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Surgical Site Infection Rates in Breast Cancer Surgery at a University Hospital in Nairobi, Kenya

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Abstract

Background: Surgery is the mainstay of treatment for breast cancer and with it the attendant risk of surgical site infection (SSI). Breast cancer surgery, though classified as a clean procedure presents with a relatively higher rate of infection than similar operations and it remains unclear whether extended antibiotic regimes improve this outcome. This study sought to evaluate SSIs using validated detection protocols.

Methods: A prospective surveillance study for patients undergoing breast cancer surgery using the National Nosocomial Infections Surveillance (NNIS) system.

Results: Sixty nine patients who underwent breast cancer related surgery at Aga Khan University Hospital-Nairobi were recruited over the period from September 2013 to April 2014, with 2 lost to follow-up. Six percent (n=4) of patients developed SSI, with 1 case of CDC Class I, and 3 cases CDC Class II. Various risk factors such as obesity, diabetes, age >65 years and prolonged drain duration were noted to be important contributors increasing the risk of SSI development. Only one patient required operative management of their infection.

Conclusion: This study demonstrates the successful introduction of an SSI surveillance protocol at a tertiary facility with an subsequent infection rate lower than reported in other studies that utilize only pre-operative antibiotics. We recommend a randomized controlled trial to compare outcomes between pre-operative only and pre- plus post-operative antibiotic use in order to explore this further.

Keywords: Infection; Breast Surgery; Antibiotic; Prophylaxis

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Background

Surgery is the mainstay of treatment for breast cancer, a major cause of morbidity and mortality in both pre- and post-menopausal women [1-4]. The evolution from debilitating extensive procedures in the earlier years to the low morbidity procedures currently practised has improved the adverse events attributable to surgery.

Surgical site infection (SSI) however remains a common complication of breast surgery, with attendant increase in patient discomfort, cost of care and burden to clinical staff [5-7]. It carries the further risks of delaying adjuvant chemo-radiation and unsightly scarring [7-9] in women already traumatized by the diagnosis of cancer and the surgical procedure itself. This situation obtains despite the recommended use of single dose peri-operative antibiotics, leading to unregulated post-operative doses in an attempt to reduce infection rates. It is not known whether these extended antibiotic regimes result in reduced SSI rates. The absence of SSI surveillance protocols further compounds the scenario.

With paucity of data as regards use of post-operative antibiotics and its effect on SSI rates, the present study sought to evaluate the SSI outcomes in breast cancer surgery with the use of peri-operative and post-operative antibiotic prophylaxis using internationally validated protocols for SSI detection and SSI definitions.

Patients and Methods

The study was a prospective surveillance study at the Aga Khan University Hospital. Inclusion criterion was age above 18 with diagnosis of breast cancer. Exclusion criteria included: failure to obtain consent for inclusion; patients in whom there was already a suspected infection following

biopsy procedure or where tumor ulceration was present.

Ethical approval was sought from the institutional ethical committee of the Aga Khan University College of Health Sciences and confidentiality of patient information was secured.

In addition to standard hospital procedure with regard to patient care for breast surgery, the following aspects were instituted into the study protocols:

The patients were assessed pre-operatively for SSI risk factors using a questionnaire. Patients were scheduled to receive peri-operative chemoprophylaxis as a single dose of Cefuroxime 750 mg IV at the time of induction of anesthesia. If surgery was prolonged beyond 4 hours, patients were to receive an additional dose of Cefuroxime 750 mg IV. Where there was known allergy or any contraindication to the use of Cefuroxime, Augmentin 1.2 g IV was to be used. All patients were to receive antibiotic prophylaxis of Cefuroxime 750 mg IV 8 hourly for the first two days while in hospital. Patients undergoing BCT would receive no further treatment. Patients undergoing mastectomy would receive an additional 3 days of oral antibiotic (Cefuroxime 750mg 12 hourly) to make the total prophylaxis duration 5 days. In the event of reported allergy or contraindication to Cefuroxime use, patients were to receive Augmentin 1.2 g 8 hourly for IV prophylaxis and Augmentin 1g 12 hourly for oral prophylaxis. All patients were to be reviewed in the clinic within one week of discharge from the hospital. If SSI was detected or suspected based on CDC criteria, an aspirate or a swab would be collected where possible and sent for microbiological study in a transport medium used for standard culture and sensitivity. The drain was assessed for amount of drainage. Criteria for removal were based on volumetric analysis; removal was advised once the drainage was <30 ml/24hour. Events such as drain dislodgement and adjustment, drain unblocking or aspiration of seroma were also collected.

Patients were to be followed up for a minimum 30 days regardless of the number of clinic visits. This data was captured in the adapted NCC post-operative SSI detection form.

Primary outcome measures were rates of SSI (detected as per the protocol), calculated as a percentage of the total number of subjects analyzed over the study period; occurrence of SSI over the duration of time to assess for temporal spread; categories/ classes of SSI.

Secondary outcome measures included incidence of common risk factors for SSI development; sub-analysis to identify risk factors present in patients who developed SSI; associations between identified patient and surgical risk factors and development of SSI; Documentation of other clinical outcomes other than SSI.

Collected data were summarized in the form of tables, graphs and figures showing the variables of interest and the temporal distribution of events during the study period. The data were analyzed in form of rates and proportions.

Results

Sixty nine consenting patients who underwent breast cancer related surgery at Aga Khan University Hospital-Nairobi were recruited over a period of 8 months from September 2013 to April 2014. Two (2) patients could not be contacted subsequently and were excluded from the final analysis. All the remaining 67 patients were followed up until completion of the surveillance period of 30 days. Their characteristics are summarized in Table 1.

Table 1: Baseline patient characteristics.

Age	Mean (years)	50
	Age range (years)	21-79
	< 65 years	8
	> 65 years	59
BMI	< 20	1
	20-29.9	48
	30-34.9	9
	35-39.9	6
	> 40	3
Procedure	MRM	33
	ALND	31
	SLNB	2
	BCT	32
	ALND	28
	SLNB	4
	Simple mastectomy	2
Neoadjuvant Chemo	MRM	21
	BCT	3
Classification	Clean	65
	Contaminated	2
Diabetic	MRM	3
	BCT	3
Other comorbidity	Hypertension	13
	Dyslipidemia	2
	Retroviral disease	1
	Osteoarthritis	1
	Leiden factor deficiency	1
	Asthma	1
	Cardiac disease	1
	Pulmonary embolism	1
ASA class	I	31
	II	32
	III/IV	4
Pregnant	MRM	1
	BCT	1
Smoking		1

ASA: American Society of Anesthesiologists' classification; MRM: Modified Radical Mastectomy; BCT: Breast Conservation Therapy; ALND: Axillary Lymph Node Dissection

All mastectomy procedures and 30 BCT procedures were classified as clean operations while two of the BCT procedures were classified as clean contaminated operations (with minor breaks in sterility: contaminated diathermy cord and break of gloves). Surgical drains were used in all operations except patients who underwent BCT and sentinel lymph node biopsy (SLNB) without further axillary dissection (n=55). Only one drain was used per patient. External compression dressing for 24-48 hours was used in all patients who underwent mastectomy or had axillary dissection with any other procedure.

All patients received a stat prophylactic dose at the time of

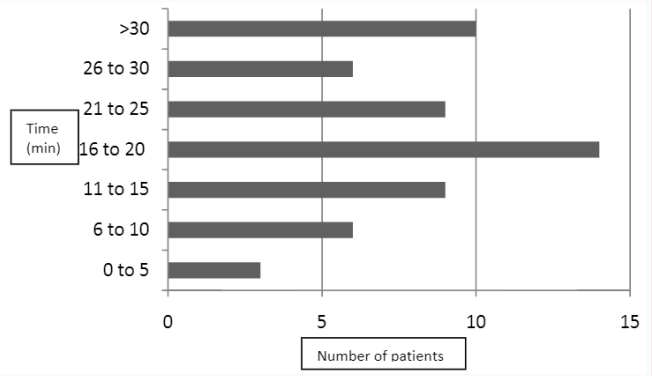

Figure 1: Bar chart of actual time of antibiotic administration prior to incision.

induction of anesthesia or before surgical incision. Thirty one patients who underwent mastectomy and a similar number who underwent BCT received Cefuroxime 1.5 g IV stat while 4 patients who underwent mastectomy and 1 who underwent BCT received Augmentin 1.2 IV stat at induction of anesthesia. There were no antibiotic-related adverse reactions. The actual pattern of antibiotic administration is summarized in Figure 1. None of the patients required a second intra-operative antibiotic dose.

Thirty one (31) post-mastectomy patients received Cefuroxime 500mg orally 12 hourly while 4 patients received Augmentin 1 g orally 12 hourly. All patients reported completion of the prophylaxis regimen as prescribed. Of patients who underwent BCT 31 received Cefuroxime 750 mg 12 hourly while 1 received Augmentin 1g 12 hourly oral medications. All patients reported completion the prophylaxis regimen as prescribed.

Strict supervision and emphasis of the antibiotic prophylaxis regimen was done, resulting in no deviation from this protocol. No patients received additional antibiotics except where SSI had been detected (4 patients).The rest of the post-operative care remained standard.

All patients were followed up with at least once-weekly clinic review as scheduled by the primary surgeon or alternatively by telephonic interview. A new data entry form was filled for each review until each patient had received at least four evaluations within the 30-day surveillance period. There was no drop-out or breach in study protocol.

Primary outcome: Rate of SSI

Four patients (6%) developed surgical site infections. Two had undergone mastectomy and the other two others breast conservation surgery. The infections were diagnosed on post-operative days 10, 18, 19 and 27. Three of the infections were CDC class II infections and one, CDC class I infection. One patient required surgical drainage of the infection. Wound swabs were taken for all infections. One culture grew *Staphylococcus aureus*. No growth was obtained from the other three cultures. All patients with SSI were treated with a combination of Amoxicillin-Clavulanic acid for 7 days. There was complete resolution of the infection during this time.

Secondary outcomes

Risk factors for SSI development: Patients who developed SSI had the following risk factors:

- Patient 1: Age >65 years, BMI of 44, diabetic, prolonged drain duration of >19 days.

Table 2: Other complications arising from breast surgery for cancer.

Seroma status	Drain Duration		Seroma	No Seroma
		< 14 days	2	5
		14 - 19 days	4	10
		> 19 days	0	8
		Blocked drain	4	0
	Volume at Removal			
		< 20ml	1	10
		> 20ml	9	9
Shoulder Dysfunction			MRM	BCT
	Axillary Dissection		31	24
	Shoulder stiffness/ Arm numbness		10	4

- Patient 2: 4 cycles of neo-adjuvant chemotherapy, blocked drain.
- Patient 3: Age >65 years, BMI 41.6, diabetic
- Patient 4: No identifiable risk factors

Other complications: Other complications are as summarized in Table 2. Only one patient an SSI that delayed administration of adjuvant chemotherapy.

Discussion

In this prospective study, a total of 67 patients undergoing breast cancer surgery were recruited and followed up until completion of the surveillance period. While there is general agreement in the literature that prophylactic antibiotics should be administered pre-operatively, there is ongoing debate whether the timing of pre-operative administration matters. Hawn et al. [10] in a large recently published retrospective cohort study involving 32,459 patients failed to demonstrate any benefit in the adherence to the recommendations on the timing of prophylaxis. However, a prospective surveillance study by Steinberg et al. [11] involving 4,472 patients using the National Nosocomial Infections Surveillance system methodology (similar to that used in this study) showed a trend towards reduced risk for SSI when antibiotics with short infusion times such as cephalosporins were given within 30 minutes of the surgical incision. Another similarly designed prospective study by Weber et al. [12] contradicts this view. We could not demonstrate an association between the timing of antibiotic prophylaxis and the occurrence of surgical site infection from our data. The present study was however not powered to evaluate the effect of this variable. It is nonetheless good clinical practice despite the ongoing debate to time prophylactic antibiotics according to their pharmacokinetic properties despite lack of strong evidence. The development of SSI is multi-factorial, and this is one of the few modifiable factors that can be addressed.

The principal finding of the study was that only 4 out of 67 patients (6%) undergoing surgery for breast cancer developed SSI; two of whom underwent mastectomy and two BCT. The rate of SSI in this study is much less than that elicited in other studies in which the standard pre- operative dose of antibiotics was used [5-7,9,13]. All four patients required additional antibiotic treatment and additional hospital visits. In addition, one patient required an additional surgical procedure to drain the infection, multiple hospital visits for local

wound care and secondary wound closure.

The cosmetic outcome in this patient was unsatisfactory and there was a delay of several weeks in starting adjuvant chemotherapy. In addition patients with SSI suffered additional psychological trauma. There was also an increase in the cost of treatment. The adverse impact of SSI has been reported by others [6-9].

Three of the 4 infections were classified as CDC class I; one patient had CDC class II infection. Vitug et al. [13] and Villar-Compte et al. [14] also found that superficial infections were commoner than deep ones. There was only one positive culture which grew *Staphylococcus aureus* (*S. aureus*). In the 5-year prospective surveillance study by Villar-Compte et al. [15], *S. aureus* was the most commonly isolated micro-organism from SSI following breast cancer surgery. In other studies of SSI following breast cancer surgery *S. aureus* comprised 48 % of 63 positive cultures [16], and 42% of 24 positive cultures [17]. This finding gives strength to the recommendation to administer intravenous prophylactic antibiotics with anti-staphylococcal activity.

Several risk factors contribute to SSI development following breast cancer surgery. Vitug et al. [13] and Xue et al. [6] identified recent biopsy (<7 days before operation), obesity, smoking, neo-adjuvant chemotherapy or radiotherapy, age >60 years and heavy alcohol intake as risk factors for SSI development. Olsen et al. [18], Hall et al. [8] and Villar-Compte et al. [19] reported additional risk factors including older age, ASA grade III and IV, intra-operative hypotension, prolonged use of a drain and compromised overall immune status. Some of these risk factors for SSI development were prevalent in our study population (Table 1). Smoking was found to be relatively uncommon (only 1% of the patients smoked) as compared to rates reported in other studies [15,18]. Obesity was the commonest risk factor in our study population, occurring in 27% of all patients, and in 50% of patients who developed SSI. Three patients who underwent mastectomy and 2 patients who had BCT were diagnosed with cancer following excision for breast lumps initially thought to be benign. All other cancers were diagnosed following core biopsy. There was no association between the biopsy procedure and development of infection. All biopsy procedures except one were done 7 days or more before surgery; and so recent biopsy was not an important risk factor. Neither of the patients who had recognized sterility breaks during surgery developed an infection. We could not draw any important conclusions regarding the role of intra-operative hypotension from this study as this was mostly due to anesthetic factors and was easily controlled. Hypotension was not due to intra-operative bleeding requiring transfusion.

Among the patients who developed SSI, the most common risk factors were diabetes, obesity, age >65 years, blocked drain and prolonged drainage exceeding 19 days. SSI occurred in 22% of the severely obese patients (BMI >35); in 25 % diabetic patients; in 25% of those aged above 65 years; in 20% each of patients who had received neo-adjuvant chemotherapy; in 13% of patients who had a drain in situ for longer than 19 days and in 25% of patients with a blocked drain.

Prolonged use of drains is known to be associated with increased risk of SSI [6,20,21]. Villar-Compte et al. [19] reported drain use exceeding 19 days to be associated with increased risk for SSI development. In the present study, the average duration of drain use was 12 days. However, out of 5 patients with prolonged use of drain (>19 days), 1 (20%) developed surgical site infection. Proneness to SSI following prolonged drain use is an important reason why some surgeons prefer to use prophylactic antibiotics postoperatively for an extended period [15,22]. In the present series additional extended antibiotics were not used for patients with prolonged drain duration, the maximum duration of drain use being 25 days post-operatively.

Seroma formation is reported to be the most common complication following breast cancer surgery [13] and occurs in 20-30% of patients. A 15% seroma formation rate was observed in the present study. All the seromas followed modified radical mastectomy. Seromas occurred more commonly when the effluent was 20 ml or more in the 24 hours prior to drain removal. Seroma formation was also commoner when drains were removed within 19 days of surgery. Philips et al. [22] and Barton et al. [23] observed that volumetric analysis of the drain effluent is a good indicator for drain removal. Most surgeons remove drains when the 24 hour drainage volume is <30ml in the previous 24 hours or at 14 days post operatively as this is associated with reduced risk of seroma formation. Obesity is associated with increased risk of fluid production and seroma formation leading to prolonged duration of drain use [20,24]. The findings in the present study related to seroma formation correlate well with observations in the contemporary literature.

Shoulder dysfunction and medial upper arm numbness collectively were reported in 21% of all patients who underwent axillary dissection, making this the most common complication. This complication was more common amongst patients undergoing MRM (32%) compared to those undergoing BCT (17%). This is a higher incidence than the 13.5% rate of shoulder dysfunction reported by Roses et al. [25], 14% reported by Box et al. [26] and 17.7% reported by Hack et al. [27]. Shoulder dysfunction is due to fibrosis during healing following axillary dissection. As part of the post-operative care program, all patients in this study were educated to perform upper arm abduction and range of motion exercises starting from the first post-operative day to help reduce the incidence and severity of this complication. These exercises were reinforced during the post-operative follow-up period to avert long-term immobility and the development of a frozen shoulder. Other authors have contested this regime of early mobilization and have reported increased wound complications and seroma formation with shoulder mobilization [28,29]. A systematic review by Shamley et al. [30] showed reduced seroma formation with delayed shoulder exercises while there was no significant difference in the incidence of shoulder dysfunction when regimens of early and delayed shoulder exercises were compared. Clinical evidence therefore supports a regimen of delayed shoulder exercises calling into review our current practice of early shoulder mobilization exercises.

Upper medial arm numbness is due to injury to the intercosto-brachial nerve during dissection [25]. Deliberate effort was made during dissection to visually identify and protect the nerve, unless it was matted within metastatic lymph nodes in which case it was sacrificed. Inadvertent minor injury can also occur during tissue retraction and is often temporary. Compared to the rates reported by others [25,27] our rate of medial upper-arm numbness is quite low. This is likely as a result of under-reporting amongst our population of patients and also lack of deliberate assessment by the clinician for this complication. It is however a major factor affecting quality of life following surgical treatment of breast cancer [27], although the natural history is one of improvement over time [25,27]. A weakness of the present study was that this complication was not independently elicited but was combined with elicitation of shoulder dysfunction. Despite reports of hematoma formation between 2 to

10% in literature [13] following breast cancer surgery, there was no hematoma formation in this study. This could be attributed to meticulous surgical technique. In summary, with the antibiotic use and strict surveillance protocols used in this study an SSI rate of 6% was observed. This was significantly less than the mean incidence of 15% (5%-30%) reported in other similar studies [5,7,13,14,31]. This reduction in observed infection rates could be attributed to the use of peri-operative antibiotics. It could also be attributed to behavioral change induced by the surveillance for taking preventive measures.

Several risk factors for SSI development were noted to be prevalent in the study population. However, age >65 years, obesity and diabetes appeared to be the most common risk factors for SSI development. By contrast smoking was not a common risk factor. Seroma formation and shoulder dysfunction/ medial upper arm numbness were also common complications. We need to review our current practice of early shoulder mobilization in view of evidence that it is associated with a higher incidence of seroma formation without a significant advantage over delayed mobilization in terms of avoidance of shoulder dysfunction.

In conclusion, there was successful introduction of a surveillance protocol for assessment of the risk of SSI following breast cancer surgery at Aga Khan University Hospital, Nairobi. An SSI rate of 6% was obtained following active and prospective surveillance of patients undergoing breast cancer surgery with the use of peri-operative antibiotics. This rate was lower than that reported in similar studies using only pre-operative prophylactic antibiotic. Various risk factors such as obesity, diabetes, age >65 years and prolonged drain duration were noted to be important contributors increasing the risk of SSI development. We recommend a randomized controlled trial comparing SSI outcomes with the use of pre-operative antibiotics only versus the use of additional post-operative antibiotics is recommended to establish whether there is any significant reduction in the rates of SSI development.

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