Nasal Carriage of *Staphylococcus aureus* as a Major Risk Factor for Wound Infections after Cardiac Surgery

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To evaluate the importance of nasal carriage of *Staphylococcus aureus* as a risk factor for the development of wound infection at the sternotomy site after cardiac surgery, a case-control study was done. The study population consisted of 1980 consecutive patients. Cases were all patients who developed a sternal wound infection from which *S. aureus* was cultured. Forty cases were identified, and 120 controls were selected. Preoperative nasal carriage of *S. aureus*, insulin-dependent diabetes mellitus, and younger age were identified as significant risk factors. The crude odds ratio of nasal carriage was 9.6 (95% confidence interval, 3.9–23.7). The median postoperative length of hospital stay for cases was 30 days longer than for controls. Mortality was also significantly higher for cases than for controls (10.0% and 0.8%, respectively).

Sternal wound infections are serious complications of thoracic surgery and cause significant morbidity and mortality [1, 2].

In our institution, deep surgical wound infections occurred in 3.9% of patients who underwent thoracic surgery [3], and more than half of these infections were caused by *Staphylococcus aureus*. Phage typing showed unique patterns for 86% of the *S. aureus* isolates, virtually ruling out cross-infection as an important mode of transmission. Therefore, it was hypothesized that a substantial number of the infections was caused by endogenous strains of *S. aureus*. This hypothesis was based on findings in several studies in the 1950s and 1960s that showed that carriers of *S. aureus* had an increased risk for development of surgical wound infections [4–6]. In the last several decades, major surgical developments have been accompanied by improvements in infection control (e.g., modernization of the operating theater with respect to air handling and use of antimicrobial prophylaxis). To evaluate the importance of nasal carriage of *S. aureus* as a risk factor for development of surgical wound infections in modern settings, we performed a case control study in patients undergoing sternotomy.

Patients and Methods

Study population. The study population comprised 1980 consecutive patients who underwent sternotomy for cardiac surgery between 1 January 1988 and 1 January 1991 at the Department of Thoracic Surgery, University Hospital, Rotterdam. This hospital is a tertiary referral center for cardiac and pulmonary surgery. Patients were routinely admitted the day before surgery. On that day, specimens were obtained for culture for nasal carriage of *S. aureus*, and body and hair were washed with povidone-iodine or chlorhexidine soap and hair was removed with depilatory cream. All patients were given systemic antibiotic prophylaxis (cefamandole or cefuroxime) for 24 h, starting 1 h before surgery. Clindamycin was given to patients reporting an allergy to β-lactam antibiotics. Sternal wound infections were treated by surgical excision and drainage and, if indicated, systemic administration of antibiotics. The choice of antibiotics was based on the organisms cultured and their susceptibility patterns.

Definition of cases and controls. Cases were all patients from the study population who developed a surgical wound infection

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...he median sternotomy site from which *S. aureus* was cul...red. The criteria used for the diagnosis of postoperative infec...ons were those defined by the Centers for Disease Control and Prevention (CDC) [7]. For each case, 3 controls were selected and matched to cases by proximity of operation date. Controls were accepted only if a preoperative nasal specimen was obtained and if they had no evidence of surgical wound infection with *S. aureus* at the sternotomy site. In the absence of clinical signs, wound cultures were not routinely done on controls. No cases or controls received antibiotic therapy before surgery or had an infection at the time of surgery.

Variables. The medical records of cases and controls were screened for the following variables: age; sex; diabetes mellitus (insulin dependent, non-insulin dependent, or both); use of immunosuppressive drugs; chronic obstructive pulmonary disease; number of underlying disorders; body mass index (kilograms per square meter); smoking history; forward heart failure; length of preoperative stay; previous sternotomy; use of an intraaortic balloon pump; *S. aureus* in the preoperative nasal culture; date of ...rgery; perioperative myocardial infarction; elective or emergency procedure; type of surgery (use of left and right internal mammary artery and cardiac valve procedures were recorded); number of coronary arteries involved; type of antibiotic used for prophylaxis; surgeons, anesthesiologist, and perfusionist; duration of surgery, extracorporeal circulation, and aortic occlusion; volume of perioperative loss of blood and peri- and postoperative blood transfusions; use of rethoracotomy for bleeding; duration of postoperative stay in the intensive care unit; outcome (discharged alive or death); date of discharge or death; length of hospital stay; and readmittance (duration was added to the postoperative length of stay). Other postoperative infections were determined by CDC criteria [7]. Site of infection, date of onset, and pathogens involved were recorded.

For cases, these additional variables were recorded: location of sternal wound infection (superficial or deep [7]), date of onset of infection, and presence of secondary bacteremia.

Microbiology. All patients had nasal swabs the day before surgery. When a surgical wound infection was suspected, the wound and, if present, purulent discharge, were cultured. *S. aur...us* was identified by standard microbiologic methods. All available *S. aureus* isolates from preoperative nasal swabs and wounds were sent to the National Institute of Public Health and Environmental Protection (Bilthoven, Netherlands) for phage typing.

Statistical analysis. Results were analyzed with the SAS statistical package [8]. Differences between groups were tested by Student's *t* test. The importance of the risk factors was determined by calculation of odds ratios and 95% confidence intervals (CIs). Odds ratios determined were Mantel-Haenszel estimates by a stratified analysis in which each stratum comprised a case and its controls. Statistical significance was accepted at $P < .05$, two-tailed analysis.

Results

Characteristics of patient population. In the study population, 40 patients (2.0%) developed a sternal wound infection with *S. aureus*. A total of 120 patients were selected as controls. Table 1 shows the general characteristics of the cases and controls. No statistically significant differences were found in sex, body mass index, type of surgery, and number of coronary arteries involved. The mean age for cases was significantly lower than for controls ($P = .026$). The median postoperative length of stay was 30 days longer for cases than controls (table 1). The total number of postoperative hospital days accrued by the 40 cases was 1901 days versus 1464 days for the 120 controls. Mortality was also significantly higher among cases ($P = .014$). Four (10%) of the sternal wound infections were superficial and 36 (90%) were deep. Eighteen (45%) of the 40 sternal wound infections with *S. aureus* were associated with a secondary bacteremia. The median onset of sternal wound *S. aureus* infections was 8 days after surgery. There was no significant difference in the incidence of postoperative infections other than sternal wound infections.

Analysis of risk factors. Table 2 shows the crude odds ratios with 95% CIs for the most important risk factors. Nasal carriage of *S. aureus* and insulin-dependent diabetes mellitus had the highest crude odds ratios. In addition to younger age (table 1), these were the only statistically significant risk factors. Two of the 4 insulin-dependent diabetes mellitus patients had *S. aureus* in their preoperative nasal cultures. To determine the minimum effect of nasal carriage, all 4 insulin-dependent diabetes mellitus patients were removed from the analysis. This analysis showed an odds ratio for nasal carriage of *S. aureus* of 8.8 with a 95% CI of 3.6–21.8. The variables not shown in table 2 were not associated with significant increased or decreased crude odds ratio.

Table 1. Characteristics of the patient population, types of surgical procedures, median postoperative length of stay, and mortality in controls and cases.

Variable	Controls ($n = 120$)	Cases ($n = 40$)
Mean age, years (SD)	63.9 (9.0)*	59.3 (11.5)*
Sex (% female)	26.7	17.5
Mean body mass index (SD)	25.4 (3.0)	25.9 (3.5)
Surgery (%)		
CABG without internal mammary artery	30.8	35.0
CABG with internal mammary artery	54.2	52.5
Procedures involving cardiac valve replacement	16.7	15.0
Other†	2.5	7.5
Emergency	5.8	10.0
Mean no. of coronary arteries involved (SD)	2.6 (1.3)	2.4 (1.1)
Median postoperative length of stay days (range)	10 (6–50)*	40 (9–145)*
Mortality (%)	0.8*	10.0*

NOTE. CABG, procedure involving coronary artery bypass grafting.

* $P < .05$.

† Other = procedures other than CABG or cardiac valve replacement.

Table 2. Crude odds ratios (ORs) and 95% confidence intervals (CIs) of the most important risk factors for wound infections with *S. aureus* after cardiac surgery.

Risk factor	No. of events/ no. of observations (%)		Crude OR (CI)
	Controls	Cases	
Nasal carriage of *S. aureus*	15/120 (12.5)	19/36 (52.8)	9.6 (3.9–23.7)
Diabetes mellitus			
Non-ID and ID	9/120 (7.5)	7/40 (17.5)	2.7 (0.9–8.0)
Non-ID	9/120 (7.5)	3/40 (7.5)	1.0
ID	0/120	4/40 (10.0)	21.0 (2.4–185.9)
Clindamycin as prophylaxis	11/120 (9.2)	0/40	0.4 (0.1–1.6)
Immunosuppressive drugs	10/120 (8.3)	6/40 (15.0)	1.9 (0.7–5.3)

NOTE. ID, insulin dependent.

Phage typing of S. aureus isolates. Nineteen cases had positive preoperative *S. aureus* nasal cultures. For 10 of the 19, both pre- and postoperative isolates were available for phage typing; these were identical for all 10. All *S. aureus* isolates were susceptible to oxacillin and aminoglycosides.

Discussion

Nasal carriage of *S. aureus*, insulin-dependent diabetes mellitus, and younger age were the most important and only statistically significant risk factors for development of sternal wound infection with *S. aureus*. Since patients with insulin-dependent diabetes mellitus have increased carriage rates of *S. aureus* and are probably at greater risk for developing *S. aureus* infections [9], these two variables could have influenced each other. Because none of the controls had insulin-dependent diabetes mellitus, multiple logistic regression analysis could not be used to evaluate this interaction. The minimum effect of nasal carriage was therefore calculated by removing all insulin-dependent diabetes mellitus patients from the analysis. This analysis showed an odds ratio for nasal carriage of *S. aureus* of 8.8, which is only slightly different from the crude odds ratio of 9.6. Thus, we conclude that nasal carriage of *S. aureus* is an important and independent risk factor for development of sternal wound *S. aureus* infections.

The importance of nasal carriage was confirmed by the 10 cases from whom pre- and postoperative isolates could be compared by phage typing. The pairs were all identical. The important role of endogenous infection also explains the heterogenous pattern of *S. aureus* isolates that caused surgical wound infections in our institution determined in a previous study [3].

The nasal carriage rate of the entire 1980 patient study population can be approximated by extrapolation of the carriage rate of the controls and cases. By so doing, ~264 (13.3%) of the 1980 patients would be nasal carriers, resulting in overall attack rates of 8.0% for carriers and 1.1% for noncarriers. This gives an attributable risk for nasal carriage of 86.3%.

Little attention has been paid to the role of nasal carriage in development of surgical wound infections for 25 years or so. In 1959, Williams et al. [6] reported that 2.1% of postoperative staphylococcal surgical wound infections in 632 patients occurred in those who never carried *S. aureus* in the nose. In 687 carriers, this incidence was 6.9% (relative risk [RR], 3.3; 95% CI, 1.8–6.1). In about half of the infected carriers, the wounds harbored a staphylococci with the same phage type as that in the nose. Also in 1959, Weinstein [5] analyzed nasal pathogens and postoperative infections in 125 patients undergoing major surgery. Those with positive preoperative nasal cultures ($n = 43$) had an infection rate of 37% versus 11% in 82 patients with negative preoperative cultures (RR, 3.4; CI, 1.6–7.0). In the nasal carriers, *S. aureus* was isolated from 94% of the infected wounds; a variety of organisms were cultured from the wounds of noncarriers. For nasal carriers with postoperative *S. aureus* infection, the phage types of the *S. aureus* isolated from the nose and wound were identical in 92% of cases. Similar results were reported by Calia et al. [4], who calculated that about half of all surgical wound infections in their population were caused by endogenous infection with *S. aureus*. The surgical wound infection rate also correlated with the density of *S. aureus* in the nasal culture.

Several studies during the 1950s and 1960s attempted to eliminate nasal carriage preoperatively, but these attempts were hampered by a lack of effective elimination strategies. However, the recent introduction of mupirocin may offer new opportunities. This topical antibiotic is highly effective for elimination of nasal carriage and is more effective than any other antibiotic studied to date [9, 10]. Thus, it should be evaluated for its value in perioperative prophylaxis.

Sternal wound infections with *S. aureus* were associated with a significant prolongation of the length of postoperative stay and a significantly higher mortality among cases. This high rate of severe infection is indicative of the unique pathogenicity of *S. aureus* in wound infections [11]. In a previous prospective surveillance study, we found that deep surgical wound infections in thoracic surgery were associated with a median prolongation of postoperative stay of 30 days [3]. This is identical to the median prolongation of hospital stay in the present study. Although the degree of prolonged hospital stay and mortality rates vary in different studies, it is generally accepted that both are common consequences of sternal wound infections [12].

Because of the severe consequences for patients and the high costs for the health care system, it is important to identify risk factors for development of sternotomy wound infections. To date, a multitude of patient- and procedure-related

risk factors have been identified [12]. The current study differs from others in that it evaluates the risk factors for development of sternal wound infections caused by one specific pathogen, *S. aureus*. Therefore, our results are not entirely comparable with those of studies that evaluated the consequences of and risk factors for development of sternal wound infections caused by a variety of pathogens.

In addition to nasal carriage, insulin-dependent diabetes mellitus and younger age were identified as risk factors for sternal wound infection with *S. aureus*. Insulin-dependent diabetes mellitus was also identified in other studies [12]. The risk factor of younger age seems paradoxical since, when age was identified as a risk factor in other studies, it was always older age [12]. A possible explanation is that some very complicated operations for congenital heart disorders were done on a small group of relatively young patients in this study. These procedures were associated with an increased risk for surgical wound infection in a previous study [3].

Surgical procedures are becoming increasingly complicated, and the population of patients operated on has more underlying diseases [13]. This increases the risk for development of surgical wound infections. Therefore, new strategies are needed to keep the surgical wound infection rate and its associated morbidity and mortality as low as possible. Although the significance of nasal carriage of *S. aureus* for development of surgical wound infections has been well defined [4–6], it has not been defined for cardiac surgery. Because of the great expense and morbidity and mortality associated with sternotomy wound infections, it is important to identify potential preventive measures. Further investigations are warranted to evaluate the effect of perioperative elimination of nasal carriage on surgical wound infection rates.

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