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Clinical Utility of Infection Control Documentation of Prior Methicillin-Resistant *Staphylococcus aureus* Colonization or Infection for Optimization of Empirical Antibiotic Therapy

Marin L. Schweizer, BS¹, Jon P. Furuno, PhD¹, Anthony D. Harris, MD, MPH¹, Jessina C. McGregor, PhD⁴, Kerri A. Thom, MD¹, Jennifer K. Johnson, PhD², Michelle D. Shardell, PhD¹, and Eli N. Perencevich, MD, MS³

¹ Department of Epidemiology and Preventive Medicine, University of Maryland School of Medicine, Baltimore, Maryland ² Department of Pathology, University of Maryland School of Medicine, Baltimore, Maryland ³ Veterans Affairs Maryland Health Care System, Baltimore, Maryland ⁴ Oregon State University College of Pharmacy, Portland, Oregon

Abstract

This 5-year study of 25,378 hospitalizations measured the utility of infection control documentation of prior methicillin-resistant *Staphylococcus aureus* (MRSA) colonization or infection for the optimization of empirical antibiotic therapy. Documented prior MRSA colonization or infection was predictive of subsequent MRSA infections (odds ratio, 4.05). Physicians appear to use this documentation when prescribing empirical therapy for suspected bacteremia.

Clinical laboratory identification of methicillin-resistant *Staphylococcus aureus* (MRSA) as the cause of bacteremia commonly requires approximately 48–72 hours.¹ Thus, physicians often initially prescribe antibiotic therapy empirically before blood culture results are known. Increasingly, many hospitals document patient history of MRSA colonization or infection in medical records to guide contact precautions. Since both colonization and infection with MRSA are known risk factors for subsequent infection, an additional benefit of this documentation may be to optimize empirical therapy. This study aimed to assess whether documented prior MRSA colonization or infection, initially documented for infection control purposes, predicts subsequent MRSA bacteremia and whether physicians appear to be using this documentation when prescribing empirical antibiotic therapy for patients with suspected bacteremia.

METHODS

This retrospective cohort study included all adults admitted to the University of Maryland Medical Center from January 17, 2001, through December 31, 2005, who had a blood culture performed and who received empirical antibiotic therapy. If multiple blood cultures were performed during a patient's hospitalization, only the first was used. This study was approved by the institutional review board of the University of Maryland, Baltimore.

Address reprint requests to Marin L. Schweizer, BS, 100 N. Greene St., Lower Level, Department of Epidemiology and Preventive Medicine, University of Maryland School of Medicine, Baltimore, Maryland, 20201 (mschweiz@epi.umaryland.edu).

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Since 1996, the University of Maryland Medical Center has documented the history of MRSA colonization or infection in a patient's medical record if the patient had a positive surveillance or clinical culture for MRSA during any hospitalization. Patients with this documentation are placed on contact precautions. During the study period, anterior nares samples for surveillance culture were obtained from patients on admission to the intensive care unit, weekly, and on discharge from the intensive care unit.

All data were abstracted from a relational database that contains medical, pharmaceutical, and microbiologic data. Blood cultures and susceptibility tests were performed as part of standard patient care. The Charlson comorbidity index was calculated according to the *International Classification of Diseases, Ninth Revision* codes for comorbid conditions.^{2,3}

We defined empirical antibiotic therapy as receipt of any antibiotic during the period 24 hours before to 24 hours after the blood sample was obtained. If the blood sample was obtained within 24 hours after hospital admission, the empirical therapy window began at the time of admission. We defined MRSA-directed empirical therapy for bacteremia as receipt of vancomycin, daptomycin, or linezolid during the empirical therapy window.

Two statistical relationships were assessed: the association between documented prior MRSA colonization or infection and a subsequent MRSA-positive blood culture result, and the association between documented prior MRSA colonization or infection and receipt of MRSA-directed empirical therapy. Bivariate analyses were performed using the χ^2 test for categorical variables and the Student *t* test or the Wilcoxon rank sum test for continuous variables. Stratification was used to test for potential effect modification. Logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs). Logistic regression models included variables that were biologically associated with prior MRSA colonization or infection and the outcomes under study. Analyses were performed using SAS software, version 9.1 (SAS).

RESULTS

Overall, 25,472 patients had a blood culture performed and received empirical therapy during the study period. Of the 25,472 patients, 94 (0.4%) were excluded because of missing data. Of the 25,378 remaining patients included in the analysis, 2,074 (8.2%) had documented prior MRSA colonization or infection, 4,455 (17.6%) received MRSA-directed empirical therapy, and 287 (1.1%) had blood culture results that were positive for MRSA. Of the 287 patients with positive blood culture results, 75 (26.1%) had a documented history of MRSA colonization or infection. Those with documented prior MRSA colonization or infection tended to be younger, have more comorbid conditions, have blood samples collected earlier in their hospitalization, and have greater exposures to antibiotics than those without documented prior MRSA colonization or infection (Table 1).

Compared with patients without documented prior MRSA colonization or infection, patients with documented prior MRSA colonization or infection had 4 times the odds of having a subsequent MRSA-positive blood culture result (3.6% vs 0.91%; OR, 4.09 [95% CI, 3.13–5.34]). The magnitude of the effect remained similar (OR, 4.05 [95% CI, 3.02–5.44]) after controlling for intensive care unit stay during the index hospitalization, receipt of antibiotics during the previous year, age, sex, calendar year, and Charlson comorbidity index (Table 2).

The relationship between documented prior MRSA colonization or infection and a subsequent MRSA-positive blood culture result was modified by the length of time the patient was hospitalized before the blood sample was collected. Of the 287 samples with positive blood culture results, 236 (82%) were collected within 24 hours after admission. Stratified analysis suggested that there was a stronger association between documented prior MRSA colonization

or infection and a subsequent positive MRSA blood culture result among patients who were hospitalized for more than 24 hours before the blood sample was collected, compared with patients who were hospitalized for 24 hours or less before the blood sample was collected (OR, 13.86 [95% CI, 7.01–27.41] vs OR, 3.01 [95% CI, 2.17–4.18]), after controlling for intensive care unit stay during the index hospitalization, receipt of antibiotics during the previous year, age, sex, calendar year, and Charlson comorbidity index.

Documented prior MRSA colonization or infection was also significantly associated with receipt of MRSA-directed empirical therapy (OR, 3.46 [95% CI, 3.14–3.80]). The magnitude of the effect decreased to 2.79 (95% CI, 2.52–3.09) after controlling for intensive care unit stay during index hospitalization, calendar year, age, sex, receipt of antibiotics during the previous year, length of stay prior to blood sample collection, and Charlson comorbidity index. Among patients who had subsequent MRSA-positive culture results, documented prior MRSA colonization or infection was not significantly associated with receipt of MRSA-directed empirical therapy (OR, 1.27 [95% CI, 0.75–2.16]).

DISCUSSION

Prior MRSA colonization or infection that had been documented in medical records was the strongest predictor of both receipt of MRSA-directed empirical therapy and subsequent MRSA-positive blood culture results. Thus, besides its use for the control of MRSA infection, the maintenance of documentation of prior MRSA colonization or infection in medical records may be useful for the optimization of empirical antibiotic therapy.

We observed that the association between documented prior MRSA colonization or infection and subsequent MRSA-positive blood culture results was stronger among patients who had blood samples collected more than 24 hours after admission. Thus, the timing of the sample collection and the documentation of prior MRSA colonization or infection should be considered together during the selection of empirical therapy.

The strong association between documented prior MRSA colonization or infection and the receipt of MRSA-directed empirical therapy indicates that physicians may use this documentation when prescribing empirical therapy. If so, physicians should be encouraged to continue this practice. Because of the retrospective nature of this study, it is not known whether physician decisions were actually influenced by the documented prior MRSA colonization or infection or if other factors were responsible for this association. Furthermore, the future development of rapid screening tests for MRSA may decrease the need for MRSA-directed empirical therapy. However, documentation of prior MRSA colonization or infection could identify a subpopulation of patients at high risk for MRSA bacteremia, for whom the rapid test could be most useful or cost-effective.

Often, infection control interventions are only implemented if they are cost-effective or cost-saving from a hospital perspective.⁴ This study identifies the increased utility of documentation of prior MRSA colonization or infection beyond contact precautions. These findings should be incorporated into future business-case analyses of surveillance interventions for MRSA, which could lead to wider adoption of these interventions and improved patient safety.

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TABLE 1

Characteristics of the Study Population Stratified by Presence of Documented Prior MRSA Colonization or Infection

Patient characteristics	With documented prior MRSA colonization or infection (n = 2,074)	Without documented prior MRSA colonization or infection (n = 23,304)	Total (n = 25,378)	P
Age, mean $\pm$ SD, years	47 $\pm$ 14	50 $\pm$ 17	50 $\pm$ 16	<.01
Female sex	860 (41)	10,133 (43)	10,993 (43)	.08
Time from admission to culture, mean $\pm$ SD, days	1.4 $\pm$ 5.2	1.7 $\pm$ 3.9	1.7 $\pm$ 4.0	<.01
Presence of comorbidities				
HIV	98 (4.7)	517 (2.2)	615 (2.4)	<.01
Diabetes mellitus	439 (21)	3,899 (17)	4,338 (17)	<.01
Renal disease	82 (4.0)	731 (3.1)	813 (3.2)	.04
Liver disease	35 (1.7)	490 (2.1)	525 (2.1)	.20
Malignancy	211 (10)	3,767 (16)	3,978 (16)	<.01
Charlson comorbidity index, mean $\pm$ SD	2.4 $\pm$ 2.5	2.1 $\pm$ 2.4	2.1 $\pm$ 2.4	<.01
ICU stay during current hospitalization	289 (14)	4,875 (21)	5,164 (20)	<.01
Receipt of antibiotic during previous year	1,689 (81)	8,606 (37)	10,295 (41)	<.01

NOTE. Data are no. (%) of patients, unless otherwise indicated. MRSA, methicillin-resistant *Staphylococcus aureus*; HIV, human immunodeficiency virus; ICU, intensive care unit; SD, standard deviation.

TABLE 2

Components of Logistic Regression Models for Association With Prior Documented MRSA Colonization or Infection

Variable	Odds ratio (95% CI)	
	Subsequent culture results positive for MRSA	Receipt of MRSA-directed empirical therapy
Documented prior MRSA colonization or infection	4.05 (3.02–5.44)	2.79 (2.52–3.09)
ICU stay during current hospitalization	1.79 (1.37–2.35)	2.18 (2.01–2.37)
Year (reference 2001)		
2002	1.72 (1.03–2.88)	1.03 (0.91–1.18)
2003	2.33 (1.43–3.78)	1.63 (1.44–1.84)
2004	2.57 (1.60–4.14)	2.22 (1.97–2.50)
2005	2.57 (1.59–4.15)	2.75 (2.44–3.09)
Female sex	0.97 (0.76–1.22)	0.95 (0.88–1.01)
Age ^a	1.00 (0.99–1.00)	1.00 (1.00–1.00)
Receipt of antibiotic during previous year	0.98 (0.76–1.28)	1.58 (1.47–1.70)
Charlson comorbidity index	1.04 (0.99–1.09)	0.98 (0.97–1.00)
LOS prior to performance of culture ^{a,b}		1.51 (1.39–1.63)

NOTE. CI, confidence interval; ICU, intensive care unit; LOS, length of stay; MRSA, methicillin-resistant *Staphylococcus aureus*.

^a Age and LOS prior to performance of culture were treated as continuous variables.

^b This characteristic was not included in the logistic regression model of the relationship between documented prior MRSA colonization or infection and subsequent blood culture results positive for MRSA because it modified this association.