Risk Factors for Surgical Site Infection following Restorative Proctocolectomy in Patients with Ulcerative Colitis in the Biologic Era

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Research Article

Keywords: ulcerative colitis, restorative proctocolectomy, postoperative complications, surgical site infection, oral antibiotic prophylaxis

Posted Date: October 14th, 2024

DOI: https://doi.org/10.21203/rs.3.rs-4936002/v1

Additional Declarations: No competing interests reported.

Version of Record: A version of this preprint was published at Techniques in Coloproctology on March 23rd, 2025. See the published version at https://doi.org/10.1007/s10151-025-03126-2.

Abstract

Background

Surgical site infection (SSI) is a critical issue in colorectal surgery because it decreases postoperative patient quality of life. The rate of SSI in patients with ulcerative colitis (UC) receiving immunosuppressive therapy is particularly high, suggesting that the SSI rate may increase with the introduction of biologic agents.

Methods

UC patients who underwent 2-stage restorative proctocolectomy at our institution between April 2012 and December 2023 were included in this study. Clinical characteristics were analyzed and compared between an SSI group and a non-SSI group; possible risk factors for SSIs were also analyzed. Additionally, the following anti-SSI measures adopted at our hospital were included as explanatory variables: laparoscopic surgery, oral antibiotic prophylaxis, and change of surgical instruments before wound closure.

Results

In total, 501 UC surgical patients were included. The incidence of overall SSIs was 45/501 (8.9%). The rates of incisional SSIs and organ/space SSIs were 26/501 (5.1%) and 30/501 (5.9%), respectively. Oral antibiotic prophylaxis was identified as a risk factor for overall SSIs (odds ratio: 0.41, 95% CI: 0.18–0.93, p = 0.02), incisional SSIs (odds ratio: 0.34, 95% CI: 0.11–1.03, p = 0.03) and organ/space SSIs (odds ratio: 0.37, 95% CI: 0.13–1.05, p = 0.04).

Conclusions

Nonadministration of oral antibiotic prophylaxis was identified as a risk factor for SSIs. Oral antibiotic prophylaxis before restorative proctocolectomy may improve the postoperative quality of life of UC patients by preventing SSIs, even in the era of minimally invasive surgery and biological agents.

Introduction

Surgical site infection (SSI) is a critical issue in colorectal surgery because it decreases postoperative patient quality of life, prolongs hospital stays, and increases medical costs. Furthermore, it is well known that SSI rates are higher among ulcerative colitis (UC) patients than among patients who have undergone other standard colorectal surgeries [1]. The reason is that UC surgery patients generally have risk factors for SSIs, such as malnutrition, anemia, and an immunosuppressed status due to medical treatment. In particular, biologics (anti-TNF agents) have been approved for the treatment of UC since 2005 in the U.S.

and Europe and since 2010 in Japan); since then, the treatment of UC has undergone a major transformation over the past decade, with a decrease in the surgery rate and a decrease in the number of cancer cases reported [2] [3]. However, the preoperative administration of biologics has been reported to be a risk factor for infectious complications, including SSIs, causing the most controversy [4] [5, 6].

Some common anti-SSI measures used in colorectal surgery include intravenous antimicrobial prophylaxis, the preoperative use of clippers, closure with antimicrobial absorbent thread, wound cleansing, intraoperative warming, and the use of wound protectants [7] [8]. In addition to the anti-SSI measures described above, various other strategies have been reported, and we have introduced several of them. The first approach is laparoscopic surgery. Laparoscopic surgery is also recommended in the guidelines, as it improves cosmesis, fertility, and pregnancy outcomes [9]. However, laparoscopic surgery for UC has been reported to contribute to a decrease in SSIs in only retrospective studies [10] [11]. The second measure is oral antimicrobial prophylaxis. In a previous series, we analyzed the efficacy of oral antimicrobial prophylaxis during surgery for UC [12]. Oral antimicrobial prophylaxis significantly reduced the overall incidence of SSIs. However, that study did not include cases of biologic administration or laparoscopic surgery. The third strategy involves changing surgical instruments before wound closure. On the basis of expert consensus, the SSI guidelines of the American College of Surgeons and Surgical Infection Society recommend the changing to new instruments for patients undergoing colorectal surgery [13]. However, the impact of changing surgical instruments on UC surgical cases is still unknown.

Therefore, we aimed to retrospectively investigate the clinical characteristics and risk factors for SSIs in UC patients in the biologic era and to determine the effectiveness of anti-SSI measures.

Materials and methods

Patient selection

UC patients who underwent restorative proctocolectomy at Hyogo Medical University between April 2012 and October 2023 were included in this study. To avoid bias due to surgical procedures, only patients who underwent 2-stage restorative proctocolectomy were included. Those who underwent modified 2-stage restorative proctocolectomy were not included in this series. UC patients were diagnosed according to the original surgical specimens at the time of the operation. The histological features of UC included lymphocytes and plasma cells in the lamina propria; neutrophils in the lamina, crypts, or surface epithelium; and changes in surface topography, epithelial damage, metaplastic changes, and mucin depletion [14]. We excluded patients with a diagnosis or suspicion of Crohn's disease (CD) on the basis of histological findings that were not included in this series. All colectomy specimens with histologic features of UC and no Crohn's-like features, such as granulomas, transmural lymphoid aggregates, or fissures, were identified. We also excluded pediatric patients due to the possibility of different postoperative outcomes [15].

The data collected included sex, age at onset, age at initial surgery, duration of disease, disease severity, blood parameters, body mass index (BMI), American Society of Anesthesiologists (ASA) score, total administered prednisolone (PSL) dose, immunomodulator (thiopurines, including azathioprine and 6-mercaptopurine) administration, calcineurin inhibitor (tacrolimus) administration, Janus kinase inhibitor (tofacitinib) administration, biologic (infliximab, adalimumab, golimumab, and vedolizumab) administration, oral antimicrobial prophylaxis (since 2017), surgical indication (cancer/dysplasia and refractory disease), urgent/emergent or elective surgery, laparoscopic surgery (since 2018), operative time, amount of blood loss, intraoperative blood transfusion, changing of surgical instruments before wound closure (from 2019 to 2020) and SSIs (within 30 days postoperatively), which were retrospectively determined from the clinical records. Severe disease was assessed primarily according to clinical features using the criteria of Truelove and Witts: 6 or more stools with blood and 1 or more of the following: a hemoglobin (hb) level < 105 g/L, an ESR > 30 mm/h, a fever > 37.8°C, or a pulse rate > 90/min [16]. Blood parameters, including the serum albumin (Alb) level, C-reactive protein (CRP) level, and hemoglobin level prior to surgery, were also retrospectively obtained from the patients' clinical records. The total amount of administered corticosteroids was converted into the PSL dose and calculated on the basis of the administered corticosteroid dose since the initial onset of UC. Patients who received immunomodulators, calcineurin inhibitors or Janus kinase inhibitors within 72 hours before surgery, regardless of the dosage, were included. All infusions given within 12 weeks before surgery were considered biologically administered.

Surgical site infection

SSIs were diagnosed and recorded according to their location after total proctocolectomy. In general, incisional SSIs included wound infections, whereas organ/space SSIs included abdominal or pelvic abscesses, such as those involving anastomotic leakage. SSIs were diagnosed by designated staff on our infection-control team who were trained in applying surveillance methods and identifying SSIs on the basis of definitions stated in guidelines issued by the NNIS system of the Centers for Disease Control and Prevention [17]. In addition, the annual incidence rates of SSIs from 2012 to 2023 were examined.

Laparoscopic surgery

We introduced laparoscopic approaches in April 2018, with indications for laparoscopic surgery, including elective surgery and urgent surgery (such as operations for refractory disease or cancer/dysplasia), and a stable general condition. We did not perform laparoscopic surgery in emergent cases, such as those involving fulminant disease, perforation, toxic megacolon, or massive bleeding.

Oral antimicrobial prophylaxis and intravenous antimicrobial prophylaxis

Oral antibiotics (500 mg of kanamycin and 500 mg of metronidazole at 2:00 p.m., 3:00 p.m., and 9:00 p.m.) and preoperative mechanical bowel preparation (1.8 l of magnesium citrate solution at 11:00 a.m.) were administered on the day before surgery. These drugs were not administered to emergency surgery patients. All patients were given intravenous antimicrobial prophylaxis with second-generation

cephalosporin (Flomoxef, Shionogi and Co., Japan) 30 minutes before surgery, with this administration repeated every 3 hours during surgery; the same antibiotics were continued for 24 hours following surgery.

Changing of surgical instruments before wound closure

The surgical nurse replaced the instruments used in the main surgical procedure (which included intestinal resection and/or anastomosis) with new tools before closure of the peritoneum. The new instruments, which included scissors, forceps, suction tubes, electronic scalpels, Kocher's forceps, muscle retractors, spatulas, tweezers, and cups for irrigation, were prepared on a separate surgical table before starting the operation. During wound closure, none of the surgical members touched the surgical instruments used in the main procedure.

Outcomes

The patients were classified into an SSI group or a non-SSI group. The primary outcome, which was defined by possible risk factors for SSIs in UC patients, was analyzed to identify significant predictors in UC patients. Additionally, the following anti-SSI measures adopted at our hospital were included as explanatory variables: laparoscopic surgery, oral antibiotic prophylaxis, and changes in surgical instruments before wound closure. We performed a multivariate analysis of risk factors for overall SSIs, incisional SSIs, and organ/space SSIs in a model with the factors identified in the univariate analysis.

Ethics approval

All study protocols were approved by the institutional review board at Hyogo Medical University (no. 4724), and informed consent and agreement for the use of patient data were obtained before surgery. Written informed consent was obtained via an opt-out method.

Statistical analysis

The statistical analysis was performed as follows. For the annual SSI rate, trends were analyzed via linear regression analysis. Categorical variables were compared via the chi-square test, ANOVA, or Fisher's exact test. Continuous variables are expressed herein as medians and ranges and were compared via the Mann–Whitney *U* test or ANOVA. Each of the anti-SSI measures was introduced at different times, but as mentioned above, oral antimicrobial prophylaxis and laparoscopic surgery are not used in emergency surgery. Therefore, the Spearman correlation was used to validate emergency surgery, oral antimicrobial prophylaxis, and laparoscopic surgery. The level of statistical significance was set at $p < 0.05$. The odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for all variables in the univariate analysis. Multivariate logistic regression analysis was performed to evaluate the risk factors for SSIs for factors with p values < 0.05. JMP version 17 (SAS Institute, Inc., Cary, North Carolina, USA) was used to perform all the analyses.

Results

Patient characteristics

We performed 717 colectomies due to a preoperative diagnosis of UC. Two-stage restorative proctocolectomy was performed in 521 patients, and other procedures were excluded. In addition, four pediatric patients and fifteen CD patients were excluded. Ultimately, 502 UC patients were analyzed in this series (Fig. 1).

Overall, 45/501 (8.9%) patients developed SSIs. The rates of incisional SSIs and organ/space SSIs were 26/405 (5.1%) and 30/501 (5.9%), respectively. The annual SSI incidence rates from 2012 to 2023 and the regression equations are shown in Fig. 2. Although there were differences across years, the linear regression revealed a decreasing trend in the SSIs. Conversely, there was an increasing trend in the rate of biologic administration, and the regression equation was $y = 0.9906x + 31.389$: $R^2 = 0.2168$.

The clinical characteristics of the patients were as follows (Table 1). Alb and Hb levels were significantly lower ($p < 0.01$). The proportion of severe cases tended to be greater in the SSI group, although this difference was not significant. The rate of ASA ≥ 3 was significantly greater ($p < 0.01$) among patients in the SSI group. With respect to pharmacotherapy, there were no significant differences between the SSI and non-SSI groups. The rate of oral antimicrobial prophylaxis was 9/45 (20.0%) in the SSI group and 176/456 (38.6%) in the non-SSI group. The rate of oral antimicrobial prophylaxis was significantly lower ($p < 0.01$) among patients in the SSI group. There were no significant differences between the SSI and non-SSI groups regarding the use of laparoscopic surgery and surgical instrument changes. The proportion of emergency/urgent surgeries tended to be greater in the SSI group, although this difference was not significant.

Table 1
UC patient characteristics

Factors	**Overall** *n* **= 501**	**SSI group** *n* **= 45**	**Non-SSI group** *n* **= 456**	***p value***
Male sex, n (%)	324 (64.6)	28 (62.2)	296 (64.9)	*0.71*
Age at surgery, years median (range)	47 (18–81)	49 (21–70)	47 (18–81)	*0.55*
Age at surgery ≥ 65 years, n (%)	53 (10.5)	3 (6.6)	50 (10.9)	*0.38*
Duration of disease, months median (range)	204.5 (2.0-590.0)	203.9 (48.8–419.0)	213.5 (2.0-590.0)	*0.06*
BMI ≥ 25, n (%)	46 (9.1)	3 (6.6)	43 (9.4)	*0.54*
Severe disease, n (%)	131 (26.1)	17 (37.7)	114 (25.0)	*0.06*
Alb	3.8 (0.7–5.3)	2.9 (0.7–4.7)	3.8 (1.1–5.3)	*< 0.01**
Hb	11.8 (5-17.3)	10.3 (7-16.6)	12 (5-17.3)	*< 0.01**
CRP	0.31 (0.0-23.8)	0.5 (0-13.7)	0.3 (0-23.8)	*0.09*
Pancolitis, n (%)	422 (84.2)	37 (82.2)	385 (84.4)	*0.69*
Cancer/dysplasia, n (%)	116 (23.1)	6 (13.3)	110 (24.1)	*0.10*
ASA ≥ 3, n (%)	111 (22.1)	16 (35.5)	95 (20.8)	*0.02**
Total PSL administration, mg, median (range)	3,000 (0–76,650)	2,960 (0–76,650)	3,042 (0–70,000)	*0.31*
Immunosuppressant administration, n (%)	212 (42.3)	15 (33.3)	197 (43.2)	*0.20*
Calcineurin inhibitor administration, n (%)	75 (14.9)	9 (20.0)	66 (14.4)	*0.49*
Janus kinase inhibitor administration, n (%)	16 (3.1)	1 (2.2)	16 (3.5)	*0.62*
Biologic administration, n (%)	186 (37.1)	17 (37.7)	169 (37.0)	*0.92*
Oral antimicrobial prophylaxis n (%)	185 (36.9)	9 (20.0)	176 (38.6)	*0.01**

Factors	Overall *n* = 501	SSI group *n* = 45	Non-SSI group *n* = 456	*p value*
Emergent/urgent surgery, n (%)	85 (16.9)	12 (26.6)	73 (16.0)	*0.06*
Laparoscopic surgery, n (%)	154 (30.7)	9 (20.0)	145 (31.7)	*0.10*
Operative time, min median (range)	241 (114–674)	228 (133–569)	243 (114–674)	*0.22*
Blood loss, ml median (range)	180 (0–2,270)	200 (10 – 1,020)	170 (0–2,270)	*0.70*
Changing surgical instruments, n (%)	18 (3.5)	2 (4.4)	16 (3.5)	*0.74*
SSI = Surgical site infection, UC = Ulcerative colitis, BMI = Body mass index, Alb = Albumin, Hb = Hemoglobin, CRP = C-reactive protein, ASA = American Society of Anesthesiologists, PSL = Prednisolone,				
The Mann–Whitney U test was performed for continuous variables. The chi-square test or Fisher's exact test was used for categorical variables. * $p < 0.05$ (indicates a significant difference)				

The incidence of SSIs according to the anti-SSI measures, divided into incisional SSIs and organ/space SSIs, is shown in Table 2. Oral antimicrobial prophylaxis was associated with a significantly lower incidence of SSIs for both incisional and organ/space SSIs, as well as overall SSIs. The use of laparoscopic surgery and surgical instrument changes did not significantly decrease the rate of SSI. However, there was a trend toward a lower incidence of SSIs for both incisional and organ/space SSIs with respect to laparoscopic surgery. Spearman's rank correlation coefficient was − 0.3128 between emergency/urgency surgery and oral antimicrobial prophylaxis and − 0.1283 between emergency/urgency surgery and laparoscopic surgery.

Table 2
Incidences of surgical site infection according to the SSI measures

	Oral antimicrobial prophylaxis			**Laparoscopic surgery**			**Changing surgical instruments**		
	Yes n= 185	**No n= 316**	***p value***	**Yes n= 154**	**No n= 347**	***p value***	**Yes n= 18**	**No n= 483**	***p value***
Overall SSIs, n (%)	9 (4.8)	36 (11.3)	*0.01**	9 (5.8)	36 (10.3)	0.10	2 (11.1)	43 (8.9)	*0.74*
Incisional SSIs, n (%)	4 (2.1)	22 (6.9)	*0.01**	4 (2.5)	22 (6.3)	0.08	2 (11.1)	24 (4.9)	*0.24*
Organ/space SSIs, n (%)	5 (2.7)	25 (7.9)	*0.01**	5 (3.2)	25 (7.2)	0.08	0 (0)	30 (6.2)	*0.27*

SSI = Surgical site infection

The chi-square test or Fisher's exact test was used for categorical variables.

* $p < 0.05$ (indicates a significant difference)

Outcomes

Univariate and multivariate analyses were performed to identify independent risk factors for SSIs. The results of the analyses of the risk factors potentially associated with overall SSIs are presented in Table 3. The four clinically and statistically significant factors, namely, severe disease, Alb level, Hb level, ASA score ≥ 3, and oral antimicrobial prophylaxis, were entered into the multivariate logistic regression analysis. Alb levels (OR = 0.49, 95% CI 0.29–0.82, *p < 0.01*) and oral antimicrobial prophylaxis (OR = 0.41, 95% CI 0.18–0.93 p = 0.02) were identified as independent risk factors for overall SSIs. The results of the analyses of the risk factors potentially associated with incisional SSIs and organ/space SSIs are presented in Tables 4 and 5, respectively. Alb levels (OR = 0.53, 95% CI 0.30–0.84, *p = 0.03*) and oral antimicrobial prophylaxis (OR = 0.34, 95% CI 0.18–0.93 *p = 0.03*) were identified as independent risk factors for incisional SSIs. An ASA score of ≥ 3 (OR = 2.32, 95% CI 1.07–5.04, *p = 0.03*) and oral antimicrobial prophylaxis (OR = 0.37, 95% CI 0.18–0.93 *p = 0.04*) were identified as independent risk factors for organ/space SSIs.

Table 3
Logistic regression analysis of the risk factors for overall SSIs

Factors	Univariate		Multivariate	
	OR (95% CI) *p value*		OR (95% CI) *p value*	
Male sex	0.89 (0.47–1.67)	*0.71*		
Age at surgery, (10-year intervals)	1.07 (0.86–1.33)	*0.51*		
Duration of disease (1-month intervals)	1.33 (0.33–5.38)	*0.69*		
BMI ≥ 25	0.68 (0.20–2.30)	*0.78*		
Severe disease	1.82 (0.96–3.45)	*0.06*		
Alb (1 g/dl intervals)	0.54 (0.39–0.75)	*< 0.01**	0.55 (0.35–0.86)	*< 0.01**
Hb (1 g/dl intervals)	0.86 (0.75–0.98)	*0.02**	1.02 (0.85–1.22)	*0.80*
CRP (1 g/dl intervals)	2.23 (0.95–1.12)	*0.43*		
Pancolitis, n (%)	0.85 (0.38–1.97)	*0.69*		
Cancer/dysplasia, n (%)	0.48 (0.19–1.17)	*0.10*		
ASA ≥ 3, n (%)	2.09 (1.09–4.01)	*0.02**	1.93 (0.99–3.77)	*0.05*
Total PSL dose (per 100 mg)	1.00 (0.99-1.00)	*0.34*		
Immunosuppressant administration	0.65 (0.34–1.25)	*0.20*		
Calcineurin inhibitor administration	0.96 (0.44–2.06	*0.92*		
Janus kinase inhibitor administration	0.60 (0.07–4.66)	*0.62*		
Biologic administration	1.03 (0.64–1.93)	*0.92*		
Oral antimicrobial prophylaxis	0.39 (0.18–	*0.01**	0.47 (0.21–	*0.04**

Factors	Univariate		Multivariate	
	OR (95% CI)	*p value*	OR (95% CI)	*p value*
	0.84)		1.01)	
Emergent/urgent surgery	1.90 (0.94–3.86)	*0.06*		
Laparoscopic surgery	0.53 (0.25–1.14)	*0.10*		
Operative time (per min)	0.99 (0.99-1.00)	*0.41*		
Blood loss (per 100 ml)	0.99 (0.99–1.13)	*0.91*		
Changing surgical instruments	1.27 (0.28–5.74)	*0.67*		

SSI = Surgical site infection, UC = Ulcerative colitis, OR = odds ratio, CI = Confidence interval, Alb = Albumin, ASA = American Society of Anesthesiologists, BMI = Body mass index, CRP = C-reactive protein, PSL = Prednisolone

* $p < 0.05$ (indicates a significant difference)

Table 4
Logistic regression analysis of the risk factors for incisional SSIs

Factors	Univariate		Multivariate	
	OR (95% CI) *p value*		OR (95% CI) *p value*	
Male sex	0.96 (0.42–2.21)	*0.93*		
Age at surgery, (10-year intervals)	1.26 (0.94–1.69)	*0.11*		
Duration of disease (1-month intervals)	0.99 (0.99-1.00)	*0.29*		
BMI ≥ 25	0.38 (0.05–2.88)	*0.33*		
Severe disease	1.82 (0.82–4.13)	*0.14*		
Alb (1 g/dl intervals)	0.50 (0.33–0.76)	*< 0.01**	0.53 (0.30–0.84)	*0.03**
Hb (1 g/dl intervals)	0.83 (0.70–0.98)	*0.03**	0.99 (0.79–1.24)	*0.95*
CRP (1 g/dl intervals)	2.23 (0.95–1.12)	*0.17*		
Pancolitis, n (%)	0.85 (0.38–1.97)	*0.69*		
Cancer/dysplasia, n (%)	0.26 (0.06–1.13)	*0.05*		
ASA ≥ 3, n (%)	1.60 (0.67–3.79)	*0.27*		
Total PSL dose (per 100 mg)	1.00 (0.99-1.00)	*0.37*		
Immunosuppressant administration	0.59 (0.25–1.38)	*0.22*		
Calcineurin inhibitor administration	0.91 (0.33–2.49)	*0.86*		
Janus kinase inhibitor administration	1.10 (0.14–8.73)	*0.92*		
Biologic administration	0.74 (0.31–1.74)	*0.49*		
Oral antimicrobial prophylaxis	0.29 (0.10–0.87)	*0.01**	0.34 (0.11–1.03)	*0.03**

Factors	Univariate		Multivariate
	OR (95% CI) *p value*		OR (95% CI) *p value*
Emergent/urgent surgery	1.50 (0.58–3.86)	*0.39*	
Laparoscopic surgery	0.39 (0.13–1.16)	*0.08*	
Operative time (per min)	0.99 (0.99-1.00)	*0.52*	
Blood loss (per 100 ml)	1.00 (0.87–1.19)	*0.78*	
Changing surgical instruments	2.39 (0.51–10.99)	*0.24*	

SSI = Surgical site infection, UC = Ulcerative colitis, OR = odds ratio, CI = Confidence interval, Alb = Albumin, ASA = American Society of Anesthesiologists, BMI = Body mass index, CRP = C-reactive protein, PSL = Prednisolone

* $p < 0.05$ (indicates a significant difference)

Table 5
Logistic regression analysis of the risk factors for organ/space SSIs

Factors	Univariate		Multivariate	
	OR (95% CI) *p value*		OR (95% CI) *p value*	
Male sex	0.91 (0.41–1.98)	*0.81*		
Age at surgery, (10-year intervals)	0.99 (0.96–1.01)	*0.61*		
Duration of disease (1-month intervals)	0.99 (0.99-1.00)	*0.12*		
BMI ≥ 25	0.69 (0.15-3.00)	*0.62*		
Severe disease	1.97 (0.92–4.21)	*0.07*		
Alb (1 g/dl intervals)	0.65 (0.44–0.96)	*0.03**	0.72 (0.43–1.18)	*0.19*
Hb (1 g/dl intervals)	0.93 (0.79–1.08)	*0.37*		
CRP (1 g/dl intervals)	1.05 (0.96–1.14)	*0.26*		
Pancolitis, n (%)	1.23 (0.41–3.62)	*0.70*		
Cancer/dysplasia, n (%)	0.82 (0.32–2.05)	*0.67*		
ASA ≥ 3, n (%)	2.50 (1.16–5.37)	*0.01**	2.32 (1.07–5.04)	*0.03**
Total PSL dose (per 100 mg)	1.00 (0.99-1.00)	*0.80*		
Immunosuppressant administration	0.77 (0.36–1.67)	*0.51*		
Calcineurin inhibitor administration	0.76 (0.28–2.03)	*0.58*		
Janus kinase inhibitor administration	0 (-)	*0.28*		
Biologic administration	0.97 (0.45–2.10)	*0.95*		
Oral antimicrobial prophylaxis	0.32 (0.12–	*0.01**	0.37 (0.13–	*0.04**

Factors	Univariate		Multivariate	
	OR (95% CI) *p value*		OR (95% CI) *p value*	
	0.85)		1.05)	
Emergent/urgent surgery	2.22 (0.98–5.05)	*0.04**	1.10 (0.37–3.22)	*0.85*
Laparoscopic surgery	0.43 (0.16–1.15)	*0.08*		
Operative time (per min)	0.99 (0.99-1.00)	*0.34*		
Blood loss (per 100 ml)	1.02 (0.89–1.18)	*0.72*		
Changing surgical instruments	0 (-)	*0.27*		

SSI = Surgical site infection, UC = Ulcerative colitis, OR = odds ratio, CI = Confidence interval, Alb = Albumin, ASA = American Society of Anesthesiologists, BMI = Body mass index, CRP = C-reactive protein, PSL = Prednisolone

* $p < 0.05$ (indicates a significant difference)

Discussion

In this study, we analyzed the risk factors for SSIs in UC patients in the biologic era and determined the effectiveness of new anti-SSI measures. The results indicated that the overall SSI rate for UC patients who underwent two-stage restorative proctocolectomy was relatively low at 8.9% in the biologic era, with a decreasing trend with annual changes in linear regression equations. Oral antimicrobial prophylaxis reduced the risk of SSIs and was found to be an effective anti-SSI measure.

With respect to SSI rates in UC patients, Fazio et al. reported that the wound infection rate was 5.8% and that the infectious complication rate was 20.6% in 1005 IPAA patients, including UC patients, from 1983 to 1993 [18]. After the advent of the biologic era, Alavi et al. reported an overall SSI rate of 22.6% for inflammatory bowel disease (IBD) surgeries via the National Surgical Quality Improvement Program [19]. Therefore, based on simple percentage comparisons alone, a prominent increase in the overall incidence of SSIs was not observed in the biologic era. Additionally, a recent large prospective multicenter cohort study reported that preoperative anti-TNF therapy was not associated with the occurrence of postoperative infectious complications or SSIs [20]. Certainly, the limitation of that study was that no specific surgical approach was defined. Another study reported that the incidence of postoperative complications significantly increased in IBD patients who underwent restorative proctocolectomy and received anti-TNFα treatment, with a 13.8-fold increase in the incidence of postoperative infection compared with that in the nontreated group [4]. However, in this study, despite the increasing trend in the rate of preoperative administration of biologics, the SSI rate remained relatively low and tended to decrease, with an acceptable coefficient of determination, even when the surgical procedure was limited

to a two-stage restorative proctocolectomy. Moreover, with respect to preoperative pharmacotherapy, there was no significant difference between the SSI group and the non-SSI group.

Risk factors for SSIs include malnutrition, ASA score ≥ 3, preoperative steroid dosage, advanced age, disease severity, emergency surgery, blood loss, and combination therapy with biologic agents and thiopurines [21–24] [25]. Risk factors for postoperative infectious complications, including SSIs, have been reported to include age, preoperative comorbidities, time from admission to surgery, smoking, anemia, hypoalbuminemia, body mass index, corticosteroid therapy, treatment with calcineurin inhibitors, biologic therapy, and emergency surgery [5] [19, 26] [27]. Therefore, while the decreasing trend in SSIs may be attributed to a decrease in the corticosteroid dose due to the administration of biologics, minimally invasive surgery, and decreased blood loss, the increase in the number of patients receiving biologics and the aging of the population and its associated comorbidities may lead to an increase in the SSI rate [28]. However, in the present study, age, corticosteroid dose, biologic treatment, laparoscopic surgery, and blood loss were not risk factors, the Alb level was identified as a risk factor for overall SSIs, and incisional SSIs and ASA scores ≥ 3 were identified as risk factors for organ/space SSIs. We reaffirmed the strong influence of the preoperative condition on the postoperative course.

A unique feature of the present study is that in addition to laparoscopic surgery, we added oral antimicrobial prophylaxis and changing surgical instruments as explanatory factors. Although laparoscopic surgery did not significantly reduce the risk of SSIs, the SSI rate tended to be lower in patients who underwent laparoscopic surgery. Furthermore, laparoscopic surgery has been reported to have certain advantages, such as cosmesis, early postoperative oral intake, and better quality of life [29, 30]. Consequently, The introduction of laparoscopic surgery is acceptable. With respect to surgical instrument changes, there was no difference in the rate of SSIs. This finding parallels that of our previous study on colorectal surgery, and consequently, instrument changes may not need to be performed routinely [31]. However, the results in cases limited to contaminated surgeries in IBD patients are unknown; therefore, in future studies, surgical instrument changes should be evaluated in patients with contaminated or infected wounds. Preoperative oral antibiotics have already been shown to be effective in open colorectal surgery in a Cochrane meta-analysis [32]. Reducing the number of aerobic and anaerobic microorganisms in the colon may have additional benefits for preventing SSIs [33]. Nevertheless, after minimally invasive surgery became more popular, only 36% of surgeons used oral antimicrobial prophylaxis, according to a 2010 report [34]. In Japan, only 18% of facilities administer oral antimicrobial prophylaxis for colorectal surgery [35]. Recently, the benefits of preoperative oral antimicrobial therapy have been reevaluated with respect to the benefits of preoperative antimicrobial therapy in general. For example, oral antimicrobial prophylaxis was reported to significantly reduce the risk of SSIs following elective laparoscopic colorectal surgery [36]. Moreover, we previously reported that oral antimicrobial prophylaxis in patients with Crohn’s disease contributed to the prevention of SSIs [37].

There are several limitations to the present study. First, this was a retrospective analysis performed at a single institution. Second, a problem with studies that examine outcomes over a given period is that concurrent changes in medical practice over time, such as changes in various medical treatments for

UC, may be a potential confounding factor. Third, the oral antimicrobial prophylaxis introduced after 2017 could have influenced the results, as it could not be administered in emergency surgery cases such as perforations. However, in the present study, no strong correlation was found between emergency/urgent surgery, antibiotics, and laparoscopic surgery in terms of the Spearman's rank correlation coefficient, which could be added to the multivariate analysis as an explanatory variable. Oral antimicrobial prophylaxis is difficult to administer before emergency surgery; consequently, future research should address the question of what measures should be taken to prevent SSIs in emergency surgeries with frequent infectious complications.

Conclusions

Preoperative Alb levels and an ASA score ≥ 3 were identified as risk factors for SSIs. Despite the increasing use of biologics, SSI rates have been declining, which suggests that anti-SSI measures may be effective. Among the three SSI-related measures, nonadministration of oral antibiotic prophylaxis was identified as a risk factor for SSIs. Oral antibiotic prophylaxis before restorative proctocolectomy may improve the postoperative quality of life of UC patients by preventing SSIs, even in the era of minimally invasive surgery and biological agents.

Abbreviations

Surgical site infection (SSI), Ulcerative colitis (UC), Crohn’s disease (CD), Body mass index (BMI), American Society of Anesthesiologists (ASA), Prednisolone (PSL), Albumin (Alb), C-reactive protein (CRP), Odds ratios (ORs), Confidence intervals (CIs)

Declarations

Acknowledgments: None

Funding: None

Author Contributions: Yuki Horio: conception and design of the study; acquisition, analysis and interpretation of the data; and drafting of the article. Kentaro Nagano, Kurando Kusunoki, Ryuichi Kuwahara, Kei Kimura, Kozo Kataoka, Naohito Beppu: conception and design of the study; acquisition, analysis and interpretation of the data. Kazuhiko Nakajima, Kaoru Ichiki, and Takashi Ueda, SSI data acquisition (infection control team). Motoi Uchino, Masataka Ikeda, Hiroki Ikeuchi: acquisition of the data, drafting of the article and critical revision of the article for important intellectual content, and final approval.

Disclosures: The authors declare no conflicts of interest.

Ethics declarations

Conflicts of interest: The authors declare that they have no competing interests.

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Figures

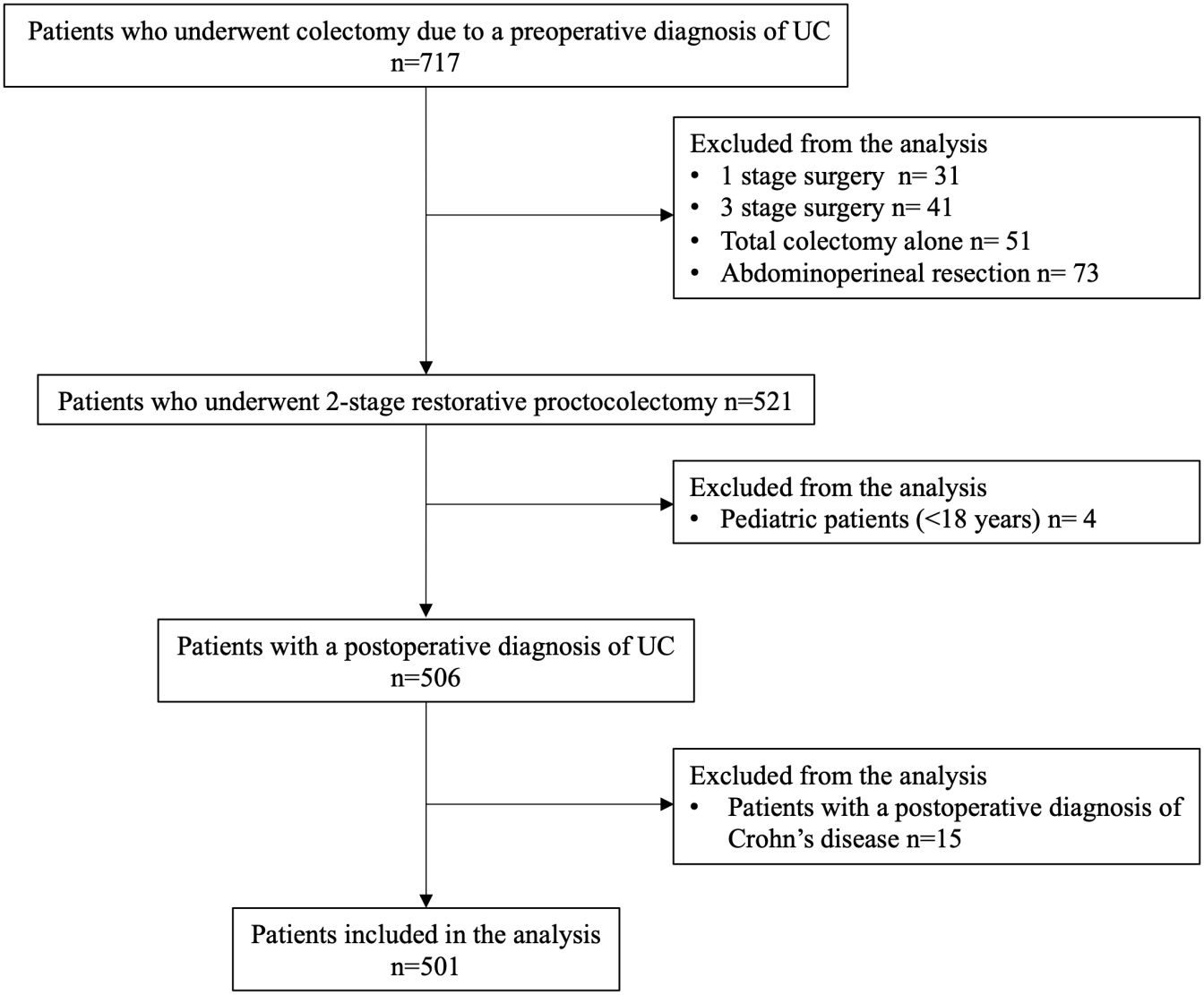

Figure 1

UC patient flow chart.

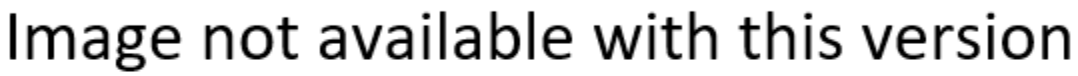

Figure 2

Annual SSI incidence rates from 2012 to 2023. Linear regression analysis was performed for overall SSI, incisional SSI, and organ/space SSI.