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Improving Efficiency in Active Surveillance for Methicillin-Resistant *Staphylococcus aureus* or Vancomycin-Resistant *Enterococcus* at Hospital Admission

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Abstract

OBJECTIVE—Mandatory active surveillance culturing of all patients admitted to Veterans Affairs (VA) hospitals carries substantial economic costs. Clinical prediction rules have been used elsewhere to identify patients at high risk of colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) or vancomycin-resistant enterococci (VRE). We aimed to derive and evaluate the clinical efficacy of prediction rules for MRSA and VRE colonization in a VA hospital.

DESIGN AND SETTING—Prospective cohort of adult inpatients admitted to the medical and surgical wards of a 119-bed tertiary care VA hospital.

METHODS—Within 48 hours after admission, patients gave consent, completed a 44-item risk factor questionnaire, and provided nasal culture samples for MRSA testing. A subset provided perirectal culture samples for VRE testing.

RESULTS—Of 598 patients enrolled from August 30, 2007, through October 30, 2009, 585 provided nares samples and 239 provided perirectal samples. The prevalence of MRSA was 10.4% (61 of 585) (15.0% in patients with and 5.6% in patients without electronic medical record (EMR)-documented antibiotic use during the past year; $P < .01$). The prevalence of VRE was 6.3% (15 of 239) (11.3% in patients with and 0.9% in patients without EMR-documented antibiotic use; $P < .01$). The use of EMR-documented antibiotic use during the past year as the predictive rule for screening identified 242.8 (84%) of 290.6 subsequent days of exposure to MRSA and 60.0 (98%) of 61.0 subsequent days of exposure to VRE, respectively. EMR documentation of antibiotic use during the past year identified 301 (51%) of 585 patients as high-risk patients for whom additional testing with active surveillance culturing would be appropriate.

CONCLUSIONS—EMR documentation of antibiotic use during the year prior to admission identifies most MRSA and nearly all VRE transmission risk with surveillance culture sampling of only 51% of patients. This approach has substantial cost savings compared with the practice of universal active surveillance.

Emerging antibiotic-resistant bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE), are leading causes of infections in hospitalized patients that result in substantial costs, morbidity, and mortality.¹⁻⁴ Efforts to decrease the incidence of healthcare-associated infections have included attempts to use active detection and isolation to reduce the transmission of antibiotic-resistant bacteria.^{5,6} MRSA and VRE have been the primary targets of active surveillance cultures, which typically are administered to all patients at admission to the hospital or to those on specific high-risk units within the hospital.⁵⁻⁸ Active surveillance cultures for MRSA are primarily based on cultures of nares samples,^{5,6,9} and those for VRE are based on cultures of perirectal samples.^{10,11}

Recent studies have come to differing conclusions regarding the benefit of using active surveillance culturing for MRSA for all patients admitted to the hospital.^{5,6} There is likely a benefit to active surveillance in some types of facilities. Many institutions have adopted active surveillance for MRSA, including all Veterans Affairs (VA) hospitals, which mandate active surveillance culturing for MRSA for all patients admitted since 2007.¹² The practice of active surveillance culturing for all patients admitted to the hospital is costly.¹³

Targeted active surveillance has been proposed to contain costs while preserving the potential benefits of active surveillance culturing.¹⁰ This method attempts to identify a group of patients at high risk for MRSA or VRE among the general population of patients admitted to the hospital.¹⁰ A prediction rule using the lone criterion of self-reported hospitalization during the past year was found to identify 76% of patients colonized with MRSA and 100% of patients colonized with VRE in a university hospital (with electronic hospital administrative data being significantly less predictive).¹⁰ Riedel et al¹¹ examined prediction rules based on electronic hospital administrative data (disregarding patient self-reporting) in a VA hospital. They found electronic medical record (EMR) documentation of hospitalization during the past year to be the best rule, predicting 70% of MRSA colonization and 71% of VRE colonization.

Other research has examined various prediction models for MRSA using many variables in more complex models. In general, these models are not feasible for screening at admission in most facilities because of the large number of variables that they include.^{14,15}

To investigate the clinical utility of alternative methods for targeted active surveillance in a VA hospital population, we formed a prospective cohort of patients. In this cohort, we identified potential prediction rules from self-reported and EMR-documented variables and performed surveillance cultures for MRSA and VRE. Prediction rules were evaluated for sensitivity, specificity, and ability to identify and prevent days of exposure to MRSA and VRE.

METHODS

We conducted a prospective cohort study of patients admitted to general acute care units at the Baltimore VA Medical Center in Baltimore, Maryland. During the period August 30, 2007, through October 30, 2009, patients admitted to the medical or surgical acute care units were approached for participation. Enrollment took place within 48 hours after admission. After giving informed consent, patients were administered a questionnaire and provided nares swab samples for MRSA testing. For a subset of these patients, perirectal swab samples were collected for VRE testing (all patients enrolled prior to September 12, 2008, when a nurse enroller left the study).

Nares swab samples were inoculated onto MRSA Select medium (Bio Rad/Sanofi) and incubated at 37°C for 24 hours. Pink colonies growing on the medium were confirmed as *S.*

aureus, and susceptibility testing was performed using the Phoenix (Becton-Dickinson Diagnostics). A D test and an oxacillin screen plate test (Becton-Dickinson Diagnostics) were also performed on each isolate. Perirectal swab samples were inoculated onto bile esculin agar supplemented with 6 µg/mL vancomycin (Becton-Dickinson Diagnostics). VRE was identified on the basis of growth on bile esculin agar with vancomycin, Gram staining, negative catalase test result, and a positive L-pyrrolidonyl-β-naphthylamide test result. Antimicrobial susceptibility testing was performed and interpreted in accordance with Clinical and Laboratory Standard Institute guidelines.

At enrollment, patients were also administered a 44-item questionnaire examining demographic characteristics and potential risk factor variables for inclusion in single-variable or multivariable prediction rules. Key variables of self-reported hospitalization or receipt of antibiotics could be answered “yes,” “no,” or “don't know.” To increase sensitivity, variables were considered present when patients responded “yes” or “don't know.” The benefit of detecting MRSA and VRE at hospital admission is the prevention of patient-to-patient transmission of these pathogens within the hospital. The variable that most directly addresses the potential for transmission is the number of subsequent inpatient days (ie, length of stay) for patients who screened positive for MRSA at admission.¹⁶ Inpatient VRE-days were calculated in the same fashion. Administrative data were obtained from the VA Maryland Health Care System's Sequel database.

Medians and frequency distributions were used to describe the characteristics of the study population. We calculated sensitivity, specificity, and days of potential exposure to MRSA or VRE to assess the ability of variables to identify patients at risk for transmitting MRSA or VRE. We then tested several single-variable prediction rules, selecting variables that predicted the most days of MRSA or VRE exposure for additional testing. Then, using Boolean logic (and/or), we assessed whether the addition of other variables would improve sensitivity without significantly decreasing specificity. The final rules to identify patients at high risk for colonization with MRSA or VRE contained the variable(s) that met these criteria. After determining the best prediction rule, we created a simple model that calculated negative predictive values and positive predictive values for the prevalence of MRSA and VRE in our patient population, as well as for hypothetical prevalences of MRSA and VRE in other hospitals.

A simple cost analysis was conducted to estimate the savings that would be associated with targeted active surveillance for either MRSA or VRE, compared with a program of universal active surveillance. Costs were determined using published estimates.^{17,18} Total costs included nursing time to obtain culture samples and laboratory time to process specimens. Individual patient costs were multiplied by the number of patients who would have undergone surveillance in each scenario. All costs were converted to 2010 US dollars by means of the medical services component of the Consumer Price Index.¹⁹ All analyses were performed using SAS statistical software, version 9.1 (SAS Institute).

RESULTS

Of 598 patients enrolled within 48 hours of hospitalization, 585 (98%) underwent anterior nares culture sampling and 239 (41%) of the 585 patients who provided nares samples also underwent perirectal culture sampling. Of 585 cultures of nares samples, 61 were positive for MRSA (prevalence, 10.4%). Of 239 cultures of perirectal samples, 15 were positive for VRE (prevalence, 6.3%).

Characteristics of the 585 patients in the sample population and of all patients admitted to the same hospital during the study period are presented in Table 1. There were no significant

differences between the final study population and the 13 patients for whom no nares culture was processed. Within the study population, median age was 63 years (interquartile range [IQR], 57–77 years), median length of stay was 2.4 days (IQR, 1.6–4.2 days), and 566 patients (97%) were male. Administrative data obtained from the VA EMR included records of hospital admission to or receipt of antibiotics from the VA Maryland Health Care System during the 365 days prior to study enrollment, length of stay for current hospitalization, clinical cultures positive for MRSA, and comorbid conditions on the basis of International Classification of Diseases, Ninth Revision, Clinical Modification codes. Of all participants, 8 (1.4%) of 585 did not give an answer regarding hospitalization during the past year and 12 (2.1%) of 585 did not give an answer regarding the contemporaneous presence or absence of a skin or soft-tissue wound.

Sensitivity, specificity, and length of MRSA or VRE exposure were examined for multiple candidate variables identified from the patient interview and the EMR. Variables with a sensitivity of greater than 60% are presented (Table 2) and analyzed for hospital days of MRSA or VRE exposure prevented (Table 3).

The prevalences of MRSA colonization and VRE colonization in high- and low-risk patient groups, as defined according to EMR-documented antibiotic use during the past year, were determined. The prevalence of MRSA colonization was 14.7% (44 of 300) in patients with EMR-documented antibiotic use during the past year and 5.6% (16 of 284) in patients with no EMR-documented use ($P < .001$). The prevalence of VRE colonization was 12.3% (14 of 114) in patients with EMR-documented antibiotic use during the past year and 0.9% (1 of 115) in patients with no EMR-documented use ($P < .001$).

The use of self-report of hospitalization as the predictive rule for MRSA screening identified 201.1 (69%) of 290.6 subsequent days of potential exposure to MRSA, whereas EMR documentation of hospitalization identified 217.1 (75%) of 290.6 MRSA-days. Either self-report of hospitalization or EMR documentation of hospitalization was able to identify 59.8 (98%) of 61.1 days of potential exposure to VRE (Table 3). Antibiotic use during the past year was the best rule for identifying subsequent MRSA-days and VRE-days. Differences between self-report and EMR documentation were compared to determine the best data source. Antibiotic use according to self-report and antibiotic use according to EMR documentation were equally good at identifying MRSA-days (244.6 [84%] of 290.6 vs 242.8 [84%] of 290.6 MRSA-days; $P = .72$). Self-reported antibiotic use revealed 57.2 (94%) of 61.0 VRE-days, and EMR-documented antibiotic use revealed 60.0 (98%) of 61.0 VRE-days ($P = .28$). EMR documentation of antibiotic use during the past year identified 301 (51%) of 585 patients as high-risk patients for whom additional testing with active surveillance culturing would be appropriate. Similar results were obtained when the 100 patients who were under contact precautions for MRSA at enrollment were excluded; self-reported antibiotic use identified 20 (69%) of 29 MRSA-colonized patients, and EMR-documented antibiotic use identified 17 (57%) of 30 MRSA-colonized patients.

A simple cost analysis revealed that, during the 26-month study period, performing active surveillance for MRSA for all non-intensive care unit patients admitted to the facility would cost \$86,773. Targeted active surveillance of with EMR documentation of antibiotic use at admission would cost \$45,255, resulting in a 48% savings. Performing active surveillance for VRE for all non-intensive care unit patients admitted to the facility would cost \$77,275, compared with \$42,468 for targeted active surveillance of patients with EMR documentation of antibiotic use, resulting in a 45% savings (if screening for both MRSA and VRE was included, screening of all non-intensive care unit patients would cost \$164,048, compared with \$87,723 for targeted screening, for an overall cost savings of 47%).

Negative predictive values and positive predictive values were calculated for the prediction rule EMR documentation of antibiotic use. In our VA hospital population, the negative predictive values and positive predictive values were 0.94 and 0.15 for MRSA colonization and 0.99 and 0.11 for VRE colonization, respectively. To assess the potential use of EMR documentation of antibiotic use as a prediction rule in other hospitals with different baseline admission prevalences of MRSA or VRE, we calculated negative predictive values and positive predictive values using variable admission prevalence from 1% to 15% (Table 4).

DISCUSSION

In a VA population with a relatively high prevalence of MRSA colonization, we found that single-variable prediction rules based on antibiotic use during the past year identified patients accounting for 84% of inpatient days of exposure to MRSA and 94%–98% of inpatient days of exposure to VRE. The use of such rules would require screening of only 51% of patients when based on EMR documentation of antibiotic use and 57% of patients when based on self-reported antibiotic use. Other tested prediction rules using single or combinations of variables were either too insensitive or nonspecific to be efficient in this population.

Prediction rules for identification of patients colonized with antibiotic-resistant bacteria have been examined in both a tertiary care center and a VA hospital.^{10,11} Investigators found prediction rules of hospitalization or antibiotic use during the prior year to have sensitivities for prediction of MRSA colonization of 69%–76%, with greater sensitivity for prediction of VRE colonization. Different conclusions were reached regarding the benefits of prediction rules. Our study focused on a slightly different variable to evaluate the benefits of prediction rules for targeted active surveillance: hospital days of exposure to MRSA or VRE.¹⁶ This variable reports more accurately the time of risk for transmission (colonization pressure) of MRSA or VRE for patients who are not under contact precautions. We believe this to be a better marker of the goals of active surveillance. We found that 84% of MRSA-days and 98% of VRE-days within our cohort were identified using a single-variable prediction rule based on EMR-documented antibiotic use during the past year. This could be implemented by screening 51% of patients at 53% of the costs associated with full active surveillance (assuming no additional costs for prediction rule identification of patients to be screened). If the EMR is not available, an intake screening question that asks patients about antibiotic use during the past year would identify patients responsible for 84% of MRSA-days and 94% of VRE-days. Metlay et al²⁰ previously showed that patients remember antibiotic use well, which is similar to our finding. The negative predictive value of the prediction rule based on EMR-documented antibiotic use is consistently greater than 0.90 if used at institutions with a broad range of admission prevalence of MRSA or VRE (1%–15%). This calculation suggests that this prediction rule should have similar efficacy at most locations that currently use active surveillance for MRSA and isolation for all admitted patients.

The use of EMR-documented antibiotic use as a prediction rule for active surveillance culturing results in not identifying 2% of VRE exposure risk and 16% of MRSA exposure risk. The potential effect of missing the patients responsible for these proportions of exposure risk is unknown. Because these patients are generally healthier, having not been hospitalized or received antibiotics during the past year, they may be less likely to transmit VRE or MRSA.

A few limitations of this study are specific to the VA healthcare system. First, it is one of the few systems in the United States in which almost all care is provided by a single source and for which a single EMR is available. In a previous study in a tertiary care center in the same geographical area, EMR-documented antibiotic use or hospitalization during the past year

were significantly less sensitive than patient self-report.¹⁰ Second, VA facilities treat a specific population with lower socioeconomic status with a high proportion of male patients, which perhaps limits generalizability beyond VA facilities. However, the VA system is the largest single-payer acute care hospital system in the United States and has mandated active surveillance culturing for MRSA for all patients at admission to the hospital. This prediction rule, if implemented throughout the VA system, could result in substantial cost savings that could be used to target other infections or quality improvement projects, such as MRSA decolonization.

The pandemic of community-associated MRSA (CA-MRSA) infection would seem to limit the utility of prediction rules for MRSA colonization that are based on risk factors for healthcare-associated MRSA colonization. CA-MRSA infection was common in Baltimore, Maryland, during the period of this study.^{4,21} Although CA-MRSA colonization has specific risk factors, we still found antibiotic use and hospitalization during the past year to be the best prediction rules in our population with a high proportion of CA-MRSA colonization. This would suggest that the prediction rules that we derived are resilient to CA-MRSA and may perform even better as the pandemic of CA-MRSA infection recedes.²² In addition, we sampled only patient nares for MRSA. This may have decreased the rate of identification of patients with MRSA colonization, although a recent study in the VA healthcare system found little benefit in screening sites beyond the nares.⁹

In conclusion, we found that the prediction rule based on EMR-documented antibiotic use during the past year identified patients responsible for 84% of MRSA exposure risk and 98% of VRE exposure risk from colonized VA inpatients, while requiring culture sampling of only 51% of patients. This prediction rule would be easily implemented within VA hospitals and could result in substantial savings.

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TABLE 1

Demographic Characteristics of Study Participants and General Inpatient Population during the Study Period

Variable	Participants (<i>n</i> = 585)	All hospitalized patients (<i>n</i> = 10,358)
Demographic characteristics		
Age, years, median (IQR)	63 (57–77)	63 (56–76)
Length of stay, days, median (IQR)	2.4 (1.6–4.2)	2.7 (1.2–5.5)
Male sex	566 (95)	9,873 (95)
EMR documentation of hospitalization during past year	321 (56) ^a	5,261 (51)
EMR documentation of antibiotic use during past year	283 (48)	5,372 (52)
Educational level, high school completed	243 (41)	NA
Past incarceration	223 (38)	NA
Employment as or residence with a HCW	52 (9)	NA
Residence with someone who has resided in a nursing home during the past year	52 (9)	NA
Nurse or other HCW visited home during past year	86 (14)	NA
Comorbidities		
Charlson comorbidity score, median (IQR)	1 (0–3)	1 (0–3)
Cerebrovascular disease	43 (7)	623 (6)
Malignancy	78 (13)	1,668 (17)
Diabetes mellitus	157 (27)	2,452 (25)
Chronic obstructive pulmonary disease	100 (17)	1,389 (14)
Heart failure	83 (14)	1,003 (10)
Renal disease	111 (19)	1,426 (15)

NOTE. Data are no. (%) of patients unless otherwise specified. AIDS, rheumatologic disease, liver disease, and peptic ulcer disease affected fewer than 5% of patients. EMR, electronic medical record; IQR, interquartile range; HCW, healthcare worker; NA, not available.

^aExcludes 8 patients for whom data were not available.

TABLE 2

Comparison of Variables for Predicting Colonization with Methicillin-Resistant *Staphylococcus aureus* (MRSA) and Vancomycin-Resistant *Enterococcus* (VRE)

Variable	MRSA, proportion (%)		VRE, proportion (%)	
	Sensitivity	Specificity	Sensitivity	Specificity
Single variables				
Hospitalization during past year				
Self-reported	41/61 (67)	236/516 (46)	14/16 (88)	99/228 (43)
EMR-documented	37/61 (61)	278/524 (53)	14/15 (93)	114/224 (51)
Antibiotic use during past year				
Self-reported	46/61 (75)	235/524 (45)	13/16 (81)	109/229 (48)
EMR-documented	44/60 (73)	268/524 (51)	14/15 (93)	114/224 (51)
Wound present, self-reported	18/58 (31)	432/515 (84)
Combination variables				
Hospitalization or antibiotic use during past year				
Self-reported	52/61 (85)	144/524 (27)	15/15 (100)	62/224 (28)
EMR-documented	47/61 (77)	195/524 (37)	15/15 (100)	85/224 (38)

NOTE. EMR, electronic medical record.

TABLE 3

Proportion of Methicillin-Resistant *Staphylococcus aureus* (MRSA) and Vancomycin-Resistant *Enterococcus* (VRE) Exposure Identified Using Different Prediction Rules

Variable	Proportion (%) of hospital days of exposure		Proportion (%) of patients necessary to screen
	MRSA	VRE	
Single variables			
Hospitalization during past year			
Self-reported	201.1/290.6 (69)	59.8/61.0 (98)	321/577 (56)
EMR-documented	217.1/290.6 (75)	59.8/61.0 (98)	283/585 (48)
Antibiotic use during past year			
Self-reported	244.6/290.6 (84)	57.2/61.0 (94)	335/585 (57)
EMR-documented	242.8/290.6 (84)	60.0/61.0 (98)	301/585 (51)
Combination variables			
Hospitalization or antibiotic use during past year			
Self-reported	261.3/290.6 (90)	61.0/61.0 (100)	432/585 (74)
EMR-documented	252.4/290.6 (87)	61.0/61.0 (100)	376/585 (64)

NOTE. EMR, electronic medical record.

TABLE 4

Negative Predictive Values and Positive Predictive Values Calculated for Hypothetical Facilities with Different Prevalences of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Colonization or Vancomycin-Resistant *Enterococcus* (VRE) Colonization in Patients at Admission Using Sensitivity and Specificity of the Prediction Rule, Electronic Medical Record Documentation of Antibiotic Use during the Past Year

Admission prevalence	Negative predictive value	Positive predictive value
MRSA colonization		
1%	0.99	0.01
2.5%	0.96	0.04
5%	0.93	0.07
10%	0.94	0.14
10.4%	0.94	0.15
15%	0.91	0.21
VRE colonization		
1%	0.99	0.02
2.5%	0.99	0.05
5%	0.99	0.09
6.3%	0.99	0.11
10%	0.98	0.17
15%	0.98	0.25