THE AMERICAN SOCIETY OF Breast Surgeons

Clinical Consensus Statement

Preoperative Antibiotics and Surgical Site Infection in Breast Surgery

Purpose

To outline recommendations for reducing and treating surgical site infections (SSIs).

Associated ASBrS Guidelines or Quality Measures

1. This document replaces the previous ASBrS Statement of Position Statement on Antibiotics and Surgical Site Infection.

2. Quality Measure: Surgical Site Infection and Cellulitis After Breast and/or Axillary Surgery

Methods

Literature review inclusive of recent randomized controlled trials evaluating the indications for and use of antibiotics to reduce and treat SSIs for patients undergoing breast surgery for both benign and malignant disease. This is not a complete systematic review but a comprehensive review of the modern literature on this subject. The ASBrS Research Committee developed a consensus document, which was reviewed and approved by the ASBrS Board of Directors.

Summary of Data Reviewed

Clinical Significance of SSI

Infections are a frequent cause of morbidity after general surgical operations. One in 25 hospitalized patients is affected by a healthcare-associated infection,[1] and in the breast surgery literature, the risk of SSI has been reported to range from 2% to 38%, with contemporary reports suggesting a range of 2% to 16%.[2-26] Breast operations are generally considered clean (Class 1 wound) cases, but reported breast SSI rates are often higher than for other clean cases, which have an expected SSI rate of less than 5%.[1,27] The search method used for documenting SSI, data source, and the SSI definition used also influence reported SSI rates. Clinical follow-up of patients versus a claims-based surrogate search, such as insurance or pharmacy claims, may also influence the reported SSI rate. [22,28-30]

Breast surgery SSI is costly and estimated to increase patient cost per episode by roughly $10,000, [4] and it is associated with significantly increased patient morbidity. Consequences of breast surgery-specific SSI include, but are not limited to, increased cost of care, delay in treatment time for adjuvant therapies, poor patient satisfaction, failed reconstruction (if

performed), and antibiotic-related complications. At least one study of breast cancer patients reported a potential detrimental relationship between SSI and local regional recurrence and survival.[23] Accordingly, the rate of SSI has become one of the most widely used quality indicators, and patients can access and compare facility SSI data.[1,31-32]

Level 1 evidence indicates that perioperative prophylactic antibiotics (PPA) decrease SSI for general and orthopedic operations. As a result, the Centers for Medicare & Medicaid Services (CMS) incorporated antibiotic quality metrics (QMs) into the Physicians Quality Reporting System (PQRS). Published data demonstrate the effectiveness of PPA for selected breast operations. Therefore, the ASBrS endorses the Surgical Care Improvement Project (SCIP) QMs for prophylactic antibiotic use in patients undergoing breast and axillary procedures. SCIP and the American College of Surgeons National Surgical Quality and Improvement Program (NSQIP) have developed infrastructure for comparison of SSI rates between different care providers and institutions. SCIP has developed prophylactic antibiotic process-of-care QMs, and NSQIP has developed specific SSI definitions along with methods of risk-adjusted peer performance comparison. All breast and axillary procedures, including those in which needles are placed for localization prior to surgery, are considered "clean" or class 1 cases by NSQIP.[29,33]

The SCIP prophylactic antibiotic QMs include the administration of antibiotics within 1 hour of surgical incision, the use of an antibiotic consistent with published guidelines, and antibiotic discontinuation within 24 hours postoperatively.[27] These SCIP QMs are publicly reported and have been incorporated into the CMS pay-for-performance incentives.[31]

Risk Factors for Development of SSI

The reported risk of SSI varies by SSI definition, duration of surveillance, type of surgery, institution, and patient co-morbidities, including obesity, diabetes, renal failure, active skin disorders, and smoking history. Other patient and clinical factors influencing SSI include advanced stage, neoadjuvant chemotherapy use, breast size, prior radiation, reoperations, operations lasting longer than 2 hours, drain placement, synchronous bilateral procedures or reconstruction, type of reconstruction, and the use of surgical compared to needle biopsy prior to definitive surgery. The risk of SSI is increased in patients undergoing mastectomy, axillary dissections, or drain placement compared to surgical excisional biopsy or partial mastectomy without axillary surgery. [4-17]

Indications for Perioperative Prophylactic Antibiotic Use

The quality of the available data is limited because of lack of uniformity of SSI definitions, definition of PPA (preoperative only versus $\leq$ 24-hour duration), duration of follow-up, inclusion of multiple different types of breast operations in most studies, and the paucity of randomized controlled trial (RCT) data. Several RCTs investigating the effect of PPA on SSI, mostly after breast operations for cancer, show contradictory results. A RCT by Platt et al[20] included more than 300 patients undergoing breast surgery per arm. They concluded that intraoperative PPA lowered SSI risk (Relative Risk (RR) 0.51). A Cochrane meta-analysis by Jones et al[34] included 11 studies (representing 2867 patients) and concluded that

intraoperative PPA lowered SSI risk. Ten of the included studies compared the use of preoperative antibiotics to no antibiotics and found that the preoperative use of antibiotics significantly decreased SSI for patients undergoing breast cancer surgery. The eleventh study compared perioperative antibiotics to no antibiotics and found no significant benefit with the use of antibiotics. The pooled RR was 0.67.

Other RCTs trended toward lower SSI risk with PPA or demonstrated no benefit with PPA. Bold et al published results of a RCT that included 200 patients undergoing axillary dissection, and found a trend towards lower SSI risk with the use of preoperative antibiotics ($p = 0.08$), with a significant reduction in the number of infections requiring hospitalization ($p = 0.033$).[35] A RCT by Hall et al[36] investigated the use of PPA in patients predominantly undergoing breast excisional biopsy and found that intraoperative PPA did not decrease SSI. Gupta et al published results of a trial involving 334 patients and also found no significant reduction in SSI rate with the use of PPA.[37] In summary, the data are conflicting regarding the benefit of PPA, but there are studies with high-level data that demonstrate a significantly lower SSI risk, and there are few studies that document PPA-related complications.

There are more recent data in the setting of implant-based breast reconstruction. The American Society of Plastic Surgeons recommends that patients undergoing implant-based reconstruction should receive a preoperative dose of an appropriate intravenous antibiotic.[38] In the absence of a drain, antibiotics should be discontinued within 24 hours. However, "if a drain is present, the role of antibiotics is less clear and should be left to physician preference. Of note, documenting a drain in proximity to the implant as a reason for continuation of intravenous antibiotics beyond the 24-hour postoperative period or switching to postoperative antibiotics within 24 hours of procedure completion is compliant with current SCIP guidelines. Presently, there is limited evidence on postoperative antibiotic prophylaxis. Overall, surgeons should adhere to their specific state and hospital guidelines on antibiotic administration."

Phillips et al[39] published a noninferiority RCT enrolling 112 patients (180 breasts) undergoing immediate implant-based reconstruction with the use of acellular dermal matrix. They compared the recommended 24 hours of PPA to PPA continued until drain removal. SSI was essentially the same in the 24-hour group and in the extended PPA group (19.4% vs 22.0%, $p = 0.82$). The 24-hour group had 4 patients who required IV antibiotics, with 3 requiring explanation (4.8%). The extended group had 7 patients who required IV antibiotics and 7 who lost their implant (14.0%). The groups were well-matched and there were no significant differences in rates of overall infection, other complications, treatment of complications, or implant loss. The 24-hour group did have more early (<30-day) infections compared to the extended group ($p = 0.04$). Interestingly, the infections seen in the 24-hour group tended to being less severe and less likely to require IV antibiotics or surgical treatment. A systematic review also published by Phillips[40] compared almost 15,000 patients (undergoing any type of breast reconstruction) who had either $\leq$24 hours of antibiotics (n =1077) to those treated with >24 hours of antibiotics (n = 13,780) and found the same rate of infection (5.78%) in both. Of the 80 studies included in this analysis, one was a RCT, and the remainder were retrospective reviews. Significant variability in antibiotic use protocol was noted. Wang et al also noted heterogeneity in studies evaluating antibiotic use in the setting of implant-based

reconstruction, and found trends in or minimally significant improvement with >24 hours of antibiotics versus <24 hours.[41]

In the setting of catheter-based accelerated partial breast radiation (APBI), infections are seen up to 14% of the time. A retrospective review by Cuttino et al[42] demonstrated a higher infection rate for patients in whom the brachytherapy device was placed after completion of breast surgery, but on multivariate analysis, the use of prophylactic antibiotics during treatment did not significantly decrease subsequent infections. Interestingly, fewer skin reactions were seen in patients on prophylactic antibiotics. Other authors have also demonstrated that timing of catheter placement influences infection risk (and infections often occur in the delayed setting after treatment is complete).[43] Reports detailing ABPI results often recommend prophylactic antibiotics while the catheter is in place, but there is no available comparison data in an adequately-sized population to determine whether this is beneficial or not.

There are risks to continuation of antibiotics postoperatively in patients who receive PPA, including drug reactions, *Clostridium difficile* infection, and increasing bacterial resistance.[28]

Perioperative Prophylactic Antibiotic Choice

The organisms responsible for breast SSI are most often staphylococcal species and other skin flora, but other gram-positive cocci, gram-negative species, and anaerobes may be cultured.[43-51] In fact, several studies have demonstrated that up to one quarter of implant-related infections involve gram negative bacteria. The incidence of methicillin resistant *staph aureus* is increasing, and many SSIs may be polymicrobial. Fungal infections are increasing but are still rare, as are mycobacterial SSIs.

Recommendations

Use of perioperative prophylactic antibiotics

- **a.** PPAs are indicated in patients undergoing mastectomy, with or without any type of axillary dissection or reconstruction, to lower the risk of SSI.
- **b.** PPAs may be indicated in patients undergoing partial mastectomy for cancer, with or without sentinel lymph node biopsy or axillary dissection.
- **c.** Oral antibiotics or PPAs may be considered in patients undergoing brachytherapy catheter device placement for APBI.
- **d.** PPAs may be used in patients undergoing simple surgical excisional biopsy, especially if specific patient or clinical risk factors for SSI are present.
- **e.** A first-generation cephalosporin is the PPA of choice, unless the patient is allergic or has a history of prior infection with MRSA.
- **f.** Continuation of antibiotics after the initial PPA is discouraged unless there is a specific clinical indication.
- **g.** If SSI occurs, aerobic and anaerobic cultures should be obtained and sensitivity of any available SSI fluid should be determined. Culture and sensitivity reports should prompt appropriate changes in antibiotic management.

h. If SSI rates are used as a QM, then standardized ascertainment measures and definitions should be used, as well as appropriate risk adjustment.

i. The ASBrS supports enrollment of patients into well-designed clinical trials regarding methods to improve the rate of breast-related SSI because reported breast SSI rates are usually higher than other "clean cases."

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