ORIGINAL ARTICLE

Identifying the Risk Factors for Hospital-Acquired Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infection among Patients Colonized with MRSA on Admission

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BACKGROUND.   Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major pathogen in hospital-acquired infections. MRSA-colonized inpatients who may benefit from undergoing decolonization have not been identified.

OBJECTIVE.   To identify risk factors for MRSA infection among patients who are colonized with MRSA at hospital admission.

DESIGN.   A case-control study.

SETTING.   A 146-bed Veterans Affairs hospital.

PARTICIPANTS.   Case patients were those patients admitted from January 2003 to August 2011 who were found to be colonized with MRSA on admission and then developed MRSA infection. Control subjects were those patients admitted during the same period who were found to be colonized with MRSA on admission but who did not develop MRSA infection.

METHODS.   A retrospective review.

RESULTS.   A total of 75 case patients and 150 control subjects were identified. A stay in the intensive care unit (ICU) was the significant risk factor in univariate analysis ($P < .001$). Prior history of MRSA ($P = .03$), transfer from a nursing home ($P = .002$), experiencing respiratory failure ($P < .001$), and receipt of transfusion ($P = .001$) remained significant variables in multivariate analysis. Prior history of MRSA colonization or infection ($P = .02$), difficulty swallowing ($P = .04$), presence of an open wound ($P = .002$), and placement of a central line ($P = .02$) were identified as risk factors for developing MRSA infection for patients in the ICU. Duration of hospitalization, readmission rate, and mortality rate were significantly higher in case patients than in control subjects ($P < .001, .001$, and $<.001$, respectively).

CONCLUSIONS.   MRSA-colonized patients admitted to the ICU or admitted from nursing homes have a high risk of developing MRSA infection. These patients may benefit from undergoing decolonization.

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Methicillin-resistant *Staphylococcus aureus* (MRSA) remains a major cause of hospital-acquired infection, although the Centers for Disease Control and Prevention (CDC) have reported that rates of invasive MRSA infection in healthcare settings have been declining.[1] MRSA infection is 4 times more frequent in MRSA carriers than in noncarriers.[2] Patients colonized with MRSA are at a significantly higher risk of developing staphylococcal infection than those colonized with methicillin-susceptible strains.[3] Since the MRSA control program at Veterans Affairs Pittsburgh Healthcare System (VAPHS)[4] was implemented, a significant decrease in the rate of MRSA transmission has been observed within the facility. As a consequence, MRSA infections with a hospital onset now occur primarily among patients who are admitted with MRSA colonization rather than those who acquire MRSA

during hospitalization. To date, no study has evaluated the risk factors for subsequent MRSA infection in MRSA carriers admitted to the hospital. In this study, we aimed to (1) identify the incidence and risk factors for subsequent MRSA infection among patients admitted with MRSA colonization and (2) identify MRSA-colonized patients who may benefit from undergoing decolonization.

MATERIAL AND METHODS

Setting and Study Population

The study was performed at VAPHS, with approval from the Institutional Review Board. VAPHS is a major tertiary care facility with 146 beds. An active surveillance program to detect MRSA colonization and prevent MRSA infection was

implemented on a surgical floor in October 2001 and then expanded to the surgical ICU in October 2003.[4] This surveillance program was later expanded to include the entire acute care division in August 2005, and in 2006 it expanded to become the national VA MRSA Prevention Initiative.[5]

Nasal secretion samples were obtained by swabbing both anterior nares and any wounds of all patients within 24 hours of admission, upon unit transfer, and upon discharge from the facility. From October 2001 until December 2007, nasal swab specimens were plated on CNA agar with broth enrichment. Beginning in December 2007, admission surveillance swab samples were processed using polymerase chain reaction (PCR) to identify MRSA (GeneOhm, Becton Dickinson) and discharge swab samples were plated on selective chromogenic agar (ChromAgar). Wound sample cultures were processed according to standard laboratory protocol that did not change during the study period. Contact precautions were implemented for patients whose test results indicated MRSA infection or colonization. MRSA infection was defined according to the current CDC definitions.[6]

Case patients were defined as patients who were admitted to VAPHS from January 2003 to August 2011, were revealed to be colonized with MRSA on admission, and then developed culture-proven MRSA infection between 48 hours after admission and 30 days after discharge. Eligible case patients were included in the study if they resided on a unit for which routine admission surveillance screening for MRSA was being performed. For the period January through September 2003, patients who were admitted to the surgical floor on which MRSA surveillance was first initiated were eligible for inclusion in the study. For the period October 2003 through September 2005, patients who were admitted to the surgical ICU were also eligible for study inclusion. Beginning in September 2005, all patients who were admitted to the acute care unit were eligible for inclusion in the study.

Patients for whom nasal swabs had MRSA-positive results were identified from infection control and microbiology records for the period January 2003 to August 2011. Patients with MRSA infection were identified from MRSA Prevention Initiative databases. If patients developed multiple MRSA infections during the study period, they were enrolled in the study for the first infection only.

For each case patient, 2 noninfected control subjects were randomly selected from the database of patients who had positive MRSA screening results on admission. Patients were not selected for inclusion as control subjects if they had received a full course of antibiotics that are empirically active against MRSA, even if no sample culture grew MRSA. Patients who experienced onset of MRSA infection within 48 hours after admission were ineligible to be included in the study as either case patients or control subjects. Case patients and control subjects were matched by calendar year of admission only.

Data Abstraction

We recorded age, sex, admission date, location, duration of stay, reason for admission, prior MRSA colonization or infection in the past 1 year, MRSA infection, transfer from a nursing home, whether bedbound or using a wheelchair, any comorbidities, immunosuppressant use, presence of indwelling devices, smoking, illicit drug use, whether overweight, whether experiencing respiratory failure, difficulty swallowing, presence of any open wounds, antimicrobial use, receipt of transfusion, surgery, duration of preoperative stay, readmission within 30 days from discharge, and death during hospitalization or within 30 days from discharge. Overweight was defined as body mass index of 25 or greater. Patients were considered to be experiencing respiratory failure if they required the use of a mechanical ventilator. Patients were considered to have difficulty swallowing if their diet was modified because of dysphagia or if they were receiving tube feeding. An open wound was defined as any surgical wound left open or any other skin breakdown.

Statistical Analysis

The Pearson χ^2 test and the t test were used for categorical variables when appropriate. Duration of ICU stay and duration of hospitalization were compared using the Mann-Whitney U test. A stepwise multivariate logistic regression model was used to select factors that were significantly associated with MRSA infection if a P value was less than .1 in univariate analysis. Two-way interactions were assessed after selection of the main effects. Analyses were performed using Stata/IC, version 10.1, and SPSS, version 20.0. All 2-tailed P values of .05 or less were considered to be significant.

RESULTS

Patient Population

The number of admissions to the facility from 2005 to 2011 was 37,421. A nasal swab sample that had positive results for MRSA was collected on admission in 34,311 cases (91.7%).

TABLE 1. Sites of Methicillin-Resistant *Staphylococcus aureus* Infection

Type of infection	No. of cases
Pneumonia	18
Line infection	15
Surgical-site infection	15
Skin and soft tissue infection	7
Urinary tract infection	6
Eye infection	5
Peritonitis	4
Osteomyelitis	1
Late graft infection	1
Perirectal abscess	1
Nasal pustule	1
Bacteremia with unknown source	1

The prevalence rate of MRSA as detected by nasal swab screening was 10.7%. The prevalence rate of MRSA as detected by clinical culture of samples collected on admission was 1.2%. The total prevalence rate of MRSA on admission was 11.9%. The average MRSA infection rate was 0.33 per 1,000 bed-days of care. The rate of MRSA surgical-site infection was 0.2%. No data were available for the period prior to 2005.

From January 2003 to August 2011, a total of 181 patients developed MRSA infection in the period between 48 hours after admission and 30 days from discharge. Among these 181 patients, 75 had evidence of MRSA colonization on admission; these individuals were included in the study as case patients. A total of 79 patients did not have evidence of MRSA colonization. Nasal swab specimens were not submitted on admission for testing for 27 patients during the period 2001–2005 because active surveillance was not performed on all floors in the facility until 2005. Of the 75 cases of MRSA colonization on patient admission, 42 were identified using plating on CNA agar and 33 were identified using PCR. Reasons for hospital admission were varied. A total of 4.0% of the case patients and 14.7% of the control subjects were admitted because of other infection; 21.3% of the case patients and 22.0% of the control subjects were admitted to undergo elective surgeries.

MRSA Infection

MRSA infection occurred at a mean of hospital-day 14 (interquartile range [IQR], 7–24 days). The observed sites of infection are presented in Table 1. Of these, hospital-acquired pneumonia was the most common; bacteremia occurred in 27 patients. Surgical-site infections occurred after a variety of surgical procedures (vascular graft surgery, laminectomy, open reduction and internal fixation for femur fracture, lower-extremity amputation, hernia repair, coronary artery

TABLE 2. Univariate Analysis: Risk Factors for Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infection

Variable	Case patients ($n = 75$)	Control subjects ($n = 150$)	P
Mean (range) age, in years	66.5 (41–86)	67 (19–94)	.78
Male sex	73 (97.3)	141 (94.0)	.27
ICU stay[a]	47 (62.7)	56 (37.3)	<.001
Prior history of MRSA colonization or infection in 1 year	40 (53.3)	49 (32.7)	.004
Hospitalization in the previous 1 year	57 (76.0)	95 (63.3)	.06
Transfer from nursing home	33 (44.0)	29 (19.3)	<.001
Bedbound or wheelchair use	15 (20.0)	21 (14.0)	.25
Diabetes	40 (53.3)	57 (38.0)	.03
End-stage renal disease	4 (5.3)	7 (4.7)	.83
End-stage liver disease	12 (16.0)	16 (10.7)	.25
Chronic obstructive lung disease	30 (40.0)	55 (36.7)	.63
Coronary artery disease	41 (54.7)	58 (38.7)	.02
Immunosuppressant use	10 (13.3)	15 (10.0)	.45
Foreign materials placement	14 (18.7)	29 (19.3)	.91
Smoking	21 (28.0)	35 (23.3)	.45
Drug use	7 (9.3)	26 (17.3)	.11
Overweight	44 (58.7)	79 (52.7)	.40
Indwelling urinary catheter	47 (62.7)	64 (42.7)	.005
Respiratory failure	27 (36.0)	13 (8.7)	<.001
Difficulty swallowing	34 (45.3)	26 (17.3)	<.001
Open wound	32 (42.7)	29 (19.3)	<.001
Decubitus ulcer	16 (21.3)	8 (5.3)	
Open surgical wound	5 (6.7)	2 (1.3)	
Skin breakdown in extremities	11 (14.7)	18 (12.0)	
Skin breakdown in other areas	3 (4.0)	2 (1.3)	
Antimicrobial use	43 (57.3)	59 (39.3)	.01
Transfusion	31 (41.3)	23 (15.3)	<.001
Central line	35 (46.7)	32 (21.3)	<.001
Surgery	27 (36.0)	53 (35.3)	.92
Long preoperative stay	2 (2.7)	9 (6.0)	.27

NOTE. Data are no. (%) unless otherwise indicated.
[a] The number of patients with MRSA infection who stayed in the intensive care unit (ICU) prior to developing infection was compared with the number of patients without MRSA infection who stayed in the ICU at any point during their hospitalization.

TABLE 3. Multivariate Logistic Regression Model: Risk Factors for Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infection

Variable	P	OR (95% CI)
Prior history of MRSA colonization or infection in 1 year	.03	2.15 (1.07–4.31)
Transfer from nursing home	.002	3.36 (1.56–7.23)
Coronary artery disease	.14	1.65 (0.85–3.22)
Respiratory failure	<.001	6.26 (2.38–16.47)
Open wound	.06	2.04 (0.96–4.25)
Transfusion	.001	6.45 (2.16–19.28)
Antimicrobial use	.65	1.21 (0.53–2.79)

NOTE. CI, confidence interval; OR, odds ratio.

bypass graft surgery, neck dissection, debridement of skin graft, hemilaryngotomy, hepatectomy, and pancreatectomy).

Risk Factors

In univariate analysis (Table 2), ICU stay, prior history of MRSA colonization or infection in the last 1 year, transfer from a nursing home, diabetes, coronary artery disease, placement of an indwelling urine catheter, respiratory failure, difficulty swallowing, presence of an open wound, antimicrobial use during hospitalization, receipt of transfusion, and presence of a central line were significantly associated with MRSA infection. In multivariate analysis (Table 3), prior history of MRSA colonization or infection, transfer from a nursing home, respiratory failure, and receipt of transfusion were significant risk factors.

Next, subgroup analysis was performed to identify risk factors for MRSA infection among patients who were and among patients who were not admitted to the ICU. In univariate analysis of ICU patients (Table 4), duration of ICU stay, respiratory failure, difficulty swallowing, presence of an open wound, and presence of a central line were significant risk factors. Duration of ICU stay prior to developing MRSA infection for case patients was compared with the total duration of ICU stay for control subjects. Among ICU patients, prior history of MRSA colonization or infection, difficulty swallowing, presence of an open wound, and placement of a central venous catheter remained significant risk factors in multivariate analysis (Table 5).

Antimicrobial use was considered to decrease the risk of infection because of the low odds ratio (OR) that occurred with this variable in multivariate analysis. We evaluated whether there was any interaction between antimicrobial use and other factors that influenced the OR statistically; however, no apparent interaction was found.

In univariate analysis of non-ICU patients (Table 6), prior history of MRSA colonization or infection, transfer from a nursing home, coronary artery disease, and smoking were significant risk factors. Transfer from a nursing home was the only significant risk factor for these patients in multivariate analysis (P = .001; OR [95% confidence interval], 5.00 [1.86–13.45]).

Outcomes

Patients who were hospitalized in the ICU and who developed MRSA infection stayed in the ICU for an additional 7 days (IQR, 0–14 days) after developing MRSA infection. The median duration of hospitalization for case patients was 17 days (IQR, 11–35 days), and for control subjects it was 5 days (IQR, 3–8 days; P < .001). A total of 25.3% of the case patients and 8.7% of the control subjects were readmitted within 30 days of hospital discharge (P = .001). A total of 24% of the case patients and 4% of the control subjects died during hospitalization or within 30 days of hospital discharge (P < .001).

DISCUSSION

This study sheds light on the risk factors for development of subsequent MRSA infection in patients admitted to the hospital with MRSA colonization. We identified populations of patients who are at high risk of developing MRSA infection after hospital admission. Admission to the ICU was a significant risk factor (P < .001) in univariate analysis. For patients in the ICU, prior history of MRSA infection or colonization, difficulty swallowing, the presence of an open wound, and the presence of a central venous catheter were risk factors. Among these patients, it is likely that both the severity of illness and the frequency of undergoing invasive procedures, such as insertion of a central venous catheter, promote infection by endogenously carried MRSA.[7] Prior history of *Staphylococcus aureus* is a known independent predictor of subsequent *S. aureus* infection.[8] Why previously identified colonization or infection with MRSA is an independent risk factor for MRSA infection is not clear from our data. It may be possible that patients with long-established colonization, as opposed to those who are recently identified as being colonized, have additional risk factors for MRSA infection that are not identified by our data.

For non-ICU patients, transfer from a nursing home was the only significant risk factor for developing subsequent MRSA infection. Most of these patients were transferred from a nearby VA long-term care facility, where the average MRSA prevalence rate is 44%; despite this high prevalence rate, how-

TABLE 4. Univariate Analysis: Risk Factors for Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infection in Intensive Care Unit (ICU) Patients

Variable	Case patients (n = 47)	Control subjects (n = 56)	P
Male sex	45 (95.7)	54 (96.4)	>.99
Mean duration of ICU stay	13.4	6.1	.01
Prior history of MRSA colonization or infection in 1 year	24 (51.1)	18 (32.1)	.07
Hospitalization in the previous 1 year	36 (76.6)	40 (71.4)	.66
Transfer from nursing home	17 (36.2)	13 (23.2)	.19
Bedbound or wheelchair use	13 (27.7)	7 (12.5)	.08
Diabetes	25 (53.2)	25 (44.6)	.43
End-stage renal disease	2 (4.3)	5 (8.9)	.45
End-stage liver disease	6 (12.8)	9 (16.1)	.78
Chronic obstructive lung disease	20 (42.6)	19 (33.9)	.42
Coronary artery disease	24 (51.1)	23 (41.1)	.33
Immunosuppressant use	6 (12.8)	3 (5.4)	.29
Foreign materials placement	7 (14.9)	12 (21.4)	.45
Smoking	10 (21.3)	17 (30.4)	.37
Drug use	4 (8.5)	11 (19.6)	.16
Overweight	27 (57.4)	25 (44.6)	.24
Indwelling urinary catheter	39 (83)	38 (67.9)	.11
Respiratory failure	27 (57.4)	13 (23.2)	.001
Difficulty swallowing	32 (68.1)	16 (28.6)	<.001
Open wound	22 (46.8)	10 (17.9)	.003
Decubitus ulcer	12 (25.5)	3 (5.4)	
Open surgical wound	3 (6.4)	1 (1.8)	
Skin breakdown in extremities	8 (17.0)	6 (10.7)	
Skin breakdown in other areas	2 (4.3)	0 (0)	
Antimicrobial use	30 (63.8)	25 (44.6)	.07
Transfusion	27 (57.4)	23 (41.1)	.12
Central line	32 (68.1)	18 (32.1)	<.001
Surgery	19 (40.4)	30 (53.6)	.24

NOTE. Data are no. (%) unless otherwise indicated.

ever, the average MRSA infection rate at this facility is 0.5 per 1,000 patient-days. This suggests that a nursing home patient experiencing an acute illness requiring transfer to acute care is at high risk for acquiring a MRSA infection if colonized at the time of transfer. However, it is important to note that our study was performed in a VA facility, where the patterns of transfer between acute care and long-term care facilities are likely to be different from those for non-VA facilities.

Although benefits have been reported of decolonizing *S.*

aureus carriers to prevent *S. aureus* surgical-site infection[9-11] and nosocomial *S. aureus* infection in ICU settings,[12] some studies have shown no benefit of decolonization.[13] The role of decolonizing MRSA carriers to decrease the risk of hospital-acquired MRSA infection has not yet been evaluated. Although our data may be insufficient to apply to other diverse patient populations, we have identified high-risk populations who would be suitable candidates on which to perform decolonization to prevent hospital-acquired MRSA infection. Patients with MRSA colonization who are admitted

TABLE 5. Multivariate Logistic Regression Model: Risk Factors for Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infection in Intensive Care Unit (ICU) Patients

Variable	P	OR (95% CI)
Duration of ICU stay	.51	1.02 (0.97–1.06)
Prior history of MRSA colonization or infection in 1 year	.02	3.69 (1.22–11.13)
Respiratory failure	.17	2.45 (0.69–8.73)
Difficulty swallowing	.04	4.17 (1.08–16.10)
Open wound	.002	6.46 (1.98–21.14)
Antimicrobial use	.03	0.25 (0.07–0.89)
Central line	.02	3.30 (1.12–9.69)

NOTE. CI, confidence interval; OR, odds ratio.

TABLE 6. Univariate Analysis: Risk Factors for Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infection in Non–Intensive Care Unit (ICU) Patients

Variable	Case patients ($n = 28$)	Control subjects ($n = 94$)	P
Male sex	28 (100.0)	87 (92.6)	.35
Prior history of MRSA colonization or infection in 1 year	16 (57.1)	31 (33.0)	.03
Hospitalization in the previous 1 year	22 (78.6)	55 (58.5)	.07
Transfer from nursing home	16 (57.1)	16 (17.0)	<.001
Bedbound or wheelchair use	2 (7.1)	14 (14.9)	.36
Diabetes	15 (53.6)	32 (34.0)	.08
End-stage renal disease	2 (7.1)	2 (2.1)	.23
End-stage liver disease	6 (21.4)	7 (7.4)	.07
Chronic obstructive lung disease	10 (35.7)	36 (38.3)	>.99
Coronary artery disease	17 (60.7)	35 (37.2)	.03
Immunosuppressant use	4 (14.3)	12 (12.8)	.76
Foreign materials placement	7 (25.0)	17 (18.1)	.43
Smoking	11 (39.3)	18 (19.1)	.04
Drug use	3 (10.7)	15 (16.0)	.76
Overweight	17 (60.7)	54 (57.4)	.83
Indwelling urinary catheter	8 (28.6)	26 (27.7)	>.99
Respiratory failure	0 (0.0)	0 (0.0)	>.99
Difficulty swallowing	2 (7.1)	10 (10.6)	.73
Open wound	10 (35.7)	19 (20.2)	.13
Antimicrobial use	13 (46.4)	34 (36.2)	.38
Transfusion	4 (14.3)	0 (0.0)	.002
Central line	3 (10.7)	14 (14.9)	.76
Surgery	8 (28.6)	23 (24.5)	.63

NOTE. Data are no. (%) unless otherwise indicated.

from nursing homes or who are admitted to ICUs and undergo invasive procedures may benefit from decolonization. This is a suitable subject to examine in future controlled trials.

There are some limitations to this study. In the VA MRSA Prevention Initiative, nasal swab sampling is used as the screening tool. Although this sampling method provides the best sensitivity to identify patients with MRSA colonization,[14] and although the results of a previous study suggested that nasal-only screening does not miss a large number of MRSA-colonized patients in VA systems,[15] we may have failed to identify some MRSA-colonized patients. Second, the patient population we studied changed over time: MRSA surveillance was initiated on a single unit and was later introduced to other units. Finally, this study was performed in a single VA hospital and as such, the result may not be able to be applied to other diverse populations.

In summary, this study has revealed that prior history of MRSA colonization or infection, transfer from a nursing home, respiratory failure, and undergoing transfusion were the significant risk factors of developing hospital-acquired MRSA infection among patients colonized with MRSA. Prior history of MRSA colonization or infection, difficulty swallowing, presence of an open wound, and central line placement were risk factors for MRSA infection in ICU patients. Although the rate of hospital-acquired MRSA infection has been decreasing in the United States, large, multicenter trials to evaluate the efficacy and cost-effectiveness of active sur-

veillance and decolonization among high-risk patients will be vital to eliminate MRSA infection in this setting.

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