Preventing Methicillin-Resistant *Staphylococcus aureus* Infections in Cardiovascular Surgery Patients: Can We Do Any Better?

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(See the article by Dodds Ashley et al. on pages 1555–60)

Mediastinitis is among the worst of the postoperative complications of cardiovascular surgery, with a mortality rate of 10%–47% [1]. Effective prevention measures, if identified, have the potential for enormous impact. But those factors that place patients at high risk for this complication are not yet completely understood, and some studies have provided conflicting results. Prior investigation has identified preoperative, operative, and postoperative factors associated with increased risk for mediastinitis. Some of these factors could themselves be altered in an attempt to reduce risk, and others, although themselves unmodifiable, could be used to identify high-risk patients for other interventions.

The elucidation of unique risk factors for methicillin-resistant *Staphylococcus aureus* (MRSA) mediastinitis, with the goal of prevention, is justifiable because MRSA is a common cause of mediastinitis, accounting for as many as 65% of cases [2]. MRSA mediastinitis may also be associated with a higher mortality rate than that associated with methicillin-susceptible *S. aureus* (MSSA) [3] and has fewer antimicrobial options available for therapy than MSSA; also, the frequent use of prolonged courses of vancomycin may promote the emergence of resistance to that drug.

If specific risk factors for MRSA mediastinitis can be identified, several targeted interventions could then be directed at the high-risk population. For example, the use of vancomycin as routine surgical prophylaxis for patients undergoing cardiovascular surgery [4] who are at high risk or the use of mupirocin intranasally for selected patients in the perioperative period [5] could be attempted. Unique risk factors that are modifiable could be addressed (e.g., tighter perioperative glucose control through the use of a more aggressive insulin regimen in patients with diabetes, reduction in the use of bone wax in high-risk patients, and avoidance of shaving in the preoperative period).

In this issue of *Clinical Infectious Diseases*, Dodds Ashley et al. [6] indicate that risk factors for postoperative mediastinitis (POM) due to MRSA could be identified and that patients with POM due to MSSA did not share these risk factors. Diabetes, female sex, and older age were all uniquely associated with increased risk for POM due to MRSA, whereas obesity was uniquely associated with POM due to MSSA. Dodds Ashley et al. [6] hypothesize that POM due to MRSA and POM due to MSSA are fundamentally different diseases and that there might be a distinct pathophysiology involved in POM due to MRSA, compared with that involved in POM due to MSSA. However, MRSA mediastinitis may merely occur in a population distinct from that in which MSSA mediastinitis occurs and still share an identical pathophysiology. The current investigation [6] studied risk factors for the disease and did not study the disease itself, and suggesting distinct pathophysiologies may be premature on the basis of the evidence presented.

Some risk factors that were differentially recognized for POM due to MRSA compared with POM due to MSSA in this study [6] have been previously recognized as consistently affecting risk for surgical wound infections in general (e.g., diabetes and obesity). Other traditional risk factors, such as duration of operation, were not found to affect risk in this study at all. These inconsistencies, together with the use of multiple comparisons to test vari-
ables, as well as a lack of strong statistical associations, may actually indicate the detection of chance occurrences that require confirmation.

Many mediastinal infections are associated with organisms other than MRSA or MSSA. In some studies, the most common cause of mediastinitis is *Staphylococcus epidermidis*. Gram-negative organisms and *Candida* species are also significant causes of mediastinitis. The exclusion of patients with non–*S. aureus* infections from this study risks ignoring common (and potentially modifiable) risk factors for mediastinitis shared with patients with *S. aureus* infections. If risk factors for MRSA are not really unique, an emphasis on MRSA when targeting interventions, as opposed to general preventive measures against mediastinitis, might result in no reduction in mediastinal infections but, rather, only result in an alteration in the flora recovered when mediastinitis occurs.

This study was also nested from a larger study of MRSA surgical site infections and, therefore, did not examine risk factors unique to cardiovascular surgery that have previously been identified. For example, the use of internal mammary arteries (IMAs), especially bilateral IMAs, for bypass grafting has been previously identified as a risk factor for sternal infection [7]. Reduced sternal blood flow has been hypothesized to be responsible for the increased incidence of sternal infection in this setting. IMA grafts may offer distinct advantages for coronary revascularization in patients with diabetes. However, IMA grafts also present greater risk for mediastinitis in patients with diabetes than in patients without diabetes [8], and the non-inclusion of IMA grafts as a variable for study in the current investigation ignores a potentially major confounder.

Perioperative blood transfusions have been identified as a risk factor for sternal infections. Transfusion may be more common in patients with diabetes [9] and in patients who undergo reoperation for bleeding, both of which conditions have been previously described as risk factors for mediastinitis. Elderly patients who receive coronary artery bypass grafts have been found to have higher incidences of blood transfusion, preoperative use of a balloon pump, and cardiogenic shock and a higher proportion of female sex than has been found in younger study groups [10]. These observations might also help to explain a higher risk of MRSA mediastinitis in patients who are elderly, female, or diabetic.

Alternatively, the findings of the Dodds Ashley study [6] may have been a result of MRSA-specific factors, as opposed to cardiovascular surgery-specific factors that were not examined. One example is the use of antibiotics, not merely perioperatively, but in the 6 months to 1 year before surgery. Would patients who are diabetic, elderly, or female have been more likely to have been treated with antibiotics and thus more likely to have harbored a resistant subpopulation of *S. aureus*? Although known MRSA colonization was evaluated as a risk factor, screening for colonization with MSSA or MRSA does not appear to have been done, which may have resulted in an underestimation of the risk associated with colonization.

A recent study of poststernotomy mediastinitis that directly compared cases associated with MRSA to those associated with MSSA did not find a significant difference between the 2 groups in mean age (65.1 years in the MRSA group, compared with 64.7 years in the MSSA group), female sex (66.7% vs. 61.5%), obesity (53.3% vs. 53.8%), or diabetes (40% vs. 23.1%) [3]. Although these data contradict those of Dodds Ashley et al. [6], such direct comparison has been criticized for overrepresenting the risk associated with antibiotic use and for not comparing risk factors in an affected population with risks in the general population from which it arose [11]. This may be true, but indirect comparisons may also lead to erroneous conclusions because of multiple comparisons and factors barely exceeding or missing thresholds of significance.

Prospective controlled investigations are needed to identify both MRSA-specific and mediastinitis-specific risk factors for MRSA mediastinitis after sternotomy. Once these risk factors are identified, targeted interventions can be investigated to reduce the burden of this devastating infection. Until then, potentially higher risk for MRSA mediastinitis in patients who are elderly, diabetic, or female may trigger a lower threshold for preoperative vancomycin prophylaxis, whether these factors are causative in themselves or are merely markers of risk for this disease.

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References

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