

Feasibility of rapid polymerase chain reaction for detection of methicillin-resistant *Staphylococcus aureus* colonization among emergency department patients with abscesses

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Purpose: In the era of community-associated methicillin-resistant *Staphylococcus aureus* (MRSA), clinicians face a difficult challenge when selecting antibiotics to treat abscesses. The lack of rapid diagnostics capable of identifying the causative organism often results in suboptimal antibiotic stewardship practices. Although not fully elucidated, the association between MRSA colonization and subsequent infection represents an opportunity to enhance antibiotic selectivity. Our primary objective was to examine the feasibility of utilizing a rapid polymerase chain reaction (PCR) system (Cepheid's GeneXpert®) to detect MRSA colonization prior to patient discharge in the emergency department (ED).

Methods: This feasibility study was conducted at a tertiary care, urban, academic ED. Patients presenting with a chief complaint related to a potential abscess during daytime hours over an 18-week period were screened for eligibility. Subjects were enrolled into either the PCR swab protocol group (two-thirds) or traditional care group (one-third). PCR swabs were obtained from known MRSA carriage sites (nasal, pharyngeal) and the superficial aspect of the wound.

Results: The two groups were similar in terms of demographics, abscess location, and MRSA history. The PCR results were available prior to patient discharge in 100% of cases. The turnaround times in minutes for the PCR swabs were as follows: nasal 73 ± 7 , pharyngeal 82 ± 14 , and superficial wound 79 ± 17 . No significant difference in length of stay was observed between the two groups. The observed ideal antibiotic selection rates improved by 45% in the PCR group, but this trend was not significant ($P = 0.08$).

Conclusion: When collected in triage, PCR swabs demonstrated turnaround times that were effective for use in the ED setting. Utilizing a rapid PCR MRSA colonization detection assay for ED patients with abscesses did not adversely impact the length of stay. Real-time determination of MRSA colonization may represent an opportunity to improve antibiotic selectivity in the treatment of abscesses.

Keywords: MRSA, carrier state, antibiotic stewardship, PCR, multiple drug resistant organisms, MDROs

Introduction

The role of antibiotics in the treatment of skin abscesses, the majority of which are now caused by community-associated (CA) methicillin-resistant *Staphylococcus aureus* (MRSA),¹ remains controversial.² The most recent Centers for Disease Control (CDC) guidelines recommend antibiotics for any purulent skin and soft tissue infection (SSTI) with systemic symptoms, severe local symptoms, or failure to respond to incision and drainage (I + D).³ Recent Infectious Disease Society of America guidelines expand

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recommended CA-MRSA antibiotic coverage to cases of purulent cellulitis (cellulitis with purulent drainage and no focal abscess) and any abscesses involving comorbidities, immunosuppression, extremes of age, difficult location to drain (face, hand, genitalia), and septic phlebitis.⁴

Although the recommendations define when to use antibiotics, clinically, the distinction between cellulitis and abscess is not always clear.⁵ To further complicate the decision to prescribe antibiotics, several recent trials have demonstrated nonsignificant trends towards increased treatment failure rates without antibiotics for uncomplicated abscesses after I + D.^{6,7} Thus, practice patterns in the use of antibiotics for abscesses are highly variable.^{8,9} Clinicians who opt to prescribe antibiotics must also consider other common causes of SSTIs, such as methicillin-sensitive *S. aureus* and group A streptococcus, which may not reliably respond to CA-MRSA-specific antibiotics. Suboptimal antibiotic stewardship practices, such as using antibiotics when unnecessary and using broad-spectrum antibiotics or multiple antibiotics, have been linked to the epidemic of multiple drug-resistant organisms.^{10–13}

MRSA colonization is a well-established risk factor for subsequent SSTIs, and this makes carriage sites an attractive target for early MRSA detection in the acute care setting.^{14–16} No one carriage site can reliably diagnose MRSA colonization, and therefore, multiple site swabs will provide more accurate information.^{17,18} Out of consideration for the cost-prohibitive nature of comprehensive polymerase chain reaction (PCR) colonization screening in the emergency department (ED) and the ease of collection during triage, in this study, only the nasal and pharyngeal sites were selected from potential colonization sites (axilla, inguinal, rectal). The anterior nares are well established as the primary colonization site for *S. aureus*, with the pharynx recognized as an important site of exclusive extranasal colonization.^{17,19–21} A rapid, reliable test to detect MRSA colonization at various sites may prove useful in the ED setting to improve antibiotic selectivity. One such system, the GeneXpert® (Cepheid, Sunnyvale, CA, USA), is a rapid PCR assay capable of detecting MRSA from both carriage and infected sites in approximately 1 hour. This assay has demonstrated 97.5% agreement with traditional laboratory testing by culture.^{22,23}

We undertook a feasibility study to examine the use of this system in the ED, with an immediate, post-triage colonization site swab protocol. Our primary objective was to analyze turnaround times, the availability of results prior to discharge, and the impact of the rapid PCR MRSA colonization detection protocol on length of stay, a key marker of

quality care in the ED. Our secondary aim was to observe whether access to MRSA colonization results influenced antibiotic selectivity. The overall purpose of this study was to provide data that would inform a future trial designed to examine the impact of rapid PCR MRSA assays on health outcomes for patients with abscesses, in the ED.

Methods

This project was designed as a single-center feasibility study, the results of which would inform the design of large-scale trials aimed at addressing the use of rapid PCR in the ED setting for patients with SSTIs. The protocol was approved by the institutional review board and utilized written informed consent. Patients presenting to the ED (tertiary care, urban, academic medical center with approximately 55,000 visits per year) with a chief complaint related to a potential abscess, during daytime hours over an 18-week period, were screened for eligibility.

In order to eliminate factors that might have restricted the choice of antibiotic, we excluded those aged <18 years, pregnant or breast feeding, allergic to any antibiotics, or who received antibiotics in the previous week. Any patients with complex abscesses, defined as requiring hospital admission, involving immunocompromised status (eg, chronic steroid usage, acquired immunodeficiency syndrome [AIDS], ongoing chemotherapy, or transplant recipients), or presenting with two or more systemic inflammatory response syndrome (SIRS) criteria, were also excluded. This study was also limited to patients who reported English as their primary language. As the aim of the study was primarily to determine the feasibility of the PCR swab protocol, and patients were enrolled with two-thirds in the PCR group and one-third in the traditional care group.

Research associates completed a data form, which included the following: demographic information (age, sex, and race), abscess location, medical history, and clinical data (exclusion criteria and history of MRSA infection or colonization). Patients in both groups had separate bilateral nasal, pharyngeal, and superficial wound swabs collected using the BBL™ CultureSwab™ (Becton, Dickinson and Company; Franklin Lakes, NJ, USA) for analysis on the Cepheid GeneXpert® system in a dedicated research laboratory. The consent process and swab collection took place immediately after nurse triage, in an adjacent exam room typically used to treat patients with low acuity complaints. Nasal swabs were collected by inserting a dry swab 1–2 cm into the nostril and rotating it against the septum for 3 seconds while applying pressure with a finger to the outside of the nose. This

was repeated using the same swab for the other nostril. For the pharyngeal swab, a dry swab was applied to both sides of the uvula and lateral walls of the posterior oropharynx. Superficial wound swabs were obtained from the middle focus of the wound, with a saline moistened swab. The Levine twirl technique,²⁴ spinning the end of the swab in a 1 cm² area for 5 seconds, was utilized. Care was taken to avoid contact with the adjacent skin margins. Pharyngeal and nasal swabs were analyzed using GeneXpert® MRSA Nasal cartridges and wound swabs with GeneXpert® MRSA/SA SSTI cartridges. PCR turnaround times, the availability of results before discharge, patient length of stay, aerobic culture result, and the discharge antibiotic (if any) were also recorded.

The three PCR swab results were simultaneously communicated by a research associate to the treating physicians of the patients in the PCR group immediately upon completion. To avoid bias in the results before discharge and length of stay measures, the treating physicians were unaware of their patient's participation until immediately after the PCR results were available. There was no chance for the physicians of the traditional care group patients to obtain MRSA PCR results, as these assays were not available for clinical use at the time of this study. As this study was not intended to examine health outcomes, providers were simply provided the PCR colonization results but were not instructed on any specific abscess management protocol, including whether or not to prescribe antibiotics or obtain aerobic cultures.

The primary outcomes were the availability of PCR results prior to patient discharge and length of ED stay, in minutes. The secondary outcome was the observed ideal antibiotic selectivity in the outpatient treatment of abscesses. The measure of ideal selection is not based on any health outcome or specific guideline but rather, the consensus of the investigators regarding adherence to the principles of antimicrobial stewardship.²⁵ For the purposes of this study, this was defined as trimethoprim/sulfamethoxazole for MRSA and any beta-lactam for non-MRSA infections. These choices represent targeted, highly effective single-agent therapy for both MRSA and non-MRSA SSTIs, respectively.^{4,26} Clindamycin is an effective single agent for most SSTIs but was specifically identified as nonideal, given emerging resistance among MRSA isolates and an unfavorable side-effect profile.^{12,27} Aerobic culture results were used as the "gold standard" to established causative organisms as either MRSA or non-MRSA.

We used SAS version 9.3 (SAS Institute Inc, Cary, NC, USA) for statistical analysis. A *P*-value < 0.05 was considered to be a significant difference. After confirming normality

with the Kolmogorov–Smirnov test, the Student's *t*-test was used to compare length of stay between the two groups. Chi-squared or Fisher's exact test were used to compare differences between the groups for antibiotics at discharge, ideal antibiotic selection, and MRSA-positive aerobic culture rates.

Results

A total of 107 patients were assessed for enrollment, with 54 randomized and 21 included in the antibiotic selectivity analysis (Figure 1). The 21 subjects were cared for by a total of 14 board-certified emergency physicians and one nurse practitioner. Patients enrolled with suspected abscesses whose final diagnosis was not abscess were not included in the analysis. The protocol involved enrollment immediately after triage, and thus, there was no way to predict who might be admitted to the hospital after physician evaluation. Our objective was to examine only patients managed on an outpatient basis because MRSA PCR turnaround times for admitted patients are less relevant, given the lack of time pressures. Thus, enrolled subjects who required admission were excluded from the analysis. In some instances, the treating physician opted to not obtain an aerobic culture as part of their routine care. This resulted in no "gold standard" to determine the causative organism. As such, these subjects were only excluded from the antibiotic selectivity analysis.

Demographic information for both groups is reported as age in years ± standard deviation (SD) and all other variables as number (percentage). The majority of our subjects self-identified as black, and ages ranged from the third to eighth decade of life. Men made up the majority of subjects in the PCR group, while women were the majority in the traditional care group. No significant differences were present between the two groups in terms of demographics, culture results, and abscess location (Table 1).

The average turnaround times from PCR swab collection to result are reported in Table 2 as minutes ± SD. The aerobic culture results demonstrated similar rates of MRSA between the two groups. In both groups, discharge antibiotics were prescribed in 100% of cases. For our primary outcomes, the PCR swab results were available to the treating physician prior to discharge in 100% of the cases and the length of stay was similar between the two groups. A nonsignificant trend towards improved ideal antibiotic selection was observed in the PCR group (Table 3).

Discussion

The combination of immense time pressures, unavailable clinical data, and a highly litigious practice environment

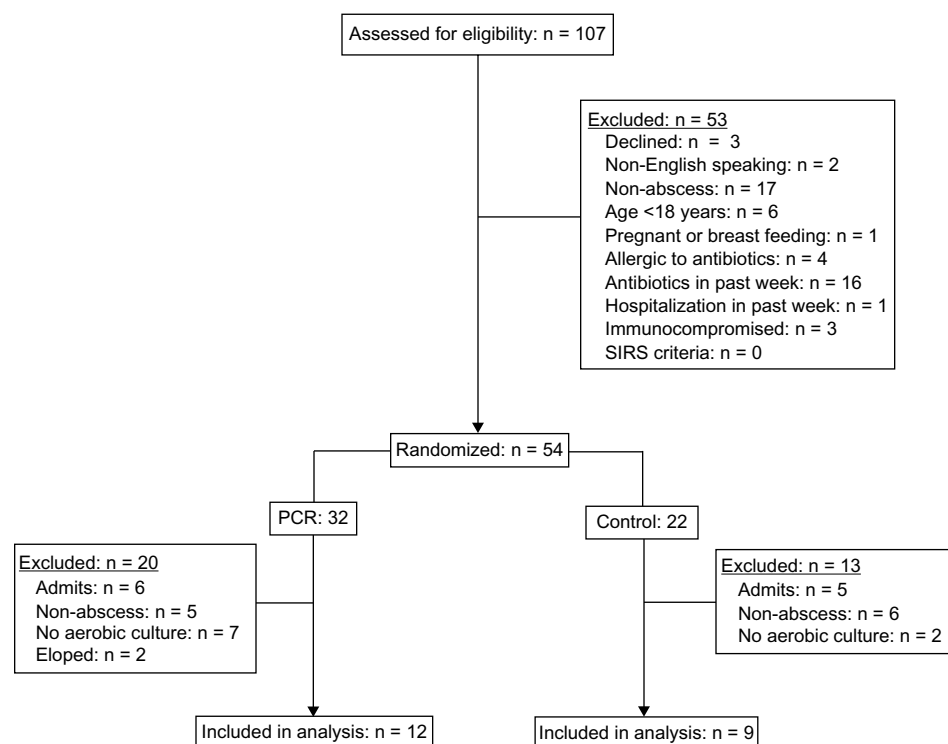


Figure 1 Study enrollment.

Abbreviations: PCR, polymerase chain reaction; SIRS, systemic inflammatory response syndrome.

makes the ED a perfect storm for antibiotic misuse. Suboptimal antibiotic stewardship practices have been linked to the rising problem of multiple drug resistant organisms.¹⁰ Newly available rapid PCR MRSA detection assays represent a golden opportunity to enhance antimicrobial stewardship in the ED with regards to SSTI treatment.

Our findings of PCR turnaround times of approximately 80 minutes from the time of collection and no impact of

length of stay support the feasibility of a triage-initiated colonization swab protocol in ED patients with abscesses. By utilizing colonization sites to detect MRSA status, as opposed to post I + D collection of purulence for analysis, in some instances, we were able to initiate the PCRs while the patients were still in the waiting room. We believe collecting these samples immediately after triage was critical in achieving 100% availability of the PCR results prior to patient discharge and the absence of any significant impact on ED length of stay. Although clinicians were not advised on how to use the colonization data and our aim was not to change clinical practice, we did observe a nonsignificant 45% improvement in discharge antibiotic selectivity for abscesses.

Our results are supported by a similar pilot study from May et al, which examined the impact of post-I + D GeneXpert® MRSA/SA SSTI assay on antibiotic usage patterns. They reported similar PCR turnaround times

Table 1 Subject baseline characteristics

Characteristic	PCR (n = 12)	Traditional care (n = 9)	P-value
Age, years – mean ± SD (range)	42 ± 16 (21–74)	37 ± 13 (23–62)	0.49
Male sex, N (%)	7 (58)	2 (22)	0.18
Race, N (%)			0.66
Black	8 (67)	7 (78)	
White	3 (25)	2 (22)	
Other	1 (8)	0 (0)	
Abscess location, N (%)			0.72
Extremity	4 (33)	4 (44)	
Groin/buttock	5 (42)	2 (22)	
Trunk/axilla	2 (17)	3 (33)	
Head and neck	1 (8)	0 (0)	
History of abscess, N (%)	5 (42)	4 (44)	1.00
History of MRSA, N (%)	2 (17)	1 (11)	1.00

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; PCR, polymerase chain reaction; SD, standard deviation.

Table 2 PCR (polymerase chain reaction) turnaround times

Swab site	Time (minutes)
Nasal	73 ± 7
Pharyngeal	82 ± 14
Superficial wound	79 ± 17

Table 3 Outcomes

Outcome	PCR (n = 12)	Control (n = 9)	Absolute difference in % or minutes (95% CI)	P-value
MRSA + culture, N (%)	6 (50)	5 (56)	6 (–43% to 54%)	P = 1.0
Discharge antibiotic, N (%)	12 (100)	9 (100)	0 (0% to 0%)	P = 1.0
Length of stay (minutes)	221 ± 129	232 ± 96	11 (–96 to 118)	P = 0.83
Ideal antibiotic selection, N (%)	8 (67)	2 (22)	45 (1% to 88%)	P = 0.08

Note: P is from Fisher's exact test or t-test.

Abbreviations: CI, confidence interval; MRSA, methicillin-resistant *Staphylococcus aureus*; PCR, polymerase chain reaction.

and improved antibiotic selectivity. Interestingly, 25% of subjects declined to wait for the post I + D PCR result, perhaps reflecting the necessity of a PCR protocol that utilizes colonization or superficial wound PCR results obtained during triage.²⁸

With an approximate 50/50 split between MRSA and non-MRSA infections in both groups, a coin toss to choose antibiotics should yield a 25% ideal antibiotic selection rate. This is reflected by the traditional care group, which only achieved a 22% ideal selection rate. It would appear that clinical judgment is no better than random chance at predicting MRSA as the causative organism in SSTIs. The 67% ideal selection rate in the PCR group is not perfect but does demonstrate a higher degree of adherence to antibiotic stewardship principles. Prior to conducting future studies aimed at improving antibiotic stewardship through colonization detection, it is critical to determine the individual and cumulative performance characteristics (sensitivity and specificity) of potential carriage site (nasal, pharyngeal, axillary, groin, and rectal) and superficial wound swabs for predicting MRSA as the causative organism in abscesses. This information will provide important guidance for clinicians in how to use real-time colonization results while making antibiotic treatment decisions.

The primary limitation of this feasibility study was our small sample size, which limits the strengths of our conclusions. Withholding patient participation from the care provider until the PCR results were available was critical to assess the ability of this protocol to produce PCR results in a meaningful timeframe for ED providers (prior to discharge). Unfortunately, this resulted in seven patients in the PCR group being excluded for lack of aerobic culture obtained during I + D. This study was conducted at a single institution, using convenience sampling, during summer months

and daytime hours only, which limits external validity. In addition, the study patient population demonstrated a high prevalence of MRSA, and these results may not be applicable to areas with low prevalence.

In conclusion, the introduction of a rapid PCR-based MRSA colonization detection protocol is feasible for the ED setting. Further research is required to determine whether real-time colonization detection can improve antibiotic stewardship or improve health outcomes for patients with abscesses.

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Disclosure

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