Surgical site infection after total en bloc spondylectomy: Risk factors and the preventive new technology

Surgical site infection after total en bloc spondylectomy: risk factors and the preventive new technology

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Abstract

Background Context

Surgical site infection (SSI) associated with instruments remains a serious and common complication in patients who undergo Total en bloc spondylectomy (TES). It is very important that the risk factors for SSI are known in order to prevent it.

Purpose

To identify independent risk factors for SSI after TES and to evaluate the positive effect of iodine-supported spinal instruments in the prevention of SSI after TES.

Study Design

Retrospective clinical study.

Patient Sample

One hundred twenty-five patients who underwent TES for vertebral tumor were evaluated.

Outcome Measures

Incidence rate of SSI, Risk factors for SSI after TES, Safety of iodine-supported spinal instrumenst.

Methods

Risk factors for SSI were analyzed using logistic regression. In recent 69 patients with iodine-supported spinal instruments, the thyroid hormone levels in the blood were examined to confirm if iodine from the implant influenced thyroid function. Postoperative radiological evaluations were performed regularly.

Results

The rate of SSI was 6.4% (8/125 patients). By multivariate logistic regression, combined anterior and posterior approach and non-use of iodine-supported spinal instruments were associated with an increased risk of SSI. The rate of SSI without iodine-supported spinal instruments was 12.5%, whereas the rate with iodine-supported spinal instruments was 1.4%. This difference was statistically significant. There were no detected abnormalities of thyroid gland function with the use of iodine-supported instruments. Among the 69 patients with iodine-supported spinal instruments, 2 patients required additional surgery due to instrument

failure. However, there were no obvious involvements with the use of iodine-supported spinal instruments.

Conclusions

This study identified combined anterior and posterior approach, and non-use of iodine-supported spinal instruments to be independent risk factors for SSI after TES. Iodine-supported spinal instrument was extremely effective for prevention of SSI in patients with compromised status, and it had no detection of cytotoxic or adverse effects on the patients.

Introduction

We have performed total en bloc spondylectomy (TES) for vertebral tumor to avoid recurrence and to control spinal paralysis with good clinical outcome [1-3]. TES is a large invasive surgical procedure and is technically demanding; thus, it has potential risks of perioperative systemic complications. In addition, patients with vertebral tumor might have poor nutritional status and are prone to immunosuppression from the effect of the disease or treatments. Patients treated by TES are, therefore, likely to surgical site infection (SSI) as one of the serious complications, and SSI may compromise the quality of treatment outcome. Jansson *et al* [4] reported that the rate of complications was 56 (20%) of 282 cases with neurological deficit due to spinal metastases. Of the 56 cases, wound infections were seen in 34 (11.3%). Demura *et al* [5] reported that the incidence of SSI was 7 (31.8%) of 22 cases with prior irradiation in spinal metastases. However, the incidence of SSI significantly decreased to 4.5% (1/22 cases) by administering prostaglandin E1 (PGE1) in cases treated with prior irradiation. Hence, we have used PGE1 to prevent SSI in all patients treated by TES from April 2006.

Recently, we developed a new procedure for anodization of iodine-containing surfaces that could be directly supported to existing titanium implants. In a basic study using Japanese white rabbits, the results indicate that iodine-supported titanium has antibacterial activity, biocompatibility, and no cytotoxicity [6]. Based on the above facts, we have performed clinical trials in spinal operation using iodine-supported spinal instruments since November 2008. Therefore, the objectives of this study are to identify independent risk factors for SSI after TES and to evaluate the positive effect of iodine-supported spinal instruments in the prevention of SSI after TES.

Materials and Methods

Patients

One hundred twenty-five patients who underwent TES for vertebral tumor between April 2006 and June 2013 were evaluated. There were 63 males and 62 females, with a median age of 53.8 years (range, 16-77 years). Of the 125 patients, 18 patients had primary vertebral tumors and 107 with metastatic tumors. The histology of primary vertebral tumors included giant cell tumor in 9 patients, symptomatic hemangioma in 2, and others in 7 patients. The histology of metastatic vertebral tumors was comprised of kidney cancer in 29 patients, breast cancer in 15, thyroid cancer in 13, lung cancer in 9, leiomyosarcoma in 5, chondrosarcoma in 3, bladder cancer in 2, colon cancer in 2, liver cancer in 2, rectal cancer in 2, chordoma in 2, liposarcoma in 2, osteosarcoma in 2, unknown in 4, and others in 15 patients. In addition, 69 patients were treated with iodine-supported spinal instruments, whereas these were not used in 56 patients. Table 1 compares the characteristics of patients with and without iodine-supported spinal instruments.

Outcome measure

In this study, we evaluated the incidence of SSI and its association with the following 15 parameters: age (< 60 or ≥ 60 years), gender, body mass index (< 25 or ≥ 25 kg/m^2), smoking status, diabetes, nutrition (albumin <3.5 or ≥ 3.5 g/dL), prior irradiation, preoperative chemotherapy (within 3 months), tumor histology (primary or metastasis), previous surgery at surgical site, operation time (< 600 or ≥ 600 minutes), intraoperative blood loss (< 1000 or ≥ 1000 ml), surgical approach (posterior only or combined anterior and posterior), number of resected vertebrae (< 2 or ≥ 2), and with or without iodine-supported spinal instruments.

In recent 69 patients with iodine-supported spinal instruments, thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4) were examined to confirm if iodine from the implant influenced thyroid function. Blood samplings were conducted before surgery and at 1 month after surgery. Postoperative radiological evaluations were performed regularly; wherein, loosening and failure of the instruments were checked. In these patients, the mean follow-up period was 14.0 months (range, 2-37 months). This study was approved by the ethics committee of Kanazawa University. Written informed consent was obtained from 69 patients with iodine-supported spinal instruments.

Statistical Analysis

Univariate methods were used to detect differences between the incidence of SSI and risk factors. Contingency tables were used to assess association using Fisher exact tests. Statistical significance was set at a *P* value of less than 0.05. For multivariate analysis, multivariable stepwise logistic regression was used to identify independent risk factors for SSI. The variables with univariate *P* values of less than 0.2 were considered as candidates for multiple logistic regression. SPSS statistical software version 19 (SPSS, Inc., Chicago, Illinois) was used to perform the statistical analysis.

Results

Incidence of SSI

During the period of this study, the incidence of SSI was 6.4% (8/125 patients). Among the 8 patients, 1 was involved with iodine-supported spinal instruments while the rest of the 7 patients were not. Microorganisms isolated from the SSI were Methicillin-resistant *Staphylococcus aureus* in 4 patients, coagulase-negative *Staphylococcus* in 2, *Enterococcus faecalis* in 1, and *Escherichia coli* in 1 patient (Table 2). All patients were complicated by SSI within 1 month and classified as having deep SSI, and 4 of the 7 patients without iodine-supported spinal instruments underwent revision surgery because the antibiotics were not effective. On the other hand, antibiotics worked on the sole infected patient with iodine-supported spinal instruments. In addition, no patient died within 3 months, and the survival rate after TES was 91.2% at 1 year in this study.

Risk factors for SSI

The results of the univariate analysis of risk factors are shown in Tables 3 and 4. Operation time (≥ 600 minutes), surgical approach (combined anterior and posterior approach), and spinal instruments (without iodine-supported spinal instruments) were significant risk factors for SSI after TES. In this study, both univariate analysis and multivariate analysis were used to evaluate potential risk factors. Stepwise regression analysis included the 3 significant factors ($P < 0.05$) and 3 factors that were relatively large, with P values of less than 0.2 by univariate analysis. These 6 factors were age, tumor histology, previous surgery at surgical site, operation time, surgical approach, and spinal instruments. Only surgical approach was the significant independent risk factor by multivariate logistic regression. Combined anterior and posterior approach was significantly associated with an increased risk of SSI, with an adjusted odds ratio (OR) of 11.6 (95% confidence interval [CI], 2.21 - 61.26). Among the 5 factors with the exception of surgical approach, the multivariate analysis results demonstrated that spinal instrument was the significant risk factor for SSI. The use of iodine-supported spinal instruments was significantly associated with a decreased risk of SSI, with an adjusted OR of 0.1 (95% CI, 0.01 - 0.86) (Table 5).

Safety of Iodine-supported Spinal Instruments

The TSH levels (μIU/ml), FT3 levels (pg/ml) and FT4 levels (ng/dl) were within the normal range. (Figure 1). There were no detected abnormalities of thyroid gland function with the use of iodine-supported instruments. None of the implants loosened during the follow-up period. However, among the 69 patients with iodine-supported spinal instruments, 2 patients (2.9%) required additional surgery due to instrument failure. One patient required revision surgery due to breakage of instruments caused by subsidence of cage at 12 months after the initial surgery. Another patient developed instrument failure due to a new metastatic tumor of the adjacent vertebra at 21 months after the initial surgery, and revision TES was subsequently performed. On the other hand, in the other 56 patients without iodine-supported spinal instrument, 4 patients (7.1%) required additional surgery due to instrument failure.

Discussion

SSI associated with instruments remains a serious and common complication in spinal surgery. For the patients who undergo a major surgery, such as TES, SSI is a more serious complication [7, 8]. Thus, it is very important that the risk factors for SSI are known in order to prevent it.

Several risk factors for SSI in spinal metastasis have been identified. Xu *et al* [9] reported that wound infection occurred in 17 (18.7%) of 91 patients with metastatic spinal tumors who underwent thoracic vertebrectomy via anterior, posterior, or combined approaches. In their study, the posterior approach was associated with the highest incidence of wound infection compared with anterior and combined approaches. Sundaresan *et al* [10] reported that wound breakdown and infection occurred in 11 (14%) of 80 cases with spinal metastases. Major risk factors for the surgery of spinal metastases were age over 65 years, paraparesis, and prior use of radiation, chemotherapy, or both. In our previous study (Demura *et al* [5]), prior irradiation was the significant independent risk factor by multivariate logistic regression. In the current study, however, prior irradiation was not a significant risk factor. Among the 15 risk factors for SSI, operation time over 10 hours, combined anterior and posterior approach, and non-use of iodine-supported spinal instruments were associated with a high incidence of SSI by univariate analysis in this study. By multivariate logistic regression, combined anterior and posterior approach and non-use of iodine-supported spinal instruments were associated with an increased risk of SSI.

Few reports have been published regarding the difference in infection rate by surgical approaches in patients with spinal metastases. Xu [9] and Quan [11] and their colleagues reported that the posterior approach was associated with the highest incidence of SSI compared with other approaches. Conversely, the combined anterior and posterior approach was significantly associated with an increased risk of SSI in this study. Potential disadvantages of the combined anterior and posterior approach are the need for patient repositioning and possibly a staged procedure, increased operative time, and extent of surgical trauma. In addition, more extensive invasion is needed in patients with history of previous surgery. Thus, we think that the rate of SSI is high in patients with combined anterior and posterior approach. On the other hand, there are several studies that describe the benefit of combined anterior and posterior approach. Roy-Camille *et al* [12] have suggested that a 2-stage operation is required at the lumbar level because both the psoas and iliac muscles have insertions on the vertebral body, as well as the vascular lumbar pedicles, which makes the posterior single approach impossible. Kawahara *et al* [13] reported that complete en bloc excision of the spinal tumor at L4 or L5 (while preserving the lumbar nerves) could be safely achieved through gentle dissection of the lumbar nerve roots, surrounding musculatures, and major vessels in a combined posterior-anterior approach. Therefore, it is necessary to select the surgical approaches based on risk-benefit assessment.

In case of spinal metastases, the rate of SSI is reported from 6.8% to 20% [4, 5, 9, 10, 14]. Similarly, the rate of SSI without iodine-supported spinal instruments was 12.5% (7/56 cases) in this study. On the other hand, the use of iodine-supported spinal instruments revealed a lower rate at 1.4% (1/69 cases). Moreover, it is notable that the patient with SSI even with the use of iodine-supported spinal instruments recovered without removal of the instruments. It is usually difficult to cure infections without removing the instruments if an instrument-associated infection arises. Our results suggest that iodine-supported spinal instruments can be very effective in the prevention of SSI after TES. The antibacterial spectrum of iodine is very broad. The antimicrobial effect acts not only on general bacteria but also on viruses, tubercle bacilli, and even fungi. In addition, iodine does not cause drug resistance as induced by the administration of antibiotics [15]. By application of these advantages, the results of this study acquired good clinical outcome.

In order to reduce the incidence of implant-associated infections, several biomaterial surface treatments have been proposed [16-18]. There have also been reports on antibacterial alloy implants [19]. In particular, silver has attracted the interest of many investigators because of its good antimicrobial action and low toxicity, although some toxicity against human cells have been observed [20]. In our opinion, therefore, safety of silver-coated implants is unestablished. On the other hand, iodine is a trace metal and an essential component of the thyroid hormone. If iodine is released from the instrument, it is biologically safe because it can be excreted by the kidneys. In this study, the TSH, FT3, and FT4 levels were within the normal range during the study period. Abnormalities of thyroid gland function were not detected, as well.

Mechanical strength is another factor necessary for the spinal instruments. There is no problem concerning the mechanical strength of iodine-supported spinal instruments because this is simply anodized titanium, and titanium is widely used for implants [6]. In this study, among the 69 patients with iodine-supported spinal instruments, 2 patients required additional surgery due to instrument failure. However, there was no obvious relationships between these events and the use of iodine-supported spinal instruments.

The current study has several limitations, including the retrospective design, small sample size, and diversity of patient background. Therefore, a prospective randomized clinical trial on a large scale is necessary to demonstrate the statistical significance of the infection rate. Although the small patient size limits the significance of the current study, the positive effect of iodine-supported spinal instruments to prevent of SSI after TES is encouraging and warrants merits.

In conclusion, combined anterior and posterior approach and non-use of iodine-supported spinal instruments were associated with an increased risk of SSI after TES. Iodine-supported spinal instruments were effective for prevention of SSI in patients with compromised status. Moreover, this clinical trial of iodine-supported spinal instruments was performed with no detection of cytotoxic or adverse effects on the patients.

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Figure Legend

Figure 1. Thyroid hormone levels: TSH levels (lIU/ml), FT3 levels (pg/ml), and FT4 levels (ng/dl) were within the normal range.

Table 1. Comparison of Patient Characteristics with and without Iodine-supported Instruments

	Iodine-supported instruments	
	W/ (69)	W/O (56)
Age	55.1 (16-73)	52.1 (19-77)
Gender (male/female)	38/31	25/31
Diabetes	10 (14.5%)	6 (10.7%)
Irradiation	23 (33.3%)	12 (21.4%)
Chemotherapy	33 (47.8%)	12 (21.4%)
Tumor histology (Primary/Metastasis)	3/66	15/41
Operation time	480±137	594±155
Intraoperative blood loss	672±831	1140±842
Surgical approach (Posterior only/Combined anterior and posterior)	58/11	37/19

Table 2. Types of Organisms Cultured From Postoperative Infections

Organism	No. of cases
W/ iodine-supported instruments	
Methicillin-resistant *Staphylococcus aureus*	1
W/O iodine-supported instruments	
Methicillin-resistant *Staphylococcus aureus*	3
coagulase-negative *Staphylococcus*	2
Enterococcus faecalis	1
Escherichia coli	1
Incidence of SSI	8/125 (6.4%)

Table 3. Univariate Analysis of Patient Characteristics

Factor	No. (%) with SSI	95% CI	*P*
Age			0.116
< 60	7/77 (9.1%)		
≥ 60	1/48 (2.1%)	0.03-1.77	
Gender			0.632
Male	4/63 (6.3%)	0.24-4.12	
Female	4/62 (6.5%)		
BMI			0.355
< 25	5/92 (5.4%)		
≥ 25	3/33 (9.1%)	0.39-7.72	
Smoking			0.336
Yes	4/46 (8.7%)	0.42-7.41	
No	4/79 (5.1%)		
Diabetes			0.323
Yes	0/16 (0%)		
No	8/109 (7.3%)		
Nutrition			0.324
Alb < 3.5	2/18 (11.1%)		
Alb ≥ 3.5	6/107 (5.6%)	0.09-2.56	
Irradiation			0.397
Yes	3/35 (8.6%)	0.36-7.06	
No	5/90 (5.6%)		
Chemotherapy			0.601
Yes	3/45 (6.7%)	0.24-4.71	
No	5/80 (6.3%)		
Tumor histology			0.089
Primary	3/18 (16.7%)		
Metastasis	5/107 (4.7%)	0.05-1.13	
Previous surgery			0.195
Yes	2/13 (15.4%)	0.58-17.88	
No	6/112 (5.4%)		

The *P* values were calculated with Fisher exact test.

Table 4. Univariate Analysis of Surgery-Related Characteristics

Factor	No. (%) with SSI	95% CI	*P*
Operation time			0.03*
< 600	3/92 (3.3%)		
≥ 600	5/33 (15.1%)	1.19-23.58	
Intraoperative blood loss			0.666
< 1000	6/93 (6.5%)		
≥ 1000	2/32 (6.3%)	0.19-5.05	
Surgical approach			0.002*
Posterior only	2/95 (2.1%)		
Combined anterior and posterior	6/30 (20.0%)	2.21-61.26	
Number of resected vertebrae			0.596
< 2	4/60 (6.7%)		
≥ 2	4/65 (6.2%)	0.22-3.84	
Spinal instruments			0.015*
W/ iodine-supported instruments	1/69 (1.4%)	0.01-0.86	
W/O iodine-supported instruments	7/56 (12.5%)		

The *P* values were calculated with Fisher exact test. *Significant values (< 0.05)

Table 5. Multivariate Analysis Results

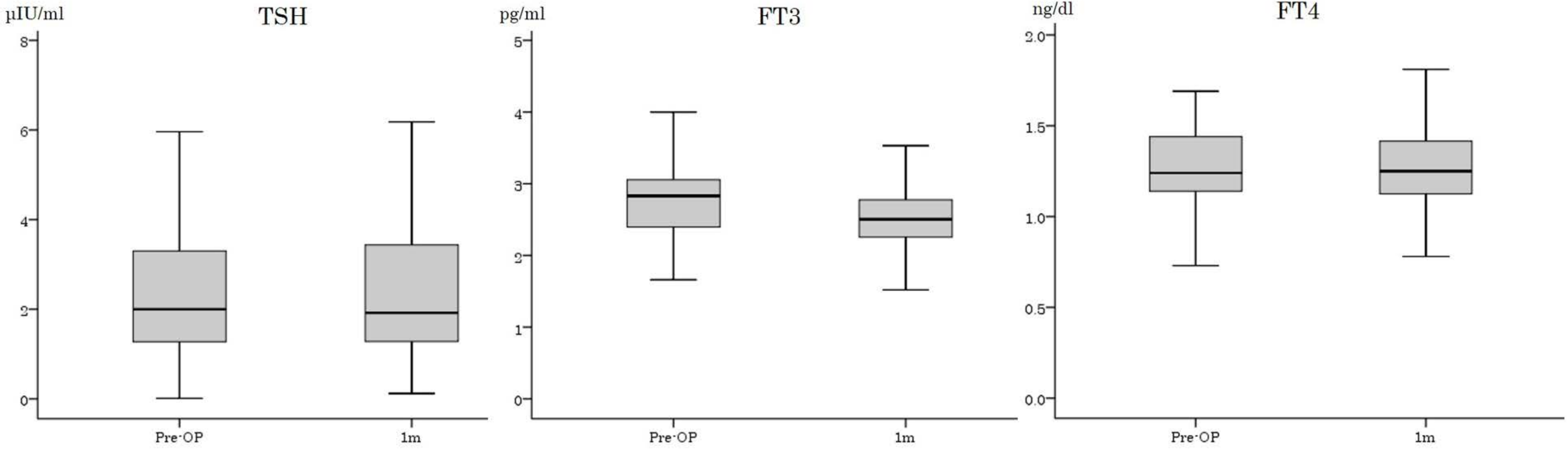
Factor	Adjusted OR	95% CI	*P*
Surgical approach	11.6	2.21-61.26	0.004*

Of the 6 factors, only surgical approach was the significant independent risk factor by multivariate logistic regression.

Factor	Adjusted OR	95% CI	*P*
Spinal instruments	0.1	0.01-0.86	0.036*

Among the 5 factors with the exception of surgical approach, the multivariate analysis results demonstrated that spinal instrument was the significant risk factor for SSI.

*Significant values (< 0.05)



μIU/ml
TSH
8
6
4
2
0
Pre-OP
1m
pg/ml
FT3
5
4
3
2
1
0
Pre-OP
1m
ng/dl
FT4
2.0
1.5
1.0
0.5
0.0
Pre-OP
1m