MAJOR ARTICLE

Randomized Controlled Trial of Chlorhexidine Gluconate for Washing, Intranasal Mupirocin, and Rifampin and Doxycycline Versus No Treatment for the Eradication of Methicillin-Resistant *Staphylococcus aureus* Colonization

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(See the editorial commentary by Bradley on pages 186–9)

Background. Eradication of methicillin-resistant *Staphylococcus aureus* (MRSA) carriage may reduce the risk of MRSA infection and prevent transmission of the organism to other patients.

Methods. To determine the efficacy of decolonization therapy, patients colonized with MRSA were randomized (3:1 allocation) to receive treatment (2% chlorhexidine gluconate washes and 2% mupirocin ointment intranasally, with oral rifampin and doxycycline for 7 days), or no treatment. Follow-up samples for MRSA culture were obtained from the nares, perineum, skin lesions, and catheter exit sites monthly for up to 8 months. The primary outcome measure was detection of MRSA at 3 months of follow-up. Univariate and multivariable analyses were performed to identify variables associated with treatment failure.

Results. Of 146 patients enrolled in the study, 112 patients (87 treated; 25 not treated) were followed up for at least 3 months. At 3 months of follow-up, 64 (74%) of those treated had culture results negative for MRSA, compared with 8 (32%) of those not treated ($P = .0001$). This difference remained significant at 8 months of follow-up, at which time, 54% of those treated had culture results negative for MRSA ($\chi^2 = 64.4$; $P < .0001$, by log-rank test). The results of the multivariable analysis indicated that having a mupirocin-resistant isolate at baseline was associated with treatment failure (relative risk, 9.4; 95% confidence interval, 2.8–31.9; $P = .0003$), whereas decolonization therapy was protective (relative risk, 0.1; 95% confidence interval, 0.04–0.4; $P = .0002$). Mupirocin resistance emerged in only 5% of follow-up isolates.

Conclusions. Treatment with topical mupirocin, chlorhexidine gluconate washes, oral rifampin, and doxycycline for 7 days was safe and effective in eradicating MRSA colonization in hospitalized patients for at least 3 months.

Staphylococcus aureus remains one of the most important human bacterial pathogens. Infections due to methicillin-resistant *S. aureus* (MRSA) have been associated with excess morbidity and mortality and with increased costs [1–3]. Transmission of a limited number of clones appears to be responsible for most community-associated and health care–associated MRSA disease [4]. Colonization with MRSA generally precedes the development of MRSA infection and plays a major role in the dissemination of this organism in health care facilities [5].

Decolonization, primarily with topical mupirocin, has been successful in reducing the risk of *S. aureus* infection in select patient populations [6, 7], but in other studies, this approach has not been effective [6, 8, 9]. In health care facilities, MRSA decolonization has also been used, along with other interventions, as an outbreak-management strategy [10, 11]. However, the role of decolonization as an infection-control intervention remains controversial, largely because no anti-

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microbial agents have been found to be effective in long-term eradication of MRSA carriage in hospitalized patients [12–16]. Indeed, a recent Cochrane Collaboration review concluded that "there is insufficient evidence to support use of topical or systemic antimicrobial therapy for eradicating MRSA" [17, p. 8].

The present study was designed to determine the efficacy of therapy using a combination of topical and systemic antimicrobial agents (chlorhexidine gluconate washes and intranasal mupirocin plus oral rifampin and doxycycline) for eradication of MRSA colonization. We were also interested in identifying variables that would predict success or failure of decolonization therapy.

PATIENTS AND METHODS

Study population and setting. Patients hospitalized in any of 8 hospitals (6 acute-care hospitals, 1 rehabilitation hospital, and 1 chronic-care hospital) in Toronto or Hamilton, Ontario, between 1 July 2000 and 30 June 2003 who were colonized with MRSA were eligible for inclusion in this study, provided that they were >18 years of age and were expected to survive for ⩾3 months. Patients were considered to be colonized with MRSA if the organism was recovered by culture of samples from ⩾1 body site obtained at 2 separate times within 2 weeks and if there was no evidence of infection on the basis of standard criteria [18]. Potentially eligible patients were identified by MRSA screening done at each hospital at admission or as part of outbreak investigation. Eligible patients who consented to participate in the study had pretreatment (baseline) samples for screening cultures obtained from the anterior nares, perianal area, any skin lesions, and catheter or medical device exit site(s).

Exclusion criteria were concurrent treatment with antimicrobials for an infection; an MRSA decolonization attempt in the previous 6 months (prior treatment for an MRSA infection was not an exclusion criterion); allergy to any of the study medications; known antimicrobial resistance to any of the study medications before randomization (if the isolate was subsequently found to be drug resistant after completion of treatment, the patient was not excluded); inability to take medications by mouth or by enteral feeding tube; pregnancy or breast-feeding; the presence of known hepatic cirrhosis or liver function test abnormalities (abnormal international normalized ratio or serum aspartate aminotransferase or alanine aminotransferase levels >5 times the upper limit of normal); or planned surgery in the following 3 months. The study was approved by the Institutional Review Board at each participating hospital and by the University of Toronto.

Study design. This was an open-label, randomized study comparing decolonization treatment with no treatment. Patients were randomized to treatment or no treatment in blocks of 8 stratified by hospital in a 3:1 ratio. Patients randomly assigned to treatment received a 7-day course of daily washes with 2% chlorhexidine gluconate, 2% mupirocin ointment (~1 cm) applied to the anterior nares with a cotton-tipped applicator 3 times daily, rifampin (300 mg twice daily), and doxycycline (100 mg twice daily). Treatment was started within 4 days of a culture result indicating the presence of MRSA. Compliance with study medications and the occurrence of adverse reactions were monitored.

Baseline demographic and clinical information was obtained by patient interview and review of the medical records. The presence of medical comorbidities was determined by documentation in the medical records or by a physician diagnosis. Baseline functional status was assessed using the Katz index of activities of daily living [19], a validated measure of function in the chronically ill.

Follow-up cultures for MRSA were obtained from the anterior nares, perianal area, skin lesions, catheter or other medical device exit site(s), and any other site that had previously yielded MRSA. They were obtained weekly for 4 weeks after randomization and then monthly for an additional 7 months. Clinical data were obtained to identify the development of MRSA infection for up to 8 months of follow-up.

Laboratory methods. Specimens for MRSA culture were processed within 8 h of procurement. To optimize the recovery of MRSA, the swabs were incubated overnight in a tryptone-based broth containing 7.5% sodium chloride and 1% mannitol (Difco m *Staphylococcus* broth; Becton Dickinson) and then subcultured onto mannitol-salt agar supplemented with oxacillin (2 μg/mL; Quelab) and incubated at 37°C for up to 48 h [20]. MRSA was identified using standard methods, including a latex agglutination test for detection of penicillin-binding protein 2a (MRSA-Screen; Denka Seiken). Specimens were processed by laboratory staff who were blinded to the study purpose and treatment allocation.

In vitro susceptibilities to mupirocin, rifampin, and tetracycline were determined by broth microdilution, in accordance with Clinical and Laboratory Standards Institute guidelines [21]. High-level resistance to mupirocin was defined as an MIC of ⩾512 μg/mL; low-level mupirocin resistance was defined as an MIC of 8–256 μg/mL [22]. To determine whether a second isolate from a patient represented relapse with the same strain or acquisition of a new strain, isolates were typed by PFGE using *Sma*I digests of genomic DNA [23, 24].

Statistical analysis. Descriptive statistics were calculated for baseline demographic and clinical variables. Univariate analysis was done using 2-sided Student's t tests, χ^2, and Fisher's exact tests as appropriate.

The primary outcome was eradication of MRSA from all sites 3 months after completion of therapy in the treatment group and 3 months after randomization in those not treated. Secondary outcomes included survival analysis to compare the probabilities of remaining free of MRSA colonization in all

evaluable study subjects; a separate survival analysis was done excluding those subjects who acquired a new strain of MRSA during follow-up, as determined by PFGE. Log-rank tests were used to assess the significance of treatment allocation.

Multivariable logistic regression analysis was performed to assess the relationship of predictor variables of interest to treatment failure at the primary end point of 3 months. The variables included those identified in the univariate analysis as possibly being associated with treatment failure ($P < .10$) and other variables that had been implicated in previous studies or were biologically plausible. Before analysis, predictor variables were assessed for the presence of collinearity.

All analyses were carried out using SAS software, version 9.1 (SAS Institute). All statistical tests were 2-tailed, with $P < .05$ considered to be statistically significant.

Sample size calculation. We assumed a priori that 20% of untreated subjects would have culture results negative for MRSA after 3 months of follow-up [16] and that 20% of subjects would be lost to follow-up by 3 months. To detect a 30% difference in MRSA decolonization rates ($\alpha = .05$; $\beta = .20$), a sample size of 78 evaluable patients (100 enrolled) in the treatment group and 26 evaluable patients (33 enrolled) in the no-treatment group would be required.

RESULTS

A total of 146 eligible consenting patients were recruited for the study; 111 were randomized to receive decolonization therapy, and 35 were randomized to receive no treatment. Thirty-four patients (23%) were not evaluable at 3 months, leaving 112 patients for the analysis of primary outcome (87 in the treatment group and 25 in the no-treatment group) (figure 1). Baseline demographic and clinical characteristics were similar between groups (table 1). There were also no significant differences in these characteristics for those subjects not completing 3 months of follow-up, compared with those subjects who did complete 3 months of follow-up (data not shown).

At 3 months following treatment (or randomization, for those not treated), 64 patients (74%) in the treatment group had all results of follow-up cultures negative for MRSA, compared with only 8 patients (32%) in the no-treatment group (relative risk [RR], 1.55; 95% CI, 1.17–2.04; $P = .0003$). Survival analysis (figure 2*A*) demonstrated a significant difference in the recovery of MRSA from treated patients, compared with patients who were not treated, over time ($\chi^2 = 64.4$; $P < .0001$, by log-rank test).

A total of 110 (98%) of the initial MRSA isolates obtained at baseline (86 from treated patients and 24 from untreated patients) were available for antimicrobial susceptibility testing and genotyping by PFGE. Twenty-one (19%) of these MRSA isolates were subsequently found to have high-level resistance

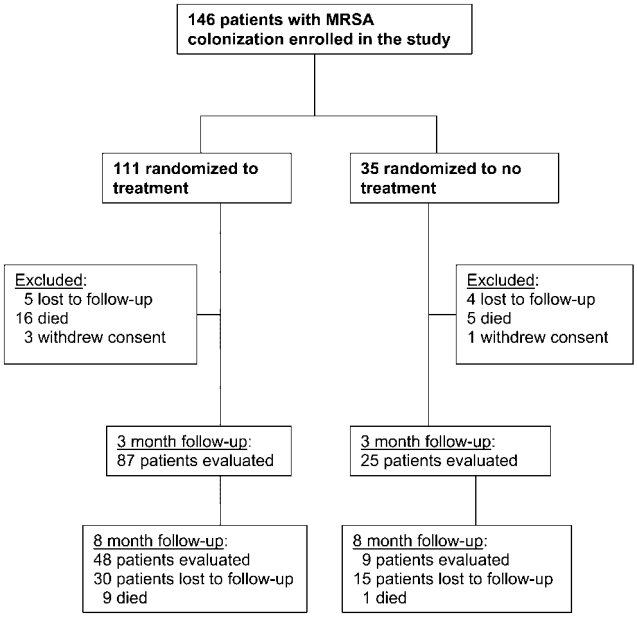

Figure 1. Disposition of patients colonized with methicillin-resistant *Staphylococcus aureus* (MRSA) in a study of decolonization treatment.

to mupirocin. Only 5 baseline isolates (5%) had low-level mupirocin resistance.

The most commonly identified MRSA strains were CMRSA-2 (46%; identical to or closely resembling USA100 ST5) and CMRSA-1 (24%; USA600 ST45). This genotype distribution was representative of that seen in hospitalized patients in southern Ontario [23]. Only 1 isolate was identified as CMRSA-7 (USA400 ST1), and none had the USA300 profile. There was no difference in the genotype distribution of the isolates obtained at baseline between subjects randomized to treatment and subjects randomized to no treatment. Most (82%) of the 72 patients with MRSA recovered in follow-up cultures had follow-up strains that were identical to their baseline isolates, as determined by PFGE typing. Thirteen patients (18%) had initial and follow-up isolates that represented different strains by PFGE typing (9 patients in the treatment group and 4 patients not receiving decolonization therapy). Because these cases represented acquisition of a new strain of MRSA, rather than failure to eradicate the initial colonizing strain, Kaplan-Meier survival curves were created excluding these 13 patients (figure 2*B*). This analysis also demonstrated a significant difference in rates of recovery of MRSA over time in treated patients, compared with untreated patients ($\chi^2 = 50.1$; $P < .0001$, by log-rank test).

Three (5%) of 61 treated study participants with baseline MRSA isolates that were susceptible to mupirocin had follow-up cultures that yielded MRSA with high-level resistance to mupirocin. In 2 of these patients, the genotypes of the initial and follow-up isolates, as determined by PFGE, were distinct,

Table 1. Demographic and clinical characteristics at baseline of study patients who completed ⩾3 months of follow-up.

Characteristic	Randomized to treatment[a] (n = 87)	Randomized to no treatment[b] (n = 25)	P
Age, mean years ± SD	77.3 ± 11.6	76.2 ± 12.2	.68
Female sex	32 (37)	8 (32)	.66
Katz index of activities of daily living score			
A	7 (8)	3 (12)	.29
B	16 (18)	7 (28)	
C	10 (11)	6 (24)	
D	6 (7)	2 (8)	
E	11 (13)	1 (4)	
F	11 (13)	3 (12)	
G	26 (30)	3 (12)	
Dementia	26 (30)	11 (44)	.19
Stroke	28 (32)	5 (20)	.23
Chronic lung disease	25 (29)	9 (36)	.49
Cardiac disease	29 (33)	12 (48)	.19
Diabetes mellitus	23 (26)	5 (20)	.51
Immunosuppression	7 (8)	3 (12)	.69
Skin lesions	33 (38)	7 (28)	.36
Hospitalized in previous 6 months	46 (53)	13 (52)	.90
Nursing home in previous 6 months	17 (20)	6 (24)	.65
Surgery in previous 30 days	11 (13)	3 (12)	.99
Antibiotic treatment in previous 30 days	40 (46)	13 (52)	.63
Previously treated for MRSA infection	1 (1)	0 (0)	1.00
Urinary catheter	19 (22)	8 (32)	.30
Intravascular catheter	24 (28)	7 (28)	.97
Tracheostomy	5 (6)	2 (8)	.68
Percutaneous enteral feeding tube	21 (24)	2 (8)	.08
MRSA recovered from >1 body site	56 (64)	18 (72)	.48
MRSA resistant to mupirocin at baseline	16 (18)	5 (20)	.98
MRSA resistant to rifampin at baseline	3 (3)	0 (0)	.99
MRSA resistant to tetracycline at baseline	1 (1)	0 (0)	1.00

NOTE. Data are no. (%) of patients with the specified characteristic, unless otherwise indicated. MRSA, methicillin-resistant *Staphylococcus aureus*.

[a] A total of 111 patients were randomized to receive treatment; of these, 87 completed ⩾3 months of follow-up.

[b] A total of 35 patients were randomized to receive no treatment; of these, 25 completed ⩾3 months of follow-up.

suggesting acquisition of a new strain of MRSA. In the third patient, the initial and follow-up isolates had indistinguishable PFGE profiles. One of the follow-up mupirocin-resistant isolates in a treated patient was also resistant to tetracycline; this isolate had a PFGE genotype different from that of the initial MRSA strain recovered from this patient. None of the follow-up isolates developed resistance to rifampin.

In univariate analysis, patients who remained colonized with MRSA at 3 months after treatment or randomization were more likely to have had a mupirocin-resistant isolate at baseline (40% vs. 7%; RR, 2.89; 95% CI, 1.90–4.39; $P = .0002$) and were less likely to have been randomized to receive decolonization therapy (58% vs. 89%; RR, 0.26; 95% CI, 0.12–0.55; $P = .0001$) (table 2). In the multivariable analysis, having a mupirocin-resistant isolate at baseline (RR, 9.37; 95% CI, 2.76–31.9; $P = .0003$) remained independently associated with recovery of MRSA in culture by 3 months of follow-up. Receipt of decolonization therapy was protective, associated with negative results of culture for MRSA at 3 months of follow-up (RR, 0.12; 95% CI, 0.04–0.36; $P = .0002$) (table 3).

Compliance with decolonization therapy was good, with 102 patients (92%) completing at least 6 days of treatment and the remaining 9 subjects completing 2–5 days of treatment. Adverse reactions possibly related to medications were reported in 22

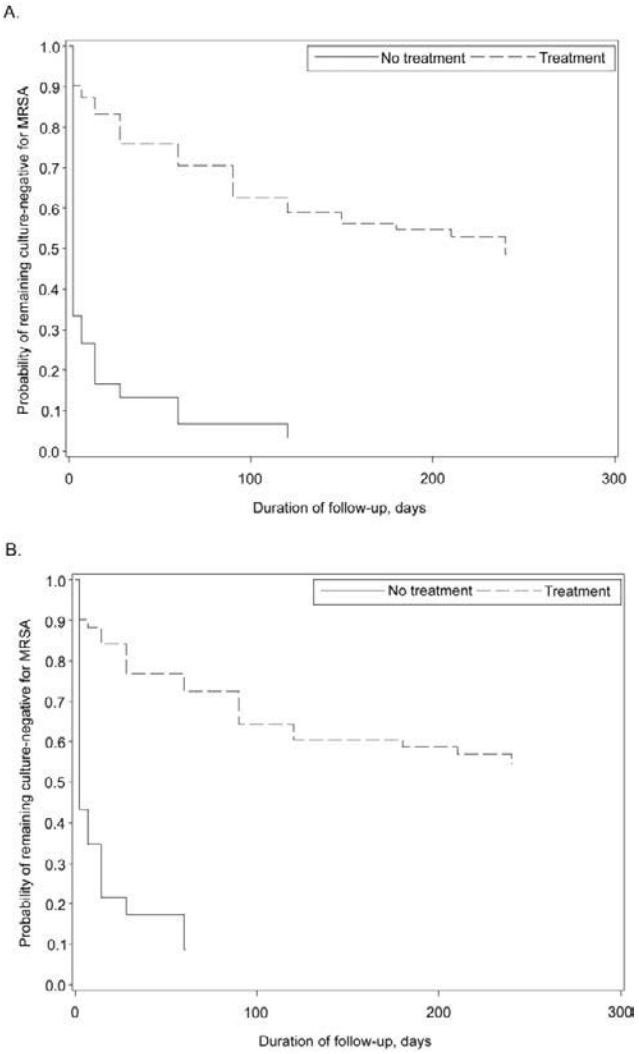

Figure 2. *A,* Kaplan-Meier curve demonstrating the probability of remaining culture-negative for methicillin-resistant *Staphylococcus aureus* (MRSA) over time in patients receiving decolonization therapy (2% chlorhexidine soap, 2% mupirocin ointment, plus oral rifampin and doxycycline), compared with patients randomized to receive no treatment. This analysis includes all randomized patients with follow-up of ⩾3 months (χ^2 = 64.4; $P < .0001$, by log-rank test). *B,* Kaplan-Meier curve demonstrating the probability of remaining culture negative for MRSA over time in patients receiving decolonization therapy (2% chlorhexidine soap, 2% mupirocin ointment, oral rifampin and doxycycline), compared with patients randomized to receive no treatment. This analysis excludes 13 patients with follow-up MRSA isolates distinct from their initial baseline isolates, as determined by pulsed-field gel electrophoresis typing (χ^2 = 50.1; $P < .0001$, by log-rank test).

(25%) of the treated patients. All of these reactions were considered to be mild and included nausea or vomiting (15 patients), diarrhea (9 patients), and dyspepsia (5 patients). Antimicrobial therapy was discontinued in 4 patients (5%) because of adverse effects. Thirty-one study participants died during the study: 25 (23%) of the patients randomized to receive decolonization therapy and 6 (17%) of the patients randomized to no treatment ($P = .64$). None of the patients developed an MRSA infection during the study.

DISCUSSION

Eradication of MRSA carriage may reduce the risk of subsequent MRSA infection in individual patients and could decrease MRSA transmission by eliminating a reservoir for the organism. Indeed, recommendations to consider decolonization of hospitalized patients with nasal carriage of MRSA have been made [25]. Colonization with *S. aureus* or MRSA in health care workers, who are generally healthy young adults, may be successfully eradicated with a short course of intranasal mupirocin ointment [26]. Up to now, however, attempts to eradicate MRSA colonization in hospitalized patients have had little success [27].

Although short-term MRSA decolonization has been accomplished in several observational and uncontrolled studies [10, 12, 28, 29], only 1 randomized controlled trial has demonstrated efficacy for eradication of MRSA carriage for up to 90 days [30]. Previous studies have generally been underpowered, have had short-term (<1 month) follow-up, or have failed to show efficacy [13–17, 31–33]. The results of this study, using a combination of topical and oral systemic antimicrobial agents, indicate that MRSA decolonization may be achieved for prolonged periods of time and that such treatment is generally well tolerated without significant adverse effects. At the end of decolonization treatment for 7 days, 92% of patients cleared MRSA from all sites, and 74% remained free of MRSA at 3 months of follow-up. Eight months after treatment, more than one-half (54%) of those available for follow-up still had negative results of culture for MRSA. Emergence of mupirocin resistance occurred infrequently.

Colonization with MRSA in hospitalized patients is not necessarily benign. In a study of patients in an intensive care unit, the risk of developing MRSA bacteremia in patients colonized with MRSA was higher than the risk of developing staphylococcal bacteremia in patients colonized with susceptible strains of *S. aureus* [34]. Huang et al. [35] found that 29% of 209 hospitalized patients newly identified as having MRSA colonization developed a subsequent MRSA infection in up to 18 months of follow-up; these infections occurred a mean of 102 days after the initial MRSA culture result. Even without infection, implementation of isolation precautions to limit transmission of MRSA may be associated with diminished quality of care and decreased patient safety [36]. These adverse consequences associated with MRSA colonization suggest that even partially effective decolonization, such as that achieved in this study, could be useful in reducing the burden of disease caused by MRSA.

Possible explanations for failure to eradicate MRSA colonization in previous studies may include the use of agents with

Table 2. Comparison of demographic and clinical characteristics of patients with and patients without methicillin-resistant *Staphylococcus aureus* (MRSA) colonization at 3 months of follow-up.

Variable	MRSA isolated at 3 months (n = 40)	MRSA not isolated at 3 months (n = 72)	Relative risk (95% CI)	P
Age, mean years ± SD	76.9 ± 11.3	77.1 ± 11.9		.93
Female sex	17 (43)	23 (32)	1.18 (0.87–1.61)	.26
Katz index of activities of daily living score A or B	30 (75)	40 (56)	1.24 (0.65–2.35)	.50
Dementia	12 (30)	25 (35)	0.93 (0.72–1.21)	.61
Stroke	13 (33)	20 (28)	1.06 (0.81–1.39)	.67
Chronic lung disease	14 (35)	20 (28)	1.11 (0.85–1.45)	.43
Cardiac disease	13 (33)	28 (39)	0.92 (0.69–1.22)	.56
Renal disease	10 (25)	16 (22)	1.04 (0.83–1.29)	.74
Diabetes mellitus	10 (25)	18 (11)	1.00 (0.80–1.25)	1.00
Immunosuppression	2 (5)	8 (20)	0.94 (0.84–1.04)	.49
Skin lesions	13 (33)	27 (38)	0.93 (0.70–1.22)	.60
Hospitalized in previous 6 months	24 (60)	35 (49)	1.34 (0.85–2.11)	.19
Nursing home in previous 6 months	6 (15)	17 (24)	0.90 (0.75–1.09)	.31
Surgery in previous 30 days	5 (13)	9 (13)	1.01 (0.87–1.61)	1.00
Antibiotic treatment in previous 30 days	20 (50)	33 (46)	1.11 (0.76–1.64)	.58
Previously treated for MRSA infection	0 (0)	1 (1)	0.99 (0.96–1.01)	1.00
Urinary catheter	11 (28)	16 (22)	1.07 (0.85–1.35)	.53
Intravascular catheter	9 (23)	12 (17)	1.11 (0.83–1.32)	.36
Tracheostomy	3 (8)	4 (6)	1.02 (0.92–1.13)	.68
Percutaneous enteral feeding tube	11 (28)	12 (17)	1.15 (0.93–1.43)	.17
Any medical device	22 (55)	40 (56)	0.99 (0.64–1.52)	.95
MRSA recovered from >1 body site	29 (73)	45 (63)	1.36 (0.76–2.45)	.28
MRSA resistant to mupirocin at baseline	16 (40)	5 (7)	2.89 (1.90–4.39)	.0002
MRSA resistant to rifampin at baseline	2 (5)	1 (1)	1.91 (0.83–4.43)	.29
MRSA resistant to tetracycline at baseline	0 (0)	1 (1)	0.99 (0.97–1.01)	1.00
Randomized to decolonization therapy	23 (58)	64 (89)	0.26 (0.12–0.55)	.0001

NOTE. Data are no. (%) of patients, unless otherwise indicated.

only marginal in vitro activity against the organism or the use of agents (such as ciprofloxacin and fusidic acid) that induce the development of resistance during therapy [31, 32]. Alternatively, decolonization may, in fact, succeed, but the patient is re-exposed to the organism and becomes colonized with a new strain of MRSA. This likely occurred in 13 (18%) of the patients in the current study. In several previous studies, failure to eradicate MRSA carriage has been associated with multiple extranasal sites of colonization [15, 37]. The gastrointestinal tract is recognized as a potentially important reservoir for the organism [38], and intranasal treatment alone is unlikely to eradicate intestinal carriage. In the current study, the presence of MRSA at multiple body sites was not associated with recovery of MRSA in follow-up cultures, possibly because topical treatment was combined with effective oral systemic drugs. Similarly, impaired functional status (as measured by the Katz index of activities of daily living [19]), and the presence of medical devices or skin lesions (such as decubitus ulcers) were not associated with recolonization or persistence of MRSA, despite the association of these variables with MRSA colonization in health care facilities [29, 39]. However, it is important to note that the power of this study to identify risk factors was limited.

Because previous studies have reported failure of MRSA decolonization in association with mupirocin resistance [16, 40], patients known to have a mupirocin-resistant isolate before randomization were excluded from our study. However, the results of mupirocin susceptibility testing were not always available before randomization, so 21 patients colonized with MRSA with high-level mupirocin resistance were enrolled in the study. As previously reported [40], colonization with MRSA with high-level mupirocin resistance was associated with failure of decolonization therapy. The significance of low-level resistance could not be assessed, because only 5 study subjects had isolates with low-level resistance. Although we observed a relatively low rate of mupirocin resistance developing in follow-up MRSA isolates from study subjects, the potential for the emergence of

Table 3. Results of multivariable logistic regression analysis to determine variables independently associated with recolonization with methicillin-resistant *Staphylococcus aureus* (MRSA) within 3 months of follow-up.

Variable	Relative risk (95% CI)	*P*
Katz index of activities of daily living score[a]	0.45 (0.16–1.31)	.14
Presence of skin lesions	0.71 (0.27–1.87)	.48
Presence of a medical device[b]	1.56 (0.62–3.94)	.35
MRSA recovered from >1 body site	1.39 (0.53–3.70)	.50
Mupirocin-resistant MRSA at baseline	9.37 (2.76–31.87)	.0003
Randomized to received decolonization therapy[c]	0.12 (0.04–0.36)	.0002

[a] Katz index of activities of daily living score of A or B vs. index score C, D, E, F, or G.
[b] For example, intravascular catheter, urinary catheter, tracheostomy, or percutaneous enteral feeding tube.
[c] Decolonization therapy consisting of treatment for 7 days with chlorhexidine soap, intranasal mupirocin ointment, oral rifampin, and oral doxycycline.

such resistance occurring with widespread use of mupirocin is of concern, and even limited development of resistance emphasizes the importance of using this agent judiciously [41].

Strengths of the current study include its study design, relatively long follow-up period, and inclusion of a sample size adequate for determination of treatment efficacy and for assessment of variables associated with treatment failure. The use of a broth culture enhanced sensitivity for the laboratory detection of MRSA, and the study was also able to examine the risk of emergence of mupirocin resistance in MRSA isolates recovered from study participants. Molecular typing by PFGE enabled us to distinguish relapse from acquisition of a new strain of MRSA in follow-up cultures.

This study also has limitations. Although it was a randomized trial, the study was not placebo-controlled and was not a double-blind study. However, this should not have affected the outcome measurement, because MRSA persistence or recolonization after 3 months of follow-up was determined by culture, without knowledge of allocation to receive treatment or to not receive treatment. As anticipated, there were patients lost to follow-up. Although those lost to follow-up appeared to be similar to those who were evaluable with regard to demographic and clinical characteristics, it is possible that some unmeasured differences were important. The study included only hospitalized patients with MRSA, and the results may not be generalizable to other patient populations, such as residents of nursing homes, or to those with community-associated MRSA.

In summary, the results of this study indicate that hospitalized patients colonized with MRSA may be successfully decolonized with a 7-day course of chlorhexidine gluconate washes, intranasal 2% mupirocin ointment, and oral rifampin and doxycycline. With this treatment, approximately three-quarters of patients are likely to remain decolonized for at least 3 months, and more than one-half will still have cultures negative for MRSA up to 8 months later. The study reaffirms the clinical significance of high-level mupirocin resistance and suggests that susceptibility testing should be done in advance if treatment with mupirocin is being considered. Because MRSA decolonization has now been demonstrated to be feasible in a substantial proportion of hospitalized patients, the role of decolonization therapy as an infection control strategy deserves serious consideration and evaluation.

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