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Staphylococcus aureus Bacteremia in Patients Infected With COVID-19: A Case Series

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Background. Previous viral pandemics have shown that secondary bacterial infections result in higher morbidity and mortality, with *Staphylococcus aureus* being the primary causative pathogen. The impact of secondary *S. aureus* bacteremia on mortality in patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) remains unknown.

Methods. This was a retrospective observational case series of patients with coronavirus disease 2019 (COVID-19) who developed secondary *S. aureus* bacteremia across 2 New York City hospitals. The primary end point was to describe 14-day and 30-day hospital mortality rates of patients with COVID-19 and *S. aureus* bacteremia. Secondary end points included predictors of 14-day and 30-day hospital mortality in patients with COVID-19 and *S. aureus* bacteremia.

Results. A total of 42 patients hospitalized for COVID-19 with secondary *S. aureus* bacteremia were identified. Of these patients, 23 (54.8%) and 28 (66.7%) died at 14 days and 30 days, respectively, from their first positive blood culture. Multivariate analysis identified hospital-onset bacteremia (≥4 days from date of admission) and age as significant predictors of 14-day hospital mortality and Pitt bacteremia score as a significant predictor of 30-day hospital mortality (odds ratio [OR], 11.9; 95% CI, 2.03–114.7; $P = .01$; OR, 1.10; 95% CI, 1.03–1.20; $P = .02$; and OR, 1.56; 95% CI, 1.19–2.18; $P = .003$, respectively).

Conclusions. Bacteremia with *S. aureus* is associated with high mortality rates in patients hospitalized with COVID-19. Further investigation is warranted to understand the impact of COVID-19 and secondary *S. aureus* bacteremia.

Keywords.: bacteremia; COVID-19; SARS-CoV-2; *Staphylococcus aureus*.

The rapid spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has resulted in the worldwide pandemic of coronavirus disease 2019 (COVID-19). Clinical manifestations of COVID-19 vary significantly [1, 2]. Severe complications from COVID-19 include acute respiratory distress syndrome (ARDS), cardiovascular complications, thromboembolic events, septic shock, and multi-organ failure [3, 4]. Complications from bacterial infection, particularly bacteremia, are now being reported. One study described bacteremia rates of 1.6%–3.8%, with *Staphylococcus aureus* accounting for 13.3% of bacteremia cases [5]. The impact of secondary *S. aureus* bacteremia on mortality in patients infected with SARS-CoV-2 remains unknown.

S. aureus has been previously described as the primary causative pathogen of secondary bacterial infections in previous viral pandemics [6, 7]. Onset of secondary bacterial infections with influenza is typically seen within the first 6 days of influenza infection, when viral shedding is the highest [7]. Among patients infected with influenza, bacteremia has been associated with mortality approaching 50%, compared with 1.4% in patients with influenza but without bacteremia [8].

The onset of secondary bacterial infections, particularly with *S. aureus*, in patients infected with SARS-CoV-2 remains unknown. Our work aims to describe the clinical characteristics, mortality rates, and risk factors for mortality of adults hospitalized for COVID-19 who have secondary *S. aureus* bacteremia.

METHODS

Study Design and Definitions

This was a retrospective observational case series study of patients with COVID-19 disease admitted to either the Mount Sinai Hospital or Mount Sinai Queens in New York City (NYC). Adult patients were included if they were admitted between March 1, 2020, and May 31, 2020, tested positive for SARS-CoV-2 via nasopharyngeal PCR swab during that admission, and had at least 1 positive blood culture for *S. aureus* during the same admission. Patients were excluded if bacteremia onset was >24 hours

before a positive SARS-CoV-2 PCR. Organism identification and susceptibility were determined by the Clinical Microbiology Laboratory at the Mount Sinai Hospital. Preliminary organism identification was performed by ePlex, and identification was confirmed by matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF). Susceptibility testing was performed by Microscan, in accordance with Clinical and Laboratory Standards Institute (CLSI) criteria [9].

Patient baseline characteristics including demographics, comorbidities, laboratory values, blood culture results, and therapies received were obtained from the Mount Sinai Data Warehouse and confirmed by manual chart review. Laboratory values were recorded from the date of admission. Source of bacteremia was specifically obtained from infectious disease provider notes and verified by 2 independent physicians. Patients were categorized as having a central line if it was present within 48 hours before positive blood culture. Chest imaging was collected at the time of positive blood culture. Antibiotics received were categorized as empiric (within the first 5 days after blood culture collection) or definitive therapy (>5 days after blood culture collection). Severity of bacteremia was determined by Pitt bacteremia scores [10–13]. Bacteremia onset was categorized as hospital-onset bacteremia, defined as a positive blood culture on or after the fourth day after hospital admission, in accordance with National Healthcare Safety Network criteria [14]. Bacteremia was also categorized as polymicrobial in patients with a positive blood culture with 1 or more organisms, other than *S. aureus,* within the same 24-hour period.

The primary end point was 14-day and 30-day hospital mortality rates of patients with COVID-19 and *S. aureus* bacteremia. Mortality was measured from the date of the first positive blood culture until the date of hospital death. Secondary end points included predictors of 14-day and 30-day hospital mortality associated with *S. aureus* bacteremia in patients infected with SARS-CoV-2.

Statistical Analysis

Differences in patient characteristics were assessed by the chi-square or Fisher exact test for categorical variables, by the *t* test for parametric continuous variables, or by the Kruskal-Wallis test for nonparametric continuous variables. Predictors of 14-day or 30-day hospital mortality were identified by a univariate logistic regression. Variables yielding a *P* value ≤.20 from the univariate analysis were included in a backwards, stepwise, multivariate logistic regression model. Variance of inflation was also assessed for initial variable inclusion to eliminate collinearity between variables. Statistical significance was measured by a *P* value <.05. All statistical analyses were performed using R (version 4.0.0).

Patient Consent Statement

The Icahn School of Medicine Institutional Review Board approved this retrospective case series. Informed consent was not required, because the overall benefits of the research outweighed the minimal risks to the subjects since no interventions were performed and patient information was protected.

RESULTS

Across 2 NYC hospitals, a total of 42 out of 2679 (1.57%) patients hospitalized for COVID-19 between March 1, 2020, and May 31, 2020, were identified to have *S. aureus* bacteremia. Overall baseline demographics, comorbidities, and laboratory values, along with therapies received, are displayed in Table 1. The mean age was 65.6 ± 13.7 years, and 21 (50.0%) were male. The median body mass index (BMI; interquartile range [IQR]) was 27.5 (23.8–33.0). Twenty-nine (69.0%) patients had baseline hypertension, 19 (45.2%) had cardiovascular disease, and 21 (50.0%) patients had diabetes. Median baseline

Table 1.   Patient Baseline Demographics and Comorbidities

	Total Cases (n = 42)
Age, mean ± SD, y	65.6 ± 13.7
Male, No. (%)	21 (50.0)
BMI, median [IQR], kg/m^2	27.5 [23.8–33.0]
Race, No. (%)	
African American	7 (16.7)
White	8 (19.0)
Other	27 (64.3)
Ethnicity, No. (%)	
Hispanic	17 (40.5)
Non-Hispanic	21 (50.0)
Unknown	4 (9.5)
Medical history, No. (%)	
Cardiovascular disease[a]	19 (45.2)
Hypertension	29 (69.0)
Diabetes	21 (50.0)
Chronic kidney disease	6 (14.3)
Malignancy	5 (11.9)
Lung disease[b]	7 (16.7)
End-stage renal disease	4 (9.5)
Transplant	3 (7.1)
Liver disease	1 (2.4)
Baseline admission labs, median [IQR]	
White blood cell, ×10^3/L	10.3 [7.48–13.2]
Platelet count, ×10^3/L	228.0 [160.1–306.5]
Serum creatinine, mg/dL	0.98 [0.75–2.36]
Bilirubin, mg/dL	0.66 [0.45–0.94]
Procalcitonin, ng/mL[c]	0.42 [0.19–1.36]
C-reactive protein, mg/L[c]	155.1 [88.2–244.2]
D-dimer, μg/mL[c]	1.65 [1.21–3.83]
Ferritin, ng/mL[c]	1045 [462.6–2521]
Interleukin-6, pg/mL[c]	151.2 [74.8–349.9]

Abbreviations: BMI, body mass index; IQR, interquartile range.

[a]Cardiovascular disease includes coronary artery disease, atrial fibrillation, heart failure, and cerebrovascular accident.

[b]Lung disease includes asthma and chronic obstructive pulmonary disease.

[c]Missing values present: procalcitonin (n = 1), C-reactive protein (n = 1), D-dimer (n = 2), ferritin (n = 2), interleukin-6 (n = 12).

inflammatory markers, including C-reactive protein, D-dimer, ferritin, and interleukin-6, were elevated at baseline.

Twenty-three of the 42 patients had *S. aureus* bacteremia (54.8%) with methicillin-susceptible *S. aureus* (MSSA) (Table 2). There were no significant differences in characteristics and outcomes between bacteremia with MSSA and methicillin-resistant *S. aureus* (MRSA). Seven (16.7%) patients were categorized as having a polymicrobial infection. These organisms included *Enterococcus faecalis* (n = 3), *Candida* spp. (n = 2), *Klebsiella* spp. (n = 2), *Escherichia coli* (n = 1), *Bacillus* spp. (n = 1), *Micrococcus* spp. (n = 1), *Staphylococcus epidermidis* (n = 1), and *Proteus mirabilis* (n = 1). The source of bacteremia was unknown or not documented for 29 (69.0%) patients. Of the 13 patients with a known source of bacteremia, the most common source was pneumonia (n = 8, 19.0%). Six of the patients with a pneumonia source had hospital-onset bacteremia with onset ranging from 9 to 48 days (median [IQR], 32.7 [16.3–45.3] days).

Median WBC count and procalcitonin at the time of blood cultures (IQR) were elevated from admission (WBC: 14.7 [9.20–20.2]; procalcitonin: 1.02 [0.28–3.47]). Patients were typically febrile at time of blood culture, with a mean temperature of 38.0°C ± 0.98°C. The median Pitt bacteremia score (IQR) was elevated at 5.0 (2.0–7.0). Thirty-one patients (73.8%) were mechanically ventilated, and 19 (45.2%) had a central venous catheter in place within 48 hours before positive blood culture. Central venous catheters were noted to be removed/replaced in 12 (63.2%) of the patients with central venous catheters. A total of 41 (97.6%) had an infectious disease consult. A transthoracic echocardiogram was obtained for 29 (47.6%) patients, and only 1 was positive for a vegetation.

The most common empiric antimicrobial regimen used was vancomycin and cefepime (n = 24, 58.5%) (Table 2). The median time from blood culture collection to antibiotic initiation (IQR) was 0 (0–24) hours. Definitive antimicrobials received in patients with MRSA bacteremia were predominantly vancomycin (n = 13), with 3 patients concomitantly receiving a β-lactam (ie, cefazolin, meropenem, or piperacillin/tazobactam), linezolid (n = 1), or daptomycin (n = 1). Definitive therapy received in patients with MSSA bacteremia was predominantly cefazolin (n = 10), followed by ceftriaxone (n = 3), nafcillin (n = 2), along with 1 patient receiving linezolid for polymicrobial bacteremia. Definitive therapy was not available for individuals who died within 2 days of culture.

Twenty-eight (66.7%) patients were considered to have hospital-onset bacteremia. The median time from admission to bacteremia onset (IQR) was 8.0 (0.02–21.0) days. Forty-one patients had a positive SARS-CoV-2 PCR result within the first 2 days of hospital admission, and 1 patient was positive on hospital day 4.

Twenty-three (54.8%) and 28 (66.7%) patients had hospital mortality at 14 and 30 days, respectively, from their first positive blood culture. The median time from blood culture to death (IQR) was 7.88 (2.00–18.5) days. The median hospital length of stay for survivors at the 30-day mortality mark (IQR) was 22.5 (10.3–35.8) days. The time from admission to blood culture (IQR) was longer in patients with mortality at 14 days compared to patients surviving at 14 days (13.0 [5.5–23.5] days vs. 4.5 [0.0–14.0] days; *P* = .06).

Median Pitt bacteremia scores (IQR) were significantly higher in patients with 14-day and 30-day hospital mortality as compared with patients surviving at 14 and 30 days (3.0 [0.50–5.0] vs 7.0 [4.5–7.0] days; *P* = .004; and 2.0 [0.25–5.0] vs 6.5 [4.0–7.0] days; *P* = .001, respectively) (Table 2). On univariate logistic regression, every 1-unit increase in Pitt bacteremia score was found to predict a 44% and 56% increased risk of mortality for 14-day and 30-day mortality, respectively (Table 3). Patients with central venous catheters present within 48 hours of positive blood culture were also more likely to have 14-day and 30-day mortality (26.3% vs 60.9%; *P* = .05; and 21.4% vs 57.1%; *P* = .05, respectively) (Table 2). On univariate logistic regression, central venous catheter presence had a 4.36 and 4.89 increased odds of 14-day and 30-day mortality (Table 3).

Higher mean age was also more common in patients with 14-day and 30-day mortality compared to patients surviving (69.0 ± 10.6 vs 61.58 ± 16.11; *P* = .08; and 67.0 ± 13.4 vs 62.8 ± 14.3; *P* = .35, respectively). Age was identified as a significant predictor of 14-day hospital mortality on multivariate logistic regression analysis, where for every 1-year increase in age there was a 10% increased risk of 14-day mortality (Table 4). There were also higher rates of 14-day and 30-day mortality in patients with hospital-onset bacteremia (52.6% vs 78.3%; *P* = .15; and 57.1% vs 71.4%; *P* = .56, respectively) (Table 3). Multivariate analysis identified hospital-onset bacteremia as a significant predictor of 14-day hospital mortality (11.9; 95% CI, 2.03–114.7; *P* = .01). Pitt bacteremia score was a significant predictor of 30-day hospital mortality (OR, 1.56; 95% CI, 1.19–2.18; *P* = .003) (Table 4). Median Pitt bacteremia score (IQR) was elevated in patients with hospital-onset bacteremia compared with patients without hospital-onset bacteremia (6 [5–7] vs 2 [2–3.75]; *P* = .01).

DISCUSSION

We report 42 cases of *S. aureus* bacteremia in patients admitted with COVID-19 across 2 hospitals in NYC during the time the city was the epicenter of the pandemic in the United States. *S. aureus* bacteremia during a COVID-19 admission was only seen in 1.6% (42/2679) of patients, but was associated with a high mortality rate. The 14-day hospital mortality rate from the first positive blood culture was 54.8%, and the 30-day hospital mortality rate was 66.7%. These rates are much higher than

Table 2. Bacteremia Related Characteristics and Treatments

	Total Cases (n = 42)	14-Day Survival (n = 19)	14-Day Mortality (n = 23)	P Value	30-Day Survival (n = 14)	30-Day Mortality (n = 28)	P Value
MSSA, No. (%)	23 (54.8)	8 (42.1)	15 (65.2)	.24	5 (35.7)	18 (64.3)	.15
Polymicrobial, No. (%)[a]	7 (16.7)	1 (5.3)	6 (26.1)	.11	1 (7.1)	6 (21.4)	.39
Source of bacteremia, No. (%)							
Vascular[b]	3 (7.1)	2 (10.5)	1 (4.3)	.19	1 (7.1)	2 (7.1)	.31
Osteomyelitis	1 (2.4)	1 (5.3)	0		1 (7.1)	0	
Skin	1 (2.4)	1 (5.3)	0		1 (7.1)	0	
Pneumonia	8 (19.0)	5 (26.3)	3 (13.0)		3 (21.4)	5 (17.9)	
Unknown	29 (69.0)	10 (52.6)	19 (82.6)		8 (57.1)	21 (75.0)	
Bacteremia definitions							
Hospital-onset bacteremia,[c] No. (%)	28 (66.7)	10 (52.6)	18 (78.3)	.15	8 (57.1)	20 (71.4)	.56
Time from admission to bacteremia onset, median [IQR], d	8.0 [0.02–21.0]	4.5 [0–14.0]	13.0 [5.5–23.5]	.06	5.2 [0.25–14.3]	11.0 [0.06–22.0]	.30
No admission blood culture, No. (%)	6 (14.3)	4 (21.1)	2 (8.7)	.38	2 (14.3)	4 (14.3)	1.0
Characteristics collected at time of blood culture							
White blood cell, median [IQR], ×10^3/L	14.7 [9.20–20.2]	12.3 [8.20–20.5]	15.8 [12.6–20.0]	.27	12.3 [8.38–18.8]	15.6 [11.8–21.2]	.21
Procalcitonin, median [IQR], ng/mL	1.02 [0.28–3.47]	1.16 [0.34–5.09]	1.02 [0.28–2.04]	.65	0.87 [0.33–3.29]	1.04 [0.30–3.33]	.89
Temperature, mean ± SD, °C	38.0 ± 0.98	38.1 ± 0.84	38.0 ± 1.10	.64	38.0 ± 0.94	38.1 ± 1.02	.86
Abnormal chest x-ray, No. (%)	36 (85.7)	17 (89.5)	19 (82.6)	.67	13 (92.9)	23 (82.1)	.65
Pitt bacteremia score, median [IQR]	5.0 [2.0–7.0]	3.0 [0.50–5.0]	7.0 [4.5–7.0]	.004	2.0 [0.25–5.0]	6.5 [4.0–7.0]	.001
Mechanical ventilation, No. (%)	31 (73.8)	13 (68.4)	18 (78.3)	.71	9 (64.3)	22 (78.6)	.54
Central venous catheter,[d] No. (%)	19 (45.2)	5 (26.3)	14 (60.9)	.05	3 (21.4)	16 (57.1)	.05
Empiric antibiotics received, No. (%)[e]							
Vancomycin/cefepime	24 (58.5)	12 (63.2)	12 (52.2)	.76	9 (64.3)	15 (53.6)	.28
Vancomycin/other β-lactam[f]	9 (22.0)	3 (15.8)	6 (26.1)		1 (7.1)	8 (28.6)	
Vancomycin	7 (17.1)	3 (15.8)	4 (17.4)		3 (21.4)	4 (14.3)	
Piperacillin/tazobactam	1 (2.4)	1 (5.3)	0		1 (7.1)	0	
Time from blood culture to antibiotic initiation, median [IQR], h	0 [0–24.0]	0 [0–23.6]	0 [0–23.4]	.90	1.0 [0–23.8]	0 [0–22.8]	.90

Differences in patient characteristics were assessed by the chi-square or Fisher exact test for categorical variables or by t test for parametric continuous variables or Kruskal-Wallis test for nonparametric continuous variables.

Abbreviations: IQR, interquartile range; MSSA, methicillin-susceptible *Staphylococcus aureus*.

[a]Polymicrobial includes other infecting organisms, including *Enterococcus faecalis* (n = 2), *Candida* spp. (n = 2), *Klebsiella* spp. (n = 2), *Escherichia coli* (n = 1), *Bacillus* spp. (n = 1), *Micrococcus* spp. (n = 1), *Staphylococcus epidermidis* (n = 1), and *Proteus mirabilis* (n = 1).

[b]Includes cardiovascular devices or line.

[c]Hospital-onset bacteremia was defined as a positive blood culture on or after the fourth day after hospital admission.

[d]Central line was present within 48 hours before positive blood cultures.

[e]One patient was excluded because they died before antibiotics could be given.

[f]Other β-lactams include piperacillin/tazobactam (n = 3), cefazolin (n = 2), aztreonam (n = 1), cefriaxone (n = 1), meropenem (n = 1), and amoxicillin (n = 1).

Table 3.   Univariate Logistic Regression Predictors of Mortality[a]

Predictor	14-Day In-Hospital Mortality		30-Day In-Hospital Mortality	
	OR [95% CI]	*P* Value	OR [95% CI]	*P* Value
Demographics and patient characteristics				
Age	1.04 [1.00–1.10]	.09	1.02 [0.98–1.08]	.34
BMI, kg/m^2	1.05 [0.97–1.15]	.23	1.02 [0.94–1.12]	.60
Hispanic	1.99 [0.57–7.38]	.29	2.17 [0.57–9.45]	.27
Pitt bacteremia score	1.44 [1.12–1.93]	.01	1.56 [1.19–2.18]	.003
Mechanical ventilation	1.66 [0.41–6.93]	.47	2.04 [0.48–8.58]	.33
Abnormal chest x-ray	0.56 [0.07–3.25]	.53	0.35 [0.02–2.52]	.37
Central venous catheter	4.36 [1.22–17.6]	.03	4.89 [1.21–25.3]	.04
Bacteremia characteristics				
MSSA bacteremia	2.58 [0.75–9.38]	.14	3.24 [0.88–13.2]	.09
Pneumonia source	0.42 [0.08–1.99]	.28	0.80 [0.16–4.45]	.78
Time from blood culture to antibiotic initiation	1.00 [0.96–1.04]	.94	1.00 [0.97–1.05]	.82
Hospital-onset bacteremia[b]	3.24 [0.88–13.2]	.09	1.87 [0.48–7.28]	.36

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; OR, odds ratio.

[a]Predictors of 14-day or 30-day hospital mortality were identified by univariate logistic regression.

[b]Hospital-onset bacteremia was defined as a positive blood culture on or after the fourth day after hospital admission.

Table 4.   Multivariate Logistic Regression Model Predictors of Mortality[a]

14-Day In-Hospital Mortality			30-Day In-Hospital Mortality		
Predictor	OR [95% CI]	*P* Value	Predictor	OR [95% CI]	*P* Value
Hospital-onset bacteremia[b]	11.9 [2.03–114.7]	.01	Pitt bacteremia score	1.56 [1.19–2.18]	.003
Age	1.10 [1.03–1.20]	.02			

Abbreviation: OR, odds ratio.

[a]A backwards, stepwise, multivariate logistic regression model was utilized. Variables initially included in this multivariate model had yielded a *P* value ≤.10 from the univariate logistic regression analysis. Variance of inflation was also assessed for initial variable inclusion to eliminate collinearity between variables.

[b]Hospital-onset bacteremia was defined as a positive blood culture on or after the fourth day after hospital admission.

reported mortality rates for patients hospitalized for COVID-19, with rates of up to 25% in patients who were mechanically ventilated [4, 15, 16]. Reported mortality rates for patients with *S. aureus* bacteremia are up to 30% [17–19]. As the median days from positive blood culture to death was <8, *S. aureus* bacteremia was likely to have contributed to the deaths.

S. aureus infections are a known complication of other viral pandemics, such as the Spanish flu in 1918–1919 and the H1N1 influenza pandemic in 2009–2010 [8, 20]. *S. aureus* is known to act synergistically in all influenza seasons, increasing mortality and severity of disease [7, 21, 22]. The proposed mechanisms of viral-induced bacterial co-infections include viral modification of airway structures, as well as initiation of immune-suppressive responses [23–25]. Viruses can upregulate ligands for bacterial adherence to virus-infected respiratory tract cells [23, 24] and can initiate immune-suppressive cytokines to reduce neutrophil recruitment [25]. Eight patients in our case series were determined to have a pneumonia source, with only 2 patients having community-onset *S. aureus* pneumonia. We also found that the majority of patients had hospital-onset bacteremia, which suggests that the interaction of *S. aureus* with SARS CoV-2 is

dissimilar to influenza. Further clinical and translational research is warranted to further define this relationship.

Bacterial infections in patients with COVID-19 have been reported [26]. A systematic review and meta-analysis of 30 studies of patients infected with SARS-CoV-2 identified that out of 3834 patients, 7% had bacterial co-infections [27]. The authors performed a pooled analysis and found an increased risk of death with bacterial co-infections (OR, 5.82; 95% CI, 3.4–9.9; I^2 = 85.4%), but they did not explore specific sites of infections or pathogens such as *S. aureus* [27]. There have been 2 reports from other centers in NYC about bacteremia in patients with COVID-19. Sepulveda et al. reported that through March 31, 1.6% of COVID-19 patients had bacteremia, with *S. aureus* as the second most common pathogen accounting for 13% of bacteremias [5]. Nori et al. reported similar findings, with 1.9% of COVID-19 patients with bacteremia with *S. aureus* as the most common etiology, accounting for 44% of bacteremias [26]. Neither of these studies evaluated timing of bacteremia with COVID-19 infection or association with mortality [5, 26]. In comparison with these studies, our case series found a greater percentage of patients who specifically had *S. aureus*

bacteremias, which may be explained by our longer observation time that included the entire admission of the patient.

The majority of our patients were also found to have hospital-onset bacteremia. Hospital-onset bacteremia was a predictor of 14-day mortality on multivariate analysis but not of 30-day mortality. Hospital-onset bacteremia has previously been reported to be associated with increased mortality [28–30]. We also identified age as a predictor of 14-day hospital mortality on multivariate analysis, which is consistent with previous findings that older patients with COVID-19 have a higher risk of death [31].

Our patients also had elevated Pitt bacteremia scores, which was a predictor of 14-day and 30-day mortality on univariate analysis and 30-day mortality on multivariate analysis. Although the Pitt bacteremia score was first developed to predict gram-negative bacteremia mortality, a score ≥2 has indicated a significant risk of mortality for *S. aureus* [12, 13]. Comparatively, our median Pitt bacteremia score (IQR) of 5.0 (2.0–7.0) is higher than previously published *S. aureus* bacteremia studies [13, 32]. One study reported a median Pitt bacteremia score (IQR) of 0 (0–2), whereas another study found the mean Pitt bacteremia score to be 4 [13, 32]. We found that the median Pitt bacteremia score was elevated in patients with hospital-onset bacteremia, which likely contributed to the association between hospital-onset bacteremia and 14-day mortality.

Our study is limited by its retrospective design and small sample size, which limited our power to detect all predictors of *S. aureus* mortality. Variables with multiple categories such as antimicrobial therapy received and source of infection could not be adequately explored. These variables have been shown to impact mortality and potentially confound our results [33, 34]. Lastly, few patients in our population underwent transthoracic echocardiogram, and none underwent transesophageal echocardiogram. The limited number of patients who underwent echocardiogram may have limited adequate source control and confounded the outcome of mortality.

To limit uncertainty about timing of active COVID-19 disease, our study was limited to the admission during which the patient was diagnosed with COVID-19. Thus, only in-hospital mortality was measured in this study, which means deaths after discharge that were still within the 30-day post–positive culture range were not captured. However, the median in-hospital length of stay for survivors was 22.5 days. Similarly, COVID-19 patients readmitted with *S. aureus* bacteremia were not included.

CONCLUSIONS

This is one of the first descriptions of *S. aureus* bacteremia in patients infected with SARS-CoV-2 and the first to evaluate predictors of mortality. *S. aureus* bacteremia was found to be uncommon but associated with high mortality rates in patients hospitalized with COVID-19. Risk factors associated with higher mortality included hospital-onset bacteremia, older age, and elevated Pitt bacteremia score. Further investigation is warranted on the relationship between COVID-19 and secondary *S. aureus* bacteremia.

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