CLINICAL RESEARCH STUDY

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Quality Improvement of *Staphylococcus aureus* Bacteremia Management and Predictors of Relapse-free Survival

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ABSTRACT

PURPOSE: The purpose of this study is to improve the quality of care and patient outcomes for *Staphylococcus aureus* bacteremia.

METHODS: A quasi-experimental pre- and postintervention study design was used to compare process and clinical endpoints before and after a quality-improvement initiative. All inpatients >18 years of age with a positive blood culture for *S. aureus* during the specified pre- and postintervention period with clinical information available in the electronic medical record were included. An institutional protocol for the care of patients with *S. aureus* bacteremia was developed, formalized, and distributed to providers using a pocket card, an electronic order set, and targeted lectures over a 9-month period.

RESULTS: There were 167 episodes of *S. aureus* bacteremia (160 patients) identified in the preintervention period, and 127 episodes (123 patients) in the postintervention period. Guideline adherence improved in the postintervention period for usage of transesophageal echocardiogram (43.9% vs 20.2%, $P < .01$) and adequate duration of intravenous therapy (71% vs 60%, $P = .05$). In a multivariate Cox proportional hazard model, the variables associated with increased relapse-free survival were postintervention period (hazard ratio [HR] 0.48; confidence interval [CI], 0.24-0.95; P .035) and appropriate source control (HR 0.53; CI, 0.24-0.92; P .027). Regardless of intervention, presence of cancer was associated with an increased risk of relapse or mortality at 90 days (HR 2.88; $P < .0001$; CI, 1.35-5.01).

CONCLUSION: A bundled educational intervention to promote adherence to published guidelines for the treatment of *S. aureus* bacteremia resulted in a significant improvement in provider adherence to guidelines as well as increased 90-day relapse-free survival.

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Staphylococcus aureus bacteremia is one of the most common causes of bloodstream infections worldwide and causes extensive morbidity and mortality, with death rates ranging from 20%-40%.[1-4] Numerous studies have demonstrated that treatment of *S. aureus* bacteremia in consultation with Infectious Disease specialty services or evidence-based bundled interventions can improve mortality rates.[5] In this study, we present the results of a quality improvement initiative to improve management and outcomes of *S. aureus* bacteremia. This paper describes the process improvement methods and results, and also predictors of

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90-day survival or freedom from relapse. Previous studies mostly used 30-day mortality as the primary clinical endpoint. Relapses of deep-seated infections often lead to readmissions, increased health care costs, and significant morbidity for patients. Given the propensity of *S. aureus* to relapse from deep sources if undertreated and prolonged effects on survival, 90-day freedom from relapse or survival may be a more meaningful marker of cure for *S. aureus* bacteremia.

The objectives of this study were to 1) improve adherence to current guidelines for treatment of *S. aureus* bacteremia, and 2) to measure impact of improved adherence on survival and freedom from relapse at 90 days.

CLINICAL SIGNIFICANCE

- A resident-run and trainee-focused educational initiative led to increased rates of transesophageal echocardiography and longer treatment duration for patients with *Staphylococcus aureus* bacteremia.
- Improved adherence to guidelines led to a decrease in the relapse rate for *S. aureus* bacteremia.
- This intervention was successful in a resource-limited hospital, and could be implemented in numerous other clinical settings.

METHODS

Setting, Intervention, and Design

The intervention was performed at Parkland Memorial Hospital, a 784-bed public academic hospital in Dallas County, Texas, which averages 40,000 admissions annually. The facility serves as the main teaching hospital for the University of Texas Southwestern Medical Center. The patient population comprises largely uninsured minority patients with a large burden of HIV, diabetes, and end-stage renal disease.[6-8] The study was designed as a resident-initiated and resident-run quality-improvement (QI) initiative with pre- and postintervention analysis. The effort was initiated and led by an Internal Medicine resident (JT) under faculty supervision (PS). The preintervention period was 1 year long, between October 1, 2010 and September 30, 2011. The intervention period was from December 2012 to September 2013. Postintervention data collection included the 6-month period from October 1, 2013 through March 28, 2014. The follow-up period ended June 28, 2014, giving a minimum of 90-day follow-up for postintervention cases. A timeline of the intervention is presented in **Figure 1**. Quality measures for the QI intervention were derived from published society guidelines, available at the time of study design, regarding treatment of *S. aureus* infections. Key definitions and treatment recommendations were extracted from the 2009 methicillin-resistant *S. aureus* (MRSA) treatment guidelines,[9] the 2005 endocarditis guidelines from the American Heart Association,[10] and the Infectious Diseases Society of America guidelines for treatment of catheter-related infections.[11] The target measures were presented to the Infectious Disease Division for consensus review, and the Division endorsed them as the institutional standard of care for *S. aureus* bacteremia at Parkland. The Infectious Disease division's recommendations for universal transesophageal echocardiogram (TEE) in *S. aureus* bacteremia at Parkland were discussed at a noninvasive cardiology meeting and endorsed by the Division of Cardiology. Simplified recommendations regarding universal TEE, treatment duration by infection complexity, and first-line agents were compiled into an order set in the electronic medical record for treatment of *S. aureus* bacteremia as well as a pocket teaching card for house staff (**Figure 2**). A total of 160 surgical and medical house staff were given teaching cards. In

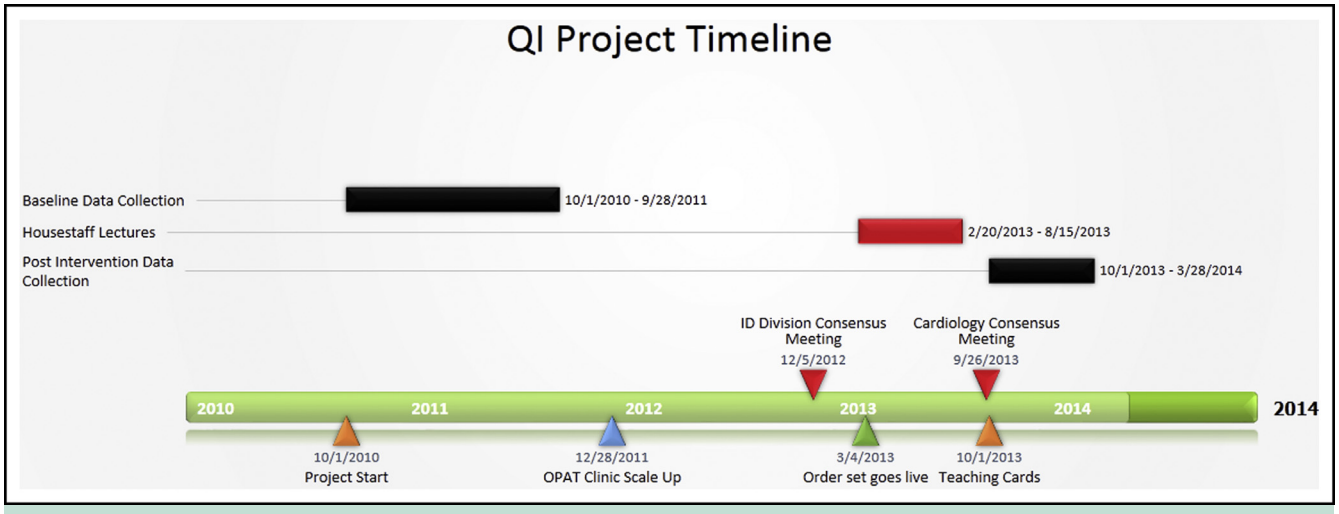

Figure 1 Project timeline for quality improvement initiatives for *Staphylococcus aureus* bacteremia, October 2010-March 2014.

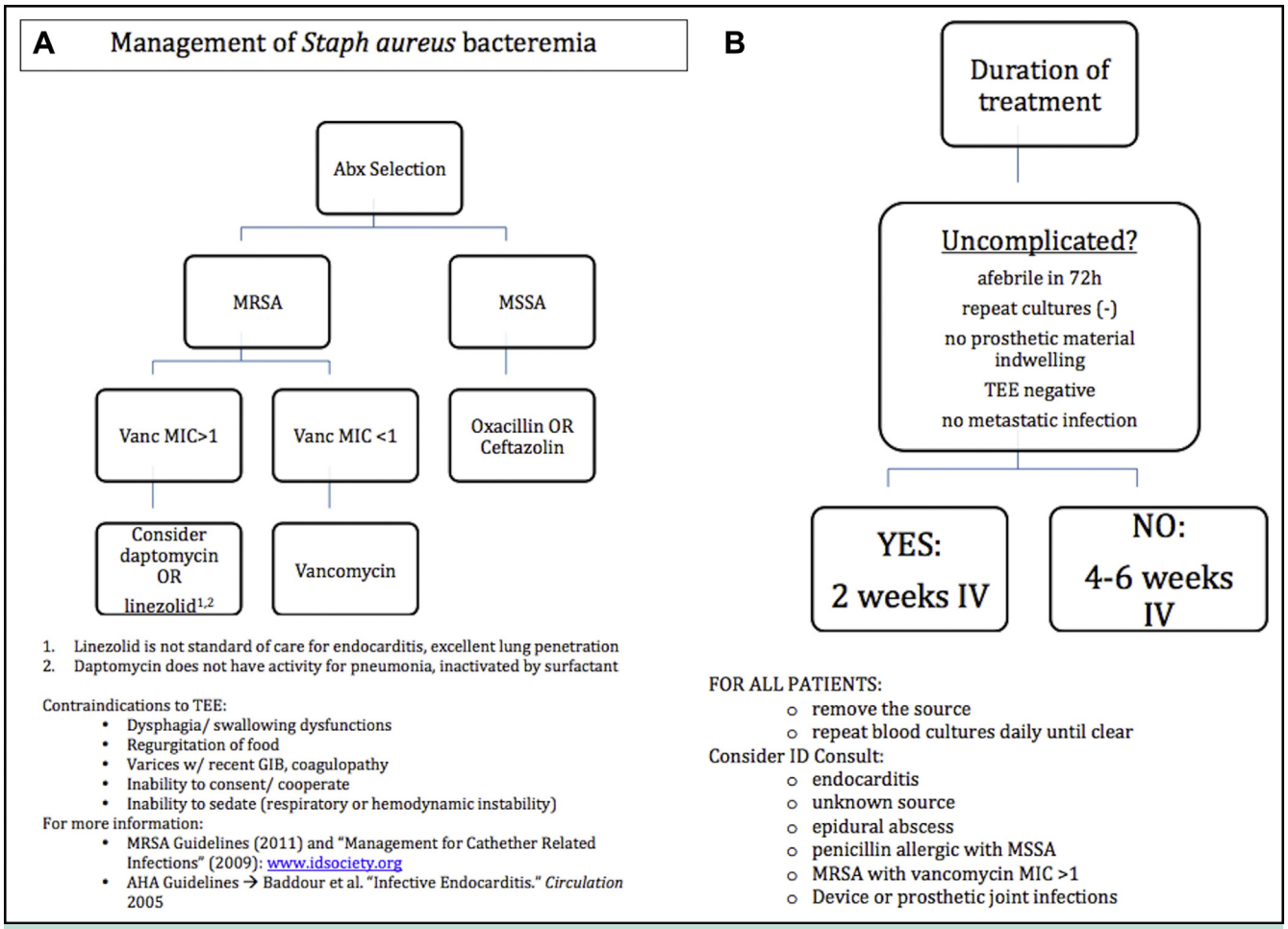

Figure 2 Pocket cards distributed to providers summarizing institutional protocol for *Staphylococcus aureus* bacteremia. Abx = antibiotic; AHA = American Heart Association; GIB = gastrointestinal bleed; IV = intravenous; MIC = minimum inhibitory concentration; MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-susceptible *Staphylococcus aureus*; TEE = transesophageal echocardiogram.

addition, the primary author delivered 2 1-hour lectures on the treatment of *S. aureus* bacteremia to Internal Medicine residents (total 160 residents), a 5-minute talk to General Surgery residents (45 residents), and a 20-minute talk to the Cardiology Division (6 faculty, 3 fellows present), followed by distribution of teaching cards at the respective lectures. Twenty teaching cards were distributed in the Emergency Department during the intervention, although no formal talks were given to their staff.

Data Collection

All consecutive episodes of *S. aureus* bacteremia, defined as ≥1 positive blood culture during the preintervention period and the postintervention period, were identified from the blood culture reports of the Parkland Microbiology Laboratory. Patients were excluded if they were <18 years old, or had no clinical data available. The study was reviewed by the UT Southwestern Institutional Review Board and designated exempt as a QI project. Pre- and postintervention data collection through review of electronic medical records was done retrospectively at the end of the respective periods. Data including demographics, clinical features, treatment course, and outcomes of *S. aureus* bacteremia cases were reviewed by the primary author (JT) and ambiguities were adjudicated by the senior author (PS) when necessary. Confirmatory data on 90-day mortality were obtained by querying the Death Master file maintained by the Social Security Administration. Patients without follow-up data in the electronic medical record at 90 days were assumed to be free of relapse, as the majority of patients at the study institution return for follow-up care. Thirty-day follow-up records were available for all episodes of bacteremia, and 90-day follow-up records were available for 236/294 (80.3%) episodes.

Definitions

The primary process outcome assessed for guideline adherence was the number of patients undergoing TEE. Secondary process outcomes included median duration of antimicrobial treatment, time to appropriate antimicrobial treatment, follow-up blood cultures ordered, and source

control measures performed during the initial admission. The primary clinical endpoint was relapse-free survival at 90 days from the date of initial positive blood culture. Relapse was defined as the return of signs or symptoms of a deep-seated and persistent staphylococcal infection, or development of new late complications (eg, endocarditis, osteomyelitis, recurrent *S. aureus* bacteremia) after a period of initial remission and hospital discharge. Relapse criteria included isolation of *S. aureus* with the same susceptibility pattern as the index episode, from the blood or other clinical specimen, recurrence of previous symptoms, or radiographic evidence of worsening at the site of the previous source.

A body site was considered the source of *S. aureus* bacteremia if the symptoms at that site were present at the time of or preceding the bacteremia. Metastatic infections were defined as bacteremia episodes with evidence of embolic secondary foci, including radiographic evidence of septic emboli to the lungs, central nervous system, spinal column, or joints. If no source was apparent after the hospital workup, the source was classified as unknown. Endocarditis cases were diagnosed if the patient met or exceeded the definite category of the Modified Duke Criteria.[12]

Infections were classified as community-onset if the patient had a positive blood culture for *S. aureus* or symptoms present within 72 hours of admission and no preceding health care contact. Patients with health care contact before admission (dialysis, hospitalization, nursing home residence, or home health care) with bacteremia in the first 72 hours were classified as "community-onset, health care-associated." If the *S. aureus* bacteremia occurred after the patient had been hospitalized for 72 hours, the infection was considered hospital-onset. Bacteremia was considered uncomplicated if all of the following criteria were met: catheter-associated bloodstream infection with catheter removed, negative follow-up blood cultures drawn within 48-96 hours of initial positive blood culture, afebrile within 72 hours, no evidence of endocarditis on TEE (or transthoracic echocardiogram if no TEE was performed due to contraindications or low suspicion of endocarditis by treating physician), no indwelling prosthetic material, no evidence of deep or metastatic infection.[9,13] For a complete list of criteria, see **Table 1**.[4] Duration of bacteremia was defined as the time between the first positive blood culture and the first negative blood culture. A patient was considered to have undergone source control if they had complete drainage of an abscess, catheter removal, valve replacement, or removal of infected hardware. In the case of an early prosthetic joint infection, if the patient underwent a washout of the infected space, source control was considered to be adequate. In the case of a spinal hardware infection, if the patient underwent complete drainage of the involved site, but the hardware was retained for spinal stability, source control was considered adequate.

Both empiric and definitive treatment regimens were recorded, including antibiotic name, route, time to administration from positive blood culture, total duration, and total intravenous duration. Regimens were classified as first-line, acceptable, or inappropriate as follows for methicillin-susceptible *S. aureus*: first-line (nafcillin or cefazolin), acceptable (ceftriaxone, piperacillin/tazobactam, clindamycin, cefepime), inappropriate (vancomycin and all others). Classification for MRSA was as follows: first-line (vancomycin), acceptable (clindamycin, daptomycin, linezolid, ceftaroline), inappropriate (all others). Treatment duration was considered to be appropriate if $\geq$14 days in uncomplicated cases, and $\geq$28 days in complicated cases. The number of patients seen by the Infectious Disease consult service and the outpatient parenteral antibiotic therapy (OPAT) clinic were also recorded.

Table 1 Criteria for Complicated Bacteremia

Follow-up blood cultures positive between 48 and 96 h
Febrile beyond 72 h of initial blood culture
Endovascular infection
Evidence of endocarditis on TTE or TEE, or both
Septic thrombophlebitis
Indwelling prosthetic device
Intracardiac device
Prosthetic joint
Ureteral stent
Endovascular graft
Abdominal mesh at site of infection
Indwelling vascular catheter
Complicated pneumonia
Loculated pleural effusions
Cavitary lesions
Empyema requiring drainage
Prolonged intubation >48 h
Prolonged shock >48 h
Complicated skin and soft tissue infection
Phlegmon or undrained abscess
Myositis
Metastatic infection at a secondary site
Unamputated osteomyelitis
Pericarditis
Mediastinitis
Endophthalmitis
Meningitis

TEE = transesophageal echocardiogram; TTE = transthoracic echocardiogram.

Statistical Analysis

Clinical features of *S. aureus* bacteremia, overall relapse rate, readmission rate, and source of infection were reported for each unique *S. aureus* bacteremia episode (n = 294). Demographics and mortality figures were calculated for unique patients (n = 283). Guideline adherence measures were calculated for each unique episode, excluding cases in which the patient died before blood culture results were available to providers (within 48 hours of blood cultures)

Table 2 Comparison of Demographics, Clinical Features, and Outcomes of SAB Episodes Pre- and Postintervention

	Preintervention n (%)	Postintervention n (%)	*P*-Value
Demographics of patients (n = 283)	(n = 160)	(n = 123)	
Male	103 (64.4)	82 (66.7)	.31
Age, y: median (IQR)	52 (41-58)	52 (42-60)	.91
Hispanic ethnicity	49 (30.6)	50 (40.7)	.04*
Past medical history			
Diabetes mellitus	64 (40)	54 (43.9)	.28
End-stage renal disease	24 (15.0)	24 (19.5)	.25
Malignancy	20 (12.5)	19 (15.4)	.39
Cirrhosis	20 (12.5)	11 (8.9)	.19
Steroids or immunosuppression	7 (4.4)	13 (10.6)	.01*
Indwelling hardware	13 (8.1)	11 (8.9)	.45
HIV	11 (6.9)	7 (5.7)	.48
Clinical features of all SAB episodes (n = 294)	(n = 167)	(n = 127)	
Number of positive blood cultures per admission (mean, range)	2 (1-11)	3 (1-12)	.06
Patients with positive follow-up blood cultures at 48-96 h	15 (9.0)	27 (21.3)	<.001*
Time to blood culture clearance (hours)	61.42 (39-92)	67.25 (36-99)	.61
Fever >72 h	8 (4.8)	4 (3.1)	.56
MRSA	88 (52.7)	43 (33.9)	<.001*
Epidemiology			
Hospital-onset SAB	29 (17.4)	23 (18.1)	.87
Community-acquired SAB	50 (29.9)	40 (31.5)	.77
Community-onset — health care-associated	88 (52.7)	64 (50.4)	.70
Complicated bacteremia	91 (54.5)	76 (59.8)	.36
Metastatic at onset	23 (13.8)	19 (15.0)	.77
Source			
Bone and joint	40 (24.0)	27 (21.3)	.59
Catheter	30 (18.0)	32 (25.2)	.13
Skin and soft tissue	40 (24.0)	21 (16.5)	.12
Respiratory	32 (19.2)	19 (15.0)	.35
Unknown	7 (4.2)	13 (10.2)	.04*
Endocarditis (primary and secondary)	5 (3.0)	17 (13.4)	.60
Urinary	7 (4.2)	7 (5.5)	.60
Other	8 (6.3)	2 (1.2)	.39
Outcomes by patient (n = 283)	(n = 160)	(n = 123)	
Overall 30-day mortality	14 (8.8)	9 (7.3)	.66
Complicated bacteremia (n = 91 pre, n = 76 post)	4 (4.4)	6 (7.9)	.51
Uncomplicated bacteremia (n = 32 pre, n = 66 post)	10 (31.3)	3 (4.5)	.24
Overall 90-day mortality	20 (12.5)	15 (12.2)	.94
Outcomes by episode (n = 294)	(n = 167)	(n = 127)	
Length of hospital stay (d, median, IQR)	14 (7-26)	13 (8-21)	.68
Length of ICU stay (d, mean, range)	3.1 (0-58)	5.3 (0-211)	.25
30-day readmission, n (%)	49 (30.6)	25 (20.3)	.06
Complicated bacteremia	29 (31.9)	9 (11.8)	<.001*
Uncomplicated bacteremia	16 (50.0)	20 (30.3)	.54
Relapse within 90 d	19 (11.9)	3 (2.4)	<.001*
Complicated bacteremia	17 (18.7)	3 (3.9)	<.001*
Uncomplicated bacteremia	2 (6.3)	0 (0.0)	.52

Data are presented as no. (%) unless otherwise specified.

HIV = human immunodeficiency virus; ICU = intensive care unit; IQR = interquartile range; MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-susceptible *Staphylococcus aureus*; SAB = *Staphylococcus aureus* bacteremia.

**P*-values considered significant if <.05.

(n = 286). Candidate predictor variables for freedom from recurrence and survival were selected based on clinical judgment and published literature.[4,14-16] Comparisons between pre-and postintervention demographics, guideline adherence measures, and outcomes were done using chi-squared test or Fisher's exact test, as appropriate.

Kaplan-Meier curves were generated in Stata 13, and univariate comparisons were made using log-rank tests.[17] Stata 13 was used to build the Cox proportional hazards multivariate model. Forward selection using the Akaike Information Criteria (AIC) was used to select covariates that would build a model that best fit the data and were parsimonious. AIC was evaluated for a decrease in value after each new variable was added to the model. Once the AIC value increased, it then became unnecessary to add additional variables to the model.

RESULTS

A total of 167 eligible episodes of *S. aureus* bacteremia (in 160 patients) were identified in the preintervention period, and 127 episodes (in 123 patients) in the postintervention period, for a total of 294 episodes of *S. aureus* bacteremia in 283 unique patients. Age, race, and comorbid conditions were not significantly different between these groups (**Table 2**), with a large percentage being male, non-White ethnicity, and diabetic. Clinical features were similar in the postintervention group compared with preintervention, with the exceptions of immunosuppression (10% vs 4.4%, *P* .01), MRSA (33.9% vs 52.7%, *P* <.01), and unknown source (10.2% vs 4.2%, *P* .04). Over 80% (242/294) of cases were community-onset, and 150/242 (62%) of the community-onset infections were health care associated. A majority of the bacteremias (54.5% preintervention and 59.8% postintervention) were complicated. The percentage of patients diagnosed with endocarditis rose significantly from 3.0% preintervention to 13.4% postintervention (*P* <.01), while other sources remained stable.

Comparison of outcomes pre- and postintervention is shown in **Table 2**. All-cause mortality was not significantly different pre- and postintervention (8.1% vs 7.7% at 30 days, *P* = .66). The rate of relapse at 90 days dropped in the postintervention period, from 11.9% to 2.4% (*P* <.01), which was most marked for patients with complicated bacteremia. In the uncomplicated group, 2 patients relapsed at 90 days, neither of which had a TEE. The 30-day readmission rate for complicated bacteremia also improved significantly postintervention.

In the multivariate Cox proportional hazard model, the variables associated with increased relapse-free survival were postintervention period (hazard ratio [HR] 0.48; confidence interval [CI], 0.24-0.95; *P* .035) and appropriate source control (HR 0.53; CI, 0.24-0.92; *P* .027) (**Table 3**). The following variables were entered into the multivariate model: cancer, postintervention, source control, source of infection, and duration of intravenous (IV) therapy. Source of infection and adequate duration of IV therapy were not significantly associated with a decrease in the endpoint when controlling for the other variables. The Kaplan-Meier survival curves showing the difference in relapse-free survival pre- and postintervention are shown in **Figure 3**.

Table 3 Multivariate Cox Proportional Hazards Models for Predictors of Combined 90-day Mortality and Relapse

	Adjusted Hazard Ratio	Confidence Intervals	*P*-Value
90-day mortality or relapse (n = 294)*			
Cancer	2.88	1.35-5.01	.004†
Source control	0.53	0.24-0.92	.027†
Post intervention	0.48	0.24-0.95	.035†

*Model adjusted for source of infection and duration of intravenous antibiotic treatment in addition to the variables shown.
†*P*-values considered significant if <.05.

Adherence to target guidelines increased in the postintervention period. Changes in adherence to guideline measures in the postintervention period are presented in **Table 4**. The most significant changes were an increase in the number of TEEs performed within 14 days of *S. aureus* bacteremia (from 20.2% to 43.9%, *P* = .001), a decrease in the time to appropriate antibiotic therapy (5.0 hours to 0.9 hours, *P* <.001), and an increase in the average duration of IV therapy from 18 days to 21 days (*P* = .001). In the group with complicated infections, 38/73 patients (52%) underwent TEE in the postintervention period, compared with 24/90 (26.7%) preintervention. The percentage of echocardiograms performed overall (82.3% of episodes) and TEEs performed for complicated patients (54.3%) in the postintervention period are among the highest reported.[14,18] Over 70% of the patients in the postintervention period received an adequate duration of IV

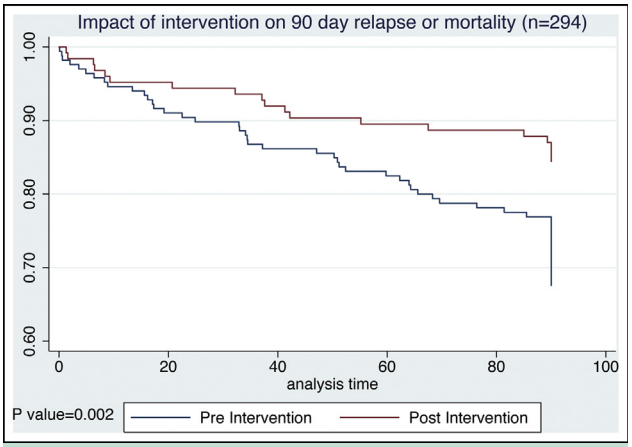

Figure 3 Impact of intervention on combined 90-day relapse or mortality. Time to event curve, univariate Cox proportional hazard model.

Table 4 Comparison of Adherence to Recommended SAB Management Process Measures Pre- and Postintervention

Process Endpoints by Episode† (n = 286)	Preintervention n = 163 n (%)	Postintervention n = 123 n (%)	95% CI	*P*-Value
Order set usage	0 (0)	16 (13)	5.2-1022	<.001*
Surveillance blood cultures at 48-96 h	127 (77.9)	102 (82.9)	0.75-2.50	.290
Transthoracic echocardiogram performed	133 (81.6)	104 (84.6)	0.66-2.32	.510
Transesophageal echocardiogram performed	33 (20.2)	54 (43.9)	1.83-5.20	<.001*
Complicated bacteremia	24 (26.7)	38 (54.3)	1.55-5.75	<.001*
Uncomplicated bacteremia	9 (12.3)	16 (30.2)	1.34-8.37	.008*
Adequate empiric therapy‡	109 (66.9)	99 (80.5)	1.20-3.55	.01*
Source control done (if indicated)§	145 (91.8)	73 (83.9)	0.1-1.05	.060
Use of recommended agent for definitive treatment‖	111 (68.1)	89 (72.3)	0.71-2.01	.510
Adequate duration of IV therapy¶	96 (60.0)	87 (71.3)	1.001-2.74	.049*
Hours to appropriate antibiotic (median, IQR)	5.0 (1-16)	0.9 (1.0-4.0)	-	<.001*
Inpatient IV duration (median, IQR)	13(6-18)	10.5 (6.2-16.6)	-	<.001*
Complicated bacteremia (median, IQR)	14 (8-22)	12.4 (8.2-21.5)	-	NS
Uncomplicated bacteremia (median, IQR)	9.0 (4.3-13.9)	8 (5.0-15.0)	-	NS
Outpatient IV duration (median, IQR)	1.0 (0.0-14.0)	9.9 (0.8-22.8)	-	NS
Complicated bacteremia (median, IQR)	6.0 (0.0-25.0)	17.0 (1.9-28.8)	-	<.001*
Uncomplicated bacteremia (median, IQR)	0.0 (0.0-9.0)	6.0 (0.4-11.8)	-	.033*
Total IV duration (median, IQR)	18 (14-35)	21 (15-43)	-	.001*
Complicated bacteremia (median, IQR)	28 (16-46)	38 (20-47)	-	.037*
Uncomplicated bacteremia (median, IQR)	15 (11-18)	16 (14-20)	-	NS
Total duration (IV and PO) (median, IQR)	19 (14-35)	23 (16-44)	-	NS
Complicated bacteremia (median, IQR)	28 (17-47)	41 (20-49)	-	.037*
Uncomplicated bacteremia (median, IQR)	16 (13.5-19.0)	16 (14-20)	-	NS
Infectious disease consultation	58 (35.6)	65 (52.8)		.005*
Outpatient parenteral antibiotic clinic referral	30 (18.4)	56 (45.5)		<.001*
Oral antibiotics only	18 (11.0)	6 (4.9)	0.93-5.53	.080
Inappropriate antibiotic days (mean, range)	3.0 (0-28)	2.6 (0-45)	-	NS

Data are presented as No. (row %) unless otherwise specified.
IQR = interquartile range; IV = intravenous; NS = nonsignificant; PO = per os (by mouth).
**P*-values considered significant if <.05.
†Excluding patients who died in <48 hours, before providers aware of blood culture results.
‡Administration of active drug based on sensitivities within 12 hours of blood culture.
§Presence of a deep focus of infection, such as abscess, catheter, device, prosthetic joint.
‖Vancomycin (methicillin-resistant *Staphylococcus aureus*) or nafcillin/cefazolin (methicillin-susceptible *Staphylococcus aureus*) used for >50% of treatment course.
¶For uncomplicated infection ≥14 days IV therapy, for complicated infections ≥28 days IV therapy with an active agent.

therapy, with a median of 38 days in complicated cases. The median duration of IV therapy increased in the post-intervention period from 28 to 38 days ($P = .037$) for complicated infections, and from 15 to 16 days for uncomplicated infections ($P > .05$). The order set was used in 16/123 episodes (13%) in the postintervention period.

DISCUSSION

Our study demonstrates the ability of a resident-initiated and resident-run QI initiative to improve management and outcomes of patients with staphylococcal bacteremia. A striking finding of our study was that a relatively modest intervention resulted in a significant change in hospital-wide treatment of *S. aureus* bacteremia. QI interventions in teaching hospitals have the potential to be successful due to close peer relationships through which high-yield education is multiplied internally. If well engrained in one generation of residents, patterns of practice have the potential to perpetuate year after year in a training program in a way that is not possible among independently practicing physicians. The uptake of the order set was poor and was likely not a significant contributor to guideline adherence. Because this intervention succeeded in a resource-limited safety-net hospital, this intervention strategy may be generalizable to other academic medical centers as well.

The success of the intervention may also have stemmed from the fact that we targeted not only provider education, but also institutional barriers to consistent guideline adherence. A key ingredient of the intervention's impact was the development of an institutional standard of care through multidisciplinary consensus. Successful treatment

of *S. aureus* bacteremia often requires assistance from multiple specialties, including Cardiology, Surgery, Infectious Disease, and outpatient services (OPAT Clinic). During the study period, the conversations between study staff and the above-mentioned parties helped to reduce variations in practice that are a common source of frustration for trainees as well as patients.

While previous bundles have relied on sporadic or mandatory Infectious Disease consultations,[19] the present intervention was designed to equip a large segment of providers to manage this common infection according to guidelines. While the number of patients with Infectious Disease consultations increased substantially in the post-intervention period, this was not an independent predictor of clinical success in the multivariate model. Similarly, the number of patients referred to the OPAT specialty clinic also increased, but this did independently predict success when adjusting for the other elements of the intervention. In short, the impact of the intervention was greater than the sum of its parts.

Our study was limited by being a single-center intervention with a smaller sample size than other studies conducted for *S. aureus* bacteremia. We found a very low baseline mortality rate despite a high level of comorbid illness, approaching the lower limits of what has been reported for *S. aureus* bacteremia.[20-22] We speculate that the mortality may be low in our study group due to a low mean age, the large number of blood cultures done in uncomplicated skin and soft tissue infections, and around-the-clock availability of multiple subspecialty services to assist with source control measures. We acknowledge that there may be unmeasured (eg, factors affecting community incidence of *S. aureus* bacteremia and factors affecting the proportion of methicillin resistance in our study population) variables that may have served as confounding factors and influenced the outcomes in our study.

CONCLUSION

While *Saureus* bacteremia remains a common and dangerous infection across the nation and the world, evidence is growing that regular adherence to evidence-based guidelines can have a positive impact on patient outcomes. Health care systems should equip providers with the knowledge of current guidelines and remove systemic barriers to adherence when they arise.

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