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Decreased rate of surgical site infection after spinal surgery with instrumentation using bundled approach including surveillance and intrawound vancomycin application

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Abstract

Surgical site infections (SSIs) increase the risk of mortality, postsurgery, extend hospital stay, and increase the costs of healthcare. Our aim in this study was to evaluate the effectiveness of a multidisciplinary, evidence-based, surveillance program combined with intrawound application of vancomycin in lowering the incidence rate of SSI after spinal surgery with instrumentation.

We conducted a retrospective analysis of 637 patients who underwent spinal fusion with instrumentation in our institution at 3 different time periods: prior to our surveillance program (control group), surveillance only (surveillance group 1), and surveillance combined with intrawound vancomycin application (surveillance group 2). The following covariates were considered in the evaluation of between-group differences in SSI rate: sex, age, surgical site, National Nosocomial Infection Surveillance (NNIS) risk index, American Society of Anesthesiologists (ASA) physical status classification, and other health comorbidities. The causative organism in cases of SSI was confirmed in all cases.

The rate of SSI was significantly lower in the surveillance group 2 (1.4%) than in the control group (4.6%; $P = .04$). On multivariate logistic regression analysis, steroid use (adjusted odd's ratio (OR), 6.06; 95% confidence interval (CI), 1.45–23.6) and operative time (adjusted OR.1.01; 95% CI, 1.00–1.01) were identified as independent risk factors of SSI. *Staphylococcus* species and *Propionibacterium* acnes were the principal causative organisms.

A bundled approach that includes surveillance and intrawound application of vancomycin is an effective strategy to lower the risk of SSI after spinal fusion with instrumentation. The use of steroid and longer operative time are risk factors of SSI.

Our findings support the implementation of a program of surveillance, combined with intrawound vancomycin application, to reduce the incidence rate of SSIs in spinal surgery.

Abbreviations: ASA = American Society of Anesthesiologists, BMI = body mass index, DM = diabetes mellitus, ICT = Infection Control Team, JANIS = Japan Nosocomial Infections Surveillance, NNIS = National Nosocomial Infection Surveillance, OR = odds ratio, RA = rheumatoid arthritis, SSI = surgical site infection.

Keywords: duration of operation, intrawound vancomycin application, steroid use, surgical site infection, surveillance

1. Introduction

Surgical site infection (SSI) increases the overall risk of mortality postsurgery,[1,2] extends hospital stay[1–3] and increases the costs of healthcare due to additional treatment needed.[1,3] In their 2014 survey of SSIs across multiple states in the United States, Magill et al[4] reported 66,100 cases of SSI, with an incidence rate of 2.0% to 4.4%.[5–8] The National Nosocomial Infection Surveillance (NNIS) system was established by the Centers for Disease Control and Prevention in 1970 to identify strategies to eliminate SSIs. Cruse and Food[9] reported on the benefit of implementing active surveillance in lowering the incidence rate of SSIs to 1.0% to 2.6%. Similarly, Brandt et al[10] reported a decrease in the risk of SSI to 0.75 after a 3-year program of SSI surveillance, an outcome which was further confirmed by Schneeberger et al[11] for elective orthopedic surgeries. In Japan, the Japan Nosocomial Infections Surveillance (JANIS) program was established by the Ministry of Health, Labor, and Welfare in 2002 to conduct SSI surveillance, using the guidelines and definitions of the NNIS system. In 2007, the JANIS program reported an incidence rate of SSI after spinal fusion of 1.1%. In comparison, the incidence rate of SSI after spinal fusion with instrumentation in our institution, between 2004 and 2007, was as high as 4.6%. To address this issue, we established an SSI surveillance program, in cooperation with the Infection Control Team (ICT), and expanded our perioperative protocol to include the use of antibiotic prophylaxis,[12–15] perioperative glycemic control[16] and intrawound application of vancomycin powder.[17,18] Our aim in this study was to evaluate the

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effectiveness of our multi-disciplinary, evidence-based surveillance program, combined with intrawound application of vancomycin, in lowering the incidence rate of SSI after spinal surgery with instrumentation.

2. Material and methods

2.1. Patient data and surveillance

We conducted a retrospective analysis of 637 patients who underwent spinal surgery with instrumentation at our institution, between January 2004 and June 2016, during 3 different types of surveillance periods: before formal surveillance and the perioperative protocol were established (January 2004–May 2007, n = 152, control group); surveillance period 1, after implementation of surveillance and the perioperative protocol (June 2007–July 2011, n = 199, surveillance group 1); and surveillance period 2, after implementation of surveillance, the perioperative protocol and intrawound application of vancomycin (August 2011–June 2016, n = 286, surveillance group 2). All procedures of surveillance were performed according to the NNIS guidelines and definitions.[19] The following covariate information was extracted from the medical analysis for inclusion in the analysis: age, sex, body mass index (BMI), current smoking status, use of steroids (defined as any systemic steroid provided at any dosage, but not including locally applied steroids). The following variables were extracted for analysis: use of immunosuppressants, past history of diabetes mellitus (DM), and rheumatoid arthritis (RA), location of surgical site (cervical/thoracic/lumbar), operative time, volume of intraoperative blood loss, number of spinal levels fused; and use of bone graft for fusion. The risk index for SSI was calculated using the methods described in the NNIS system, with the index ranging between "0" and "3," with higher scores indicative of a higher risk for SSI. Patients' physical status prior to surgery was assessed using the American Society of Anesthesiologists (ASA) physical status classification system.

Approval by Kyoto university ethics committee was obtained for this study.

2.2. Perioperative protocol

The following perioperative protocol was used for all patients, including: preoperative bathing with soap[20] and intranasal mupirocin treatment, with application of mupirocin ointment for decolonization in patients with nasal *Staphylococcus aureus*;[12–14] antibiotic prophylaxis, consisting of administration of 1 g of cephazolin 30 minutes before incision, with intraoperative redosing if the procedure exceeded 3 hours, and additional 6 doses administered up to 48 hours after surgery;[12] frequent wound irrigation, using saline, including after instrumentation;[21] double gloving and a change of the outer pair before handling the instrumentation and before wound closing;[22] storage of bone grafts in the plastic box with a cover to prevent bacterial contamination; perioperative glycemic control, measured using an insulin sliding scale;[16] and intrawound application of vancomycin powder. Since August 2011, we added 1 g of vancomycin powder to the bone graft and scattered 1 g of vancomycin around the instrumentation.[17,18]

2.3. Statistical analysis

Differences between the control (before formal surveillance) and the surveillance groups (surveillance period 1 and 2) with regard to age, number of spinal levels fused, volume of blood loss, and BMI were evaluated using Dunnett's test. Between-group differences and sex distribution, rate of SSI, and risk factors were valuated using Pearson's test. Lastly, a chi-squared test was used to compare the NNIS risk index and ASA classification between groups. Univariate analysis and multivariate regression analysis were performed to identify the variables associated with SSI, with variables selected using a stepwise method. All analyses were performed using JMP Pro 11 (SAS, United States), with significance set a *P*-value of .05. Steroid use and operative time were used for the calculation of the adjusted odds ratio (OR).

3. Results

Patient characteristics were comparable between the 3 groups, with the exception of a higher mean age for surveillance 2 group compared to the control group. Surgical characteristics were comparable between groups. The incidence rate of SSI was significantly lower for the surveillance group 2 (1.4%) than for the control group (4.6%; $P = .04$; Table 1; Fig. 1). Considering the subgroup of patients who developed an SSI only, no between-group differences in operative parameters were identified (Table 2). The distribution of deep SSI was as follows: 6 in the control group, 5 in the surveillance 1 group and 3 in the surveillance group 2 (Table 3). The SSI rate at the main surgical site was significantly lower in the surveillance group 2 than in the control group ($P = .02$; Table 3; Figure).

Staphylococcus species and *Propionibacterium* acnes were major causative organisms of SSI (Table 4). Of note, only 1 case of methicillin resistant *S aureus* (MRSA) and 1 case of *Mycobacterium abscessus* were detected from samples of main surgical wounds, with 1 case of methicillin susceptible *S aureus* s detected at the iliac bone graft site in the surveillance group 2.

In univariate analysis, steroid use and a longer operative time were associated with a higher incidence rate of SSI ($P = .01$; Table 5). The rate of SSI was also higher among patients with RA ($P = .05$). Smoking, immunosuppressant therapy, previous surgeries, DM, number of levels of fusion, intraoperative volume of

Table 1

Patient demographics in total.

	Control	Surveillance 1	Surveillance 2	Total
The number of patients	152	199	286	637
Age (mean ± SD)	57.9 ± 15.3	61.0 ± 16.5	64.6 ± 15.4	61.9 ± 15.9
$P^{\dagger}$		.11	<.001***	
Sex (male/female)	64/88	85/114	132/154	281/356
$P^{\ddagger}$		.91	.42	
SSI	7	6	4	17
$P^{\ddagger}$		.43	.04*	
Surgical sites				
Cervical	68	67	68	203
Thoracic	49	55	91	195
Lumbar	72	119	195	386
Duration of operation (min, mean ± SD)	303 ± 223	268 ± 126	283 ± 139	283 ± 160
$P^{\dagger}$		0.07	0.33	
Blood Loss (mL, mean ± SD)	484 ± 745	438 ± 534	360 ± 548	414 ± 598
$P^{\dagger}$		.68	.07	

† Dunnett's test.
‡ Pearson's test.
* $P < .05$.
*** $P < .001$
SD = standard deviation.

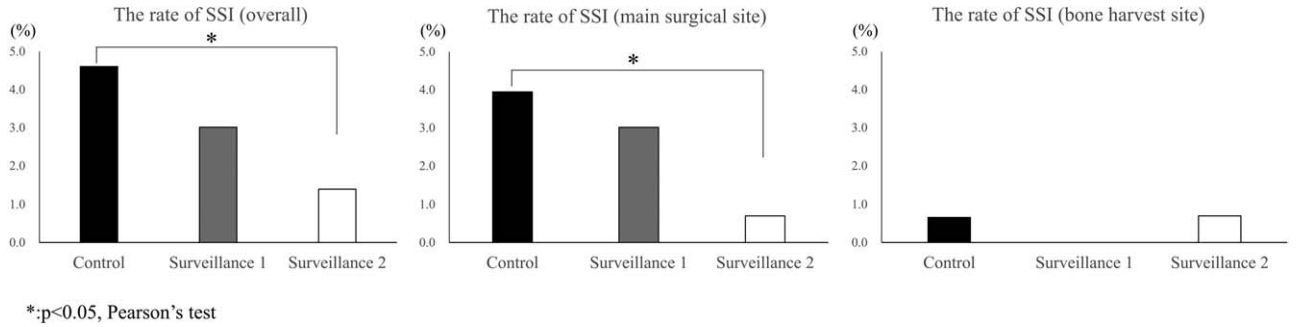

Figure 1. The overall rate of surgical site infection (SSI) was4.6% for the control group, 3.0% for surveillance group 1 and 1.4% for surveillance group 2. The incidence rate of SSI was significantly lower for the surveillance group 2 than the rate for the control group (left panel). The SSI rate at the main surgical site was 4.0%, 3.0%, 0.7%, respectively, for the control, surveillance 1 and surveillance 2 groups. The SSI rate at the main surgical site was significantly lower in the surveillance 2 group than in the control group (middle panel). The SSI rate at the bone harvest site was 0.7%, 0%, 0.7%, respectively. There were no significant differences between groups (right panel).

Table 2

Patient demographics in SSI subgroup.

	Control	Surveillance 1	Surveillance 2
The number of patients	7	6	4
Age (mean ± SD)	56.9 ± 13.9	66.3 ± 11.4	64.5 ± 6.8
P†		.29	.51
Sex (male/female)	4/3	4/2	2/2
P‡		0.72	0.82
Surgical sites			
Cervical	4	4	2
Thoracic	3	3	1
Lumbar	2	2	1
Duration of operation (min, mean ± SD)	379.4 ± 201.7	392.3 ± 159.0	360.3 ± 171.6
P†		.97	.99
Blood Loss (mL, mean ± SD)	680.3 ± 730.6	842.0 ± 953.6	120.5 ± 108.3
P†		.75	.50

SD = standard deviation, SSI = surgical site infection.
† Dunnett's test.
‡ Pearson's test.

blood loss, BMI, the NNIS risk index, and the ASA classification were not associated with SSI incidence. On multivariate logistic regression analysis, an increase in operative time was associated with an increased incidence of SSI (adjusted OR, 1.01; 95% confidence interval (CI), 1.00–1.01), with steroid use resulting in a 6.06-fold increase in SSI incidence (OR, 6.06; 95%CI, 1.45–23.6; Table 6).

Table 3

Classification of SSI.

	Control	Surveillance 1	Surveillance 2
Deep	6 (4.0%)	5 (2.5%)	3 (1.1%)
Superficial	1 (0.7%)	1 (0.5%)	1 (0.3%)
Total	7 (4.6%)	6 (3.0%)	4 (1.4%)
Main surgical site	6 (4.0%)	6 (3.0%)	2 (0.7%)
Bone harvest site	1 (0.7%)	0 (0%)	2 (0.7%)
Total	7 (4.6%)	6 (3.0%)	4 (1.4%)

SSI = surgical site infection.

Table 4

Causative organisms of SSI.

Bacterial Species	Control	Surveillance I	Surveillance II	Total
MSSA*	2	2	1	5
Propionibacterium acnes	2	1		3
MRSA†	1		1	2
MRS (*S epidermidis*)‡	1	1		2
Pseudomonas aeruginosa		1		1
Proteus mirabilis (ESBL)§		1		1
Mycobacterium abscessus			1	1
Undetected	1		1	2
	7	6	4	17

* MSSA; Methicillin susceptible *Staphylococcus aureus*.
† MRSA; Methicillin resistant *Staphylococcus aureus*.
‡ MRS; Methicillin resistant *Staphylococcus epidermidis*.
§ ESBL; extended spectrum beta lactamase.

4. Discussion

We were successful in significantly reducing the incidence rate of SSI after spinal instrumentation surgery through a combination of surveillance, implemented by an ICT, and intrawound application of vancomycin powder. Following the American study on the efficacy of nosocomial infection control (SENIC project),[23] active surveillance was implemented in Europe,[10,24–28] Australia,[29] and Asia,[30,31] and has played an important role in the prevention of SSIs. Although most surveillance programs have been effective in reducing the rate of SSI, surveillance alone was insufficient in our study. Although this unexpected result may be due, in part, to the small sample size of our study, the most likely explanation is the increased detection of SSI with surveillance.[32] Moreover, a previously published prospective study reported that surveillance of SSIs by surgeons alone was not as effective as surveillance performed in cooperation with an ICT.[33] Considering this, the rate of SSI might be underestimated when not implemented by an ICT.

Several risk factors have been associated with SSI after spinal surgery, and these can be classified into 3 broad groups: patient characteristics, surgical procedure and postoperative care.[34] At the level of patient characteristics, older age,[8,35] obesity,[5–8,36,37] DM,[2,6–8,21,38] alcohol abuse,[8,39] smoking,[2,8,35,37] low platelet count,[40,41] and previous SSI[7,8] all contribute to increasing the risk for SSI after instrumented spinal surgery. At the level of

Table 5

Correlations between risk factors and SSI occurrence during surveillance period.

Risk factors		SSI (+)	SSI (−)	Total	P
Smoking†		3	81	84	.28
Steroid use†		4	59	63	.01*
Immunosuppressant‡		1	45	46	.96
RA†		3	49	52	.05
Previous operation†		3	97	100	.46
Diabetes mellitus†		3	65	68	.14
NNIS‡;					.35
	0	2	131	133	
	1	4	182	186	
	2	1	104	105	
	3	3	58	61	
ASA‡;					.76
	1	1	113	114	
	2	7	282	289	
	3	2	80	82	
Number of fusion§		4.8±2.3	3.6±3.0	3.6±3.0	.20
Blood loss, mL§		553±805	388±537	392±544	.34
BMI†		21.5±4.6	22.9±4.0	22.9±4.0	.25
Age§ (mean±SD)		65.6±9.4	63.1±16.1	63.1±16.0	.62
Duration of operation§ (min, mean±SD)		380±155	274±133	277±134	.01*

ASA PS = American Society of Anesthesiologists Physical Status classification system, BMI = body mass index, NNIS = National Nosocomial Infections Surveillance, SSI = surgical site infection.

† Pearson's test.

‡ Chi-squared test.

§ Dunnett's test.

* $P < .05$.

surgical procedures, use of a posterior approach,[5,35] a volume of intraoperative blood loss >1 L,[7,35] a longer operative time,[2,7,36] and the need for blood transfusion[40,42] have been identified as common risk factor for postsurgical SSI. At the level of postoperative care, not using a postoperative drain,[40] prolonged postoperative wound drainage[39] and postoperative incontinence[5] are recognized as potential risk factors for SSI. In our study cohort, we identified operative time and steroid use as independent risk factors for the development of SSI. Previous studies have reported an OR of operative time for SSI ranging between 1.33 to 2.08,[2,7,36] although different cutoff values have been used in different studies. In our study, we expressed operative time as a continuous variable. Therefore, our OR of 1.01 indicates that extending the operative time by 60 minutes results in a 1.8-fold increase in the rate of SSI. The association between SSI and use of steroids can be explained by the effects of corticosteroids suppressing cell-mediated immunity.[36,43,44]

The combination of systemic antibiotic prophylaxis, consisting of first generation cephalosporins and local vancomycin application, has been associated with excellent outcomes in lowering the incidence rate of SSI after spinal surgery with instrumentation to levels of 0–0.8%.[17,18,35] Both *S aureus* and *S epidermidis* bacteria can form a biofilm, increasing their resistance to antibiotics. The combination of vancomycin and β-lactam antibiotics provides a synergistic effect against biofilm forming MRSA.[45] Vancomycin alone, at a concentration >64 μg/mL, can eradicate biofilm forming *S epidermidis* for up to 4 hours.[46] The average concentration of intrawound vancomycin used 48 h after hip revision surgeries, using impaction bone grafting mixed with vancomycin, is 265 μg/mL.[47] Therefore, an effective local application of vancomycin must be sustained for at least 2 days postsurgery. Considering that a sufficient concentration of vancomycin was used over a sufficient time period in our surveillance 2 protocol, the occurrence of one case of MRSA-associated SSI indicates that not all MRSA infections can be controlled by intrawound application of vancomycin. The issue is to balance an effective local dose of vancomycin with tissue tolerance. An *in vitro* study reported that human osteoblasts can survive up to vancomycin concentrations of 2000 μg/ml.[48] In humans, thus far, the maximum reported concentration of vancomycin used locally was 1400 μg/mL over a 48-hours period, without any sign of nephrotoxicity.[49] Further research is warranted to clearly delineate the effects of intrawound vancomycin on the bone fusion rate at the graft site.

Table 6

Multivariate logistic analysis of SSI occurrence.

	Crude OR (95%CI)	Adjusted OR (95%CI)	P
Duration of operation, minutes	1.00 (1.00–1.01)	1.01 (1.00–1.01)	.01
Steroid use	4.70 (1.29–17.1)	6.06 (1.45–23.6)	.02

OR = odds ratio, SSI = surgical site infection.

The limitations of our study need to be acknowledged. First, the bias introduced by the lower mean age of patients in the control versus surveillance group 2 on measured outcomes could not be accounted for in our statistical analysis. Age is an important covariate to consider as higher patient age correlates with higher incidence rates of SSI.[8,35] Moreover, not all risk factors for SSI could be identified from the medical records of patients in the control group, as these risk factors were not systematically recorded prior to the implementation of SSI surveillance. As the majority of our patients underwent spinal fusion with instrumentation of the cervicothoracic and thoracolumbar regions of the spine, a reliable evaluation of the effect of surgical site on the incidence rate of SSI could not be performed. As well, the local or serum concentration of vancomycin was not measured and, therefore, a dose–effect relationship could not be evaluated. Lastly, although steroid use was identified as an independent risk factor for SSI, again, we did not consider the dose-effect. As we were not able to identify research that clearly evaluated the dose effect of steroids on SSI, further research on this issue is needed.

In conclusion, topical administration of vancomycin in combination with surveillance can be effective in lowering the incidence rate of SSI after spinal fusion with instrumentation. Steroid use and longer operative time are risk factors for SSI.

Author contributions

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