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Methicillin-resistant *Staphylococcus aureus* and Vancomycin Prescribing in the Emergency Department: A Single-center Study Assessing Antibiotic Prescribing

Joshua D. Niforatos MD, MTS[1], Jeremiah S. Hinson MD, PhD[1], Richard E. Rothman MD, PhD[1], Sara E. Cosgrove MD[2], Kate Dzintars PharmD[2], Eili Y. Klein PhD[1]

[1]*Department of Emergency Medicine, The Johns Hopkins University School of Medicine, Baltimore, Maryland, USA*
[2]*Division of Infectious Diseases, Department of Medicine, The Johns Hopkins University School of Medicine, Baltimore, Maryland, USA*

Correspondence

Joshua D. Niforatos, MD, MTS, Department of Emergency Medicine, The Johns Hopkins University School of Medicine, 1830 Bldg, 1830 E Monument St suite 6-100, Baltimore, MD, USA. Email: jnifora1@jh.edu

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Abstract

Objectives: Given the support for methicillin-resistant *Staphylococcus aureus* (MRSA) antimicrobial stewardship in the 2021 Surviving Sepsis Campaign Guidelines, we sought to measure the use of vancomycin in the emergency department (ED) in the years preceding these recommendations.

Methods: A retrospective cohort study was conducted of all patients aged ≥ 18 years presenting to 5 emergency departments within a university-based health system who were given intravenous (IV) vancomycin during their ED index visit. The primary outcome assessed the proportion of patients with MRSA-positive blood cultures who received IV vancomycin in the ED. We also measured associations between clinical attributes associated with any MRSA infection.

Results: Of the 20,212 unique ED visits for patients who received IV vancomycin, 63% (n = 12,755) had at least 1 MRSA risk factor. Only 2.4% (n = 494) and 14.1% (n = 2850) of patients receiving IV vancomycin in the ED were found to have MRSA bacteremia or any MRSA-positive culture, respectively. A total of 3160 patients met Sepsis-3 criteria and received IV vancomycin, though 65% (n = 2064) had no MRSA risk factors. For any patient with culture-proven MRSA, 63.8% (n = 315) and 43.4% (n = 1236) received an MRSA antimicrobial in the ED. MRSA risk factors were not associated with MRSA bacteremia (≥1 MRSA risk factor: odds ratio, 1.3, 95% CI, 0.9-1.8) or an MRSA-positive culture of any type (odds ratio, 0.9, 95% CI, 0.7-1.1).

abstract continues

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Abstract (continued)

Conclusion: Within our hospital system, MRSA was an infrequent cause of bacteremia for patients presenting to the ED with sepsis or septic shock. Although vancomycin is frequently used in the ED, many patients with culture-proven MRSA did not receive MRSA antimicrobials. Notably, one-third of patients with culture-proven MRSA had no MRSA risk factors. MRSA risk factors were not predictive of culture-proven MRSA, thus highlighting the complexity of antimicrobial stewardship in the ED without validated clinical decision rules.

Keywords: *emergency medicine, MRSA, antibiotic prescribing, clinical practice variation, clinical guidelines*

1 INTRODUCTION

1.1 Background

Sepsis accounts for over 850,000 emergency department (ED) visits annually and is associated with significant mortality.[1–3] Previous research has shown improved survival with early administration of antimicrobials in patients with septic shock,[4–7] though debate exists regarding the precise timing of antimicrobials.[8–10]

Based on the 2016 Surviving Sepsis Campaign (SSCG) recommendations, routine empiric antimicrobial coverage for methicillin-resistant *Staphylococcus aureus* (MRSA) was required,[11] which includes the antimicrobial vancomycin and subsequently is considered a composite measure for reimbursement by Centers for Medicare and Medicaid Services.[12]

1.2 Importance

The 2021 SSCG revised recommendations on managing sepsis and septic shock.[13] The guidelines provided a new best practice statement to provide empiric MRSA antimicrobials *only* in adults with sepsis or septic shock at high risk for MRSA infection.[13] This recommendation was based on research that MRSA accounts for less than 5% of all culture-positive infections,[14–17] as well as observational data that administration of MRSA antimicrobials is associated with increased mortality in undifferentiated patients with pneumonia or community-acquired sepsis.[18–20] For patients with MRSA infections, the literature is mixed on whether 24- to 48-hour delays in MRSA antimicrobials are associated with increased mortality.[13] A recent observational study suggests that administering a β-lactam antimicrobial before vancomycin improved 48-hour and 7-day mortality in ill-appearing patients with bacteremia.[21] Finally, the MRSA antimicrobial vancomycin has a known association with acute kidney injury when given individually and synergistically with gram-negative antimicrobials.[22–24]

1.3 Goals of This Investigation

Given support for MRSA antimicrobial stewardship in the 2021 SSCG, this study aimed to measure the use of vancomycin in the ED in the years preceding these recommendations.

2 METHODS

2.1 Study Design and Setting

This single-center retrospective study of patient visits to 5 EDs within a university-based health system in the Baltimore-Washington, DC, region occurred between 2017 and 2019. The system includes 2 urban academic EDs and 3 suburban community EDs with an annual patient volume of over 255,000 patients. The Johns Hopkins University School of Medicine Institutional Review Board approved this study with a waiver of informed consent.

2.2 Selection of Participants

This study included adult patients aged (≥18 years) who received ≥1 intravenous (IV) vancomycin administration during the ED index visit. We also included all adult patients with MRSA-positive cultures during their ED index visit for sensitivity analyses.

2.3 Data Collection

An experienced data user (EYK) extracted clinical information from a relational database that underlies the electronic health record (her) of our institution (Epic) using Microsoft SQL Server Management Studio 18 (Microsoft Corporation), as previously described.[25–27] Extracted data are in Table 1. The presence or absence of MRSA risk factors and MRSA alert for contact precautions in the patient's chart during the ED visit were also collected. The Sepsis-3 definition using the Sequential Organ Failure Assessment score was a reference standard to define sepsis groups (sepsis without shock and septic shock).[28] This was abstracted using previously described methods (Table 1).[29] Septic shock was defined as those patients with sepsis who required vasopressor initiation with lactate values >2.0 mmol/L. Patients who did not meet Sepsis-3 criteria were categorized as not septic. JDN manually reviewed a random sample of charts to ensure that automated data extraction accurately captured clinical information.

2.4 Methods of Measurement

Data were coded as continuous, ordinal, or categoric. According to previously established physiologic cut-offs, vital signs were recoded into categoric variables as normal or abnormal (eg, heart

The Bottom Line

The 2021 Surviving Sepsis Campaign guidelines recommend methicillin-resistant *Staphylococcus aureus* antimicrobials only for patients with sepsis/septic shock at risk for methicillin-resistant *Staphylococcus aureus*. This single-center study found that methicillin-resistant *Staphylococcus aureus* bacteremia was an infrequent cause of sepsis/septic shock. Two-thirds of patients who met Sepsis-3 criteria and one-third of patients with any culture-proven methicillin-resistant *Staphylococcus aureus*, respectively, had no methicillin-resistant *Staphylococcus aureus* risk factors. The risk factors of methicillin-resistant *Staphylococcus aureus* were not associated with methicillin-resistant *Staphylococcus aureus* bacteremia (≥1 methicillin-resistant *Staphylococcus aureus* risk factor: odds ratio, 1.3, 95% CI, 0.9-1.8) or an methicillin-resistant *Staphylococcus aureus*–positive culture of any type (odds ratio, 0.9, 95% CI, 0.7-1.1), thus highlighting the complexity of antimicrobial stewardship in the ED.

rate < 100 or ≥100 bpm). Laboratory data were recoded into categoric variables based on institutional reference ranges. Missing data were not excluded or imputed according to our hypothesis that these data may not be missing at random,[30,31] as previously described in the emergency medicine literature,[25,32] and were included in all analyses. Given nosocomial infections are those considered to have occurred after 48 hours of hospital admission, an MRSA-positive culture was considered present at the ED index visit if it was present in cultures collected either in the ED or within 48 hours of hospital admission. Patients with no cultures collected were categorized as MRSA-negative. An MRSA alert in the patient's electronic health records (EHRs) identified past MRSA infection events. All culture data of any type were also collected for each patient and categorized by organ system/kind of culture (Supplementary Appendix 1).

The Johns Hopkins Antibiotic Guideline was used to identify general and local patient risk factors for MRSA infection,[33] of which are included in Supplementary Appendix 1. Additional risk factors for MRSA infection included positive blood cultures in the 14 days preceding the ED index visit, positive MRSA culture of any type within the last 90 days, and ED visits or hospital admission within 30 or 60 days. A cumulative MRSA "risk score" was calculated for each patient based on the presence and absence of risk factors, for which each risk factor was given 0 points if absent and 1 point if present, with a minimum of 0 points and a maximum of 9 points. Intravenous drug use (IVDU) is challenging to capture in EHRs,[34] and a previously identified published algorithm was used to create a category of patients deemed at high risk for IVDU history.[35]

2.5 Primary and Secondary Outcome

The primary outcome of this study assessed the proportion of patients with MRSA-positive blood cultures who received guideline-concordant IV vancomycin in the ED. We also measured associations between clinical attributes associated with MRSA infection. We hypothesized there would be no significant associations between vancomycin prescribing and MRSA blood culture positivity rate, the presence of MRSA risk factors, and whether the patient met Sepsis-3 criteria during the ED index visit. The secondary outcome sought to identify clinical predictors of MRSA infection.

2.6 Data Analysis

Descriptive statistics were calculated using median with IQR, and frequency count with percentage (%) as appropriate. Pearson's chi-squared test and the Wilcoxon rank sum test were used to assess associations for categoric and continuous data, respectively. For the primary outcome, the rate of MRSA-positive cultures among patients prescribed vancomycin was calculated as the percentage of visits with occurrence. We then compared the proportion of patients with Sepsis-3 criteria who received vancomycin based on MRSA positivity using Pearson's chi-squared test. A subgroup analysis of all adult ED patients with MRSA bacteremia or any MRSA-positive culture was identified to classify missed opportunities for vancomycin administration. A sensitivity analysis was performed on this cohort of patients regarding exposure to any antimicrobial with MRSA coverage during the ED index visit (Supplementary Appendix 1).

For the secondary outcome, we used the combined cohort of all patients receiving vancomycin in the ED and those with any MRSA-positive cultures (Table S1). Univariable and multivariable logistic regression was used to assess the relationship between MRSA risk factors identified in the literature, its association with Sepsis-3 criteria, and patient-level characteristics known to the emergency clinician at the index visit for MRSA infection (model 1). MRSA risk factors were coded as binary: 0 pt or ≥1 pt. Given clinical significance and association with the outcome in prior literature, all variables were retained in the model even if they were not statistically significant. Multilevel mixed-effects logistic regression models were used when appropriate to predict MRSA infection (blood

TABLE 1. Baseline characteristics of the patients.

Characteristic -	Vancomycin cohort N = 20,212	MRSA + blood cultures N = 494	MRSA+ any culture N = 2850
Patient age (y)	62 (47-75)	60 (41-72)	55 (38-69)
Sex	-	-	-
Female	46% (9356)	43% (210)	43% (1239)
Male	54% (10856)	57% (284)	57% (1611)
Race	-	-	-
Black	29% (5914)	33% (164)	33% (944)
Other	11% (2133)	6% (29)	8% (231)
White	60% (12,165)	61% (301)	59% (1675)
Charlson comorbidity index	-	-	-
90% 10 y survival	32% (6535)	27% (134)	29% (827)
50%-75% 10 y survival	22% (4508)	25% (122)	20% (584)
< 20% 10 y survival	26% (5190)	37% (185)	22% (639)
Null	20% (3979)	11% (53)	28% (800)
IVDU history: yes	6.1% (1229)	16.2% (80)	10.7% (307)
ESI	-	-	-
ESI 4-5	4% (720)	1% (7)	11% (312)
ESI 3	50% (10,146)	47% (233)	56% (1604)
ESI 1-2	46% (9346)	51% (254)	33% (934)
MRSA risk factors	-	-	-
No MRSA RF	37% (7457)	29% (145)	39% (1122)
>1 MRSA RF	63% (12,755)	71% (349)	61% (1728)
Admission level of care	-	-	-
Non-ICU	91% (18,448)	83% (410)	91% (2605)
ICU/IMC	9% (1764)	17% (84)	9% (245)
ED shift at presentation			
Morning	42.7% (8622)	35.4% (175)	43.3% (1235)
Afternoon	43.0% (8682)	45.5% (225)	41.1% (1171)
Overnight	14.4% (2908)	19.0% (94)	15.6% (444)
ED with care area	-	-	-
ED with not high acuity	24.6% (4970)	22.1% (109)	36.1% (1028)
ED with high acuity	75.4% (15,242)	77.9% (385)	63.9% (1822)
ED LOS (h, median, IQR)	8 (6-14)	8 (5-13)	8 (5-14)
Hospital LOS (d, median, IQR)	5 (3-8)	9 (6-15)	6 (4-11)
Sepsis 3 criteria present[a]	-	-	-
Sepsis 3: yes	15.6% (3160)	28.1% (139)	11.0% (313)
Positive blood cultures	-	-	-
Yes	33.6% (6788)	100.0% (494)	100.0% (2850)
Vasopressors given	3% (526)	7% (35)	2% (62)
Minimum SBP (median, IQR)	114 (98-132)	110 (93-128)	115 (101-130)
Maximum HR (median, IQR)	103 (88-119)	108 (94-124)	98 (86-112)
Maximum temp (median, IQR)	99 (98-101)	100 (98-102)	99 (98-100)
Minimum temp (median, IQR)	37 (36-37)	37 (36-37)	37 (36-37)
Maximum RR (median, IQR)	20 (18-24)	20 (18-26)	18 (18-22)

(Continues)

TABLE 1. (Continued)

Characteristic -	Vancomycin cohort N = 20,212	MRSA + blood cultures N = 494	MRSA+ any culture N = 2850
Lactate (maximum)			
Normal lactate level (<2 mmol/L)	35% (7068)	37% (182)	34% (983)
Hyperlactemia (≥2 but < 4 mmol/L)	21% (4305)	25% (123)	14% (403)
High lactate level (≥4 mmol/L)	9% (1795)	9% (46)	5% (132)
Null	35% (7044)	29% (143)	47% (1332)
WBC (maximum)			
Normal WBC (<12 $\times 10^9$/L)	43% (8788)	30% (149)	41% (1159)
High WBC (≥12 and <20 $\times$ 10^9/L)	34% (6873)	38% (187)	33% (945)
Very High WBC (≥20 $\times$ 10^9/L)	16% (3326)	26% (126)	18% (499)
Null	6% (1225)	6% (32)	9% (247)
MRSA flag at the index visit	14.1% (2853)	39.5% (195)	35.6% (1016)
MRSA-positive culture within 90 d	3.1% (621)	14.8% (73)	11.4% (326)
MRSA-positive NAT within 90 d	1.4% (291)	6.1% (30)	4.5% (129)
Any positive blood culture within 14 d	3.7% (739)	4.5% (22)	3.6% (103)
ED or hospital visit within 60 d	54.4% (10,995)	57.3% (283)	52.2% (1488)
ED or hospital visit Within 60 d	31.2% (6312)	28.3% (140)	27.7% (790)
Hospital ED	-	-	-
BMC	21.2% (4284)	25.9% (128)	26.6% (758)
HCGH	21.9% (4434)	19.6% (97)	18.2% (520)
JHEM	28.2% (5690)	31.6% (156)	33.9% (965)
SH	18.5% (3748)	16.4% (81)	13.3% (379)
SMH	10.2% (2056)	6.5% (32)	8.0% (228)

BMC, Bayview Medical Center; ED, emergency department; ESI, emergency severity index; HCGH, Howard County General Hospital; HR, heart rate; ICU, intensive care unit; JHEM, Johns Hopkins Hospital Emergency Medicine; IMC, intermediate care unit; IVDU, intravenous drug use; LOS, length of stay; MRSA, methicillin-resistant *Staphylococcus aureus*; NAT, Nucleic acid testing; RF, risk factors; RR, respiratory rate; SBP, systolic blood pressure; SH, Suburban Hospital; SMH, Sibley Memorial Hospital; Temp, temperature.

[a] A patient who met the criteria for infection with at least 1 Sequential Organ Failure Assessment criterion present, including (1) vasopressor initiation, (2) initiation of mechanical ventilation, (3) doubling in serum creatinine level, (4) decrease by 50% of estimated glomerular filtration rate relative to baseline, (5) bilirubin level >2.0 mg/dL and doubling from baseline, (6) platelet count less than 100 $\times$ 10^9/L and >50% decline from baseline (baseline had to be >100 $\times$ 10^9/L), or (7) lactate > 2.0 mmol/L.

cultures and any culture, respectively) at the patient level while accounting for random effects of patients presenting to different ED locations. A sensitivity analysis was conducted that coded MRSA risk factors as a continuous variable (model 2) and an ordinal variable (0 pt, 1 pt, and ≥ 2 pts; model 3). Models 2 and 3 were compared with model 1 using likelihood ratio tests. Odds ratios (ORs) and 95% CIs were reported.

All significance testing was done at an α level of 0.05. Data were analyzed using Stata version 17.0 software (StataCorp). Results reporting conforms to STROBE guidelines.

3 RESULTS

3.1 Characteristics of Study Subjects

A total of 20,212 unique adult ED visits for patients who received IV vancomycin were included in the primary analysis. Patient demographic characteristics and clinical characteristics are shown in Table 1. Included patients were predominately male (54% [95% CI, 53%-55%], n = 10,856) and White (60% [95% CI, 59%-61%], n = 12,165) with a median age of 62 years (IQR, 47-75). 63% (95% CI, 62%-64%; n = 12,755) had at least 1 MRSA risk factor, and 6.1% (95% CI, 5.8%-6.4%, n = 1,229) were considered high risk for IVDU history. Almost half of ED visits (46.2% [95% CI 45%-47%]) were triaged as high acuity (level 1 or 2), with 9% (95% CI, 8.3%-9.1%) admitted to intermediate care or intensive care units. Approximately 86% of patients (95% CI, 85%-87%, n = 17,437) had blood cultures drawn within 48 hours of the ED index visit, of which 33.6% (95% CI, 33%-34%) had positive blood cultures (ie, bacteremia) and 15.6% (95% CI, 15.1-16.1%, n = 3,160) of this cohort met Sepsis-3 criteria. In total, 93% of patients (95% CI, 92.4%-93.2%, n = 18,765) had blood, urine, or non-MRSA nucleic acid testing (NAT) respiratory cultures obtained in the ED or

within 48 hours of hospital admission, of which 53% (95% CI, 52.2%-53.6%, n = 10,696) were found to have a positive culture of any type.

Of patients who received vancomycin in the ED, 85% (95% CI, 84.4%-85.4%) had blood cultures obtained in the ED, 88% (95% CI, 87.3%-88.2%; n = 17,750) had either blood, urine, or non-MRSA NAT respiratory cultures obtained in the ED, and 19% (95% CI, 18.4%-19.6%) met Sepsis-3 criteria, with 91.3% (95% CI, 88%-94%; n = 451) found to have MRSA bacteremia.

3.2 Prevalence of MRSA Infection Among Patients Receiving IV Vancomycin

In total, 2.4% (95% CI, 2.2%-2.6%) and 14.1% (95% CI, 13.6%-14.6%) of patients receiving IV vancomycin in the ED had either MRSA bacteremia or any MRSA-positive culture (Table 1), respectively.

3.3 Vancomycin Over-/Under-Prescribing

In total, 3160 patients (15.6%, 95% CI, 15.1%-16.1%) met Sepsis-3 criteria in the ED and thus met 2016 SSC Guideline criteria for empiric administration of vancomycin. Only 34.7% (95% CI, 33%-36.4%, n = 1095) had ≥ 1 MRSA risk factor.

In one subgroup analysis of ED patients with MRSA bacteremia (n = 494, Table 1), 63.8% (95% CI, 59.3%-68%, n = 315) received IV vancomycin in the ED. In another subgroup analysis of ED patients with any MRSA-positive culture (n = 2850, Table 1), 43.4% (95% CI, 41.5%-45.2%, n = 1236) received IV vancomycin in the ED. A sensitivity analysis of any MRSA antibiotic given to patients with either MRSA bacteremia or any MRSA-positive culture found that an additional 2 (0.4%) and 10 (0.62%) patients received alternative MRSA antibiotics in the ED, respectively.

3.4 MRSA Risk Factors and MRSA Bacteremia

In the multilevel mixed-effects logistic regression model (Table 2), nonvital sign or laboratory predictor variables with the most significant increase in odds of MRSA bacteremia included a Charlson comorbidity index associated with < 20% 10-year survival (OR, 1.5, 95% CI, 1.2-2.0), lower acuity level (emergency severity index [ESI] level 3, OR, 2.3, 95% CI, 1.1-5.0), Sepsis-3 criteria (OR, 1.6, 95% CI, 1.3-2.1), high-risk history for IVDU (OR, 2.8, 95% CI, 2.1-3.6), vasopressor use within the first 48 hours (OR, 1.6, 95% CI, 1.1-2.2), MRSA alert in the EHR (OR, 2.3, 95% CI, 1.8-3.0), and an MRSA-positive culture within the last 90 days (OR, 2.7, 95% CI, 1.9-3.7). Patients had lower odds of having MRSA bacteremia if they were neither black nor white (OR, 0.7, 95% CI, 0.4-0.99). The presence of any MRSA risk factor was not associated with an increased likelihood of MRSA bacteremia (≥ 1 MRSA risk factor: OR, 1.2, 95% CI, 0.9-1.7). The sensitivity analyses showed no statistically significant difference between the regression models when MRSA risk factors were coded as either an ordinal variable (0 pt, 1 pt, and ≥ 2 pts) or a continuous variable. An additional sensitivity analysis was performed on 17,169 patients who received blood cultures in the ED. Of this group, 15,525 patients (88.9%, 95% CI, 88.3%-89.3%) received blood cultures before administration of IV antibiotics with a median time of 43 minutes (IQR, 14-96 minutes) between blood cultures and antibiotics. Additionally, 369 (74.7%, 95% CI, 70.6%-78.5%) of all MRSA-positive blood cultures were in this group. The proportion of patients who met Sepsis-3 criteria was 18.9% (95% CI, 18.4%-19.6%, n = 3160), with 9.7% (95% CI, 9.3%-10.1%, n = 1663) requiring vasopressor support and IMC/ICU level of care. A similar multilevel mixed-effects logistic regression model was performed, but no statistically significant difference in any variable was found in this subgroup analysis.

3.5 MRSA Risk Factors and MRSA-Positive Cultures (Any Type)

In the multilevel mixed-effects logistic regression model (Table 2), nonvital sign or laboratory predictor variables with the most significant increase in odds of MRSA-positive culture of any type included male sex (OR, 1.1, 95% CI, 1.0- 1.2), high-risk history for IVDU (OR, 1.3, 95% CI, 1.1-1.6), MRSA alert in the EHR (OR, 3.0, 95% CI, 2.6-3.3), an MRSA-positive culture within the last 90 days (OR, 2.4, 95% CI, 2.0-2.9), and an MRSA-positive NAT within the last 90 days (OR, 1.4, 95% CI, 1.1-1.8). Patients had lower odds of having MRSA bacteremia if they were ≥ 65 years of age (OR, 0.9, 95% CI, 0.8-0.97), non-Black race (see Table 2), ESI levels 1 to 2 (OR, 0.3, 95% CI, 0.3-0.4) and ESI level 3 (OR, 0.5, 95% CI, 0.4-0.6) compared with lowest acuity level (ESI levels, 4-5), and a positive blood cultures within the 14 days (OR, 0.6, 95% CI, 0.5-0.8). The presence of any MRSA risk factor was not associated with an increased likelihood of an MRSA-positive culture of any type (OR, 0.9, 95% CI, 0.8, 1.1). In the sensitivity analyses, there was no statistically significant difference between regression models when MRSA risk factors were coded as either an ordinal variable (0 pt, 1 pt, and ≥ 2 pts) or a continuous variable. In the multilevel mixed-effects logistic regression model, the random intercept for the ED site was statistically significant, and this model was used over the single-level model.

4 LIMITATIONS

This study has several limitations. First, this study did not examine the presenting chief complaint or admission diagnosis and its association with IV vancomycin prescribing. A preliminary chart review of a subset of patients revealed that the information entered for the chief complaint and admission diagnosis was unreliable for determining the clinical problems associated with the ED visit. Second, there was no systematic way in the EHR to capture the presence of active IVDU during the ED index visit to determine its role as a predictor

TABLE 2. Regression modeling

Multivariable regression of predictors of MRSA bacteremia or any MRSA+ culture				
	MRSA bacteremia[a]		Any MRSA + culture[b]	
Variable	**OR (95% CI)**	***P*-value**	**OR (95% CI)**	***P*-value**
Age (reference age: 18-64) y				
Over 65 y	0.9 (0.7, 1.1)	.3	0.9 (0.8, 0.97)	.01
Sex (reference: female)				
Male	1.2 (1.0, 1.4)	.1	1.1 (1.0, 1.2)	.0
Race (reference: Black)				
Other	0.7 (0.4, 0.99)	.05	0.8 (0.7, 0.9)	.0
White	1.1 (0.9, 1.4)	.2	0.9 (0.8, 1.0)	.01
Charlson comorbidity index (reference: 90% 10-y survival)				
50%-75% 10-y survival	1.2 (0.9, 1.5)	.2	1.1 (0.9, 1.2)	.4
< 20% 10-y survival	1.5 (1.2, 2.0)	.0	1.0 (0.9, 1.1)	.9
Null	0.7 (0.5, 0.99)	.04	1.4 (1.2, 1.5)	.0
Triage acuity (reference: ESI 4-5)				
Acuity level 3	2.3 (1.1-5.0)	.03	0.5 (0.4, 0.6)	.0
Acuity levels 1-2	1.9 (0.9, 4.1)	.1	0.4 (0.3, 0.4)	.0
MRSA risk factors (reference: no MRSA RF)				
>1 MRSA RF	1.2 (0.9, 1.7)	.3	0.9 (0.8, 1.1)	.3
SEP3 criteria present (reference: SEP3: No)				
SEP3: yes	1.6 (1.3, 2.1)	.0	1.0 (0.9, 1.2)	.9
IVDU Hx: Yes	2.8 (2.1-3.6)	.0	1.3 (1.1, 1.6)	.0
SBP (minimum) (reference: low SBP, <90 mm Hg)				
Normal SBP (≥90 mm Hg)	1.0 (0.8, 1.3)	.9	1.1 (1.0, 1.3)	.1
Null	1.5 (0.2, 3.5)	.8	1.3 (0.7, 2.5)	.7
Heart rate (maximum) (reference: normal HR, <100 bpm)				
High HR (≥100 bpm)	1.3 (1.02, 1.6)	.03	0.9 (0.8, 1.0)	.2
Null	0.8 (0.2, 4.39)	.8	0.12 (0.1, 0.3)	.0
Respiratory rate (maximum) (reference: normal RR, ≥20)				
High RR (>20)	1.3 (1.1, 1.7)	.0	1.1 (1.0, 1.2)	.2
Null	1.9 (0.9, 4.0)	.07	1.3 (0.9, 1.9)	.2
Temperature (maximum) (reference: normal Temp, <38 °C)				
High Temp (≥38 °C)	1.6 (1.3, 2.0)	.0	0.7 (0.6, 0.8)	.0
Null	1.1 (0.6, 2.2)	.6	0.8 (0.6, 1.1)	.2
Lactate (maximum) (reference: normal lactate level (<2 mmol/L)				
Hyperlactemia (≥2 but <4 mmol/L)	0.9 (0.7, 1.1)	.2	0.7 (0.6, 0.8)	.0
High lactate level (≥4mmol/L)	0.7 (0.5, 1.0)	.07	0.5 (0.4, 0.7)	.0
Null	0.98 (0.8, 1.2)	.7	1.5 (1.4, 1.7)	.0
WBC (maximum) (reference: normal WBC)				
High WBC (> 12 and < 20)	1.6 (1.3, 2.1)	.0	1.3 (1.2, 1.5)	.0
Very high WBC (≥ 20)	2.0 (1.6, 2.6)	.0	1.6 (1.4, 1.9)	.0
Null	1.4 (0.9, 2.2)	.1	1.7 (1.4, 2.0)	.0
Vasopressor use (reference: 0)				
1	1.6 (1.1, 2.2)	.0	1.1 (0.9, 1.4)	.2

(Continues)

TABLE 2. (Continued)

Multivariable regression of predictors of MRSA bacteremia or any MRSA+ culture				
	MRSA bacteremia[a]		Any MRSA + culture[b]	
Variable	**OR (95% CI)**	***P*-value**	**OR (95% CI)**	***P*-value**
MRSA flag at index visit (reference: MRSA flag absent)				
MRSA flag present	2.3 (1.8, 3.0)	.0	3.0 (2.6, 3.3)	.0
MRSA-positive culture within 90 d (reference: 0)				
1	2.7 (1.9, 3.7)	.0	2.4 (2.0, 2.9)	.0
MRSA-positive NAT within 90 d (reference: 0 d)				
1	1.2 (0.8, 1.9)	.3	1.4 (1.1, 1.8)	.0
Positive culture within 14 d (reference: 0 d)				
1	0.8 (0.5, 1.2)	.3	0.6 (0.5, 0.8)	.0
Visit within 30 d (reference: 0 d)				
1	0.8 (0.7, 1.1)	.2	0.9 (0.8, 1.0)	.08
Visit within 60 d (reference: 0 d)				
1	0.8 (0.6, 1.1)	.2	0.9 (0.8, 1.1)	.4

ED, emergency department; ESI, emergency severity index; HR, heart rate; Hx, history; ICU, intensive care unit; IMC, intermediate care unit; IVDU, intravenous drug use; LOS, length of stay; MRSA, methicillin-resistant *Staphylococcus aureus*; NAT, nucleic acid testing; OR, odds ratio; RF, risk factors; RR, respiratory rate; SBP, systolic blood pressure; SEP 3, Sepsis 3; Temp, temperature; WBC, white blood cell count.

[a] Results of the multilevel model with a random intercept at the hospital level were not statistically significant (chi-square 0.33, $P = .3$) compared with the single-level model; thus, results from the single-level model are shown.

[b] Results of the multilevel model with a random intercept at the hospital level were statistically significant (chi-square 82.11, $P = .000$) compared with the single-level model; thus, results from the multilevel model are shown, with the random effects intercept "Department' explaining 2% to 23% (95% CI) of the variance."

for MRSA infection. Third, we did not follow all patients longitudinally to assess morbidity and mortality from vancomycin administration or lack of administration. Fourth, given the paucity of blood cultures with MRSA, the model for MRSA bacteremia is likely overfit. Finally, this was a single-center study in the Baltimore-DC area, which may represent a population at higher risk for MRSA infection, given the high rates of IVDU use in this region.[36] Despite this limitation, the robustness of the data available in different ED settings within this single center is a strength of this study.

5 DISCUSSION

In this study of vancomycin prescribing in the ED, 20,212 unique patient encounters received IV vancomycin, with only 2.4% and 14.1% of encounters later found to have MRSA bacteremia or any MRSA-positive culture, respectively. These results are consistent with prior research that MRSA accounts for less than 5% of all culture-positive infections.[14–17] Previous ED-based studies have looked at the likelihood of therapeutic benefit from a single dose of IV vancomycin,[37] decision support tools for appropriate IV vancomycin dosing,[38,39] clinical appropriateness criteria of IV vancomycin prescribing based on clinical guidelines,[38,40,41] as well as estimating the prevalence of community-acquired MRSA skin and soft tissue and infections.[42]

Our study provides new data suggesting that up to 65% of patients with Sepsis-3 criteria (n = 2605) may not necessarily require IV vancomycin empirically. Administering vancomycin is not without potential harm, including its associations with increased mortality in certain undifferentiated patients,[18–20] and its association with acute kidney injury.[22,24] Furthermore, data are mixed on whether prolonged delays in vancomycin administration are associated with changes in mortality.[13] Given the results of our study, it is conceivable that the 2016 SSC guideline recommendations for empiric MRSA coverage likely and unintentionally contributed to some degree of routine patient harm as an unintentional consequence.[43–47]

Perhaps most importantly, our study highlights the challenge of identifying patients in the ED at risk for MRSA bacteremia or any clinically significant MRSA-positive culture. Only two-thirds and one-half of patients with MRSA bacteremia and any MRSA-positive culture, respectively, received IV vancomycin or any MRSA antibiotic while in the ED. For patients with culture-proven MRSA, MRSA risk factors were *not* associated with MRSA bacteremia; however, an MRSA alert in the EHR and an MRSA-positive culture within the last 90 days were associated with MRSA bacteremia. Sepsis-3 criteria were associated with MRSA bacteremia, though not any MRSA-positive culture. Data other than previous MRSA infections or alerts make predicting who might have culture-proven MRSA almost uninterpretable, ranging from elevated white blood cell counts (WBCs) to not having any laboratory ordered. Previous research suggests using the Shorr score for MRSA pneumonia,[48,49] though conflicting research finds the

Shorr score and other similar clinical decision rules to result in over-recommending vancomycin when it is not indicated in community-acquired pneumonia.[50]

The MRSA nasal swab polymerase chain reaction assay has been proposed to identify MRSA risk for patients with pneumonia, SSTI, and sepsis/septic shock.[51] A recent review on this topic shows that the MRSA swab has a high negative predictive value but a low positive predictive value.[51] Given the paucity of data, the authors suggest that MRSA swabs should not be used for presumed sepsis or septic shock. Our study adds to the literature by suggesting that MRSA swabs may help predict who has an MRSA infection, though waiting for these results may delay antibiotic administration. Nevertheless, the current literature on MRSA bacteremia suggests that delaying the administration of MRSA antimicrobials in patients without septic shock until diagnostic testing is completed is unlikely to change patient-oriented outcomes, such as mortality.

6 CONCLUSION

Within our hospital system, MRSA was an infrequent cause of bacteremia for patients presenting to the ED with sepsis or septic shock. Although vancomycin is frequently used in the ED, many patients with culture-proven MRSA did not receive MRSA antimicrobials. Notably, one-third of patients with culture-proven MRSA had no MRSA risk factor. MRSA risk factors were *not* predictive of culture-proven MRSA, thus highlighting the complexity of antimicrobial stewardship in the ED without validated clinical decision rules.

AUTHOR CONTRIBUTIONS

Contribution (JDN, JSH, RER, SEG, KD, EYK), data collection (EYK), data analysis (JDN), critical review and evaluation of the results (JDN, JSH, RER, SEG, KD, EYK), review and editing of the paper (JDN, JSH, SEG, KD, EYK), and procurement of grant or other funding (EYK).

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CONFLICT OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

ORCID

Joshua D. Niforatos MD, MTS https://orcid.org/0000-0003-4702-7465

Joshua D. Niforatos MD, MTS 𝕏 https://twitter.com/reverendofdoubt

Jeremiah S. Hinson MD, PhD 𝕏 https://twitter.com/Hinson_EM

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SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.acepjo.2024.100021

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