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ORIGINAL ARTICLE

# Factors predicting incisional surgical site infection in patients undergoing open radical cystectomy for bladder cancer

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**Abstract**
*Background* The risk factors of incisional surgical site infection (iSSI) after open radical cystectomy (ORC) have not been fully investigated. The aim of the present study is to examine factors correlated with iSSI development after ORC with intestinal urinary diversion.
*Methods* A total of 178 patients who had undergone ORC with intestinal urinary diversion between 2003 and 2012 at our institution were included in this retrospective study. Correlations between different perioperative factors and iSSI development were determined using univariate and multivariate logistic regression analyses.
*Results* iSSI was observed in 53 patients (29.8 %). In the univariate analysis, age, diabetes mellitus, thickness of subcutaneous fat (TSF), and allogeneic transfusion were significant predictors of iSSI development. Although subcutaneous closed-suction drainage (SCSD) was not a significant factor in univariate analysis, SCSD, age, and TSF were all finally identified as independent predictors of iSSI development ($P = 0.020$, $P < 0.001$, and $P = 0.022$, respectively). Further analyses demonstrated that SCSD was frequently used in patients with relatively thick subcutaneous fat tissue and that SCSD significantly decreased iSSI development in these patients.
*Conclusions* Advanced patient age, thick subcutaneous fat tissue, and the absence of SCSD were significantly associated with iSSI development in bladder cancer patients who underwent ORC with intestinal urinary diversion. SCSD may be a useful procedure for iSSI prevention, especially in patients with relatively thick subcutaneous fat tissue.

**Keywords** Bladder cancer · Radical cystectomy · Surgical site infection · Subcutaneous closed-suction drainage

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## Introduction

Open radical cystectomy (open RC; ORC) with urinary diversion is a standard treatment for invasive bladder cancer [1]. However, the complication rates of ORC are not particularly low, with reported incidence rates in previous studies ranging from 28 to 60 % [2–4]. ORC with intestinal urinary diversion is classified as a contaminated operation according to the Centers for Disease Control and Prevention (CDC) wound classification [5, 6], and in several reports, the incidence of surgical site infection (SSI) according to CDC criteria was relatively high, ranging from 18 to 33 % [7–9]. SSI is among the most common sources of nosocomial morbidity after general surgery. Furthermore, wound infection has been strongly associated with a prolonged length of stay in hospital, decreased health-related quality of life, and increased total medical costs [10, 11]. Thus, SSI prevention during the perioperative period is a major issue.

Several risk factors for SSI such as obesity [measured in terms of body mass index (BMI) and thickness of subcutaneous fat (TSF)], prolonged operation time, and blood loss have been reported in the general surgery field [5, 6]. Additionally, several groups have investigated the efficacy of subcutaneous closed-suction drainage (SCSD) for the prevention of incisional SSI (iSSI) in patients who have undergone various types of surgery [12, 13]. However, only a few studies have focused on iSSI following RC, and a definitive method with which to prevent iSSI after ORC has not yet been fully investigated.

The aim of this study was to investigate the perioperative risk factors for iSSI in bladder cancer patients who underwent ORC with intestinal urinary diversion at our institution.

## Materials and methods

This study was conducted according to the ethical guidelines for clinical studies of the Ministry of Health, Labor and Welfare in Japan and was approved by the ethics committee at our facility. We retrospectively reviewed the medical records of 204 patients with bladder cancer who underwent RC at our institution between April 2003 and June 2012. The indications for RC included muscle-invasive tumors and high-grade non-muscle-invasive tumors with no evidence of distant metastasis or bacillus Calmette–Guerin-resistant carcinoma in situ. All patients had undergone transurethral resection of the bladder tumor prior to RC, and no patients had received neoadjuvant chemotherapy. Of the 204 patients, 6 who underwent ureterocutaneous urinary diversion, 3 hemodialysis patients, 1 who underwent abdominal radiation therapy prior to surgery, 12 who underwent robotic-assisted RC, and 4 with insufficient data were excluded. A total of 178 patients who underwent ORC were thus included in the present study.

### Perioperative management

Preoperative urine cultures were routinely obtained from all patients. An oral antibiotic preparation of clindamycin hydrochloride plus polymyxin B sulfate was administered to all patients until November 2005 but was not routinely administered thereafter, and oral antibiotic preparations were completely discontinued in December 2009. All patients underwent preoperative mechanical bowel preparation with sennosides and a polyethylene glycol electrolyte solution on the day before surgery. A regimen of systemic prophylactic antibiotics, including second-generation cephalosporins or sulbactam/ampicillin, was strictly followed in all cases, beginning 30 min before incision. However, for patients with preoperative bacteriuria, antibiotic administration was initiated one day before surgery. The patient's abdominal hair was removed by shaving immediately before surgery if the hair around the incision site would interfere with the operation. Members of the surgical team who had direct contact with the sterile operating field washed their hands and forearms by scrubbing using povidone–iodine or chlorhexidine gluconate immediately before donning sterile gowns and gloves. Povidone–iodine was used for abdominal skin preparation before ORC.

ORC was performed through a periumbilical midline incision in the traditional manner [14]. The peritoneum and fascia were sutured with interrupted 1–0 polyfilament or monofilament absorption string. After the subcutaneous space was irrigated with saline, contraction of the dead space by a subcutaneous suture was performed with interrupted 3–0 polyfilament, and the skin was closed with staples. The wound was protected with a sterile dressing for 48 h. Staples were typically removed on postoperative day 6. Prophylactic antibiotic infusion was continued postoperatively for 3 days, in accordance with the Japanese guidelines for the prevention of perioperative infections [5]. Oral antibiotics were not routinely administered.

In some cases, we performed SCSD by inserting a 10-Fr Blake silicone drain (Ethicon, Somerville, NJ, USA) with a 150-mL J-VAC suction reservoir (Ethicon, Somerville, NJ, USA) into the subcutaneous space. We used SCSD mainly in obese patients (BMI $\geq$25 kg/m$^2$), after considering the thickness of the subcutaneous fat. The SCSD was inserted for at least 3 days and was removed when the drainage measured $<$10 mL over a 24-h period.

### Data analyses

iSSI was defined according to the CDC criteria [6]. In the present study, superficial and deep iSSI were combined into the same category of iSSI diagnosis on the basis of a previous report [15]. The analyzed variables included age, gender, BMI, TSF, comorbidity [diabetes mellitus (DM)], smoking history, presence of bacteriuria, type of bowel preparation, type of urinary diversion, preoperative hematocrit level, operation time, transfusion (allogeneic and autologous transfusion), intraoperative blood loss (IBL), SCSD, and year during which surgery took place. Cases were classified into 3 categories considering the above-mentioned changes in perioperative management: April 2003–November 2005 (period 1), December 2005–December 2009 (period 2), and January 2010–June 2012 (period 3). TSF was preoperatively evaluated using computed tomography or magnetic resonance imaging at a location just below the umbilicus, as previously reported [16].

IBL was calculated using the formula advocated by Gross in 1983 [17], with minor modifications. Briefly, the following formula was used to calculate the IBL: $\mathrm{IBL} = \mathrm{IBTV} + \mathrm{EBV} \times \mathrm{Hi\text{-}Hf/Hav}$, in which IBTV refers to the intraoperative blood transfusion volume, EBV is the patient's estimated blood volume, Hi is the initial hematocrit at the beginning of surgery, Hf is the final hematocrit at the end of surgery, and Hav is the average of the patient's initial and final hematocrit.

The correlations between variables and iSSI were analyzed using univariate analysis with the Pearson chi-squared test or Fisher's exact test. Multivariate logistic regression analysis with a forward stepwise selection procedure was performed to identify independent predictors of iSSI. A potentially significant relationship with iSSI development (univariate analysis $P < 0.25$) was used as the criterion for including a variable in the multivariate stepwise modeling procedure [18]. A $P$ value of <0.05 was considered statistically significant. All statistical analyses were performed using STATA (ver. 11.0; StataCorp, College Station, TX, USA).

## Results

Patient characteristics are shown in Table 1. iSSI was observed in 53 patients (29.8 %). According to the Clavien Classification Grade, iSSI was graded as I in 23 patients, II in 14, IIIa in 6, and IIIb in 3. The univariate analyses revealed that age, DM, TSF, and allogeneic transfusion were significantly associated with iSSI development (Table 2). The date of surgery was not associated with iSSI development ($P = 0.319$). Although SCSD was not significant in univariate analysis ($P = 0.197$), SCSD, age, and TSF were ultimately identified as independent predictors of iSSI development in multivariate analysis ($P = 0.020$, $P < 0.001$, and $P = 0.022$, respectively; Table 3).

We further performed multivariate analyses of various combinations of SCSD and other factors in order to identify factors that affected the association between SCSD and iSSI development. Consequently, SCSD was found to be a significant predictor of iSSI only when adjusted for TSF (a $P$ value of 0.197 in multivariate logistic regression analysis changed to 0.028 after adjusting for TSF). TSF differed significantly between patients with and without SCSD (21 vs. 16.5 mm; $P = 0.0041$). On dichotomization at the median TSF value of 18 mm, SCSD was significantly associated with a decrease in iSSI incidence in patients with a TSF ≥18 mm ($P = 0.033$; Table 4).

## Discussion

SSI is the most common type of nosocomial infection in patients who undergo surgical procedures. The risk factors for SSI can be classified as patient- and procedure-related factors. Patient-related factors include age, obesity, DM, and cigarette smoking, whereas procedure-related factors include the type of surgery, blood transfusion, operation time, and IBL. In the present study, univariate analysis indicated that age, TSF, DM, and allogeneic transfusion were significantly associated with iSSI development. The first 3 factors are patient related and the last is procedure related. These risk factors are consistent with those reported in previous studies of patients undergoing gastrointestinal or gynecological surgery [12, 19–22].

Furthermore, multivariate analysis demonstrated that age, TSF, and SCSD were independent predictors of iSSI. Obesity, which was expressed as TSF in the present study, has been previously reported as a risk factor for iSSI

**Table 1** Patient characteristics of 178 bladder cancer patients who underwent radical cystectomy with intestinal urinary diversion at our institution

| Characteristics | |
|---|---|
| Age, years; median (IQR) | 71 (62–76) |
| Gender, *n* (%) | |
| Male | 143 (80.3) |
| Female | 35 (19.7) |
| BMI, kg/m$^2$; median (IQR) | 22.7 (20.8–25.3) |
| TSF, mm; median (IQR) | 18 (13–22) |
| DM, *n* (%) | |
| No | 153 (86.0) |
| Yes | 25 (14.0) |
| Smoking history, *n* (%) | |
| No | 88 (49.4) |
| Yes | 90 (50.6) |
| Preoperative bacteriuria, *n* (%) | |
| No | 123 (69.1) |
| Yes | 55 (30.9) |
| Bowel preparation, *n* (%) | |
| Chemo + mechanical | 90 (50.6) |
| Mechanical only | 88 (49.4) |
| Preoperative hematocrit level, mg/dl; median (IQR) | 34.3 (31.2–36.9) |
| Operative time, min; median (IQR) | 397 (338–458) |
| Intraoperative transfusion, *n* (%) | |
| Allogeneic transfusion | 97 (54.5) |
| Allogeneic transfusion + autologous transfusion | 157 (88.2) |
| IBL, ml; median (IQR) | 1066 (738–1611) |
| Type of urinary diversion, *n* (%) | |
| Ileal conduit | 109 (61.2) |
| Ileal neobladder | 69 (38.8) |
| SCSD, *n* (%) | |
| No | 144 (80.9) |
| Yes | 34 (19.1) |
| Surgery year, *n* (%) | |
| April 2003–November 2005 (period 1) | 61 (34.3) |
| December 2005–December 2009 (period 2) | 90 (50.6) |
| January 2010–June 2012 (period 3) | 27 (15.1) |

*IQR* interquartile range, *BMI* body mass index, *TSF* thickness of subcutaneous fat, *DM* diabetes mellitus, *IBL* intraoperative blood loss, *SCSD* subcutaneous closed-suction drainage

**Table 2** Univariate analyses of perioperative parameters for the prediction of incisional surgical site infection development in 178 patients who underwent radical cystectomy

| Parameter | *P* value | AUC |
|---|---|---|
| Age (continuous) | 0.033 | 0.594 |
| Gender (male vs. female) | 0.516 | 0.521 |
| BMI (continuous) | 0.091 | 0.573 |
| TSF (continuous) | <0.001 | 0.72 |
| DM (no vs. yes) | 0.036 | 0.561 |
| Smoking history (no vs. yes) | 0.794 | 0.511 |
| Preoperative bacteriuria (no vs. yes) | 0.825 | 0.508 |
| Bowel preparation (chemomechanical vs. mechanical) | 0.694 | 0.516 |
| Preoperative hematocrit level (continuous) | 0.734 | 0.522 |
| Operative time (continuous) | 0.224 | 0.552 |
| Intraoperative transfusion | | |
| Allogeneic transfusion (no vs. yes) | 0.02 | 0.596 |
| Allogeneic transfusion + autologous transfusion (no vs. yes) | 0.259 | 0.53 |
| Intraoperative blood loss (continuous) | 0.081 | 0.591 |
| Type of urinary diversion (ileal conduit vs. neobladder) | 0.234 | 0.548 |
| SCSD (without vs. with) | 0.197 | 0.542 |
| Surgery year | 0.319 | 0.54 |

*AUC* area under the curve, *BMI* body mass index, *TSF* thickness of subcutaneous fat, *DM* diabetes mellitus, *SCSD* subcutaneous closed-suction drainage

**Table 3** Multivariate logistic regression analyses with a stepwise selection procedure of perioperative parameters for the prediction of incisional surgical site infection following radical cystectomy

| Predictive factor | Coefficient | Odds ratio | 95 % CI | *P* value |
|---|---|---|---|---|
| Age (continuous) | 0.05 | 1.05 | 1.01–1.10 | 0.022 |
| TSF (continuous) | 0.14 | 1.15 | 1.08–1.22 | <0.001 |
| SCSD (without vs. with) | −1.23 | 0.29 | 0.10–0.82 | 0.020 |

*CI* confidence interval, *TSF* thickness of subcutaneous fat, *SCSD* subcutaneous closed-suction drainage

**Table 4** The incidence of incisional surgical site infection after radical cystectomy depends on the thickness of subcutaneous fat

| TSF value | With SCSD | Without SCSD | *P* value[a] |
|---|---|---|---|
| TSF $<18$ mm ($n = 87$)[b] | 10 % (1/10) | 17 % (13/77) | 0.495 |
| TSF $\geq 18$ mm ($n = 91$) | 25 % (6/24) | 49 % (33/67) | 0.033 |

*TSF* thickness of subcutaneous fat, *SCSD* subcutaneous closed-suction drainage

[a] Fisher's exact test

[b] Median value of thickness of subcutaneous fat

because of its association with decreased topical blood flow, decreased oxygen tension, and the ease of formation of dead space caused by aseptic liquefaction [23, 24]. Older patients have been reported as having impaired host immunity, which leads to delayed epithelialization and results in increased iSSI development [20, 25]. In contrast, it has been suggested that SCSD prevents iSSI by removing hematomas and the exudate containing wound-healing inhibitory factors, decreasing bacterial colonization, and improving blood flow and tissue oxygenation [26, 27].

To the best of our knowledge, this is the first study to show that age, TSF, and SCSD are significant predictors of iSSI in patients who undergo ORC with intestinal urinary diversion. Additionally, no previous published studies have evaluated the efficacy of SCSD for iSSI prevention in patients who undergo ORC. Although several groups have investigated the usefulness of SCSD for iSSI prevention in abdominal surgery, the efficacy of this treatment remains controversial [12, 13, 19, 28, 29]. Possible explanations for this discrepancy include differences in surgical skill, the types and cleanliness of surgical procedures, SCSD management, and patient selection bias. In the present study, SCSD was not a significant predictor of iSSI development in univariate analysis; however, SCSD was found to be a significant predictor of iSSI development in multivariate analysis. These results suggest that there might be risk factor-related differences between patients with SCSD and those without SCSD. Finally, we determined that TSF was a confounding factor in evaluating the efficacy of SCSD. This must have been due to the existing patient selection bias in our cohort, since in the present study, SCSD was mainly performed in obese patients (BMI $\geq$25 kg/m$^2$), as determined by the thickness of the subcutaneous fat.

This study provides important insights into the risks of iSSI in bladder cancer patients undergoing ORC with intestinal urinary diversion; however, it does have some limitations. First, this is a retrospective analysis of data collected from a single institution, and thus, the number of cases available for study is small. Second, because ethnic differences in the amount and distribution of adipose tissues do exist [30], we hope that, in future, the results of the present study can be validated in cohorts of different races and countries. Third, although we demonstrated that SCSD might be more effective in patients with relatively thick subcutaneous fat tissue, we could not identify specific patients who benefitted most from this intervention in the present study. Further studies to develop a risk-stratification model might help with the selection of appropriate candidates for SCSD and reduce unnecessary medical expenditure. Despite the limitations, the risk factors identified in this study could help to identify patients at a high risk of iSSI development and could be useful in counseling patients before surgery. We believe that our results could help prevent iSSI development after ORC, thereby potentially shortening the length of hospital stay and reducing excessive medical costs due to iSSI treatment.

## Conclusions

The present study showed that advanced patient age, thick subcutaneous fat tissue, and the absence of SCSD are independent predictors of iSSI after ORC with intestinal urinary diversion in patients with bladder cancer. SCSD would be a useful surgical intervention with which to reduce the iSSI incidence, especially in patients with thick subcutaneous fat tissue. However, a prospective randomized study is required to verify these results.

**Conflict of interest** The authors declare that they have no conflict of interest.

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