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# Risk Factors for Surgical Site Infection Following Major Breast Surgery

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## Abstract

**Background—**Surgical site infections following breast surgery result in increased length of hospital stay, antibiotic utilization, and morbidity. Understanding SSI risk factors is essential to develop infection prevention strategies and improve surgical outcomes.

**Methods—**A retrospective case-control design was used to determine independent risk factors for surgical site infection in subjects selected from a cohort of patients who had mastectomy, breast reconstruction or reduction surgery between January 1998 and June 2002 at a tertiary-care university affiliated hospital. SSI cases within 1 year after surgery were identified using ICD-9-CM diagnosis codes for wound infection or complication and/or positive wound cultures. The medical records of 57 case patients with breast SSI and 268 randomly selected uninfected control patients were reviewed. Multivariate logistic regression was used to identify independent risk factors for SSI.

**Results—**During the 4.5-year study period, 57 patients developed SSIs involving a breast incision and 10 patients developed SSIs involving a donor site incision. Significant independent risk factors for SSI involving the breast incision included insertion of a breast implant or tissue expander (odds ratio (OR) 5.3, 95% confidence interval (CI):2.5–11.1), suboptimal prophylactic antibiotic dosing (OR 5.1, 95% CI: 2.5–0.2 ), transfusion (OR 3.4, 95% CI: 1.3–9.0), mastectomy (OR 3.3, 95% CI: 1.4–7.7), previous chest irradiation (OR 2.8, 95% CI: 1.2–6.5), and current or recent smoking (OR 2.1, 95% CI: 0.9–4.9). Local infiltration of an anesthetic agent was associated with significantly reduced risk of SSI (OR 0.4, 95% CI: 0.1–0.9).

**Conclusions—**Suboptimal prophylactic antibiotic dosing is a potentially modifiable risk factor for SSI following breast surgery. Risk of SSI was increased in patients undergoing mastectomy and in patients who had an implant or tissue expander placed during surgery. Knowledge of these

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risk factors can be used to develop a specific risk stratification index to predict SSI in breast surgery and infection preventive strategies tailored for breast surgery patients.

## INTRODUCTION

Variation in risk of surgical site infection (SSI) after clean surgery, such as breast surgery, may occur because of differences in the type of surgery, duration of operation, underlying patient comorbidities, and other perioperative therapy. SSIs have been reported in approximately 2% of mastectomy patients, according to the most recent report by the National Nosocomial Infection Surveillance System (NNIS) (1). Infection rates reported in the breast surgical literature tend to be higher, with reported rates ranging from 1–30%, depending on the type of surgery, definitions used for infection, specific characteristics of the patients, length of postoperative follow-up, and reporting institution (2). The NNIS risk index, developed to predict risk of SSI, uses only 3 characteristics to predict infection; duration of operation greater than the 75$^{th}$ percentile for the specific operation, American Society of Anesthesiologist's score, and wound class. The predictive ability of the NNIS risk index is better when comparing risk after different types of surgery rather than risk to individuals undergoing the same type of surgical procedure, since the variability in the characteristics used to predict risk is greater between different types of surgical procedures than within an individual type of surgical procedure (3).

Knowledge of specific risk factors for SSI is essential in order to create a SSI risk stratification index specific to breast surgery and other types of surgical procedures. A variety of risk factors for SSI following breast cancer surgery have been reported, including older age (4–6), obesity (7,8), heavy alcohol use (7), smoking (7), diabetes (7), malignant tumor (4), previous open biopsy (9), breast-conservation surgery (10), previous radiation therapy (11–13), previous chemotherapy or radiation therapy (8,14,15), trainee surgeon responsible for the surgery (7), seroma development (16), prolonged duration of drainage after surgery (8), immediate reconstruction (15), and lack of antibiotic prophylaxis at the time of surgery (17,18). Many of these risk factors have been identified in only single studies and have not been verified. Only limited conclusions can be drawn from some of the previous reports, since they focused on only one or a small list of potential risk factors for infection (9,11,14,19).

Multivariate analyses to control for the occurrence of several risk factors within individual patients have been reported in 8 studies (4,7,8,10,13,15,17,20), but only Vilar-Compte (8), Sørensen (7) and Platt (17) included a sufficient number of infected patients (> 20) to permit definitive conclusions concerning risk factors. The SSI rate was most likely underestimated in Sørensen's study, since only infections that occurred within two weeks after surgery were recorded. The standard definition of SSI, developed by the Centers for Disease Control and Prevention (CDC) and NNIS which is used by most hospital epidemiologists and infection control practitioners worldwide, specifies surveillance for SSIs for 30 days after surgery in procedures without implants, and one year after surgery when an implant is placed (21). Sørensen's study may also be biased due to misclassification of the outcome, since individuals who developed SSI after two weeks could have been included in the uninfected category. This misclassification would result in loss of power to detect significant risk factors for SSI.

Many of the studies identifying risk factors for SSI after breast surgery described above included large percentages of patients who had breast-conserving surgery (4,5,15,17,22,23). Unique risk factors for SSI after more extensive surgery such as mastectomy or reconstructive surgery may exist which would not be identified in the studies in which the majority of patients had breast-conserving surgery. To more precisely determine

independent risk factors for SSI in breast surgical patients undergoing more extensive surgery, we performed a case-control study of patients undergoing breast reduction, mastectomy, and breast reconstruction. We used breast reduction surgery as the comparison group, because this operative procedure involves a similarly long incision with removal of a large volume of breast tissue, and in many other respects is more comparable to mastectomy than other breast procedures, such as breast-conserving surgery (comparable duration of surgery, general anesthesia, use of drains to prevent fluid accumulation, and overnight hospital stay). In addition breast reduction creates dead space with the potential for seroma formation, similar to mastectomy. We excluded procedures such as needle-localized incisional biopsy in order to keep the surgeries as comparable as possible. We included a comprehensive list of potential risk factors derived from the breast surgical and infection control literature, and used rigorous statistical methods for analysis. The goal of this study was to identify relevant and new independent risk factors for SSI in patients undergoing breast surgery.

## METHODS

### Study Design and Population

A case-control design was used to assess the relationship between potential risk factors and development of SSI in breast surgical patients. Procedures eligible for inclusion included all breast reduction, mastectomy, and breast reconstruction surgical procedures performed at Barnes-Jewish Hospital from January 1, 1998 through June 30, 2002. ICD-9-CM procedure codes were used to identify eligible surgical admissions, including breast reduction, mastectomy, breast reconstruction with transverse rectus abdominis myocutaneous (TRAM) or other myocutaneous flap, and insertion of breast implant or tissue expander (codes 85.31 – 85.48, 85.50, 85.53, 85.54, 85.7, 85.85, 85.95). Admissions for excisional biopsy, lumpectomy, partial mastectomy, cosmetic augmentation, nipple reconstruction, or mastopexy only were excluded. A subset of the admissions included in this case-control study were derived from a cohort of breast surgical patients (from July 1999 through June 2002) described in a previous publication describing the hospital-associated costs of breast surgery SSI (24). The data analyzed in the prior publication (24) were derived solely from electronic data obtained for the entire cohort of patients with these surgical procedures during the study period. In this current study the data for the case-control subset was obtained by chart review, as described below. Approval for this study was obtained from the Washington University School of Medicine Human Studies Committee.

SSI occurring in the original surgical admission or resulting in readmission to the hospital (inpatient or outpatient surgery) were identified by an electronic method of surveillance based on ICD-9-CM diagnosis codes suggestive of wound infection (998.5, 998.51, 998.59, 996.69, 682.2, 682.3) or breast surgery complication (611.0, 996.79, 998.3, 998.83), positive microbiology wound cultures and/or excess antibiotic utilization (24,25). All electronic surveillance data were obtained from the BJH Medical Informatics database. Potential wound infections identified by electronic surveillance were verified by review of the medical records to determine if an infection occurred within one year following surgery which met the CDC/NNIS definitions for deep or superficial incisional SSI. These definitions require that signs and symptoms of superficial incisional SSI occur within 30 days after surgery for patients without an implant, and up to one year for patients with an implant. We have previously found that the onset of SSI can be delayed in breast cancer surgical patients (24). In addition, many breast cancer surgical patients receive implants/ expanders, and for these reasons we extended the time period for detection of all SSIs to one year after surgery.

### Data and Statistical Methods

Case patients were identified as described above. Uninfected control patients (n = 278) were selected using a random number generator in SPSS (SPSS Inc., Chicago, IL) with frequency matching by year of surgery. Ten control patients were excluded from the study due to missing medical records, resulting in 268 control patients for analysis. Data concerning potential risk factors for SSI were collected from the medical records for the original surgical admission for all cases and controls using a standardized data collection tool. Pathologic diagnosis and tumor stage were verified using data from our institutional Oncology Data Services tumor registry. Post-operative follow-up data, including signs and symptoms of SSI were collected from all records available in the subjects' electronic medical record and hard-copy records, as necessary.

All data were double-entered into a Microsoft Access database (Microsoft Corp, Redmond WA), with double-entry checks performed to identify entry errors. All statistical analyses were performed in SPSS 14.0. All possible logic-check combinations were performed to ensure accuracy of the data, with discrepant results corrected through re-review of the medical record. Associations between SSI and potential categorical risk factors were analyzed using the chi-square test or Fisher's exact test and calculation of odds ratio (OR) and 95% confidence intervals (95% CI). Significant differences for continuous variables were determined using the student's T-test or Mann-Whitney U test, as appropriate. A 2-tailed $p$ value less than 0.05 was considered significant in all statistical tests. Multivariate logistic regression was used to identify independent risk factors for SSI. Variables eligible for inclusion in the multivariate models included those associated with increased risk of SSI from the literature or with clinical/biologic plausibility, and those with $p$-values < .20 in the univariate analyses. Risk factors with less than five occurrences in any cell of the contingency tables were excluded from the multivariate analysis, due to the inability to make statistical inferences with such small numbers. After identification of the main effects in the logistic regression models, all clinically meaningful 2-way interaction factors were tested in the models. The final model(s) were checked for goodness of fit (Hosmer and Lemeshow) and by collinearity and residuals diagnostics, to ensure they were well-specified and fit the data (26).

## RESULTS

During the four and one-half-year time period of the study, a total of 63 patients were diagnosed with 72 SSIs within one year of their breast surgery. During this time period 1298 admissions for breast reduction, mastectomy, or breast reconstruction were identified, resulting in an SSI rate of 4.9% within one year of surgery. Sixty-one SSIs in 57 patients involved the breast incision(s) (5 bilateral), while 10 patients had SSIs involving the donor site incision (TRAM or latissimus dorsi flap donor site). Four patients were diagnosed with both breast and donor site SSIs. 20 (27.8%) SSIs were classified as deep infections (involving the muscle or fascial layers). The deep SSIs in 17 patients involved breast implants (permanent or tissue expanders), and involved abdominal mesh in 2 patients following TRAM reconstruction. One patient had a deep breast SSI without an implant following delayed reconstruction with a pedicled TRAM flap. The remaining 52 (72.2%) SSIs in 44 patients were classified as superficial.

Four patients (6.3%) were diagnosed with SSIs during their original surgical admission, four patients were diagnosed as outpatients (6.3%), and the remaining 55 patients (87.3%) were diagnosed at readmission (inpatient or outpatient surgical) to the hospital. 41 of the 57 patients with SSIs involving the breast incision were diagnosed with infection ≤ 30 days after surgery (71.9%). Breast SSIs in 7 of the 16 patients (43.8%) diagnosed > 30 days after surgery required removal of an implant, while 10/41 (24.4%) of the breast SSIs diagnosed ≤

30 days after surgery required implant removal. Five of the 10 SSIs (50%) involving the donor site incision were diagnosed > 30 days after surgery, and infection in 2 of the 5 patients required abdominal mesh removal (compared to 0/5 for donor site SSIs diagnosed ≤ 30 days after surgery).

The microbiology of breast and donor site SSI is shown in Table 1. *Staphylococcus aureus* (sensitive or methicillin-resistant) was isolated from 58% (25/43) of the patients with breast SSIs in whom cultures were obtained and in one patient with a donor site SSI. *Pseudomonas aeruginosa* was isolated in 19% of the breast SSI cases and from 3 of the 8 patients with donor site SSIs in which cultures were performed. Mixed cultures containing three or more organisms were obtained from 16% of patients with breast SSIs and 50% (4/8) of patients with donor site SSIs whose wounds were cultured. Coagulase-negative Staphylococci were isolated in pure culture from only 7% of patients with breast SSI.

The comprehensive list of potential risk factors included in the case-control study is shown in Table 2, and selected results of the univariate analysis for categorical risk factors are shown in Table 3. Factors significantly associated with breast SSI in univariate analysis included ASA score greater than 2, obesity (BMI > 30) or morbid obesity (BMI > 35), mastectomy with 0–2 lymph nodes removed, mastectomy with 3 or more lymph nodes removed, diagnosis of current breast cancer, diagnosis of breast cancer at any time (current or past), diagnosis of carcinoma *in situ,* breast implant placed during surgery (tissue expander or permanent implant), reduction surgery only (decreased risk), and local anesthetic infiltration (decreased risk). Local anesthetic was used significantly more often in breast reduction surgery than in other types of breast surgical procedures (32/71 reductions vs. 40/254 non-reduction breast surgeries, $p < .001$). Local anesthetic was associated with significantly decreased risk of SSI only in the subset of patients who did not undergo mastectomy ($p = .025$), and not in the patients who had mastectomy (alone or in combination with immediate reconstruction, $p = .734$).

Receipt of a sub-optimal dose of prophylactic antibiotic was associated with increased risk of breast SSI. Patients included in this category included individuals with a BMI greater than 30 who received 1 gram of cefazolin instead of the recommended 2 grams, and patients with no prophylactic antibiotic recorded in the anesthesiologists' or nurses' notes. We included the 7 subjects without documented prophylactic antibiotic in the sub-optimal prophylactic antibiotic dose and sub-optimal prophylactic antibiotic timing, despite the fact that none of them developed an SSI. There was no association between sub-optimal timing of prophylactic antibiotic, defined as no antibiotic given or antibiotic given > 60 minutes before surgery or after incision, and SSI risk ($p = .844$). There was also no association between sub-optimal prophylactic antibiotic administration, including timing of the 1$^{st}$ dose and either lack of receipt of a 2$^{nd}$ dose for surgeries with duration > 6 hours, or administration of the second dose > 6 hours after incision in long surgeries ($p = .743$).

Among the continuous variables, only BMI was associated with significantly increased risk of breast SSI ($p = .007$, student's T-test). There was a trend towards increased risk of breast SSI with increasing breast weight ($p = .095$; Mann-Whitney U test), although breast weight was missing in over half of the pathology reports. There was no association between breast SSI and number of lymph nodes removed, age, estimated blood loss, or duration of surgery.

There was no difference in preoperative blood glucose values between tested patients with SSI and control uninfected patients (p = .992). Postoperative blood glucose levels within 5 days after surgery were significantly higher in patients with SSI compared to uninfected control patients (mean value 223 vs. 174 mg/dL, $p = .025$, Mann-Whitney U test) although only 89 (27%) patients had postoperative glucose testing performed.

Multivariate logistic regression was used to identify independent risk factors for breast incisional SSI. The independent factors significantly associated with breast SSI included mastectomy, having a breast implant/expander placed during the surgery, sub-optimal dosing of the prophylactic antibiotic, receiving one or more units of transfused packed red blood cells or platelets during or after surgery, and a history of chest irradiation prior to surgery. Current or recent smoking was associated with marginally increased risk of breast SSI, while local infiltration of an anesthetic agent at surgery was associated with significantly decreased risk of breast SSI. No significant interactions between variables were identified. The c-statistic for the model was .782, indicating acceptable discrimination of the model.

Case subjects with breast SSIs caused by gram-negative organisms (n = 12) were also compared to the cases with breast SSI caused by only gram-positive organisms (n = 24), to determine if there were unique risk factors associated with gram-negative bacterial infections. Morbid obesity (BMI > 35) was more common in patients with gram-negative SSIs (any gram-negative bacteria in the cultures) compared to patients with SSIs caused solely by gram-positive bacteria (6/10 morbidly obese patients had gram-negative SSIs vs. 6/26 patients with BMI < 35, $p = .053$, Fisher's exact test). Current smoking was more frequent in patients with gram-negative SSIs than in those with gram-positive SSIs (5/7 current smokers had gram-negative SSIs, vs. 2/7 with a history of previous smoking, and 5/22 in patients who never smoked, $p$ for linear trend = .028). Patients with previous chest irradiation were more likely to have gram-negative SSIs (3/3 patients with previous chest irradiation had gram-negative SSIs vs. 9/33 with no history of chest irradiation, $p = .031$, Fisher's exact test), as were patients who had undergone TRAM reconstruction (4/5 TRAM patients had gram-negative SSIs vs. 8/31 patients who did not have TRAM reconstruction, $p = .034$, Fisher's exact test). There were no other significant differences between SSI case-patients with infection caused by gram-negative bacteria compared to those with gram-positive bacterial infections.

Half of the SSI case-patients with positive cultures of their breast wound were infected with bacteria susceptible to cefazolin (18/36). In addition, 10/19 (56%) obese patients with suboptimal dosing of prophylactic antibiotic were infected with bacteria susceptible to cefazolin.

## DISCUSSION

This study identifies specific new independent risk factors for breast SSI in patients undergoing extensive breast surgery, some of which are potentially amenable to interventions to reduce this risk. SSIs occurred more frequently in surgeries involving placement of a breast implant or expander, particularly in combination with mastectomy. Approximately one-fourth of the SSIs were classified as deep infections, necessitating surgical removal of an implant/expander in all but one case. Although the remainder of the SSIs were classified as superficial, they resulted in excess morbidity and length of stay for the affected patients, as demonstrated in our previous study describing the hospital costs associated with SSI in this population (24).

### Independent Risk Factors for SSIs Identified by Multivariate Analysis

The adjusted odds ratio for breast SSI associated with placement of a breast implant or tissue expander was equal to 5.3. This is the first study, to our knowledge, to document increased risk of SSI associated with implants in multivariate analysis. The majority of the studies of postoperative wound infection in breast surgery have focused on one subset of surgical procedures (primarily mastectomy only, or mastectomy and lumpectomy), and thus risk associated with a particular procedure or with implants has not been studied in any detail.

Three more recent studies have described SSI following implant surgeries, but there were no control groups in these studies without implants for comparison.(13,14,27) Additional investigation is needed in this area, due to the increasing frequency of immediate reconstruction following mastectomy, particularly in younger women. In addition it will be important to determine whether there is increased risk associated with delayed placement of tissue expanders or permanent implants in cancer patients, or whether the apparent increased risk of SSI is associated only with implant placement immediately after mastectomy. Tissue expanders are often used in immediate reconstruction when the mastectomy flaps have just been compromised by the excision of their primary blood supply and are in a stage of vascular shock. Permanent implants are usually placed in a delayed fashion after the flaps have had an opportunity to recover from the effects of the mastectomy and collateral circulation has improved the overall blood supply. The comparison of SSI rates in patients receiving immediate vs. delayed placement of implants will lead to insight concerning the underlying mechanism and pathogenesis of SSI development, since it is not clear whether the implant alone is responsible for the increased risk of SSI, or if it is the combination of mastectomy followed immediately by implant placement that confers increased risk of SSI.

Receipt of a sub-optimal dose of prophylactic antibiotic was associated with 5.1-fold increased odds of breast SSI. The increased dosage of prophylactic antibiotic is necessary in obese persons since antibiotic penetration into fat is relatively poor (28). In our multivariate analysis, obesity did not have as strong an association with SSI, and was displaced in the regression model by the sub-optimal dose variable. This implies that the risk associated with obesity may be somewhat reduced by proper dosing of prophylactic antibiotics to account for increased tissue mass. Proper antibiotic dosing may not reduce the risk completely, since only half of the SSI case-patients with suboptimal dosing of prophylactic antibiotics and with positive breast wound cultures were infected with bacteria susceptible to cefazolin. There was no association between sub-optimal prophylactic antibiotic timing and SSI risk. Appropriate timing of prophylactic antibiotic was very high in this breast surgical population, with over 80% of patients receiving a dose of antibiotic within 60 minutes before incision.

Transfusion was also significantly associated with increased SSI risk, although excessive blood loss during the operation was not associated with increased risk. We have previously reported that transfusion of packed red blood cells is associated with increased risk of SSI following spinal surgery and increased risk of leg and chest SSI after coronary artery bypass graft surgery (29–31). It is unclear if this increased risk is a true reflection of the risk associated with the blood transfusion itself, or is due to residual confounding by severity of illness or operative factors associated with increased blood loss after surgery, such as reoperation for bleeding.

Mastectomy was associated with increased risk of breast SSI. Since our case-control population consisted of persons undergoing cancer-related surgeries and those undergoing non-cancer related reductions, this indicates increased risk of SSI in patients undergoing cancer-related surgery. This is an important finding, since the risk of SSI is much higher in patients undergoing mastectomy compared to patients undergoing breast reduction surgery, despite the fact that the operations have very similar durations and length of incisions. Previously we reported the incidence of SSI to be 1.1% after breast reduction, while the incidence after mastectomy was 4.4% in our breast surgical population from 1999–2002 (24). The incidence of SSI after implant placement for breast augmentation was zero, while the incidence of SSI after delayed implant/expander placement in cancer patients was 7.7%. Thus it is apparent there is increased risk of SSI in breast cancer surgical patients compared to non-cancer patients undergoing similarly extensive surgeries. It is not clear if the increased risk associated with mastectomy is due to disruption of lymphatic drainage, length

of time drains were in place, or some other operative or non-operative factors. We were unable to detect any association between SSI and the number of drains used, number of lymph nodes removed during surgery, and pre- or postoperative chemotherapy. We were unable to determine the total duration of drain time since drains were removed primarily during outpatient or home health visits, and thus we could not determine whether the length of time drains were left in the place was associated with increased risk of SSI.

Previous chest irradiation was associated with a 2.7-fold increased risk of breast infection. This confirms previous reports of increased risk of infection with irradiation (11–13), although in the study by Nahabedian and colleagues the risk factor analyzed consisted of any irradiation (either pre- or post-operative). Increased risk of SSI due to previous chest irradiation is biologically plausible, due to underlying tissue damage resulting in postoperative wound ischemia.

The final independent risk factor for breast SSI in our logistic regression model was current or recent smoking. Smoking has been presumed to be a risk factor for SSI in general, due to constriction of blood vessels with resulting delay in wound healing caused by nicotine (21). In a careful multivariate analysis, Sørensen and colleague found a dose-response between smoking quantity (light vs. heavy smoking) and risk of wound infection following breast cancer surgery (7). These same authors more recently found decreases in excisional wound infection rates (non-breast) in smokers assigned to abstinence therapy compared to current smokers in a randomized control trial (32). Thus our result is consistent with the combined results reported by Sørensen and colleagues, and suggests increased risk of SSI in individuals who continue to smoke or have recently quit smoking prior to surgery.

Local infiltration in the breast of an anesthetic agent during surgery was associated with significantly lower risk of SSI in our multivariate model. Although anesthetic agents used for local infiltration have been shown to have antibacterial properties both in vitro and in vivo (33,34), the protective effect observed in this study was most likely due to the type of surgery. Local anesthetic agents were used more often in breast reduction surgery than in other types of breast surgery. In addition, the association of local anesthetic with SSI was confined to the non-mastectomy population in univariate analysis, suggesting that the protective effect observed was related to the type of surgery rather than antibacterial properties of the anesthetic agents.

Although not significant in multivariate analysis, postoperative hyperglycemia was associated with increased risk of breast SSI. This is consistent with results from multiple studies that have shown increased risk of mediastinitis in diabetic patients with poorly controlled diabetes following coronary artery bypass graft surgery (35–37), and suggests that peri-operative hyperglycemia may increase the risk of SSI in surgeries other than just cardiac surgery. Glucose control in diabetic patients after cardiac surgery has been shown to reduce the risk of SSI to that observed in non-diabetic patients (38–40). In addition, peri-operative hyperglycemia may also identify patients at increased risk of SSI who have not been previously diagnosed with diabetes (41).

We also found significant associations between morbid obesity, current smoking, and TRAM reconstruction with gram-negative bacterial SSI compared to SSI caused only by gram-positive bacteria (based on the microbial species present in aerobic breast wound cultures). These results must be interpreted with caution since the number of subjects available for these analyses was very small. It is intriguing to speculate that certain patient characteristics may predispose patients to infection with gram-negative bacteria, rather than with the predominant gram-positive bacterial skin flora. This finding requires confirmation with a larger number of case patients from multiple institutions.

Limitations of this study include the acquisition of cases and controls during a period of 4.5 years, during which time some changes in procedures and personnel obviously occurred. The long duration of this study was necessary to accrue a sufficient number of SSI case patients for analysis. In addition, the retrospective case-control design, the small number of patients with some important risk factors (e.g., neoadjuvant chemotherapy), and the limited number of case patients with SSI involving the breast incision precluded the ability to analyze in depth some potential risk factors specific to breast cancer patients. In addition, we could not examine some potentially important interactions, such as history of cancer and previous surgery, because of the small numbers of patients with both characteristics. A larger cohort study restricted to breast cancer patients would allow for more detailed examination of risk factors unique to these patients, including previous and postoperative irradiation, neoadjuvant and adjuvant chemotherapy, and axillary dissection.

The strengths of this study include the large number of cases of SSI analyzed relative to most other studies in the literature, and the extensive nature of the potential risk factors analyzed. In addition, the use of multivariate analysis allowed for the identification of new independent risk factors for breast incisional infection after controlling for the occurrence of multiple risk factors in individual patients, which has rarely been done in prior published reports.

### Conclusions

Using multivariate analysis and a retrospective case-control study design, this study demonstrates that placement of a breast implant/expander in cancer patients, suboptimal dosing of prophylactic antibiotic, transfusion, mastectomy, previous chest irradiation, and current or recent smoking independently increase the risk of SSI following major breast surgery. Local infiltration of an anesthetic agent was associated with significantly reduced risk of SSI, most likely due to use of these agents primarily in breast reduction surgeries. Identification of these risk factors should allow for the development of specific interventions to decrease the risk of SSIs, with the goal of improving outcomes and decreasing morbidity, hospital length of stay and hospital costs in breast surgery patients. In addition, knowledge of these risk factors may allow for better patient selection for reconstruction procedures, and for the development of pre-operative algorithms to predict SSI, giving surgeons more specific information to tailor their pre-and postoperative management strategies to individual patients.

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## Table 1

Microbiology of SSI Associated with Breast Surgery

| **Organism – Breast SSI (n = 43)**[a] | **No. (%) of Patients** |
|---|---|
| Methicillin-sensitive *Staphylococcus aureus* (+/− other organisms) | 18 (41.9%) |
| Methicillin-resistant *Staphylococcus aureus* (+/− other organisms) | 7 (16.3%) |
| Coagulase-negative Staphylococcus only | 3 (7.0%) |
| *Streptococcus viridans* group (+ other organisms) | 2 (4.7%) |
| *Pseudomonas aeruginosa* (+/− other organisms) | 8 (18.6%) |
| *Proteus mirabilis* | 1 (2.3%) |
| *Serratia marcescens* | 2 (4.7%) |
| Mixed flora | 7 (16.3%) |
| No growth[b] | 4 (9.3%) |
| **Organism – Donor Site SSI (n = 8)**[c] | |
| Methicillin-resistant *Staphylococcus aureus* (+/− other organisms) | 1 |
| Coagulase-negative Staphylococcus only | 1 |
| *Pseudomonas aeruginosa* (+/− other organisms) | 3 |
| *Proteus mirabilis* | 1 |
| Mixed flora | 4 |
| No growth | 1 |

[a] Cultures not performed for 14 patients with breast SSI. Percentages calculated based on number cultured (n = 43).

[b] Two of the four cultures that had no growth had organisms visible on gram stain.

[c] Cultures not performed for 2 patients with donor site SSI.

## Table 2

Potential Risk Factors for Surgical Site Infection After Breast Surgery Included in Study

| **Potential Risk Factors for Breast Surgical Site Infections** | | |
|---|---|---|
| **Preoperative** | **Intraoperative** | **Postoperative** |
| Age | Skin antisepsis | Serum Glucose |
| Gender | Razor shaving vs. clipping | Hemoglobin, hematocrit |
| Medicaid | Prophylactic antibiotics (type, duration prior to incision, 2nd dose for surgeries with duration > 6 hours) | Transfusions (number and type received during and/or after operation, before discharge from surgical admission) |
| Body mass index | Local infiltration | Pathology |
| | | Carcinoma in-situ |
| | | Invasive carcinoma |
| | | Histologic grade and stage |
| | | Weight of removed breast tissue |
| | | Tumor stage (TNM) |
| Diabetes, including form of control | Use of operating microscope (TRAM abdomen only) | Postoperative antibiotics |
| | | Duration |
| | | Type(s) |
| Serum Glucose | Intraoperative irrigation | Discharged on antibiotics |
| Smoking history | Hemostatic agent | Postoperative complications |
| | | Hematoma |
| | | Seroma |
| Alcohol use | Type of procedure | |
| | Mastectomy | |
| | Implant | |
| | Flap | |
| | Reduction only | |
| Menopausal status | Breast implant | |
| | Tissue expander vs. permanent | |
| Skin disorders | If implant, antibiotic/antiseptic soaked | |
| Previous breast surgery | Type of flap | |
| Previous needle or open biopsy | Lymph node dissection | |
| | Sentinel node | |
| | Axillary dissection | |
| | No. of nodes removed | |
| Steroid therapy | Duration of surgery | |
| Preoperative chemotherapy or irradiation | Estimated blood loss | |
| ASA class | Drains (number and type) | |
| Hemoglobin, hematocrit | Surgeon(s), resident surgeon(s) | |

## Table 3

Univariate Comparisons of Risk Factors in Patients With and Without Breast Incisional SSI

| Characteristic | No. (%) patients with breast SSI (n = 57) | No. (%) uninfected patients (n = 268) | Odds ratio (95% CI) | *p* |
|---|---|---|---|---|
| Body mass index | | | | |
| 25 or less | 15 (26) | 89 (33) | | |
| 25–30 | 10 (18) | 88 (33) | 0.7 (0.3,1.6) | .365 |
| 30–35 | 15 (26) | 45 (17) | 2.0 (0.9,4.4) | .095 |
| > 35 | 17 (30) | 46 (17) | 2.2 (1.0,4.8) | .049 |
| Obesity (BMI > 30) | 32 (56) | 91 (34) | 2.5 (1.4,4.5) | .002 |
| Diabetes | 12 (21) | 37 (14) | 1.7 (0.8,3.4) | .165 |
| Any glucose > 200 mg/dL[a] | 10 (20) | 22 (12) | 1.9 (0.8,4.4) | .116 |
| Diabetes or any glucose > 200 mg/dL[a] | 14 (25) | 40 (15) | 1.9 (0.9,3.7) | .076 |
| Current smoking or quit within past 6 months | 12 (21) | 38 (14) | 1.6 (0.8,3.3) | .192 |
| ASA class 3 or 4 | 21 (37) | 54 (20) | 2.3 (1.2,4.2) | .007 |
| Skin disorders at time of surgery | 10 (18) | 29 (11) | 1.8 (0.8,3.8) | .156 |
| Prior chest irradiation | 12 (21) | 39 (15) | 1.6 (0.8,3.2) | .220 |
| Previous chemotherapy (any) | 16 (28) | 47 (18) | 1.8 (1.0,3.5) | .068 |
| Recent chemotherapy (within 6 months before surgery) | 9 (16) | 29 (11) | 1.5 (0.7,3.5) | .289 |
| Tamoxifen therapy at time of surgery | 9 (16) | 25 (9) | 1.8 (0.8,4.1) | .148 |
| Breast biopsy within 1 year | | | | |
| None | 13 (23) | 91 (34) | | |
| Needle only | 23 (40) | 93 (35) | 1.7 (0.8,3.6) | .145 |
| Any open biopsy or surgery | 21 (37) | 84 (31) | 1.8 (0.8,3.7) | .145 |
| Mastectomy | | | | |
| No mastectomy | 8 (14) | 90 (34) | | |
| 0–2 lymph nodes removed | 13 (23) | 45 (17) | 3.3 (1.3,8.4) | .015 |
| ≥3 lymph nodes removed | 36 (63) | 133 (50) | 3.0 (1.4,6.9) | .007 |
| Axillary dissection[b] | 34 (60) | 134 (50) | 1.5 (0.8,2.6) | .186 |
| Current breast cancer | 45 (79) | 174 (65) | 2.0 (1.0,4.0) | .040 |
| Current or past breast cancer | 54 (95) | 204 (76) | 5.6 (1.7,18.7) | .002 |
| Current diagnosis | | | | |
| None/history of malignancy | 12 (21) | 94 (35) | | |

| Characteristic | No. (%) patients with breast SSI (n = 57) | No. (%) uninfected patients (n = 268) | Odds ratio (95% CI) | *p* |
|---|---|---|---|---|
| Carcinoma *in situ* only | 9 (16) | 21 (8) | 3.4 (1.3,9.0) | .016 |
| Invasive carcinoma | 36 (63) | 153 (57) | 1.8 (0.9,3.7) | .088 |
| Breast implant | | | | |
| No implant | 36 (63) | 225 (84) | | |
| Permanent implant | 6 (11) | 13 (5) | 2.9 (1.0,8.1) | .044 |
| Tissue expander | 15 (26) | 30 (11) | 3.1 (1.5,6.4) | .002 |
| Local infiltration of anesthetic agent | 7 (12) | 65 (24) | 0.4 (0.2,1.0) | .048 |
| Reduction surgery only | 3 (5) | 68 (25) | 0.2 (0.0,0.5) | .001 |
| Sub-optimal prophylactic antibiotic dose | 29 (51) | 78 (29) | 2.5 (1.4,4.5) | .001 |
| Sub-optimal timing of prophylactic antibiotic (none, or > 60 minutes before or after incision) | 10 (18) | 50 (19) | 0.9 (0.4, 2.0) | .844 |
| Any sub-optimal timing of prophylactic antibiotic administration (sub-optimal timing of 1st dose as above, or for surgeries with duration > 6 hrs, no 2nd dose or 2nd dose > 6 hrs after incision) | 15 (26) | 65 (24) | 1.1 (0.6, 2.1) | .743 |
| Estimated blood loss during operation (mL)[c] | | | | |
| ≤50 | 17 (29.8) | 77 (28.7) | | |
| 51 – 200 | 19 (33.3) | 104 (38.8) | 0.8 (0.4, 1.7) | .605 |
| 201 – 499 | 17 (29.8) | 66 (24.6) | 1.2 (0.6, 2.5) | .686 |
| ≥500 | 4 (7.0) | 21 (7.8) | 0.9 (0.3, 2.8) | .808 |
| Transfusion | 9 (16) | 21 (8) | 2.2 (1.0,5.1) | .060 |

[a] Serum glucose from blood collected during preoperative clinic visit or in the hospital before surgery, or within 5 days after surgery.

[b] Axillary dissection as described in operative note

[c] Estimated blood loss was missing for 46 patients (17.2%), and was assumed to be ≤ 50 mL for analysis. The results did not change when these patients were excluded from analysis.

## Table 4

Multivariate Logistic Regression Model for Developing Breast Surgical Site Infection[a]

| Risk Factor | Adjusted Odds Ratios (95% CI) | *p* |
|---|---|---|
| Breast implant/expander | 5.3 (2.5,11.1) | <.001 |
| Sub-optimal prophylactic antibiotic dosing | 5.1 (2.5,10.2) | <.001 |
| Transfusion | 3.4 (1.3,9.0) | .012 |
| Mastectomy | 3.3 (1.4,7.7) | .007 |
| Chest irradiation prior to surgery | 2.8 (1.2,6.5) | .013 |
| Recent or current smoking | 2.1 (0.9,4.9) | .080 |
| Local infiltration of anesthetic agent | 0.4 (0.1,0.9) | .033 |

[a]The c statistic for the model = .782 The Hosmer and Lemeshow goodness of fitness chi-square $p = .749$ (7 df), and the Nagelkerke $R^2 = .249$.