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Risk Factors for Wound Infection After Surgery for Colorectal Cancer: A Matched Case – Control Study

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1. Introduction

Elective surgery for colorectal cancer involves a semi-contaminated operation, with a 3% to 26% incidence of postoperative wound infection (1). Risk factors for postoperative wound infection include high body-mass index (BMI) (2, diabetes mellitus(3), body-weight loss(4), advanced age(5), smoking(6), blood transfusion(7), and high intraoperative blood loss (8). The development of wound infections can cause considerable discomfort and stress, as well as prolong the hospital stay, substantially increasing healthcare costs. Measures to prevent wound infections have been refined by adjusting the duration of antibiotic treatment and improving techniques for preoperative bowel preparation and drain placement. We performed a matched case-control study to clarify risk factors for perioperative wound infection in patients who underwent standard surgery for colorectal cancer, performed by the same operator at the same hospital. All patients received similar levels of perioperative care.

2. Subjects and methods

From January 2004 through December 2006, a total of 264 patients underwent surgery in our hospital for primary colorectal cancer with a solitary lesion. The same surgeon (T.N.) served as the operator or assistant. Preoperatively, all patients received mechanical bowel preparation. Two tablets of sennoside were given orally 2 days before surgery, and 1 packet of magnesium citrate and 1 bottle of sodium picosulfate were given the day before surgery. For wound closure, the peritoneum and fascia were sutured together with interrupted, polydioxanone absorbable sutures (0-PDS II™, Johnson and Johnson Co. Ltd). The same suture material was used to close the abdomen in patients who underwent laparoscopic surgery and those who underwent open surgery.
In patients who underwent high-pressure irrigation of their wounds, the muscle layer was sutured, and the subcutaneous tissue was washed with warm physiological saline solution applied under high pressure, using a 23-gauge ophthalmic washing catheter attached to a 20-mL syringe. The tip of the needle was positioned about 10 cm from the wound (Fig. 1). The applied volume of physiological saline solution was 400 mL for open surgery, and 200

mL for laparoscopic surgery. After irrigation, the skin was closed with polydioxanone absorbable sutures (4-0 PDS II™, Johnson and Johnson Co., Ltd.).

Fig. 1. Before closure of the abdomen during surgery, high-pressure irrigation of the subcutaneous tissue after muscle layer suturing

In patients who did not undergo high-pressure irrigation (non-high-pressure irrigation group), the peritoneum and fascia were sutured together with interrupted, polydioxanone absorbable sutures (0-PDS II™, Johnson and Johnson Co., Ltd.) Then, In the non-high-pressure lavage group, no syringe was used. The subcutaneous tissue was just washed with 500 mL of warm physiological saline solution.

The subcutaneous adipose tissue was sutured with polyglactin 910 absorbable sutures (3-0 Vicryl™, Johnson and Johnson Co., Ltd.), and the skin was closed with a skin stapler.

During the 19 months from January 2004 through July 2005, a total of 145 patients underwent surgery without high-pressure irrigation. During 16 months from August 2005 through December 2006, a total of 119 patients underwent surgery with high-pressure irrigation. The two groups were matched for the following 6 variables: sex, age (± 5 years), tumor location (right side of colon, transverse colon, left side of colon, rectum), surgical procedure (laparoscopic surgery, open surgery), tumor-node-metastasis (TNM) classification, and BMI (± 1). We studied a total of 100 patients: 50 in the high-pressure irrigation group and 50 in the non-high-pressure irrigation group (Table 1).

As for the demographic characteristics of the patients, the American Society of Anesthesiologists' physical status classification was class I in 37 patients (74%), class II in 10 (20%), and class III in 3 (6%) in the high-pressure irrigation group and class I in 37 patients (4%), class II in 11 (22%), and class III in 2 (4%) in the non-high-pressure irrigation group. The difference between the groups was not significant ($p = 0.884$). No patient had a preoperative hemoglobin level of ≤8.0 g/dL. Four patients received blood transfusions during surgery.

	High-pressur irrigation group (n=50)	Non High-high irrigation group (n=50)
No.of patients	50	50
Sex (male : femail)	36 : 14	36 : 14
Age(years)	66(42-87)	67(40-90)
Tumor location		
Cecum , Ascending colon	13	13
Transverse colon	6	6
Descending colon , Sigmoid colon	15	15
Rectum	16	16
Tumor diameter(cm)	4.1(0.8-8.0)	3.5(1.0-7.5)
Surgical procedure(laparoscopy : open surgery)	37 : 13	37 : 13
pTNM stage		
0	3	3
Ⅰ (pT1N0)	6	6
Ⅰ (pT2N0)	4	4
Ⅱ (pT3N0)	20	20
Ⅲ (pT3N1)	13	13
Ⅳ	4	4
Wound infection (presence : absence)	2 : 28	9 : 31
BMI(kg/m^2)	21.9(17.6-28.3)	22.8(16.6-26.8)
Median follow-up period (months) (range)	15(7-30)	30(21-39)

Table 1. Demographic characteristics of the patients

Laparoscopic surgery was performed if tumors invaded the lamina propria (Tis), the submucosa (T1), or the muscularis propria (T2). Open surgery was performed if tumors directly invaded other organs or structures and/or perforated the visceral peritoneum (T4, AI). If tumors invaded through the muscularis propria into the subserosa or into non-peritonealized pericolic or perirectal tissues (T3, A), the surgical procedure was decided in a randomized control trial after obtaining informed consent from the patient. Laparoscopic surgery was not switched to open surgery in any subject.

After skin closure, the wound was applied a polyurethane film dressing for 48 hours in all patients. Subsequently, the wound was uncovered and was not sterilized. To prevent infection during and after surgery, cefmetazole sodium (1 g/time) or flomoxef sodium (1 g/time) was given as a continuous intravenous infusion 1 hour before surgery and at 3-hour intervals thereafter. On the day after surgery, antibiotics were administered only one time.

After the operator confirmed the wound, wound infection was evaluated according to the 1999 Guidelines for the Prevention of Surgical Site Infection (SSI)(9). These guidelines do not require the results of culture studies to assess wound infection. In our study, however, a wound culture was performed if fluid or discharge was exuded from the wound. The median postoperative follow-up period was 15 months (range, 7 to 30) in the high-pressure irrigation group and 30 months (range, 21 to 39) in the non-high-pressure irrigation group. During follow-up, patients visited the outpatient clinic at 2- to 4-week intervals. Follow-up examinations included examination of the surgical wound, administration of adjuvant chemotherapy, and computed tomography (CT) of the chest and abdomen. The preoperative and postoperative status of each patient was retrospectively examined on the basis of medical records.

A total of 10 potential risk factors for wound infection were compared between the groups: the presence or absence of high-pressure irrigation before wound closure, sex, age (<65 years, ≥65 years), BMI (≤25 kg/m^2, >25 kg/m^2), tumor location (colon, rectum), surgical procedure (laparoscopic surgery, open surgery), operation time (<180 minutes, ≥180 minutes), bleeding volume (<100 mL, ≥100 mL), tumor stage (I or II, III or IV), and antibiotic treatment (cefmetazole, flomoxef), (Table 1).

Chi-square tests with Yates' correction and multivariate logistic regression analysis were performed to identify variables with p values of less than 0.1. P values of less than 0.05 were considered to indicate statistical significance. SPSS version 8.0J (SPSS Inc., Chicago, USA) software was used for analysis.

3. Results

Wound infections developed after colorectal cancer surgery in 11 (11%) of the 100 patients. On univariate analysis, wound infection was significantly associated with tumors located in the rectum (p = 0.011), open surgery (p = 0.032), and non-high-pressure irrigation of wounds (Table 2). On multivariate analysis, independent risk factors for wound infection were wound treatment (non-high-pressure irrigation) (p = 0.034; odds ratio, 5.968) and surgical procedure (open surgery) (p = 0.039; odds ratio, 4.266) (Table 3).

	Wound infection(+) (n=11)	Wound infection (-)(n=89)	*p*-value
Sex (male:female)	6 : 5	66 : 23	0.189
Age (years)(≦65 : 65<)	6 : 5	39 : 50	0.710
Tumor location (Colon : Rectum)	3 : 8	60 : 29	0.011
BMI(kg/m2)(<25 : 25≦)	3 : 8	60 : 29	0.837
Surgical procedure (laparoscopy : open surgery)	5 : 6	69 : 20	0.032
Operation time (<180 : 180≦)	5 : 6	29 : 60	0.837
Intraoperative bleeding volume (ml)(<100 : 100≦)	8 : 3	65 : 24	0.983
High-pressure irrigation (presence : absence)	2 : 9	48 : 41	0.021
TNMstage(I-II : III, IV)	7 : 4	59 : 30	0.861
Antibiotics (CMZ : FMOX)	4 : 7	37 : 52	0.739

BMI:Boddy Mass Index,;TNM,Tumor node metastasis;CMZ:cefmetazole sodium, FMOX:flomoxef sodium

Table 2. Wound infection detected free of wound infection

Wound infection developed in 5 (7%) of the 74 patients who underwent laparoscopic surgery and 6 (23%) of the 26 patients who underwent open surgery. Wound infection occurred in 2 (4%) of the 50 patients in the high-pressure irrigation group and 9 (18%) of the 50 patients in the non-high-pressure irrigation group. The mean duration of the hospital stay after surgery was 8 days (range, 5 to 31) in patients without wound infection, as compared with 15 (range, 7 to 40) in those with wound infection. This difference was significant (p = 0.041). During observation after discharge, there was no flare-up of wound infection, wound dehiscence, or adhesive ileus.

	Odds ratio	95%CI	*p*-valeue
Surgical procedure Open surgery : laparoscopy	4.266 : 1	1.079-16.866	0.039
High-pressure irrigation absence : presence	5.968 : 1	1.150-30.963	0.034

CI:confidence interval

Table 3. Results of multivariate analysis of risk for wound infection

The American Society of Anesthesiologists' Physical Status Classification was class I in 56 patients (76%), class II in 15 (20%), and class III in 3 (4%) in the laparoscopic surgery group and class I in 16 patients (67%), class II in 6 (23%), and class III in 2 (7%) in the open surgery group. The difference between the groups was not significant (p = 0.884).
Pus samples from infected wounds were cultured in 9 of the 11 patients with wound infection (2 in the high-pressure irrigation group and 7 in the non-high-pressure irrigation group). Pus cultures were positive in all patients in both the high-pressure irrigation group and the non-high-pressure irrigation group. The most common pathogen was bacteroides in 6 patients, followed by *Staphylococcus aureus* in 2 and *Pseudomonas aeruginosa* in 1. Pathogens did not differ between the high-pressure irrigation group and the non-high-pressure irrigation group. Strains isolated from the 6 patients with bacteroides infections and the 2 with *Staphylococcus aureus* infections were sensitive to the prophylactically administered antibiotics.

4. Discussion

Our study showed that that non-high-pressure irrigation and open surgery were independent risk factors for postoperative wound infection in patients with colorectal cancer. To minimize potential effects of confounding factors, our study was conducted under consistent conditions, i.e., the same operator performed surgery and perioperative management in the same hospital.
Carlos et al. performed a randomized control trial to evaluate whether syringe pressure irrigation of surgical wounds decreases wound infection after appendectomy (10). Patients were randomly assigned to receive prophylactic antibiotics alone before surgery or prophylactic antibiotics plus syringe pressure irrigation of their wounds. Irrigation was performed by applying 300 mL of physiological saline solution under high pressure with the use of a 20-mL syringe with a 19-gauge intravenous catheter. The tip of the catheter was placed about 2 cm from the wound. Among the 283 patients confirmed to have appendicitis, 95 (33.6%) had complications. Of these 95 patients, wound infection developed in 9 (16.3%) of the 55 patients who received prophylactic antibiotics plus wound irrigation, as compared with 29 (72.5%) of the 40 patients who received prophylactic antibiotics alone (p = 0.0006).

Johnson et al. prospectively studied the incidence of SSI in 715 patients who underwent a cesarean section procedure (11)・The use of subcuticular sutures for skin closure was associated with a significantly higher incidence of SSI than was the use of staples (7.9%, 20/252 vs. 13.0%, 59/459; p = 0.021).

To our knowledge, no previous study has evaluated high-pressure irrigation at the time of wound closure after muscle-layer suture in patients with colorectal cancer. This technique was originally developed in our hospital. A bacterial count of greater than 10^5 bacteria per gram of tissue is considered necessary for the development of wound infection(12). We believe that our method for high-pressure irrigation after muscle-layer suture effectively decreases the bacterial count in subcutaneous tissue.

Our study showed that the incidence of postoperative wound infection was significantly lower after laparoscopic surgery than after open surgery. Some previous studies have reported that the incidence of wound infection after laparoscopic surgery was similar to that after open surgery, whereas others have found that the incidence of wound infection was significantly lower after laparoscopic surgery(13). A meta-analysis performed by Abraham et al. showed that the incidence of postoperative wound infection was significantly lower after laparoscopic surgery (3.9%) than after open surgery (8.9%) ($p<0.005$). Our findings support the results of this meta-analysis(14).

The presence of suture material in a closed wound has been reported to increase the number of bacteria to 10^4 per gram of tissue (15)・ Open surgery requires a longer skin incision and more stitches than laparoscopic surgery, increasing the bacterial count and potentially increasing the risk of wound infection. One study reported that the incidence of wound infection after laparoscopic surgery was 2.7% at the trocar site and 10.8% at the site of colorectal removal (16). In our hospital, no patient has had wound infection at the trocar site, and the incidence of wound infection at the site of colorectal removal was only 4%, which was lower than that reported previously(17). In general, wound infection has been reported to occur at an incidence of about 20% after open surgery, which is consistent with the incidence of 23% in our study.

The relation between surgical wound infection and diabetes mellitus in patients who undergo surgery for colorectal cancer remains unclear. The risk of SSI after cardiac surgery has been reported to be 2 to 3 times higher in patients with diabetes mellitus than in those without diabetes mellitus, even after adjustment for other risk factors (3). The higher risk of SSI may be related to long-term metabolic and microcirculatory disorders induced by diabetes mellitus, perioperative hyperglycemia, and other risk factors associated with diabetes mellitus, such as obesity. Because we strictly control blood levels before and after surgery in our hospital, diabetes mellitus was not a risk factor for wound infection.

As for the relation between BMI and wound infection, Smith et al. reported that the incidence of wound infection increases in parallel to BMI (2)・ In their study, 53% of the patients had a BMI of ≥25 kg/m^2 or higher. In contrast, only 21% of our patients had a BMI of ≥25 kg/m^2. This lower proportion of patients with an increased BMI may have accounted for BMI not being a risk factor for wound infection.

In patients with a BMI of ≥25 kg/m^2, we close the wound with subcuticular sutures after inserting a closed subcutaneous drain to maintain fluid drainage. However, firm evidence supporting the use of a subcutaneous drain after colorectal cancer surgery has yet to be obtained. The insertion of a drain may increase healthcare costs and negatively affect patients' ability to walk after surgery. Therefore, further studies are needed.

Many surgical wound infections are caused by bacteroides and *Staphylococcus aureus*. Although these bacteria were sensitive to the antibiotics we administered prophylactically in our study, wound infection developed. The dose and duration of treatment with antibiotics should thus be reassessed. Further multicenter studies are needed to more clearly define risk factors and establish the most effective prophylactic treatment for wound infection.

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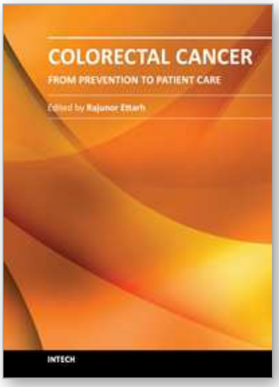

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The projections for future growth in the number of new patients with colorectal cancer in most parts of the world remain unfavorable. When we consider the substantial morbidity and mortality that accompanies the disease, the acute need for improvements and better solutions in patient care becomes evident. This volume, organized in five sections, represents a synopsis of the significant efforts from scientists, clinicians and investigators towards finding improvements in different patient care aspects including nutrition, diagnostic approaches, treatment strategies with the addition of some novel therapeutic approaches, and prevention. For scientists involved in investigations that explore fundamental cellular events in colorectal cancer, this volume provides a framework for translational integration of cell biological and clinical information. Clinicians as well as other healthcare professionals involved in patient management for colorectal cancer will find this volume useful.