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Risk Factors of Methicillin-Resistant *Staphylococcus aureus* Infection and Correlation With Nasal Colonization Based on Molecular Genotyping in Medical Intensive Care Units

A Prospective Observational Study

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Abstract: Methicillin-resistant *Staphylococcus aureus* (MRSA) is a common and important cause of colonization and infection in medical intensive care units (ICU). The aim of this study was to assess association factors between MRSA nasal colonization and subsequent infections in medical ICU patients by clinical investigation and molecular genotyping.

A prospective cohort observational analysis of consecutive patients admitted to medical ICUs between November 2008 and May 2010 at a tertiary teaching hospital were included. To detect MRSA colonization, the specimens from the nares were obtained within 3 days of admission to the ICU and again 1 week following admission to the ICU. Genetic relatedness for colonized and clinical isolates from each study patient with MRSA infection were analyzed and compared.

A total of 1266 patients were enrolled after excluding 195 patients with already present MRSA infections. Subsequent MRSA infection rates were higher in patients with nasal colonization than in those without (39.1% versus 14.7%, respectively). Multivariate Poisson regression analysis demonstrated that nasal MRSA colonization (relative risk [RR]: 2.50; 95% confidence interval [CI]: 1.90–3.27; $P < 0.001$) was independent predictors for subsequent MRSA infections. History of tracheostomy, however, was a protective predictor in all patients (RR: 0.38; 95% CI: 0.18–0.79; $P = 0.010$) and in patients with MRSA nasal colonization (RR: 0.22; 95% CI: 0.55–0.91; $P = 0.037$). Molecular genetics studies revealed that most MRSA isolates were healthcare-associated clones and that nasal and clinical isolates exhibited up to 75% shared identity.

Methicillin-resistant *S. aureus* nasal colonization was significantly associated with subsequent MRSA infection among medical ICU patients. Previous MRSA infection was associated with subsequent MRSA infections, and history of tracheostomy associated with reducing this risk. Most MRSA isolates were healthcare-associated strains that were significantly correlated between nasal and clinical isolates.

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Abbreviations: CI = confidence interval, ICU = intensive care unit, MLST = multilocus sequence typing, MRSA = methicillin-resistant *Staphylococcus aureus*, MSSA = methicillin-susceptible *Staphylococcus aureus*, PCR = polymerase chain reaction, PFGE = pulsed-field gel electrophoresis, PVL = Pantone-Valentine leukocidin, RR = relative risk, SD = standard deviation.

INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a common and important cause of infection in the intensive care unit (ICU) setting. Preceding MRSA colonization is a risk factor for subsequent MRSA infections.[1] The colonizing bacterial strains may serve as endogenous reservoirs for overt clinical infections or may spread to other patients.[2–7] Several studies have demonstrated a link between *S. aureus* carriage and subsequent infection in continuous peritoneal dialysis patients, nonsurgical patients, critical neonates, and medical ICU patients.[8–12] The routine MRSA surveillance to prevent MRSA infections among ICU patients, however, is still a controversial policy.[13] Controversy also exists about eliminating nasal MRSA carriage to prevent consequent MRSA infections. It is important to confirm the linkage between nasal carriage and clinical MRSA isolates to develop the best strategy to avoid systemic infection by decolonization methods. In 2000, 53% to 83% of *S. aureus* isolates attributed to nosocomial infections in 12 Taiwanese major hospitals were resistant to methicillin.[14] In our adult ICUs, MRSA accounted for 77% of nasal *S. aureus* isolates with a high colonization rate (up to 32%) during a surveillance study in 2010.[15]

A prospective cohort observational study of medical ICU patients was undertaken to examine MRSA nasal colonization status and the development of MRSA infection. Our research goals were to determine the clinical association between nasal carriage of MRSA and subsequent MRSA infections and to identify additional risk factors associated with MRSA infection. The relationship between nasal and clinical isolates was also investigated using pulsed-field gel electrophoresis (PFGE) and multilocus sequence typing (MLST) analysis.

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MATERIALS AND METHODS

Study Settings and Design

Chang-Gung Memorial Hospital, Lin-Kuo branch, is a university-affiliated 3700-bed tertiary teaching hospital in northern Taiwan that provides healthcare ranging from primary to tertiary care. A prospective cohort observational analysis of consecutive patients admitted to the 2 medical ICUs (44 beds) between November 2008 and May 2010 was performed. The Institutional Review Board of Chang-Gung Memorial Hospital reviewed and approved the study (IRB No.: 96–0104B) and the requirement for written informed consent was waived.

For patients with multiple medical ICU admissions, only the first admission was included in the analysis. Nasal surveillance specimens for MRSA were collected. To detect MRSA colonization, the specimens from the nares were obtained within 3 days of admission to the ICU and again 1 week following admission to the ICU. Methicillin-resistant *S. aureus* isolates recovered from clinical diagnostic samples (beyond survey culture specimens) submitted to the clinical microbiology laboratory were defined as clinical isolates. True MRSA infections were defined by the following criteria. Bloodstream infection required a positive blood culture. Pneumonia required a positive respiratory culture, a compatible chest radiograph with symptoms and signs of lower respiratory tract infection and a decision to treat. Urinary tract infection required a positive urine culture and either a decision to treat or the growth of $>100{,}000$ CFU/ml plus at least 50 leukocytes per high-power field. All other sites, including pleural effusion, ascites, skin, and soft tissue required a positive culture and a decision to treat.

To identify potential risk factors for MRSA infection, the following data were collected from each patient: baseline demographics, characteristics, underlying and current diseases, clinical covariates, dates of previous and current hospitalizations, date of ICU admission, previous MRSA infection, already present MRSA infection, and subsequent MRSA infection. Previous infection was defined as MRSA infection diagnosed at least 2 weeks before the current hospitalization. Already present infection was defined as MRSA infection diagnosed during this hospitalization but before admission to medical ICU or within 24 hours after ICU admission.

Microbiology

Nasal and clinical isolates from each study patient with MRSA infection were genotyped and compared. Survey specimens for MRSA culture were obtained with a cotton swab, placed in transport medium (Venturi Transystem, Copan Innovation Ltd, Limmerick, Ireland), and processed in the microbiology laboratory within 4 hours. Coagulase tests were carried out by using rabbit plasma to make sure the identification of *S. aureus* after incubation and subcultivation. Based on the recommendation of Clinical and Laboratory Standards Institute (CLSI), Cefoxitin test was used to differentiate the MRSA from methicillin-susceptible *S. aureus* (MSSA).[16]

Molecular genotyping analysis was performed on a total of 65 clinical isolates and 43 nasal isolates from 36 randomly selected patients with MRSA infections. PFGE was used to fingerprint all MRSA isolates according to procedures described previously.[12,17–19] Genotypes were allocated in alphabetical order, as in our prior studies; any new genotype, if identified, was allocated consecutively.[12,17,18] Pulsed-field gel electrophoresis patterns with less than 4 band differences from an existing genotype were defined as subtypes of that genotype. Two isolates were regarded to be indistinguishable, highly related, or distinct if they had the similar subtype (no band difference), the same genotype (less than 4-band differences), or a different type ($\geq$4-band differences), respectively. According to the measures described previously, Staphylococcal chromosome cassette *mec* (SCC*mec*) type and presence of Pantone-Valentine leukocidin (PVL) genes were established by polymerase chain reaction (PCR) assays.[12,18,20,21] Multilocus sequence typing was performed for selective strains of representative PFGE patterns as described elsewhere.[22]

Statistical Analysis

Statistical analyses were performed using SPSS for Windows software version 21.0 (IBM, Armonk, N Y). Continuous data obtained were expressed as the mean $\pm$ standard deviation (SD) and frequencies were calculated for categorical data. Relative risk (RR) and 95% confidence interval (CI) were calculated using Poisson regression. Potential predictors of colonization with $P < 0.05$ in univariate analysis were further analyzed with a multivariate Poisson regression model in SPSS. Two-sided P values<0.05 were considered significant for multivariate analysis.

RESULTS

A total of 1461 patients admitted to the medical ICUs were evaluated. Excluding 195 patients who had already present MRSA infections, 1266 patients were enrolled in this study. Of these 1266 study patients, the initial MRSA nasal colonization rate was 16.4% (207/1266), and the rate of subsequent MRSA infections was 39.1% (81/207) (Figure 1). The subsequent MRSA infection rate of non-MRSA colonization patients was significantly lower than MRSA colonization patients (14.7% versus 39.1%, OR: 3.72; 95% CI: 2.68–5.16; $P < 0.001$). Overall, the MRSA infection rate during hospitalization was 18.7% (237/1266). For the patients with MRSA nasal colonization, true infection occurred 12.3 days (median, 7 days; interquartile range, 3–15 days) after colonization, and 16.9 days (median, 12 days; interquartile range, 7–20 days) after ICU admission, respectively. There was a significant difference in the meantime from ICU admission to the true MRSA infection between patients with MRSA colonization (16.9 days) and those without colonization (24.3 days) ($P = 0.002$). Of these 1266 study patients, 939 patients (74.2%) were experiencing respiratory failure with mechanical ventilation. There were 119 patients (9.4%) who underwent tracheostomy, which were all done before ICU admission, and all need ventilator support.

Table 1 shows the characteristics and risk factors of nasal MRSA colonization in these enrolled patients. The colonized MRSA patients were older than noncolonized patients (71.8 ± 15.7 versus. 68.9 ± 15.2, $P = 0.023$). In addition, the nasal MRSA patients had higher instances of hospitalization within the previous year ($P = 0.029$), old cerebrovascular accidents ($p = 0.047$), and MRSA infections previous to this admission ($P < 0.001$). Furthermore, multivariate Poisson regression analysis demonstrated that previous MRSA infections (RR: 2.19; 95% CI: 1.56–3.08; $P < 0.001$) were independent predictors for nasal MRSA colonization.

Table 2 shows that nasal MRSA colonization was an independent predictor for subsequent MRSA infections. Patients with nasal MRSA colonization had significantly higher rates of subsequent MRSA infections than those without colonization (RR: 2.50; 95% CI: 1.90–3.27; $P < 0.001$). History of

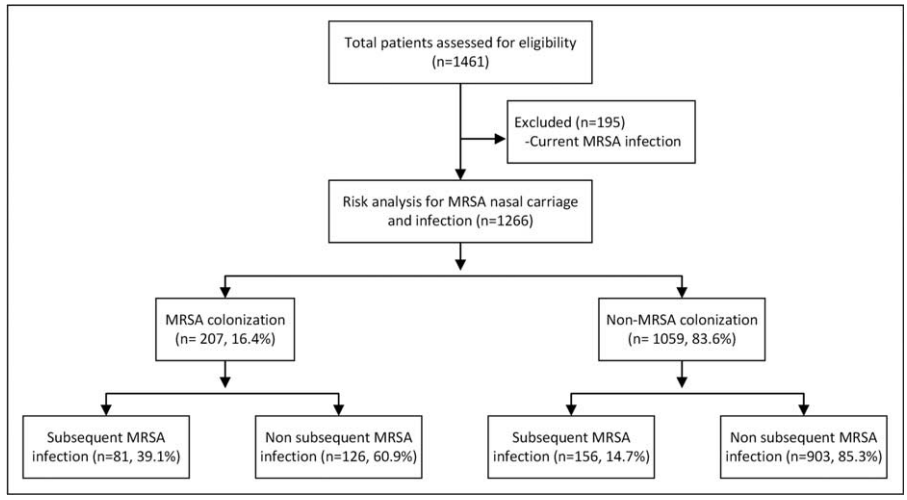

FIGURE 1. Schematic of analysis for medical intensive care unit patients by either MRSA infection or methicillin-resistant *S. aureus* nasal colonization. ICU, intensive care unit; MRSA, methicillin-resistant *Staphylococcus aureus*.

tracheostomy (RR: 0.38; 95% CI: 0.18–0.79; $p = 0.010$), however, was an independent protective predictor for subsequent MRSA infection. Methicillin-resistant *S. aureus* nasal colonization was noted for 81 (34.2%) of 237 patients with MRSA infections. Methicillin-resistant *S. aureus* nasal colonization was also noted for 93 (65.5%) of 142 patients with previous MRSA infections. In patients with MRSA nasal colonization, subsequent MRSA infections decreased significantly only with the history of tracheostomy (RR: 0.22; 95% CI: 0.55–0.91; $P = 0.037$) (Table 3).

Molecular genotyping analysis was performed on a total of 65 clinical isolates and 43 nasal isolates from 36 patients with true MRSA infections (Table 4). Of these 36 patients, 14 patients (38.9%) had 2 to 7 clinical isolate for analysis. The

TABLE 1. Risk Factors Associated With Nasal MRSA Colonization (N = 1266)

				Univariate		Multivariate	
Characteristics	**Total (N = 1266)**	**Colonized (N = 207)**	**Noncolonized (N = 1059)**	***P* Value**	**Relative Risk (95% CI)**	***P* Value**	**Relative Risk (95% CI)**
Age (years, mean ± SD)	69.4 ± 15.3	71.8 ± 15.7	68.9 ± 15.2	0.023	1.01 (1.00–1.02)	0.056	
Male gender (%)	794 (62.7)	128 (61.8)	666 (62.9)	0.793			
APACHE II score (mean ± SD)	23.8 ± 6.5	23.6 ± 6.7	23.9 ± 6.6	0.928			
Nasogastric tube (%)	1125 (88.9)	191 (92.3)	934 (88.2)	0.122			
Endotracheal tube (%)	938 (74.1)	162 (78.3)	776 (73.3)	0.172			
Tracheostomy (%)	119 (9.4)	21 (10.1)	98 (9.3)	0.713			
CVC (%)	779 (61.5)	140 (67.6)	639 (60.3)	0.072			
Foley catheterization (%)	1034 (81.7)	178 (86.0)	856 (80.8)	0.110			
From nursing home (%)	101 (8.0)	19 (9.2)	82 (7.7)	0.524			
Hospitalization within 1 year (%)	583 (46.1)	111 (53.6)	472 (44.6)	0.029	1.36 (1.03–1.78)	0.322	
Underlying diseases (%)							
Old CVA	199 (15.7)	43 (20.8)	156 (14.7)	0.047	1.41 (1.01–1.97)	0.435	
COPD	46 (3.6)	6 (2.9)	40 (3.8)	0.573			
DM	376 (29.7)	66 (31.9)	310 (29.3)	0.492			
Hemodialysis	41 (3.2)	7 (3.4)	34 (3.2)	0.907			
Cancer	249 (19.7)	31 (15.0)	218 (20.6)	0.091			
Current illness							
Pneumonia (%)	190 (15.0)	39 (18.8)	151 (14.3)	0.124			
Previous MRSA infection before this admission (%)	142 (11.2)	48 (23.2)	94 (8.9)	<0.001	2.39 (1.73–3.30)	<0.001	2.19 (1.56–3.08)

APACHE II = Acute Physiology and Chronic Health Evaluation II, CI, confidence interval = COPD = chronic obstructive pulmonary disease, CVA = cerebrovascular accident, CVC = central venous catheter, DM = diabetes mellitus, MRSA = methicillin-resistant *Staphylococcus aureus*.

TABLE 2. Risk Factors for Patients With Subsequent MRSA Infection

Characteristics	Total (N = 1266)	MRSA Infection (N = 237)	Non-MRSA Infection (N = 1029)	Univariate		Multivariate	
				P Value	Relative Risk (95% CI)	*P* Value	Relative Risk (95% CI)
Age (years, mean ± SD)	69.4 ± 15.3	72.3 ± 15.0	68.7 ± 15.4	0.004		0.059	
Male gender (%)	794 (62.7)	156 (65.8)	638 (62.0)	0.323			
Nasogastric tube (%)	1125 (88.9)	225 (94.9)	900 (87.5)	0.004	2.35 (1.32–4.20)	0.071	
Endotracheal tube (%)	938 (74.1)	193 (81.4)	745 (72.4)	0.010	1.53 (1.11–2.13)	0.514	
Tracheostomy (%)	119 (9.4)	9 (3.8)	110 (10.7)	0.004	0.38 (0.20–0.74)	0.010	0.38 (0.18–0.79)
CVC (%)	779 (61.5)	167 (70.5)	612 (59.5)	0.005	1.49 (1.13–1.97)	0.058	
Foley catheterization (%)	1034 (81.7)	208 (87.8)	826 (80.3)	0.016	1.61 (1.09–2.37)	0.405	
From nursing home (%)	101 (8.0)	20 (8.4)	81 (7.9)	0.793			
Hospitalization within 1 year (%)	583 (46.1)	103 (43.5)	480 (46.6)	0.424			
Underlying diseases (%)							
Old CVA	199 (15.7)	39 (16.5)	160 (15.5)	0.755			
COPD	46 (3.6)	10 (4.2)	36 (3.5)	0.630			
DM	376 (29.7)	78 (32.9)	298 (29.0)	0.280			
Hemodialysis	41 (3.2)	7 (3.0)	34 (3.3)	0.804			
Cancer	249 (19.7)	38 (16.0)	211 (20.5)	0.160			
Current illness (%)							
Pneumonia	190 (15.0)	45 (19.0)	145 (14.1)	0.087			
Previous MRSA infection before this admission (%)	142 (11.2)	36 (15.2)	106 (10.3)	0.054			
MRSA nasal colonization (%)	207 (16.4)	81 (34.2)	126 (22.0)	<0.001	2.66 (2.03–3.47)	<0.001	2.50 (1.90–3.27)

CI = confidence interval, COPD = chronic obstructive pulmonary disease, CVA = cerebrovascular accident, CVC = central venous catheter, DM = diabetes mellitus, MRSA = methicillin-resistant *Staphylococcus aureus*.

TABLE 3. Risk Factors for MRSA Infection in Patients With Nasal MRSA Colonization (N = 207)

Characteristics	Infection (n = 81)	No Infection (n = 126)	*P* Value	Relative Risk (95% CI)
Age (mean ± SD)	73.9 ± 14.7	70.4	±16.2	0.221
Male gender (%)	52 (64.2)	76 (60.3)	0.662	
Nasogastric tube (%)	76 (93.8)	115 (91.3)	0.601	
Endotracheal tube (%)	68 (84.0)	94 (74.6)	0.217	
Tracheostomy (%)	2 (2.5)	19 (15.1)	0.037	0.22 (0.55–0.91)
CVC (%)	55 (67.9)	85 (67.5)	0.959	
Foley catheterization (%)	68 (84.0)	110 (87.3)	0.597	
From nursing home (%)	7 (8.6)	12 (9.5)	0.867	
Hospitalization within 1 year (%)	40 (49.4)	71 (56.3)	0.445	
Underlying diseases (%)				
Old CVA	16 (19.8)	27 (21.4)	0.821	
COPD	1 (1.2)	5 (4.0)	0.387	
DM	29 (35.8)	37 (29.4)	0.450	
Hemodialysis	4 (4.9)	3 (2.3)	0.441	
Cancer	12 (14.8)	19 (15.1)	0.968	
Current illness (%)				
Pneumonia	15 (18.5)	24 (19.0)	0.941	

CI = confidence interval, COPD = chronic obstructive pulmonary disease, CVA = cerebrovascular accident, CVC = central venous catheter, DM = diabetes mellitus, MRSA = methicillin-resistant *Staphylococcus aureus*.

TABLE 4. Molecular Genotyping of 65 Clinical and 43 Nasal Colonized MRSA Isolates From 36 Patients With MRSA Infections

Classification of Isolates	No. of Isolates	No. of Genotypes	PFGE Patterns No. (%) of Isolates			
			A	F	B	Others
Infection	65	9	31 (48)	16 (25)	11 (17)	7 (10)
Colonized	43	10	16 (37)	13 (30)	5 (12)	9 (21)
SCC*mec* type			III, IIIA	II, Untypeable	III, untypeable	II, IV, V_T, untypeable
Sequence type			239	5	239	1, 5, 30, 59, 89
PVL-positive			0	0	0	7*

MRSA = methicillin-resistant *Staphylococcus aureus*, PFGE = pulsed-field gel electrophoresis, PVL = Panton-Valentine leukocidin, SCC*mec* = staphylococcal chromosome cassette *mec*.

* PVL genes were not identified in the major PFGE types, but were identified in 5 isolates of ST59-PFGE D-SCC*mec* V_T and 2 isolates of ST 30-PFGE AG-SCC*mec* IV.

source of the 65 clinical isolates included bloodstream (46 isolates), sputum (14 isolates), pleural effusion (3 isolates), and ascites (2 isolates). A total of 11 PFGE patterns were identified and 2 major patterns were type A and type F. Within 65 clinical isolates, the ratios of type A and type F are 48% and 25%, respectively. Of the 43 nasal isolates, types A and F accounted for 37.2% and 30.2% of the patterns, respectively. Seventeen isolates with various PFGE patterns were selected for MLST analysis and 2 sequence types (ST 239 and ST 5) were identified. Most isolates with PFGE type A and B sequenced as ST 239, whereas those with PFGE type F sequenced as ST 5. Overall, most MRSA isolates belonged to 1 of 2 major clones characterized as ST239/PFGE A/SCC*mec* III or IIIA/PVL negative (43.5%), and ST5/PFGE F/SCC*mec* II/PVL negative (26.9%). Both clones have been recognized as healthcare-associated clones in Taiwan.

The genetic correlation between clinical and nasal colonized isolates was analyzed in 32 patients with MRSA infections after excluding 4 patients who had multiple nasal MRSA colonization or clinical isolates with different genotypes (Table 5). The infection sources in these 32 patients were: bacteremia (19), pneumonia (8), thoracic empyema (2), peritonitis (1), combined thoracic empyema with bacteremia (1), and combined pneumonia with peritonitis (1). The nasal and clinical isolates were indistinguishable in 24 patients (75.0%), highly related in 6 patients (18.8%), and distinct in 2 patients (6.2%) based on PFGE and MLST analyses.

DISCUSSION

In this study of medical ICUs patients, we found the subsequent MRSA infection rate of patients with nasal MRSA colonization to be significantly higher than that of patients without nasal MRSA colonization. History of hospitalization within 1 year, old cerebrovascular accidents, and previous MRSA infections were risk factors for nasal MRSA colonization. Nasal MRSA colonization was an independent predictor for subsequent MRSA infections. History of tracheostomy, however, was a protective predictor against subsequent MRSA infection. Molecular study revealed that most MRSA isolates were ST239/PFGE A/SCC*mec* III or IIIA/PVL (−) and ST5/PFGE F/SCC*mec* II/PVL (−), which have been classified as healthcare-associated clones.

Nosocomial *S. aureus* bacteremia is 3 times more frequent in *S. aureus* nasal carriers than in noncarriers (1.2% versus 0.4%).[11] Methicillin-resistant *S. aureus* colonization was the leading risk factor for subsequent MRSA infection in patients with chronic skin ulcers during the same admission.[7] In general, nasal MRSA colonization, either present at admission to the hospital or acquired during hospitalization, increases the risk of MRSA infection compared with patients without nasal colonization (25% versus 2%).[2] Furthermore, the impact of colonization leading to infection may be prolonged up to 18 months after hospital discharge.[23] In our study patients, we also found that patients with nasal MRSA colonization had higher rates of subsequent MRSA infections than patients without nasal colonization (39.1% versus 14.7%). Although 1 study showed that nasal MRSA colonization was a poor predictor of ICU-acquired MRSA infections requiring antibiotic treatment,[24] a recent study observed that active surveillance cultures of MRSA yielded high specificity and negative predictive values for ventilator-associated pneumonia.[25] In this study, we also found nasal MRSA colonization was 1 important risk factors of MRSA infection. One possible explanation for these different observations is that different ICU patient groups respond differently to the same strategy.

Furthermore, we found that tracheostomy, but not translaryngeal endotracheal tubes, was associated with lower risk for MRSA infection with or without previous nasal MRSA colonization. Previous studies have also found that early tracheostomy patients had significantly lower rates of mortality and pneumonia compared with patients with prolonged translaryngeal endotracheal tubes.[26] Translaryngeal endotracheal tubes may provide a direct route from the upper airway—often colonized with pathologic organisms—to the lower airway. Translaryngeal endotracheal tubes keep the vocal cords open and that the bacteria from the back of the throat pass through the cords and then pass the cuff, get into the airway, reflux into the tube infect the biofilm in the endotracheal tubes tube, and finally translocate into the lungs. Tracheostomy is protective against nosocomial infection acquired from upper airway because of better hygiene and oral care. Therefore, tracheostomy, rather than a translaryngeal endotracheal tube to bypass the upper airway, may potentially decrease the risk for bacteria colonization and subsequent infection.

In this study, the rate of subsequent MRSA infection in patients with nasal MRSA colonization on admission was 39.1%. Clinical infection isolates were genotypically indistinguishable from nasal colonized isolates in 75.0% (24 in 32) of

TABLE 5. Genetic Correlation Between Clinical and Nasal Colonized MRSA Isolates From 32 Patients With MRSA Infections

Isolates	Indistinguishable Clone No. (%)	Highly Related Clone No. (%)	Distinct Clone* No. (%)
Clinical colonized	24 (75)	6 (18.8)	2 (6.2)
PFGE patterns			
A (N = 11)	8	3	
F (N = 9)	8	1	
B (N = 4)	2	2	
Others (N = 6)	6	0	

MRSA = methicillin-resistant *Staphylococcus aureus*, PFGE = pulsed-field gel electrophoresis.
* Two patients with distinct clones between clinical and colonized isolates: PFGE types A54 versus. AF4 and F4 versus B2, respectively.

the cases based on PFGE patterns and MLST analysis. We demonstrated a significant association between nasal MRSA colonization and subsequent infections based on genotyping by PFGE in medical ICU patients. In other groups, such as mixed ICU and general ward patients, continuous peritoneal dialysis patients, surgical patients and neonates, the association rate ranged from 67% to 84.6%.[8–12] One study also demonstrated that *S. aureus* nasal carriage and clinical isolates belong to similar genetic clusters using MLST, despite differences in sequence type assignments.[27]

There has been controversy about the benefits of reducing subsequent infection rates by decolonization. The Cochrane database of systematic reviews showed that application of intranasal mupirocin reduced infection rates only in dialysis and surgical patients.[28] Bode et al showed that rapid screening to identify nasal carriers, followed by decolonization with both nasal mupirocin nasal ointment and chlorhexidine soap, could prevent hospital-acquired infection with *S. aureus* in surgical patients.[29] Notably, a recent large-scale cluster-randomized trial among 74,256 patients concluded that universal decolonization was superior to both targeted decolonization and screening and isolation in both reducing rates of MRSA clinical isolates and bloodstream infection from any pathogen.[30] Although this practice benefited from infection rate control and obviated the need for MRSA surveillance tests, further surveillance for mupirocin and chlorhexidine resistance remains an essential issue if the universal decolonization practice implemented widely.[31,32]

There are some limitations in this study. First, although this was a large study, these results reflected the association between nasal colonization and infection at a single medical center, and may not be generalized to other hospitals. Second, we did not obtain colonization specimens from anatomic sites other than nostrils, which may also contribute to subsequent MRSA infections. Third, our study was performed in 2 different ICUs. Differences in compliance to infection-control programs to prevent horizontal transmission of MRSA in these 2 ICUs may affect the occurrence of nasal MRSA colonization and subsequent infections. Finally, molecular genotyping analysis was performed randomly on a subset of the total strains, which could not represent all the strains.

In conclusion, nasal MRSA colonization was significantly associated with subsequent MRSA infection among medical ICU patients. Previous MRSA infection was associated with subsequent MRSA infections, and history of tracheostomy could reduce this risk. Molecular and genetic studies determined that most MRSA isolates were healthcare-associated strains with significant correlations between colonized nasal and clinical isolates. In future studies, this information may support a decolonization strategy for the medical ICU patients.

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