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Original Article

Impact of Active Surveillance and Contact Isolation on Transmission of Methicillin-resistant *Staphylococcus aureus* in Intensive Care Units in an Area With High Prevalence

*Jann-Tay Wang,[1] Tsai-Ling Lauderdale,[2] Wen-Sen Lee,[3] Jeng-Hua Huang,[4] Tsung-Hsi Wang,[5] Shan-Chwen Chang[1]**

Background/Purpose: Previous research has suggested that active surveillance and early initiation of contact isolation (ASI) can control the nosocomial spread of methicillin-resistant *Staphylococcus aureus* (MRSA), especially among intensive care unit (ICU) patients. However, these interventions have never been implemented in Taiwan.

Methods: This study was conducted from September 2005 to October 2006 to evaluate the effect of ASI on the spread of MRSA in two medical centers in Taiwan with a high prevalence of MRSA. One ICU from each hospital was selected as a study site. In phase I (the first 6 months), only active surveillance was introduced. In phase II (the final 6 months), ASI for patients who had positive MRSA cultures was implemented.

Results: The incidence of acquiring MRSA during ICU stay did not differ significantly during phases I and II in hospital A ($p = 0.940$) and hospital B ($p = 0.810$). The independent risk factors for acquiring MRSA in the ICU were length of stay and presence of respiratory tract diseases.

Conclusion: This study demonstrated that, given the current resource limitations, ASI alone could not reduce MRSA transmission in two ICUs in Taiwan, where the MRSA prevalence was high.

Key Words: intensive care units, methicillin-resistant *Staphylococcus aureus*, patient isolation, surveillance

Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the main pathogens responsible for nosocomial infections.[1,2] Previous studies have suggested that MRSA is not part of a patient's endogenous flora.[3] Other studies have indicated that acquisition of MRSA is associated highly with subsequent MRSA infection.[4] Prevention of transmission among hospitalized patients appears to be the major method for the control of MRSA infection.[3]

Two major guidelines in the United States have provided important recommendations for

[1]Department of Internal Medicine, National Taiwan University Hospital, [3]Department of Internal Medicine, Wan Fang Hospital, [4]Department of Internal Medicine, Taipei Cathay General Hospital, [5]Center for Disease Control, Taipei, [2]Division of Clinical Research, National Health Research Institute, Zhunan, Taiwan.

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***Correspondence to:** Dr Shan-Chwen Chang, Department of Internal Medicine, National Taiwan University Hospital, 7 Chung-Shan South Road, Taipei 100, Taiwan.
E-mail: changsc@ntu.edu.tw

the control of MRSA transmission.[3,5] These guidelines agree on many issues. However, there is one major difference. The guidelines of the Society of Healthcare Epidemiology of America recommend the use of active surveillance of MRSA for all high-risk patients, especially those who have stayed in an intensive care unit (ICU).[3] In contrast, the guidelines of the Centers for Disease Control and Prevention Healthcare Infection Control Practices Advisory Committee (HICPAC) recommend the use of active surveillance of MRSA only after other interventions have failed to control transmission.[5]

During the past 2 decades, many United States hospitals have adopted the HICPAC recommendations,[6] but the incidence of MRSA infection has continued to increase.[1] It has been argued that unrecognized MRSA carriers become continuous sources of MRSA because they are not placed in isolation. This has prompted some hospitals to implement active surveillance for MRSA in target patients.[3,7] Although several studies have reported that active surveillance successfully controls MRSA infection,[8–10] others have reported inconsistent or negative results.[11–14]

A high proportion of MRSA (up to 80%) among all nosocomial *S. aureus* isolates has been noted in Taiwan.[15,16] Taiwanese hospitals have followed the HICPAC recommendations for many years, but these have provided no obvious benefits.[17,18] In addition to the controversies concerning MRSA-control guidelines, the effectiveness of active surveillance and early initiation of contact isolation (ASI) in an area with a high proportion of MRSA among all nosocomial isolates of *S. aureus* has never been studied. In addition, some adjuvant interventions such as rapid detection of MRSA using polymerase chain reaction methods, preemptive isolation, and bedside bathing using chlorhexidine-containing solutions are not applicable currently in Taiwan because of limitations in resources and/or lack of acceptance by patients and their families.[7,14,19]

We conducted the present study to investigate the impact of active surveillance on the transmission of MRSA among high-risk patients in the ICUs of two hospitals in Taiwan.

Methods

Hospital settings, patients, and study period

This study was conducted from September 1, 2005 to October 31, 2006 at two medical centers (Hospitals A and B) in Northern Taiwan. These two hospitals offered primary and tertiary care. Hospital A had a capacity of 623 beds and four ICUs (43 beds in total). Hospital B had a capacity of 756 beds and three ICUs (59 beds in total). The 13-bed medical ICU of hospital A and the 32-bed surgical ICU of hospital B were selected as the study sites. The distance between bed centers in these two ICUs was at least 2.1 m. The proportion of MRSA among all *S. aureus* that caused nosocomial infections in both hospitals during the past 5 years was around 85.4% and 86.3%, respectively. The nosocomial MRSA infection rates in the ICU of hospital A were 2.2, 1.4, 0.9, 1.4, and 0.9 per 1000 patient days from 2000 to 2004, respectively. The nosocomial MRSA infection rates in the ICU of hospital B were 1.75, 1.09, 1.71, 0.97, and 0.93 per 1000 patient days from 2000 to 2004, respectively.

Study protocol

The study was approved by the Institute Review Boards of the two hospitals. This 14-month study consisted of three phases: phase I (the first 6 months), wash-out phase (the following 2 months), and phase II (the last 6 months). Active surveillance was performed in phases I and II. The active surveillance procedures were as follows: (1) all patients who were in ICUs on the first day of phases I and II had surveillance cultures taken on day 1 of each phase; (2) patients who were newly admitted to the ICU had surveillance cultures taken within 24 hours of admission; (3) for all patients, surveillance cultures were taken every 3 days and on the day that they left the ICU; and (4) the culture sites of every surveillance culture were the nostril,[20–22] throat (or sputum if the patient was intubated),[23,24] axillae,[3] inguinal area,[3] and wound (if present).[21,22] During phases I and II, all healthcare workers in the two ICUs were screened monthly for nasal

carriage of MRSA. All culture swabs were sent immediately to the central laboratory at the National Health Research Institute (Zhunan, Taiwan).

During phase I, the results of active surveillance were not given to the healthcare workers. Only infection control interventions suggested by HICPAC, except those related to active surveillance, were adopted in these two ICUs.[5] Therefore, in phase I, patients were placed in isolation only when cultures of their clinical specimen yielded MRSA and/or other multidrug-resistant bacteria, or if they suffered from contagious diseases. During the washout phase, an education program (designed by three senior infectious diseases specialists) was used to train healthcare workers on isolation procedures that would be adopted in phase II. During phase II, patients who tested positive for MRSA by surveillance and clinical specimen cultures were put on contact isolation immediately after the culture results were available. The procedures of contact isolation in phase II were: (1) patients were moved to private rooms or cohort areas as soon as possible; (2) non-critical devices were used exclusively in those isolated patients; (3) healthcare workers were instructed to wash their hands with chlorhexidine-based disinfectants (4% w/v) or alcohol-based hand rubs before entering and after leaving the private rooms or cohort areas; (4) healthcare workers were instructed to put on gowns and gloves before entering the private rooms or cohort areas; (5) healthcare workers were instructed to take off gowns and gloves after leaving the private rooms or cohort areas; (6) the beds and surrounding environment were cleaned and disinfected with 0.5% sodium hypochlorite after patient discharge; (7) study assistants were instructed to monitor the adherence of healthcare workers to procedures 3–5 twice daily; and (8) contact isolation continued until the patient was discharged.

Microbiology

Each swab was plated onto a sheep blood agar plate, and a CHROMagar MRSA plate, after which it was placed in a tube of enrichment (salt) broth that contained 5 mL Trypticase Soy Broth with 7.5% NaCl. After overnight incubation, the enrichment broth was subcultured on a CHROMagar *S. aureus* plate. All plates were incubated at 35°C in ambient air and were checked for the presence of *S. aureus* and/or MRSA at 24 and 48 hours after incubation. Isolates suspected to be *S. aureus* from sheep blood agar were first checked by catalase and Gram stain if deemed necessary, and all *S. aureus* was confirmed by coagulase latex agglutination. *S. aureus* isolates from blood agar plates and CHROMagar *S. aureus* plates were spotted onto CHROMagar MRSA plates to check for methicillin resistance, whereas confirmed *S. aureus* isolates from CHROMagar MRSA plates were assumed to be MRSA.

All isolates were subcultured to a fresh blood agar plate and stored at −80°C for subsequent drug susceptibility tests. Susceptibility to chloramphenicol, ciprofloxacin, clindamycin, erythromycin, gentamicin, linezolid, rifampin, teicoplanin, tetracycline, trimethoprim/sulfamethoxazole, and vancomycin was determined using the disc diffusion method.[25] All media and identification reagents were purchased from Becton, Dickinson and Co., Franklin Lakes, NJ, USA), unless indicated otherwise.

Data collection and definitions

A standardized case record form was used to record demographic, clinical, and microbiological data. The demographic data included patient age and sex. The clinical data consisted of dates of ICU admission and discharge, length of ICU stay, Acute Physiology and Chronic Health Evaluation II (APACHE II) score upon admission to the ICU,[26] underlying diseases, recent operations, invasive therapeutic procedures, and prior use of antimicrobial agents. The microbiological data included the first date when a culture tested positive for MRSA, and the body sites where positive cultures were found. The prevalence of patients carrying MRSA on admission and during their stay in the ICU, as well as the incidence of MRSA transmission (newly acquired MRSA) during ICU stay were recorded and compared.

The APACHE II scores were divided into low and high groups, with a cutoff point of 17, as

suggested previously.[27,28] Initially, antibiotics were classified into 15 groups: Group 1, penicillins without anti-pseudomonal effect and not combined with β-lactamase inhibitors; Group 2, anti-pseudomonal penicillins; Group 3, penicillins combined with β-lactamase inhibitors; Group 4, first-generation cephalosporins; Group 5, second-generation cephalosporins; Group 6, third-generation cephalosporins without anti-pseudomonal effect; Group 7, third-generation cephalosporins with anti-pseudomonal effect; Group 8, fourth-generation cephalosporins; Group 9, carbapenems; Group 10, monobactams; Group 11, glycopeptides; Group 12, anti-anaerobic agents and antibiotics with activity against atypical pathogens; Group 13, aminoglycosides; Group 14, antifungals; and Group 15, fluoroquinolones. Subsequently, antibiotics of groups 2, 6, 7, 8, 9, 10, 13, and 15 were classified further as broad-spectrum antibiotics.

Prior use of antibiotics was defined as use within 15 days before acquisition of MRSA (for those who were positive for MRSA), or 15 days before ICU admission to the day of ICU discharge (for those who were negative for MRSA).[29] Invasive therapeutic procedures included use of central venous catheters (CVCs), arterial catheters, Port A catheters, endotracheal tubes, nasogastric/nasoduodenal tubes, peripheral venous catheters, thoracentesis, and paracentesis within 7 days prior to acquisition of MRSA (for these who were positive for MRSA), or within the meanwhile from 7 days before ICU admission to the day of ICU discharge (for those who were negative for MRSA). Recent operation was defined as: (1) a simple procedure performed under local anesthesia within 7 days prior to acquisition of MRSA (for those who were positive for MRSA), or within the meanwhile from 7 days before ICU admission to the day of ICU discharge (for those who were negative for MRSA); or (2) an operation performed under general anesthesia within 30 days prior to acquisition of MRSA (for those who were positive for MRSA), or within the meanwhile from 30 days before ICU admission to the day of ICU discharge (for those who were negative for MRSA).[30]

Transmission of MRSA was defined as patients being negative for MRSA on first active surveillance culture upon admission to the ICU, but being positive for MRSA in the following active surveillance cultures or the clinical cultures during their stay in the ICU.

Statistical analysis

Statistical analysis was performed with SAS 9.1.3 (SAS Institute Inc., Cary, NC, USA). Continuous variables were compared using Student's t test. Categorical variables were compared with a χ^2 test or, if the expected values were < 10, Fisher's exact test. The primary end point was the incidence of MRSA transmission during ICU stay (new acquisition of MRSA). Nosocomial MRSA infection rates were also compared. The method described by Oleinick and Mantel was used to compare the incidence in phases I and II.[31] Predictors for acquisition of MRSA during ICU stay were identified using a logistic regression model, by comparing the characteristics of patients with newly acquired MRSA (including new colonization and new infection) to those who were never positive for MRSA by all active surveillance cultures and clinical cultures while staying in the ICU. All parameters were tested initially by univariate analysis. Parameters with a p value less than 0.05 from the univariate analysis were used for multivariate analysis. Parameters with collinearity (variance inflation > 10, as determined by a linear regression model using the VIF option in SAS) were not considered in the final model simultaneously. A stepwise model comparison and selection were used to determine the final model of multiple variables analysis. All tests were two-tailed and $p < 0.05$ was considered statistically significant.

Results

Table 1 shows the demographic and clinical data of the enrolled patients. Chronic renal insufficiency was the most common (79.4%) genitourinary tract disease, and diabetes mellitus was the most common (98.0%) endocrine disease. For

Table 1. Demographic and clinical data of the enrolled patients*

Parameters	Hospital A			Hospital B		
	Phase I ($n=231$)	Phase II ($n=329$)	*p*	Phase I ($n=464$)	Phase II ($n=601$)	*p*
Age (yr)	69.5 ± 13.8	69.5 ± 14.6	0.962	65.3 ± 17.8	66.6 ± 18.2	0.245
Sex, male:female	132:99	192:137	0.774	305:159	362:239	0.066
Length of stay (d)	10.1 ± 25.4	7.9 ± 8.9	0.352	9.8 ± 14.1	9.1 ± 11.7	0.383
APACHE II > 17	93 (40.3)	115 (35.0)	0.201	86 (18.5)	172 (28.6)	< 0.001
Smoking	86 (37.2)	107 (32.5)	0.249	158 (34.1)	203 (33.8)	0.925
Diseases						
Cardiovascular	123 (53.2)	205 (62.3)	0.033	270 (58.2)	350 (58.2)	0.988
Respiratory tract	35 (15.2)	43 (13.1)	0.484	113 (24.4)	161 (26.8)	0.367
Hepatobiliary tract	19 (8.2)	22 (6.7)	0.492	45 (9.7)	49 (8.2)	0.378
GU tract	55 (23.8)	61 (18.5)	0.130	127 (27.4)	192 (31.9)	0.106
GI tract	19 (8.2)	49 (14.9)	0.017	60 (12.9)	94 (15.6)	0.213
Mucocutaneous	2 (0.9)	0	0.091	1 (0.2)	0	0.255
Cerebrovascular	31 (13.4)	57 (17.3)	0.211	78 (16.8)	129 (21.5)	0.057
Endocrine	90 (39.0)	91 (27.7)	0.006	156 (15.4)	215 (35.8)	0.465
Autoimmune	3 (1.3)	3 (0.9)	0.662	1 (0.2)	1 (0.2)	0.854
Malignant	13 (5.6)	23 (7.0)	0.517	27 (5.8)	56 (9.3)	0.035
Immunodeficiency	0	0	0.854	2 (0.4)	8 (1.3)	0.131
Recent operation	12 (5.2)	8 (2.4)	0.083	208 (44.8)	292 (48.6)	0.223
CVC	62 (26.8)	111 (33.7)	0.082	265 (57.1)	368 (61.2)	0.175
Arterial line	94 (40.7)	186 (56.5)	< 0.001	172 (37.1)	258 (42.9)	0.053
Nasogastric tube	80 (34.6)	169 (51.4)	< 0.001	202 (43.5)	346 (57.6)	< 0.001
Urinary catheters	91 (39.4)	187 (56.8)	< 0.001	331 (71.3)	478 (79.5)	0.002
Endotracheal tube	61 (26.4)	116 (35.3)	0.027	181 (39.0)	304 (50.6)	< 0.001
Antibiotics						
Group 1	5 (2.2)	7 (2.1)	0.976	110 (23.7)	121 (20.1)	0.161
Group 2	24 (10.4)	35 (10.6)	0.925	51 (11.0)	130 (21.6)	< 0.001
Group 3	25 (10.8)	50 (15.2)	0.135	30 (6.5)	25 (4.2)	0.092
Group 4	38 (16.5)	51 (15.5)	0.762	233 (50.2)	288 (47.9)	0.458
Group 5	66 (28.6)	93 (28.3)	0.937	28 (6.0)	62 (10.3)	0.013
Group 6	43 (19.5)	80 (24.3)	0.109	54 (11.6)	50 (8.3)	0.071
Group 7	3 (1.3)	19 (5.8)	0.007	47 (10.1)	25 (4.2)	0.000
Group 8	8 (3.5)	7 (2.1)	0.335	26 (5.6)	36 (6.0)	0.789
Group 9	3 (1.3)	12 (3.6)	0.090	32 (6.9)	62 (10.3)	0.051
Group 10	8 (3.5)	1 (0.3)	0.003	0	1 (0.2)	0.379
Group 11	25 (10.8)	36 (10.9)	0.964	86 (18.5)	101 (16.7)	0.462
Group 12	38 (16.5)	66 (20.1)	0.279	65 (14.0)	92 (15.3)	0.553
Group 13	22 (9.5)	33 (10.0)	0.843	171 (36.9)	254 (42.3)	0.074
Group 14	5 (2.2)	9 (2.7)	0.670	41 (8.8)	52 (8.7)	0.916
Group 15	37 (16.1)	80 (24.3)	0.017	96 (20.7)	116 (19.3)	0.574

**Data presented as mean ± standard deviation or n(%). APACHE II = Acute Physiology and Chronic Health Evaluation II; GU = genitourinary; GI = gastrointestinal; CVC = central venous catheter.*

Table 2. Patients positive for methicillin-resistant *Staphylococcus aureus* in hospitals A and B*

	Hospital A		Hospital B	
	Phase I	Phase II	Phase I	Phase II
Patients screened	231	329	464	601
Patient-times screened	514	731	895	1563
Episodes of MRSA infections	2	1	13	15
Patients positive for MRSA	74 (32.0)	76 (23.1)	160 (34.5)	197 (32.7)
Acquired before ICU	61 (26.4)	58 (17.6)	123 (26.5)	152 (25.3)
Acquired in ICU	13 (7.6)†	18 (6.6)†	37 (10.8)†	45 (10.0)†
Time lag from admission to acquiring MRSA (d)	9.6±8.5	9.4±8.7	13.0±14.4	10.8±8.2

**Data presented as n, n (%) or mean±standard deviation; †number of patients at risk, not the total number screened. MRSA = Methicillin-resistant Staphylococcus aureus; ICU = intensive care unit.*

patients in hospital A, more patients in phase I consumed alcohol, had endocrine diseases, and used monobactams. More patients in phase II had cardiovascular and gastrointestinal diseases; used arterial lines, nasogastric and endotracheal tubes, and used third-generation cephalosporins with anti-pseudomonal effects (Group 7), and fluoroquinolones (Group 15). In hospital B, more patients in phase I used third-generation cephalosporins with anti-pseudomonal effects (Group 7). More patients in phase II had APACHE II scores > 17, underlying malignancy; use of nasogastric tubes, urinary catheters and endotracheal tubes; and use of anti-pseudomonal penicillins (Group 2) and second-generation cephalosporins (Group 5).

During phase I, we screened 695 patients (1309 patient-times in total). The proportion of surveillance cultures missed was 5.6%. The total number of patient days for both ICUs was 6286. A total of 234 patients (33.7%) were positive for MRSA through active surveillance. Only 50 patients, all of whom belonged to those identified by surveillance cultures, were found positive for MRSA through routine culture of clinical specimens. Among the 234 MRSA-positive patients, 184 were found to have been positive for MRSA by active surveillance at ICU admission (which indicated that they had carried MRSA at the time of admission to the ICU). The other 50 patients (13 in hospital A and 37 in hospital B) acquired MRSA during their stays in the ICU. The time lag from ICU admission to acquisition of MRSA for the 13 patients in hospital A was 9.6±8.5 days, and that for the 37 patients in hospital B was 13.0±14.4 days. During this phase, there were 15 episodes of nosocomial MRSA infections in these two ICUs (Table 2).

During phase II, we screened 930 patients (2249 patient-times in total). The proportion of surveillance cultures missed was 4.5%. The total number of patient days for both ICUs was 6743. Two hundred and seventy-three patients (29.4%) were positive for MRSA through active surveillance. Only 59 patients, all of whom belonged to those identified by surveillance cultures, were positive for MRSA through routine culture of clinical specimens. Among these 273 MRSA-positive patients, 210 were found to have been positive by active surveillance for MRSA at admission to the ICU. The other 63 patients (18 in hospital A and 45 in hospital B) acquired MRSA during their stay in the ICU. The time lag from admission to ICU to acquisition of MRSA for the 18 patients in hospital A was 9.4±8.7 days, and that for the 45 patients in hospital B was 10.8±8.2 days. During this phase, there were 16 episodes of nosocomial MRSA infections in these two ICUs (Table 2). All patients with nosocomial MRSA infection were found to be carriers of MRSA by active surveillance at 3–21 days before the development of infection.

Table 3. Incidence of methicillin-resistant *Staphylococcus aureus* transmission and infection in both hospitals A and B

	Hospital A			Hospital B		
	Phase I	Phase II	*p*	Phase I	Phase II	*p*
Total patient days (d)	2009	2607		4528	5440	
Patient days at risk for acquiring MRSA (d)	1354	1803		2659	3329	
Incidence of MRSA infection (%)	1.00	0.38	0.719	2.87	2.76	0.932
Incidence of MRSA transmission (%)	9.60	9.98	0.940	13.92	13.52	0.810

MRSA = Methicillin-resistant Staphylococcus aureus.

Nasal carriage of MRSA by healthcare workers did not differ significantly between the two phases (hospital A: 8/32 *vs.* 7/25, $p = 0.768$; hospital B: 14/55 *vs.* 11/58, $p = 0.507$).

Table 3 shows the incidence of MRSA transmission during phases I and II in both hospitals. A comparison of phases I and II indicated no significant differences in the incidence of MRSA transmission (hospital A, $p = 0.940$; hospital B, $p = 0.810$), MRSA infection (hospital A, $p = 0.719$; hospital B, $p = 0.932$), and the time lag from admission to the ICU to acquiring MRSA (hospital A, $p = 0.96$; hospital B, $p = 0.42$).

Among the 507 patients who were positive through active surveillance for MRSA, 90.9% had positive nasal swab cultures, 87.5% had positive sputum or throat swab cultures, 62.6% had positive axillary swab cultures, 71.1% had positive perineal swab cultures, and 11.8% had positive wound cultures.

There were 420 MRSA isolates collected in phase I and 415 in phase II available for drug susceptibility tests. Susceptibility to chloramphenicol was 54.1% in phase I and 55.2% in phase II; ciprofloxacin, 17.8% and 14.8%; clindamycin, 15.5% and 18.8%; erythromycin, 4.8% and 4.0%; gentamicin, 13.3% and 10.6%; linezolid, 100% and 100%; rifampin, 88.8% and 77.6%; teicoplanin, 100% and 100%; tetracycline, 21.9% and 24.6%; sulfamethoxazole, 32.1% and 32.3%; and vancomycin, 100% and 100%. There was no significant difference in the drug susceptibilities between the two phases.

To determine adherence of healthcare workers to contact precautions, we made 701 observations. For hospital A, the adherence rates for washing hands using antiseptics before entering a private room or cohort area, washing hands using antiseptics after leaving a private room or cohort area, putting on gloves before entering a private room or cohort area, taking off gloves after leaving a private room or cohort area, putting on gowns before entering a private room or cohort area, and taking off gowns after leaving a private room or cohort area were 63.3%, 81.8%, 83.8%, 80.2%, 87.4%, and 88.2%, respectively. The corresponding rates for hospital B were 33.1%, 52.2%, 64.8%, 42.1%, 67.1%, and 67.3%, respectively.

Univariate analysis determined that the following factors increased the risk of acquisition of MRSA (Table 4): prolonged ICU stay; female sex; high APACHE II score at admission; use of CVCs, nasogastric tubes and endotracheal tubes; respiratory tract, genitourinary tract and endocrine diseases; recent operation; use of penicillin combined with β-lactamase inhibitors; and use of second-generation cephalosporins, glycopeptides, aminoglycosides, fluoroquinolones, and broad-spectrum antibiotics. Active surveillance plus contact isolation was not a significant factor (odds ratio, 0.884; 95% confidence interval, 0.599–1.306; $p = 0.540$). Multivariate analysis indicated that prolonged ICU stay and the presence of respiratory tract diseases were independent risk factors for acquiring MRSA in the ICU (Table 5).

Table 4. Risk factors for acquiring methicillin-resistant *Staphylococcus aureus* during intensive care unit stay

Variables	Odds ratio (95% confidence interval)	*p*
Length of stay in ICU	1.089 (1.071–1.108)	< 0.001
Sex, male to female	0.663 (0.450–0.977)	0.038
APACHE II score > 17	4.008 (2.317–6.934)	< 0.001
Central venous catheters	1.808 (1.078–3.033)	0.025
Nasogastric tube	3.740 (2.163–6.465)	< 0.001
Endotracheal tube	2.412 (1.381–4.218)	0.002
Respiratory tract diseases	2.762 (1.787–4.268)	< 0.001
Genitourinary tract diseases	1.605 (1.028–2.506)	0.037
Endocrine diseases	2.042 (1.334–3.125)	0.001
Recent operation	2.017 (1.365–2.979)	0.000
Group 3 antibiotics	2.037 (1.109–3.742)	0.022
Group 5 antibiotics	2.167 (1.292–3.634)	0.003
Group 11 antibiotics	2.057 (1.163–3.639)	0.013
Group 13 antibiotics	2.248 (1.373–3.681)	0.001
Group 15 antibiotics	2.425 (1.478–3.980)	< 0.001
Broad-spectrum antibiotics	5.450 (3.249–9.143)	< 0.001

ICU = Intensive care unit; APACHE II = Acute Physiology and Chronic Health Evaluation II.

Table 5. Risk factors for acquiring methicillin-resistant *Staphylococcus aureus* during intensive care unit stay

Variables	Odds ratio (95% confidence interval)	*p*
Length of stay in ICU	1.072 (1.045–1.099)	< 0.001
Respiratory tract diseases	2.066 (1.092–3.910)	0.026

Discussion

The present study demonstrated that ASI did not reduce the transmission of MRSA and MRSA infection in ICU patients in two Taiwanese hospitals. For our ICU patients, the overall prevalence rate of MRSA carriage was 31.2%. However, the incidence of nosocomial MRSA infection was low: 0.65 per 1000 patient days in hospital A, and 2.81 per 1000 patient days in hospital B. Only 21.5% patients who carried MRSA could be identified using routine clinical cultures. Nasal swab cultures had the higher yield rate to find MRSA carriage.

Some previous studies have suggested that ASI reduces the transmission of MRSA,[8,10,12] and two major guidelines to control nosocomial infection advocate the use of ASI.[3,5] However, the studies of Cepeda et al and Harbarth et al have shown that implementation of these procedures had no effect.[11,13] The different conclusions of these studies might have been the result of differences in study design, simultaneous application of other interventions (e.g. chlorhexidine bathing and topical mupirocin) other than ASI, differences in patient populations, and differences in the baseline prevalence of MRSA.

Despite the controversies about the effectiveness of ASI, we can suggest five reasons for the negative results in our study. First, we did not adopt preemptive isolation for patients who were newly admitted to the ICU. According to the surveillance results, 77.7% of patients who were positive for MRSA carried MRSA upon ICU admission. In this study, it took about 3 days to obtain culture results, which was similar to the routine practices in Taiwanese hospitals. Therefore, it is possible that transmission of MRSA to patients

negative for MRSA on admission from those who carried MRSA on admission occurred during this time interval. However, universal preemptive isolation for all patients admitted to ICUs is not generally acceptable to most Taiwanese hospitals.[19] Second, we did not use intranasal mupirocin and chlorhexidine bathing to reduce the colonization pool. This procedure has been reported previously as being effective in reducing MRSA colonization and infection.[7] A nasal preparation of mupirocin is currently not available in Taiwan, and chlorhexidine bathing is not acceptable to Taiwanese patients and their families at the present time.[19] Third, the prevalence of MRSA carriage among ICU patients (31.2%) was much higher in our study than in previous studies from other countries (11.4–15.7%).[6–8] The high prevalence of MRSA among our patients might have led to a higher overall probability of transmission.[14] Fourth, more of the patients in phase II of our study had significant clinical conditions, in particular high APACHE II scores, use of devices, and underlying diseases, compared with those in phase I. Patients with more complicated clinical conditions might have a higher risk of acquiring MRSA. Fifth, adherence of our healthcare workers to contact precautions was not good. A breach in isolation precautions unquestionably increases the risk of MRSA transmission.

Our study also showed that ASI did not decrease nosocomial MRSA infections in ICU patients. In addition to the reasons listed above, a low MRSA infection rate (0.65 per 1000 patient days at hospital A, and 2.8 per 1000 patient days at hospital B) compared with that in United States hospitals (2.0–8.9 per 1000 patient days) was found in the present study.[14,32] The cases of nosocomial infection in our two ICUs were defined according to the United States Centers for Disease Prevention and Control.[33] Therefore, the possibility of underestimating the MRSA infection was less likely. The low baseline MRSA infection rate might be a possible factor hindering the impact of ASI. Furthermore, a recent report by Robicsek et al demonstrated that surveillance cultures in ICUs alone do not result in a decrease in MRSA infections, but universal surveillance of the whole hospital does decrease infection.[32] This might also partly explain the negative results of our study, because a large proportion of our patients who were positive for MRSA were positive at the time of ICU admission, which indicated that they were likely to have acquired MRSA in other wards of the hospital. In addition, the nosocomial MRSA infection rates were much higher in the ICU of hospital B in phase I of the study compared with those noted from 2000 to 2004. It might be possible that, if active surveillance were not conducted, the nosocomial MRSA infection rate in the ICU of hospital B would continue to increase. Therefore, active surveillance might, in fact, have been helpful in controlling the nosocomial MRSA infection rate in the ICU of hospital B. However, this phenomenon could not be demonstrated in the ICU of hospital A.

Compared with hospitals in the United States, we noted a higher prevalence of MRSA carriage, but a lower MRSA infection rate. This finding is worthy of further study.

Our finding that routine clinical cultures detected only 21.5% of the MRSA colonization pool is similar to that (15%) reported by Salgado et al.[9] Previously reported risk factors for acquiring MRSA have included use of systemic antibiotics, prior residence in a long-term care facility, prior hospitalization, prior operation, need for dialysis, use of CVCs or long-term venous access devices, and use of urinary tract catheters.[34] We identified prolonged ICU stay and presence of respiratory diseases as the two independent risk factors for acquiring MRSA. It seems obvious that a prolonged ICU stay will increase the risk for acquiring MRSA. Presumably, the presence of respiratory diseases might facilitate colonization or infection of the airway with MRSA as a result of a breach in the defensive barriers of the normal airway.

In conclusion, our study demonstrated that ASI did not reduce MRSA transmission and infection among ICU patients in two Taiwanese hospitals where there was a high prevalence of MRSA. The negative results of ASI could reflect the current

situation in Taiwanese hospitals, where a relative low adherence rate to isolation precaution by healthcare workers was present, and limited resources compromised the implementation of other adjuvant infection control interventions. In addition, the major burden of nosocomial infections in Taiwan currently is caused by drug-resistant Gram-negative bacilli.[35] ASI for MRSA might not have a high priority as a mandatory infection control measure in Taiwan before the situation changes.[36] Prolonged ICU stay and the presence of respiratory diseases were independent risk factors for acquiring MRSA in ICUs.

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References

1. NNIS System. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. *Am J Infect Control* 2004;32:470–85.
2. Wang JT, Fang CT, Chen YC, et al. Staphylococcal cassette chromosome *mec* in MRSA, Taiwan. *Emerg Infect Dis* 2007; 13:494–7.
3. Muto CA, Jernigan JA, Ostrowsky BE, et al. SHEA guideline for preventing nosocomial transmission of multidrug-resistant strains of *Staphylococcus aureus* and *Enterococcus*. *Infect Control Hosp Epidemiol* 2003;24:362–86.
4. Huang SS, Platt R. Risk of methicillin-resistant *Staphylococcus aureus* infection after previous infection or colonization. *Clin Infect Dis* 2003;36:281–5.
5. Siegel JD, Rhinehart E, Jackson M, et al. *Management of Multidrug-resistant Organisms in Healthcare Settings*. Atlanta, GA: Centers for Disease Control and Prevention Healthcare Infection Control Practices Advisory Committee, 2006.
6. Boyce JM. New insights for improving hand hygiene and practice. *Infect Control Hosp Epidemiol* 2004;25:187–8.
7. Ridenour G, Lampen R, Federspiel J, et al. Selective use of intranasal mupirocin and chlorhexidine bathing and the incidence of methicillin-resistant *Staphylococcus aureus* colonization and infection among intensive care unit patients. *Infect Control Hosp Epidemiol* 2007;28:1155–61.
8. Huang SS, Yokoe DS, Hinrichsen VL, et al. Impact of routine intensive care unit surveillance cultures and resultant barrier precautions on hospital-wide methicillin-resistant *Staphylococcus aureus* bacteremia. *Clin Infect Dis* 2006; 43:971–8.
9. Salgado CD, Farr BM. What proportion of hospital patients colonized with methicillin-resistant *Staphylococcus aureus* are identified by clinical microbiological cultures? *Infect Control Hosp Epidemiol* 2006;27:116–21.
10. Singh N, Squier C, Wannstedt C, et al. Impact of an aggressive infection control strategy on endemic *Staphylococcus aureus* infection in liver transplant recipients. *Infect Control Hosp Epidemiol* 2006;27:122–6.
11. Cepeda JA, Whitehouse T, Cooper B, et al. Isolation of patients in single rooms or cohort to reduce spread of MRSA in intensive-care units: prospective two-centre study. *Lancet* 2005;365:295–304.
12. Gould IM, MacKenzie FM, MacLennan G, et al. Topical antimicrobials in combination with admission screening and barrier precautions to control endemic methicillin-resistant *Staphylococcus aureus* in an intensive care unit. *Int J Antimicrob Agents* 2007;29:536–43.
13. Harbarth S, Fankhauser C, Schrenzel J, et al. Universal screening for methicillin-resistant *Staphylococcus aureus* at hospital admission and nosocomial infection in surgical patients. *JAMA* 2008;2999:1149–57.
14. Harbarth S, Masuet-Aumatell C, Schrenzel J, et al. Evaluation of rapid screening and pre-emptive contact isolation for detecting and controlling methicillin-resistant *Staphylococcus aureus* in critical care: an interventional cohort study. *Crit Care* 2006;10:R25.
15. Chang SC, Sun CC, Yang LS, et al. Increasing nosocomial infections of methicillin-resistant *Staphylococcus aureus* at a teaching hospital in Taiwan. *Int J Antimicrob Agents* 1997;8:109–14.
16. Ho M, McDonald L, Lauderdale T, et al. Surveillance of antibiotic resistance in Taiwan, 1998. *J Microbiol Immunol Infect* 1999;32:239–49.
17. Hsueh PR, Chen WH, Teng LJ, et al. Nosocomial infections due to methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci at a university hospital in Taiwan from 1991 to 2003: resistance trends, antibiotic usage and *in vitro* activities of newer antimicrobial agents. *Int J Antimicrob Agents* 2005;26:43–9.
18. Wang JT, Sheng WH, Chang SC. Isolation precautions in hospitals. *Nosocomial Infect Control J* 2002;12:376–81.
19. Yu WL, Chang WH, Chuang YC. Nosocomial infections and surveillance for drug-resistant bacteria. *Infect Control J* 2007;17:254–62.
20. Garner JS, Jarvis WR, Emori TG, et al. CDC definition for nosocomial infections, 1988. *Am J Infect Control* 1988; 16:128–40.
21. Papia G, Louie M, Tralla A, et al. Screening high-risk patients for methicillin-resistant *Staphylococcus aureus* on

admission to the hospital: is it cost effective? *Infect Control Hosp Epidemiol* 1999;20:473–7.
22. Sanford MD, Widmer AF, Bale MJ, et al. Efficient detection and long-term persistence of the carriage of methicillin-resistant *Staphylococcus aureus*. *Clin Infect Dis* 1994;19: 1123–8.
23. Salgado CD, Sheppe S, Dill J. The sensitivity of MRSA follow-up cultures. Presented at the 11th Annual Meeting of the Society for Healthcare Epidemiology of America; April 1–3, 2001; Toronto, Ontario, Canada. Abstract 40.
24. Shahin R, Johnson IL, Jamieson F, et al. Methicillin-resistant *Staphylococcus aureus* carriage in a child care center following a case of disease. *Arch Pediatr Adolesc Med* 1999;153: 864–8.
25. Clinical and Laboratory Standards Institute (CLSI): Performance Standards for Antimicrobial Disk Susceptibility Tests. Approved Standard M2 – A9. CLSI documents, Wayne, PA, 2006.
26. Knaus WA, Draper EA, Wagner DP, et al. APACHE II: a severity of disease classification system. *Crit Care Med* 1985;13:818–29.
27. Chow JW, Yu VL. Combination antibiotic therapy versus monotherapy for gram-negative bacteraemia: a commentary. *Int J Antimicrob Agents* 1999;11:7–12.
28. Smolyakov R, Borer A, Riesenberg K, et al. Nosocomial multi-drug resistant *Acinetobacter baumannii* bloodstream infection: risk factors and outcome with ampicillin-sulbactam treatment. *J Hosp Infect* 2003;54:32–8.
29. Harris AD, Smith D, Johnson JA, et al. Risk factors for imipenem-resistant *Pseudomonas aeruginosa* among hospitalized patients. *Clin Infect Dis* 2002;34:340–5.
30. Levin AS, Levy CE, Manrique AE, et al. Severe nosocomial infections with imipenem-resistant *Acinetobacter baumannii* treated with ampicillin/sulbactam. *Int J Antimicrob Agents* 2003;21:58–62.
31. Oleinick A, Mantel N. Family studies in systemic lupus erythematosus. II. Mortality among siblings and offspring of index cases with a statistical appendix concerning life table analysis. *J Chronic Dis* 1970;22:617–24.
32. Robicsek A, Beaumont JL, Paule SM, et al. Universal surveillance for methicillin-resistant *Staphylococcus aureus* in 3 affiliated hospitals. *Ann Intern Med* 2008;148:409–18.
33. Garner JS, Jarvis WR, Emori TG, et al: CDC definitions for nosocomial infections, 1988. *Am J Infection Control* 1988; 16:128–40.
34. Naimi TS, LeDell KH, Como-Sabetti K, et al. Comparison of community- and health care-associated methicillin-resistant *Staphylococcus aureus* infection. *JAMA* 2003;290:2976–84.
35. Taiwan Nosocomial Infections Surveillance System (TNIS). *Annual Report of Nosocomial Infections, 2007*. Taipei: TNIS, 2008.
36. Weber SG, Huang SS, Oriola S, et al. Legislative mandates for use of active surveillance cultures to screen for methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci: position statement from the Joint SHEA and APIC Task Force. *Am J Infect Control* 2007;35:73–85.