Optimizing Treatment of Hand Infections: Is MRSA Coverage Always Necessary?

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Background: Multiple publications have highlighted the prevalence of methicillin resistant *Staphylococcus aureus* (MRSA) as a cause of hand infections. We hypothesized that these publications have shifted the empiric treatment of hand infections. The aim of this study was to identify the current standard of care, the most common causative bacteria, and factors leading to extended length of stay for hand infection patients at a suburban hospital to improve treatment and establish an optimized care protocol.

Methods: Retrospective cohort analysis was conducted to identify all patients admitted for hand infections over an 8-year period. A comprehensive chart review of each patient's hospital course was completed.

Results: A total of 70 patients were included. Maximum white blood cell count ≥ 12 was associated with a significantly longer hospital length of stay (9.1 days versus 5.4 days) compared to WBC values < 12 ($P < 0.05$). Also, 11 out of 23 (47.8%) underwent two or more incision and drainages (I&D's), compared with patients with maximum WBC < 12. Vancomycin use as an empiric antibiotic was widespread (68 patients, 97.1%), despite only 14 (20%) having MRSA positive cultures. Univariate analysis identified a significant increased likelihood for increased length of stay ($P < 0.05$) and rise in creatinine ($P < 0.05$) in patients with an initial vancomycin trough level > 20.

Conclusions: This analysis of hand infection treatment in a suburban hospital demonstrates the incidence of MRSA hand infections may not be universally high across institutions. Each hospital should review its own data to optimize hand infection treatment and its associated costs. (*Plast Reconstr Surg Glob Open 2021;9:e3619; doi: 10.1097/GOX.0000000000003619; Published online 15 June 2021.*)

INTRODUCTION

Hand surgeons commonly encounter patients with hand infections. Optimal outcomes rely on the accuracy of initial diagnosis and treatment strategy.[1] However, upon initial presentation, the responsible organism is often unknown due to unavailable culture data, which requires empiric antibiotic selection upon initial presentation.[2,3] Treatment protocols for hand infections often include broad-spectrum antibiotic therapy (eg, vancomycin and piperacillin-tazobactam or ampicillin-sulbactam), attempting to cover for all potential gram-positive and gram-negative infecting organisms. Recent literature demonstrating a rising incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) as the cause of hand infections requiring surgical intervention has led providers to use vancomycin therapy as the first line treatment.[2–4] While effective against MRSA, vancomycin is dosed based on renal function and takes multiple doses to reach target concentration, requiring close monitoring over several days. Given these limitations, we hypothesize that vancomycin treatment in hand infections is associated with delays in achieving therapeutic levels with concomitant increased morbidity due to these delays.

The aim of this study was to analyze the course of treatment for all patients who presented to our institution with a primary diagnosis of a hand infection. This evaluation included an analysis of antibiotic selection and its effect on patient outcomes. Specifically, we aimed to evaluate whether the increasing incidence of MRSA hand infections is leading to an increased unindicated use of vancomycin. Through this study, we attempt to lay the groundwork to support larger trials to test different interventions to best optimize the current state of hand infection care and its

Disclosure: *All the authors have no financial interest to declare in relation to content of this article.*

associated costs. Findings from this study will help guide clinical decision-making for all plastic surgeons who treat patients suffering from hand infections in the development of pharmacologic and surgical protocols to decrease the current systemic burden of antibiotic resistance and misuse.

MATERIALS AND METHODS

This was a retrospective cohort analysis using the Stanford Translational Research Integrated Database Environment to identify all patients admitted to Stanford Hospital & Clinics for a hand infection from May 1, 2008–April 30, 2016. After obtaining institutional review board approval, subjects aged ≥ 18 years who were admitted to Stanford Hospital & Clinics for a primary diagnosis of hand infection were included by screening all admissions associated with one of the ICD-9 codes listed in Appendix 1. (**See Appendix, Supplemental Digital Content 1**, which shows ICD-9 codes utilized for screening patients for inclusion in this study. http://links.lww.com/PRSGO/B687.) All admissions to medicine or surgery services were included. Exclusion criteria consisted of the following: patient aged < 18 years, primary infection site at or proximal to the elbow, postoperative infections, septic arthritis, and hospital acquired hand infections.

Patient demographic data collected included sex, age, body mass index, medical comorbidities, current smoking status, and current intravenous (IV) drug use. An analysis of patient care characteristics included laboratory tests (creatinine, white blood cell count (WBC), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR)), MRSA nares swab results, wound cultures, organism strain and number of organisms isolated, vancomycin trough level, and antibiotic usage. The reference range at our institution for normal WBC is 4–11 (×1000 cells/mL). We chose 12 as the reference value for elevated WBC, to allow for one point of deviation from the upper limit of normal. Laboratory tests were performed upon admission and typically were performed daily until they began to trend downward. The primary outcomes of interest were hospital length of stay (LOS) and number of bedside or operative incision and drainage (I&D) procedures for each patient. The secondary outcome of interest was change in serum creatinine level. Acute kidney injury (AKI) was defined as an increase in serum creatinine by 0.3 mg/dl compared with the admission laboratories.[5]

Data analysis was conducted by utilizing analysis of variance, chi-square, and two-tailed Student t-tests as appropriate at $P < 0.05$. Dichotomous variables identified were diabetes mellitus (DM), end-stage renal disease (ESRD), immunocompromised status, smoking status, IV drug use status, and laboratory values (if a threshold was used). Nondichotomous categorical variables included MRSA nares swab status, number of organisms cultured, isolated organisms, and number of antibiotics administered. Finally, multivariate linear regression was conducted for the primary outcome measure of hospital LOS. A post hoc power analysis was used to assess power for nonsignificant variables.

RESULTS

A total of 70 patients were included: 23 (32.9%) women and 47 (67.1%) men. The mean age was 52.0 years (SD 18.4). Comorbidity data and patient characteristics are listed in Table 1. Clinical care characteristics can be found in Table 2. Of the 70 patients, 13 (18%) received MRSA nares swabs at admission; two of the three positive MRSA nares swabs were associated with a positive MRSA wound culture, and two of the 10 negative MRSA nares swabs were associated with a positive MRSA wound culture. Overall, 68 of the 70 patients (97%) were treated with at least one dose of vancomycin for empiric treatment of a MRSA infection, but only 14 of the 70 patients (20%) were culture positive for MRSA. Of the 68 patients receiving vancomycin, this antibiotic was discontinued within 24 h in 16 of the 68 patients receiving vancomycin (24%). Vancomycin and piperacillin/tazobactam, the two most commonly prescribed antibiotics, were administered at a mean of 13.2 and 10.1 hours, respectively, from the time of initial intake in the emergency department. They were continued for a mean duration of 66.5 and 60.6 hours, respectively.

Medical comorbidities and clinical data were analyzed to determine correlations with clinical outcomes (Table 3). DM status was not associated with the number of I&Ds in this cohort. Diabetes was associated with a substantial increase in hospital LOS, yet not statistically significantly in univariate analysis ($P = 0.07$), from a mean of 5.5 days (no DM) to 10.1 days (+ DM). However, on multivariate linear regression analysis, DM was significantly associated with increased LOS ($P < 0.05$). Neither ESRD, an immunocompromised state, nor IV drug use significantly increased number of I&Ds or LOS. However, none of these parameters were sufficiently powered based on post hoc power analysis to reveal a difference if one was present. Data revealed that active smoking was associated with an increased length of stay from a mean of 4.8 days (nonsmokers) to 7.9 days (smokers) ($P < 0.05$).

Of the laboratory values analyzed, a WBC ≥ 12 (×1000 cells/mL) during the hospital stay was found to be associated with a significantly increased number of I&Ds and increased hospital LOS. AKI, as defined by an increased creatinine of 0.3 mg/dL, was present in 14 of the 65 patients (22%) in whom creatinine was measured and was associated with a significantly increased LOS from a mean of 5.4–12.9 days ($P < 0.05$). There

Table 1. Patient Characteristics

Gender	
Women	23 (32.9)*
Men	47 (67.1)*
Age (y)	52.0 (18.4)†
Body mass index (kg/m²)	25.7 (5.8)†
Comorbidities	
DM	17 (24.3)*
ESRD	3 (4.3)*
Immunocompromised	13 (18.6)*
Smoker	37 (52.9)*
IVDU	10 (14.3)*

*Values are number of patients (%).
†Values are mean (SD).
IVDU, intravenous drug use.

Table 2. Care Characteristics

Admission laboratories	
Creatinine (mg/dL)	1.3 (1.3)
WBC (×1000 cells/mL)	10.5 (5.3)
CRP (mg/L)	8.8 (10.4)
ESR (mm/h)	47.9 (40.3)
MRSA nares swab [no. patients (%)]	
Positive	3 (4.3)
Negative	10 (14.3)
Not performed	57 (81.4)
Wound cultures taken [no. patients (%)]	61 (87.1)
No. organisms isolated (%)	
0	7 (10)
1	45 (64.3)
2	6 (8.6)
3+	12 (17.1)
No. patients with listed organism isolated (%)	
MRSA	14 (20)
MSSA	17 (24.3)
Group A Strep	7 (10)
Coag negative Staph	7 (10)
Strep dysgalactiae	3 (4.3)
Strep intermedius	2 (2.9)
Other	19 (27.1)
Vancomycin trough	
No. patients drawn on (%)	40 (57.1)
Initial vancomycin trough (SD)	12.5 (7.8)
No. antibiotics received during admission (%)	
0	0
1	1 (1.4)
2	20 (28.6)
3	24 (34.3)
4	15 (21.4)
5	6 (8.6)
6	3 (4.9)
7	1 (1.4)
8	0
No. patients receiving listed antibiotic (%)	
Vancomycin	68 (97.1)
Zosyn	46 (65.7)
Unasyn	11 (15.7)
Clindamycin	17 (24.3)
Cefazolin	11 (15.7)
Nafcillin	8 (11.4)
Meropenem	4 (5.7)
Metronidazole	2 (2.9)
Bactrim	11 (15.7)
Ciprofloxacin	8 (11.4)
Levofloxacin	3 (4.3)
Moxifloxacin	2 (2.9)
Daptomycin	2 (2.9)
Ceftriaxone	9 (12.9)
Doxycycline	3 (4.3)
Augmentin	7 (10.0)
Linezolid	5 (7.1)
Cephalexin	4 (5.7)
Penicillin G	4 (5.7)
Penicillin VK	1 (1.4)
Azithromycin	1 (1.4)
Cefepime	1 (1.4)
Flexor tenosynovitis (%)	7 (10)
Length of stay, d (SD)	6.6 (6.1)
I&D	
No. patients with bedside I&D (%)	17 (24.3)
Average number of bedside I&D per patient (SD)	0.3 (0.5)
No. patients with OR I&D (%)	54 (77.1)
Average number of OR I&D per patient (SD)	1.0 (1.0)
No. patients with any I&D, bedside or OR (%)	61 (87.1)
Average number of any I&D per patient, bedside or OR (SD)	1.3 (1.0)

Table 3. Number of Incision and Drainage (I&D) Procedures Performed and Length of Stay

	Number I&D's	P	Length of Stay (d)	P
Diabetes				
Yes	1.7 (1.6)	0.17	10.1 (9.6)	0.07
No	1.2 (0.7)		5.5 (4.0)	
ESRD				
Yes	3.0 (3.6)	0.48	14.0 (15.1)	0.47
No	1.2 (0.7)		6.3 (5.4)	
Immunocompromised				
Yes	0.9 (0.8)	0.09	7.8 (6.1)	0.44
No	6.4 (6.1)		6.4 (6.1)	
Smoker				
Yes	1.2 (0.5)	0.43	4.8 (5.8)	**0.05**
No	1.4 (1.2)		7.9 (6.3)	
IVDU				
Yes	1.3 (0.5)	0.94	6.5 (8.4)	0.95
No	1.3 (1.1)		6.7 (5.7)	
Admit WBC				
≥12	1.8 (1.5)	**0.04**	8.9 (8.0)	0.12
<12	5.8 (5.0)		5.8 (5.0)	
Max WBC				
≥12	1.7 (1.4)	**0.03**	9.1 (7.6)	**0.04**
<12	1.1 (1.7)		5.4 (4.8)	
Creatinine increase ≥ 0.3				
Yes	1.6 (1.8)	0.37	12.9 (9.1)	**0.01**
No	1.2 (0.7)		5.4 (3.9)	
Admit CRP				
≥3	1.4 (1.3)	0.31	7.8 (7.5)	0.21
<3	1.2 (0.7)		5.8 (4.8)	
Admit ESR				
≥30	1.4 (1.3)	0.55	8.1 (7.4)	0.12
<30	1.2 (0.7)		5.6 (4.8)	
No. organisms cultured				
0	1.1 (0.7)	0.10	6.3 (5.0)	0.76
1	1.3 (0.7)		7.1 (6.1)	
2+	2.0 (1.8)		8.8 (8.6)	
Organism cultured				
No growth	1.1 (0.7)	0.16	6.3 (5.0)	0.61
MRSA	1.9 (1.6)		8.8 (7.6)	
MSSA	1.4 (0.7)		7.3 (7.7)	
Group A Strep	2.3 (2.2)		11.3 (9.5)	
Coag negative Staph	1.1 (0.7)		6.4 (3.8)	
Other	1.2 (0.7)		6.5 (5.1)	
Flexor tenosynovitis				
Yes	1.3 (1.0)	0.31	6.9 (6.3)	0.06
No	1.3 (0.5)		4.4 (2.5)	
Initial vancomycin trough (µg/mL)				
<10	1.1 (0.7)	0.35	6.5 (4.6)	**0.005**
10–15	1.3 (0.7)		6.2 (5.4)	
15–20	0.9 (0.6)		7.0 (4.5)	
>20	2.4 (2.7)	0.12	16.6 (9.0)	
Vancomycin use >24 h				
Yes	1.3 (1.0)	0.34	7.5 (6.5)	0.01
No	1.1 (0.8)		4.2 (3.8)	

Values are mean (SD). Analysis of variance performed for situations with multiple categories.
Bold numbers indicate significant differences at $p \leq 0.05$.

were no differences between patients based on CRP or ESR, culture results, or presence of flexor tenosynovitis, none of which were sufficiently powered based on post-hoc power analysis to reveal a difference if one was present. Elevated vancomycin troughs and vancomycin use for more than 24 hours were both associated with an increased LOS. Use of piperacillin-tazobactam or ampicillin-sulbactam alone or in combination with vancomycin did not influence LOS or number of I&D procedures.

There was a statistically significant rise in creatinine with increased vancomycin trough levels (Table 4). Of the 43 patients receiving vancomycin for >36 hours, 34 patients (79%) had a vancomycin trough measured.

Multivariate linear regression for LOS (Table 5) controlling for all comorbidities confirmed a significant correlation between increased LOS and increased serum

creatinine level > 0.3 mg/dL ($P < 0.05$) as well as a diagnosis of DM ($P < 0.05$). Furthermore, multivariate linear regression was performed for likelihood of an I&D (Table 6), which revealed a significant association after controlling for all comorbidity data between need for I&D and maximum WBC > 12 ($P < 0.05$). No other variable analyzed for multivariate regression revealed significant associations with LOS or I&D.

DISCUSSION

Effective management of acute hand infections necessitates timely diagnosis and a directed treatment regimen to avoid complications and to preserve hand function.[6] Due to the heterogenous nature of these infections, including the presence of MRSA depending on the hospital and patient population, broad spectrum empiric antibiotics often are chosen for initial treatment of hand infections.[7] In this study, we aimed to evaluate whether the increasing incidence of MRSA hand infections is leading to an increased *unindicated* use of vancomycin. As shown above, the empiric use of vancomycin by emergency department, medicine, and hand surgery physicians for MRSA coverage may be unnecessary for all patients and may have negative effects on population health and patient safety.

Prior studies have shown that community-acquired MRSA has continued to increase in incidence over the past several decades, both in the United States and worldwide.[8] Outbreaks in the community have been associated with a number of at-risk populations, including prison inmates, IV drug abusers, athletes participating in contact sports, and patients in long-term care facilities.[9–13] Specifically in hand infections, the incidence of community-acquired MRSA isolates has been reported to be as high as 40%–73% percent in urban populations in the United States.[8,14,15] These community-acquired strains have been shown to be more responsive to antibiotics such as clindamycin, sulfamethoxazole/trimethoprim, and linezolid compared with the nosocomial MRSA strains.[16]

To achieve therapeutic levels of vancomycin while decreasing the risk of vancomycin-induced nephrotoxicity from supratherapeutic levels of vancomycin, trough concentrations of vancomycin often are monitored.[17] Pharmacist-managed dosing of vancomycin has been associated with improved outcomes, including reduced renal impairment.[18] However, these pharmacist-managed programs tend to be resource-intensive, which may pose a challenge to many institutions.[19] Given the limitations of

Table 4. Increase in Creatinine

	Increase in Creatinine (mg/dL)	P
Initial vancomycin trough (μg/mL)		
<10	0.2 (0.4)	**0.007**
10–15	0.4 (1.1)	
15-20	0.3 (0.5)	
>20	1.5 (0.8)	

Values are mean (SD). Analysis of variance performed for situations with multiple categories.
Bold numbers indicate significant differences at $p \le 0.05$.

Table 5. Multivariate Linear Regression Analysis for Length of Stay

	t Stat	Lower 95%	Upper 95%	P
DM	2.15	0.24	6.51	**0.04**
ESRD	0.46	−5.29	8.40	0.65
Immunocompromised	0.83	−1.95	4.70	0.41
Smoker	−1.94	−5.36	0.09	0.06
IVDU	0.48	−3.02	4.94	0.63
Polymicrobial—yes/no	0.93	−2.03	5.57	0.36
FTS	−0.71	−5.69	2.73	0.48
On vanc > 24 h	1.22	−1.27	5.24	0.23
Elevated vanc Trough (>20)	−0.14	−5.56	4.82	0.89
Max WBC > 12	0.62	−1.98	3.74	0.54
Cr increase > 0.3	3.22	2.42	10.36	**0.002**

Bold numbers indicate significant differences at $p \le 0.05$.

Table 6. Multivariate Linear Regression Analysis for Incision and Drainage

	t Stat	Lower 95%	Upper 95%	P
DM	1.06	−0.27	0.88	0.29
ESRD	1.72	−0.18	2.32	0.09
Immunocompromised	−1.22	−0.98	0.24	0.23
Smoker	−0.53	−0.63	0.36	0.60
IVDU	0.21	−0.65	0.80	0.84
Polymicrobial—yes/no	1.61	−0.13	1.25	0.11
FTS	−0.18	−0.84	0.70	0.85
On vanc > 24 h	0.03	−0.59	0.60	0.98
Elevated vanc Trough (>20)	0.01	−0.94	0.95	0.99
Max WBC > 12	2.05	0.01	1.06	**0.05**
Cr increase > 0.3	0.02	−0.72	0.73	0.98

Bold numbers indicate significant differences at $p \le 0.05$.

vancomycin treatment, there may be a role for the use of other antibiotics active against MRSA in the treatment of hand infections.

In this study, vancomycin use was widespread with 97.1% of patients receiving it for empiric treatment of a MRSA infection. However, in our patient population, only 20% of hand infections grew MRSA in culture. This suggests that more judicious use of vancomycin may need to be considered for multiple reasons. At a population level, vancomycin-intermediate *Staphylococcus aureus* (VISA) and vancomycin-resistant *Staphylococcus aureus* (VRSA) infections have become increasingly prevalent.[20] One strategy to slow the spread VISA and VRSA is improved antibiotic stewardship among prescribers. However, even at the patient level, we found that vancomycin use > 24 hours and elevated vancomycin trough levels were associated with increased length of stay and acute kidney injury. These findings from our study and a need for improved antibiotic stewardship to slow the spread of VISA/VRSA suggest that there may be a role for more judicious use of vancomycin for empiric treatment of hand infections.

In 1988, Spiegel and Szabo[21] presented a treatment protocol for severe hand infections which they implemented in the treatment of 69 patients. This consisted of immediate I&D in the operating room, culture of the infected area, and IV antibiotic therapy with sensitivity against anaerobic and aerobic organisms according to culture results. By implementing these accelerated measures of care, the authors noted a decreased length of hospital stay, expedited healing, and lower risk of developing complications following operative management.

Our analysis identified four statistically significant predictive factors for increased LOS: maximum WBC > 12 (×1000 cells/mL), active smoking status, initial vancomycin trough level >20 μg/mL, and vancomycin use > 24 hours. As patients with initial vancomycin trough levels > 20 μg/mL were noted to have a mean increase in creatinine of 1.5 mg/dL, the increased length of stay in these patients may be due to additional treatment required for management of acute kidney injury; however, this study was not designed to address this specific question. Moreover, on multivariate linear regression analysis, we identified that elevated vancomycin trough level, while significantly associated with increased LOS on univariate analysis, did not maintain its significant correlation. We suspect this is due to the fact that elevated vancomycin trough levels and Cr increase > 0.3 mg/dL were associated with one another (see Table 4), and Cr increase > 0.3 mg/dL was significantly associated with increased LOS. Thus, we advocate for more judicious utilization of vancomycin in such instances. When these complications associated with vancomycin use are evaluated in the context of the relatively low incidence of MRSA in our patient population (20%), we propose an algorithm for reference when prescribing empiric vancomycin treatment (see algorithm in Fig. 1). We believe other hospitals that closely examine their MRSA rate may find similarly high rates of unnecessary use of vancomycin.

The potential effect of underlying medical comorbidities or risk factors (ie, DM, long-term steroid treatment, IV drug abusers, and acquired immunodeficiency syndromes) on the efficacy of infection management should not be underestimated and is critical when considering empiric antibiotic therapy. Specifically, in the hand infection literature, DM has been identified as a predictor for more severe morbidity, leading to amputation rates of 63%–100% in the presence of impending renal failure or transplant.[22] In one study, 39 patients with known DM who presented with purulent hand infections were identified to have polymicrobial (52%) infections with 51% Gram-negative organisms. This led to an amputation rate of 18% in the study cohort, with significant factors contributing to the worse prognosis in patients with DM being evidence of poor glycemic control, delayed presentation, and prior intervention for hand infection.[23] In our study, patients with DM were found to have a slightly increased likelihood to need more than one I&D and an increased LOS on multivariate linear regression.

This study has several limitations. First, the patient data set, derived from a single academic institution, may lack generalizability. However, our patient demographics and study design are similar to those seen in other studies,[14,15] and the size of our analyzed cohort is similar to or larger than some prior published studies.[21,22] Furthermore, the number of patients and patient variability limits meaningful subgroup analyses. Although this study entailed a rigorous chart review of patient data, there is the risk in retrospective review of inaccurate assessments of patient course due to coding errors and missing data. Finally, post-hoc power analysis revealed we were underpowered to detect differences in ESRD,
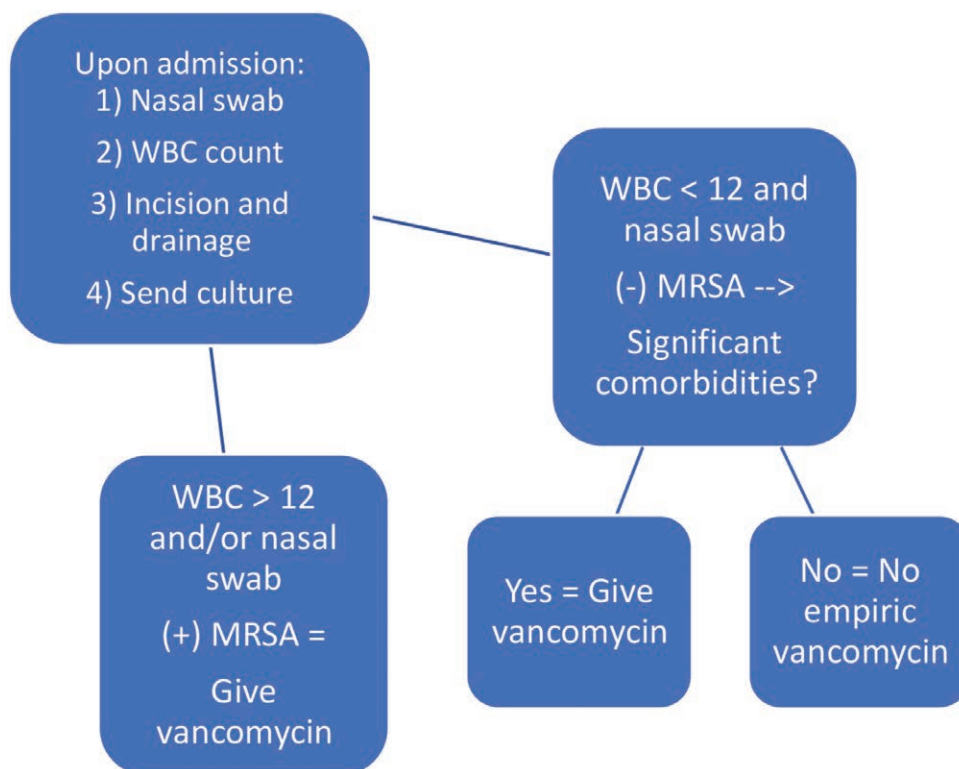

Fig. 1. Algorithm for vancomycin administration in suspected hand infection. WBC, white blood cell count; MRSA, methicillin resistant *Staphylococcus aureus*.

immunocompromised status, IV drug use, and presence of flexor tenosynovitis, due to low patient numbers. These parameters should be targeted in future studies to accurately identify potential risk factors in these patient populations.

CONCLUSIONS

This analysis of hand infection treatment at a suburban hospital serves as a framework for further studies to optimize the current state of hand infection treatment at institutions seeing varied patient populations. In this cohort, almost 98% of patients who presented to our institution with a hand infection received vancomycin; however, only 20% of these patients had a culture confirmed MRSA infection. On univariate analysis, we identified an association between vancomycin use and increased hospital LOS and AKI. Multivariate regression revealed significant associations between maximum WBC > 12 and increased I&D likelihood, as well as increased serum creatinine level > 0.3 mg/dL and DM with increased hospital LOS. Given these findings, we conclude that despite multiple publications documenting increased MRSA prevalence in hand infections, this is not true in all populations and widespread vancomycin use in hand infection patients may be unindicated and lead to negative sequelae impacting patient outcomes.

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ACKNOWLEDGMENTS

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