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Comparison of Microbial Respiratory Cultures versus MRSA Nasal Screen to Guide Vancomycin De-escalation in Patients Hospitalized for Bacterial Pneumonia

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ABSTRACT

Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) nasal screen identifies the presence of MRSA nasal colonization, which can be used as a valuable antimicrobial stewardship tool to de-escalate empiric vancomycin therapy in patients with pneumonia. Current practices at a Florida hospital include using respiratory culture and MRSA nasal screening results to assist in treating MRSA pneumonia infections. This study aimed to evaluate the total duration of vancomycin therapy in patients with suspected MRSA respiratory tract infections.

Methods: This was a single-center, retrospective chart review conducted at a tertiary medical center. Adult patients were assigned to either the respiratory culture-directed group or the MRSA nasal screening-directed group. The primary outcome was the duration of vancomycin therapy, in hours, in patients who were started on vancomycin for suspected pneumonia. Secondary outcomes included new onset acute kidney injury, length of stay, 30-day in-hospital mortality, number of vancomycin levels obtained, cost-avoidance analysis, and duration of mupirocin therapy before MRSA nasal screening.

Results: Thirty-four patients were evaluated in the culture-directed group and 56 in the MRSA nasal screen-directed group (N = 90). The MRSA nasal screen-directed cohort had a statistically significant reduction in the duration of vancomycin therapy compared to the culture-directed group (24 vs. 94 hours; $p < .00001$).

Discussion: The empiric vancomycin therapy duration was significantly lower in the MRSA nasal screen cohort compared to the respiratory culture cohort. Hospitals could have a beneficial, cost-saving impact by utilizing MRSA nasal screening for patients with a lower respiratory tract infection.

***Keywords*:** Vancomycin, de-escalation, MRSA, pneumonia

BACKGROUND

Methicillin-resistant *Staphylococcus aureus* (MRSA) is recognized as a common pathogen in pulmonary infections (Kalil et al., 2016). Current Infectious Disease Society of America community-acquired bacterial pneumonia guidelines recommend empiric anti-MRSA antibiotics in select patients at a higher risk for a MRSA pneumonia infection (*i.e.,* prior intravenous antibiotic use within 90 days or recent hospitalization) (Metlay et al., 2019). When empiric anti-MRSA antibiotics (*e.g.,* vancomycin) are initiated,

assessing for clinically appropriate de-escalation opportunities is essential.

Methicillin-resistant *Staphylococcus aureus* nasal screening can be used as a valuable antimicrobial stewardship tool to assist in determining the clinical appropriateness for empiric anti-MRSA antimicrobial de-escalation in patients with pneumonia. Clinical studies have shown that MRSA nasal screening rapidly identifies the presence of MRSA nasal colonization, with a high negative predictive value (NPV) of approximately 97%. This data reinforces the clinical utility supporting MRSA nares results in patients with a suspected MRSA pneumonia infection. A negative MRSA nasal screen can dictate when to de-escalate empiric therapy if appropriate (Carr et al., 2018; Shenoy et al., 2014; Baby et al., 2017).

Current practices at this study hospital for managing suspected bacterial pneumonia include utilizing microbial culture and MRSA nasal screening results to assist in treating MRSA pneumonia infections. Practitioners are encouraged to utilize MRSA nasal screening when a MRSA pulmonary infection is suspected; however, the decision to utilize microbial cultures, MRSA screening, or both is left up to each practitioner. When comparing the two microbial identification methods, according to Infectious Disease Society of America guidelines, the rate of obtaining a good quality pneumococci respiratory culture result is 86% (Metlay et al., 2019). Regarding utilizing a respiratory culture, some factors that could delay the clinical utility of respiratory culture results may include inadequate sample collection and requiring multiple days until culture identification and speciation. In comparison, MRSA nasal screening results could help guide the decision to de-escalate empiric vancomycin therapy within approximately 2 hours of the MRSA nasal screen if empiric gram-positive coverage is no longer indicated. Due to these reasons, this study evaluated the clinical utility of using MRSA nasal screening for appropriate anti-MRSA antimicrobial de-escalation compared to culture-directed results in patients being treated for pneumonia. The purpose of this study was to evaluate the total duration of vancomycin therapy in patients with suspected MRSA respiratory tract infections.

METHODS

Study Design

This was a single-center retrospective chart review conducted at a tertiary medical center from June 30, 2022, to February 20, 2023. All adult patients who received vancomycin for pneumonia in the selected timeframe were screened from the hospital's paper antimicrobial records and appropriately allocated into each cohort by the primary investigator. The culture-directed cohort consisted of adult patients placed on vancomycin empiric therapy for suspected pneumonia from whom a respiratory culture was collected. The MRSA nasal screening cohort consisted of adult patients placed on vancomycin empiric therapy for suspected pneumonia from whom a MRSA nasal screen was collected. Patients who were found to have both a respiratory culture and MRSA nasal screen collected were included in the MRSA nasal screen group, and the concordance between results was utilized for internal purposes. Exclusion criteria for the study included pregnancy, incarceration, structural lung disease (cystic fibrosis, bronchiectasis, or chronic tracheostomy), infection outside the indication of pneumonia, mortality within 72 hours of vancomycin initiation, receipt of anti-MRSA antibiotics more than 48 hours before MRSA nasal screen collection, and evidence of MRSA growth in MRSA nasal screen or respiratory culture within seven days.

Study Outcomes

The primary outcome was to assess the duration (in hours) of vancomycin therapy in patients who were started on empiric therapy for suspected pneumonia. Duration, or time to de-escalation, was determined by the difference in van-

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comycin administration start time and order discontinuation by a physician. Secondary outcomes included the incidence of new-onset acute kidney injury (AKI) defined using the Kidney Disease Improving Global Outcomes criteria (Stevens & Levin, 2013), total length of stay, 30-day in-hospital mortality, and the total number of vancomycin levels obtained.

Data Analysis

Twenty subjects per cohort were needed to achieve 80% power to detect a mean difference of 1.5 days. Baseline and continuous variables were analyzed using the Kruskal-Wallis test, and categorical baseline variables were compared using Fisher's Exact test. The primary outcome of duration of empiric vancomycin therapy, time, was compared between cohorts using the Kruskal-Wallis test. The secondary outcomes of the number of vancomycin levels and length of stay were compared using the Kruskal-Wallis test. The secondary outcomes of new-onset AKI and 30-day in-hospital mortality were compared using Fisher's Exact test. A priori analysis determined *that* $p < .05$ was considered statistically significant. We used SAS software, version 9.4 (SAS Institute Inc), for all the analyses.

RESULTS

Two hundred twelve patients on empiric vancomycin therapy for suspected community-acquired bacterial pneumonia were screened. Of these, 34 patients were included in the culture-directed cohort, and 56 were included in the MRSA nasal screening-directed cohort (Figure 1). Baseline demographics between cohorts were not significantly different except for ICU-admission and dialysis-dependent patients (Table 1). The primary outcome, median duration of vancomycin therapy, was 93.5 hours in the culture-directed cohort and 23.9 hours in the MRSA nasal screening-directed cohort ($p < .00001$) (Figure 2).

Secondary outcomes were assessed (Table 2). The median number of vancomycin levels obtained per cohort was 2.5 and 0 in the culture-directed cohort and MRSA nasal screening-directed cohort, respectively ($p < .00001$). Length of stay had a median of 12 days versus 6 days ($p < .00001$). No significant differences

Figure 1

Patient Screening

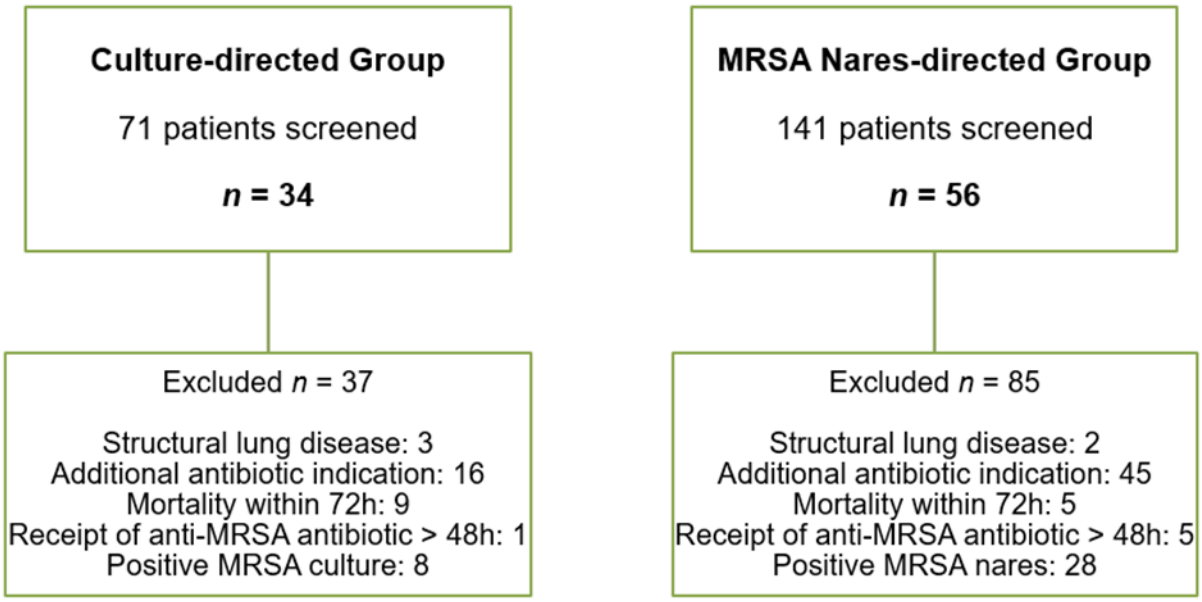


Table 1

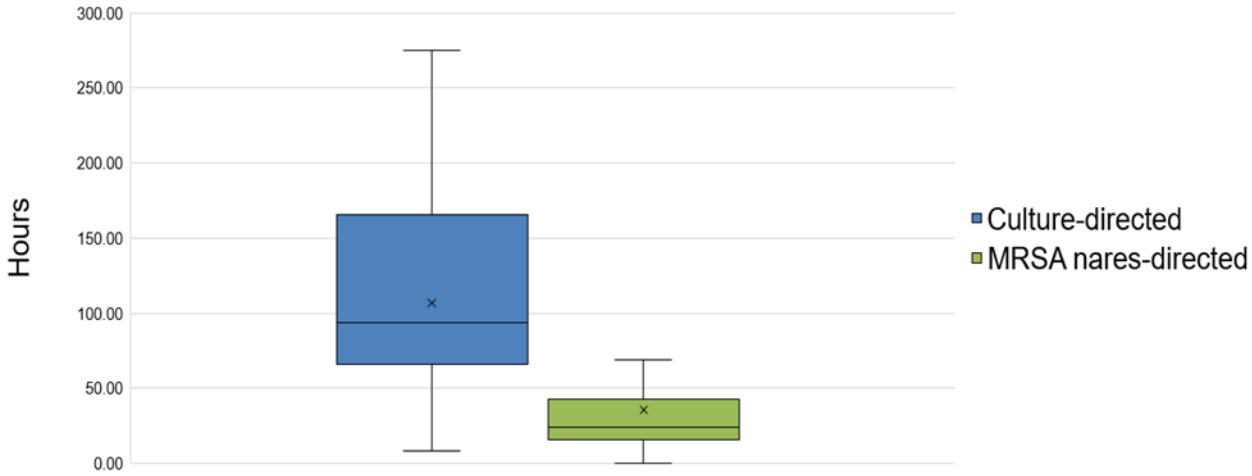
Baseline Characteristics

Characteristic	Culture-directed Cohort (*n* = 34)	MRSA nasal screening-directed Cohort (*n* = 56)	*p* value
Age (years), median (IQR)	78.5 (68-85)	80.0 (67.8-91)	.519
Sex, male, *n* (%)	21.0 (61.8)	31.0 (55.4)	.706
Weight (kg), median (IQR)	73.1 (63.8-82)	70.8 (57.9-80)	.216
BMI (kg/m^2), median (IQR)	26.5 (22-29)	25.0 (21.8-28)	.255
Baseline SCr (mg/dL), median (IQR)	0.9 (0.6-1.1)	0.8 (0.6-1)	.115
ESRD on dialysis, *n* (%)	5.0 (14.7)	0 (0)	.006
ICU admission	12.0 (35.3)	5.0 (8.9)	.004

Note. SCr: serum creatinine; BMI: body mass index; ESRD: end stage renal disease; ICU: intensive care unit

Figure 2

Median Duration of Vancomycin Therapy



Note. $p < .00001$

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Table 2

Secondary Outcomes

Characteristic	Culture-directed Cohort (*n* = 34)	MRSA nasal screening-directed Cohort (*n* = 56)	*p* value
Number of vancomycin levels, median (IQR)	2.5 (0-3)	0 (0-1)	< .00001
New onset AKI, *n* (%)	5.0 (14.7)	2.0 (3.6)	.099
Length of stay, days, median (IQR)	12 (7-20)	6 (4-8)	< .00001
Total 30-day in-hospital mortality, *n* (%)	5.0 (14.7)	2.0 (3.6)	.099
ICU admission, *n* (%)	3.0 (8.8)	0 (0)	.051

were shown between the culture-directed or MRSA nasal screening-directed cohort for incidence of new-onset AKI (14.7% vs. 3.6%, *p* = .99) or 30-day in-hospital mortality (14.7% vs. 3.6%, *p* = .99).

DISCUSSION

Current practices at the study hospital include the predominant utilization of vancomycin therapy for the empiric coverage of MRSA in patients with suspected MRSA pneumonia infection. This study was designed to assess the total duration of vancomycin therapy in patients with suspected MRSA pneumonia who were eligible for further anti-MRSA antimicrobial de-escalation when using respiratory culture-directed versus MRSA nasal screening-directed practices at our institution. To determine the total duration of empiric vancomycin therapy, our primary outcome was to assess the duration (in hours) of vancomycin therapy with patients who only had a pneumonia infection type to prevent confounders from increasing the duration of therapy.

Prior studies have shown the clinical utility of using MRSA nasal screening to assist in further anti-MRSA antimicrobial de-escalation. Our findings showed agreement with previously published studies regarding our primary outcome duration of vancomycin therapy (Marinucci et al., 2023; Woolever et al., 2020; Dadzie et al., 2019). Within the MRSA nasal screening-directed cohort, three individuals had avoidance of vancomycin when using MRSA nares due to the collection of nares at a time prior to the start of vancomycin therapy. Vancomycin doses were discontinued before administration due to negative results, further demonstrating the benefit of MRSA nasal screening as a valuable antimicrobial stewardship tool. Aligning with the primary outcome of reduced antibiotic duration, the MRSA nasal screening-directed cohort also had a significantly lower number of vancomycin levels obtained. Additional findings of an overall decrease in length of stay were found in the MRSA nasal screening-directed cohort, which could potentially lead to the prevention of hospital-acquired infections, increased costs, and other adverse events (Siddique et al., 2021). Lastly, this study also found a reduced incidence of new-onset AKI and 30-day in-hospital mortality in the MRSA nasal screening-directed cohort compared to the culture-directed cohort, although this was not statistically significant. The reduc-

tion could be attributed to more patients being admitted to the ICU in the culture-directed cohort.

A cost analysis was performed to evaluate the total cost of managing vancomycin therapy in patients eligible for appropriate antimicrobial de-escalation (Figure 3). An average of $417.65 was spent per person in the culture-directed cohort and $172.98 per person in the MRSA nasal screening-directed cohort. For each cohort, $21 per hour was assigned for the estimated microbiology technician time based on institutional salary information. To analyze and report respiratory culture results for microbiology technicians, an estimated 2 hours was assigned for the culture-directed cohort compared to the 1 hour for MRSA nasal screening results. A monetary value was also applied for the average estimated cost of analyzing and reporting a vancomycin trough level ($110 for each trough level collection), estimated cost of 1 gram vancomycin dose ($16 for each dose), and estimated cost of $33.60 per MRSA nares collection kit (Knack et al., 2023). The hourly rate of pharmacist pay of $60 per hour was used with an assumed 30 minutes per dose to perform vancomycin dosing and pharmacokinetic monitoring. Overall, it was estimated that using a MRSA nasal screening-directed method versus culture-directed would result in a $245 cost savings per person receiving empiric vancomycin therapy for suspected MRSA pneumonia. This analysis did not include the cost associated with hospital length of stay, cost per nursing personnel, and cost of managing clinical AKI due to the potential for over or underestimating associated costs.

Limitations

Limitations of this study include restricting our study population to patients only with the infection indication of pneumonia. Patients were excluded if they initially presented with extrapulmonary infections such as cellulitis. Newer literature suggests a clinical utility for utilizing MRSA nasal screening in these patient populations; however, current practices at our institution do not reflect this practice. In addition, our data collection process depended on analyzing paper charts locally in the pharmacy, which could present a form of collection bias via convenience sampling. Lastly, it is important to note potential variability and human error while collecting microbial samples and interpreting results.

In the literature, the NPV of MRSA nasal screening decreases from approximately 97-99% to 95% in patients receiving at least two doses of mupirocin. Due

Figure 3

Cost Avoidance Analysis

Culture-directed Cohort cost estimate (*n* = 34)		MRSA Nares-directed Cohort cost estimate (*n* = 56)	
Microbiology technician time	$1,428	Microbiology technician time	$1,176
Pharmacist time	$2,160	Pharmacist time	$ 930
Vancomycin trough	$7,920	Vancomycin trough	$ 3,410
Vancomycin dose	$2,692.04	Vancomycin dose	$ 2,289.04
		MRSA nares kit	$1,881.60
Total cost	$14,200.04		$9,686.64
Average cost per person	**$417.65**	**Average cost per person**	**$172.98**

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to the nature of our small subset of patients that fit into this category, we could not accurately identify if mupirocin administration affected the NPV of MRSA nasal screening (Chaudhry et al., 2020). Out of 56 patients in the MRSA nasal screening-directed cohort, 13 patients were initiated on mupirocin therapy before collecting the MRSA nasal screen. Of those 13 patients, three were administered mupirocin therapy for greater than or equal to 24 hours before the MRSA nares screening collection. None of these patients had a new onset AKI or mortality event.

At our institution, a pneumonia sputum (polymerase chain reaction) PCR panel was implemented in December 2022, which should also be considered moving forward with the generalizability of the study. The PCR pneumonia sputum panel allows for rapid identification of common bacterial and viral pathogens found in the sputum, which can also allow for empiric therapy modification if clinically indicated. Some areas of interest moving forward include determining best practice methods to identify common sputum pathogens and determining the clinical utility of MRSA nasal screening in patients with additional indications outside of pneumonia (*i.e.,* cellulitis) (Ferrer et al., 2023).

CONCLUSION

Methicillin-resistant *Staphylococcus aureus* nasal screening to guide empiric vancomycin de-escalation was statistically significant in reducing the total duration of vancomycin therapy compared to culture-directed methods. Additional findings suggest a reduction in the total number of vancomycin levels and length of stay. An estimated $245 cost savings per person was shown in patients on empiric vancomycin therapy for suspected MRSA pneumonia who were eligible for appropriate anti-MRSA therapy de-escalation. Further studies should evaluate the clinical impact of how to effectively interpret MRSA nasal screening results when patients receive greater than 24 hours of mupirocin decolonization.

DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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