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The Incidence of Decolonizing Patients of Staphylococcus Aureus Nasal Carriage Undergoing Breast Cancer Surgery In The Netherlands.

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ABSTRACT

Staphylococcus aureus (S. aureus) is the leading nosocomial (hospital acquired) pathogen in hospitals globally, resulting in substantial morbidity, mortality and additional costs. Breast cancer wound infection can delay and even cause the omission of necessary adjuvant oncological treatment. Nasal carriers of S. aureus are a well defined risk factor for subsequent infections with this organism. Decolonization of nasal and extra nasal sites preoperative can reduce the risk of surgical site infections (SSIs) with S. aureus. The aim of this study was to evaluate the effect of patients screened with S. aureus nasal carriage on the incidence of SSI in a breast cancer surgery population. A prospective cohort study was performed between April 2009 and December 2016 including all patients undergoing a breast cancer surgery. Patients were screened for S. aureus nasal carriage and, when tested positive, were subsequently treated with mupirocin nasal ointment and chlorhexidine soap. The control group was a cohort of patients from April 2009 till July 2011, who were not screened and not received treatment. A total of 1543 patients were included in this study. The rate of S. aureus infection was 1.1% (12 of 1071) for patients who were screened for S. aureus nasal carriage as compared with 2.5 % (12 of 472) for patients who were not screened for S. aureus carriage (relative risk of infection, 0.48; 95% confidence interval [CI], 0.194 to 0.974; p=0.038). The number of surgical site for patients infected with S. aureus who were also operated for breast cancer can be significantly reduced by screening and decolonizing nasal carriers of S. aureus on admission.

Keywords: Screening, Treatment, Nasal carriage

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INTRODUCTION

In the Netherlands, breast cancer is the second leading cause of death in women.[1] Although breast cancer treatment entails a clean surgical procedure, the rate of breast surgical site infections (SSI) range from 0 to 9.6 percent in the Netherlands, depending on definition of SSI, type of operation, comorbidities of the patients, time of follow up, perioperative therapy and reporting institution as described in the PREZIES protocol.[2] PREZIES is a national nosocomial infection surveillance system in the Netherlands which records SSI data.

SSI of the breast do not only result to longer hospital stay and increased hospital cost, it also leads to delay and omission of necessary adjuvant oncological treatment and psychological trauma.[3-4] SSI contamination occurs probably during the perioperative phase, with the main sources of microorganisms being the patients gastro-intestinal and the respiratory tracts and skin (endogenous). *Staphylococcus aureus* (*S. aureus*) nasal carriage is associated with an increased risk of developing a health care-related infection with this micro-organism.[5] The risk of infection in nasal carriers is estimated to be two to twelve times higher than in those who are not colonized with *S. aureus*.[6]

Little is known about the results of treatment of nasal carriage caused by breast cancer surgery, despite *S. aureus* being reported as the leading cause of SSI during breast cancer surgery in the Netherlands.[7] The objective of this study is to minimize *S. aureus* nasal carriage related SSIs through the screening for *S. aureus* of patients with breast cancer.

MATERIALS AND METHOD

Study population

A prospective cohort study was performed from April 1st 2009 until December 31st 2016 at the Department of Surgery, Alrijne Hospital, Leiderdorp, Netherlands. A total of 1543 patients operated for breast cancer were included in this study. The surgical procedures included mamma ablation and mamma lumpectomy. Exclusion and inclusion criteria were defined in agreement with PREZIES protocol.[2]

Screening patients on *S. aureus* nasal carriage started from July 1st, 2011. In the remaining parts of this study, this group of patients would be referred as the intervention group. From April 2009 until July 2011, patients were not routinely screened because screening was not part of the infection strategy of the Alrijne hospital. This group of patients are further indicated as the control group.

Intervention

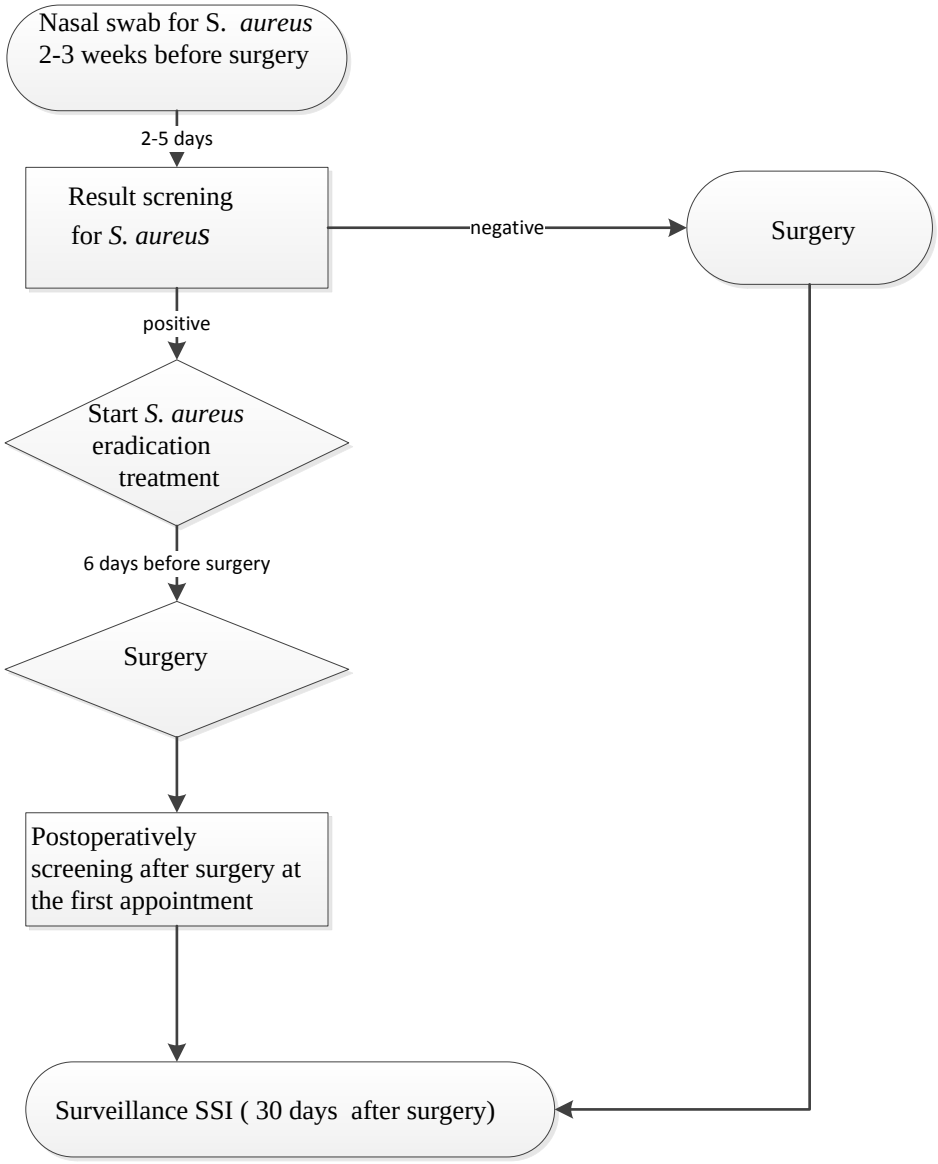
Patients in the intervention group were screened for nasal *S. aureus* carriage, determined by the nasal swab culture preoperatively. The screening was performed using a dry sterile swab, which was rotated in each nostril. The swab was placed in the WASP (Walk Away Specimen

Processor, Copan). At the WASP, a blood and mannitol salt agar were inoculated and incubated 48 hours at 35°C. Strains that were suspected for *S. aureus* were identified in the MALDI-TOF MS (Matrix Assisted Laser Desorption/Ionisation and Time-Of Flight MassaSpectrometrie, Microflex LT, Bruker Daltonik GmbH).

Within 5 days, all patients received the result of their test. Patients with a positive culture for *S. aureus* were instructed to apply mupirocin (Bactroban®, GlaxoSmithKline) ointment 20 mg/g three times a day in each nostril for 5 consecutive days starting 6 days before the surgery. Additionally, these patients showered with chlorhexidine gluconate (HiBiScrub®, SSL Healthcare Nederland BV) 40 mg/ml respectively 1 and 5 days before surgery including the hair.

All patients that received eradication therapy completed the full protocol. Patients with positive cultures for *S. aureus* were screened postoperatively till January 2016 to evaluate the efficiency of our eradication protocol. The postoperatively screening took place at the first appointment with the surgeon after operation (Figure 1).

Figure 1:Screening and treating schedule for patients *S. aureus* nasal carriage



Outcome

Patients' characteristics such as gender, age and the use of implant were assessed as defined by American Society of Anesthesiology (ASA).[8] If a wound was collected, the cultured microorganism(s) were documented.

SSI after the initial procedure at 30 days was defined based on PREZIES criteria.[2]

Each SSI was characterized as superficial or deep. A superficial SSI involves only skin or subcutaneous tissue of the incision and at least 1 of the following: (1) purulent drainage from the incision with or without laboratory confirmation; (2) organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision; (3) at least 1 of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat; and deliberate opening of superficial incision by surgeon, unless the incision is culture-negative. A deep SSI involves deep tissues and at least 1 of the following: (1) purulent

drainage from the incision; (2) the incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least 1 of the following signs or symptoms: temperature higher than 38°C or localized pain or tenderness, unless site is culture-negative; (3) an abscess or other evidence of infection involving the incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination.

Patients with positive cultures for *S. aureus* were screened postoperatively to evaluate efficiency of the eradication protocol. To determine whether *S. aureus* eradication was associated with a decreased risk of SSI, the number needed to treat was calculated. Patients were examined routinely by a physician assistant. Signs of SSI were documented on a case report form (CRF). All patients and infections were discussed and confirmed by a surgeon and an infection prevention controller.

Statistics

The characteristics of the study sample by group (control and intervention) were presented as means and standard deviations for continuous variables, and as percentages for ordinal variables. For group comparisons, continuous variables were analysed with an independent Student's t-test and with a chi-square test for nominal data.

To determine whether *S. aureus* eradication was associated with a decreased risk of SSI descriptive statistics, including frequencies for the independent, variables were included.

Continuous data are presented as means. Categorical data are presented as counts and percentages. Pearson's chi-square and Fisher's exact tests were used for categorical variables and t tests were used for continuous independent variables. In all analyses, statistical under certainties were quantified using corresponding 2-sided 95% CIs and a P-value of < 0.05 was considered significant. Statistical analyses were performed with SPSS for Windows, release 21.0 (SPSS Inc., Chicago, IL, USA).

RESULTS AND DISCUSSION

Study population

In total, 1543 patients were included for the study in the Alrijne hospital. Of this 1543 patients, 1071 (69.4%) were screened for *S. aureus* nasal carriage (intervention group) and 472 (30.6%) patients were not screened for *S. aureus* nasal carriage (control group). In the intervention group, 221 patients (20.6%) turned out to be *S. aureus* carriers as at the time of screening, of which two patients screened positive for MRSA (Methicillin Resistant *S. aureus*). All patients were subsequently treated. On January 2016, we stopped screening postoperatively because patients (including the MRSA patients) who were screened a second time postoperatively "remained" clean.

Patient characteristics

In the baseline characteristics, there were no significant differences between the intervention and the control group (Table 1).

Table 1: Baseline characteristics of 1543 study patients*

Characteristics	Screened (n=1071)	Not screened (n=472)	P value
Mean (SD) age	64 (12.2)	64.5 (13.3)	0.218
Seks,Male/Female(% female)	8/1063 (99)	4/468 (99)	1.000
Implant used n(%)	102 (9.5)	59 (13)	0.078
ASA (%)			
1	227 (21.2)	158 (33.5)	0.788
2	720 (67.2)	233 (49.4)	0.723
3	74 (6.9)	41 (8.7)	0.934
4	2 (0.2)	1 (0.2)	
unknown	48 (4.5)	39 (8.3)	

* April 1st 2009 until December 31st 2016

Infection rates

The total SSIs were 20 (1.8%) in the intervention group and 12 (2.5%) in the control group (p=0.392). Of these SSIs, 12 (1.1%) wound swabs tested positive for *S. aureus* in the intervention group versus 12 (2.5%) in the control group (p=0.038). All SSIs with *S. aureus* were deep-seated (Table 2).

Table 2: Infection rates in the intervention and control group

	Screened (n=1071)	Not screened (n=472)	RR	95% CI; P value
Total SSI (%)	20 (1.9)	12 (2.5)	0.48	0.354-1.505;P=0.391
Non *S. aureus* SSI (%)	8 (0.75)	0 (0,0)		
Type				
aerobic and anaerobic flora	2			
Haemolyticus streptococcus G	1			
Streptococcus oralis	1			
E.coli	1			
Staphylococcus capitis		1		
Unable to obtain culture	2			
***S. aureus* SSI (%)**	12 (1,1)	12 (2,5)		0.194-0.974;P=0.038

* April 1st 2009 until December 31st 2016

Sub analysis in the intervention group showed that 4 (1.8%) patients who screened positive for *S. aureus*, despite treatment and screening negative postoperatively, developed a SSI with *S. aureus*. It also shows that 8 patients (0.9%) who screened negative postoperatively for *S. aureus* also developed a SSI with *S. aureus* (Table 4*)*.

In this study, all strains of *S. aureus* were sensitive for mupirocin. No serious side effects of either mupirocin and chlorhexidine gluconate were encountered and most importantly, the eradication strategy did not postpone further treatment in any way.

DISCUSSION

This prospective cohort study showed that surgical site infections in breast cancer surgery are a frequent and serious complication and most of the SSIs are caused by *S. aureus* (75%). The relationship in occurrence of SSI with *S. aureus* between screening and treating patients of *S. aureus* nasal carriage and patients who were not screened of *S. aureus* nasal carriage is significant (Table 2).

Some authors opted for a treat-all strategy instead of the screen-and-treat strategy that used in this study.[9] The rationale for treating all patients without screening is reduced cost compared to screen and treat. According to our result the number patient needed to treat was 76. While treating all patients and omitting the screening process is a lot cheaper than the screen-and-treat method, the treatall strategy is associated with the probability of developing bacterial resistance.[10]

Although, not included in the scope of this study, it was striking to see patients who screened positive preoperatively, were treated and screened negative postoperatively and patients who screened negative preoperatively, develop a surgical site infection with *S.* aureus (Table 3).

Table 3: Sub analysis infection rates in the intervention group*

	Screened positive (=221)	**Screened negative (n=850)**	**95% CI; P-value**
Total SSI (%)	6 (2.7)	14 (1.6)	0.633-4.387;P=0.275
Non *S. aureus* SSI (%)	2 (0,9)	6 (0.7)	
Type			
aerobic and anaerobic flora	1	1	
Haemolyticus streptococcus G		1	
Streptococcus oralis		1	
Staphylococcus capitis		1	
Unable to obtain culture		2	
Escherichia coli	1		
***S. aureus* SSI (%)**	4 (1.8)	8 (0.9)	0.579-6.503;P=0.283

*July 1st 2011 until December 31st 2016

The cause of these surgical SSIs may be exogenous and several studies show that microorganisms can originate from the operation room (OR) environment[11-12- 13- 14] however, Gabriel Birgand *et al.* reported that the impact of operating-room behaviours on the risk of infection were limited and heterogeneous.[15]

This study has several limitations. Baselines characteristics as diabetes mellitus, smoking and Body Mass Index are not taken in account in this study. These baselines are associated with higher risks of SSI outcomes[16-17] and may have influenced the development of a SSI in this study.

CONCLUSION

In conclusion, this study shows that our screen-and-treat strategy prescribing mupirocin nasal ointment and chlorhexidine soap for patients requiring breast surgery due to cancer with positive nasal swab cultures for *S. aureus,* resulted in significantly less SSIs with *S. aureus*. We recommend this strategy to reduce complications arising from SSIs with *S. aureus* in breast cancer surgery, because additional advantages are lack of major side effects, treatment did not delay surgery and might saves both life years and medical costs at the same time. However, more research is needed to investigate if there is a possible correlation between *S. aureus* originating from the environment and the risk of SSI during breast cancer surgery, which could lead to a further reduction in SSIs with *S. aureus*.

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