Sustained Reduction in Methicillin-Resistant Staphylococcus aureus Wound Infections After Cardiothoracic Surgery

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Background: Methicillin-resistant Staphylococcus aureus (MRSA) wound infections after cardiac surgery have increased in recent years and carry significant morbidity and mortality. In our hospital, MRSA accounted for 56% of postoperative infections.

Methods: Postoperative wound infection rates were compared for the 3 years before (baseline period) and after (intervention period) introduction of a comprehensive MRSA intervention program. The intervention included preoperative screening for MRSA colonization, administration of intravenous vancomycin prophylaxis for identified carriers, administration of intranasal mupirocin calcium ointment to all patients regardless of colonization status for 5 days beginning the day before surgery, and application of mupirocin to chest tube sites at the time of removal.

Results: Postoperative MRSA wound infections decreased by 93% (32 infections per 2767 cases in the baseline period vs 2 infections per 2496 cases in the intervention period; relative risk, 0.069; P < .001). Overall wound infection rates decreased from 2.1% to 0.8% (59 infections per 2769 cases vs 20 infections per 2496 cases; P < .001). During the intervention period, there was no change in the number of MRSA infections after noncardiac surgery.

Conclusion: This MRSA intervention program, in which all patients receive intranasal mupirocin and patients colonized with MRSA receive vancomycin prophylaxis, has resulted in a near-complete and sustained elimination of MRSA wound infections after cardiac surgery.

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Surgical Site Infections (SSIs) after cardiothoracic (CT) surgery carry significant morbidity and mortality as well as substantial monetary costs. Although the overall incidence of serious deep sternal or mediastinal wound infections is relatively low, ranging from 0.5% to 3%, prolonged hospitalization or readmission for extensive surgical debridement of the chest followed by lengthy antibiotic therapy is often required. Staphylococcus aureus is implicated in approximately half of these infections, with coagulase-negative staphylococci, gram-negative bacilli, and yeast organisms less frequently responsible. During the past 2 decades, the proportion of SSIs due to methicillin-resistant Staphylococcus aureus (MRSA) after cardiac surgery has steadily increased at many institutions. In contrast to many other pathogens, antibiotic therapy for MRSA is suboptimal and, even when combined with surgical debridement treatment, failure is not uncommon. Therefore, some institutions have developed strategies directed at preventing staphylococcal surgical wound infections, and specifically MRSA infections, after cardiac surgery. Because it has generally been assumed that SSIs are caused by patients’ endogenous flora, most control measures have focused on preoperative identification of MRSA carriers, with subsequent isolation, decolonization with intranasal mupirocin calcium ointment, and intravenous vancomycin for prophylaxis.

The success of these efforts has been variable, although placebo- and historically controlled intervention studies have reported reductions of 37% to 90% in S aureus SSIs, including those due to MRSA.

See Invited Commentary at end of article

Rochester General Hospital, Rochester, New York, is a community-based, 520-bed, medical-surgical hospital in which approximately 900 cardiac surgical procedures requiring median sternotomy are performed annually. Since the introduction of MRSA into the hospital in 1986, the
incidence of MRSA SSIs has steadily increased. Despite persistent educational efforts with an emphasis on standard control measures that included weekly screening for MRSA colonization of patients in the CT intensive care unit and administration of vancomycin prophylaxis to known MRSA carriers, MRSA accounted for 54% of all SSIs in the 3 years from 2004 through 2006. In an attempt to reduce this rate, a novel comprehensive MRSA control program was instituted that has resulted in a nearly complete elimination of MRSA SSIs that has been sustained for 36 months.

## METHODS

### PATIENT POPULATION

Data from all patients who underwent cardiac surgery and required a median sternotomy incision from January 1, 2004, through January 31, 2010, are included in this report. Before this period, the cardiac surgical service used industrial engineering methods to standardize all components of preoperative, intraoperative, and postoperative care. These methods included skin cleansing and preoperative preparation with chlorhexidine alcohol and vigorous intraoperative and postoperative glucose control. Most patients were admitted electively or immediately after cardiac catheterization to a 24-bed CT surgical floor before surgery. A few patients were first admitted to general medical or cardiology floors before transfer to the CT service when the need for surgical intervention was identified. Elective admissions underwent preoperative evaluation, including nasal culture for MRSA, in a dedicated room on the CT floor 24 to 72 hours before admission. The same 3 surgeons performed all procedures with assistance from dedicated physician assistants and nursing staff. Whenever feasible, endoscopic saphenous vein harvest was performed, and most coronary artery bypass procedures included implantation of the left internal mammary artery. Other standardized components of the CT program included dedicated CT operating suites, nursing personnel, cardiac bypass pump teams, and anesthesiologists. Intravenous cefazolin, administered for 48 hours, was standard prophylaxis, with the exception that patients with a history of an internal penicillin allergy received vancomycin. After surgery, all patients were transferred to a 13-bed CT intensive care unit for a minimum of 16 hours and then, when stable, to the CT surgical floor until hospital discharge, generally on postoperative day 4 or 5. Patients were seen within 2 weeks of discharge in the CT office for routine postoperative evaluation, including inspection of chest and leg incisions.

### IDENTIFICATION OF POSTOPERATIVE WOUND INFECTIONS

The same active and passive screening of all patients was used to identify infections throughout the period. A single infection prevention practitioner (L.G.) made daily rounds in the CT intensive care unit and on the CT unit to discuss postoperative cases or readmissions with the staff. After discharge, all surgical site cultures collected in the cardiac surgical office were reviewed, as were any cultures collected on readmission to Rochester General Hospital. Readmissions to other hospitals were also reviewed when possible. Classification of infections as superficial or deep and identification of the infecting organism were made by the infection prevention practitioner according to Centers for Disease Control and Prevention and National Healthcare Safety Network guidelines. Infections were attributed to the surgery if they occurred within 30 days or 1 year if the sternum or deep-organ space was involved. Infections resulting in hospitalization were reviewed with an infectious disease specialist and a CT surgeon.

### MRSA INTERVENTION PROGRAM

A quality improvement program specifically designed to reduce MRSA infections on the CT service was initiated on February 1, 2007, when the following 5 measures were instituted: (1) at the outset of the program, all CT staff were screened for nasal carriage of MRSA and decolonized if identified; (2) all patients were screened for nasal MRSA carriage 1 to 3 days before surgery or as soon as possible after admission in the case of transfers from other institutions or in emergency cases (oxacillin-sensitive *S aureus* was not identified), followed by the addition of vancomycin prophylaxis for carriers; (3) mupirocin calcium nasal ointment was applied to the anterior nares of all patients regardless of colonization status beginning 1 day before surgery or on admission for emergency cases and continued for 5 days or until discharge if earlier than day 5; (4) all patients were rescreened for MRSA colonization on discharge from the hospital; and (5) on removal of chest and mediastinal tubes, the exit site was covered with a 4 × 4 sterile gauze pad coated with mupirocin. The intervention was reviewed by the Rochester General Hospital Clinical Investigation Committee and was considered exempt since it was a quality improvement program.

### MICROBIOLOGY

Nasal swabs were collected from the anterior nares of patients and cultured for MRSA on chromagar plates using standard procedures. *Staphylococcus aureus* was confirmed as coagulase positive. Mupirocin sensitivity testing using an E test strip (AB BioDisk, Solna, Sweden) was performed on 12 randomly selected hospital MRSA isolates that had been collected before the initiation of the program and on 10 isolates that had been collected in January 2010.

### STATISTICAL ANALYSIS

The SSI rates were compared using the χ² test, and relative risk (RR) reduction and 95% confidence intervals (CIs) were calculated. *P* ≤ .05 was considered significant.

### RESULTS

An average of 877 CT surgical cases were performed annually from 2004 through January 2010, with minor year-to-year variation (Table 1). A total of 2766 patients underwent surgery between January 1, 2004, and January 31, 2007 (baseline cohort), and a total of 2496 patients underwent surgery from February 1, 2007, through January 31, 2010 (intervention cohort). During the baseline period, 59 SSIs were identified, for an incidence of 2.1%. Of these, 32 (54%) were attributable to MRSA, yielding a 1.2% MRSA SSI rate during the 37-month baseline period.

Before the initiation of the MRSA intervention program, 98 CT surgical staff members, including the 3 surgeons, were screened for MRSA colonization. Two nurses were positive (2% colonization rate) and were decolonized with a 5-day course of intranasal mupirocin. Subsequent screening of staff was not done after the program began. After implementation of the program on
February 1, 2007, all patients were assessed for nasal MRSA carriage before or just after admission. Fifty-six of the 2496 patients (2.2%) were colonized with MRSA on admission to the CT service. All but 3 of the colonized patients were negative on subsequent nasal culture before discharge (95% eradication rate). Most MRSA-colonized patients received intravenous vancomycin in addition to the standard cefazolin prophylaxis, with the exception of several patients who were taken to the operating room emergently and in whom MRSA screening cultures were not available until the following day. According to protocol, all patients, regardless of MRSA colonization status, received intranasal mupirocin for up to 5 days after surgery.

After implementation of the program, 2 of 2496 patients (0.08%) developed an MRSA SSI. This number represents a 93% reduction in MRSA SSIs from the baseline period (32/2766 vs 2/2496; RR, 0.069; 95% CI, 0.016-0.286; \( P < .001 \)). If only patients who completed 6 months of postoperative follow-up are considered, the MRSA SSI rate is similar (2 MRSA infections per 2220 surgical procedures). In the first month after the program was initiated, one of the infections was identified in a patient who was not colonized on admission, and the other occurred in a patient who was transferred from another hospital for emergency bypass surgery at the beginning of the second year. The latter patient was colonized with MRSA on admission, and although intranasal mupirocin therapy was provided, vancomycin prophylaxis was not admin-

<table>
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<tr>
<th>Table 1. Number of Cardiothoracic Surgical Procedures Requiring Median Sternotomy and the Number of Methicillin-Resistant Staphylococcus aureus (MRSA) Infections in the Baseline Period (January 1, 2004, to January 31, 2007) and After the Intervention (February 1, 2007, to January 31, 2010)</th>
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<td>Total</td>
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Abbreviation: SSIs, surgical site infections

a Excludes February, which is included in the baseline period.

b Compared with baseline period, \( P < .001 \).

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<th>Table 2. Incidence of Methicillin-Resistant Staphylococcus aureus (MRSA) Surgical Site Infections (SSIs) on Noncardiac Surgical Services at Rochester General Hospital, Rochester, New York, During 2004 Through 2009</th>
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<td>Variable</td>
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<td>No. of surgical cases</td>
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<td>Total SSIs, No. (%)</td>
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<td>SSIs due to MRSA, No. (%)</td>
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Abbreviation: NA, not available.
Staphylococcus aureus is consistently the most common pathogen associated with postoperative SSIs after CT surgery, and, in some institutions, as in ours, MRSA is more common than methicillin-sensitive isolates. Antibiotic therapy for serious MRSA infections is unsatisfactory, with high relapse rates, especially for isolates with vancomycin minimum inhibitory concentrations of 1.5 µg/mL or higher. At Rochester General Hospital, MRSA accounted for 54% of the SSIs on the CT service from January 2004 through January 2007, and standard measures emphasizing hand hygiene and isolation of known colonized or infected patients were ineffective at reducing postoperative MRSA infections. However, after introduction of the intervention, the incidence of MRSA SSIs declined immediately and dramatically. Including only patients in whom a 6-month postoperative follow-up period was complete, there was a greater than 90% reduction in MRSA SSIs that was sustained for at least 30 months. Using these data, the number needed to treat to prevent 1 postoperative MRSA wound infection was 93. Although other centers have also been able to reduce MRSA SSIs after CT surgery, the reported reductions have generally been lower and similar to the decline in rates of all S aureus SSIs. Our inability to detect a statistically significant decrease in oxacillin-sensitive S aureus infections is attributable to their relatively infrequent occurrence during the baseline period.

Since our program was initiated, only 2 cases of MRSA SSIs have been identified. It is possible that the first failure had a false-negative MRSA nasal screening culture result and thus would not have received vancomycin prophylaxis. It has been suggested that use of polymerase chain reaction assays to detect colonization might be more sensitive. The second failure, an emergency case that was not recognized as MRSA colonized until after surgery, did not receive vancomycin prophylaxis. These 2 failures suggest that vancomycin prophylaxis may be an important component to the intervention program for MRSA-colonized persons and that inoculation of the operative site may have occurred during surgery.

The design of our MRSA control program accounted for several variables that could be responsible for the development of MRSA infection. First, we assumed that not all MRSA SSIs develop as a result of contamination during the surgical procedure by endogenous flora of MRSA-colonized patients. We speculated, as have others, that for many patients bacteria reach the wound later in the hospital course, after a patient becomes colonized with MRSA in the postoperative period. In one study, 57% of the MRSA SSIs occurred in persons whose screening results were negative on admission. We also considered the possibility that mediastinal drain tubes might provide a conduit for pathogens to reach the sternum and mediastinal tissues, especially at the time of their removal. It is possible that MRSA, either in a newly colonized patient or from the hands of medical personnel, could enter the vacated chest tube track. Finally, the program was designed to circumvent the reality that hand hygiene of medical staff is sometimes suboptimal. To address each of these possibilities, we included several elements in the control program. To target vancomycin prophylaxis, rather than use it for all patients, it is necessary to screen all patients for MRSA colonization. We found that 2.2% of patients were colonized before surgery, similar to rates reported by others. This relatively low rate supports the concept that many wounds are seeded after the chest is closed in patients who are not originally colonized with MRSA. Assuming a similar preoperative MRSA colonization rate of 2.2% during the baseline period, this would mean that more than 50% of the patients would have had to develop an MRSA infection to account for the number of MRSA infections in the baseline period. Therefore, we believed that it was important not only to decolonize MRSA carriers but also to prevent postoperative colonization by treating all patients with intranasal mupirocin regardless of colonization status. This strategy appeared to be effective as only 9 of 2440 patients (0.4%) acquired MRSA colonization after the program was initiated. This rate is 5-fold lower than the rate reported from the United Kingdom, in which only MRSA-colonized patients were decolonized. It should be noted that in most studies mupirocin is administered only to patients with positive screening culture results or until cultures are finalized as negative if the therapy is initially begun in all patients. Our decision to add vancomycin to standard cefazolin prophylaxis for MRSA carriers, rather than to replace it, was in response to recent suggestions that β-lactam antibiotics provide better bactericidal activity than vancomycin for oxacillin-sensitive S aureus infections in addition to maintaining gram-negative antimicrobial coverage.

A potential adverse consequence of our program is the emergence of mupirocin resistance among gram-positive organisms. It is important to stress that although we did not find emergence of mupirocin resistance, it must be noted that a very small number of isolates were tested. A more comprehensive ongoing monitoring program for such a development would be required, as resistance has been reported in Europe after widespread mupirocin use. Should mupirocin resistance become prevalent, it is likely that we will observe a rebound in MRSA SSIs on the CT service. Furthermore, we did not find any vancomycin-resistant enterococcal infections on the CT service or a change in hospital-wide MRSA sensitivity to vancomycin therapy during the intervention period.

One factor that was clearly beneficial for the success of this program was the long-standing use of industrial engineering methods for the design and operation of the CT surgical service. These engineering methods provided a rigorous consistency in patient flow and procedures, thus reducing the chance of random factors affecting patient outcome. Implementation of a regimented MRSA reduction intervention was relatively easy in such an environment and ensured a high level of compliance by the staff.

Several limitations of our findings should be recognized. Our analysis used data from a historical control group for comparison to data collected after an intervention was initiated rather than data from a double-blind, randomized, placebo-controlled study design. Al-
though the latter provides a more rigorous assessment of the intervention, we believe that the use of the temporally proximal 3-year baseline period is reasonable since all other standardized procedures were in effect during the baseline period. During the 6 years encompassing the baseline and intervention periods, there were no major changes in surgical staff, technical procedures, or standard infection control measures. The only exception was the addition of the Premier Safety Surveillance (Cereplex Inc, Germantown, Maryland) Web-based infection control program to our standard surveillance methods during the intervention period. This program should have had the effect of detecting additional infections. Furthermore, the New York State public reporting law requires all hospitals to report SSIs to the facility in which the procedure was performed, and it also provides for validation of SSI data by on-site review. Nevertheless, it is possible that factors unrelated to the intervention program could have affected our observed MRSA SSI rates. For instance, a change in hospital-wide adherence to hand hygiene practices, a factor we did not rigorously measure, could have influenced MRSA SSI rates, or it is possible that the admission MRSA colonization rate during the baseline period was significantly higher than our measured rate during the intervention. However, hospital-wide rates of nosocomial MRSA SSIs on other surgical services did not change significantly during the intervention period, suggesting that other such effects were not operative. Another limitation is that we did not use a fastidious SSI detection method, such as routine 30-day postoperative telephone calls, to ascertain possible infectious complications but instead relied on physician- and staff-generated culture data and readmissions. Although our method for detecting infections may underestimate superficial wound infections, it is not likely to overlook serious deep wound infections. Finally, it should be noted that we cannot differentiate the beneficial effect of mupirocin therapy from vancomycin prophylaxis for MRSA carriers, as both measures were introduced simultaneously, and both have been independently associated with reductions in MRSA SSIs after cardiac surgery.12

In summary, we observed a sustained 93% reduction in MRSA SSIs after introduction of a program that included preoperative screening of all patients for MRSA carriage, with vancomycin prophylaxis for identified carriers; preoperative and postoperative intranasal mupirocin therapy for all patients regardless of colonization status; and application of mupirocin to chest tube sites on their removal.

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REFERENCES

Surgical site infections (SSIs) cause significant patient morbidity and mortality and add $10 billion annually to health care expenditures. Staphylococcus aureus is the most common pathogen, with methicillin-resistant S aureus (MRSA) accounting for up to 65% of poststernotomy mediastinitis. Compared with infections due to methicillin-susceptible S aureus (MSSA), MRSA has been associated with increased mortality, treatment failure, length of hospital stay, and costs.

The optimal strategy to prevent MRSA SSIs remains elusive, and data to support the benefit of any single MRSA-specific intervention, such as MRSA screening and decolonization or use of perioperative prophylaxis to cover MRSA, are limited and, at times, conflicting. For example, a meta-analysis of 7 randomized trials in patients undergoing cardiac surgery failed to show any overall benefit of routine prophylaxis with vancomycin compared with β-lactams. A randomized, double-blind, placebo-controlled trial of 4000 patients found no benefit of treatment with mupirocin compared with placebo in reducing S aureus SSI rates, but a more recent randomized clinical trial showed that the combination of mupirocin and chlorhexidine soap reduced the rate of S aureus SSIs by 60% among S aureus nasal carriers, although no patients with MRSA were encountered in that study.

Finally, 2 studies came to opposite conclusions regarding the effectiveness of MRSA screening used in combination with topical decolonization; that approach reduced hospital-associated MRSA disease in a 3-hospital organization, while no benefit was observed in the study that included more than 20,000 surgical patients and also adjusted perioperative antibiotic therapy for MRSA carriers. In the absence of more conclusive data, institutions often struggle to develop the most effective solutions to reduce their MRSA SSI rates.

The Online First article by Walsh et al details one institution’s successful approach to MRSA SSI prevention. The authors present a single-center, interrupted time series analysis that was designed to evaluate the impact of a comprehensive MRSA control program after reinforcement of standard control measures was insufficient to reduce MRSA SSIs among patients undergoing cardiothoracic surgery. During the 3-year baseline period, weekly screening for MRSA colonization with isolation and administration of vancomycin prophylaxis to carriers was performed in addition to standard infection control measures. During the intervention period, the following measures were implemented: (1) MRSA screening of all cardiothoracic staff and decolonization of carriers; (2) preoperative MRSA nasal screening of all patients; (3) perioperative vancomycin prophylaxis of MRSA carriers; (4) perioperative administration of intranasal mupirocin to all patients independent of colonization status; and (5) application of mupirocin to all chest tube sites on removal. Compared with the baseline period, overall SSI rates decreased by 62%, and there was a dramatic 93% reduction in MRSA SSIs.

Walsh and colleagues’ comprehensive approach to MRSA SSI prevention included screening of both the staff and the patients. All cardiothoracic staff members were screened for MRSA, and the 2 individuals (2%) that were found to be nasal carriers were decolonized with mupirocin. Although subsequent screening was not performed to assess the efficacy of decolonization during the 3-year intervention period, most studies suggest that mupirocin decolonization is most effective in the short term, with recolonization occurring in 50% to 70% of patients by 6 months to 1 year after treatment. Unless these individuals were extremely efficient in transmission, it seems unlikely that they contributed significantly to these infections, although molecular testing to establish strain relatedness was not available. Screening and decolonization of health care workers remain controversial issues.

Walsh and coauthors screened all patients for MRSA carriage before surgery to target the use of vancomycin for perioperative prophylaxis. It is interesting that they chose to use the MRSA screening results to guide prophylaxis only and not mupirocin use, hypothesizing that universal administration of mupirocin would prevent postoperative colonization, which raises the question, “Is screening necessary at all?” One alternate approach supported by existing guidelines is to administer vancomycin prophylaxis to all patients who are undergoing cardiac surgery in institutions where there are high endemic rates of MRSA SSIs. The extent to which mupirocin use in MRSA noncarriers contributed to their results is unclear; ie, how many MRSA SSIs were averted by treating this group? In a large, randomized clinical trial, mupirocin use had no impact on S aureus SSIs or other nosocomial infections among those who were noncarriers, while it reduced the rate of nosocomial S aureus infections (but not SSIs) among nasal carriers.