



CLINICAL RESEARCH STUDY

Evaluating the Probability of Previously Unknown Carriage of MRSA at Hospital Admission

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ABSTRACT

PURPOSE: We determined the prevalence and risk profile of patients with previously unknown carriage of methicillin-resistant *Staphylococcus aureus* (MRSA) at hospital admission.

SUBJECTS AND METHODS: We conducted a 7-month, prospective case-controlled study in adult inpatients admitted to a university hospital with endemic MRSA. Multivariate conditional logistic regression for data sets matched 1:4 was performed to identify the risk profile of newly identified MRSA carriers.

RESULTS: Overall, 399 of 12072 screened admissions (prevalence, 3.3%) were found colonized ($n = 368$, 92%) or infected ($n = 31$, 8%) with MRSA. In 204 cases (prevalence, 1.7%), MRSA carriage was newly identified. Without screening on admission, 49% (196/399) of MRSA carriers would have been missed. We identified nine independent risk factors for newly identified MRSA carriage at admission (adjusted odds ratio): male sex (1.9); age greater than 75 years (2.0); receipt of fluoroquinolones (2.7), cephalosporins (2.1), and carbapenems (3.2) in the last 6 months; previous hospitalization (1.9) or intravenous therapy (1.7) during the last 12 months; urinary catheter at admission (2.0); and intrahospital transfer (2.4). A risk score (range, 0-13) was calculated by adding points assigned to these variables. On the basis of analysis of 1006 patients included in the case-controlled study, the probability of MRSA carriage was 8% (28/342) in patients with a low score (≤ 1), 19% (92/482) in patients with an intermediate score (2-4), and 46% (84/182) in patients with a high score (≥ 5). The risk score had good discrimination (c-statistic, 0.73) and showed excellent calibration ($P = .88$).

CONCLUSIONS: On-admission prevalence of previously unknown MRSA carriers was high. Applying the risk score to newly admitted patients with an intermediate or high probability of MRSA carriage could allow a more effective MRSA control strategy. © 2006 Elsevier Inc. All rights reserved.

KEYWORDS: Methicillin-resistant *Staphylococcus aureus*; Prevalence; Infection control; Prediction; Admission

Carriage of antimicrobial-resistant pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA) places patients at high risk of antibiotic-resistant nosocomial infection.^{1,2} Early identification of patients colonized with MRSA and subsequent prevention of patient-to-patient spread through proper infection control and barrier precau-

tions are considered the most potent interventions to control endemic MRSA and reduce its clinical impact.^{3,4}

Various studies have investigated risk factors for MRSA carriage and infection.^{5,6} Despite the great merit of these reports, they focused mainly on patients already hospitalized and did not exclude previously known MRSA carriers from the risk factor analysis. For clinical practice, however, a crucial issue remains how to identify patients with unknown, asymptomatic MRSA carriage.

Determining the epidemiology of previously unknown MRSA carriage at hospital admission could help optimize control measures, facilitate cost evaluations of different surveillance strategies, and guide clinicians in the identifi-

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cation of patients with MRSA.^{7,8} Therefore, our prospective, case-controlled investigation of a large group of adult patients sought to determine the prevalence and risk profile of MRSA carriage at hospital admission in patients not previously known to be colonized with MRSA; generate a risk score that could stratify patients into low- and high-risk groups; and assess the effect of screening on the incidence of MRSA bacteremia.

METHODS

Study Setting

This study was undertaken at the University of Geneva Hospitals, a 2220-bed health care center providing primary and tertiary care for Geneva (Switzerland) and the surrounding areas. An increase in the number of new patients colonized and/or infected by MRSA was observed at this center since 1999, after the positive impact of different control efforts initiated between 1994 and 1998, including a computerized laboratory alert system, topical decolonization of known MRSA carriers, and a hospital-wide campaign promoting the use of alcohol-based hand disinfection.⁹⁻¹² Standard control strategies, including screening of roommates as soon as a new MRSA carrier has been identified, have failed so far to decrease MRSA cross-infections. In 2002, the incidence of MRSA colonization or infection reached 1.91 new cases per 100 admissions (including both screening specimens and clinical cultures).

Study Population

From January 20 to August 31, 2003, MRSA screening was performed within 24 hours after admission by systematic sampling (anterior nares; perineal region; skin lesions, if present; and other sites when clinically indicated) of all consecutive adult inpatients. Specimens were collected with a Dacron-tipped swab premoistened with sterile saline solution. Patients were excluded if they refused screening or stayed less than 24 hours. The study protocol was approved by the institutional review board as a continuous quality improvement project. No informed consent was therefore required.

Microbiologic Methods

Identification was performed on ORSA plates (Oxoid, Basingstoke, United Kingdom). Further identification of MRSA was based on Pastorex agglutination (Bio-Rad, Reinach, Switzerland), DNase reaction on agar, and growth on Mueller-Hinton oxacillin plates (6 µg of oxacillin per mil-

liliter).^{13,14} This selective enrichment broth has a sensitivity of 88% for detecting MRSA in screening specimens.¹³ MRSA identification was confirmed with Vitek 2 identification and susceptibility testing cards for gram-positive bacteria (bioMérieux, Marcy l'Etoile, France).

CLINICAL SIGNIFICANCE

- The prevalence of previously unknown methicillin-resistant *Staphylococcus aureus* carriage at admission to large tertiary care centers is high.
- Nine patient characteristics predicted unknown methicillin-resistant *Staphylococcus aureus* carriage on admission and stratified patients into risk groups.
- The derived risk score had good accuracy and showed excellent calibration. Its application could decrease the volume of methicillin-resistant *Staphylococcus aureus* screening cultures and allow a more effective methicillin-resistant *Staphylococcus aureus* control strategy.

Case-Controlled Study

A case-controlled study with prospective recruitment of cases and controls was performed to determine the risk factors of newly identified MRSA carriage on admission. A new MRSA case was defined as any patient not previously identified as an MRSA carrier who was found to be colonized or infected with MRSA on admission. MRSA isolates from clinically indicated specimens not associated with infection were classified as colonization.¹⁵ For each case, we randomly selected as controls four patients from whom MRSA had not been isolated in the past or on admission screening and who were admitted within 2 days to the same hospital sector as the case patient.

Data Collection and Variables

The following potential risk factors for newly identified MRSA carriage were selected for the current investigation: age; sex; origin of patient; comorbid conditions; severity of underlying illness¹⁶; Charlson comorbidity index¹⁷; degree of disability (three grades defined by the degree of physical support required)¹⁸; nurse acuity score as measured by the "Project Research in Nursing" system¹⁹; patient's prior location and transfer status; sector of admission (acute, sub-acute, or chronic care)²⁰; history of previous hospitalization or surgery (past 12 months); presence of urinary catheter, tracheotomy, intravenous catheters, drains, or skin lesions at admission; and antibiotic use (past 6 months).

Information about any exposure to a risk factor was extracted from patient files and nursing records. A standardized questionnaire was developed and pilot-tested. The information retrieval was carried out by trained infection control nurses under supervision of an experienced study coordinator. Data quality was enhanced by double data entry and consistency checks.

Statistical Analyses

Data were first entered into a relational database (Access 2000, Microsoft Corp, Redmond, Wash) and then converted into a Stata file (STATA 8.0, College Station, Tex). We expressed continuous variables as the mean (\pm standard deviation) or the median (interquartile range), if their dis-

Table 1 Overall Prevalence of Methicillin-Resistant *Staphylococcus Aureus* Carriage at Admission to Different Hospital Sectors

Hospital Sector	Proportion of MRSA Carriers/All Patients	Prevalence (%)
Emergency department	151/5430*	2.8
Internal medicine	26/886	2.9
Surgery	63/1953	3.2
Obstetrics/gynecology	2/819	0.2
Neurology and dermatology	17/1285	1.3
Subacute care and rehabilitation units	63/1096	5.7
Chronic care wards	77/603	12.8
Total	399/12 072	3.3

MRSA = methicillin-resistant *Staphylococcus aureus*.

*Sixty-five MRSA-positive patients were transferred to internal medicine, 37 were transferred to subacute or chronic care, 36 were transferred to surgery, 9 were transferred to neurology and dermatology units, and 4 were transferred to other units.

tribution was skewed. Univariate analysis of variables from the entire patient population was performed using chi-square tests and two-sample *t* tests for continuous data. Multivariate conditional logistic regression for data sets matched 1:4 was used to identify independent risk factors associated with previously unknown MRSA case status on admission as primary outcome. Models were fitted including all variables associated with the outcome at a *P* value less than .2. Any variable was subsequently eliminated from the model if the chi-square statistic of the likelihood ratio test indicated no statistical significance ($P > .05$) and no substantial confounding of odds ratio estimates for the other variables was observed. Possible effect modification was analyzed by fitting interaction terms between variables; resulting models were compared by likelihood ratio tests. Results are presented as crude (unadjusted) and multivariate (adjusted) odds ratios and their 95% confidence intervals.

An additional analysis was done to generate a risk index for identifying patients who had an increased probability of previously unknown MRSA carriage. All variables from the multivariable analysis that were independently associated with the outcome of interest were included. For calculation of the risk score and to simplify its use, we assigned points to each independent risk factor based on the beta coefficients.²¹ Variables with regression coefficients closer to 0.5 were assigned 1 point, and those with a value closer to 1 (intrahospital transfer; receipt of fluoroquinolones, cephalosporins, or carbapenems) received 2 points. Goodness-of-fit of the risk score was assessed using the Hosmer-Lemeshow statistic. A concordance index (c-index), equal to the area under the curve for logistic regression, was calculated to assess the discriminative accuracy of the model.

Random bootstrap sampling with 1000 replications was performed to validate covariate selection in the multivariate analysis.²² Briefly, the bootstrap method constructs alternative cohorts by sampling the study population with replacement and refitting the regression models. With this methodology, one can determine the stability of a predictive model's effect estimates.²³

RESULTS

From January to August 2003, 12 072 of 13 440 hospital admissions were screened. In 1368 admissions (10%), screening for MRSA could not be performed for different reasons (eg, time constraints, patient refusal). Screening was performed in the emergency department (45% of patients), surgery (16%), subacute and chronic care (14%), neurology and dermatology (10%), internal medicine (7%), and obstetric-gynecology wards (7%).

Prevalence

Overall, 399 of 12 072 admissions (prevalence, 3.3%) were found colonized ($n = 368$, 92%) or infected ($n = 31$, 8%) with MRSA. Leading sources of MRSA infection were the urinary tract ($n = 10$), skin or surgical wound ($n = 8$), and bone and joints ($n = 5$). The prevalence of positive admissions varied for different hospital sectors (Table 1); it was highest in the subacute (5.7%) and chronic care sectors (12.8%).

In 204 of 399 patients (51%), MRSA carriage was newly identified by on-admission screening. Among the 151 previously known carriers, MRSA colonization had persisted for more than 1 year in 55 of 151 patients (36%). Forty-four MRSA-positive patients (11%) were readmitted during the study period. Thus, without the general screening strategy on admission and using only clinical isolates of infected sites or targeted screening of previously identified MRSA carriers, 49% (196/399) of all MRSA carriers would have been missed on admission.

Characteristics of Methicillin-Resistant *Staphylococcus Aureus* Carriers

After excluding the 44 MRSA-positive patients who were readmitted during the study period, we performed an unmatched comparison of the characteristics at first hospital admission of 355 patients with any type of MRSA carriage with 1372 patients without MRSA. Patients who were MRSA-positive on admission differed in several ways from those who were free of MRSA (Table 2). MRSA carriers

Table 2 Characteristics of Patients With and Without Methicillin-Resistant *Staphylococcus Aureus* Carriage on Admission

Characteristic	Patients With MRSA (n = 355)*	Patients Without MRSA (n = 1372)	P Value
	Number (%), mean \pm SD		
Age (y)	75 \pm 16	71 \pm 18	<.001
Male sex	203 (57)	603 (44)	<.001
Residency in Switzerland	343 (97)	1306 (97)	.93
Health care worker	2 (1)	29 (2)	.07
Emergency admission	171 (48)	666 (50)	.56
Origin of patient			
Home	227 (64)	1041 (76)	<.001
Nursing home	30 (8)	55 (4)	.001
Intrahospital transfer	81 (23)	184 (13)	<.001
Referral from another hospital	17 (5)	92 (7)	.19
Hospitalization during the last year	286 (81)	672 (49)	<.001
Number of hospital stays during last 12 mo	1.5 \pm 1.3	0.8 \pm 1.1	<.001
History of surgery during the last 12 mo	131 (37)	263 (19)	<.001
History of stay (past 12 mo) in			
Surgery	136 (38)	250 (18)	<.001
Internal medicine	125 (35)	246 (18)	<.001
Intensive care	25 (7)	46 (3)	.002
Subacute and chronic care	145 (41)	272 (20)	<.001
Underlying conditions			
Ischemic heart disease	90 (25)	236 (17)	<.001
Solid organ neoplasm	88 (25)	231 (17)	<.001
Diabetes mellitus	82 (23)	232 (17)	.007
Chronic renal disease	71 (20)	163 (12)	<.001
Chronic heart failure	44 (12)	127 (9)	.08
Chronic obstructive pulmonary disease	44 (12)	146 (11)	.34
Peripheral vascular disease	42 (12)	114 (8)	.04
Dementia	40 (11)	123 (9)	.19
Gastrointestinal disorder	40 (11)	167 (12)	.64
Severity of underlying disease			
Nurse acuity score	48 \pm 26	35 \pm 20	<.001
Charlson comorbidity index	2.6 \pm 2.3	1.8 \pm 2.1	<.001
Rapidly or ultimately fatal disease	89 (25)	245 (18)	<.001
Complete dependence for daily activities	57 (16)	103 (8)	<.001
Previous antibiotic receipt (past 6 mo)			
Any exposure	226 (64)	401 (29)	<.001
Cephalosporins	92 (26)	101 (7)	<.001
Fluoroquinolones	74 (21)	121 (9)	<.001
Penicillin agents	66 (19)	117 (9)	<.001
Carbapenems	30 (8)	14 (1)	<.001
Macrolides	22 (6)	36 (3)	.001
Presence at admission of			
Peripheral catheter	47 (13)	137 (10)	.08
Central venous catheter	13 (4)	50 (4)	.70
Indwelling urinary catheter	64 (18)	66 (5)	<.001
Mechanical ventilation	9 (3)	17 (1)	.09
Tracheotomy	4 (1)	3 (0)	.04
Drains	18 (5)	9 (1)	<.001
Open skin lesions	66 (19)	90 (7)	<.001

MRSA = methicillin-resistant *Staphylococcus aureus*; SD, standard deviation.

*Repeat admissions (n = 44) of MRSA-positive patients were excluded.

were more likely to have one or several of the following risk factors (all $P < .001$): older age; male sex; more comorbidities and greater severity of underlying illness; prior hospitalization or surgery; transfer from nursing home or intrahospital transfer; recent antibiotic exposure; and more invasive procedures.

Predictor Variables of Newly Identified Methicillin-Resistant *Staphylococcus Aureus* Carriage

All but 13 case patients were matched to four controls each; consequently, the final data set comprised 204 new MRSA

Table 3 Risk Factors for Methicillin-Resistant *Staphylococcus Aureus* Carriage on Admission in 204 Patients Not Previously Identified as Methicillin-Resistant *Staphylococcus Aureus* Carriers (Conditional Logistic Regression Analysis)

Risk Factor	Odds Ratio (95% confidence interval)	
	Univariable	Multivariable
Male sex	1.7 (1.2-2.3)	1.9 (1.3-2.7)
Age \geq 75 y	2.0 (1.4-2.8)	2.0 (1.3-2.9)
Health care worker	0.2 (0.1-1.8)	
Emergency admission	0.9 (0.7-1.3)	
Origin of patient		
Home	0.4 (0.3-0.7)	
Nursing home	1.3 (0.6-2.5)	
Intrahospital transfer	3.3 (1.9-5.5)	2.4 (1.3-4.4)
Referral	1.4 (0.7-2.9)	
Hospitalization during the last year	3.2 (2.3-4.6)	1.9 (1.2-3.0)
History of surgery (past 12 mo)	2.5 (1.8-3.6)	
History of intravenous therapy (past 12 mo)	3.4 (2.4-5.0)	1.7 (1.1-2.8)
History of stay (past 12 mo) in		
Surgery	2.8 (2.0-4.0)	
Internal medicine	2.4 (1.6-3.4)	
Intensive care	1.7 (0.8-3.5)	
Subacute and chronic care	2.3 (1.6-3.4)	
Underlying conditions		
Ischemic heart disease	1.6 (1.1-2.4)	
Solid organ neoplasm	1.5 (1.0-2.4)	
Diabetes mellitus	1.2 (0.8-1.8)	
Chronic renal disease	1.4 (0.9-2.2)	
Chronic heart failure	1.1 (0.7-1.9)	
Chronic obstructive pulmonary disease	1.5 (0.9-2.4)	
Peripheral vascular disease	1.4 (0.8-2.4)	
Dementia	0.9 (0.5-1.5)	
Gastrointestinal disorder	0.8 (0.4-1.4)	
Trauma	1.0 (0.6-1.6)	
Severity of underlying disease		
Charlson comorbidity index	1.5 (1.2-1.8)	
McCabe classification		
Ultimately fatal disease	1.5 (0.9-2.3)	
Rapidly fatal disease	2.2 (1.2-4.1)	
Complete dependence for daily activities	4.4 (2.3-8.2)	
Antibiotic receipt (past 6 mo)		
Any exposure	4.4 (3.1-6.3)	
Carbapenems	6.9 (2.9-16.3)	3.2 (1.2-8.9)
Cephalosporins	3.9 (2.5-6.1)	2.1 (1.3-3.5)
Fluoroquinolones	3.3 (2.1-5.2)	2.7 (1.6-4.4)
Penicillin agents	2.1 (1.4-3.3)	
Macrolides	2.3 (1.1-4.8)	
Presence at admission of		
Peripheral catheter	1.5 (0.9-2.6)	
Indwelling urinary catheter	3.5 (2.1-5.9)	2.0 (1.1-3.6)
Central venous catheter	0.9 (0.3-2.3)	
Mechanical ventilation	2.0 (0.6-6.2)	
Drains	5.3 (1.9-15.4)	
Open skin lesions	2.3 (1.4-3.8)	

MRSA = methicillin-resistant *Staphylococcus aureus*.

cases and 802 matched control patients. A total of 23 variables were significantly associated with newly identified MRSA carriage in the univariate conditional regression analysis (Table 3). In the multivariable analysis, we identified nine categorical risk factors for newly identified MRSA carriage at admission (adjusted odds ratio; Table 3): male sex (1.9); age greater than 75 years (2.0); exposure during

the past 6 months to fluoroquinolones (2.7), cephalosporins (2.1), and carbapenems (3.2); previous hospitalization (1.9) or intravenous therapy (1.7) during the last 12 months; urinary catheter at admission (2.0); and intrahospital transfer (2.4).

In the bootstrap validations, the same variables actually included in the primary model entered the bootstrap-derived

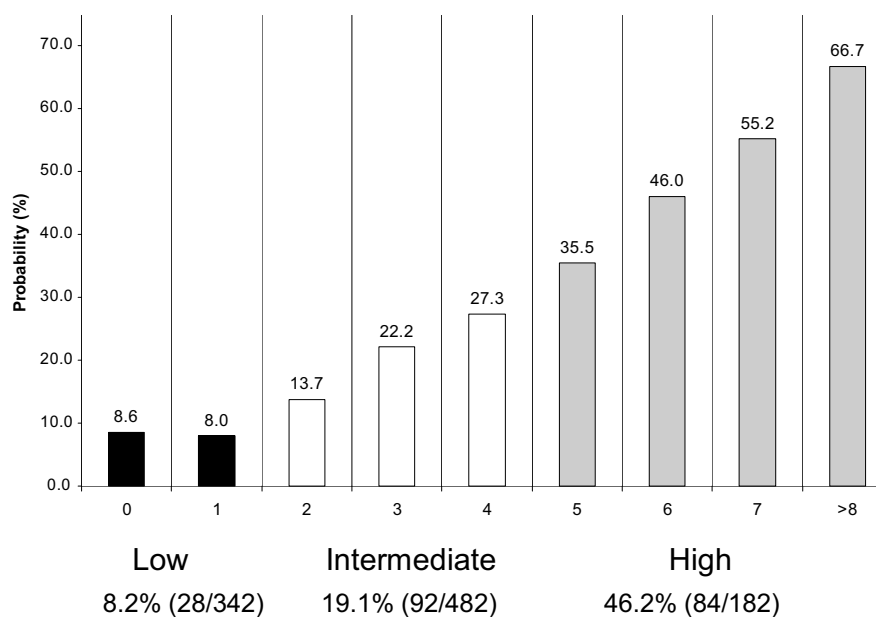


Figure 1 Probability of previously unrecognized carriage of methicillin-resistant *Staphylococcus aureus* (MRSA) on admission. Application of the full risk score to the population of 1006 patients included in the case-controlled study. Indicated under the graph are the average probability of previously unrecognized MRSA carriage and the proportion of patients in each probability category (low probability defined as a score of 0 and 1, intermediate probability defined as a score of 2-4, and high probability defined as a score of ≥ 5).

model most frequently. The stability of the coefficient estimates was evaluated, and there was little difference for eight predictors in either the beta coefficients or the standard errors. However, for carbapenem therapy the beta coefficients and standard errors were much larger: $\beta = 1.17 \pm 0.52$ in the initial model versus $\beta = 2.09 \pm 4.33$ in the bootstrap validation. This suggests that the odds ratio for this variable is less stable than the other effect estimates.

Risk Score Model

By using the multivariate regression coefficients, a probability score was calculated by adding points assigned to these variables. For each patient, the score could range from 0 to 13 points. According to the analysis of 1006 patients included in the case-controlled study, the probability of previously unknown MRSA carriage was 8% (28/342) in patients with a low score (≤ 1 point), 19% (92/482) in those with an intermediate score (2-4 points), and 46% (84/182) in those with a high score (≥ 5 points). The probability of previously unknown MRSA carriage for each score is detailed in Figure 1. The risk model had good discrimination (c-index, 0.73; 95% confidence interval, 0.69-0.77) and showed excellent calibration (Hosmer-Lemeshow χ^2 -statistic, $P = .88$). With bootstrap validation, beta coefficients and standard errors did not differ between the risk model and the bootstrap sample (0.41 ± 0.04 in both models).

Screening at admission of patients with an intermediate or high score (≥ 2 points) would have reduced the screening volume by more than 30%, producing a sensitivity of 86% (176/204) to identify previously unknown MRSA carriers. Limiting on-admission screening to patients with a high score

(20% of patients) would have identified 84 MRSA carriers (sensitivity, 41%).

Simplified Model for the Acute Care Sector

Although the full model provided good discriminating ability, it could be difficult to use in daily practice because of the large number of predictors. Therefore, we explored the performance of a simplified model that included only patients admitted to the acute care sector (cases, 119; controls, 475). We included in that model only predictors readily available at admission (age >80 years, previous hospitalization within past 12 months, previous antibiotic use within past 6 months, and urinary catheter present on admission). In the presence of any of these risk factors, this model would have identified 84% of patients (100/119) and decreased the number of patients to be screened by at least 36%.

Incidence of Methicillin-Resistant *Staphylococcus Aureus* Bacteremia

The incidence of MRSA bacteremia increased from 0.79/1000 admissions in 2002 to 1.17/1000 admissions in 2003 (risk ratio, 1.48; $P = .07$). From January to August 2003, 34 patients experienced at least one episode of MRSA bacteremia. Among the 30 patients with nosocomial MRSA bacteremia, 15 had a positive and 15 had a negative on-admission screening before their first episode of MRSA bacteremia. After exclusion of screening specimens and duplicate isolates, the rate of MRSA in any type of clinical cultures did not change between 2002 and 2003 (risk ratio, 1.0; $P = .58$).

DISCUSSION

This large, prospective, case-controlled investigation showed that the prevalence of previously unknown MRSA carriage at admission to our institution is high, despite the adoption of an aggressive control policy during the last 10 years, which has been based on systematic, in-hospital screening of roommates of newly identified MRSA carriers and computer alerts to rapidly install contact precautions for all known patients with MRSA.^{9,11} It is therefore likely that screening solely previously known MRSA carriers and roommates of patients with MRSA found in clinical specimens will not detect a large proportion of colonized patients.

Previous studies conducted in acute-care settings have yielded a prevalence of MRSA carriage on admission ranging between 1% and 12%.^{7,24-32} In several recent reports from the United States, the on-admission prevalence of community-acquired MRSA has dramatically increased.³³ In contrast, in our population, the number of patients with community-acquired, leukocidin-producing MRSA was still very low ($n = 4$).¹⁴

There are several strengths of the current investigation that are not shared by previously conducted studies that examined MRSA carriage on admission.²⁴⁻³¹ Our study enrolled more than 12 000 consecutive patients, making it one of the largest on-admission screening studies ever conducted on a hospital-wide scale. In contrast, most of the previously conducted studies enrolled fewer cases and focused on specific patient populations. Our analysis was designed to detect the clinically most relevant group of previously unknown MRSA carriers. Most previous studies did not discriminate between known and unknown MRSA carriers at admission and included previously known MRSA carriers in the multivariate analysis. Finally, no previous hospital-wide study has established a risk index to better identify newly admitted patients colonized with MRSA.

Findings from our risk-factor analysis suggest that several variables reflecting prior contact with the health care setting are associated with previously unknown MRSA carriage on admission. By using these predictors, we calculated a point system to estimate the likelihood of unknown MRSA carriage and to create a risk index that recommends not screening patients at low risk of MRSA carriage and obtaining, at least, on-admission swabs from high-risk patients. This risk index, which was validated by a bootstrapping procedure, may assist hospital epidemiologists and clinicians in assessing which patients are most likely to be colonized with MRSA on admission.

Although risk factors of nosocomial MRSA acquisition have been described for more than 30 years, only few investigators have developed practical tools to identify previously unknown MRSA carriage at hospital admission.^{8,25,29} In the study by Troillet and colleagues,²⁵ three patient characteristics (diabetes, antibiotic treatment within 6 months, and exposure to a health care facility within the past year) predicted MRSA carriage with a high sensitivity. Two recent studies looking at MRSA bacteremia at time of hospital admission identified

previous hospitalization, receipt of antibiotics, presence of indwelling catheters, diabetes mellitus, and nursing home residence as independent risk factors.^{34,35} In contrast with these studies, the presence of diabetes mellitus did not increase the likelihood of MRSA carriage in the present study. Finally, our finding that men are at a higher risk of MRSA carriage concurs with that of other studies.^{26,36,37}

Prior receipt of cephalosporins, carbapenems, and fluoroquinolones was independently associated with MRSA carriage on admission. Other studies found discrepant results about the effect of antibiotic exposure.^{28,38} Yet, evidence is accumulating that antibiotic selection pressure plays a pivotal role in MRSA acquisition and dissemination.^{5,39}

There may be barriers to the adoption of our screening tool in daily hospital practice. Although it has been shown that on-admission screening to intensive care units may be cost-beneficial,⁴⁰ convincing cost evaluations are still lacking for screening policies in general wards with endemic MRSA. Our results that 64% of admitted acute-care patients have to be screened to obtain a sensitivity of greater than 80% using the simplified score is a logistic and financial obstacle arguing against extensive on-admission screening. Furthermore, detailed information on recent use of specific antibiotics may not be available in all settings. This concern would not be an issue if our simplified tool for the acute care setting was used, because it does not rely on retrieving data on particular antibiotics.

Despite a large-scale screening campaign and contact isolation of more than 200 previously unknown MRSA carriers, the incidence of MRSA bacteremia increased during the study period. This worrisome finding probably reflects the increase in "colonization pressure," that is, the overall prevalence of patients with MRSA hospitalized at our institution.⁴¹ In contrast, in a recently published mathematical model,⁴² it was suggested that a policy of screening newly admitted patients for MRSA coupled with rapid contact isolation could reduce nosocomial MRSA infection. Several uncontrolled investigations attempted to confirm this hypothesis.^{32,43} Yet, hospital-wide, on-admission screening for MRSA carriage remains a controversial issue.

Our study has potential limitations. Recall bias occurs in case-control studies if patients remember past exposures differently from controls. In this study, recall bias regarding previous antibiotic use might have led to overestimation of the effect of antibiotics on MRSA carriage. However, external data and medical records were used to confirm previous antibiotic exposure and may have minimized this source of bias. Selection bias may affect the results of matched case-control studies. In our study, the subset of control patients in whom the risk score was established may not be entirely representative of the source population of all patients hospitalized during the study period. For the calculation of the full risk score, this bias may have caused an overestimation of the number of patients to be screened on admission. Therefore, we generated a simplified risk score for the acute-care sector, excluding controls from subacute and chronic care wards.

CONCLUSION

On-admission prevalence of previously unknown MRSA carriers was high in the present study. More important, our data could help to improve strategies to better identify the unknown reservoir of hospitalized patients carrying MRSA on admission. We are currently conducting a controlled clinical trial to test the hypothesis that the application of our simplified risk score and a new molecular technique enabling rapid detection of MRSA carriage at admission can substantially reduce the incidence of MRSA infections in surgical patients.

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References

- Pujol M, Pena C, Pallares R, et al. Nosocomial *Staphylococcus aureus* bacteremia among nasal carriers of methicillin-resistant and methicillin-susceptible strains. *Am J Med.* 1996;100:509-516.
- Garroute-Orgeas M, Timsit JF, Kallel H, et al. Colonization with methicillin-resistant *Staphylococcus aureus* in ICU patients: morbidity, mortality, and glycopeptide use. *Infect Control Hosp Epidemiol.* 2001;22:687-692.
- Muto CA, Jernigan JA, Ostrowsky BE, et al. Guideline for preventing nosocomial transmission of multidrug-resistant strains of *Staphylococcus aureus* and *Enterococcus*. *Infect Control Hosp Epidemiol.* 2003;24:362-386.
- Cooper BS, Stone SP, Kibbler CC, et al. Isolation measures in the hospital management of methicillin resistant *Staphylococcus aureus* (MRSA): systematic review of the literature. *BMJ.* 2004;329:533-541.
- Harbarth S, Liassine N, Dharan S, Herrault P, Auckenthaler R, Pittet D. Risk factors for persistent carriage of methicillin-resistant *Staphylococcus aureus*. *Clin Infect Dis.* 2000;31:1380-1385.
- 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.
- Davis KA, Stewart JJ, Crouch HK, Florez CE, Hospenthal D. Methicillin-resistant *Staphylococcus aureus* (MRSA) nares colonization at hospital admission and its effect on subsequent MRSA infection. *Clin Infect Dis.* 2004;39:776-782.
- Furuno JP, Harris AD, Wright MO, et al. Prediction rules to identify patients with methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci upon hospital admission. *Am J Infect Control.* 2004;32:436-440.
- Pittet D, Safran E, Harbarth S, et al. Automatic alerts for methicillin-resistant *Staphylococcus aureus* surveillance—role of a hospital information system. *Infect Control Hosp Epidemiol.* 1996;17:496-502.
- Harbarth S, Dharan S, Liassine N, Herrault P, Auckenthaler R, Pittet D. Randomized, placebo-controlled, double-blind trial to evaluate the efficacy of mupirocin for eradicating carriage of methicillin-resistant *Staphylococcus aureus*. *Antimicrob Agents Chemother.* 1999;43:1412-1416.
- 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.
- Pittet D, Hugonnet S, Harbarth S, et al. Effectiveness of a hospital-wide program to improve compliance with hand hygiene. *Lancet.* 2000;356:1307-1312.
- Blanc DS, Wenger A, Bille J. Evaluation of a novel medium for screening specimens from hospitalized patients to detect methicillin-resistant *Staphylococcus aureus*. *J Clin Microbiol.* 2003;41:3499-3502.
- Francois P, Renzi G, Pittet D, et al. A novel multiplex real-time PCR assay for rapid typing of major staphylococcal cassette chromosome *mec* elements. *J Clin Microbiol.* 2004;42:3309-3312.
- Garner JS, Jarvis WR, Emori TG, Toran TC, Hughes JM. CDC definitions for nosocomial infections. *Am J Infect Control.* 1988;16:128-140.
- McCabe WR, Jackson GG. Gram-negative bacteremia I. Etiology and ecology. *Arch Intern Med.* 1962;110:847-855.
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40:373-383.
- Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The index of ADL: a standardized measure of biological and psychosocial function. *JAMA.* 1963;185:914-919.
- O'Brien-Pallas L, Cockerill R, Leatt P. Different systems, different costs? An examination of the comparability of workload measurement systems. *J Nurs Adm.* 1992;22:17-22.
- Sax H, Hugonnet S, Harbarth S, Herrault P, Pittet D. Variation in nosocomial infection prevalence according to patient care setting: a hospital-wide survey. *J Hosp Infect.* 2001;48:27-32.
- Harbarth S, Pestotnik SL, Lloyd JF, Burke JP, Samore MH. The epidemiology of nephrotoxicity associated with conventional amphotericin B therapy. *Am J Med.* 2001;111:528-534.
- Steyerberg EW, Harrell FE Jr, Borsboom GJ, Eijkemans MJ, Vergouwe Y, Habbema JD. Internal validation of predictive models: efficiency of some procedures for logistic regression analysis. *J Clin Epidemiol.* 2001;54:774-781.
- Steyerberg EW, Bleeker SE, Moll HA, Grobbee DE, Moons KG. Internal and external validation of predictive models: a simulation study of bias and precision in small samples. *J Clin Epidemiol.* 2003;56:441-447.
- Hoefnagels-Schuermans A, Borremans A, Peetermans W, Van Lierde S, Reybrouck G, Van Eldere J. Origin and transmission of methicillin-resistant *Staphylococcus aureus* in an endemic situation: differences between geriatrics and intensive care. *J Hosp Infect.* 1997;36:209-222.
- 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.
- Samad A, Banerjee D, Carbarns N, Ghosh S. Prevalence of methicillin-resistant *Staphylococcus aureus* colonization in surgical patients, on admission to a Welsh hospital. *J Hosp Infect.* 2002;51:43-46.
- Casas I, Esteve M, Andres I, et al. Prevalence and risk factors of methicillin-resistant *Staphylococcus aureus* carriage at hospital admission. ECCMID 2003; Glasgow. Abstract O 342. European Society of Clinical Microbiology and Infectious Diseases.
- Jernigan JA, Pullen AL, Flowers L, Bell M, Jarvis WR. 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.
- Lucet JC, 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: results of a multicenter study. *Arch Intern Med.* 2003;163:181-188.
- Fishbain JT, Lee JC, Nguyen HD, et al. Nosocomial transmission of methicillin-resistant *Staphylococcus aureus*: a blinded study to establish baseline acquisition rates. *Infect Control Hosp Epidemiol.* 2003;24:415-421.

31. Ho PL. Carriage of methicillin-resistant *Staphylococcus aureus*, ceftazidime-resistant Gram-negative bacilli, and vancomycin-resistant enterococci before and after intensive care unit admission. *Crit Care Med*. 2003;31:1175-1182.
32. Boyce JM, Havill NL, Kohan C, Dumigan DG, Ligi CE. Do infection control measures work for methicillin-resistant *Staphylococcus aureus*? *Infect Control Hosp Epidemiol*. 2004;25:395-401.
33. Young DM, Harris HW, Charlebois ED, et al. An epidemic of methicillin-resistant *Staphylococcus aureus* soft tissue infections among medically underserved patients. *Arch Surg*. 2004;139:947-951.
34. Rezende NA, Blumberg HM, Metzger BS, Larsen NM, Ray SM, McGowan JE Jr. Risk factors for methicillin-resistance among patients with *Staphylococcus aureus* bacteremia at the time of hospital admission. *Am J Med Sci*. 2002;323:117-123.
35. Tacconelli E, Venkataraman L, De Girolami PC, D'Agata EM. Methicillin-resistant *Staphylococcus aureus* bacteraemia diagnosed at hospital admission: distinguishing between community-acquired vs. healthcare-associated strains. *J Antimicrob Chemother*. 2004;53:474-479.
36. Murphy S, Denman S, Bennett RG, Greenough WB 3rd, Lindsay J, Zelesnick LB. Methicillin-resistant *Staphylococcus aureus* colonization in a long-term-care facility. *J Am Geriatr Soc*. 1992;40:213-217.
37. Cox RA, Bowie PE. Methicillin-resistant *Staphylococcus aureus* colonization in nursing home residents: a prevalence study in Northamptonshire. *J Hosp Infect*. 1999;43:115-122.
38. Asensio A, Guerrero A, Quereda C, Lizan M, Martinez-Ferrer M. Colonization and infection with methicillin-resistant *Staphylococcus aureus*: associated factors and eradication. *Infect Control Hosp Epidemiol*. 1996;17:20-28.
39. Monnet DL, MacKenzie F, López-Lozano JM, et al. Antimicrobial drug use and methicillin-resistant *Staphylococcus aureus*, Aberdeen, 1996-2000. *Emerg Infect Dis*. 2004;10:1432-1441.
40. 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.
41. 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.
42. Cooper BS, Medley GF, Stone SP, et al. Methicillin-resistant *Staphylococcus aureus* in hospitals and the community: stealth dynamics and control catastrophes. *Proc Natl Acad Sci U S A*. 2004;101:10223-10228.
43. Tomic V, Svetina Sorli P, Trinkaus D, Sorli J, Widmer AF, Trampuz A. Comprehensive strategy to prevent nosocomial spread of methicillin-resistant *Staphylococcus aureus* in a highly endemic setting. *Arch Intern Med*. 2004;164:2038-2043.