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Original Article

Screening for nasal carriage of *Staphylococcus aureus* among patients scheduled to undergo orthopedic surgery: Incidence of surgical site infection by nasal carriage

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ABSTRACT

Background: *Staphylococcus aureus* (*S. aureus*), including MRSA, is considered to be the leading cause of surgical site infection (SSI) after orthopedic surgery. We screened for nasal carriers of *S. aureus* among patients who were scheduled to undergo orthopedic surgery at our hospital to reveal the effect of nasal *S. aureus* carriage on SSI. Our study design clearly has the intent of finding *S. aureus* nasal carriage and eradicating MRSA when found, and this strategy is to verify whether it's effective for preventing orthopedic surgical infections.

Methods: Subjects were 4148 patients who underwent preoperative screening for nasal carrier and subsequently underwent orthopedic surgery during a 7-year period between April 2007 and March 2014. The incidence of SSI among patients who were operated in our department was investigated, and the rates were compared between patients with and without nasal carriage to reveal the effect of preoperative nasal carriage on SSI.

Results: In total, 1036 patients were nasal carriers of *S. aureus* (carriage rate, 25.0%), whereas 140 patients carried MRSA (carriage rate, 3.4%). SSI developed in 24 patients [incidence, 0.58% (24/4148)] consisting of 12 non-carriers [0.39% (12/3112)] and 12 carriers [1.16% (12/1036)] with a significant difference in the incidence between the groups. Among 24 cases of SSI, more than half (13 cases) were caused by bacterial species other than *S. aureus* or those that could not be detected by the tests used. Only 7 patients out of 24 SSI patients, *S. aureus* was the bacterium detected in preoperative nasal cultures and the causal bacterium for SSI (concordance rate of 29.2%).

Conclusions: It was difficult to reduce the incidence rate of SSI in eradication group to the same level as nasal culture negative group. However, nasal carriage of *S. aureus* or MRSA may be a risk factor for SSI in orthopedic surgery.

1. Introduction

Staphylococcus aureus (*S. aureus*), including methicillin-resistant *S. aureus* (MRSA), may be the leading cause of surgical site infection (SSI) after orthopedic surgery. Causal bacteria for SSI are divided into two groups based on their origins: exogenous agents, such as intraoperative airborne bacteria, and endogenous agents, such as bacteria carried by patients themselves. While exogenous origins have always been considered important, recent studies focus more attention to endogenous infection caused by bacteria originating in patients. However, it is currently unclear whether nasal bacterial carriage is an endogenous risk factor for SSI.

2. Objectives

To reveal the effect of nasal *S. aureus* carriage on SSI, we screened for nasal carriers of *S. aureus* (including MRSA) among patients who were scheduled to undergo orthopedic surgery at our hospital. Our study design clearly has the intent of finding *S. aureus* nasal carriage and eradicating MRSA when found, and this strategy

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is to verify whether it's effective for preventing orthopedic surgical infections.

3. Subjects and methods

We calculated the annual rates of nasal *S. aureus* and MRSA carriage in 4148 patients who had undergone outpatient preoperative screening for nasal bacterial carriage prior to hospital admission for orthopedic surgery during a 7-year period between April 2007 and March 2014.

At our hospital, patients with nasal carriage of MRSA are treated with topical "mupirocin (MUP)" three times a day for three days to eradicate MRSA before surgery. In addition, preoperative prophylactic administration of vancomycin is performed. Therefore, in this study, the proportion of patients subjected to nasal cultures after eradication and the proportion of those who had successful MRSA eradication were determined to reveal the efficacy of MUP. In addition, we investigated background diseases in patients with preoperative carriage of MRSA.

We then compared the incidence rates of SSI between patients with and without nasal carriage during the corresponding period to reveal whether preoperative nasal bacterial carriage affects SSI. A diagnosis of SSI was made in accordance with the definition used in the Guideline for Prevention of Surgical Site Infection published by the United States Centers for Disease Control and Prevention (CDC) [1].

This article has got institutional review board (IRB) approval for all the investigation of human subjects in our institution.

4. Results

In total, 1036 (25.0%) patients carried nasal *S. aureus*, whereas 140 (3.4%) were carrier of MRSA.

The annual incidence of nasal *S. aureus* was 22.9% in 2007, 23.2% in 2008, 26.2% in 2009, 27.5% in 2010, 25.2% in 2011, 25.4% in 2012, and 23.7% in 2013, with a mean rate of 25.0%, while the incidence of nasal MRSA in the same period was 2.4%, 2.3%, 5.9%, 3.1%, 2.7%, 3.5%, and 3.4%, respectively, with a mean rate of 3.4% (Table 1).

The rate of conducting post-MUP nasal cultures was 44.3% (62/140), and the rate of MRSA eradication by MUP was 75.8% (47/62) (Table 2). Primary diseases/surgeries in the 140 patients positive for MRSA culture were 38 (27.1%) spine surgeries, including 17 (12.1%) spinal fusions with implants; 62 (44.3%) joint replacement surgeries including revision surgeries, consisting of 25 (17.9%) total hip arthroplasty (THA) and 37 (26.4%) total knee arthroplasty (TKA); and 40 (28.6%) other surgeries such as femoral head replacement and osteosynthesis.

The CDC defines SSI as infection occurring within 30 days of any operative procedure or occurring within one year after surgery with implants. Based on this definition, 24 (incident rate of 0.58%) patients (ten female and fourteen male, mean age at surgery 67.3 years (range, 39–88 years)) had SSI in this study after 19 spine surgeries, consisting of 13 spinal fusions with implants; 4 joint replacement surgeries, consisting of one each of THA, TKA, revision THA, and revision TKA; and one invasive osteosynthesis. 24 cases of SSI include 10 female and 14 male. The average age at the time of surgery was 67.3 (39–88) years (Table 3). In addition, causal agents were MRSA in 3 patients, *methicillin-sensitive S. aureus (MSSA)* in 8, *Staphylococcus epidermidis* in 6, *Streptococcus* in 2, *Enterococcus faecalis* in 2, coagulase-negative *Staphylococcus (CNS)* in 1, *Escherichia coli* in 1, *Bacteroides fragilis* in 1, and no bacterium detected in 4. Multiple bacteria were detected in 2 patients. Among 24 cases of SSI, more than half (13 cases) were caused by bacterial species other than *S. aureus* or those that could not be detected by the tests used (Table 4). After dividing 24 patients with SSI into those with ($n = 12$) or without ($n = 12$) nasal carriage, the incidence of SSI were analyzed using the Chi-square test, with the significance set at $P < 0.01$. The results showed that the rate was 1.16% (12/1036) and 0.39% (12/3112) in patients with and without nasal carriage, respectively, with a significantly high incidence of SSI in patients carrying bacteria (Fig. 1).

Onset of SSI was a postoperative average of 2.1 months (range, 0.5–12 months). In 7 patients, *S. aureus* was the bacterium detected in preoperative nasal cultures and the causal bacterium for SSI (concordance rate of 29.2%) (Table 5). However, in this study, we did not elucidate whether SSI was caused by endogenous factors, that is, nasal *S. aureus*, in these patients.

Table 1
By year nasal culture colonization rate.

Year	*S. aureus*	MRSA
2007	22.9% (75/327)	2.4% (8/327)
2008	23.2% (122/526)	2.3% (12/526)
2009	26.2% (141/539)	5.9% (32/539)
2010	27.5% (160/581)	3.1% (18/581)
2011	25.2% (168/666)	2.7% (18/666)
2012	25.4% (188/740)	3.5% (26/740)
2013	23.7% (182/769)	3.4% (26/769)
Total	**25.0% (1036/4148)**	**3.4% (140/4148)**

Table 2
The rate of conducting post-MUP nasal culture and MRSA eradication by MUP.

Year	Post-MUP nasal culture	MRSA eradication by MUP
2007–2010	39.1% (27/69)	77.8% (21/27)
2011–2014	49.3% (35/71)	74.3% (26/35)
Total	**44.3% (62/140)**	**75.8% (47/62)**

It was divided into a first half and a second half.

5. Discussion

Once patients develop SSI after orthopedic surgeries, especially those with implants such as joint replacement surgery and spinal fusion, it is often necessary to remove the implants, aggravating their dysfunction. Matsushita et al. [2] emphasized the importance of preventing SSI in bone and joints because of the difficulty treating this type of infection even today with technological advances in the field of antibiotics.

Against this background, the Japanese Orthopaedic Association developed Japanese Orthopaedic Association (JOA) Clinical Practice Guideline on the Prevention of Surgical Site Infections in Bone and Joint [3]. To improve treatment outcome and patient prognosis, the guideline recommends currently most appropriate preventive, diagnostic, and treatment strategies for musculoskeletal disorders. Also at our hospital, we developed the Guidelines for Healthcare Hazard Control and Safety Management in April 2007 and have subsequently established various preventive measures against infection, including the Infection Control Committee and a SSI surveillance system. Around the same time, our orthopedic surgery department started routine preoperative screening for nasal bacterial carriage as a part of the surveillance system.

When MRSA is detected in preoperative nasal cultures at our hospital, we perform the intranasal application of topical MUP three times a day and chlorhexidine wipes at surgical sites once a day for three days before surgery to eradicate MRSA. In addition, vancomycin is administered intra-operatively as a preventive measure. It is ideal to perform the whole-body washing of patients

Table 3
Primary disease and operative procedure of SSI 24 cases.

Case	Age at surgery	Gender	Primary disease	Operative procedure
1	77	F	Old vertebral compression fractures	Thoracolumbar spinal fusion
2	60	F	Destructive spondyloarthropathy	Lumbar spinal fusion
3	60	F	Rheumatoid arthritis (RA)	TKA
4	59	M	Lumbar spinal canal stenosis	Lumbar laminectomy
5	78	F	Degenerative lumbar stenosis	Lumbar spinal fusion
6	49	M	Avascular necrosis of the femoral head	THA
7	66	M	Old vertebral compression fractures	Thoracolumbar spinal fusion
8	39	M	Lumbar disk herniation	Lumbar disk herniotomy
9	85	M	Osteoarthritis of the knee joint	TKA revision
10	62	M	Lumbar spinal canal stenosis	Lumbar laminectomy
11	75	F	Degenerative lumbar scoliosis	Lumbar spinal fusion
12	48	F	Degenerative spondylolisthesis	Lumbar spinal fusion
13	67	M	Lumbar spinal canal stenosis	Lumbar laminectomy
14	88	F	Degenerative spondylolisthesis	Lumbar spinal fusion
15	56	M	Destructive spondyloarthropathy	Lumbar spinal fusion
16	58	M	Lumbar spinal canal stenosis	Lumbar spinal fusion
17	81	F	Old vertebral compression fractures	Thoracolumbar spinal fusion
18	77	M	Cervical spondylotic myelopathy	Cervical laminoplasty
19	82	M	Lumbar spinal canal stenosis	Lumbar spinal fusion
20	64	M	Lumbar disk herniation	Lumbar disk herniotomy
21	63	F	Degenerative spondylolisthesis	Lumbar spinal fusion
22	72	M	Degenerative spondylolisthesis	Lumbar spinal fusion
23	80	M	Osteoarthritis of the hip joint	THA revision
24	70	F	Calcaneous fracture	Osteosynthesis
Average	67.3 (39–88)		F 10, M 14	

with chlorhexidine, but instead, we currently wipe surgical sites with chlorhexidine because of various issues such as equipment.

Regarding the timing of the eradication of nasal MRSA after screening, we think it is best to initiate eradication 1 week before surgery. At our hospital, patients are admitted 2 days before their surgery. Therefore, to prevent nosocomial spread to other in-patients, MRSA carriers who are scheduled to undergo surgery should complete the eradication of MRSA by the day before hospital admission. Another reason to complete the eradication of MRSA immediately prior to surgery, if possible, is the uncertainty about how long the effect of eradication lasts. Although we did not investigate the recurrence rate of nasal MRSA carriage among the present patients, we previously examined nasal screening of MRSA carriers multiple times before they underwent elective surgeries for different diseases at different times, and found that even after eradication, patients who were once a carrier were more likely to become infected again. We think this issue needs to be investigated further.

The present findings showed that patients with nasal carriage of *S. aureus* had a higher incidence of SSI than those without. We hypothesize that in patients who carry nasal *S. aureus* and have poor health such as a weakened immune system, surgery requiring general anesthesia via intratracheal intubation may induce the intraoperative or postoperative transmission of the bacteria to the trachea and lungs, causing adverse events. In other words, it is possible that relatively harmless resident bacteria turn into opportunistic pathogens because of the declining clinical status of the patient, causing systemic infection and thus SSI [6,14,15,17,18]. Therefore, nasal *S. aureus* eradication is important in terms of avoiding this kind of situation, too.

Table 4
Causal bacteria of SSI.

Detected bacteria (SSI 24 cases)	Cases
MRSA	3
Methicillin-sensitive S. aureus	8
S. epidermidis	6
Streptococcus	2
Enterococcus	2
Coagulase negative Staphylococcus	1
Escherichia coli	1
Bacteroides fragilis	1
Not detected	4

There have been several reports on the importance of pre-operative eradication. The Society for Healthcare Epidemiology of America (SHEA) promotes active eradication programs in carriers of MRSA [9]. Using real-time polymerase chain reaction, Bode et al. [4] screened patients for nasal *S. aureus* carriage immediately after hospital admission and performed the intranasal application of topical MUP and the whole-body washing with chlorhexidine. These measures reduced the occurrence of SSI significantly, showing the importance of eradicating the bacterium from not only the nasal cavities, but also the entire body surface. Saitoh et al. [5] also reported recently that preoperative screening and intranasal and whole-body eradication in patients carrying bacteria could reduce the incidence of perioperative SSI.

Furthermore, Tsujihara et al. [6] have shown the importance of post-eradication cultures for identifying the improper use or tolerance of MUP. However, caution must be paid when applying MUP for a long time or on body areas other than nasal cavities because of its association with MUP resistant strains as shown in some studies [7,8].

In the present study, the rate of conducting post-MUP nasal cultures was as low as 44.3%. However, after mandating the culture in April 2014, the rate has increased to 78.6% by June 2015. In addition, the 75.8% eradication rate suggests that MUP successfully eradicates MRSA in three out of four patients.

In this study, we did not thoroughly investigate whether host factors varied between patients with and without MRSA, but the proportion of MRSA carriers tended to increase in health care workers and individuals who had recently been admitted to a hospital or care facility.

From time to time, studies in the field of orthopedic surgery have shown the involvement of nasal carriage of *S. aureus* including MRSA in SSI [10–13]. The association between nasal MRSA carriage and infection in other body areas has also been shown occasionally

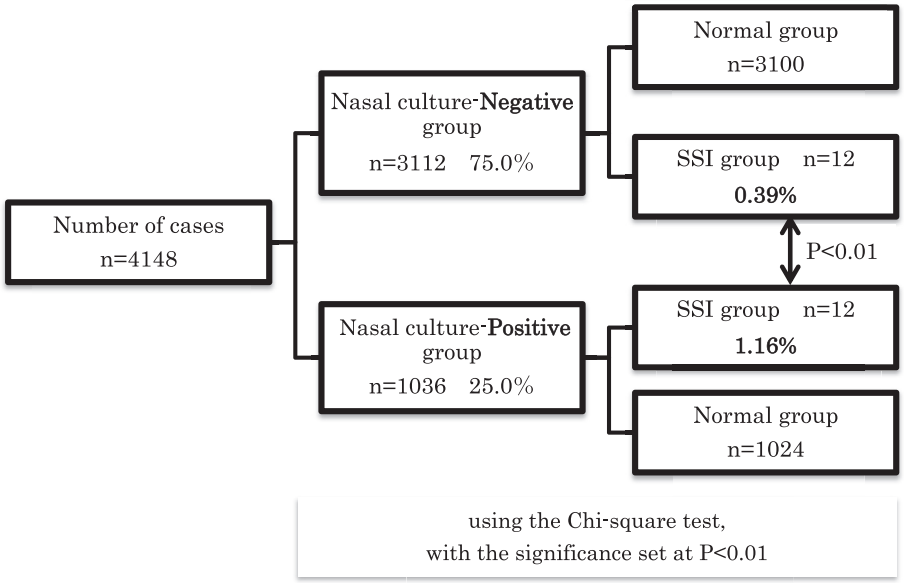

Fig. 1. Flow chart shows a comparison of surgical site infection (SSI) between patients with and without nasal carriage (using the Chi-square test, with the significance set at $P < 0.01$).

[14,15]. However, other studies reported the no association between preoperative bacterial carriage and SSI [16].

In this study, the antibiotic agent mupirocin achieved eradication in 75.8%, but not all, of MRSA cases. The living environment might have been the factor differentiating successful cases from unsuccessful ones. Because of exposure to the outside world, the nasal cavity easily comes in contact with various bacterial species. When MRSA is present in the environment, patients may easily become a carrier even after eradication. However, the eradication rate of 75.8% in this study suggests that eradication was successful in 3 out of 4 patients, emphasizing the significance of the procedure.

In a previous study by another group, the occurrence of SSI could not be prevented completely even after successful preoperative eradication [10]. In our study as well, it was not possible to eradicate MRSA completely. This suggests that the occurrence of SSI is not simple because of the involvement of many factors, besides bacterial carriage, as described in the Japanese Orthopaedic Association (JOA) Clinical Practice Guideline on the Prevention of Surgical Site Infections in Bone and joint [3].

Table 5
The relationship between preoperative nasal carriage and perioperative infection bacteria of SSI 24 cases.

Case	Age at surgery	Gender	Onset of SSI (months)	Nasal culture before surgery	Infection-causing bacteria	Concordance of the bacteria
1	77	F	3	negative	*S. epidermidis*	
2	60	F	1.2	MSSA	MSSA	●
3	60	F	8.1	MSSA	*Streptococcus*	
4	59	M	1.5	negative	MRSA	
5	78	F	1.2	MSSA	*S. epidermidis*	
6	49	M	4.9	MSSA	MSSA	●
7	66	M	0.9	MSSA	*S. epidermidis*	
8	39	M	1.1	MSSA	MSSA	●
9	85	M	2	negative	negative	
10	62	M	1	negative	MSSA	
11	75	F	1	MRSA	MRSA	●
12	48	F	12	negative	*Streptococcus*	
13	67	M	1.5	MSSA	MSSA	●
14	88	F	1	negative	MSSA	
15	56	M	1	MRSA	negative	
16	58	M	0.5	MSSA	MSSA, *S. epidermidis*	●
17	81	F	1	negative	*E. coli*, *E. faecalis*, *B. fragilis*	
18	77	M	0.5	negative	negative	
19	82	M	1	MRSA	MRSA	●
20	64	M	1	negative	MSSA	
21	63	F	1	negative	negative	
22	72	M	1	negative	*E. faecalis*	
23	80	M	1.5	negative	CNS, *S. epidermidis*	
24	70	F	1	MSSA	*S. epidermidis*	
Mean	67.3		2.1			
						Concordance rate 29.2% (7/24)

This study showed that, among 24 cases of SSI, more than half (13 cases) were caused by bacterial species other than *S. aureus* or those that could not be detected by the tests used (Tables 4 and 5). What is more, only 7 patients out of 24 SSI patients, *S. aureus* was the bacterium detected in preoperative nasal cultures and the causal bacterium for SSI (concordance rate of 29.2%) (Table 5). This study compared incidence rate of SSI between nasal culture positive group and nasal culture negative group. This study did not compare between group with eradication and group without eradication. Therefore, it is difficult to judge efficacy of eradication of bacteria. One proven thing in this study was that it was difficult to reduce the incidence rate of SSI in eradication group to the same level as nasal culture negative group.

On the other hand, preoperative MUP treatment was fairly effective, achieving an approximately 75% eradication rate (Table 2), and the incidence of SSI was significantly higher in patients with nasal carriage of *S. aureus* than in those without (Fig. 1), indicating that preoperative screening and eradication measures could have prevented SSI at least in some patients.

The limitation of this study is that no genetic analysis of nasal *S. aureus* was conducted to elucidate whether the causal bacteria for SSI had originated exogenously or endogenously.

6. Conclusion

Our conclusion from this study, which is a very extensive and rigorous investigation, is that it is difficult to reduce the incidence rate of SSI in eradication group to the same level as nasal culture negative group.

Because of the involvement of various risk factors, it is difficult to explain the occurrence of SSI just by comparing patients with and without bacterial carriage. However, the findings of this study suggest that nasal carriage of regular *S. aureus* or MRSA may be a risk factor for SSI in orthopedic surgery.

Conflict of interest

The authors declare that they have no conflict of interest.

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