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Postoperative complications and prognosis based on type of surgery in ulcerative colitis patients with colorectal cancer: A multicenter observational study of data from the Japanese Society for Cancer of the Colon and Rectum

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Abstract

Background: Patients with ulcerative colitis are reported to be at increased risk of colorectal cancer and are also at high risk of postoperative complications. However, the incidence of postoperative complications in these patients and how the type of surgery performed affects prognosis are not well understood.

Methods: Data collected by the Japanese Society for Cancer of the Colon and Rectum on ulcerative colitis patients with colorectal cancer between January 1983 and December 2020 were analyzed according to whether total colorectal resection was performed with ileoanal anastomosis (IAA), ileoanal canal anastomosis (IACA), or permanent stoma creation. The incidence of postoperative complications and the prognosis for each surgical technique were investigated.

Results: The incidence of overall complications was not significantly different among the IAA, IACA, and stoma groups (32.7%, 32.3%, and 37.7%, respectively; p = 0.510). The incidence of infectious complications was significantly higher in the stoma group (21.2%) than in the IAA (12.9%) and IACA (14.6%) groups (p = 0.048); however, the noninfectious complication rate was lower in the stoma group (13.7%) than in the IAA (21.1%) and IACA (16.2%) groups (p = 0.088). Five-year relapse-free survival was higher in patients without complications than in those with complications in the IACA group (92.8% vs. 75.2%; p = 0.041) and the stoma group (78.1% vs. 71.2%, p = 0.333) but not in the IAA group (90.3% vs. 90.0%, p = 0.888).

Conclusion: The risks of infectious and noninfectious complications differed according to the type of surgical technique used. Postoperative complications worsened prognosis.

KEYWORDS

colorectal neoplasms, postoperative complication, prognosis, ulcerative colitis

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1 | INTRODUCTION

Ulcerative colitis is a chronic inflammatory disease of the colon, and the mainstay of treatment is pharmacotherapy, including 5-aminosalicylic acid, steroids, and immunosuppressive agents.¹⁻⁴ Surgery is required in patients with ulcerative colitis if they develop colorectal cancer, when drug treatment is unsuccessful, or if the condition becomes an emergency, such as toxic megacolon or intestinal perforation.⁵⁻⁷ The standard surgical procedure for ulcerative colitis is reconstruction of the intestinal tract by ileoanal anastomosis (IAA) or ileoanal canal anastomosis (IACA) after total colorectal resection.^{8,9} When intestinal anastomosis is not possible for anatomical reasons such as inability to bring the two remaining ends of the intestinal tract close enough together, or when anastomosis of the small intestine and anus or anal canal in the pelvis is not desirable for oncological reasons such as advanced cancer, a permanent ileostomy is created.

The reported overall complication rates after surgery for colorectal cancer in ulcerative colitis patients range from 9% to 65%, with infectious complication rates of 10%–45% and mortality of 0%–5.2%.^{10,11} Patients with ulcerative colitis are often treated with a variety of medications and the status of their intestinal tract is worse than that in patients without ulcerative colitis. There are postoperative complications specific to patients with ulcerative colitis, including pouch-related complications. Patients with ulcerative colitis are also at high risk of colorectal cancer and for developing postoperative complications.^{12,13} Several types of surgery are performed for patients with ulcerative colitis who develop colorectal cancer, including IAA, IACA, and permanent placement of a stoma. However, there is limited information on the risk of complications for each surgical procedure in these patients.

Postoperative complications have been reported to worsen both short-term and long-term prognosis in various types of cancer.¹⁴⁻¹⁹ Although there have been reports suggesting an association between postoperative complications and worse prognosis after surgery for colorectal cancer or liver metastases of colorectal cancer,^{20,21} little is known about this association in ulcerative colitis patients with colorectal cancer. In this study, we examined the association between postoperative complications and prognosis in these patients according to type of surgical procedure.

2 | PATIENTS AND METHODS

2.1 | Study design and setting

Information on patients who had undergone upfront radical surgery for up to stage III colorectal cancer was extracted from the Japanese Society for Cancer of the Colon and Rectum (JSCCR) data on ulcerative colitis patients with gastrointestinal cancer or dysplasia between January 1983 and December 2020 and were treated at any of 43 participating hospitals.²² Patients for whom there was no information on postoperative complications and those who underwent other types of surgery were excluded. The final study population included patients who had undergone any one of the three typical surgical procedures for ulcerative colitis comorbid with colorectal cancer, namely, total colorectal resection with ileoanal anastomosis (the IAA group), total colorectal resection with ileoanal canal anastomosis (the IACA group), or total colorectal resection with permanent placement of a stoma (the stoma group).

The incidence of postoperative complications was compared among the three surgical procedures. Postoperative complications were categorized as infectious or noninfectious and their relationship with prognosis according to type of surgical procedure was investigated. Overall survival (OS) was defined as the time interval between the date of surgery and the date of death and recurrencefree survival (RFS) was defined as the time interval between the date of surgery and the date of recurrence or death, whichever came first. Five-year OS and RFS were compared according to the presence or absence of postoperative complications. The study was approved by the Ethics Committee of Kyoto University (ID: R2348). The need for informed consent was waived in view of the anonymity of the data.

2.2 | Statistical analysis

Categorical variables are shown as the number and percentage and were compared using Fisher's exact test. Five-year OS and RFS were estimated using the Kaplan-Meier method and compared using the log-rank test. Risk factors for complications and their effect on 5-year RFS were identified using univariable and multivariable Cox proportional hazards models. Clinical factors with the potential to have a confounding effect on 5-year RFS were adjusted for in the multivariable model. All statistical analyses were performed using JMP statistical software version 15 (SAS Institute Inc.). All *p*-values were two-sided and those less than 0.05 were considered statistically significant.

3 | RESULTS

3.1 | Patient characteristics

A total of 1222 patients with gastrointestinal cancer or dysplasia comorbid with ulcerative colitis underwent surgery during the study period. Of these, 942 underwent radical upfront surgery for up to stage III colorectal cancer. After exclusion of eight patients for whom there were no data on postoperative complications and 147 who underwent other types of surgery, data for 511 patients who underwent IAA, 130 who underwent IACA, and 146 who underwent permanent stoma creation were available for analysis (Figure 1). The patient characteristics are shown in Table 1. Compared with patients in the IAA and IACA groups, those in the stoma group were older, had a shorter history of ulcerative colitis, had a higher carcinoembryonic antigen level, were more likely to have rectal cancer, more poorly differentiated cancer, a deeper -WILEY- AGSurg Annals of Gastroenterological Surgery

tumor depth, and more lymph node metastasis, and were more likely to receive adjuvant chemotherapy. There were more Stage III patients in the stoma group and patients with more advanced cancer had a greater likelihood undergoing permanent stoma creation.

The relation between presence or absence of complications and the administration of adjuvant chemotherapy in Stage III patients are shown in Table S1. Patients with postoperative complications were less likely to receive adjuvant chemotherapy than those without postoperative complications in IAA and IACA groups.

3.2 | Postoperative complications

The incidence of overall complications was not significantly different among the IAA, IACA, and stoma groups (32.7%, 32.3%, and 37.7%, respectively; p = 0.510). The incidence of infectious complications was significantly higher in the stoma group (21.2%) than in the IAA (12.9%) group and the IACA group (14.6%) (p = 0.048). Meanwhile, the incidence of noninfectious complications was higher in the IAA (21.6%) group and the IACA (16.2%)

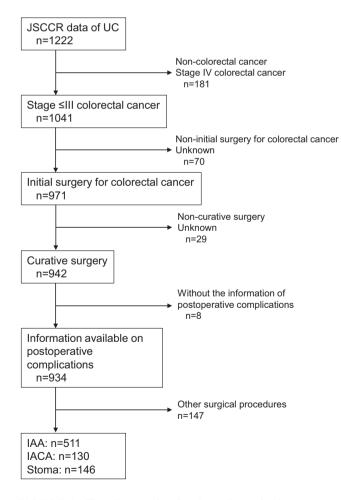


FIGURE 1 Flow diagram showing the patient selection process. IAA, ileoanal anastomosis; IACA, ileoanal canal anastomosis; JSCCR, Japanese Society for Cancer of the Colon and Rectum; UC, ulcerative colitis.

group than in the stoma group (13.7%), but the difference was not statistically significant (p = 0.088).

The incidence of anastomotic leakage tended to be higher in the IACA group than in the IAA group (6.2% vs. 3.3%; p = 0.135). The surgical site infection (SSI) rate was significantly higher in the stoma group (8.9%) than in the IAA and IACA groups (2.9% and 1.5%, respectively; p = 0.004). The incidence of high output syndrome/ diarrhea/dehydration tended to be higher in the IAA group than in the IACA and stoma groups (2.7% vs. 0.8% and 0.0%, respectively; p = 0.051). There were no significant between-group differences in the rates of other complications. Details of complications are shown in Table 2.

3.3 | Recurrence patterns based on surgical technique

The recurrence patterns are shown in Table S2. Lymph node recurrence and lung metastasis were significantly more frequent in stoma group (4.8%, 5.5%, respectively) than in IAA group (0.6%, 1.2%, respectively) and IACA group (0.8%, 0.8%, respectively). The other recurrences were not significantly different among the three groups.

3.4 | Five-year OS and RFS

The 5-year OS was 93.3% in the IAA group, 94.5% in the IACA group, and 82.5% in the stoma group; the difference among the three groups was statistically significant (p = 0.001), as was the 5-year RFS (90.2%, 88.1%, and 75.5%, respectively; p < 0.001).

3.5 | Overall complications and 5-year OS and RFS

Figure 2 shows OS according to the presence or absence of postoperative overall complications for each type of surgery. In the IAA group, there was no significant difference in 5-year OS between patients without and with overall complications (93.1% vs. 93.6%; p = 0.687). In the IACA group, 5-year OS was higher in patients without overall complications than in those with overall complications, but the difference was not statistically significant (96.8% vs. 88.4%; p = 0.098). In the stoma group, there was no significant difference in 5-year OS between patients without and with overall complications (82.3% vs. 83.1%; p = 0.912).

Figure 2 also shows RFS according to the presence or absence of postoperative overall complications for each type of surgery. In the IAA group, there was no significant difference in 5-year RFS between patients without and with overall complications (90.3% vs. 90.0%, p = 0.888). The 5-year RFS was significantly higher in patients without overall complications in the IACA group (92.8% vs. 75.2%; p = 0.041) and was also higher in those without overall complications in the stoma group (78.1% vs. 71.3%; p = 0.333) but the difference was not statistically significant.

		IAA(n = 511)	511)			ACA (n = 130)	= 130)			Stoma (n = 146)	= 146)		
		Complication	tion			Complication	tion			Complication	ation		
		I		+		I		+		I		+	
Variable	Category	2	%	2	%	2	%	2	%	2	%	2	%
Age at time of	<70	330	96.5	157	95.7	78	90.7	38	90.5	64	70.3	43	78.2
surgery (years)	≥70	12	3.5	7	4.3	8	9.3	4	9.5	27	29.7	12	21.8
Sex	Σ	191	55.7	110	66.7	55	63.2	31	73.8	58	63.7	38	69.1
	ш	152	44.3	55	33.3	32	36.8	11	26.2	33	36.3	17	30.9
Extent of UC	Total colon	268	78.6	137	82.5	72	82.8	37	88.1	70	76.9	41	75.9
	Left colon	99	19.4	28	16.9	12	13.8	5	11.9	19	20.9	10	18.5
	Rectum	4	1.2	1	0.6	2	2.3	0	0.0	1	1.1	ю	5.6
	Other	S	0.9		0.0	1	1.1	0	0.0	1	1.1	0	0.0
Duration of UC	<10	56	16.5	33	20.0	18	20.9	7	17.1	20	22.0	18	32.7
(years)	10≤, <20	166	48.8	71	43.0	42	48.8	16	39.0	37	40.7	19	34.5
	20≤	118	34.7	61	37.0	26	30.2	18	43.9	34	37.4	18	32.7
CEA (ng/mL)	<5	245	88.8	141	89.8	74	91.4	34	89.5	59	73.8	42	80.8
	≥5	31	11.2	16	10.2	7	8.6	4	10.5	21	26.3	10	19.2
Approach	Open	207	60.4	81	49.1	29	33.0	15	36.6	50	54.9	32	60.4
	Lap, Rob	136	39.7	84	50.9	59	67.0	26	63.4	41	45.1	21	39.6
Tumor location	Right colon	47	13.9	24	14.5	15	17.0	7	16.7	11	12.1	ю	5.5
	Left colon	162	47.8	75	45.5	54	61.4	21	50.0	31	34.1	13	23.6
	Rectum	130	38.3	99	40.0	19	21.6	14	33.3	49	53.8	39	70.9
Pathology findings	Differentiated	268	81.5	130	77.8	73	84.9	31	77.5	66	75.9	41	77.4
	Undifferentiated	47	14.3	20	12.0	13	15.1	4	10.0	18	20.7	12	22.6
	Other	14	4.3	17	10.2	0	0.0	5	12.5	ო	3.4	0	0.0
рТ	0-2	246	73.0	113	68.9	61	69.3	28	71.8	48	53.3	25	45.5
	3, 4	91	27.0	51	31.1	27	30.7	11	28.2	42	46.7	30	54.5
Nd	0	291	85.8	140	85.4	74	84.1	38	90.5	62	69.7	37	67.3
	+	48	14.2	24	14.6	14	15.9	4	9.5	27	30.3	18	32.7
Stage	_	232	69.5	107	66.5	56	63.6	28	71.8	45	51.1	25	45.5
	=	54	16.2	30	18.6	18	20.5	7	17.9	16	18.2	12	21.8
	≡	48	14.4	24	14.9	14	15.9	4	10.3	27	30.7	18	32.7
AC	1	276	80.9	141	84.9	72	82.8	39	92.9	67	73.6	34	63.0
	+	65	19.1	25	15.1	15	17.2	ო	7.1	24	26.4	20	37.0
Abbreviations: AC, adj	Abbreviations: AC, adjuvant chemotherapy; CEA, carcinoembryonic antigen; IAA, ileoanal anastomosis; IACA, ileoanal canal anastomosis; Lap, laparoscopic; Rob, robotic-assisted; UC, ulcerative colitis.	CEA, carcino	embryonic a	ntigen; IAA, il	eoanal anasto	mosis; IACA,	ileoanal canal	anastomosis	; Lap, laparosc	opic; Rob, ro	botic-assisted	l; UC, ulcera	tive colitis.

TABLE 1 Patient characteristics

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TABLE 2 Postoperative complications	
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	IAA		IACA		Stoma		
	n = 511		n = 130		n = 146		
	n	%	n	%	n	%	p-Value
Overall complications	167	32.7	42	32.3	55	37.7	0.510
Infectious complications	66	12.9	19	14.6	31	21.2	0.048
Anastomotic leakage	17	3.3	8	6.2	-	_	0.135
Incisional SSI	15	2.9	2	1.5	13	8.9	0.004
Intraabdominal/pelvic abscess	10	2.0	2	1.5	4	2.7	0.753
Pouchitis	9	1.8	1	0.8	_	—	0.696
Colitis	4	0.8	0	0.0	1	0.7	0.831
Noninfectious complications	108	21.1	21	16.2	20	13.7	0.088
lleus/Intestinal obstruction	44	8.6	14	10.8	11	7.5	0.618
High output syndrome / diarrhea/dehydration	14	2.7	1	0.8	0	0.0	0.051
Stoma outlet obstruction	13	2.5	2	1.5	1	0.7	0.426
Thrombosis	11	2.2	0	0.0	1	0.7	0.195
Bleeding	3	0.6	1	0.8	2	1.4	0.593
Anastomotic stenosis	5	1.0	0	0.0	0	0.0	0.519

Abbreviations: IAA, ileoanal anastomosis; IACA, ileoanal canal anastomosis; SSI, surgical site infection.

3.6 | Postoperative infectious complications and 5-year OS and RFS

Figure 3 shows OS according to the presence or absence of postoperative infectious complications in each surgery group. In the IAA group, there was no significant difference in 5-year OS between patients without and with overall complications (93.5% vs. 92.7%; p = 0.985). In the IACA group, the 5-year OS was higher in patients without infectious complications, but this finding was not statistically significant (96.2% vs. 83.3%; p = 0.090). In the stoma group, there was no significant difference in 5-year OS between patients without and with infectious complications (80.1% vs. 91.8%; p = 0.269).

Figure 3 also shows the RFS according to the presence or absence of postoperative infectious complications and type of surgery performed. In the IAA group, there was no significant difference in 5-year RFS between patients without and with infectious complications (90.1% vs. 91.1%; p = 0.665). In the IACA group, 5-year RFS was significantly higher in patients without infectious complications (91.4% vs. 66.7%, p = 0.021). In the stoma group, there was no significant difference in 5-year RFS between patients without and with infectious complications (75.3% vs. 76.2%; p = 0.921).

3.7 | Noninfectious postoperative complications and 5-year OS and RFS

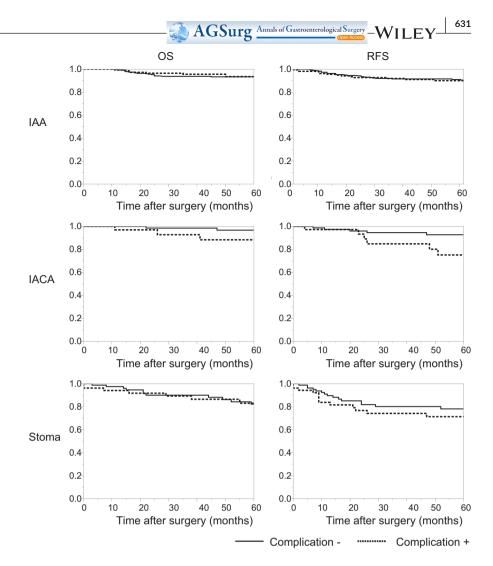
Figure 4 shows OS according to the presence or absence of noninfectious postoperative complications is shown for each type of surgery in Figure 4. In the IAA group, there was no significant difference in 5-year OS between patients without and with noninfectious complications (92.9% vs. 95.1%; p = 0.490). In the IACA group, patients without noninfectious complications had a higher 5-year OS but this finding was not statistically significant (95.9% vs. 85.9%, p = 0.067). In the stoma group, the 5-year OS was significantly higher in patients without noninfectious complications (86.2% vs. 60.3%, p = 0.008).

Figure 4 also shows the RFS according to the presence or absence of postoperative noninfectious complications for each type of surgery. In the IAA group, there was no significant difference in 5-year RFS between patients without and with noninfectious complications (90.3% vs. 90.4%, p = 0.771). In the IACA group, 5-year RFS was higher in patients without noninfectious complications, but the difference was not statistically significant (89.9% vs. 75.4%, p = 0.178). In the stoma group, the 5-year RFS was significantly higher in patients without noninfectious complications (79.4% vs. 50.9%, p = 0.008).

3.8 | Prognostic factors affecting 5-year RFS

Prognostic factors affecting 5-year RFS were investigated in each group (Table S3). Five-year RFS was significantly associated with pT and pN disease and adjuvant chemotherapy in all surgery groups. Pathology findings were significantly associated in the IAA and stoma groups, and sex was significantly associated in the stoma group. Age, sex, pathology findings, pT and pN disease, and adjuvant chemotherapy were entered in the multivariable analysis to determine the prognostic effect of complications on 5-year RFS. FIGURE 2 Five-year overall survival and recurrence-free survival for each surgical procedure according to presence or absence of overall complications. IAA, ileoanal anastomosis; IACA, ileoanal canal anastomosis; OS, overall survival; RFS, relapse-free survival.

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3.9 | Effect of overall complications on 5-year RFS

In the multivariable analysis, there was no significant difference in 5-year RFS between patients without and with overall complications (hazard ratio [HR] 1.11, 95% confidence interval [CI] 0.58– 2.15, p = 0.751) in the IAA group. In the IACA group, 5-year RFS was higher in patients without overall complications (HR 3.47, 95% CI 0.84–14.37, p = 0.086) but did not reach statistical significance. In the stoma group, there was no significant difference in RFS between patients without and with overall complications (HR 1.09, 95% CI 0.51–2.34, p = 0.816; Table 3).

3.10 | Effect of infectious complications on 5year RFS

In the multivariable analysis, infectious complications had no significant effect on 5-year RFS in the IAA group (HR 0.91, 95% CI 0.35-2.42, p = 0.857). In the IACA group, 5-year RFS was higher in patients without infectious complications (HR 4.71, 95% CI 0.92-24.12, p = 0.063) but did not reach statistical significance. In the stoma group, there was no significant difference in 5-year RFS between patients without and with infectious complications (HR 0.88, 95% CI 0.34–2.30, p = 0.799; Table 3).

3.11 | Effect of noninfectious complications on 5-year RFS

In multivariable analysis, there was no significant between-group difference in 5-year RFS (IAA group, HR 1.18, 95% CI 0.56–2.50, p = 0.666; IACA group, HR 1.31, 95% CI 0.23–7.36, p = 0.756; stoma group, HR 1.66, 95% CI 0.72–3.84, p = 0.236; Table 3).

3.12 | Subgroup analysis of 5-year OS and 5-year RFS according to stage

Five-year OS and RFS according to stage were shown in Table 4. Overall, patients in the IAA group did not have a worse prognosis due to complications (Figure 2). However, patients with complications in stage II or stage III tended to have worse 5-year OS and 5-year RFS than those without complications in the IAA group.

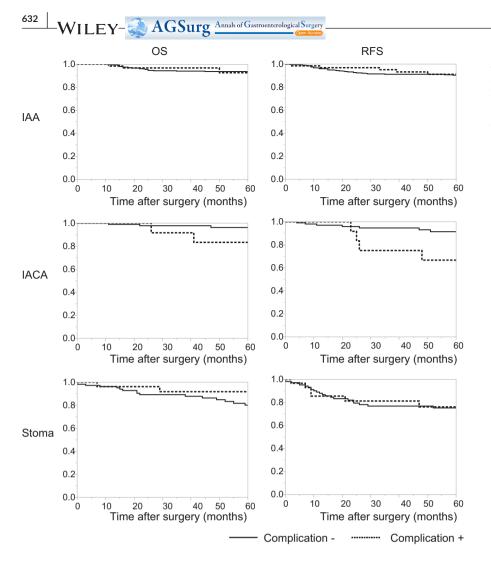


FIGURE 3 Five-year overall survival and recurrence-free survival for each surgical procedure according to presence or absence of infectious complications. IAA, ileoanal anastomosis; IACA, ileoanal canal anastomosis; OS, overall survival; RFS, relapse-free survival.

4 | DISCUSSION

In this study, we investigated three common surgical techniques used in ulcerative colitis patients with colorectal cancer, namely, IAA, IACA, and stoma creation, and found differences in patient characteristics and the incidence of postoperative complications among these techniques. We also showed that postoperative complications may worsen the prognosis in these patients.

Ileoanal anastomosis is considered the first choice for ulcerative colitis patients with colorectal cancer in Japan and was the most frequently performed procedure in this study. Although IACA or stoma creation may be the first choice in some institutions, IACA or stoma creation may be selected when IAA is not indicated for anatomical reasons or because of tumor progression. The survival curves for OS and RFS indicate that the degree of deterioration was greater for RFS than for OS in patients with postoperative complications. This would suggest a close association of postoperative complications with recurrence of disease.

Although we found no significant difference in the overall incidence of postoperative complications among the three surgical techniques, the incidence of infectious complications was higher in the stoma group. This finding could possibly have reflected the significantly higher incidence of incisional SSI in the stoma group. However, a temporary ileostomy was also created in the IAA and IACA groups, and the higher incidence of infectious complications, including incisional SSI, in patients who underwent permanent stoma creation was more likely to reflect their poor general condition, such that reconstruction was not possible, than creation of the stoma per se. On the other hand, noninfectious complications, including ileus/intestinal obstruction, high output syndrome/ diarrhea/dehydration, and thrombosis, were more common in the IAA and IACA groups and might be due to the extra operation time required for intestinal reconstruction and the increased postoperative burden resulting from delayed postoperative weaning and prolonged intestinal edema.

Postoperative complications can worsen the prognosis, not only directly but also indirectly, by causing delays in the start of drug treatment.^{23,24} The mechanism by which postoperative complications worsen prognosis is not fully understood; one possibility is that they are associated with inflammation, which in turn induces an immunosuppressive state.^{15,21,25} Furthermore, postoperative complications can lead to general debility and failure to receive adjuvant chemotherapy or delay its start, which has been shown to have an adverse prognostic impact in patients with colorectal cancer.^{26,27} In this study, patients with postoperative complications were less likely to receive adjuvant chemotherapy than

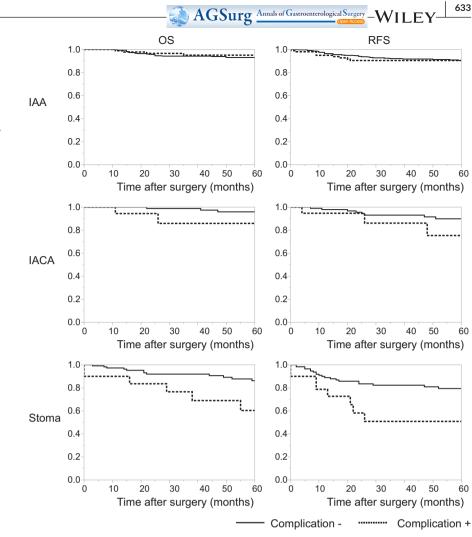


TABLE 3 Multivariable analyses of postoperative complications affecting 5-year RFS

		IAA			IACA			Stoma		
Complication		HR	95% CI	p-Value	HR	95% CI	p-Value	HR	95% CI	p-Value
Overall	+/-	1.11	0.58-2.15	0.751	3.47	0.84-14.37	0.086	1.09	0.51-2.34	0.816
Infectious	+/-	0.91	0.35-2.42	0.857	4.71	0.92-24.12	0.063	0.88	0.34-2.30	0.799
Noninfectious	+/-	1.18	0.56-2.50	0.666	1.31	0.23-7.36	0.756	1.66	0.72-3.84	0.236

Abbreviations: CI, confidence interval; HR, hazard ratio; IAA, ileoanal anastomosis; IACA, ileoanal canal anastomosis; RFS. relapse-free survival.

those without postoperative complications in Stage III patients in IAA and IACA groups, suggesting that patients who experienced postoperative complications may have missed the opportunity to receive adjuvant chemotherapy as a result of these complications in addition to their already poor general condition. For patients in the IAA group overall, complications did not worsen the prognosis. However, complications worsened the prognosis in higher stages. In addition, the prognosis of patients with complications in the IACA group was particularly poor, largely due to the lower rate of adjuvant chemotherapy.

The strength of this study is that it included a large number of cases from many facilities throughout Japan, which allowed us to examine the effects of the three typical surgical methods used to treat colorectal cancer in patients with ulcerative colitis. Given that the patient's general health status is an important consideration when selecting the surgical procedure, inclusion of such a large number of patients allowed us to consider each procedure separately, thereby minimizing the possibility of selection bias.

However, the study also had some limitations. First, it had a retrospective observational design, which meant that the potential influence of other factors on the association between postoperative complications and prognosis may not have been completely eliminated. Nevertheless, we believe that our findings reflect the reality of clinical practice. Second, because the study period was extended

FIGURE 4 Five-year overall survival and recurrence-free survival for each surgical procedure according to presence or absence of noninfectious complications. IAA, ileoanal anastomosis; IACA, ileoanal canal anastomosis; OS, overall survival; RFS, relapse-free survival.

		IAA			IACA			Stoma		
		I	П	111	I	П	111	I	П	111
5-year overall survival										
Overall complication	-	95.7	93.0	79.5	100.0	90.9	90.9	100.0	74.1	55.5
	+	99.0	90.4	65.2	93.3	100.0	50.0	92.0	83.3	70.7
	p-Value	0.176	0.912	0.504	0.103	0.602	0.093	0.056	0.438	0.539
Infectious complication	-	96.2	94.8	77.0	100.0	90.9	84.6	96.4	73.2	58.5
	+	100.0	78.8	68.6	85.7	100.0	_	100.0	100.0	71.4
	p-Value	0.217	0.134	0.751	0.009	0.602	_	0.476	0.267	0.651
Noninfectious complication	_	96.3	90.0	77.7	98.0	92.3	90.9	100.0	82.1	65.5
	+	98.3	100.0	63.6	100.0	100.0	50.0	77.8	66.7	53.6
	p-Value	0.511	0.240	0.534	0.726	0.782	0.093	< 0.001	0.730	0.376
5-year relapse-free survival										
Overall complication	-	94.5	88.3	70.2	97.8	76.9	90.9	100.0	77.0	40.4
	+	96.8	91.2	51.7	80.8	66.7	66.7	87.6	88.9	40.3
	p-Value	0.495	0.604	0.215	0.024	0.972	0.127	0.022	0.393	0.785
Infectious complication	-	94.4	91.3	66.8	95.7	78.0	85.9	96.4	76.6	41.6
	+	100.0	81.5	53.6	71.4	66.7	-	92.9	100.0	38.6
	p-Value	0.135	0.371	0.710	0.008	0.885	-	0.623	0.248	0.763
Noninfectious complication	-	95.4	86.5	67.7	92.2	80.4	90.9	98.1	84.5	43.8
	+	94.9	100.0	55.4	100.0	0.0	50.0	77.8	66.7	28.6
	p-Value	0.737	0.160	0.207	0.458	0.354	0.066	0.003	0.647	0.417

Abbreviations: IAA, ileoanal anastomosis; IACA, ileoanal canal anastomosis.

in order to collect a larger number of cases, we were unable to control for the prognostic impact of improved surgical methods or advances in drug treatment over time.

5 | CONCLUSION

The incidence of infectious and noninfectious postoperative complications differed in ulcerative colitis patients with colorectal cancer according to the surgical technique used. Postoperative complications worsened prognosis.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest for this article.

ETHICAL STATEMENTS

Approval of the research protocol: The protocol for this research project has been approved by the Ethics Committee of Kyoto University (Approval No. R2348).

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REFERENCES

- 1. Ungaro R, Mehandru S, Allen PB, Peyrin-Biroulet L, Colombel JF. Ulcerative colitis. Lancet. 2017;389:1756–70.
- Biondi A, Zoccali M, Costa S, Troci A, Contessini-Avesani E, Fichera A. Surgical treatment of ulcerative colitis in the biologic therapy era. World J Gastroenterol. 2012;18:1861–70.
- Ananthakrishnan AN, Kaplan GG, Bernstein CN, Burke KE, Lochhead PJ, Sasson AN, et al. Lifestyle, behaviour, and environmental modification for the management of patients with inflammatory bowel diseases: an International Organization for Study of inflammatory bowel diseases consensus. Lancet Gastroenterol Hepatol. 2022;7:666–78.
- Ferretti F, Cannatelli R, Monico MC, Maconi G, Ardizzone S. An update on current pharmacotherapeutic options for the treatment of ulcerative colitis. J Clin Med. 2022;11:2302.
- Bohl JL, Sobba K. Indications and options for surgery in ulcerative colitis. Surg Clin North Am. 2015;95:1211–32.
- Ryan DP, Doody DP. Surgical options in the treatment of ulcerative colitis. Semin Pediatr Surg. 2017;26:379–83.

- AGSurg Annals of Gastroenterological Surgery -WILEY
- Andersson P, Söderholm JD. Surgery in ulcerative colitis: indication and timing. Dig Dis. 2009;27:335–40.
- McGuire BB, Brannigan AE, O'Connell PR. Ileal pouch-anal anastomosis. Br J Surg. 2007;94:812–23.
- Saito Y, Sawada T, Tsuno N, Watanabe T, Higuchi Y, Shinozaki M, et al. Total colectomy and ileorectal anastomosis in ulcerative colitis. J Gastroenterol. 1995;30:131–4.
- Peyrin-Biroulet L, Germain A, Patel AS, Lindsay JO. Systematic review: outcomes and post-operative complications following colectomy for ulcerative colitis. Aliment Pharmacol Ther. 2016; 44:807–16.
- Bernstein CN, Ng SC, Lakatos PL, Moum B, Loftus EV, Epidemiology and Natural History Task Force of the International Organization of the Study of Inflammatory Bowel Disease. A review of mortality and surgery in ulcerative colitis: milestones of the seriousness of the disease. Inflamm Bowel Dis. 2013;19:2001–10.
- 12. Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut. 2001;48:526–35.
- Yashiro M. Ulcerative colitis-associated colorectal cancer. World J Gastroenterol. 2014;20:16389–97.
- Savioli F, Edwards J, McMillan D, Stallard S, Doughty J, Romics L. The effect of postoperative complications on survival and recurrence after surgery for breast cancer: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2020;155:103075.
- Chok KS, Ng KK, Poon RT, Lo CM, Fan ST. Impact of postoperative complications on long-term outcome of curative resection for hepatocellular carcinoma. Br J Surg. 2009;96:81–7.
- Yu F, Huang C, Cheng G, Xia X, Zhao G, Cao H. Prognostic significance of postoperative complication after curative resection for patients with gastric cancer. J Cancer Res Ther. 2020; 16:1611–6.
- Li SS, Udelsman BV, Parikh A, Klempner SJ, Clark JW, Roeland EJ, et al. Impact of postoperative complication and completion of multimodality therapy on survival in patients undergoing gastrectomy for advanced gastric cancer. J Am Coll Surg. 2020;230:912–24.
- Hirai T, Yamashita Y, Mukaida H, Kuwahara M, Inoue H, Toge T. Poor prognosis in esophageal cancer patients with postoperative complications. Surg Today. 1998;28:576–9.
- Howard TJ, Krug JE, Yu J, Zyromski NJ, Schmidt CM, Jacobson LE, et al. A margin-negative RO resection accomplished with minimal postoperative complications is the surgeon's contribution to long-term survival in pancreatic cancer. J Gastrointest Surg. 2006;10:1338-45.
- Law WL, Choi HK, Lee YM, Ho JW. The impact of postoperative complications on long-term outcomes following curative resection for colorectal cancer. Ann Surg Oncol. 2007;14:2559–66.
- Mavros MN, de Jong M, Dogeas E, Hyder O, Pawlik TM. Impact of complications on long-term survival after resection of colorectal liver metastases. Br J Surg. 2013;100:711–8.
- Noguchi T, Ishihara S, Uchino M, Ikeuchi H, Okabayashi K, Futami K, et al. Clinical features and oncological outcomes of intestinal cancers associated with ulcerative colitis and Crohn's disease. J Gastroenterol. 2023;58:14–24.
- Wasserman DW, Boulos M, Hopman WM, Booth CM, Goodwin R, Biagi JJ. Reasons for delay in time to initiation of adjuvant chemotherapy for colon cancer. J Oncol Pract. 2015;11:e28–35.
- Elkrief A, Redstone G, Petruccelli L, Ali A, Thomas D, Fernandez M, et al. Reasons for delay in timely administration of adjuvant chemotherapy for patients with stage III colon cancer: a multicentre cohort study from the McGill University Department of oncology. BMJ Open Qual. 2021;10:e000934.
- Okamura Y, Takeda S, Fujii T, Sugimoto H, Nomoto S, Nakao A. Prognostic significance of postoperative complications after hepatectomy for hepatocellular carcinoma. J Surg Oncol. 2011; 104:814-21.

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-WILEY- AGSurg Annals of Gastroenterological Surgery

- 26. Turner MC, Farrow NE, Rhodin KE, Sun Z, Adam MA, Mantyh CR, et al. Delay in adjuvant chemotherapy and survival advantage in stage III colon cancer. J Am Coll Surg. 2018;226:670-8.
- 27. Kim YW, Choi EH, Kim BR, Ko WA, Do YM, Kim IY. The impact of delayed commencement of adjuvant chemotherapy (eight or more weeks) on survival in stage II and III colon cancer: a national population-based cohort study. Oncotarget. 2017;8:80061-72.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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