BRIEF REPORT



Disparity in Quality of Infectious Disease vs Addiction Care Among Patients With Injection Drug Use–Associated *Staphylococcus aureus* Bacteremia

David Phillip Serota,^{1,0} Emily D. Niehaus,² Marcos C. Schechter,¹ Jesse T. Jacob,¹ Jeb Jones,³ Susan M. Ray,^{1,4} Colleen F. Kelley,¹ and Russell R. Kempker¹

¹Division of Infectious Diseases, Department of Medicine, and ²Department of Medical Education, Emory University School of Medicine, Atlanta, Georgia; ³Department of Epidemiology, Emory University Rollins School of Public Health, Atlanta, Georgia; ⁴Grady Health System, Atlanta, Georgia

Evidence-based interventions for *Staphylococcus aureus* bacteremia (SAB) are well known, but it is unclear how they are implemented among patients with injection drug use-associated (IDU) SAB. Of 46 patients with IDU-SAB identified, all received high-quality SAB management; however, few received appropriate recognition or treatment of their underlying substance use disorder.

Keywords. bacteremia; endocarditis; injection drug use; *Staphylococcus aureus*; substance use disorder.

Invasive infections with *Staphylococcus aureus* account for a large proportion of injection drug use–associated (IDU) infections, and rates of IDU-associated *Staphylococcus aureus* have been increasing across the United States [1]. *Staphylococcus aureus* bacteremia (SAB) is associated with a 30-day mortality rate of approximately 20%, high morbidity, prolonged hospital stays, and high health care costs [2]. Despite the focus on improving the quality of SAB management in the general population [3], the implementation of IDU-specific interventions among patients with IDU-SAB has received lower priority, even though successful management of IDU-associated infections requires addressing the underlying substance use disorder (SUD) [4]. We sought to evaluate the quality of care among patients with IDU-SAB in the southern United States, especially

Open Forum Infectious Diseases®

SUD treatment metrics, and to identify areas for improvement in the management of patients with IDU-SAB.

METHODS

We conducted a retrospective cohort study of all IDU-SAB cases in 3 hospitals in Atlanta, Georgia, including a county hospital and 2 academic medical centers from March 1, 2012, to October 31, 2017. All cases of community-onset SAB (CO-SAB) (defined as a positive blood culture drawn within 72 hours of admission to the hospital) were reviewed to evaluate if the bacteremia was caused by IDU. Each episode of bacteremia was evaluated separately as a unique case. Data used to determine if a case of CO-SAB was IDU-associated included clinical notes, prior episodes of IDU-associated infections, and labs including hepatitis C antibody, HIV, and urine drug screens. An episode was considered IDU-associated if there was explicit mention of IDU within 30 days of admission in the notes, clear evidence on physical exam (eg, abscess in the antecubital fossa), or recent admission for IDU-associated infections, with labs as supporting evidence.

All data were obtained through medical record review. The Charlson Comorbidity Index (CCI) was used to assess the burden of chronic disease [5]. A metastatic site of infection was defined as a discrete focus of infection remote from the initial infection source. Diagnosis of infective endocarditis (IE) was made by the treating physicians and was based on Duke criteria. SAB quality measures included use of echocardiography, repeat blood cultures to document clearance, infectious diseases (ID) consultation, and use of antistaphyloccocal beta-lactam antibiotics for methicillin-sensitive *Staphyloccocus aureus* (MSSA) [3, 6].

To evaluate SUD interventions, we assessed inpatient provision of medications for addiction treatment (MAT) and reviewed the chart for consultation by psychiatry or toxicology. Discharge summaries, social work notes, and progress notes were used to identify SUD treatment plans or recommendations.

Assessment of SAB quality measures was restricted to patients who survived \geq 72 hours from admission [3]. Analyses regarding follow-up, readmission rate, death after discharge, and SUD interventions were restricted to patients who survived to discharge. This study was approved by the internal review board of Emory University and the research oversight committee of Grady Health System.

RESULTS

Forty-six cases of IDU-SAB were identified between the 3 hospitals during the study period (Table 1). The median age (interquartile range [IQR]) was 34 (29–46) years. Forty-six percent

Received 21 March 2019; editorial decision 13 June 2019; accepted 17 June 2019.

Correspondence: D. P. Serota, MD, MSc, Division of Infectious Diseases, Department of Medicine, Emory University, 1518 Clifton Rd NE, GCR 420, Atlanta, GA 30322 (dpserota@gmail. com).

[©] The Author(s) 2019. Published by Oxford University Press on behalf of Infectious Diseases Society of America. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (http://creativecommons.org/licenses/ by-nc-nd/4.0/), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact journals.permissions@oup.com DOI: 10.1093/ofid/ofz289

Table 1. Characteristics of Patients With Injection Drug Use-Associated Staphylococcus aureus Bacteremia

Variable	Overall (n = 46) No. (%)
Age, median (IQR), y	34 (29–46)
Female	21 (46)
Race	
White	25 (54)
Black	19 (41)
Native American	1 (2)
Asian/Pacific Islander	1 (2)
Hispanic	1 (2)
Chronic hepatitis Cª	28 (62)
Cirrhosis	2 (4)
HIV infection	9 (20)
Charlson Comorbidity Index, median (IQR)	1 (0-2)
Psychiatric illness	9 (20)
Alcohol use disorder	4 (9)
Injected drug	
Heroin	41 (89)
Cocaine or crack	10 (22)
Methamphetamine	5 (11)
Other opioid	5 (11)
Multiple injected drugs	14 (30)
Taking MAT at hospital admission	0 (0)
Methicillin-resistant SAB	29 (63)
Metastatic sites of infection (≥1 site)	37 (80)
Endocarditis	20 (43) ^{b,c}
Septic pulmonary emboli	14 (30)
Septic arthritis	11 (24)
Other abscess	7 (15) ^d
Vertebral osteomyelitis and/or epidural abscess	7 (15)
Empyema	2 (4)
Nonvertebral osteomyelitis	2 (4)
Endovascular graft infection	2 (4)
Source control procedure performed, ≥1	19 (41)
Native joint incision and drainage	6
Vertebral osteomyelitis/epidural abscess surgical debridement	4
Debridement of skin or muscle abscess	4
Chest tube or VATS for empyema	2
Native cardiac valve replacement	1
Prosthetic cardiac valve replacement	1
Prosthetic joint incision and drainage with retention	1
Other procedure ^e	4
Completed antibiotic course in hospital (n = 42)	12 (29)
Discharged with PICC ($n = 42$)	23 (55)
Disposition from index hospitalization	
Home	11 (24)
Skilled nursing facility	19 (41)
Left hospital AMA	12 (26)
Hospice/died	4 (9)
Confirmed death after discharge ^f	3
Readmitted for persistent/recurrent <i>S. aureus</i> infection (n = 42) ^g	8 (19)

Abbreviations: AMA, against medical advice; CO, community-onset; IQR, interquartile range; MAT, medications for addiction treatment; PCR, polymerase chain reaction; PICC, peripherally inserted central catheter; SAB, *Staphylococcus aureus* bacteremia; VATS, video-assisted thorascopic surgery; WBC, white blood cell count in 1000 cells/mm³. ^aPositive hepatitis C antibody and detectable RNA PCR.

2 • OFID • BRIEF REPORT

were female, and 41% were African American. The prevalence rates of chronic hepatitis C virus and HIV were 62% and 20%, respectively. Heroin use was the most common drug injected (89%), and crack/cocaine (22%) and methamphetamine (11%) were next most common.

SAB Quality Measures

All patients had repeat blood cultures to document clearance after initiation of antimicrobials, and 98% had an ID consultation. All had a transthoracic echocardiogram (TTE), and 84% had a transesophageal echocardiogram (TEE). All patients with MSSA were treated with beta-lactams. The planned length of treatment was \geq 28 days for all patients (median [IQR], 42 [42–43] days).

Complications of SAB and Hospital Course

Among 46 cases, 44 survived \geq 72 hours and could be fully evaluated for infective endocarditis (IE), with a rate of 45% (43% of the total cohort). Of patients with IE, 75% had echocardiographic evidence. Eighty percent had complicated SAB, and 41% had a source control procedure performed. Two of 20 patients with endocarditis had valve replacement surgery.

In-hospital mortality was 9% (4/46), including 1 patient who was discharged to hospice. Eleven (24%) were discharged home, and 19 (41%) went to a skilled nursing facility (SNF). Twelve (24%) left the hospital against medical advice (AMA), none with any oral or intravenous antibiotics or follow-up appointments. The median length of hospital stay (IQR) was 23 (14–43) days. Of the patients who survived to hospital discharge, 45% were readmitted to the same hospital within 1 year after a median (IQR) of 29 (12–146) days. Three additional patients died after discharge, for an overall 6-month mortality of 15%. All deaths after hospital discharge occurred among females aged 27–33 who left AMA. One death was due to drug overdose, and 2 were infection related.

Substance Use Disorder Interventions

SUD was listed as an active hospital problem on the discharge summary for 52% of patients who survived to discharge. Twenty-six percent of patients received a "recommendation of abstinence" as the only intervention for their SUD, and 62% received at least 1 other intervention for their SUD (Table 2). In the last 2 months of the study period, the toxicology consult service at 1 hospital began assessing patients with opioid use disorder and initiating inpatient buprenorphine. Thirty-three

^eOne each: endovascular aspiration of tricuspid valve vegetation, debridement of retropharyngeal abscess, thoracentesis, vascular graft partial removal, and washout. ^fAll died within 6 months of discharge.

⁹Forty-two patients survived to discharge.

 $^{^{\}rm b}{\rm Endocarditis}$ identified in 20/44 (45%) patients who survived long enough for full evaluation (>72 hours).

^cMitral valve 1, tricuspid valve 15, aortic valve 2, prosthetic tricuspid valve 2. ^dBrain 1, renal 1, muscle 5.

 Table 2.
 Interventions for Substance Use Disorder for Patients With

 Injection Drug Use–Associated Staphylococcus aureus
 Bacteremia who

 Survived Until Discharge (n = 42)
 Survived Until Discharge (n = 42)

Variable	No. (%)
SUD on discharge summary as active problem	22 (52)
Abstinence recommended as only SUD intervention	11 (26)
Received ≥1 of the following SUD interventions	26 (62)
Psychiatry consult	12 (29)
Toxicology consult ^a	2 (5)
Received any buprenorphine in hospital	3 (7)
Received any methadone in hospital	7 (17)
Prescribed naloxone on discharge	0 (0)
Discharged with clear plans for outpatient addiction care	1 (2)
Discharged to inpatient SUD rehabilitation	1 (2)
Recommended outpatient treatment without clear plans	13 (31)

Abbreviation: SUD, substance use disorder.

^aBecame available only at Grady Memorial Hospital, and no other site, in the last 2 months of the study period.

percent had a psychiatry or toxicology consult while admitted. Twenty-two percent (10/42) received \geq 1 dose of buprenorphine (n = 3) or methadone (n = 7) during their hospital stay. No patients were discharged with a naloxone prescription or documented recommendation to obtain naloxone.

DISCUSSION

In this retrospective cohort in 3 Atlanta hospitals, we identified 46 cases of IDU-SAB. In contrast to national data on the demographics of the opioid epidemic—predominantly young white men—almost half of our cases were nonwhite and female. Most patients used heroin, but a quarter also used stimulants, which have no effective MAT. Although patients received excellentquality care with regards to evidence-based interventions for SAB, only half of the patients we identified with IDU-SAB had documentation of SUD as a medical problem, and few received any treatment interventions. This may have contributed to the high rate of AMA discharge and 6-month mortality. These data highlight that SUD is not treated with parity compared with other medical problems, even when it is the underlying cause of the acute medical illness.

We found that despite reports of stigmatization of people who inject drugs [7], patients with IDU-SAB received all of the appropriate ID-related interventions, which were associated with improvements in mortality [3, 6]. However, this care broke down for those who left AMA, none of whom received intravenous or oral antibiotics or medical follow-up. It is possible that precipitous AMA departures interfered with suitable care plans, and also possible that it was lack of attention to SUD that led directly to these hasty departures.

Several efforts might mitigate the problem of incomplete care and early hospital departure. First, all efforts should be made to prevent AMA discharge. This includes addressing the underlying causes of AMA discharge, which might include inadequate treatment of pain or withdrawal. Second, to reduce harm, providers should have an "antimicrobial contingency plan" so that oral antibiotics can be rapidly obtained and directly dispensed to patients before they leave. Third, patients should be offered low-barrier access to outpatient ID follow-up regardless of the terms by which they are discharged. Leaving AMA should not be a reason not to provide the best possible treatment, including outpatient follow-up.

The literature consistently describes insufficient, inconsistent efforts to treat addiction among patients admitted with IDUassociated infections, including initiation of lifesaving MAT [8-10]. Addiction medicine consultation results in more MAT, more frequent completion or antibiotic therapy, and fewer AMA discharges (87% vs 17%, 79% vs 40%, and 16% vs 49%, respectively) [11]. These results highlight the need to scale up programs to engage hospitalized patients with SUD into addiction care. We found a higher proportion of African American patients than other cohorts of IDU-associated infections [8, 10]. This is important because African Americans with opioid use disorder (OUD) appear less likely to receive appropriate addiction treatment [12]. Although OUD is readily treatable with MAT, consistent with epidemiologic data, we found a quarter of patients with concomitant stimulant use. Although MAT for OUD may mitigate some of the risks of IDU-associated infections in this population, ongoing stimulant use is an emerging problem [13].

The limitations of our study include a retrospective design, small sample size, and lack of a non-IDU-SAB comparison group. Identification of recent IDU can be difficult based on chart review alone; thus some IDU-SAB cases were likely missed. There could have been selection bias in which patients reported IDU or had objective evidence of recent IDU. Because we used time of first positive blood culture in the hospital to identify potential cases, we may have underestimated IDU-SAB, especially in those transferred from other facilities.

This cohort of IDU-SAB patients was characterized by young age and lack of comorbidity, which may be protective against early mortality; however, we identified complicated infection in 80% and frequent inadequate treatment due to AMA discharge. Postdischarge deaths occurred only among those who left AMA and were due to both addiction and infection. The provision of evidence-based SUD interventions should be prioritized for patients with IDU-SAB, in addition to appropriate antibiotic and surgical management.

Acknowledgments

Financial support. This work was unfunded. Dr. Serota receives grant funding from the Georgia Clinical and Translational Science Alliance (UL1TR002378 and TL1TR002382).

Potential conflicts of interest. All authors: no reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Author contributions. D.P.S. and R.R.K. came up with the research question and plan, and R.R.K. served as principal investigator. D.P.S. and E.D.N. abstracted all data from the medical record. D.P.S., E.D.N., and J.J. performed data analysis. All authors were involved in data interpretation and the writing of the manuscript.

References

- Jackson KA, Bohm MK, Brooks JT, et al. Invasive methicillin-resistant Staphylococcus aureus infections among persons who inject drugs - six sites, 2005–2016. MMWR Morb Mortal Wkly Rep 2018; 67:625–8.
- 2. Holland TL, Arnold C, Fowler VG Jr. Clinical management of *Staphylococcus aureus* bacteremia: a review. JAMA **2014**; 312:1330–41.
- Goto M, Schweizer ML, Vaughan-Sarrazin MS, et al. Association of evidence-based care processes with mortality in *Staphylococcus aureus* bacteremia at Veterans Health Administration Hospitals, 2003–2014. JAMA Intern Med 2017; 177:1489–97.
- Serota DP, Kraft CS, Weimer MB. Treating the symptom but not the underlying disease in infective endocarditis: a teachable moment. JAMA Intern Med 2017; 177:1026–7.
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987; 40:373–83.

- Pérez-Rodríguez MT, Sousa A, López-Cortés LE, et al. Moving beyond unsolicited consultation: additional impact of a structured intervention on mortality in *Staphylococcus aureus* bacteraemia. J Antimicrob Chemother **2019**; 74:1101-7.
- 7. Bearnot B, Mitton JA, Hayden M, Park ER. Experiences of care among individuals with opioid use disorder-associated endocarditis and their healthcare providers: results from a qualitative study. J Subst Abuse Treat **2019**; 102:16–22.
- Rosenthal ES, Karchmer AW, Theisen-Toupal J, et al. Suboptimal addiction interventions for patients hospitalized with injection drug use-associated infective endocarditis. Am J Med 2016; 129:481–5.
- 9. Medications for Opioid Use Disorder Save Lives. Washington, DC: National Academies Press; 2019.
- Jicha C, Saxon D, Lofwall MR, Fanucchi LC. Substance use disorder assessment, diagnosis, and management for patients hospitalized with severe infections due to injection drug use. J Addict Med 2019; 13:69–74.
- Marks LR, Munigala S, Warren DK, et al. Addiction medicine consultations reduce readmission rates for patients with serious infections from opioid use disorder. Clin Infect Dis 2019; 68:1935–7.
- Santoro TN, Santoro JD. Racial bias in the US opioid epidemic: a review of the history of systemic bias and implications for care. Cureus 2018; 10:e3733.
- Kariisa M, Scholl L, Wilson N, et al. Drug overdose deaths involving cocaine and psychostimulants with abuse potential - United States, 2003–2017. MMWR Morb Mortal Wkly Rep 2019; 68:388–95.