

## Postoperative surgical site infection: risk factors and prevention

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### DISCLOSURES

Dr. Bennett-Guerrero is the coordinating center principal investigator for 2 large multicenter clinical trials involving a gentamicin collagen sponge (Innocoll Ltd) in which the primary objective is to show the efficacy of this sponge at reducing postoperative surgical site infection. In this capacity his institution (Duke University) and he (indirectly) have received research support from Innocoll Ltd.

Dr. Bennett-Guerrero is the coordinating center principal investigator for a multicenter clinical trial involving the Rapid Sternal Closure System (KLS Martin LP) in which an objective is to show the efficacy of rigid fixation with sternal plating in reducing postoperative surgical site infection. In this capacity his institution (Duke University) and he (indirectly) have received research support from KLS Martin.

Over 27 million patients undergo surgery in the United States annually<sup>(1)</sup>. Despite the use of prophylactic systemic antibiotics and other routine interventions, postoperative surgical site infection (also called surgical wound infection) is a significant complication. It is estimated that over 700,000 surgical site infections occur annually in the US<sup>(2)</sup> with these infections accounting for \$10 billion in costs annually<sup>(3)</sup>. Deep infections are associated with significant suffering, cost, increased hospital stay and long-term mortality. Many patients require a long term (several weeks) course of antibiotics and surgical debridement. Infections involving an implant, e.g. from an orthopedic procedure, can result in loss of the implant and need for reoperation. Although superficial surgical wound infections are less morbid, they remain a significant medical problem and give rise to visits to the emergency room and/or surgical clinic/office, prescription of antibiotics, and concern in patients and family members.

Despite the routine use of standard surgical scrub/prep and prophylactic antibiotics in many surgical patients, up to 10-20% of certain high-risk patient populations are at risk for wound infection<sup>(4,5)</sup>. For example, in one study involving a high risk surgical population (colorectal surgery) the incidence of surgical wound infection was 18.4%<sup>(5)</sup>. One can also define high risk based on patient factors, some examples being diabetes, obesity, and use of immunosuppressive drugs. For example, in a study of 2,000 cardiac surgical patients the incidence of deep sternal wound infection was 9.8% in patients with diabetes (defined as those requiring treatment preoperatively with oral medication or insulin)<sup>(4)</sup>, which is higher than that reported for "all comers" presenting for cardiac surgery. We will look at sternal wound infection as an example of a surgical site infection in a specific surgical procedure.

Surgical procedures involving a full median sternotomy, where the two parts of the breastbone (manubrium and sternum) are divided with a saw and then reapproximated with wire at the end of the surgical procedure, are routinely performed in the United States for cardiac and other thoracic surgeries. The majority of these surgeries are coronary artery bypass graft (CABG) and/or heart valve repair/replacement procedures. Although there have been some efforts to develop "minimally invasive techniques", eg minithoracotomy approach, most CABG and/or valve procedures, including "off-pump" CABG, are performed through a routine full median sternotomy.

Postoperative sternal wound infection is one of the most feared and devastating complications after sternotomy. The development of significant sternal wound infection is associated with significant suffering, cost<sup>(2,6)</sup>, increased hospital stay<sup>(7,8)</sup> and long-term mortality<sup>(9)</sup>. For example, in one study, patients with sternal wound infection had increased long term mortality (22 vs 0.6%) and spent 20 additional

days in the hospital, compared with uninfected individuals<sup>(10)</sup>. In this study the incremental cost of sternal wound infection was estimated to be \$20,000 USD<sup>(10)</sup>. Consistent with this value, Friberg et al. found that the cost of sternal wound infection was 14,500 Euros<sup>(6)</sup>. In another study, the mean cost of hospitalization for cardiac surgery was doubled in patients with sternal wound infection<sup>(11)</sup>.

Depending on patient risk factors and the rigor with which infections are assessed, reported incidences have ranged from as low as 1 or 2 to 10%<sup>(6,8,10,12-21)</sup>. Sternal wound infections can become clinically overt anytime from one or two weeks after surgery to approximately 2 or 3 months postoperatively<sup>(22)</sup>. Jonkers et al. studied 1,885 patients and observed incidences of sternal wound infection of 4.0, 6.8 and 9.0% at hospitalization, at 30 and at 90 days postoperatively, respectively<sup>(22)</sup>. Therefore, studies that assessed patients for only 30 days likely underreported the true incidence of this complication.

Infection can be localized in any of the following areas: skin, subcutaneous tissues, superficial fascia, sternal fixation wires, bone (osteomyelitis) and mediastinum (area under the sternum). Mediastinitis generally refers to infection involving the mediastinum. Deep sternal wound infections often require rehospitalization, several weeks of intravenous antibiotics, surgical debridement and in some cases muscle or omental flaps. Although superficial sternal wound infections are less morbid, these remain a significant medical problem and give rise to visits to the emergency room and/or surgical clinic/office, prescription of antibiotics and concern in patients and family members.

It is difficult to definitively ascertain the microbiology of sternal wound infection because some cultures are negative in subjects with overt infection. In one series of 3,008 subjects, 91 subjects required surgery for deep infection, and 24% of these subjects had negative cultures<sup>(17)</sup>. Similarly, Lu et al. observed negative cultures in 45% of subjects with sternal wound infection<sup>(21)</sup>. However, other studies have demonstrated a low incidence of negative culture. For example, in an 885-subject, randomized trial, only 3% of subjects were culture-negative<sup>(23)</sup>. In another example, only 6% of cultures were negative in a large series of cardiac surgical subjects<sup>(8)</sup>.

Pathogens observed in sternal wound infections include methicillin-sensitive and -resistant *Staphylococcus aureus*,

coagulase-negative staphylococci, enterococci, *Propionibacterium acnes*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Acinetobacter* spp, *Klebsiella* spp, *Enterobacter cloacae*, *Proteus mirabilis*, *Serratia marcescens*, and Group B species *Streptococcus*<sup>(8,10,13,16,17,21,23,24)</sup>. Since the incidences of these different pathogens varies by hospital and also over time, it is difficult to provide an accurate estimate of the incidence of these pathogens in sternal wound infections in the United States at the present time. Anecdotal reports suggest that the incidence of methicillin-resistant *S. aureus* (MRSA) has increased over the last decade. There does not appear to be a significant difference between pathogens cultured from deep vs. superficial sternal wounds<sup>(16)</sup>.

Risk factors for sternal wound infection have been explored in numerous studies. Although there have been some reports to the contrary<sup>(12,13)</sup>, a large number of studies have demonstrated that diabetes<sup>(6,8,14-18)</sup> and overweight or obesity<sup>(6,10,14-17,19-21)</sup> are significant risk factors for sternal wound infections. Numerous other potential risk factors have been reported including use of immunosuppressive medications (eg prednisone), use of single or bilateral internal mammary artery grafts, reoperation, shaving<sup>(25)</sup>, and increased duration of surgery. There is mostly anecdotal evidence or non-randomized data showing that control of hyperglycemia with insulin may reduce the incidence of sternal wound infection<sup>(26-28)</sup>. However, to date no large multicenter randomized trials have confirmed these observations.

Given the major impact of surgical site infections numerous interventions have been studied, with most unfortunately showing no clear benefit. For example, a Cochrane analysis of 7 previous trials showed that use of plastic adhesive drapes did not reduce the incidence of surgical site infections<sup>(29)</sup>. Another Cochrane analysis related to use of chlorhexidine or other antimicrobials as part of a preoperative shower showed no benefit to this practice<sup>(30)</sup>. Systemic prophylactic antibiotics have been shown to be beneficial and there are national guidelines regarding their use in surgery<sup>(31-34)</sup>. However, despite the use of systemic prophylactic antibiotics and other interventions the incidence of surgical site infections remains unacceptably high, especially in higher risk surgeries or patients. Therefore there is a long and unmet need for strategies that can reduce the incidence of this complication in high risk patients.

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