Institutional Prescreening for Detection and Eradication of Methicillin-Resistant Staphylococcus aureus in Patients Undergoing Elective Orthopaedic Surgery

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Institutional Prescreening for Detection and Eradication of Methicillin-Resistant *Staphylococcus aureus* in Patients Undergoing Elective Orthopaedic Surgery

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Background: Surgical site infection has been identified as one of the most important preventable sources of morbidity and mortality associated with medical treatment. The purpose of the present study was to evaluate the feasibility and efficacy of an institutional prescreening program for the preoperative detection and eradication of both methicillin-resistant and methicillin-sensitive *Staphylococcus aureus* in patients undergoing elective orthopaedic surgery.

Methods: Data were collected prospectively during a single-center study. A universal prescreening program, employing rapid polymerase chain reaction analysis of nasal swabs followed by an eradication protocol of intranasal mupirocin and chlorhexidine showers for identified carriers, was implemented. Surgical site infection rates were calculated and compared with a historical control period immediately preceding the start of the screening program.

Results: During the study period, 7019 of 7338 patients underwent preoperative screening before elective surgery, for a successful screening rate of 95.7%. One thousand five hundred and eighty-eight (22.6%) of the patients were identified as *Staphylococcus aureus* carriers, and 309 (4.4%) were identified as methicillin-resistant *Staphylococcus aureus* carriers. A significantly higher rate of surgical site infection was observed among methicillin-resistant *Staphylococcus aureus* carriers (0.97%; three of 309) compared with noncarriers (0.14%; seven of 5122) ($p = 0.0162$). Although a higher rate of surgical site infection was also observed among methicillin-sensitive *Staphylococcus aureus* carriers (0.19%; three of 1588) compared with noncarriers, this difference did not achieve significance ($p = 0.709$). Overall, thirteen cases of surgical site infection were identified during the study period, for an institutional infection rate of 0.19%. This rate was significantly lower than that observed during the control period (0.45%; twenty-four cases of surgical site infection among 5293 patients) ($p = 0.0093$).

Conclusions: Implementation of an institution-wide prescreening program for the identification and eradication of methicillin-resistant and methicillin-sensitive *Staphylococcus aureus* carrier status among patients undergoing elective orthopaedic surgery is feasible and can lead to significant reductions in postoperative rates of surgical site infection.

Level of Evidence: Therapeutic Level III. See Instructions to Authors for a complete description of levels of evidence.

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Staphylococcus aureus is considered to be the most important pathogen in terms of surgical site infection. Epidemiologic studies have demonstrated that most cases of surgical site infection are caused by strains of *Staphylococcus aureus* that are brought into the hospital environment by patients themselves; i.e., most patients who develop a *Staphylococcus aureus* surgical site infection are carriers of the strains causing the infection. The anterior nares may be the most common niche for *Staphylococcus aureus* among carriers, and multiple studies have established that nasal carrier status is a significant risk factor for the development of surgical site infection with *Staphylococcus aureus*[1].

Methicillin-resistant forms of *Staphylococcus aureus* are particularly virulent and are especially of concern for a number of reasons. Specifically, methicillin-resistant *Staphylococcus aureus* has been associated with higher rates of morbidity and mortality following infection[2], these bacteria can survive on inanimate surfaces and in dry environments for as long as twenty days[3], and the overall prevalence of methicillin-resistant *Staphylococcus aureus* appears to be increasing[4].

Increased morbidity associated with surgical site infection translates directly into increased costs associated with medical care. On the average, surgical site infection is associated with a two-week increase in hospital stay, double the rate of rehospitalization, and triple the overall cost of treatment[5]. Moreover, most capitated payor systems consider surgical site infection to be a "preventable complication" and do not provide hospitals additional payment to cover treatment costs, further increasing the financial burden of this complication on institutions.

Multiple studies have identified nasal carriage status of *Staphylococcus aureus* as the most important risk factor for the development of a surgical site infection. The rate of surgical site infection appears to be two to nine times higher in carriers than in noncarriers[1,6,7]. In cases of surgical site infection, *Staphylococcus aureus* isolates have been reported to match those from the nares 85% of the time[8]. One study identified nasal carriage of *Staphylococcus aureus* as the only independent risk factor for the development of surgical site infection following orthopaedic implant surgery[9]. Comparable findings have been reported in the fields of cardiac and vascular surgery[10,11].

Intranasal mupirocin is currently the most efficient method of eradicating intranasal *Staphylococcus aureus* and appears to be successful for a majority of treated carriers[8]. Multiple clinical studies have demonstrated efficacy in reducing the rate of *Staphylococcus aureus* infection in different patient populations, including dialysis, cardiac, and orthopaedic surgery patients[8,12-18].

The purpose of the present study was to evaluate the feasibility and efficacy of an institution-wide prescreening program for the identification of *Staphylococcus aureus* carrier status and eradication of *Staphylococcus aureus* nasal colonization among patients undergoing elective orthopaedic surgery. The hypothesis was that successful implementation of such a program would significantly decrease the institutional rate of surgical site infection.

Materials and Methods

Study Design and Patient Population

This prospective clinical study received institutional review board approval. We evaluated adults undergoing elective inpatient orthopaedic surgery at a single institution between July 2006 and September 2007. Eligible procedures included arthroplasty, spine, and sports medicine procedures requiring at least one overnight hospital stay. A consecutive series of all patients undergoing elective orthopaedic surgery during that interval participated in the present study. The rates of surgical site infection during the study period were compared with those observed during a control period immediately preceding implementation of the screening program (between October 2005 and July 2006). A comparison of the two patient populations indicated that basic demographic variables were comparable (Table I).

Study Intervention: Screening and Eradication Protocol

In vitro antibiotic susceptibility testing of all cultured isolates was performed according to methods recommended by the National Committee for Clinical Laboratory Standards[19]. Nasal cultures were performed by swabbing a sterile saline solution-moistened polyester (Dacron) swab for five seconds along the interior walls of each naris. All culture specimens were obtained by a dedicated technician who had been initially trained and subsequently supervised by a microbiology supervisor. Rapid preoperative screening of patients with use of a polymerase chain reaction-based diagnostic test (Cepheid, Sunnyvale, California) was used to identify methicillin-resistant *Staphylococcus aureus* carriers. Standard microbiologic culture methods were used to identify methicillin-sensitive *Staphylococcus aureus* strains. This institution-wide program was applied to all patients undergoing elective surgery. However, the vast majority of procedures performed at this specialty hospital are

TABLE I Demographic Data

	Study Period (July 2006 to September 2007)	Control Period (October 2005 to July 2006)
No. of patients screened	7019	5293
Sex *(%)*		
Male	44.6	46.4
Female	55.4	53.6
Age* *(yr)*		
Male	59.2	59.2
Female	61.6	62.0

*The values are given as the mean.

orthopaedic in nature, and the current analysis focuses on the elective orthopaedic surgery experience.

Patients who tested positive for either methicillin-resistant or methicillin-sensitive *Staphylococcus aureus* were managed with intranasal 2% mupirocin ointment (Bactroban; GlaxoSmithKline, Middlesex, United Kingdom), which was applied to the interior of each naris twice daily for five days, and a shower wash with 2% chlorhexidine (Hibiclens; Mölnlycke Health Care, Norcross, Georgia), which was performed once daily for five days. The polymerase chain reaction test was then repeated to confirm eradication of the carrier status. Initial telephone contacts by trained hospital personnel provided direct personalized education and instruction regarding the importance of carrier status and proper implementation of the eradication protocol. A follow-up telephone call that was made several days later to confirm appropriate treatment was critical to achieving a high level of compliance. Patients in whom the carrier status was eliminated did not undergo isolation precautions while in the hospital but did receive preoperative antibiotic prophylaxis with vancomycin in lieu of routine medication with cefazolin. Patients who continued to demonstrate positive carrier status on follow-up testing were managed with routine methicillin-resistant *Staphylococcus aureus*-isolation precautions in addition to receiving preoperative antibiotic prophylaxis with intravenous vancomycin. Patients who were identified as carriers of methicillin-sensitive *Staphylococcus aureus* were similarly managed with five days of intranasal mupirocin and three days of chlorhexidine showers. Follow-up polymerase chain reaction testing was not performed on these individuals. If any patient underwent surgery prior to completion of the five-day course of mupirocin, treatment was completed following surgery.

During the period of the study, no additional systemic changes in the infection-control protocol were instituted. Also, to limit the potential bias that might be introduced by a general increase in the awareness of the risks of surgical site infection and increased adherence to routine infection-control measures, no institutional surgical site infection-related promotional campaign was performed.

Surveillance, Outcomes, and Definitions

Surveillance for nosocomial infection has been performed continuously at this institution since October 2005 with use of previously validated methods[20,21]. Healthcare-associated infections were identified according to criteria recommended by the Centers for Disease Control and Prevention[22,23]. A surgical site infection was considered to be present if one of the following findings was noted within thirty days after the operation: (1) the wound drained purulent material, (2) the wound drained serosanguineous material, the edges of the wound and surrounding tissues were erythematous, and the wound culture yielded a pathogen, or (3) a physician stated in the medical record that the surgical site was infected. In addition, when non-human tissue-derived implants were used, inpatient procedures were followed postoperatively for a minimum of one year. Stitch abscesses were not considered to be surgical site infections. Each case identified by the infection control manager was then reviewed by the hospital epidemiologist to ensure that the criteria for infection were met. Surgeons participated in a post-discharge surveillance system on a bimonthly basis that demonstrated 95% participation. Surgeon compliance with the surveillance system was promoted by annual reporting of the individual infection rates for each surgeon to the hospital credentialing committee.

The risk index developed by the National Nosocomial Infections Surveillance System was used to predict risk, and standardized infection ratios were calculated. The primary outcome measure was defined as the overall rate of surgical site infection with *Staphylococcus aureus* (including methicillin-resistant *Staphylococcus aureus*) among all inpatients undergoing surgery. Additional data collection included demographic information and associated comorbidities.

Statistical Analysis

The rate of surgical site infection was determined with use of the number of persons who presented for elective orthopaedic surgery during the relevant time period as the denominator. The primary comparison was made between the rates of surgical site infection during the study period and the control period. Secondary comparisons were made between the rates

TABLE II Screening Results*

	No. of Patients	No. of Cases of Infection	Rate of Surgical Site Infection (per 100)	No. of Cases of MSSA Infection	No. of Cases of MRSA Infection
Patients screened	7019	13	0.19	9	4
Noncarrier	5122 (73.0%)	7	0.14	6	1
Carrier (MSSA + MRSA)	1897 (27.0%)	6	0.32	3	3
MSSA carrier	1588 (22.6%)	3	0.19	3	0
MRSA carrier	309 (4.4%)	3	0.97	0	3

*MSSA = methicillin-sensitive *Staphylococcus aureus,* and MRSA = methicillin-resistant *Staphylococcus aureus.*

TABLE III Rates of Surgical Site Infection According to Carrier Status*

	MRSA Carriers	Noncarriers	P Value (Fisher Exact Test)	MSSA Carriers	Noncarriers	P Value (Fisher Exact Test)
No. of patients	309	5122		1588	5122	
No. of cases of surgical site infection (rate)	3 (0.97%)	7 (0.14%)	0.0162	3 (0.19%)	7 (0.14%)	0.7093

*MRSA = methicillin-resistant *Staphylococcus aureus,* and MSSA = methicillin-sensitive *Staphylococcus aureus.*

of surgical site infection in methicillin-resistant *Staphylococcus aureus* carriers and methicillin-sensitive *Staphylococcus aureus* carriers compared with noncarriers during the study period. The chi-square test was used unless one or more subgroups was five or fewer, in which case the Fisher exact test was utilized.

Source of Funding
There was no external funding source for this study.

Results

During the study period, 7019 patients underwent screening with both the polymerase chain reaction test for methicillin-resistant *Staphylococcus aureus* and routine cultures for methicillin-sensitive *Staphylococcus aureus*. Seven thousand three hundred and thirty-eight inpatient surgical procedures were performed during the same period, yielding a successful screening rate of 95.7%. Thirteen cases of surgical site infection were identified among the 7019 screened patients, for a surgical site infection rate of 0.19% during the study period (Table II). These cases included three infections with methicillin-resistant *Staphylococcus aureus* in previously identified methicillin-resistant *Staphylococcus aureus* carriers and three infections with methicillin-sensitive *Staphylococcus aureus* in previously identified methicillin-sensitive *Staphylococcus aureus* carriers. Seven infections (including one infection with methicillin-resistant *Staphylococcus aureus* and six infections with methicillin-sensitive *Staphylococcus aureus*) arose in noncarriers and presumably reflect true hospital-acquired infections or failure of the screening culture. Among screened patients, 1588 patients (22.6%) were identified as methicillin-sensitive *Staphylococcus aureus* carriers, and 309 patients (4.4%) were identified as methicillin-resistant *Staphylococcus aureus* carriers. The remaining 5122 patients (73%) were noncarriers. Comparing methicillin-resistant *Staphylococcus aureus* carriers with noncarriers, there were three cases of surgical site infection (all with methicillin-resistant *Staphylococcus aureus*) among 309 methicillin-resistant *Staphylococcus aureus* carriers and seven cases of surgical site infection (including one infection with methicillin-resistant and six infections with methicillin-sensitive *Staphylococcus aureus*) among the 5122 noncarriers; this difference in rates was significant (0.97% compared with 0.14%; $p = 0.016$) (Table III). There were three cases of surgical site infection among 1588 methicillin-sensitive *Staphylococcus aureus* carriers (0.19%), and, although this rate was also higher than that observed among noncarriers (0.14%), the difference was not significant ($p = 0.709$).

Surgical site infection rates were compared between the study and control periods. During the control period, twenty-four cases of infection were observed among 5293 inpatient orthopaedic surgery patients, for a rate of 0.45% (Table IV). Therefore, during the study period, a 59% reduction in the infection rate was observed ($p = 0.0093$). The reduction in the infection rate was relatively greater for methicillin-resistant *Staphylococcus aureus*-associated surgical site infection (0.06% compared with 0.19%; $p = 0.0315$), which was associated with a threefold reduction, than for methicillin-sensitive *Staphylococcus aureus*-associated surgical site infection (0.13% compared with 0.26%; $p = 0.0937$), which was associated with a twofold reduction.

The majority of identified methicillin-resistant *Staphylococcus aureus* carriers were previously unaware of their carrier status and therefore would not have received appropriate antibiotic prophylaxis or isolation precautions. Among identified methicillin-resistant *Staphylococcus aureus* carriers, only eight (2.6%) of 309 patients were aware of their status or had

TABLE IV Comparison of Surgical Site Infection Rates Between Study and Control Periods*

	Study Period (July 2006 to September 2007)	Control Period (October 2005 to July 2006)	P Value (Chi-Square Test)
No. of cases of MRSA infection (rate)	4 (0.06%)	10 (0.19%)	0.0315
No. of cases of MSSA infection (rate)	9 (0.13%)	14 (0.26%)	0.0937
Total no. of cases of surgical site infection (rate)	13 (0.19%)	24 (0.45%)	0.0093

*MRSA = methicillin-resistant *Staphylococcus aureus,* and MSSA = methicillin-sensitive *Staphylococcus aureus.*

available medical documentation indicating their status as carriers. Of the 309 methicillin-resistant *Staphylococcus aureus* carriers who were identified during the study period, 85% successfully completed all components of the eradication protocol and were subsequently retested. Seventy-eight percent of these carriers had negative results on retesting, whereas 22% were found to be persistently colonized. During the study period, only one (0.02%) of 5122 patients developed a methicillin-resistant *Staphylococcus aureus* surgical site infection following a negative screening result. Six (0.12%) of 5122 patients developed a methicillin-sensitive *Staphylococcus aureus* surgical site infection following a negative screening result.

Discussion

The present study suggests the potential efficacy of a comprehensive institutional screening and selective treatment program for methicillin-resistant *Staphylococcus aureus* and methicillin-sensitive *Staphylococcus aureus* carriers in terms of achieving a significant reduction in the rate of surgical site infection. A polymerase chain reaction-based screening test for methicillin-resistant *Staphylococcus aureus* allowed for the rapid identification of carrier status, among patients undergoing elective orthopaedic surgery, during routine prescreening hospital visits. Ultimately, the screening and treatment program was associated with a 59% reduction in the rate of surgical site infection in comparison with that during the control time period.

There have been two previously reported studies of large institutional efforts to reduce the rates of *Staphylococcus aureus* or methicillin-resistant *Staphylococcus aureus* infection in patients undergoing surgery[8,24]. Although both studies yielded essentially negative results, the failure to demonstrate a significant reduction in infection rates appears to have been largely due to methodological issues. Perl et al. conducted a large randomized, placebo-controlled, double-blind trial of intranasal mupirocin treatment for a group of patients undergoing elective cardiothoracic, general, oncologic, gynecologic, or neurosurgical procedures[8]. Three thousand eight hundred and sixty-four patients were analyzed, and no difference was observed in the rate of surgical site infection with *Staphylococcus aureus* between patients managed with mupirocin and those receiving placebo. However, although nasal cultures were performed to determine carrier status, preoperative screening was not used to identify carriers prior to surgery, and the primary analysis was therefore performed without regard to carrier status. Among patients who were identified as *Staphylococcus aureus* nasal carriers, mupirocin treatment was actually associated with a significant and nearly 50% reduction in the rate of nosocomial infection with *Staphylococcus aureus* (4.0% compared with 7.7%). Among nasal carriers, the risk of surgical site infection with *Staphylococcus aureus* was 4.5 times higher among those receiving placebo compared with those managed with mupirocin (95% confidence interval, 2.47 to 8.21; $p < 0.001$). Therefore, the negative study result appears to have been largely due to the failure to select nasal carriers as the population at risk and the failure to define the primary study question in terms of how treatment might affect the rate of surgical site infection in this target population.

The other major study, by Harbarth et al., was a large prospective interventional cohort study of a universal screening program for methicillin-resistant *Staphylococcus aureus*[24]. A rapid polymerase chain reaction screening test for methicillin-resistant *Staphylococcus aureus* was compared with no screening in a group of 21,754 mixed surgical patients in a crossover study design. Identified methicillin-resistant *Staphylococcus aureus* carriers were managed with intranasal mupirocin and chlorhexidine body wash. No significant difference in the rates of surgical site infection with methicillin-resistant *Staphylococcus aureus* was observed between the screened and unscreened groups. A major problem with the study, however, was that the vast majority of patient screening was performed at the time of hospital admission, with a relatively small percentage (12%) of patients undergoing outpatient prescreening prior to admission. Among methicillin-resistant *Staphylococcus aureus* carriers who were actually identified and managed in an outpatient setting prior to admission, there were no infections with methicillin-resistant *Staphylococcus aureus*. Another important consideration with respect to that study is that 57% (fifty-three) of the ninety-three patients who developed a methicillin-resistant *Staphylococcus aureus* nosocomial infection following screening were methicillin-resistant *Staphylococcus aureus*-negative at the time of admission, suggesting an endemic methicillin-resistant *Staphylococcus aureus* problem affecting the study institution. In hospitals without endemic methicillin-resistant *Staphylococcus aureus* contamination, universal screening protocols would be expected to be more effective.

In contrast to the findings in the study by Harbarth et al.[24], only one patient in the present study developed a methicillin-resistant *Staphylococcus aureus*-associated surgical site infection following a negative screening result. Three of the four observed cases of methicillin-resistant *Staphylococcus aureus*-associated surgical site infection occurred in patients who were identified as methicillin-resistant *Staphylococcus aureus* carriers during the screening process, two of whom failed to demonstrate successful eradication of carrier status following treatment. This relatively low rate of infection in uncolonized patients contrasts with the high (59%) rate of de novo infection observed in the study by Harbarth et al.[24]. Previous surveillance of our institution did not demonstrate a problem with endemic *Staphylococcus aureus* or methicillin-resistant *Staphylococcus aureus* contamination, and this difference in hospital environments likely explains the greater efficacy of screening in our study.

More recently, a study of universal screening and selective decolonization for *Staphylococcus aureus* in a population of patients undergoing elective total joint arthroplasty was reported by Rao et al.[25]. That study was very similar in design to the current study but had a much smaller sample size. One hundred and sixty-four (26%) of 636 patients were identified as nasal carriers and completed a five-day course of intranasal mupirocin and chlorhexidine baths. This group was compared

with both a concurrent and a historical control population, and an overall reduction in the rate of surgical site infection, from 2.6% to 1.5%, was observed. A basic cost-benefit analysis suggested a net economic savings for the institution of $231,741 per year.

The major limitation of our study is the use of historical controls. The potential for confounding was highlighted in a study by Kalmeijer et al. from the University of Amsterdam[26]. In that prospective, double-blind, placebo-controlled study in which intranasal mupirocin treatment was compared with placebo in patients undergoing orthopaedic surgery with implants, no significant reduction in the rate of surgical site infection was observed, despite successful eradication of intranasal carriage status in 83.5% of patients managed with mupirocin as compared with only 27.8% of those receiving placebo. In their analysis of the possible explanations for the negative result, the investigators pointed to an apparent reduction in the overall rate of surgical site infection during the study period and suggested a potential surveillance effect. The existence and strength of such a confounding effect would have clear implications for the use of historical controls.

Nevertheless, despite the limitations inherent in the use of historical controls, we believe that such a study design is reasonable in the setting of an adverse event that is relatively rare, as is the case with surgical site infection following orthopaedic implant-associated surgery, particularly when an institution-wide screening program is the intervention under investigation. Our study demonstrates the feasibility of implementing a hospital-wide prescreening program for detecting previously unidentified methicillin-resistant *Staphylococcus aureus* and methicillin-sensitive *Staphylococcus aureus* carriers with use of a rapid polymerase chain reaction-based assay. Practically, such a program allows early identification of methicillin-resistant *Staphylococcus aureus*-colonized patients, treatment, adjustment of preoperative antibiotic prophylaxis, and early isolation and contact precautions for those who continue to remain colonized with methicillin-resistant *Staphylococcus aureus*. Treatment of carriers with intranasal mupirocin and chlorhexidine showers also may be associated with a significant decrease in the rate of surgical site infection, most notably in methicillin-resistant *Staphylococcus aureus* carriers. However, it must be emphasized in this case that identification of previously unrecognized methicillin-resistant *Staphylococcus aureus* carriers and switching of preoperative antibiotic prophylaxis to vancomycin may have played an important role. Efficacy may require the absence of an endemic *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* contamination problem. Finally, despite relatively high compliance with such a program and a reduction in surgical site infection rates, previously identified methicillin-resistant *Staphylococcus aureus* carriers appear to remain at increased risk for developing surgical site infection following orthopaedic implant-associated surgery. ■

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