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Risk Factors for Wound Infection After Laparoscopic Surgery for Colon Cancer

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Objective: To clarify risk factors for wound infection after laparoscopic surgery for colon cancer.

Subjects and Methods: The study group comprised 1144 patients. Univariate and multivariate analyses were performed to assess the following 14 postoperative risk factors for wound infection.

Results: Univariate analysis showed that the following 4 risk factors were related to wound infection: tumor location right-sided colon cancer, a preoperative serum albumin level of ≤2.5 g/dL, anastomotic technique [functional end-to-end anastomosis (FEEA)], and sutures used at the time of wound closure non–polydioxanone sutures (PDS)-Plus. Multivariate analysis indicated that 3 factors were independent risk factors for wound infection: a preoperative serum albumin level of ≤2.5 g/dL, FEEA, and the use of non-PDS-Plus sutures wound closure.

Conclusions: Risk factors for wound infection after laparoscopic surgery for colon cancer were a preoperative serum albumin level of ≤2.5 g/dL, FEEA, and the use of non-PDS-Plus sutures.

Key Words: functional end-to-end, PDS Puls, risk factor, retrospective study

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Elective surgery for colorectal cancer is semi-contaminated surgery, and postoperative wound infection develops in 3% to 26% of patients.[1–3] Diabetes mellitus and malnutrition,[4] a body mass index of ≥25,[5] open surgery,[6–8] and the use of non–polydioxanone sutures (PDS)-Plus sutures at the time of wound closure[9–11] have been reported to be risk factors for postoperative wound infection. Wound infection can cause pain and distress and prolong the hospital stay of patients, markedly increasing health care costs. Therefore, measures against wound infection have been taken, including modification of the period of treatment with antibiotics given to prevent wound infection, preoperative bowel preparation, and the placement of drainage tubes. The aim of our study was to retrospectively analyze wound infections that developed during perioperative care in patients who underwent standard laparoscopic surgery for colon cancer in the same hospital and to thereby clarify risk factors for wound infection.

SUBJECTS AND METHODS

The study group comprised 1144 patients with an initial single colorectal carcinoma who underwent laparoscopic surgery in our hospital from January 2010 through December 2017. Patients who underwent elective laparoscopic surgery for primary single colon cancer were included in the study. Patients who underwent emergency surgery or who had a diverting stoma were excluded from the study. There were 650 men (57%) and 494 women (43%), with a mean age of 67.6 years (range, 22 to 93 y). Patients who preoperatively received chemotherapy, underwent emergency surgery, or were switched to open surgery were excluded from the study. Right-sided colectomy was performed in 474 patients (41.4%), and left-sided colectomy was performed in 670 patients (58.6%). The following 14 risk factors for wound infection were studied: sex (male vs. female), age (below 65 y vs. 65 y and above), body mass index (kg/m^2), American Society of Anesthesiologists physical status classification score (class I or class ≥II), the presence or absence of diabetes mellitus, tumor location (The cecum, the ascending colon, and the transverse colon were defined as the right-sided colon. The descending colon, the sigmoid colon, and the rectosigmoid colon were defined as the left-sided colon.), preoperative serum hemoglobin levels (<10 or ≥10 g/dL), preoperative serum albumin levels (<2.5 or ≥2.5 g/dL), operation time (<180 or ≥180 min), bleeding volume (<50 or ≥50 mL), anastomotic technique [functional end-to-end anastomosis (FEEA) or other procedures], tumor diameter (<4 or ≥4 cm), pathologic tumor stage (≤II or ≥III), and sutures used at the time of wound closure (PDS-Plus or non-PDS-Plus) (Table 1).

Surgical Procedure

At the start of surgery, a small surgical incision was made in the umbilical region regardless if the lesion was present in the right or left side of the colon. A12-mm port was placed in the umbilical incision. Carbon dioxide was delivered at a mean rate of 8 mm Hg/h to induce pneumoperitoneum. A 5-mm laparoscopic flexible fiberscope was inserted into the 12-mm port. While examining the abdominal cavity, two 5-mm ports each were placed in the left and right sides of the middle-lower abdomen. A total of 5 ports were used.

In patients with right-sided colon cancer, the dissection sites of arteries were determined on the basis of the sites and stages of tumors arising in the region of the ileocolic artery, right colic artery, and the middle colic artery. As for intestinal dissection and anastomosis, the umbilical wound was extended to about 4 to 7 cm. The intestine including lesions was adequately exposed outside of the body, and FEEA was performed. In

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TABLE 1. Clinical Characteristics of 1144 Patients

	N = 1144	%
Sex		
Male:Female	650:494	57:43
Age	67.6 (± 11.1)	
ASA score		
1:2:3	437:626:81	38:55:7
BMI (kg/m^2)	22.9 (± 3.5)	
Tumor site		
Right colon (C:A:T): left colon (D:S:Rs)	112:248:114:77:406:187	10:22:10:7:35:16
Preoperative hemoglobin level (g/dL)	12.5 (± 2.2)	
Preoperative albumin level (g/dL)	3.9 (± 0.6)	
Diabetes mellitus		
Yes:no	158:986	14:86
Operation time (min)	2014.7 (± 563.8)	
Bleeding volume (mL)	52.7 (± 202.1)	
Anastomotic method		
FEEA:no FEEA	596:545	52:48
Tumor diameter (cm)	4.0 (± 2.3)	
pStage		
0:I:II:III:IV	59:322:332:347:84	6:28:29:30:7
Suture (at the time of wound closure)		
PDS:no PDS	856:288	75:25

ASA indicates American Society of Anesthesiologists; BMI, body mass index; FEEA, functional end-to-end anastomosis; no PDS, non-PDS-Plus; PDS, PDS-Plus; tumor site, right side of colon: cecum, ascending, transverse, left side of colon: descending, sigmoid, rectosigmoid.

patients with left-sided colon cancer, dissection was extended to the root of the inferior mesenteric artery if the depth of invasion was diagnosed to be clinical T3 or deeper. As for intestinal dissection and anastomosis, the umbilical wound was extended to about 3 to 5 cm depending on the status of the lesion. FEEA was performed if the lesion could be adequately exposed. If the intestine could not be exposed outside the body, the mesentery was treated in the body, and the distal colon was then cut using an automatic suturing device. The lesion was pulled out of the body from a small surgical wound, and the proximal colon was transected. Subsequently, the tip of an automatic anastomosis device was placed in the resected margin of the proximal colon, and the proximal colon was returned to the abdominal cavity. Patients who underwent elective laparoscopic surgery for primary single colon cancer were included in the study. Patients who underwent emergency surgery or who had a diverting stoma were excluded from the study.

Preoperative and Postoperative Management

All patients underwent mechanical bowel preparation before surgery (Two tablets of sennoside were given orally 2 days before surgery. On the day before surgery, a pack of magnesium citrate and a pack of sodium picosulgate were given orally.) Chemical intestinal preparation was not performed. In principle, cefmetazole sodium (1 g) was given as prophylactic treatment by intravenous infusion at the time of surgery and thereafter was additionally given every 3 hours. On the day after surgery, cefmetazole was given only once.

Wound Closure

For surgical wound closure, in principle, the peritoneum and fascia were closed with en bloc sutures. 0-PDS sutures (Johnson and Johnson, New Brunswick, NJ) were used from January 2010 through March 2012, and 0-PDS-Plus sutures (Johnson and Johnson) were used from April 2012 through December 2017. After suturing the peritoneum and fascia, the subcutaneous tissue was irrigated with 200 mL of warmed physiological saline applied under high pressure. For dermal sutures, similarly, 4-0-PDS sutures (Johnson and Johnson) were used from January 2010 through March 2012, and 4-0-PDS-Plus sutures (Johnson and Johnson) were used from April 2012 through December 2017. After closure, the surgical wound was covered with a polyurethane film dressing for 48 hours after surgery. Thereafter, the wound was left open and was not sterilized.

Assessment of Wound Infection

The wound was assessed by surgeons (operators, ward doctors, etc.) and nurses (ward nurses and infection control specialist nurses). If exudate fluid or pus was found on the wound, culture tests were performed in accordance with the guidelines for the prevention of surgical-site infection (SSI). The presence of wound pain or redness alone was not considered a sign or symptom of wound infection.

Postoperative Course

As for the period of postoperative follow-up, patients were followed up for 30 days after surgery. After discharge, patients presented at an outpatient clinic once every 2 to 4 weeks to confirm the wound site. In patients with pathologic stage III or higher tumors, adjuvant chemotherapy was begun within 4 to 8 weeks after surgery. The preoperative and postoperative courses were retrospectively studied on the basis of the medical records.

Statistical Analysis

Multivariate logistic regression analysis was performed with the use of χ^2 tests (with Yate's correction). Variables with P-values of <0.2 were analyzed, and P-values of <0.05 were considered to indicate statistical significance. These statistical analyses were performed using SPSS software, version 8.0J (SPSS Inc., Chicago, IL).

RESULTS

Complications after laparoscopic surgery for colon cancer occurred in 16.9% (193/1144) of the patients, including wound infection in 4.5% (51/1144), suture failure in 4.4% (50/1138), and intestinal obstruction in 3.6% (41/1144). No patient died. The median postoperative hospital stay was 14 days in patients with wound infection and 8 days in those without wound infection ($P = 0.0001$). No flare-up of wound infection or wound dehiscence occurred during the follow-up period after discharge. All patients underwent culture tests of pus from infected wounds, and 50 patients (98%) had positive results. The causative pathogens were Bacteroides in 27 patients (53%), Enterococcus in 10 (20%), Enterobacter in 8 (16%), *Pseudomonas aeruginosa* in 3 (6%), *Escherichia coli* in 1, and Clostridium sepsis in 1.

On univariate analysis, there were 4 risk factors for wound infection: tumor site (right-sided colon cancer, $P = 0.0149$), preoperative serum albumin levels (≤ 2.5 g/dL, $P = 0.0249$), anastomotic technique (FEEA, $P = 0.0005$), and sutures used at the time of wound closure (non-PDS-Plus, $P = 0.0279$) (Table 2).

Multivariate analysis showed that there were 3 independent risk factors for wound infection: preoperative serum albumin levels (≤ 2.5 g/dL) (odds ratio, 4.0690; $P = 0.0069$), anastomotic

TABLE 2. Univariate Analysis

	Infection (N = 51)	No Infection (N = 1093)	*P*
Sex (male:female)	26:25	624:469	0.4737
Age (< 69: ≥ 70) (y)	22:29	588:505	0.1777
ASA score (I: ≥ II)	14:37	422:671	0.1453
BMI (< 25: ≥ 25) (kg/m^2)	33:18	766:327	0.7298
Tumor site (right side of colon:left side of colon)	30:21	444:649	0.0149
Preoperative hemoglobin (< 9: ≥ 10) (g/dL)	10:41	145:948	0.2783
Preoperative albumin (g/dL) (< 2.5: ≥ 2.5)	7:44	33:1060	0.0249
Diabetes mellitus (present:absent)	9:42	149:944	0.5454
Operation time (< 180: ≥ 180) (min)	16:35	465:628	0.1514
Bleeding (< 50: ≥ 50) (mL)	38:13	897:196	0.2380
Anastomotic technique (FEEA:no FEEA)	12:39	533:557	0.0005
Tumor diameter (< 3: ≥ 3) (cm)	18:33	460:633	0.4145
pStage (0-II: ≥ III)	27:24	686:407	0.2051
Sutures used at wound closure (P:NP)	31:20	825:268	0.0279

ASA indicates American Society of Anesthesiologists; BMI, body mass index; FEEA, functional end-to-end anastomosis; NP, non-PDS-Plus; P, PDS-Plus; Tumor site, right side colon: cecum, ascending, transverse, left side colon: descending, sigmoid, rectosigmoid.

technique (FEEA) (odds ratio, 3.2097; $P = 0.0005$), and sutures used at the time of wound closure (non-PDS-Plus; odds ratio, 2.2045; $P = 0.0087$) (Table 3).

DISCUSSION

We studied wound infections occurring after laparoscopic surgery under the same conditions in patients who underwent surgery for colon cancer by standardized surgical procedures and received perioperative care (before, during, and after surgery) in a single hospital. The incidence of wound infection was 4.5%, which was lower than that in most previous studies (3% to 26%). Our results showed that a preoperative serum albumin level of ≤ 2.5 g/dL, anastomotic technique (FEEA), and sutures used at the time of wound closure (non-PDS-Plus) were 3 independent risk factors for wound infection.

In previous studies, the incidence of wound infection after laparoscopic surgery for colorectal cancer was 3% at the trocar site[12] and 10.8% at the wound site after exposure of the intestine.[13] In our hospital, there were no infections at the trocar site, and the intestine was exposed at the umbilical region in all patients. The rate of infection (4.5%) was lower than that in previous studies.

TABLE 3. Multivariate Analysis

	Odds Ratio	95% CI	*P*
Tumor site (right colon)	1.0943	0.5011-2.3896	0.8211
Preoperative albumin (< 2.5) (g/dL)	4.0690	1.4709-11.2560	0.0069
Anastomotic technique (FEEA)	3.2097	1.6573-6.2163	0.0005
Sutures used at closure (P:NP)	2.2045	1.2210-3.9802	0.0087

FEEA indicates functional end-to-end anastomosis; NP, non-PDS-Plus; P, PDS-Plus.

The 2016 World Health Organization Guidelines for the Prevention of SSI[14] claimed that SSI is the most preventable health care–associated infection. Additional medical costs required for the treatment of SSI represent a heavy burden.

The development of wound infections after surgery prolonged the mean length of the hospital stay by 7 days and required about US$540 of medical cost per patient.

As for malnutrition and wound infection, decreased preoperative serum albumin levels are considered an important cause of postoperative complications. Gibbs et al[15] reported that the incidence of complications and the mortality rate within 30 days after surgery exponentially increased when the preoperative serum albumin level ranged from 4.6 to 2.1 g/dL. They also reported that a preoperative serum albumin level of 3.5 g/dL was associated with wound-site complications after surgery for colorectal cancer, an increased risk at the time of surgery, and prolonged postoperative recovery, leading to a prolonged hospital stay.[16,17] Mangram et al[18] recommended that nutritional therapy should be preoperatively given for 7 to 14 days before surgery to malnourished patients. In our study, a serum albumin level of ≤ 2.5 g/dL was a risk factor for wound infection. This value was lower than that in previous studies of risk factors for wound infection.

Only a few previous studies have shown that anastomotic technique (FEEA) is a risk factor for wound infection. Few studies have examined risk factors for wound infection in only patients who underwent laparoscopic surgery. Ojima et al[19] compared the closed method for FEEA using cartridges 4 times with the open method using cartridges 2 times and found that the closed method was associated with a significantly lower incidence of wound infection. They reported that FEEA performed by the open method required a longer suture line than did the closed method and was more economical because a stapler was used only twice. However, the open method was associated with a significantly higher incidence of wound infection because the intestine had to be released once at the time of anastomosis. In our study, the surgical technique was limited to laparoscopic surgery, and all patients underwent the closed method. Therefore, further studies are needed to establish new anastomotic techniques and to define the optimal environment at the time of anastomosis as countermeasures against wound infection.

Previous studies examining the relation between wound infections and sutures have shown that the use of antimicrobial sutures such as triclosan-coated polydioxanone sutures (PDS-Plus PDP771D, Ethicon Inc.) is a promising method for decreasing the incidence of SSI.[9–11] Nakamura et al[20] performed a randomized controlled trial examining risk factors for postoperative wound infection in 410 patients with colorectal cancer and found that the incidence of wound infection was significantly lower in patients in whom triclosan-coated sutures were used (4.3%) than in the control group (9.3%) although 45% of the patients underwent open surgery. These findings are consistent with our results. In a randomized controlled trial (PROUD study) conducted by Diener et al,[21] the incidence of wound infection was 16.1% in patients in whom nonantimicrobial sutures (PDS II) were used for wound closure and 14.8% in patients in whom antimicrobial sutures were used, with no significant difference. In contrast to our study, their patients underwent elective abdominal surgery, and the most common disease was colon cancer, which was

only present in only 34% of patients. Therefore, their results cannot be directly accepted. In their study, the fascia was closed with a continuous suture technique using PDS-Plus sutures. The skin was closed with skin staples, instead of using subcuticular sutures. This point largely differed from our study. Subgroup analysis showed that the incidence of SSI after surgery was 18.0% in patients in whom PDS-Plus sutures were used and 17.3% in patients in whom nonantimicrobial PDS II sutures were used. This difference was not significant.

Our results indicate that preoperative nutritional status should be improved as much as possible at the time of wound closure to prevent wound infection particularly in patients who have a preoperative serum albumin level of ≤ 2.5 g/dL. Wound edge protection or anastomosis within the body was considered an important factor to consider when the intestine is pulled outside the body at the time of reconstruction. In patients who undergo FEEA, the incidence of wound infection may be further decreased by using PDS-Plus antimicrobial sutures at the time of wound closure.

Further large randomized clinical studies should be performed in Japan to determine risk factors for wound infection, thereby allowing more effective preventive treatment to be established.

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