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ORIGINAL ARTICLE

Epidemiology of Methicillin-Resistant *Staphylococcus aureus* Colonization in a Surgical Intensive Care Unit

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BACKGROUND.   Methicillin-resistant *Staphylococcus aureus* (MRSA) is a cause of healthcare-associated infections among surgical intensive care unit (ICU) patients, though transmission dynamics are unclear.

OBJECTIVE.   To determine the prevalence of MRSA nasal colonization at ICU admission, to identify associated independent risk factors, to determine the value of these factors in active surveillance, and to determine the incidence of and risk factors associated with MRSA acquisition.

DESIGN.   Prospective cohort study.

SETTING.   Surgical ICU at a teaching hospital.

PATIENTS.   All patients admitted to the surgical ICU.

RESULTS.   Active surveillance for MRSA by nasal culture was performed at ICU admission during a 15-month period. Patients who stayed in the ICU for more than 48 hours had nasal cultures performed weekly and at discharge from the ICU, and clinical data were collected prospectively. Of 1,469 patients, 122 (8%) were colonized with MRSA at admission; 75 (61%) were identified by surveillance alone. Among 775 patients who stayed in the ICU for more than 48 hours, risk factors for MRSA colonization at admission included the following: hospital admission in the past year (1-2 admissions: adjusted odds ratio [aOR], 2.60 [95% confidence interval {CI}, 1.47-4.60]; more than 2 admissions: aOR, 3.56 [95% CI, 1.72-7.40]), a hospital stay of 5 days or more prior to ICU admission (aOR, 2.54 [95% CI, 1.49-4.32]), chronic obstructive pulmonary disease (aOR, 2.16 [95% CI, 1.17-3.96]), diabetes mellitus (aOR, 1.87 [95% CI, 1.10-3.19]), and isolation of MRSA in the past 6 months (aOR, 8.18 [95% CI, 3.38-19.79]). Sixty-nine (10%) of 670 initially MRSA-negative patients acquired MRSA in the ICU (corresponding to 10.7 cases per 1,000 ICU-days at risk). Risk factors for MRSA acquisition included tracheostomy in the ICU (aOR, 2.18 [95% CI, 1.13-4.20]); decubitus ulcer (aOR, 1.72 [95% CI, 0.97-3.06]), and receipt of enteral nutrition via nasoenteric tube (aOR, 3.73 [95% CI, 1.86-7.51]), percutaneous tube (aOR, 2.35 [95% CI, 0.74-7.49]), or both (aOR, 3.33 [95% CI, 1.13-9.77]).

CONCLUSIONS.   Active surveillance detected a sizable proportion of MRSA-colonized patients not identified by clinical culture. MRSA colonization on admission was associated with recent healthcare contact and underlying disease. Acquisition was associated with potentially modifiable processes of care.

Staphylococcus aureus is one of the most frequent causes of nosocomial infection in intensive care unit (ICU) patients.[1] The proportion of *S. aureus* isolates with methicillin resistance is increasing in both the United States and several European countries.[2,3] Nasal colonization with *S. aureus* predisposes to subsequent infection, particularly in surgical patients.[4-6] Infections caused by methicillin-resistant *S. aureus* (MRSA) have been associated with increased mortality and hospital costs, compared with methicillin-susceptible strains.[7-9]

Unidentified MRSA carriers serve as a potential reservoir for transmission.[10] Active surveillance for MRSA, using screening cultures and aggressive contact precautions, has been shown to reduce MRSA transmission.[10-12] The use of active surveillance helps in the determination of the prevalence and incidence of MRSA colonization in a given area or institution, though some studies have had incomplete data for admission screening cultures,[13,14] potentially leading to biased estimates of these values. In addition, screening of all patients may be an overwhelming and costly task. Screening of patients at high-risk and those with known risk factors for MRSA colonization may be more feasible. Selective screening of patients for MRSA, combined with aggressive infection control measures, has been demonstrated to be an effective and cost-effective method to reduce MRSA transmission.[11,12,15,16] However, selective screen-

ing methods are often chosen on the basis of generalized risk factors rather than identified patient-specific risk factors in a given patient population.

The purpose of this study was to implement active surveillance for MRSA in a surgical ICU and to obtain high capture rates for admission surveillance cultures in order to accurately determine the prevalence of MRSA nasal colonization at ICU admission. Independent risk factors associated with MRSA colonization on admission were also ascertained, and the predictive value of the multivariate model was determined to assess the value of these factors as a screening tool for future active surveillance. In addition, we sought to determine the incidence of and risk factors associated with MRSA acquisition.

METHODS

This was a 15-month prospective cohort study conducted from December 2002 through February 2004 in the surgical ICU at Barnes-Jewish Hospital (BJH). BJH is a 1,251-bed, urban, tertiary care teaching hospital in St. Louis, Missouri. The burn, trauma, and surgical ICU has 24 beds and approximately 1,400 admissions per year.

MRSA active surveillance was instituted in the surgical ICU by the hospital infection control department in December 2002. Nasal culture for *S. aureus* was performed for all patients admitted to the ICU who stayed for more than 12 hours. Nasal swab specimens for culture were also obtained weekly and at discharge from the ICU for all patients who stayed in the ICU for more than 48 hours. A specimen was collected from both anterior nares of each patient. Collected specimens were transported and stored at room temperature. Mannitol salt agar plates (Becton Dickinson) were inoculated directly with swab specimens. The mannitol salt agar plates were incubated for 24-48 hours at 35°C and examined for growth. Strains that produced yellow colonies on the screening mannitol salt agar plates were confirmed as *S. aureus* by means of Gram staining, 3% catalase testing, and coagulase testing with the Staph Latex agglutination assay (LifeSign). Detection of MRSA was performed by subculturing confirmed *S. aureus* isolates in Trypase soy broth with 5% sheep blood (Becton Dickinson), then on oxacillin screening agar containing 6.0 μg/mL of oxacillin (Becton Dickinson). Plates were incubated at 35°C for 18-24 hours and examined for evidence of growth. Strains showing distinct growth were considered to be methicillin resistant.

Data collected for all study patients included demographic characteristics, hospital and ICU admission dates, admission to BJH in the past 12 months, location prior to hospital admission (ie, home, another hospital, or a long-term care facility), use of contact precautions, and hospital and ICU discharge dates and discharge status. Additional data were collected for patients who remained in the ICU for more than 48 hours, including past medical history, ICU processes of care and medications received, and use of mechanical ventilation and/or central venous catheters. Each nasoenteric tube used was identified as a nasogastric or Dobhoff tube. Each percutaneous feeding tube was defined as a gastrostomy, jejunostomy, or gastrojejunostomy tube. In accordance with hospital policy, patients found to be colonized or infected with MRSA, vancomycin-resistant enterococci (VRE), *Clostridium difficile* (associated with diarrhea), and certain multidrug-resistant, gram-negative bacilli were placed under contact precautions. In addition, patients with a history of colonization with these organisms were identified and placed under contact precautions at admission. Decolonization therapy for MRSA was not routinely done. All positive clinical culture results and ICU-related infections were recorded. Infections were defined using the National Nosocomial Infection Surveillance system criteria.[17]

MRSA colonization at admission was defined as an admission nasal surveillance culture positive for MRSA or any clinical culture positive for MRSA within 48 hours after ICU admission. MRSA acquisition was defined as an admission nasal surveillance culture negative for MRSA and subsequent isolation of MRSA from a surveillance or clinical culture performed more than 48 hours after admission. Incidence density was calculated as the number of cases of MRSA acquisition per 1,000 total patient-days and per 1,000 days at risk for MRSA colonization (ie, days on which a given patient had no MRSA detected). At-risk ICU-days were calculated by excluding from the denominator the ICU-days of patients colonized with MRSA on admission, and only including patient-days occurring prior to MRSA colonization for those acquiring MRSA in the ICU.

Statistical analysis was performed using SPSS for Windows, version 12.0 (SPSS). Sensitivity, specificity, and positive and negative predictive values were all calculated using standard methodology.[18] Categorical variables were analyzed using the χ^2 test or Fisher's exact test, as appropriate, and analysis of continuous variables was performed using the Wilcoxon rank-sum test. Two-tailed tests were used, and $P < .05$ was considered statistically significant. Previously known risk factors or clinically relevant significant variables from the univariate analysis were considered for inclusion in multivariate logistic regression analysis. Backward stepwise logistic regression was performed, and the model that was considered biologically plausible and had the lowest -2 log likelihood ratio was chosen as the final model. Variables were tested for first-order interaction effects, and none were noted. The Hosmer and Lemeshow goodness-of-fit test was used to assess model fit. The Washington University Institutional Review Board approved this study.

RESULTS

During the study period, 1,469 (98%) of 1,494 patients admitted to the ICU had an admission nasal culture performed.

TABLE 1. Demographic Characteristics of 775 Patients Who Stayed in the Surgical Intensive Care Unit (ICU) for More Than 48 Hours for Whom a Nasal Swab Specimen Was Obtained at Admission

Variable	Value
Baseline patient characteristics	
Male sex	458 (59)
Age in years	
Median (range)	60 (17-97)
Mean	58
White race	585 (76)
Contact precautions at time of ICU admission	82 (11)
Admission to BJH in past 12 months	
None	539 (70)
1-2 admissions	170 (22)
>2 admissions	66 (8)
Location prior to hospital admission	
Home	608 (78)
Long-term care facility	21 (3)
Other hospital	146 (19)
Pre-ICU LOS in days	
Median (range)	0 (0-143)
Mean	4
Conditions present at admission	
Congestive heart failure	79 (10)
COPD	106 (14)
Malignancy (current diagnosis)	129 (17)
Chemotherapy (in the past 28 days)	11 (1)
Chronic skin disease	8 (1)
Diabetes mellitus	187 (24)
Systemic corticosteroid use (in the past 28 days)	58 (8)
Baseline renal function	
Normal	690 (89)
Chronic renal failure	58 (8)
Chronic renal failure with dialysis	27 (4)
Cirrhosis	36 (5)
Solid organ or bone marrow transplant	15 (2)
Surgical procedure	
Prior to admission (within past 3 months)	150 (19)
Current hospitalization	633 (82)
Burn patient	11 (1)
Antibiotic use and resistant organisms	
MRSA isolated in past 6 months	29 (4)
Any infection in past 3 months	143 (18)
Antibiotic use in past 3 months	160 (21)
C. difficile–associated diarrhea in past 3 months	19 (2)
VRE isolated in past 3 months	38 (5)
MRSA colonized on admission	82 (11)
ICU-related events	
Tracheostomy	
None	585 (76)
Present on admission to ICU	27 (3)
Performed while in ICU	163 (21)
Decubitus ulcer in ICU	171 (22)
CVC	
Present	539 (71)
Duration, median total CVC–days (range)	7 (0-63)

(Continued)

TABLE 1. *(Continued)*

Variable	Value
Mechanical ventilation	
Received	592 (76)
Median ventilator-days (range)	4 (0-66)
Reintubation	85 (11)
Systemic corticosteroid use	73 (9)
Antacid use	41 (5)
H_2 antagonist use	667 (86)
Sucralfate use	7 (1)
Vasopressor use	299 (39)
Enteral nutrition	
None	483 (62)
Via nasoenteric tube[a]	212 (27)
Via percutaneous tube[b]	43 (6)
Via nasoenteric and percutaneous tube	37 (5)
Total parenteral nutrition	224 (29)
Outcomes	
Median ICU LOS in days (range)	6 (3-76)
Median hospital LOS in days (range)	19 (4-219)
Hospital discharge status	
Death	109 (14)
Discharged home	349 (45)
Discharged to LTC facility	277 (36)
Discharged to other hospital	40 (5)

NOTE. Data are no. (%) of patients, unless otherwise specified. BJH, Barnes-Jewish Hospital; COPD, chronic obstructive pulmonary disease; CVC, central venous catheter; LOS, length of stay, LTC, long-term care; MRSA, methicillin-resistant *Staphylococcus aureus;* VRE, vancomycin-resistant enterococci.
[a] Nasoenteric tube includes nasogastric tubes and Dobhoff tubes.
[b] Percutaneous tube includes gastrostomy, jejunostomy, and gastrojejunostomy tubes.

Of those from whom a nasal swab specimen was obtained, 122 (8%) were colonized with MRSA on admission to the ICU. Of these 122 patients, 75 (61%) had MRSA colonization detected by surveillance culture alone while they were in the ICU. Two patients (2%) had MRSA colonization detected by clinical culture alone.

Risk factor analysis was performed only for the 775 (53%) patients who stayed in the ICU for more than 48 hours and had a nasal swab specimen obtained at admission (Table 1). The median age of admitted patients was 60 years (range, 17-97 years), and 458 (59%) were male. Eighty-two (11%) of 775 patients who stayed in the ICU more than 48 hours were colonized with MRSA (Table 2). Patients with MRSA colonization on admission were likely to have had recent healthcare contact, defined as admission to BJH in the past year, admission from a long-term care facility or from another hospital, or a pre-ICU hospital length of stay of at least 5 days, compared with patients who were not colonized on admission (85% vs 52%, $P < .001$). On multivariate testing, factors independently associated with MRSA colonization on

TABLE 2.   Comparison of Patients With and Patients Without Methicillin-Resistant *Staphylococcus aureus* (MRSA) Colonization on Admission to the Surgical Intensive Care Unit (ICU)

| Variable | Univariate analysis, value | | | Multivariate analysis: aOR[a] (95% CI) |
	Patients with MRSA (*n* = 693)	Patients without MRSA (*n* = 82)	*P*	
Male	408 (59)	50 (61)	.714	
Median age in years (range)	59 (17-97)	67 (23-96)	.008	
Race (white)	520 (75)	65 (79)	.400	
Admission to BJH in past 12 months				
None	507 (73)	32 (39)	Ref[b,c]	Ref
1-2 admissions	140 (20)	30 (37)	<.001	2.60 (1.47-4.60)
>2 admissions	46 (7)	20 (24)	<.001	3.56 (1.72-7.40)
Location prior to hospital admission				
Home	552 (80)	56 (68)	Ref[b]	
Long-term care facility	13 (2)	8 (10)	<.001	
Other hospital	128 (18)	18 (22)	.257	
Pre-ICU LOS of ≥5 days	132 (19)	36 (44)	<.001	2.54 (1.49-4.32)
Conditions present at admission				
Congestive heart failure	63 (9)	16 (20)	.003	
COPD	84 (12)	22 (27)	<.001	2.16 (1.17-3.96)
Malignancy (current diagnosis)	114 (16)	15 (18)	.672	
Chemotherapy (in the past 28 days)	8 (1)	3 (4)	.101	
Chronic skin disease	7 (1)	1 (1)	.593	
Diabetes mellitus	152 (22)	35 (43)	<.001	1.87 (1.10-3.19)
Systemic corticosteroid use (in the past 28 days)	49 (7)	9 (11)	.204	
Baseline renal function				
Normal	623 (90)	67 (82)	Ref[b]	
CRF	45 (6)	13 (16)	.004	
CRF with dialysis	25 (4)	2 (2)	.692	
Cirrhosis	32 (5)	4 (5)	.786	
Solid organ or bone marrow transplant	14 (2)	1 (1)	1.0	
Surgical procedure				
Prior to admission (in the past 90 days)	120 (17)	30 (37)	<.001	
During current ICU stay	562 (81)	71 (87)	.224	
Burn patient	11 (2)	0 (0)	.617	
Tracheostomy present at admission	20 (3)	7 (8)	.018	
Antibiotic use and resistant organisms				
MRSA isolated in past 6 months	11 (2)	18 (22)	<.001	8.18 (3.38-19.79)
Any infection in past 3 months	108 (16)	35 (43)	<.001	
Antibiotic use in past 3 months	125 (18)	35 (43)	<.001	
C. difficile–associated diarrhea in past 3 months	11 (2)	8 (10)	<.001	
VRE isolated in past 3 months	26 (4)	12 (15)	<.001	

NOTE.   Data are no. (%) of patients, unless otherwise specified. aOR, adjusted odds ratio; BJH, Barnes-Jewish Hospital; *C. difficile, Clostridium difficile;* COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; LOS, length of stay; Ref, reference category; VRE, vancomycin-resistant enterococci.

[a] Other variables considered for inclusion into the final model: admission from a long-term care facility, infection in the past 3 months, antibiotic use in past 3 months, *C. difficile*–associated diarrhea in past 3 months, VRE colonization in past 3 months, and surgical procedure in the 3 months prior to admission.

[b] Obtained from univariate logistic regression analysis.

[c] χ^2 for trend, 48.31; *P* < .001.

admission were as follows: 1 or 2 admissions to BJH in the past year (adjusted odds ratio [aOR], 2.60 [95% confidence interval {CI}, 1.47-4.60]), more than 2 admissions to BJH in the past year (aOR, 3.56; 95% CI, 1.72-7.40]), a hospital length of stay of 5 days or more prior to admission to the surgical ICU (aOR, 2.54 [95% CI, 1.49-4.32]), chronic ob-structive pulmonary disease (aOR, 2.16 [95% CI, 1.17-3.96), diabetes mellitus (aOR, 1.87 [95% CI, 1.10-3.19), and iso-lation of MRSA in the past 6 months (aOR, 8.18 [95% CI, 3.38-19.79]) (Table 2).

The predictive ability of the model to detect MRSA col-onization on admission in patients who stayed in the ICU

TABLE 3.   Sensitivity and Specificity of Independent Risk Factor Variables for Prediction of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Colonization Among Patients Who Stayed in the Surgical Intensive Care Unit (ICU) for More Than 48 Hours

Variable	Sensitivity, %	Specificity, %	Percentage of patients admitted to ICU
One predictor variable			
A: Admission to BJH in past year	61	73	30
B: Pre-ICU LOS of ≥5 days	44	81	22
C: MRSA isolated in the past 6 months	22	98	4
D: Chronic obstructive pulmonary disease	27	88	14
E: Diabetes mellitus	43	78	24
Predictor variable A, B, or C	79	61	43
Any predictor variable	89	45	58

NOTE.   BJH, Barnes-Jewish Hospital; LOS, length of stay.

for more than 48 hours is shown in Table 3. Presence of at least 1 of the independent risk factors had a sensitivity of 89% and a specificity of 45% for identification of a patient with MRSA colonization on admission. Use of the risk factors as a screening tool for active surveillance would lower the percentage of ICU patients from whom admission surveillance swab specimens were required to 58%. In this cohort, the positive predictive value of this screening method was 16%, and the negative predictive value was 97%.

Of the 693 patients who were initially culture negative for MRSA and who remained in the ICU for more than 48 hours, 669 (97%) had at least 1 follow-up nasal surveillance culture performed (range, 1-10 cultures). One additional patient did not have a follow-up nasal culture performed but was found to be MRSA positive by routine clinical culture and was included in the analysis (Figure). Sixty-nine patients (10%) were newly colonized with MRSA on follow-up (9.5 cases per 1,000 ICU-days; 10.7 cases per 1,000 patient-days at risk). The median time to culture positivity was 8 days (range, 2-24 days). Twenty-seven (39%) of 69 patients were identified by surveillance culture alone, and another 5 (7%) were detected by routine clinical culture alone. The time from the culture date (ie, the date the swab specimen for culture was obtained) to the availability of results was a median of 3 days. Of the patients who acquired MRSA, 16 (23%) developed an MRSA infection during their ICU stay (8 bloodstream infections, 3 cases of ventilator-associated pneumonia, and 5 other infections [eg, intra-abdominal abscess, surgical site infection, or pneumonia]).

Risk factors associated with acquisition of MRSA in the surgical ICU on univariate analysis are shown in Table 4. Risk factors included in the final multivariate model were tracheostomy in the ICU (aOR, 2.18 [95% CI, 1.13-4.20]), development of a decubitus ulcer while in the ICU (aOR, 1.72 [95% CI, 0.97-3.06]), and enteral nutrition via nasoenteric tube (aOR, 3.51 [95% CI, 1.74 to 7.07]), via percutaneous feeding tube (aOR, 2.35 [95% CI, 0.74-7.49]), or both nasoenteric and percutaneous tube (aOR, 3.33 [95% CI, 1.13-9.77]) (Table 4). The presence of decubitus ulcers was retained in the multi-

variate model, even though the *P* value was greater than .05, because the aORs of the other variables changed more than 10% when the risk factor was removed from the model.

DISCUSSION

Multiple studies have performed active surveillance for MRSA and examined risk factors associated with MRSA colonization, though few have achieved the extremely high initial surveillance culture capture rates achieved in this study population. Nasal specimens for surveillance culture were obtained from 98% of all patients admitted to the ICU in this study, increasing the validity of the MRSA prevalence estimate. Eight percent of all patients admitted to this ICU were already colonized with MRSA. Other ICU populations have reported admission prevalence rates of 4%-9%.[12-14,19] Of the patients colonized with MRSA on admission, 61% never had an MRSA-positive clinical culture during their ICU stay.
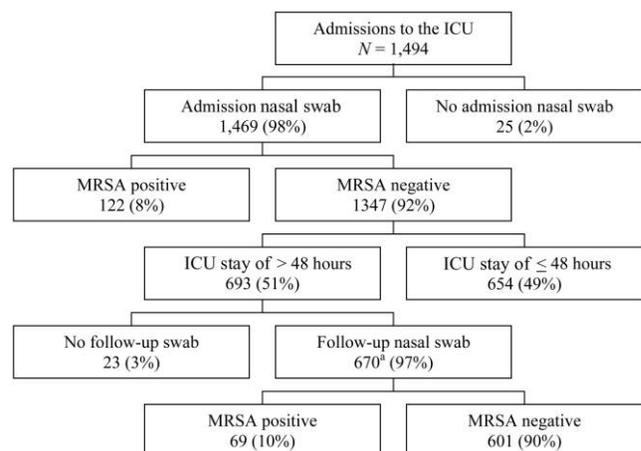

FIGURE   Distribution of the study population. Data are no. (%) of patients. ICU, intensive care unit, MRSA, methicillin-resistant *Staphylococcus aureus*. [a]One patient did not have a follow-up nasal swab specimen obtained but was determined to be MRSA positive by clinical culture and was included in the analysis.

TABLE 4. Analysis of Risk Factors and Outcomes Associated With Acquisition of Methicillin-Resistant *Staphylococcus aureus* (MRSA) During Surgical Intensive Care Unit Stay

Variable	Univariate analysis, value			Multivariate analysis: aOR[a] (95% CI)
	Patients with MRSA (n = 601)	Patients without MRSA (n = 69)	P	
Patient characteristics				
Male sex	353 (59)	41 (59)	.913	
Age, median years (range)	60 (17-94)	57 (19-96)	.998	
White race	453 (75)	48 (70)	.293	
Conditions present at admission				
Congestive heart failure	52 (9)	11 (16)	.049	
COPD	68 (11)	14 (20)	.031	
Malignancy (current diagnosis)	105 (18)	7 (10)	.122	
Chemotherapy (in the past 28 days)	8 (1)	0 (0)	1.0	
Chronic skin disease	6 (1)	1 (1)	.534	
Diabetes mellitus	126 (21)	21 (30)	.072	
Systemic corticosteroid use (in the past 28 days)	42 (7)	5 (7)	1.0	
Renal function				
Normal	540 (90)	62 (90)	Ref[b]	
CRF	37 (6)	7 (10)	.249	
CRF with dialysis	24 (4)	0 (0)	.998	
Cirrhosis	32 (5)	0 (0)	.065	
Solid organ or bone marrow transplant	14 (2)	0 (0)	.382	
Surgical procedure				
Prior to admission (in the past 90 days)	110 (18)	7 (10)	.091	
Current admission	486 (81)	63 (91)	.033	
Burn patient	9 (2)	1 (1)	1.0	
Antibiotic use and resistant organisms				
MRSA isolated in past 6 months	6 (1)	4 (6)	.013	
Any infection in past 3 months	91 (15)	12 (17)	.599	
Antibiotic use in past 3 months	112 (19)	9 (13)	.253	
C. difficile–associated diarrhea in past 3 months	11 (2)	0 (0)	.615	
VRE isolated in past 3 months	20 (3)	4 (6)	.297	
ICU-related events				
Tracheostomy performed while in ICU	106 (18)	37 (54)	<.001	2.18 (1.13-4.20)
Decubitus ulcer	115 (19)	32 (46)	<.001	1.72 (0.97-3.06)[c]
CVC				
Present	404 (67)	58 (84)	.004	
Duration, median CVC-days (range)	7 (0-63)	14 (0-62)	<.001	
Mechanical ventilation				
Received	443 (74)	62 (90)	.003	
Duration, median ventilator-days (range)	3 (0-66)	15 (0-60)	<.001	
Reintubation	60 (10)	13 (19)	.025	
Systemic corticosteroid use	53 (9)	7 (10)	.715	
Antacid use	31 (5)	4 (6)	.775	
H₂ antagonist use	515 (86)	62 (90)	.343	
Sucralfate use	6 (1)	0 (0)	1.0	
Vasopressor use	206 (34)	40 (58)	<.001	
Enteral nutrition				
None	400 (67)	17 (25)	Ref[b]	Ref
Via nasoenteric feeding tube	148 (25)	38 (55)	<.001	3.51 (1.74-7.07)
Via percutaneous feeding tube	28 (5)	5 (7)	.008	2.35 (0.74-7.49)
Via nasoenteric and percutaneous tube	25 (4)	9 (13)	.001	3.33 (1.13-9.77)
Total parenteral nutrition	163 (27)	20 (29)	.742	
Outcomes				
Median ICU LOS in days (range)	6 (3-66)	18 (3-76)	<.001	
Median hospital LOS in days (range)	18 (4-219)	28 (7-96)	<.001	
Death during hospitalization	65 (11)	14 (20)	.021	

NOTE. Data are no. (%) of patients, unless otherwise specified. aOR, adjusted odds ratio; *C. difficile, Clostridium difficile;* COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; CVC, central venous catheter; LOS, length of stay; Ref, reference category; VRE, vancomycin-resistant enterococci.

[a] Other variables considered for inclusion into the model: no. of CVC-days, no. of mechanical ventilation–days, and vasopressor use.

[b] Obtained from univariate logistic regression.

[c] Retained in final model because of its confounding effect (see Methods).

Other studies have found similar detection rates, with only 25%-60% of all MRSA-colonized patients detected by routine clinical culture.[12,19-22] There is ongoing debate concerning the effectiveness of contact precautions to reduce transmission of MRSA or other antibiotic-resistant organisms.[22] However, reliance on routine clinical cultures alone leaves many MRSA carriers undetected, which is likely to compromise the overall success of infection control measures.

Patients with a history of MRSA colonization in the previous 6 months were 8 times more likely to be colonized with MRSA on admission to the ICU. Estimates of long-term persistence of MRSA colonization vary widely, from several months to more than 3 years.[23-26] Decolonization therapy, including intranasal mupirocin therapy and chlorhexidine baths, have been used with varying degrees of success to decrease the prevalence of long-term colonization.[27] The efficacy of these methods depends on the antimicrobial agent, the body site, and whether MRSA is endemic in a particular setting.[27] Future studies are planned in our ICU in which decolonization therapy will be implemented to reduce the prevalence of MRSA colonization.

Recent healthcare contact was a predominant risk factor associated with MRSA colonization on admission in the surgical ICU in this study, which is a common finding in other investigations.[12,19,20] Both previous admission to BJH and a hospital length of stay of 5 days or more prior to admission to the surgical ICU were associated with increased risk, which suggests ongoing institutional transmission of MRSA. Eighty-five percent of the patients colonized with MRSA on admission had had some form of recent healthcare contact (recent hospital admission, admission from a long-term care facility or from another hospital, or a hospital length of stay of 5 days or more prior to admission to the surgical ICU). However, 15% of patients colonized with MRSA at admission did not have some identifiable healthcare contact in the past year, which raises the possibility of community-acquired MRSA colonization. Without molecular typing of isolates for determinants associated with community-acquired MRSA, such as SCC*mec* type IV,[28] this cannot be proven at this time.

Patients with chronic diseases, such as COPD or diabetes mellitus, had a higher likelihood of MRSA colonization on admission. Diabetes has been identified as a risk factor for MRSA colonization at hospital admission,[29] but COPD is generally not recognized as a common risk factor. Although it is controversial, antibiotic therapy is frequently prescribed for COPD exacerbations and may lead to increased antibiotic resistance in these patients.[30] There was no difference in antibiotic use in the 3 months prior to admission between patients with and patients without COPD, which would argue against this explanation. However, there were limited data available to establish a patient's history of antibiotic use prior to hospital admission, and it is unlikely that information on all previous antibiotic use was captured, particularly antibiotic therapy received at other hospitals or through outpatient treatment.

Active screening of all patients on admission is labor- and resource intensive. Girou et al.[12] found that selective screening for MRSA based on risk factors was as effective as screening all patients in detecting colonized patients, but this selective strategy was not determined to be a cost-effective strategy in a larger study.[19] In our study, screening by significant predictor variables from multivariate analysis would identify 89% of MRSA colonized patients at admission and would decrease the total number of admission surveillance cultures required by 42%, assuming that the group of all patients admitted to the ICU had the same frequency of risk factors as did the group who stayed in the ICU for more than 48 hours. Whether this approach would identify sufficient numbers of patients colonized with MRSA on admission to reduce transmission in this setting remains to be determined. Increased community-acquired MRSA may also alter the efficacy of such risk-based screening.

In this study, 10% of patients in the surgical ICU acquired MRSA. Estimates in the literature of rates of acquisition in an ICU vary from 4% to 11%.[12-14] The MRSA acquisition rate in our ICU was 10.7 cases per 1,000 ICU-days at-risk. This value reflects a more accurate estimate of incidence, as it accounts for length of stay in the ICU before the time of MRSA colonization, as opposed to including all ICU-days in the denominator. Others have used the total number of patient-days to calculate the incidence density of MRSA colonization,[31,32] which would underestimate the true acquisition rate.

This study mainly focused on patient risk factors and processes of care associated with MRSA acquisition. All of the predictors in the multivariate model are indicators of increased severity of illness, which potentially raises the intensity of care and time of contact with healthcare professionals. MRSA colonization in wounds and skin ulcers is well documented.[21,25,33] Microbial contamination of tube feeding solution has been associated with nosocomial infection.[34] In this study, tube feeding via a percutaneous tube alone did not significantly elevate the risk of MRSA acquisition in the multivariate model, suggesting that the route was the risk factor, rather than tube feeding solution itself. Dziekan et al.[35] identified the presence of a nasogastric tube as a risk factor for MRSA colonization, further supporting this theory. More research is needed to determine the impact of nasoenteric tubes on MRSA nasal colonization.

There are some limitations to this study. Because of logistical constraints, comorbidity and process of care data were collected only for patients who remained in the ICU for more than 48 hours; brief ICU stays may contribute to the transmission of MRSA but were not captured by this analysis. In addition, a severity-of-illness measure (eg, Acute Physiology and Chronic Health Evaluation II score) was not available for all patients for inclusion in risk factor analysis. However, surrogate markers, such as information on vasopressor use and use of mechanical ventilation, were available. Other information that could not be reliably ascertained for all subjects was admission to other healthcare facilities in the past

year, which may have been a risk factor for MRSA colonization on admission.

Specimens for surveillance culture were only taken from the nares. The use of nasal cultures alone for the detection of MRSA colonization has a sensitivity of 78%-85%,[12,19,21] compared with use of surveillance cultures of specimens from multiple body sites. Therefore, several patients who were classified as having acquired MRSA may have already been colonized at admission. Four of 10 patients with a history of prior MRSA colonization were culture negative for MRSA on admission and were culture positive on subsequent follow-up testing, suggesting they were colonized with MRSA on admission. Performance of additional cultures of specimens from other body sites may increase the detection of MRSA carriage but would result in increased cost of surveillance. In addition, surveillance cultures were only performed weekly and at discharge, which may underestimate the overall incidence density. Finally, molecular typing of MRSA isolates would enhance our understanding of MRSA transmission in this population but was not feasible with current resources.

A significant number of patients admitted to the ICU in this study were colonized with MRSA. Sixty-one percent of MRSA-colonized patients identified by nasal culture on admission would not have been identified by routine clinical culture in the ICU. Risk factors for MRSA colonization on admission include recent colonization with MRSA, recent healthcare contact, and presence of an underlying illness, such as COPD, which is not a commonly identified risk factor. Another 10% of patients acquired MRSA despite infection control measures. Acquisition was associated with acuity of care and processes of care, including enteral feeding via nasoenteric tube. This important baseline data will facilitate future interventions necessary to limit MRSA transmission in this ICU.

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REFERENCES

1. Ibelings MM, Bruining HA. Methicillin-resistant *Staphylococcus aureus*: acquisition and risk of death in patients in the intensive care unit. *Eur J Surg* 1998; 164:411-418.

2. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. *Am J Infect Control* 2004; 32:470-485.

3. Tiemersma EW, Bronzwaer SL, Lyytikainen O, et al. Methicillin-resistant *Staphylococcus aureus* in Europe, 1999-2002. *Emerg Infect Dis* 2004; 10: 1627-1634.

4. Corbella X, Dominguez MA, Pujol M, et al. *Staphylococcus aureus* nasal carriage as a marker for subsequent staphylococcal infections in intensive care unit patients. *Eur J Clin Microbiol Infect Dis* 1997; 16:351-357.

5. Davis KA, Stewart JJ, Crouch HK, Florez CE, Hospenthal DR. Methicillin-resistant *Staphylococcus aureus* (MRSA) nares colonization at hospital admission and its effect on subsequent MRSA infection. *Clin Infect Dis* 2004; 39:776-782.

6. Mest DR, Wong DH, Shimoda KJ, Mulligan ME, Wilson SE. Nasal colonization with methicillin-resistant *Staphylococcus aureus* on admission to the surgical intensive care unit increases the risk of infection. *Anesth Analg* 1994; 78:644-650.

7. Cosgrove SE, Sakoulas G, Perencevich EN, Schwaber MJ, Karchmer AW, Carmeli Y. Comparison of mortality associated with methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* bacteremia: a meta-analysis. *Clin Infect Dis* 2003; 36:53-59.

8. Blot S, Vandewoude K, Hoste E, Colardyn F. Outcome and attributable mortality in critically Ill patients with bacteremia involving methicillin-susceptible and methicillin-resistant *Staphylococcus aureus*. *Arch Intern Med* 2002; 162:2229-2235.

9. Engemann JJ, Carmeli Y, Cosgrove SE, et al. Adverse clinical and economic outcomes attributable to methicillin resistance among patients with *Staphylococcus aureus* surgical site infection. *Clin Infect Dis* 2003; 36:592-598.

10. Jernigan JA, Titus MG, Groschel DH, Getchell-White S, Farr BM. Effectiveness of contact isolation during a hospital outbreak of methicillin-resistant *Staphylococcus aureus*. *Am J Epidemiol* 1996; 143:496-504.

11. Harbarth S, Martin Y, Rohner P, Henry N, Auckenthaler R, Pittet D. Effect of delayed infection control measures on a hospital outbreak of methicillin-resistant *Staphylococcus aureus*. *J Hosp Infect* 2000; 46:43-49.

12. Girou E, Pujade G, Legrand P, Cizeau F, Brun-Buisson C. Selective screening of carriers for control of methicillin-resistant *Staphylococcus aureus* (MRSA) in high-risk hospital areas with a high level of endemic MRSA. *Clin Infect Dis* 1998; 27:543-550.

13. Merrer J, Santoli F, Appere-De Vecchi C, Tran B, De Jonghe B, Outin H. "Colonization pressure" and risk of acquisition of methicillin-resistant *Staphylococcus aureus* in a medical intensive care unit. *Infect Control Hosp Epidemiol* 2000; 21:718-723.

14. Marshall C, Harrington G, Wolfe R, Fairley C. Acquisition of methicillin-resistant *Staphylococcus aureus* in a large intensive care unit. *Infect Control Hosp Epidemiol* 2003; 24:322-326.

15. Chaix C, Durand-Zaleski I, Alberti C, Brun-Buisson C. Control of endemic methicillin-resistant *Staphylococcus aureus*: a cost-benefit analysis in an intensive care unit. *JAMA* 1999; 282:1745-1751.

16. Girou E, Azar J, Wolkenstein P, Cizeau F, Brun-Buisson C, Roujeau JC. Comparison of systematic versus selective screening for methicillin-resistant *Staphylococcus aureus* carriage in a high-risk dermatology ward. *Infect Control Hosp Epidemiol* 2000; 21:583-587.

17. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. *Am J Infect Control* 1988; 16:128-140.

18. Hennekens CH, Buring JE. Screening. In: Mayrent SL, ed. *Epidemiology in Medicine*. 1st ed. Boston: Little, Brown and Company; 1987:327-347.

19. Lucet J, Chevret S, Durand-Zaleski I, Chastang C, Regnier B. Prevalence and risk factors for carriage of methicillin-resistant *Staphylococcus aureus* at admission to the intensive care unit. *Arch Intern Med* 2003; 163:181-188.

20. Jernigan J, Pullen A, Flowers L, Bell M, Jarvis W. Prevalence of and risk factors for colonization with methicillin-resistant *Staphylococcus aureus*

at the time of hospital admission. *Infect Control Hosp Epidemiol* 2003; 24:409-414.

21. Coello R, Jimenez J, Garcia M, et al. Prospective study of infection, colonization and carriage of methicillin-resistant *Staphylococcus aureus* in an outbreak affecting 990 patients. *Eur J Clin Microbiol Infect Dis* 1994; 13:74-81.

22. Boyce J, Havill N, Kohan C, Dumigan D, Ligi C. Do infection control measures work for methicillin-resistant *Staphylococcus aureus*? *Infect Control Hosp Epidemiol* 2004; 25:395-401.

23. Scanvic A, Denic L, Gaillon S, Giry P, Andremont A, Lucet JC. Duration of colonization by methicillin-resistant *Staphylococcus aureus* after hospital discharge and risk factors for prolonged carriage. *Clin Infect Dis* 2001; 32:1393-1398.

24. Sanford MD, Widmer AF, Bale MJ, Jones RN, Wenzel RP. Efficient detection and long-term persistence of the carriage of methicillin-resistant *Staphylococcus aureus*. *Clin Infect Dis* 1994; 19:1123-1128.

25. Bradley SF, Terpenning MS, Ramsey MA, et al. Methicillin-resistant *Staphylococcus aureus:* colonization and infection in a long-term care facility. *Ann Intern Med* 1991; 115:417-422.

26. Muder RR, Brennen C, Wagener MM, et al. Methicillin-resistant staphylococcal colonization and infection in a long-term care facility. *Ann Intern Med* 1991; 114:107-112.

27. Boyce JM. MRSA patients: proven methods to treat colonization and infection. *J Hosp Infect* 2001; 48(Suppl A):S9-S14.

28. Ma XX, Ito T, Tiensasitorn C, et al. Novel type of staphylococcal cassette chromosome *mec* identified in community-acquired methicillin-resistant *Staphylococcus aureus* strains. *Antimicrob Agents Chemother* 2002; 46: 1147-1152.

29. Troillet N, Carmeli Y, Samore MH, et al. Carriage of methicillin-resistant *Staphylococcus aureus* at hospital admission. *Infect Control Hosp Epidemiol* 1998; 19:181-185.

30. Wilson R. Bacteria, antibiotics and COPD. *Eur Respir J* 2001; 17:995-1007.

31. Lucet JC, Paoletti X, Lolom I, et al. Successful long-term program for controlling methicillin-resistant *Staphylococcus aureus* in intensive care units. *Intensive Care Med* 2005; 31:1051-1057.

32. Grundmann H, Hori S, Winter B, Tami A, Austin DJ. Risk factors for the transmission of methicillin-resistant *Staphylococcus aureus* in an adult intensive care unit: fitting a model to the data. *J Infect Dis* 2002; 185: 481-488.

33. Roghmann MC, Siddiqui A, Plaisance K, Standiford H. MRSA colonization and the risk of MRSA bacteraemia in hospitalized patients with chronic ulcers. *J Hosp Infect* 2001; 47:98-103.

34. Thurn J, Crossley K, Gerdts A, Maki M, Johnson J. Enteral hyperalimentation as a source of nosocomial infection. *J Hosp Infect* 1990; 15: 203-217.

35. Dziekan G, Hahn A, Thune K, et al. Methicillin-resistant *Staphylococcus aureus* in a teaching hospital: investigation of nosocomial transmission using a matched case-control study. *J Hosp Infect* 2000; 46:263-270.

Note Added in Proof.   During the interval between publication of this article online and publication in print, errors were noted in tables 2 and 4. The corrected tables are given in an erratum in this issue of the journal (pages 1140-1141).