Risk Factors for Complications in Children with *Staphylococcus aureus* Bacteremia

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Objectives To determine risk factors for complications in children with *Staphylococcus aureus* (*S aureus*) bacteremia, including methicillin resistance.

Study design Single center, retrospective cohort study of children ≤18 years of age hospitalized with *S aureus* bacteremia. We compared clinical characteristics and outcomes between those with methicillin-sensitive *S aureus* (MSSA) and methicillin-resistant *S aureus* (MRSA) bacteremia. Multivariate regression models identified risk factors associated with developing complications and with longer duration of bacteremia.

Results We identified 394 episodes of *S aureus* bacteremia, 279 (70.8%) with MSSA, and 115 (29.2%) with MRSA. Primary site of infection was catheter-related in 34%, musculoskeletal in 30%, skin/soft tissue in 10.2%, pneumonia in 6.4%, and endovascular in 6.6%. Eight children (2.0%) died within 30 days because of *S aureus* bacteremia, 15 (3.5%) had recurrence within 30 days, and 38 (9.6%) had complications including septic emboli or a metastatic focus of infection. Methicillin resistance was associated with development of a complication (aOR 3.31; 95% CI 1.60-6.85), and catheter-related infections were less likely to be associated with a complication (aOR 0.40; 95% CI 0.15-1.03). In a Poisson regression analysis on duration of bacteremia, methicillin resistance, musculoskeletal infection, endovascular infection, black race, and delayed intervention for source control were significantly associated with longer duration of bacteremia.

Conclusions In this cohort of children with *S aureus* bacteremia, MRSA infections ere associated with longer duration of bacteremia and a higher likelihood of complications. *(J Pediatr 2019;208:214-20)*.

Staphylococcus aureus (*S aureus*) is among the most common causes of bloodstream infections in hospitalized children, accounting for approximately 10% of nosocomial bloodstream infections in children.[1-3] The mortality attributed to *S aureus* bacteremia in children has been reported as 0.7%-5.1%,[4-8] and as many as one-third of patients with *S aureus* bacteremia develop complications.[4,9] A recent study reported risk factors for mortality in children with *S aureus* bacteremia including age <1 year, endocarditis, pneumonia, sepsis, and treatment with vancomycin (especially with methicillin-sensitive *S aureus* [MSSA]).[6]

The proportion of *S aureus* resistant to methicillin is evolving over time and varies greatly by geographic location.[10,11] Recent, single center studies in the US of *S aureus* bacteremia in children have reported methicillin-resistant *S aureus* (MRSA) rates between 19% and 44%.[5,12,13] Clinical outcomes of patients with MRSA bacteremia appear to differ compared with those with MSSA bacteremia. In adults, methicillin resistance is a strong risk factor for mortality in patients with *S aureus* bacteremia.[14] Although most pediatric studies have not shown a significant difference in mortality between patients with MRSA and MSSA,[6,13,15] a meta-analysis that pooled results of 7 cohort studies reported that risk of mortality in patients with MRSA was double that of patients with MSSA bacteremia.[16] MRSA bacteremia in children has also been associated with sepsis,[17] longer hospital length of stay,[6] and longer duration of bacteremia[18] compared with MSSA sepsis.

S aureus bacteremia can disseminate, leading to complications including septic emboli, thrombosis, and metastatic foci of infection.[19] In adults, MRSA infections are twice as likely as MSSA infections to cause hematogenous complications[20]; however, this has not been well studied in children. The objective of this study is to determine risk factors for complications in children with *S aureus* bacteremia, including methicillin resistance.

CHOP	Children's Hospital of Philadelphia
MIC	Minimum inhibitory concentration
MRSA	Methicillin-resistant *S aureus*
MSSA	Methicillin-sensitive *S aureus*
S aureus	Staphylococcus aureus

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Methods

All patients younger than 19 years of age hospitalized at Children's Hospital of Philadelphia (CHOP), a 520-bed children's hospital in Philadelphia, Pennsylvania between January 1, 2007 and November 17, 2014 with a blood culture positive for *S aureus* were evaluated for inclusion in the study. We defined an episode of *S aureus* bacteremia as a single blood culture positive for *S aureus* in a patient with signs consistent with an infection. Patients with polymicrobial bloodstream infections or transferred from another institution with incomplete laboratory or drug administration data were excluded. For subjects with more than 1 episode of *S aureus* bacteremia, only the first episode was included. Patients who died within 48 hours of onset of bacteremia were excluded because exposures such as source control intervention would not have had the opportunity to occur in those patients and to reduce immortal time bias for the secondary outcome duration of bacteremia.

Microbiologic Methods

Blood isolates of *S aureus* were included in our cohort. Methicillin resistance was defined as an isolate that was resistant to oxacillin (minimum inhibitory concentration [MIC] ≥4 mcg/mL) or cefoxitin (≥8 mcg/mL). Clinical samples were processed at the CHOP microbiology laboratory according to standard operating procedures. The Vitek 2 system (bioMérieux, Marcy-l'Étoile, France) was used for pathogen identification and antibiotic susceptibility testing. Any vancomycin MIC of ≥2 mcg/mL was verified by E-test.

Data Collection

Laboratory databases were used to identify all *S aureus* blood cultures during the study period. All clinical data were extracted from electronic health records through structured chart review.

Data abstracted through chart review included (1) demographic information; (2) presence of clinically significant underlying comorbidities present prior to the onset of bacteremia; (3) critical illness, defined as vasopressor use within 48 hours of onset of *S aureus* bacteremia; (4) site of infection, categorized as catheter-related as defined by the National Healthcare Safety Network,[21] skin and soft tissue, musculoskeletal (osteomyelitis, septic arthritis, or pyomyositis), endovascular (including endocarditis defined as ≥2 positive cultures more than 12 hours apart and echocardiogram findings consistent with endocardial involvement or suppurative thrombophlebitis), pneumonia, or other; (5) community-onset (bacteremia from culture obtained <48 hours after admission) vs hospital-onset; (6) surgical intervention for source control, categorized as none performed, performed within 3 days of bacteremia onset, performed beyond 3 days of bacteremia onset; (7) removal of catheter, categorized into not removed, removed within 3 days of bacteremia onset, removed beyond 3 days of bacteremia onset; (8) antibiotic treatment data from the hospital medication administration record; and (9) *S aureus* susceptibility to methicillin, clindamycin, and trimethoprim-sulfamethoxazole. All cases of endocarditis were adjudicated by 2 infectious diseases physicians. Removal of catheter was considered source control for catheter-related infections. Source control intervention, including catheter removal, was considered delayed if it occurred beyond 3 days of bacteremia onset.[22-24] Time to first antistaphylococcal antibiotic was defined as number of days between first positive blood culture and first dose of an antibiotic to which the *S aureus* isolate was susceptible. A subset of this cohort was included in a multicenter study (focused only on MRSA) in previously published work.[9] This study was approved by the CHOP Institutional Review Board.

Study Outcomes

The primary outcome was development of a complication from *S aureus* bacteremia. A complication was defined as hematogenous dissemination including new septic embolus or new thrombus as identified by ultrasound, metastatic focus of infection such as osteomyelitis or pyomyositis, or endocarditis identified at least one day after onset of bacteremia; progression of infection, such as an increase in size of thrombus or abscess; *S aureus*-attributable mortality within 30 days (when blood culture was positive for *S aureus* at the time of death, *S aureus* infection was listed in the medical record as cause of death, or death occurred within 14 days of first day of *S aureus* bacteremia without an alternate explanation as determined by the study investigators); or need for extracorporeal membranous oxygenation or development of stroke.

Additional outcomes included recurrence of bacteremia within 30 days (a new blood culture positive for *S aureus* within 30 days of discontinuing antibiotic therapy and separated by at least 7 days from the last positive blood culture for *S aureus*, with documentation of at least one negative blood culture in the interim time period); duration of bacteremia, defined as the number of days from the first to the last positive blood cultures; and readmission within 30 days of hospital discharge attributable to *S aureus* bacteremia. It is standard practice at our institution to obtain daily blood cultures for patients with *S aureus* bacteremia.

Statistical Analyses

We compared baseline characteristics and clinical outcomes between those with MSSA and MRSA bacteremia using χ^2 test for dichotomous and *t* test or Wilcoxon-Mann-Whitney for continuous variables. The prevalence of complications was determined and expressed as a point estimate (percent) and 95% CI within the group of patients with MSSA and with MRSA. For variables with missing data (race and ethnicity), race that was not reported (n = 2) was categorized as non-black when race was dichotomized, and ethnicity that was not reported (n = 94) was categorized as non-Hispanic.

For our primary analysis, logistic regression was used to determine aORs with 95% CIs of complications associated with risk factors of interest among all patients with *S aureus*.

Table I. Baseline characteristics of children with *S aureus* bacteremia

Baseline characteristics	Total *S aureus* (n = 394)	MSSA (n = 279)	MRSA (n = 115)	*P* value
Age in y, mean (SD)	5.4 y (5.5)	5.2 y (5.6)	5.9 y (5.3)	.27
Infants <1 y (%)	37.1%	40.1%	29.6%	.048
Neonates <30 d (%)	11.2%	14.7%	2.6%	.001
Premature infants <36 wk gestation (%)	10.4%	11.1%	8.7%	.48
Female (%)	41.7%	43.8%	36.5%	.18
Race				
Caucasian (%)	42.8%	56.5%	9.6%	<.001
Black (%)	30.2%	25.2%	42.2%	.001
Other (%)	26.7%	18.0%	47.8%	<.001
Not reported (%)	0.5%	0.7%	0	
Ethnicity				
Hispanic (%)	9.6%	9.7%	9.6%	.97
Non-Hispanic (%)	66.5%	67.4%	64.4%	.97
Not reported (%)	23.6%	22.7%	26.1%	.46
Comorbid medical conditions				
Any (%)	68.3%	74.9%	52.2%	<.001
Cardiac (%)	22.8%	26.5%	13.9%	.007
Respiratory (%)	8.1%	5.4%	14.8%	.002
Oncologic (%)	7.1%	7.5%	6.1%	.61
Neuromuscular (%)	4.8%	2.9%	9.6%	.005
Hospital onset	38.3%	43.4%	26.1%	.001
Critically ill	21.8%	20.8%	24.4%	.44
Primary source of infection				
CLABSI	134 (34.0%)	108 (38.7%)	26 (22.6%)	.002
Musculoskeletal	118 (30.0%)	74 (26.5%)	44 (38.3%)	.02
SSTI	40 (10.2%)	26 (9.3%)	14 (12.2%)	.39
Endovascular	26 (6.6%)	20 (7.2%)	6 (5.2%)	.48
Pneumonia	25 (6.4%)	10 (3.6%)	15 (13.0%)	<.001
No source	34 (8.6%)	28 (10.0%)	6 (5.2%)	.12
Other source	17 (6.6 %)	13 (4.7%)	4 (3.5%)	.60
Source control intervention performed	164 (41.6%)	98 (35.%)	66 (57.4%)	<.001

CLABSI, central-line associated bloodstream infection; *SSTI*, skin/soft tissue infection.

We included in the initial model covariates that we determined a priori to be clinically significant: methicillin resistance, source control intervention performed, race, and critical illness. We also included in the initial model variables associated with development of complications in univariate analysis with *P* value of <.10. Methicillin resistance was retained in all models. Variables not significantly associated with development of complications were removed from the model one by one by backward selection. Variables were retained in the model if their removal resulted in a significant change in the model as determined by likelihood ratio test at $P < .05$. Goodness of fit of the model was tested using the Pearson goodness-of-fit test[25] with an alpha level of 0.10 necessary to conclude good fit.

For our secondary analysis, we evaluated factors associated with prolonged bacteremia >3 days in univariate analysis, and built a Poisson regression model to determine the effect of methicillin resistance on duration of bacteremia adjusting for any variable associated with prolonged bacteremia in univariate analysis with *P* value of <.05. Data were analyzed using Stata v 13.1 (StataCorp, College Station, Texas).

Results

Study Cohort

A total of 494 episodes of *S aureus* bacteremia were identified; 100 episodes were excluded: 79 occurred in patients transferred from another institution, 22 were age >18 years, and 4 died within 48 hours of bacteremia onset (some patients had overlapping exclusion criteria). Of the 394 episodes that met study inclusion criteria and were included in the cohort, 279 (70.8%) had MSSA bacteremia and 115 (29.2%) had MRSA bacteremia.

Clinical and Microbiologic Characteristics

Baseline characteristics of the cohort are described in Table I. Among the 134 patients with catheter-related infections, 54 of 134 (40.3%) underwent removal of the catheter within ≤3 days, 28 of 134 (20.9%) underwent removal of the catheter beyond 3 days, and 51 of 134 (38.1%) had their catheters retained.

The proportion of *S aureus* isolates that were methicillin-resistant declined over time, ranging from 11 of 23 (48%) in 2007 to 12 of 57 (21%) in 2014 (Figure). This declining trend was seen most notably among community-acquired infections, among which the proportion of isolates that were MRSA declined from 62% in 2007 to 25% in 2014 (Figure, B); whereas the proportion of hospital onset infections because of MRSA remained more stable over time (Figure, C). Among all *S aureus* isolates tested, 312 of 394 (79.2%) were susceptible to clindamycin, including 219 of 279 (78.5%) of MSSA isolates and 93 of 115 (80.9%) of MRSA isolates, and 382 of 387 (98.7%) were susceptible to

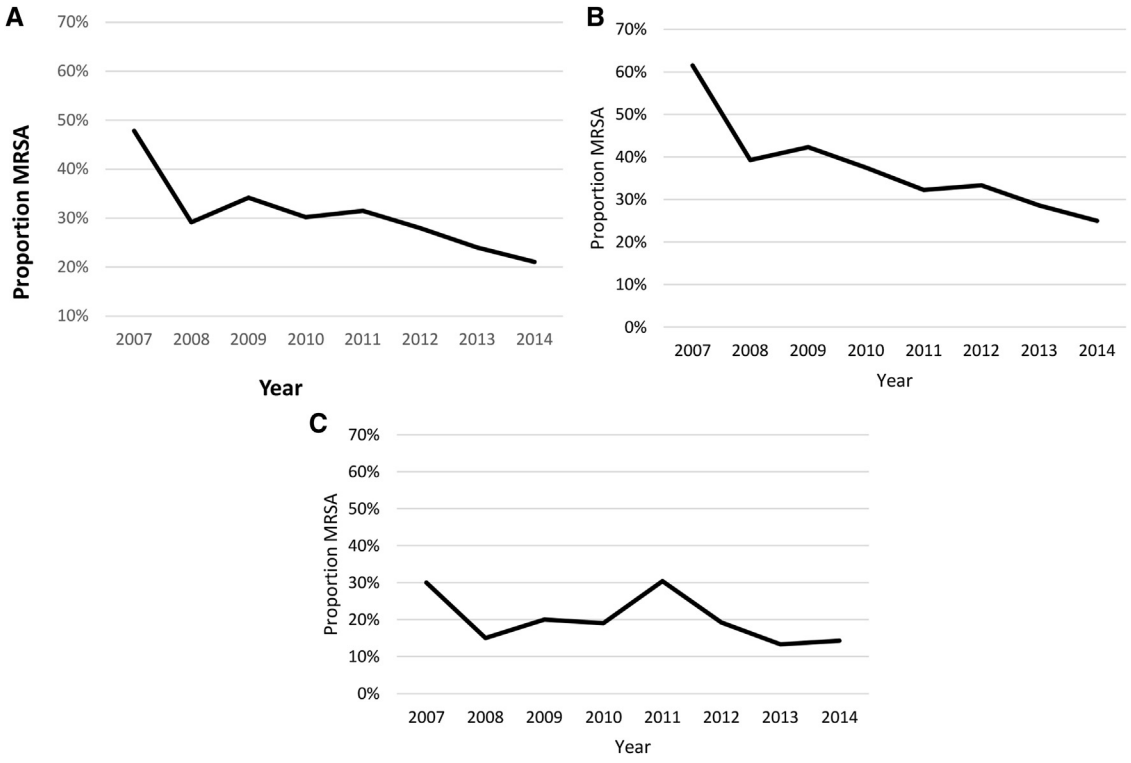

Figure. **A,** Proportion of *S aureus* isolates that were MRSA, over time. **B,** Proportion of community-acquired *S aureus* isolates that were MRSA, over time. **C,** Proportion of hospital-onset *S. aureus* isolates that were MRSA, over time.

trimethoprim-sulfamethoxazole. All isolates in this cohort were susceptible to vancomycin; 7 (1.8%) had a vancomycin MIC of 2 mcg/mL, and the remaining 98.2% had an MIC of <2 mcg/mL.

Clinical Outcomes

Clinical outcomes are summarized in **Table II**. Recurrence of infection occurred in 8 of 134 (6%) patients with catheter-related infections, including 4 of 51 (7.8%) patients whose catheter was not removed, and 4 of 82 (4.9%) patients whose catheter was removed (P = .48). Of the 8 patients who died because of *S aureus* bacteremia, 5 had pneumonia, 2 had catheter-related bloodstream infections, and 1 had endocarditis.

Risk Factors for Complications

In univariate analysis, public insurance, absence of comorbid conditions at baseline, musculoskeletal infections, pneumonia, duration of bacteremia prior to onset of complication >3 days, and methicillin resistance were associated with development of complications (with a P value of <.10 for all) (**Table III**). These variables were included in the initial multivariable logistic regression model along with the variables selected a priori to be clinically significant.

In final logistic regression model evaluating the risk of developing complications, we found that compared with MSSA, patients with MRSA were 3.31 times (95% CI 1.60-6.85) more likely to develop complications, adjusting for source control intervention (none needed, performed within 3 days, performed beyond 3 days), catheter-related infection, and duration of bacteremia prior to onset of complication. Duration of bacteremia >3 days was associated with an aOR of 2.07 (95% CI 0.94-4.56). Catheter-related infections were less likely to lead to complications (aOR 0.40; 95% CI 0.15-1.03), though this did not reach statistical significance (**Table IV**; available at www.jpeds.com). Source control was retained in the model despite not being significantly associated with complications because its removal from the model resulted in significant changes to model estimates based on the likelihood ratio test. The Pearson goodness-of-fit statistic for the final model was 10.58 (P = .83), suggesting the model is a good fit for the data.

Risk Factors for Prolonged Bacteremia

In univariate analysis of potential risk factors for prolonged duration of bacteremia (>3 days), methicillin resistance, endovascular infection, musculoskeletal infection, infection that is not catheter related, absence of underlying comorbid conditions, public insurance, black race, critical illness, and delayed source control >3 days were associated with an increased odds of having prolonged bacteremia.

In a Poisson regression model of methicillin resistance on duration of bacteremia adjusting for these covariates, we found that compared with MSSA, patients with MRSA

Table II. Clinical outcomes of children with *S aureus* bacteremia

Outcomes	Total *S aureus* (n = 394)	MSSA (n = 279)	MRSA (n = 115)	*P* value
Complications*	46/394 (11.7%)	18/279 (6.5%)	28/115 (24.3%)	<.001
Septic emboli/thrombus	18/394 (4.6%)	3/279 (1.1%)	15/115 (13.0%)	<.001
Metastatic focus of infection	12/394 (3.1%)	2/279 (0.7%)	10/115 (8.7%)	<.001
Progression of infection	13/394 (3.3%)	8/279 (2.9%)	5/115 (4.4%)	.46
Attributable 30-d mortality	8/394 (2.0%)	4/279 (1.4%)	4/115 (3.5%)	.19
Recurrence of bacteremia	15/394 (3.8%)	11/279 (3.9%)	4/115 (3.5%)	.83
Duration of bacteremia, mean (SD)	2.2 days (2.0)	1.9 days (1.6)	3.1 days (2.5)	<.0001
Persistent bacteremia >3 d	72/394 (18.3%)	35/279 (12.5%)	37/115 (32.2%)	<.001
Persistent bacteremia >5 d	27/394 (6.9%)	6/279 (2.2%)	21/115 (18.3%)	<.001
Persistent bacteremia >7 d	11/394 (2.8%)	2/279 (0.7%)	9/115 (7.8%)	<.001
Attributable readmission within 30 d	21/394 (5.3%)	10/279 (3.6%)	11/115 (9.6%)	.02
Hospital length of stay (d) from onset of bacteremia, median (IQR)	14 (7-32)	14 (7-36)	13 (8-22)	.38

*Some patients had complications from >1 category.

were bacteremic for 0.78 days longer (95% CI 0.43-1.12). Musculoskeletal infection, endovascular infection, black race, and delayed source control >3 days were independently associated with increased duration of bacteremia (**Table V**; available at www.jpeds.com).

Discussion

This study explored clinical outcomes in children with *S aureus* bacteremia at a large tertiary care children's hospital, in particular the development of complications including septic emboli, thrombi, and metastatic foci of infection. Adjusting for potential confounding factors, methicillin-resistant infections were more than 3 times more likely to lead to complications than methicillin-susceptible infections. Compared with patients with MSSA, patients with MRSA experienced bacteremia for almost 1 day longer. Musculoskeletal and endovascular infections, black race, and delayed source control intervention were also significantly associated with longer duration of bacteremia.

Our finding that methicillin resistance was an independent risk factor for the development of complications is consistent with findings in adult studies.[19] In 1 study evaluating risk factors for hematogenous bacterial seeding in a cohort of adult patients with *S aureus* bacteremia, longer symptom duration, hemodialysis dependence, presence of a long-term intravascular catheter, and infection with MRSA were significantly associated with hematogenous complications.[19] In a previously published study in children that examined the risk of complications in 376 children with *S aureus* bacteremia over a 25-year period, Le et al did not find methicillin resistance to be associated with complications. However, Le et al defined complication as having endocarditis, osteomyelitis, pneumonia, meningitis, septic arthritis, skin or soft tissue infection, splenic abscess, bacteriuria, respiratory distress syndrome, or septic thrombophlebitis, whether or not it occurred with the onset of bacteremia or after first positive culture. In a multivariate logistic regression analysis to identify predictors of *S aureus* bacteremia-related complications, methicillin-resistant infection was not found to be a risk factor for complications as defined.[4] Our work differs most notably in our definition of a complication (ie, development of a hematogenous complication including septic emboli, thrombosis, or a metastatic focus of infection that was noted at least one day after onset of bacteremia).

Host, pathogen, and treatment-related factors likely contribute to the outcome of a *S aureus* bloodstream infection. In this study, we found that methicillin resistance was an independent risk factor for the development of complications, adjusting for specific clinical factors. This may be related to expression of pathogenic virulence factors specific to strains of MRSA, or to antibiotic treatment, or both. For example, treatment with vancomycin, which is currently the first-line drug for MRSA bacteremia,[26] has been associated with higher rates of clinical failure and prolonged bacteremia in MSSA compared with treatment with beta-lactam therapy.[27] Identification of strain types, virulence factors, and host immune response to *S aureus* infection was beyond the scope of the current study, but future analyses evaluating specific strains of *S aureus* isolates and expression of virulence factors would be helpful in differentiating the contributions of each of these potential factors.

Our secondary analysis identified musculoskeletal and endovascular infections, black race, methicillin resistance, and delayed source control intervention as factors significantly associated with longer duration of bacteremia. Delayed intervention for source control, which included removal of catheter for catheter-related infection, is the one risk factor among this list that is modifiable. This finding underscores the importance of prompt removal of catheters in catheter-related *S aureus* bloodstream infections, as is recommended in current consensus guidelines,[24] to decrease the risk of complications.

Longer duration of *S aureus* bacteremia previously has been shown to be associated with development of hematogenous complications.[9,19] Presumably this is because of increased opportunity for bacterial seeding to occur. In the present study, methicillin resistance was associated with development of complications in multivariate analysis adjusting for duration of bacteremia. Methicillin resistance

Table III. Univariate analyses of risk factors associated with complications among children with *S aureus* bacteremia

	Complications	OR (95% CI)	*P* value
Age			
Infant (<1 y)	15/146 (10.3%)	0.67 (0.36-1.28)	.23
Age ≥1 y	36/248 (14.5%)	[Ref]	
Sex			
Female	20/161 (12.4%)	[Ref]	
Male	30/227 (13.2%)	1.07 (0.59-1.97)	.82
Race			
Non-black	31/274 (11.3%)	[Ref]	
Black	20/119 (16.8%)	1.58 (0.86-2.91)	.14
Ethnicity			
Not Hispanic	46/356 (12.9%)	[Ref]	
Hispanic	5/38 (13.2%)	1.02 (0.38-2.75)	.97
Insurance			
Private or self-pay	34/330 (10.3%)	[Ref]	
Public	17/63 (27.0%)	3.22 (1.66-6.22)	.001
Epidemiologic category			
Community-onset	33/243 (13.6%)	[Ref]	
Hospital-onset	18/151 (11.9%)	0.86 (0.47-1.59)	.63
Comorbid condition at baseline			
None	24/125 (19.2%)	[Ref]	
Yes (any)	27/269 (10.0%)	0.47 (0.26-0.85)	.013
Primary source			
Catheter-related	9/134 (6.7%)	0.37 (0.17-0.79)	.01
Musculoskeletal*	21/118 (17.8%)	1.78 (0.97-3.25)	0.06
Skin/soft tissue	6/40 (15.0%)	1.21 (0.48-3.05)	.68
Pneumonia	9/25 (36.0%)	4.37 (1.82-10.53)	0.001
Endovascular	4/26 (15.4%)	1.24 (0.41-3.76)	.70
No source	1/34 (2.9%)	0.19 (0.03-1.40)	.10
Other	1/17 (5.9%)	0.41 (0.05-3.15)	.39
Methicillin resistance			
MSSA	21/279 (7.5%)	[Ref]	
MRSA	30/115 (26.1%)	4.33 (2.36-7.97)	<.001
Duration of bacteremia prior to onset of complication			
≤3 d	33/327 (10.1%)	[Ref]	
>3 d	18/67 (26.9%)	3.27 (1.71-6.26)	<.001
Time until antistaphylococcal antibiotic			
0-1 d	49/382 (12.8%)	[Ref]	
≥2 d	2/12 (16.7%)	1.36 (0.29-6.39)	.70
Critical illness			
No	36/308 (11.7%)	[Ref]	
Yes	15/86 (17.4%)	1.59 (0.83-3.08)	.16
Source control intervention			
None needed	19/174 (10.9%)	[Ref]	
Within 3 d	17/118 (14.4%)	1.37 (0.68-2.77)	.69
Delayed (>3 d)	6/45 (13.3%)	1.26 (0.47-3.35)	.65

*Including osteomyelitis, septic arthritis, and pyomyositis.

was also the only factor associated in multivariate analyses with both longer duration of bacteremia and development of hematogenous complications. Patients with MRSA had bacteremia for 0.78 (95% CI 0.43-1.12) days longer than patients with MSSA; although this difference may seem slight, a previous study of MRSA bacteremia in children showed that each day of bacteremia was associated with a 50% (95% CI 26%-79%) increased odds of bacteremia-related complications.[9] Additional factors (delayed source control, musculoskeletal and endovascular infections, and black race) were associated with longer duration of bacteremia; however, these factors were not associated with development of complications in multivariate analysis. These results suggest that prolonged duration of bacteremia is not the only explanation for the association between MRSA and the development of complications.

Our study is subject to several limitations. First, as a retrospective cohort study, the data rely on documentation from medical records and is subject to missing data. Misclassification of exposures and outcomes are a potential source of bias. To minimize this, structured chart review was performed using a standard data collection form, with predefined definitions for each variable and adjudication by 2 pediatric infectious diseases physicians. Furthermore, recognition of a complication such as a thrombus after onset of bacteremia does not necessarily indicate that this finding was not present earlier. As a single-center study at a large tertiary care center, generalizability may be limited, as our patient population may not be representative of all children with *S aureus* bacteremia. Finally, the sample size may have limited the power to detect associations where true differences exist, particularly in smaller subcategories of analysis.

In our study, complications including septic emboli and metastatic foci of infection occurred in almost 10% of children hospitalized with *S aureus* bacteremia. Bloodstream

infections caused by MRSA were more than 3 times more likely to lead to complications than those caused by MSSA. Children with MRSA, with endovascular or musculoskeletal infections, black children, and those who underwent a delayed source control intervention experienced a longer duration of bacteremia. Although host immune response, antibiotic treatment, and pathogen-specific factors likely contribute to the outcomes of children with *S aureus* bacteremia, additional studies are needed to differentiate the contribution of each of these factors. ■

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Table IV. Multivariate logistic regression analysis for odds of complications among children with *S aureus* bacteremia (n = 394)

	aOR (95% CI)	*P* value
Methicillin resistance	3.31 (1.60-6.85)	.001
Catheter-related infection	0.40 (0.15-1.03)	.059
Duration of bacteremia prior to complication >3 d	2.07 (0.94-4.56)	.07
Source control within 3 d*	1.09 (0.51-2.36)	.82
Source control delayed (>3 d)*	0.97 (0.23-2.96)	.96

*Compared with no source control needed as reference.

Table V. Poisson regression on duration of *S aureus* bacteremia

	Average marginal effect (95% CI)	*P* value
Methicillin resistance	0.78 (0.43-1.11)	<.001
Musculoskeletal infection	0.60 (0.25-0.95)	.001
Endovascular infection	0.88 (0.31-1.44)	.002
Black race	0.42 (0.08-0.77)	.015
Delayed source control (>3 d)*	0.71 (0.29-1.12)	.001

*Compared with no source control needed as reference.