; *MSSA*, methicillin-sensitive *S aureus*; *OR*, odds ratio.

DISCUSSION

S aureus bacteremia has been well described worldwide and more so in the United States. However, the last 2 decades have revealed that the epidemiology of *S aureus* infections is constantly changing. The continuous pressure exerted by antibiotics, emergence of novel community-acquired MRSA virulent strains, fluctuations in resistance patterns, and spread of MRSA into the community are thought to have played a role in these shifts.[23] Furthermore, improvements in infection control, hemodialysis, and central line insertion practices have impacted the proportion of MRSA bacteremia ensuing from such sources.[24] In this context, epidemiologic studies that assess the current risk factors for MRSA BSI are needed to identify specific vulnerable patient groups. Recent studies have recognized specific clinical characteristics that predispose patients to infections with MRSA bacteremia. Some of these include intravascular catheters or devices,[25] liver cirrhosis,[26] and surgery within 3 months of infection.[26]

We identified 118 cases of MRSA BSI that fulfilled the inclusion criteria between April 2012 and October 2014. As seen in the results section, an overwhelming percentage (76%) of all *S aureus* BSI cases was community acquired or community onset. This finding reflects a change in MRSA epidemiology that was initially described in 2007.[17] Indeed, the assessment of underlying bacteremia sources in our cohort demonstrated that skin- and skin structure–related infections comprised most cases. These results are particularly critical bearing in mind the emergence of virulent MRSA strains that have caused complicated epidemics. Tattevin et al indisputably showed in 2012 that BSI secondary to USA300 emerged as a consequence of a skin and skin structure epidemic caused by the same strain.[27] Numerous recent studies in the United States and around the world have similarly implicated MRSA as the major pathogen for skin and skin structure infections with increasing prevalence.[28-31]

The case-case-control design of this study permits for the identification of predisposing factors that are unique to MRSA BSI. Although the bivariable analysis indicated an association between MRSA and several risk factors (Tables 1 & 2), the only true independent risk factor that remained significant after multivariable analysis was the recent placement of a CVC within 30 days of infection. Furthermore, a subanalysis of CVC days was conducted to determine a threshold number associated with the greatest risk for MRSA BSI. It is noteworthy to mention that the placement of a CVC for ≤2 days was not independently associated with MRSA or MSSA BSI. However, the recent (within 1 month of infection) insertion of a CVC for at least 3 days constituted a unique and robust risk factor for MRSA BSI in our cohort. The strength of this association can be seen in the calculated OR of 80.7. Central line–associated bloodstream infections (CLABSIs) caused by *S aureus* are known to cause increased mortality,[32] morbidity, and cost of care.[33] CLABSIs can also result in grave complications, such as endocarditis (native valve[34] and prosthetic valve[35]) and vertebral osteomyelitis.[2] These infections represent 10% (n = 24) of all *S aureus* BSI cases in our study. The percentage of CLABSI seen in our institution over the studied 2.5-year period is consistent with the decreases observed elsewhere in the literature. Between 2001 and 2009, the rates of CLABSI secondary to MRSA decreased by 50%.[24] This has been attributed to improvements in infection control and insertion

practices, such as those proposed by the CDC in 2002.[36] In a retrospective matched case-control study, Yoshida et al showed that retaining a central line for a prolonged period (especially >30 days) singlehandedly outweighed all other risk factors for the development of MRSA CLABSI.[37] Moreover, guidelines and studies have shown that recurrence of infection will likely occur if an infected CVC is not removed.[38] All central line catheters were removed in each documented case of *S aureus* CLABSI that we retrospectively reviewed. In the future, it would be interesting to conduct a cohort study that prospectively follows patients after central line insertions at our institution. This would allow for the determination of CVC-specific risk factors, including the number of insertion attempts, total procedure time, and anatomic site of insertion.

In the second multivariable model (MSSA vs uninfected controls), prior hospital stay for >3 days and CKD were found to be independent predictors of infection. Although the rationale for the former may not be immediately evident, similar results were encountered by Crowley et al. in the United Kingdom renal registry report for CKD and dialysis patients.[39] Crowley et al hypothesized that the more efficient screening and elimination programs aimed at MRSA within dialysis centers have favored its eradication at the expense of MSSA BSIs. Similarly, prior hospital stay was found to be independently associated with MSSA BSI in our patient population. This may be the effect of infection control practices that favor the elimination of MRSA at the expense of MSSA within the hospital setting. More studies are needed to establish and understand the relationship between CKD-HD (hemodialysis) and BSI secondary to MSSA. Prior antibiotic use in the month preceding infection seemed to be more associated with MRSA bacteremia after performing bivariable χ^2 analysis; however, both antibiotic variables consequently dropped from the multivariable model. For that reason, specific antibiotic classes were not analyzed.

As expected, patients with MRSA bacteremia fared worse than those with MSSA BSI. Specifically, patients with MRSA were more likely to develop persistent bacteremia, recurrence, prolonged hospitalization, and other hospital-acquired infections. Mortality rates did not significantly differ across both case groups. Furthermore, our analysis did not uncover any significant differences in sepsis, septic shock, acute kidney injury, or ICU admission between both case groups.

Limitations and strengths

Using multivariate logistic regression and matching *S aureus* infections in both case groups solely to BSIs served to decrease the effects of confounding variables. To reduce selection bias, cases were included only once, and a random integer generator was used to select MSSA BSI cases. Furthermore, all consecutive cases of MRSA BSI eligible for inclusion were enrolled. Because this study was not ideally designed to research treatment efficacy, MRSA isolates were not analyzed across different minimum inhibitory concentrations for vancomycin. This study is limited by its retrospective nature and the fact that it was conducted in 1 center. This design makes it especially difficult to accurately determine the severity of bacteremia, which was not included in the analysis. Every effort was made to obtain all the pertinent clinical and laboratory data needed for analysis. However, details of treatment, including antibiotics administered to patients who transferred from other hospitals, were sometimes unavailable. Moreover, 5 doctors were involved in gathering clinical data from the electronic charts, and they were furthermore unblinded to the assignments of cases and controls. Because the physicians involved in data collection had access to progress notes, it was impossible to blind them effectively from the type of case being filled. Nevertheless, the effect of this bias is minimal because the data collected are objective in nature.

CONCLUSION

This study showed that within 1 month of MRSA bacteremia, the insertion of a CVC for at least 3 days constituted an independent risk factor for infection. Furthermore, the study demonstrated that most of the *S aureus* BSIs in our hospital are now community acquired and largely associated with skin and skin structure infections. These results alerted us to re-emphasize proper central line insertion guidelines and prompt CVC removal when possible. We draw special attention to patients with CVCs as a highly vulnerable group for MRSA BSI in our institution. Given the observed strength of this association, more studies are warranted to evaluate the utility of prophylactic antibiotics within these patients. This is especially necessary because patients who developed consequent MRSA BSI suffered persistent bacteremia, recurrence, prolonged hospitalization, and other hospital-acquired infections.

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References

1. Lowy FD. Staphylococcus aureus infections. N Engl J Med 1998;339:520-2.
2. Fowler VG, Justice A, Moore C, Benjamin DK, Woods CW, Campbell S, et al. Risk factors for hematogenous complications of intravascular catheter-associated Staphylococcus aureus bacteremia. Clin Infect Dis 2005;40:695-703.
3. Fowler VG, Miro JM, Hoen B, Cabell CH, Abrutyn E, Rubinstein E, et al. Staphylococcus aureus endocarditis: a consequence of medical progress. JAMA 2005; 293:3012-21.
4. Petti CA, Fowler VG. Staphylococcus aureus bacteremia and endocarditis. Cardiol Clin 2003;21:219-33.
5. Cosgrove SE, Sakoulas G, Perencevich EN, Schwaber MJ, Karchmer AW, Carmeli Y. Comparison of mortality associated with methicillin-resistant and methicillin-susceptible Staphylococcus aureus bacteremia: a meta-analysis. Clin Infect Dis 2003;36:53-9.
6. Cosgrove SE, Qi Y, Kaye KS, Harbarth S, Karchmer AW, Carmeli Y. The impact of methicillin resistance in Staphylococcus Aureus bacteremia on patient outcomes mortality, length of stay, and hospital charges. Infect Control Hosp Epidemiol 2005;26:166-74.
7. Shurland S, Zhan M, Bradham DD, Roghmann MC. Comparison of mortality risk associated with bacteremia due to methicillin-resistant and methicillin-susceptible Staphylococcus aureus. Infect Control Hosp Epidemiol 2007;28: 273-9.
8. Schito GC. The importance of the development of antibiotic resistance in Staphylococcus aureus. Clin Microbiol Infect 2006;12(Suppl):3-8.
9. Calfee DP, Durbin LJ, Germanson TP, Toney DM, Smith EB, Farr BM. Spread of methicillin-resistant Staphylococcus aureus (MRSA) among household contacts of individuals with nosocomially acquired MRSA. Infect Control Hosp Epidemiol 2003;24:422-6.
10. Bal AM, Gould IM. Antibiotic resistance in Staphylococcus aureus and its relevance in therapy. Expert Opin Pharmacother 2005;6:2257-69.
11. Sakoulas G, Moellering RC. Increasing antibiotic resistance among methicillin-resistant Staphylococcus aureus strains. Clin Infect Dis 2008;46(Suppl):360-7.
12. Lawton RM, Fridkin SK, Steward CD, Edwards JR, Pryor ER, McGowan JE, et al. Intensive care antimicrobial resistance epidemiology (ICARE) surveillance report, data summary from January 1996 through December 1997. Am J Infect Control 1999;27:279-84.
13. National Nosocomial Infections Surveillance (NNIS) System. Data summary from January 1992-June 2001, issued August 2001. Am J Infect Control 2001; 29:404-21.
14. National Nosocomial Infections Surveillance (NNIS) System Report. Data summary from January 1992 to June 2002, issued August 2002. Am J Infect Control 2002;30:458-75.
15. National Nosocomial Infections Surveillance (NNIS) System Report. Data summary from January 1992 through June 2003, issued August 2003. Am J Infect Control 2003;31:481-98.
16. National Nosocomial Infections Surveillance (NNIS) System Report. Data summary from January 1992 through June 2004, issued October 2004. Am J Infect Control 2004;32:470-85.

17. Klevens RM, Morrison MA, Nadle J, Petit S, Gershman K, Ray S, et al. Invasive methicillin-resistant Staphylococcus aureus infections in the United States. JAMA 2007;298:1763-71.
18. Dantes R, Mu Y, Belflower R, Aragon D, Dumyati G, Harrison LH, et al. National burden of invasive methicillin-resistant Staphylococcus aureus infections, United States, 2011. JAMA Intern Med 2013;173:1970-8.
19. Fluit AC, Wielders CL, Verhoef J, Schmitz FJ. Epidemiology and susceptibility of 3,051 Staphylococcus aureus isolates from 25 university hospitals participating in the European SENTRY study. J Clin Microbiol 2001;39:3727-32.
20. Boyce JM, Cookson B, Christiansen K, Hori S, Vuopio-Varkila J, Kocagöz S, et al. Methicillin-resistant Staphylococcus aureus. Lancet Infect Dis 2005;5:653-63.
21. Tong SY, Davis JS, Eichenberger E, Holland TL, Fowler VG. Staphylococcus aureus infections: epidemiology, pathophysiology, clinical manifestations, and management. Clin Microbiol Rev 2015;28:603-61.
22. Bishara J, Goldberg E, Leibovici L, Samra Z, Shaked H, Mansur N, et al. Healthcare-associated vs. hospital-acquired Staphylococcus aureus bacteremia. Int J Infect Dis 2012;16:e457-63.
23. Fowler VG, Sakoulas G, McIntyre LM, Meka VG, Arbeit RD, Cabell CH, et al. Persistent bacteremia due to methicillin-resistant Staphylococcus aureus infection is associated with agr dysfunction and low-level in vitro resistance to thrombin-induced platelet microbicidal protein. J Infect Dis 2004;190:1140-9.
24. Lu SY, Chang FY, Cheng CC, Lee KD, Huang YC. Methicillin-resistant Staphylococcus aureus nasal colonization among adult patients visiting emergency department in a medical center in Taiwan. PLoS One 2011;6:e18620.
25. Lewis T, Chaudhry R, Nightingale P, Lambert P, Das I. Methicillin-resistant Staphylococcus aureus bacteremia: epidemiology, outcome, and laboratory characteristics in a tertiary referral center in the UK. Int J Infect Dis 2011;15:e131-5.
26. Pastagia M, Kleinman LC, de la Cruz EG, Jenkins SG. Predicting risk for death from MRSA bacteremia. Emerg Infect Dis 2012;18:1072-80.
27. Tattevin P, Schwartz BS, Graber CJ, Volinski J, Bhukhen A, Bhukhen A, et al. Concurrent epidemics of skin and soft tissue infection and bloodstream infection due to community-associated methicillin-resistant Staphylococcus aureus. Clin Infect Dis 2012;55:781-8.
28. Talan DA, Krishnadasan A, Gorwitz RJ, Fosheim GE, Limbago B, Albrecht V, et al. Comparison of Staphylococcus aureus from skin and soft-tissue infections in US emergency department patients, 2004 and 2008. Clin Infect Dis 2011;53:144-9.
29. Frazee BW, Lynn J, Charlebois ED, Lambert L, Lowery D, Perdreau-Remington F. High prevalence of methicillin-resistant Staphylococcus aureus in emergency department skin and soft tissue infections. Ann Emerg Med 2005;45:311-20.
30. Nimmo G, Coombs G, Pearson J, O'Brien F, Christiansen K, Turnidge J, et al. Methicillin-resistant Staphylococcus aureus in the Australian community: an evolving epidemic. Med J Aust 2006;184:384-8.
31. Otter JA, French GL. Molecular epidemiology of community-associated methicillin-resistant Staphylococcus aureus in Europe. Lancet Infect Dis 2010;10:227-39.
32. Chu VH, Crosslin DR, Friedman JY, Reed SD, Cabell CH, Griffiths RI, et al. Staphylococcus aureus bacteremia in patients with prosthetic devices: costs and outcomes. Am J Med 2005;118:1416.
33. Rosen AB, Fowler VG, Corey GR, Downs SM, Biddle AK, Li J, et al. Cost-effectiveness of transesophageal echocardiography to determine the duration of therapy for intravascular catheter-associated Staphylococcus aureus bacteremia. Ann Intern Med 1999;130:810-20.
34. Ehni WF, Reller LB. Short-course therapy for catheter-associated Staphylococcus aureus bacteremia. Arch Intern Med 1989;149:533-6.
35. Guerrero ML, López JJ, Goyenechea A, Fraile J, de Górgolas M. Endocarditis caused by Staphylococcus aureus: a reappraisal of the epidemiologic, clinical, and pathologic manifestations with analysis of factors determining outcome. Medicine (Baltimore) 2009;88:1-22.
36. O'Grady NP, Alexander M, Dellinger EP, Gerberding JL, Heard SO, Maki DG, et al. Guidelines for the prevention of intravascular catheter–related infections. Clin Infect Dis 2002;35:1281-307.
37. Yoshida J, Ishimaru T, Kikuchi T, Matsubara N, Ueno T, Hirata N, et al. Central line-associated bloodstream infection: is the hospital epidemiology of methicillin-resistant Staphylococcus aureus relevant? J Infect Chemother 2010;16:33-7.
38. Walker TM, Bowler IC, Bejon P. Risk factors for recurrence after Staphylococcus aureus bacteraemia. A retrospective matched case–control study. J Infect 2009;58:411-6.
39. Crowley L, Wilson J, Guy R, Pitcher D, Fluck R. Epidemiology of Staphylococcus Aureus bacteraemia amongst patients receiving dialysis for established renal failure in England in 2009 to 2011: a joint report from the health Protection Agency and the UK Renal Registry. Nephron Clin Pract 2012;120(Suppl):c233-45.