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Patient-Associated Risk Factors for Acquisition of Methicillin-Resistant *Staphylococcus aureus* in a Tertiary Care Hospital

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Abstract

BACKGROUND—Determining risk factors for acquisition of methicillin-resistant *Staphylococcus aureus* (MRSA) in hospitals is important for defining infection-control measures that may lead to fewer hospital-acquired infections.

OBJECTIVE—To determine patient-associated risk factors for acquisition of MRSA in a tertiary care hospital with the goal of identifying modifiable risk factors.

METHODS—A retrospective matched case-control study was performed. Case patients who acquired MRSA during hospitalization and 2 matched control patients were selected among inpatients admitted to target units during the period from 2001 through 2008. The odds of exposure to potential risk factors were compared between case patients and control patients, using matched univariate conditional logistic regression. A single multivariate conditional logistic regression model identifying independent patient-specific risk factors was generated.

RESULTS—A total of 451 case patients and 866 control patients were analyzed. Factors positively associated with MRSA acquisition were as follows: target unit stay before index culture; primary diagnosis of respiratory disease, digestive tract disease, injury or trauma, or other diagnosis compared with cardiocirculatory disease; peripheral vascular disease; mechanical ventilation with pneumonia; ventricular shunting or ventriculostomy; and ciprofloxacin use. Factors associated with decreased risk were receipt of a solid-organ transplant and use of penicillins, cephalosporins, rifamycins, daptomycin or linezolid, and proton pump inhibitors.

CONCLUSION—Among the factors associated with increased risk, few are modifiable. Patients with at-risk conditions could be targeted for intensive surveillance to detect acquisition sooner. The association of MRSA acquisition with target unit exposure argues for rigorous application of hand hygiene, appropriate barriers, environmental control, and strict aseptic technique for all

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procedures performed on such patients. Our findings support focusing efforts to prevent MRSA transmission and restriction of ciprofloxacin use.

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a dominant hospital pathogen in the United States and worldwide.[1–8] MRSA colonization increases the risk of infection and contributes to healthcare-associated transmission.[9,10] Determining risk factors for MRSA acquisition in hospitals is important for defining infection-control measures, which may lead to reduction in MRSA transmission and ultimately fewer MRSA hospital-acquired infections (HAIs), reduced mortality from those infections, and subsequent reduction in unnecessary healthcare expenditures. Individual patient risk factors for MRSA acquisition that have been identified in previous studies include length of stay (LOS), the presence of open wounds, the presence of a tracheostomy or nasoenteric feeding tube, perioperative hemodialysis or apheresis, high Omega score (composite of common hospital procedures), high severity of illness score, the presence of an MRSA-positive roommate, dependency in activities of daily living, and fluoroquinolone use.[11–18] Most of these studies investigated specific populations and used small numbers of subjects, and not all facilities reporting risk factors for MRSA colonization perform active surveillance for MRSA, making it impossible to determine the timing of acquisition.

Surveillance data obtained at the University of Pittsburgh Medical Center (UPMC)–Presbyterian University Hospital (PUH) during the period from 2005 through 2008 revealed an average rate of MRSA acquisition in the hospital of less than 2%. Although this is relatively low, hospitals now face the challenge of aiming for zero acquisition. A retrospective matched case-control study was conducted to determine patient-associated risk factors for MRSA acquisition at UPMC-PUH with the goal of identifying modifiable risk factors.

METHODS

Subjects and Setting

In 2001, UPMC-PUH, a 745-bed tertiary care teaching facility, implemented an MRSA prevention bundle in a target unit and then gradually increased the number of target units that participated. The bundle included MRSA active surveillance testing, hand hygiene, real-time notification of incident MRSA isolates, use of contact and droplet precautions, use of clean or dedicated equipment, enhanced environmental cleaning, and electronic flagging of patients. In 2003, UPMC-PUH implemented restriction of the use of certain antibiotics, including fluoroquinolones, carbapenems, line-zolid, tigecycline, and daptomycin. Active surveillance testing was accomplished by inoculating nasal swab samples onto BBL CHROMagar MRSA (BD Diagnostic Systems). Target units are defined as areas housing patient populations with increased risk of developing multidrug-resistant organism colonization and/or HAIs and include all intensive care units (medical, surgical, cardiothoracic, neurosurgical/neurology, solid-organ transplant, coronary care, and trauma), the orthopedic unit, and medical step-down areas. Samples for culture are obtained from all patients admitted to target units at admission, weekly, and on discharge from the target area. Target patients, defined as at-risk patients admitted from other healthcare facilities, undergo

active surveillance testing at hospital admission. Compliance with process measures is regularly monitored.

Adult patients admitted to target units during the period from January 2001 through December 2008 with initial negative results at MRSA surveillance culture were potential subjects. Case patients were defined as patients who underwent MRSA conversion and fulfilled inclusion criteria: the presence of at least 1 prior negative result at MRSA active surveillance testing culture from a sample obtained at hospital admission and any subsequent MRSA-positive culture result (from a nasal or clinical/nonnasal sample) from a sample collected in a target unit 3 or more days after hospitalization. Inclusion criteria for control patients included the presence of at least 1 negative result at active surveillance testing culture from a nasal sample collected 3 or more days after hospitalization. Potential case patients and control patients were excluded if they had a concurrent or prior MRSA-positive culture result or history, and control patients were also excluded if they had a subsequent MRSA-positive culture result during the study period. Two unique control patients per case patient were chosen when possible, matched by (1) date of the index negative culture result within 7 days of the case patient's index positive culture result; (2) hospital unit at time of culture sampling; and (3) minimum LOS, ie, the control patient's hospital stay needed to be at least as long as the number of days between the case patient's last negative culture result and the index MRSA-positive culture result. Index culture was defined as the first positive culture result for case patients and the corresponding negative culture result for control patients. Case patients were excluded if a matching control patient could not be identified.

Data from a subset of case patients (subset 1) whose negative culture results and subsequent MRSA-positive culture results were obtained during a contiguous target unit stay and whose positive culture results were obtained 3 or more days after admission to a target unit were compared with data from control patients and analyzed. Data from another subset of case patients (subset 2) whose converter status was based on a subsequent positive result at active surveillance testing culture, excluding case patients identified only on the basis of nonnasal clinical culture results, were similarly compared with data from control patients and analyzed. These subset analyses served to confirm results of the larger data set and to reduce detection bias in determining conversion from negative to positive MRSA carrier status.

Data Collection

The study was approved by the institutional review board of the University of Pittsburgh. Data were obtained from the UPMC Medical Archival Retrieval System and supplemented with data from an internal infection control database. The Medical Archival Retrieval System is the repository of information forwarded from the health system's electronic clinical, administrative, and financial databases. It is indexed on every word in the medical record and is capable of recovering information on all encounters for a given patient that occurred between specified dates.[19]

To ensure patient confidentiality, all data were deidentified with use of an honest broker system. Data collection was performed using computerized algorithms that did not discriminate between case patients and control patients. Variables collected included

demographic data; *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis and procedure codes; comorbid conditions and devices present at admission; institution of contact isolation for other multidrug-resistant organisms; medical procedures and major surgical procedures performed during hospitalization; laboratory detection of other multidrug-resistant organisms; and use of oral and intravenous antibiotics, mupirocin administered topically, H_2 blockers, proton pump inhibitors, and vasopressors during hospitalization. The Charlson comorbidity index was calculated, and laboratory values that reflected the patient's clinical condition around the time of index culture sampling were collected.

Statistical Analysis

The odds of exposure to potential risk factors for MRSA acquisition were compared for case patients and control patients using univariate conditional logistic regression analysis for both binary and continuous data, conditioning on matched sets of subjects. Matched odds ratios (ORs) for categorical variables reflect the odds of exposure to a variable for case patients compared with control patients, whereas matched ORs for continuous variables reflect the increase in matched OR for every unit increase in the value of the variable. A single multivariate conditional logistic regression model to identify independent patient-specific risk factors significantly associated with MRSA acquisition was generated using stepwise regression methods on variables that yielded a *P* value of less than .10 on univariate analysis, using a cutoff *P* value of less than .05. Goodness of fit was assessed by examining plots of Pearson and deviance residuals and influence measures. Selected biologically plausible interactions between covariates found significant on multivariate analysis were tested. Similar statistical methods were applied to subsets. Prevalence rates of MRSA-positive nasal screening culture results among UPMC patients who had chronic kidney disease, required hemodialysis, and/or had received solid-organ transplants were calculated to investigate univariate and multivariate analysis results. All analyses were performed with SAS 9.2 software (SAS Institute).

RESULTS

A total of 474 case patients were identified. Twenty-three case patients could not be matched to control patients and were excluded, resulting in 451 case patients and 866 matched control patients. Subset 1 included 359 case patients and 599 matched control patients. Subset 2 included 336 case patients and 651 matched control patients. The MRSA acquisition rate (proportion of patients who underwent MRSA conversion on the basis of nasal culture results) among patients screened with active surveillance testing during the 8-year study period was 353 of 31,448 (1.12%), decreasing from 91 of 4,312 (2.11%) during the first half of the study period to 262 of 27,136 (0.97%) during the second half of the study period. There were no outbreaks of MRSA acquisition or MRSA HAI, and MRSA HAI rates declined during the study period from 196 MRSA HAIs in 183,540 patient-days (1.07 cases per 1,000 patient-days) in 2001 to 65 MRSA HAIs in 224,458 patient-days (0.29 cases per 1,000 patient-days) in 2008.

Overall, 20 variables were identified as significant on univariate analysis (Tables 1–3). Exposure to a target unit prior to index culture sampling was the only admission characteristic significantly associated with MRSA acquisition (Table 1). Among the potential risk factors and antibiotic use examined (Tables 2 and 3), the results of univariate analysis indicated that pneumonia, use of mechanical ventilation with or without pneumonia, ventricular shunting or ventriculostomy, and H_2 blocker use were significantly associated with MRSA acquisition; ciprofloxacin use was borderline significant ($P = .054$).

Factors present at admission, including hospitalization in a UPMC facility during the past 6 months (Table 1), immunosuppression (all causes), and receipt of a solid-organ transplant prior to admission, and some procedures performed during the hospital stay, including hemodialysis, placement of an invasive vascular device, placement of a ventricular assist device, upper gastrointestinal endoscopy, and gastrointestinal surgery (Table 2), were significantly associated with decreased risk of MRSA acquisition. However, most of these factors did not enter the final model. Medication use variables, including use of proton pump inhibitors (Table 2), penicillins, cephalosporins, carbapenems, daptomycin or linezolid, and rifamycins, were significantly associated with decreased risk (Table 3).

On multivariate analysis, target unit stay prior to index culture sampling had the greatest association with MRSA acquisition (Table 4). Other risk factors for MRSA acquisition were a primary diagnosis of respiratory disease, digestive tract disease, injury or trauma, or other diagnosis, compared with cardiocirculatory disease; peripheral vascular disease; mechanical ventilation with pneumonia; ventricular shunting and/or ventriculostomy; and ciprofloxacin use. Receipt of a solid-organ transplant and use of penicillins, daptomycin or linezolid, rifamycins, cephalosporins, or proton pump inhibitors were protective. No interaction variables were significant. Elimination of extreme or influential observations did not result in any substantial changes in the main model, and thus, all observations were retained.

For subset 1 (contiguous target unit stay only), the final model had only 2 variables, mechanical ventilation with pneumonia (adjusted OR, 1.79 [95% confidence interval {CI}, 1.33–2.41]; $P < .001$) and ventricular shunting and/or ventriculostomy (adjusted OR, 1.97 [95% CI, 1.03–3.77]; $P = .04$), that were associated with MRSA acquisition. Except for rifamycin and daptomycin or linezolid use, protective factors were similar to those in the main model and had comparable adjusted ORs and *P* values (data not shown). Carbapenem use (adjusted OR, 0.58 [95% CI, 0.36–0.95]; $P = .03$) and placement of an invasive vascular device (adjusted OR, 0.60 [95% CI, 0.36–0.98]; $P = .04$) were additional protective factors.

In the final model for subset 2 (active surveillance testing culture only), 4 factors were associated with MRSA acquisition, including target unit stay prior to index culture (adjusted OR, 4.65 [95% CI, 1.37–15.76]; $P = .01$), mechanical ventilation with pneumonia (adjusted OR, 1.67 [95% CI, 1.23–2.28]; $P = .001$), ventricular shunting and/or ventriculostomy (adjusted OR, 2.26 [95% CI, 1.12–4.55]; $P = .02$), and ciprofloxacin use (adjusted OR, 1.70 [95% CI, 1.17–2.49]; $P = .006$). Protective factors were likewise similar to those in the main model (data not shown). Additional protective factors identified were cardiac catheterization and/or contrast angiography (adjusted OR, 0.61 [95% CI, 0.40–0.91]; $P = .02$) and

placement of an invasive vascular device (adjusted OR, 0.58 [95% CI, 0.34–0.99]; *P* = .047).

During the study period, the prevalence of MRSA-positive nasal culture results among MRSA-screened patients at UPMC with a diagnosis of chronic kidney disease or requirement of hemodialysis was 345 (20.2%) of 1,705, compared with 3,350 (11.3%) of 29,745 among other patients (adjusted OR, 1.98 [95% CI, 1.74–2.25]; *P* < .001 [adjusted for receipt of solid-organ transplant]); and their first nasal screening culture result was positive more often than that of patients without chronic kidney disease and who did not require hemodialysis (242 [14.2%] of 1,705 vs 2,451 [8.2%] of 29,745; adjusted OR, 1.88 [95% CI, 1.63–2.18]; *P* < .001). However, the prevalence of MRSA-positive nasal culture results among MRSA-screened patients who had received solid-organ transplants was not significantly different from that among patients who had not (318 [13.7%] of 2,317 vs 3,377 [11.6%] of 29,133; adjusted OR, 1.04 [95% CI, 0.91–1.18]; *P* = .56 [adjusted for chronic kidney disease or requirement of dialysis]).

DISCUSSION

In general, few modifiable risk factors for acquisition of MRSA were identified in this large retrospective study. The association of certain primary diagnoses and peripheral vascular disease with MRSA acquisition could be reflective of disease mechanisms, underlying health status of the patients, the long-term nature of illnesses in these diagnostic categories, or the types of procedures performed for these patients.

The association of mechanical ventilation with pneumonia and MRSA acquisition is not surprising, because mechanical ventilation is a known risk factor for hospital-acquired pneumonia and MRSA is a common pathogen in ventilator-associated pneumonia.[20,21] The link between mechanical ventilation and pneumonia may be reflective of either development of hospital-acquired MRSA pneumonia among patients receiving ventilation or pneumonia promoting MRSA acquisition among patients receiving ventilation. Mechanical ventilation with pneumonia is plausible as a risk factor, because the endotracheal tube bypasses normal upper respiratory tract defenses against aspiration and prevents coughing and clearing of secretions. Respiratory tract damage, disruption of respiratory flora, and increased secretions due to pneumonia result in a favorable environment for MRSA. In addition, intubation, suctioning, and other airway manipulation could serve as a portal of entry for MRSA from the hands or equipment of healthcare workers.

Ventricular shunting and/or ventriculostomy was the only surgical procedure associated with acquisition of MRSA. Its significance may reflect the health status of patients who undergo the procedure or the indications for the procedure. These patients often undergo multiple manipulations for drainage of cerebrospinal fluid, which might explain the increased risk of MRSA acquisition. However, ventricular shunting was performed for only 32 (7.1%) of case patients.

Requirement of hemodialysis, which is a known risk factor for MRSA infection and colonization, was not found to be a risk factor for MRSA acquisition.[3] On univariate

analysis, the requirement of hemodialysis seemed protective and chronic kidney disease trended toward being protective (Table 2). Patients with a diagnosis of chronic kidney disease or who required hemodialysis had significantly higher prevalence of MRSA-positive nasal cultures, as well as significantly higher rates of incident positive results on initial nasal screening, compared with the general hospital population. This greatly reduced the number of patients requiring hemodialysis who were eligible as case patients in our study, because we looked at converters only during hospitalization, which could account for the apparent protective effect. A healthy survivor effect among patients who had repeated healthcare exposure but were still eligible for the study may also explain why patients who received hemodialysis during hospitalization were not at higher risk for MRSA acquisition. Our data suggest that MRSA acquisition among patients with chronic kidney disease or who require hemodialysis occurs before hospitalization, such as in outpatient dialysis centers.

Ciprofloxacin use during the hospital stay was a significant risk factor for MRSA acquisition in the main model and was confirmed in the subset 2 analysis. This is consistent with previously published findings.[11,22,23] Use of fluoroquinolones as a class and of the respiratory fluoroquinolones levofloxacin and moxifloxacin were not significant risk factors. Variations in antistaphylococcal and anti-MRSA activity may explain this differential finding within the class.

Previous studies of group-level antibiotic use have shown the use of β-lactam antibiotics to be a risk factor for MRSA colonization, which is in contrast to our findings, but prevalent colonization should be distinguished from acquisition and patient-level use should be distinguished from group-level use.[11,24] Patient-level data in 1 study showed narrow-spectrum penicillins to be protective against MRSA colonization, which is consistent with our results.[23] The effect of combinations of penicillins with anti-MRSA antibiotics on MRSA acquisition is a potential mechanism or confounder because of the high proportion of vancomycin use (approximately 68%) among our patient population (Table 3). Rifamycin and daptomycin or linezolid use were also associated with a decreased risk. It is plausible that, because these agents are active against MRSA, recovery of MRSA on active surveillance testing could have been suppressed. However, anti-MRSA antibiotics would generally not be used for controlling MRSA acquisition. Additional analysis of antibiotic use is planned to further explore study findings.

Receipt of a solid-organ transplant seemed to be protective. This may be confounded by antibiotic use among transplant recipients, because several antibiotic classes were shown to be protective. The similar prevalence of MRSA-positive nasal screening culture results among the populations of UPMC patients who had or had not received solid-organ transplants is consistent with study findings. The mechanisms behind these findings are unclear and may be explored in future studies.

The use of proton pump inhibitors was also found to be associated with decreased risk of MRSA acquisition. This is difficult to explain in light of the association of the use of proton pump inhibitors with pneumonia and infection with other healthcare-associated pathogens, such as *Clostridium difficile*.[25–28]

The cardiac procedures that were found to be significant on subset analyses are consistent with the finding in the main model of comparatively lower risk of MRSA acquisition among patients with a primary diagnosis of cardiocirculatory disease, who are more likely to undergo these procedures. This finding may be reflective of the underlying good health status of subjects who undergo some of these procedures. Only a small number of patients (less than 7%) required intra-aortic balloon pump and ventricular assist device support. The emergence of these protective factors only on subset analyses may reflect differences in the method of identification of case patients and control patients in the subsets.

As a result of the matching method, it can be presumed that case patients and control patients were exposed to similar group-level antibiotic use, MRSA colonization pressure, care workload, and unit location, and thus these could not be studied as risk factors.[11,29] Similarly, LOS parameters would be reflective of matching accuracy and could not be studied as risk factors. Because subjects were chosen on the basis of results from cultures performed using samples obtained at a target unit, the resulting adjusted ORs for the dichotomous variables indicating prior exposure to a target unit may not truly reflect the odds of exposure in a general population of MRSA converters to a certain type of unit. Because target units housed populations that were at higher risk for MRSA HAIs than were populations in other units, this finding is plausible but should be interpreted with caution. Perhaps this was due to higher MRSA burden and/or performance of more invasive procedures in target units than in nontarget units.

The limitations of our study include its retrospective nature and the method of data capture by means of electronic extraction alone. The sensitivity of MRSA detection also depended on the culture sensitivity. However, these potential biases would unlikely be different between the case and control groups. As a result of multiple comparisons among many variables, the *P* value of less than .05 may be overly sensitive but was felt to be appropriate because of the study's exploratory nature. Because of study design, residual confounding may have occurred and causation cannot be determined.

We report one of the largest single-center studies of patient-associated risk factors for MRSA acquisition performed in a tertiary care hospital. Our data revealed a number of risk factors, most not modifiable but some of which could be targeted for more intensive active surveillance testing in hopes of detecting MRSA acquisition as it occurs so that precautions could be implemented sooner. Increased risk for MRSA acquisition seems to be associated with underlying primary diagnoses and exposure to conditions in target units. The significance of ciprofloxacin use as a risk factor for MRSA acquisition supports restricting its use. Overall, few medical or surgical procedures studied as possible risk factors for MRSA acquisition yielded a significant result. The use of the MRSA prevention bundle may have helped to safeguard patients undergoing procedures who might not otherwise have been protected, because this program identifies colonized patients and requires implementation of barrier precautions. However, the significance of target unit exposure indicates that there is room for improvement in curtailing MRSA spread, particularly in these settings. MRSA reduction efforts should be less focused on modifying specific patient-associated risk factors but rather on preventing transmission, with emphasis on rigorous application of basic infection control strategies, such as hand hygiene before and after

patient or environmental contact, habitual cleaning of equipment, and intensified environmental control, as well as assiduous use of and removal of barriers as appropriate. These principles and strict aseptic techniques should be applied to the care of all patients undergoing medical and surgical procedures. Because these procedures are often medically necessary, it would be impossible to reduce their frequency. Instead, consistent application of infection-control measures might decrease the risk for MRSA acquisition during these procedures, as well as during patient stays in high-risk units.

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TABLE 1

Univariate Analysis of Demographic and Admission Characteristics of Patients Who Acquired Methicillin-Resistant *Staphylococcus aureus* during Hospitalization and Matched Control Patients

Variable	Case patients (*n* = 451)	Control patients (*n* = 866)	OR (95% CI)	*P*
Age, years, mean ± SD	60.2 ± 17.5	59.2 ± 16.4	1.00 (1.00–1.01)	.35
Male sex	250 (55.4)	484 (55.9)	0.95 (0.75–1.20)	.67
Race				.98
White	330 (73.2)	639 (73.8)	1.00	
Black	42 (9.3)	79 (9.1)	1.02 (0.69–1.52)	
Other or unknown	79 (17.5)	148 (17.1)	1.02 (0.75–1.41)	
Emergent or urgent admission	401 (88.9)	767 (88.6)	1.06 (0.73–1.55)	.75
Admission from long-term care facility	41 (9.1)	51 (5.9)	1.52 (0.99–2.35)	.06
Admitting service				.52
Medical	260 (57.6)	520 (60.0)	1.00	
Surgical	183 (40.6)	329 (38.0)	1.18 (0.88–1.58)	
Other	8 (1.8)	17 (2.0)	0.92 (0.38–2.24)	
LOS, days, median (IQR)	30 (17–50)	32 (20–54)	1.00 (1.00–1.00)	.51
Prior to index culture	12 (6–24)	13 (8–24)	1.00 (1.00–1.00)	.98
In target unit	21 (12–35)	21 (12–34)	1.00 (1.00–1.00)	.29
Target unit stay prior to index culture	447 (99.1)	821 (94.8)	6.27 (2.23–17.61)	<.001
LOS in target unit prior to index culture, days, median (IQR)	9 (5–18)	10 (5–19)	1.00 (1.00–1.00)	.65
Other UPMC hospitalization during past 6 months	100 (22.2)	241 (27.8)	0.73 (0.56–0.95)	.02
Substance abuse or dependence				
Alcohol	42 (9.3)	95 (11.0)	0.84 (0.57–1.23)	.37
Drug	23 (5.1)	40 (4.6)	1.16 (0.68–1.99)	.58
Tobacco	35 (7.8)	72 (8.3)	0.89 (0.58–1.38)	.61
Primary diagnosis[a]				.08
Cardiocirculatory disease	51 (11.3)	135 (15.6)	1.00	
Respiratory disease	100 (22.2)	146 (16.9)	2.00 (1.26–3.17)	
Digestive tract disease	48 (10.7)	86 (9.9)	1.59 (0.94–2.68)	
Cerebrovascular disease	38 (8.4)	71 (8.2)	1.64 (0.87–3.06)	
Injury or trauma	98 (21.8)	186 (21.5)	1.54 (0.97–2.45)	
Other diagnosis[b]	115 (25.6)	242 (27.9)	1.38 (0.89–2.15)	
Age-adjusted Charlson comorbidity index, mean ± SD	3.8 ± 2.9	4.0 ± 3.0	0.97 (0.93–1.01)	.13
Total point value assigned for abnormal laboratory values,[c] median (IQR)	5 (4–6)	5 (4–6)	0.95 (0.87–1.03)	.18
Contact isolation for other target organism	161 (35.7)	339 (39.1)	0.83 (0.64–1.07)	.14
Discharge disposition				.15
Alive	286 (63.4)	539 (62.2)	1.00	
Deceased	112 (24.8)	193 (22.3)	1.10 (0.83–1.46)	
Unknown	53 (11.8)	134 (15.5)	0.74 (0.52–1.06)	

NOTE. Data are no. (%) of patients unless otherwise indicated. CI, confidence interval; IQR, interquartile range; LOS, length of stay; OR, odds ratio; SD, standard deviation; UPMC, University of Pittsburgh Medical Center.

[a] Excludes 1 patient whose primary diagnosis was unknown.

[b] Classified under hematology/oncology, infectious diseases, obstetrics/gynecology, rheumatology, dermatology, endocrinology, neurology, genitourinary, or psychiatry.

[c] One point given for the presence of each of the following 9 laboratory values: white blood cell count of at least 15 or less than 3×10^9 cells/L, hematocrit level less than 30% or at least 46%, albumin level less than 3.5 g/dL, bilirubin level 2 mg/dL or more, creatinine level less than 0.6 or at least 1.4 mg/dL, bicarbonate level less than 22 or at least 32 meq/L, sodium level less than 130 or at least 150 mmol/L, potassium level less than 3.5 or at least 5.5 meq/L, and $CD4^+$ count less than 200 cells/mm^3. The most extreme laboratory value within 7 days of index culture was used and designated abnormal on the basis of hospital reference ranges and clinical cutoff values.

TABLE 2

Univariate Analysis of Potential Risk Factors for Hospital Acquisition of Methicillin-Resistant *Staphylococcus aureus*

Variable	Case patients (*n* = 451)	Control patients (*n* = 866)	OR (95% CI)	*P*
Ischemic heart disease	184 (40.8)	383 (44.2)	0.86 (0.68–1.09)	.21
Peripheral vascular disease	53 (11.8)	77 (8.9)	1.40 (0.96–2.04)	.08
Chronic kidney disease	93 (20.6)	217 (25.1)	0.76 (0.58–1.01)	.06
Acute renal failure	74 (16.4)	163 (18.8)	0.84 (0.62–1.14)	.28
Requirement of hemodialysis	92 (20.4)	245 (28.3)	0.63 (0.47–0.84)	.001
Venous stasis or decubitus ulcer	76 (16.9)	117 (13.5)	1.30 (0.95–1.79)	.10
Immunosuppression[a]	163 (36.1)	368 (42.5)	0.74 (0.58–0.96)	.02
Receipt of solid-organ transplant	37 (8.2)	126 (14.5)	0.43 (0.28–0.68)	<.001
Prior to current stay	18 (4.0)	76 (8.8)	0.38 (0.21–0.67)	<.001
During current stay	19 (4.2)	50 (5.8)	0.67 (0.37–1.23)	.20
Substantial steroid use	125 (27.7)	280 (32.3)	0.79 (0.61–1.03)	.08
Pneumonia	269 (59.6)	422 (48.7)	1.62 (1.27–2.07)	<.001
Without mechanical ventilation	6 (1.3)	20 (2.3)	0.58 (0.23–1.45)	.25
Mechanical ventilation	415 (92.0)	766 (88.5)	1.86 (1.15–3.00)	.01
With pneumonia	263 (58.3)	402 (46.4)	1.69 (1.33–2.16)	<.001
Without pneumonia	152 (33.7)	364 (42.0)	0.71 (0.56–0.90)	.005
Central venous catheterization	443 (98.2)	858 (99.1)	0.52 (0.18–1.46)	.21
Nasoenteric or ostomy tube feeding	218 (48.3)	379 (43.8)	1.24 (0.98–1.58)	.08
Upper gastrointestinal endoscopy	50 (11.1)	133 (15.4)	0.61 (0.44–0.85)	.004
Cardiac catheterization or contrast angiography	92 (20.4)	208 (24.0)	0.80 (0.59–1.08)	.14
Placement of invasive vascular device[b]	38 (8.4)	116 (13.4)	0.57 (0.38–0.85)	.007
Intra-aortic balloon pump	12 (2.7)	38 (4.4)	0.55 (0.27–1.13)	.10
Ventricular assist device	14 (3.1)	53 (6.1)	0.49 (0.27–0.90)	.02
Neurosurgery	51 (11.3)	78 (9.0)	1.45 (0.94–2.24)	.09
Ventricular shunting/ventriculostomy	32 (7.1)	37 (4.3)	1.98 (1.14–3.43)	.02
Cardiothoracic surgery	80 (17.7)	160 (18.5)	0.96 (0.64–1.44)	.84
Extracorporeal membrane oxygenation	36 (8.0)	86 (9.9)	0.67 (0.38–1.18)	.17
Gastrointestinal surgery	67 (14.9)	171 (19.7)	0.67 (0.48–0.93)	.02
Colon surgery	13 (2.9)	41 (4.7)	0.58 (0.31–1.10)	.09
Total number of major surgical procedures, median (IQR)	1 (0–2)	1 (0–2)	0.93 (0.82–1.04)	.20
Vasopressor use	268 (59.4)	538 (62.1)	0.88 (0.68–1.14)	.34
Proton pump inhibitor use	224 (49.7)	514 (59.4)	0.63 (0.49–0.80)	<.001
H_2 blocker use	407 (90.2)	748 (86.4)	1.55 (1.05–2.28)	.03
Other target organism, positive culture or toxin test result	145 (32.2)	312 (36.0)	0.82 (0.64–1.06)	.14
Vancomycin-resistant *Enterococcus*	128 (28.4)	278 (32.1)	0.80 (0.62–1.05)	.10
Multidrug-resistant *Acinetobacter*	2 (0.4)	14 (1.6)	0.24 (0.05–1.10)	.07
Clostridium difficile	30 (6.7)	59 (6.8)	0.95 (0.60–1.52)	.84

NOTE. Data are no. (%) of patients unless otherwise indicated. Other variables with $P \geq .20$ not shown: congestive heart failure; cerebrovascular disease; intracranial hemorrhage; diabetes mellitus; chronic obstructive pulmonary disease; sepsis; any infection; *C. difficile*–associated disease; cirrhosis; malignancy; human immunodeficiency virus/AIDS; presence of intracardiac pacemaker or defibrillator, tracheostomy, or gastrointestinal stoma; peripheral venous or arterial and Foley catheterization; placement of subcutaneous intravenous port; transesophageal echocardiography; use of positive airway pressure ventilation; bronchoscopy; chest tube insertion; thoracentesis; percutaneous coronary intervention or stenting; lumbar puncture; blood transfusion; head and neck surgery; orthopedic surgery; vascular surgery; and other surgical subcategories. CI, confidence interval; IQR, interquartile range; OR, odds ratio.

[a] Also includes immunosuppression from pharmacotherapy or radiotherapy, malignancy, and immunodeficiency syndromes.

[b] Also includes coronary stenting and intracardiac pacemaker or defibrillator placement.

TABLE 3

Univariate Analysis of Antibiotic Use during Hospital Stay for Patients Who Acquired Methicillin-Resistant *Staphylococcus aureus* during Hospitalization and Matched Control Patients

Variable	Case patients (*n* = 451)	Control patients (*n* = 866)	OR (95% CI)	*P*
Antibiotics administered intravenously or orally				
Any antibiotic	432 (95.8)	840 (97.0)	0.73 (0.40–1.32)	.30
Penicillins	239 (53.0)	531 (61.3)	0.70 (0.55–0.89)	.003
Cephalosporins	301 (66.7)	622 (71.8)	0.77 (0.59–1.00)	.048
Carbapenems	41 (9.1)	108 (12.5)	0.67 (0.46–1.00)	.048
Vancomycin	307 (68.1)	595 (68.7)	0.96 (0.74–1.24)	.76
Daptomycin or linezolid	35 (7.8)	102 (11.8)	0.62 (0.41–0.94)	.02
Aminoglycosides	62 (13.7)	145 (16.7)	0.78 (0.57–1.08)	.14
Ciprofloxacin	106 (23.5)	166 (19.2)	1.32 (0.99–1.76)	.054
Levofloxacin or moxifloxacin	39 (8.6)	91 (10.5)	0.77 (0.49–1.20)	.25
Rifamycins	11 (2.4)	53 (6.1)	0.32 (0.16–0.67)	.003
Trimethoprim-sulfamethoxazole	71 (15.7)	156 (18.0)	0.82 (0.59–1.13)	.22
Metronidazole	211 (46.8)	429 (49.5)	0.89 (0.70–1.13)	.33
Clindamycin	22 (4.9)	47 (5.4)	0.89 (0.53–1.50)	.66
Macrolides	89 (19.7)	155 (17.9)	1.13 (0.84–1.51)	.43
Mupirocin administered topically	22 (4.9)	48 (5.5)	0.88 (0.50–1.56)	.67

NOTE. Data are no. (%) of patients unless otherwise indicated. CI, confidence interval; OR, odds ratio.

TABLE 4

Multivariate Model for Predicting Acquisition of Methicillin-Resistant *Staphylococcus aureus*

Variable	OR (95% CI)	*P*
Target unit stay prior to index culture	4.95 (1.71–14.34)	.003
Primary diagnosis		.02
Respiratory disease vs cardiocirculatory disease	2.25 (1.36–3.72)	
Digestive tract disease vs cardiocirculatory disease	2.39 (1.35–4.25)	
Injury or trauma vs cardiocirculatory disease	1.90 (1.14–3.18)	
Cerebrovascular disease vs cardiocirculatory disease[a]	1.51 (0.75–3.02)	
Other diagnosis vs cardiocirculatory disease	1.64 (1.02–2.62)	
Peripheral vascular disease	1.54 (1.01–2.33)	.04
Receipt of solid-organ transplant	0.33 (0.20–0.54)	<.001
Receipt of mechanical ventilation with pneumonia	1.75 (1.34–2.29)	<.001
Ventricular shunting or ventriculostomy[b]	2.20 (1.23–3.94)	.008
Ciprofloxacin use	1.57 (1.13–2.17)	.007
Penicillin use	0.66 (0.51–0.89)	.002
Daptomycin or linezolid use	0.56 (0.35–0.89)	.01
Rifamycin use	0.38 (0.17–0.82)	.01
Cephalosporin use	0.73 (0.55–0.98)	.03
Proton pump inhibitor use	0.68 (0.52–0.89)	.006

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

[a]The CI for this primary diagnosis category crossed 1.00, but the category is retained in the model as part of a categorical variable.

[b]Among all patients who underwent this procedure, 37 of 69 (53.6%) had an intracranial hemorrhage.