



# Postoperative complications, bowel function, and prognosis in restorative proctocolectomy for ulcerative colitis—a single-center observational study of 320 patients

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Accepted: 30 October 2021 / Published online: 9 November 2021  
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## Abstract

**Purpose** To determine the selection criteria, postoperative complications, bowel function, and prognosis of stapled ileal pouch-anal anastomosis (IPAA) and hand-sewn IPAA for ulcerative colitis (UC).

**Methods** We defined our surgical indications and strategy, and compared the postoperative complications, bowel function, and prognoses between patients who underwent stapled and hand-sewn IPAA for UC at the Yokohama City University Medical Center between 2004 and 2017.

**Results** Among 320 patients enrolled, 298 patients underwent stapled IPAA while 22 underwent hand-sewn IPAA. There was no significant difference in the postoperative complications between the two groups. Regarding postoperative bowel function, stapled IPAA caused significantly less soiling (stapled vs hand-sewn: 9.1% vs 41.0%, odds ratio (OR)=0.14,  $p < 0.0002$ ), spotting (stapled vs hand-sewn: 23.2% vs 63.6%,  $OR = 0.17$ ,  $p < 0.0001$ ), and difficulty in distinguishing feces from flatus (stapled vs hand-sewn: 39.9% vs 63.6%,  $OR = 0.36$ ,  $p < 0.026$ ). No postoperative neoplasia was observed at the final follow-up in all patients.

**Conclusion** In this study, there was no clear difference in the postoperative complications between stapled and hand-sewn IPAA, but stapled IPAA resulted in better postoperative bowel function. Postoperative oncogenesis from the residual mucosa is rare. However, future cancer risk remains; thus, careful follow-up is required.

**Keywords** Postoperative complications · Stapled ileal pouch-anal anastomosis · Hand-sewn ileal pouch-anal anastomosis · Anal transitional zone · Restorative proctocolectomy

## Introduction

In recent years, with the progress in medical treatment for ulcerative colitis (UC), therapeutic options have increased, and the rate of patients who can switch to maintenance therapy has also increased. However, there are still patients who are resistant to medical treatment, in whom severe UC develops rapidly, which may be complicated by perforation, bleeding, toxic megacolon, etc.; thus, 20–30% of patients with intractable and severe UC eventually require surgery [1–4].

Both stapled ileal pouch-anal anastomosis (stapled IPAA; the surgical procedure which involves a stapled anastomosis at the surgical anal canal without mucosectomy) and hand-sewn ileal pouch-anal anastomosis (hand-sewn IPAA; the surgical procedure which involves a hand-sewn anastomosis on the dentate line with mucosectomy) are performed

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as restorative proctocolectomy for UC. The origin of these procedures is based on hand-sewn IPAA with a resection on the dentate line, which was founded on the concept of excising the rectal mucosa without excess or deficiency. Stapled IPAA, which leaves a small part of the rectal mucosa, has become widely used owing to its better postoperative bowel function, widespread stapled anastomosis, and stable technique [5–7]. The two procedures differ based on the position of the anastomotic line and whether the anal canal (distance is approximately 1–2 cm on the dentate line) is partly preserved. However, the slight difference is vital in terms of functionality and curability. The choice between both procedures remains controversial and is currently under the discretion of the performing surgeon. Therefore, the knowledge of both surgical concepts, surgical skills, and the judgment to select the appropriate procedure is vital for the surgeon while treating each patient. We aimed to determine the selection criteria, postoperative complications, bowel function, and prognosis of stapled and hand-sewn IPAA for UC at our facility.

## Methods

We identified 320 patients who underwent stapled or hand-sewn IPAA for UC at the Yokohama City University Inflammatory Bowel Disease Center from 2004 to 2017. We determined the surgical procedure performed, indication, and treatment strategy, and retrospectively reviewed the medical records to compare postoperative complications, functional results, and prognosis. Two patients were excluded since they underwent ileal-rectal anastomosis and another four patients were excluded since they underwent abdominoperineal resection of the rectum for severe or intractable UC. The characteristics of the patients with UC are outlined

in Table 1. At our facility, stapled IPAA was the standard procedure, and hand-sewn IPAA was performed only in patients with dysplasia/colitis-associated cancer (CAC) and intractable rectal or anal problems. Postoperative complications were examined separately for early (within 30 days after surgery) and late complications (from 31 days after surgery). Regarding postoperative bowel function, we compared the daily frequency of bowel movements at 3, 6, 9, and 12 months after surgery, the presence of seepage (more than thrice weekly; soiling: stains with a diameter of  $\geq 3$  cm; spotting: stains with a diameter of  $< 3$  cm) at 12 months, the difficulty to discriminate between feces and flatus, and the use of antidiarrheal agents. We also examined carcinogenesis during the postoperative period.

## Procedure selection and surgical management (Figs. 1 and 2)

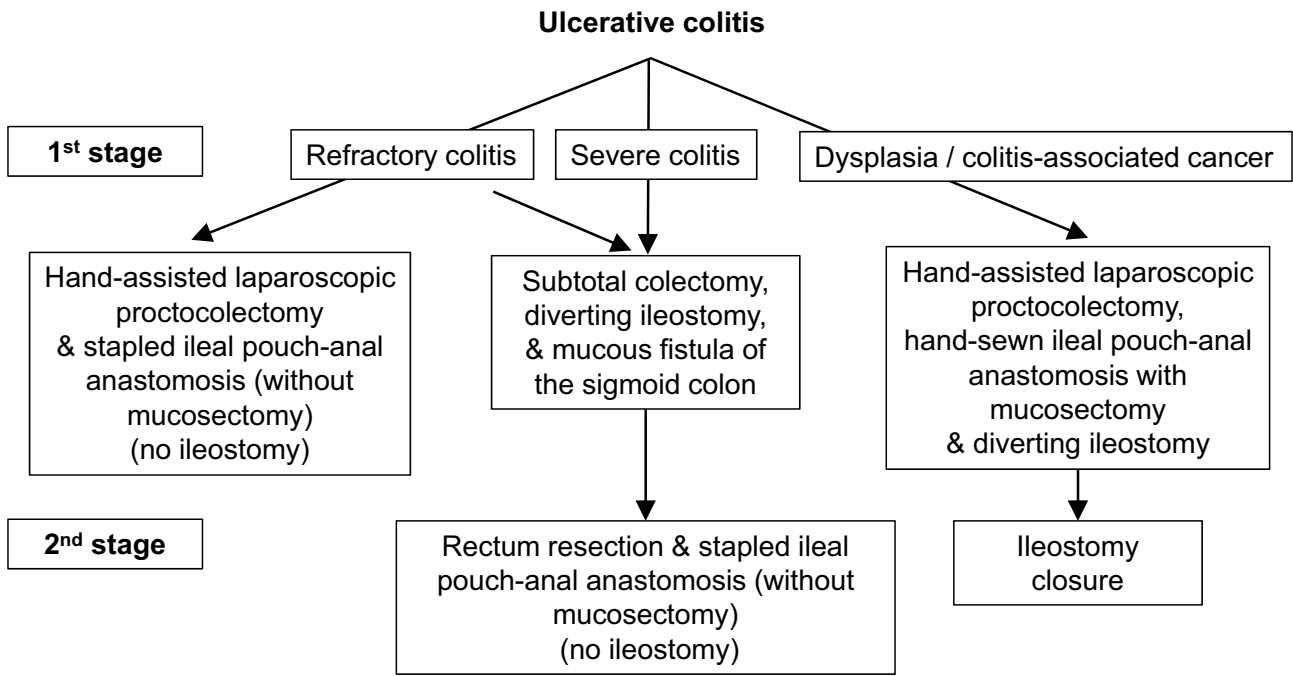
### Stapled IPAA

Single-stage surgery was performed under hand-assisted laparoscopic proctocolectomy for intractable patients, for whom standby surgery was possible. Meanwhile, emergency laparotomy with subtotal colectomy, diverting ileostomy, and mucous fistula of the sigmoid colon was performed in the initial operation for severe, urgent cases, followed by a modified two-stage surgery involving transabdominal proctectomy and stapled IPAA without ileostomy after withdrawal from steroid treatment and recovery from malnutrition (generally 12 to 24 weeks after the initial surgery). We examined the diameter of the anal canal in the lithotomy position while fully expanding it with an EEA sizer (Covidien Japan, Inc.), and selected the optimal stapler size for the anastomosis. We usually use 31-mm-sized CEEA (Covidien Japan, Inc.). At this time, we added stitches to the anterior and posterior parts of the dentate

**Table 1** Patient characteristics and demographics ( $n = 320$ )

	Stapled IPAA ( $n = 298$ )	Hand-sewn IPAA ( $n = 22$ )
Sex(male:female)	182:116	17:5
Age at onset of UC (mean/range/years)	32.3 (4–78)	28.1 (13–70)
Age at initial surgery (mean/range/ years)	38.0 (10–82)	42.2 (26–81)
<b>Surgical indication</b>		
Severe colitis (%)	81 (27.2%)	1 (4.6%)
Refractory colitis (%)	211 (70.8%)	5 (22.7%)
Dysplasia/CAC (%)	5 (1.7%)	16 (72.7%)
<b>Staged surgery</b>		
Single-staged surgery (%)	144 (48.3%)	0 (0%)
Two-staged surgery (%)	149 (50.0%)	16 (72.7%)
Three-staged surgery (%)	5 (1.7%)	6 (27.3%)
Diverting ileostomy (%)	144 (48.3%)	22 (100%)

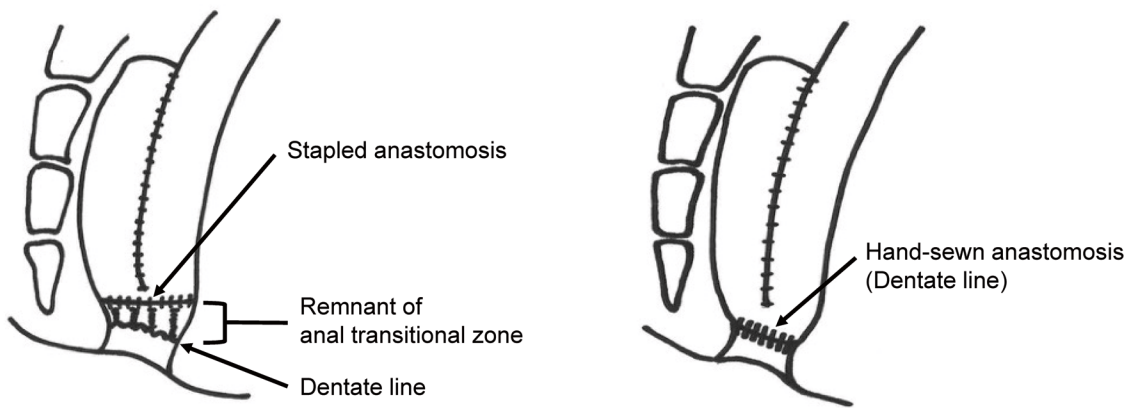
*Abbreviations: IPAA ileal pouch-anal anastomosis, UC ulcerative colitis, CAC colitis-associated cancer*



**Fig. 1** Surgical strategy and procedure selection. Severe colitis: perforation, severe hemorrhage, toxic megacolon, patients who were categorized as “severe”. Refractory colitis: medically refractory or steroid-dependent ulcerative colitis.

line to confirm the level of anastomosis by finger palpation when transecting the rectum. A 12 cm-long ileal J-pouch was constructed in all patients. The layer for exfoliating the rectum was similar to that of total mesenteric excision for rectal cancer surgery that preserves the hypogastric and pelvic nerves and was carried down to the level of the levator ani muscle. To facilitate the double stapling technique (DST) in the deep pelvic cavity, the coccyx-rectal ligament mediating between the puborectalis muscle and the lower rectum was dissected to prepare the anal canal for full movement. While transecting the

rectum, the planned resection level of the anterior and posterior walls was determined from the dentate line by relying on the tactile sensation of the stitches marked preoperatively, and the anal canal was transected with TL 30 or TX 30 (Covidien Japan, Inc.). The transection line was 20 mm on the anterior wall and 10 mm on the posterior wall (both were the median distance in our facility) from the dentate line. The anvil head was fixed to the apex of the ileal pouch, and the trocar of the CEEA was punched on the center or directly under the staple line, and anastomosis was performed using the DST. After



Stapled ileal pouch-anal anastomosis (Stapled IPAA)

Hand-sewn ileal pouch-anal anastomosis (Hand-sewn IPAA)

**Fig. 2** Schema of J pouch procedure

confirming that the anastomosis was successful using the leak test, a 26-Fr Foley catheter for decompression was inserted transanally and placed in the ileal pouch for 7–10 days. Oral ingestion was resumed on the seventh day after confirming that there was no leakage at the anastomotic site by a radiographic enema study performed at 5–7 days after the operation.

### Hand-sewn IPAA

Hand-sewn IPAA was indicated for patients who were diagnosed with dysplasia/CAC or intractable rectal or anal problems associated with UC, such as massive rectal bleeding, anal fistula, and vaginal fistula. Hand-assisted laparoscopic surgery was performed, except for emergency surgeries. Transabdominal manipulation was performed in the same manner as stapled IPAA, and the rectum was sufficiently mobilized down to the anal canal. The entire rectal mucosa was removed transanally, in strips, from the dentate line up to the top of the divided rectum. At the level of the anorectal line (Herrmann line), the muscle layer was dissected outward and the rectum was transected to complete the mucosectomy. The apex of the ileal pouch was sufficiently guided to the anal margin and anastomosed with 16–24 interrupted sutures using a 4/0 absorbable thread at the level of the dentate line. A diverting ileostomy was performed, and was closed at 12 weeks after the initial surgery.

All operations during the study period were performed by the same surgeon as either the operator or under the chief surgeon's supervision.

### Postoperative complications

Early (within the 30-day postoperative period) and late (from 31 days after surgery) complications were examined separately after anal-preserving surgery. Early complications were assessed using the Clavien–Dindo classification. The four most common late complications, including ileal pouchitis, intestinal obstruction, anastomotic site fistula, and anastomotic stenosis, were examined. The modified pouchitis activity index (mPDAI) was considered the basis for ileal pouchitis.

### Patients' follow-up

All patients were evaluated at 1, 3, 6, 9, and 12 months until 1 year after anal-preserving surgery or ileostomy closure; thereafter, they presented for regular medical examinations every 3 months. At the time of the medical examination, we inquired regarding the bowel function, with questions on the frequency of bowel movement over a

24-h period, quality of stool, frequency of nocturnal bowel movement, presence or frequency of soiling or spotting over 7 days, whether feces could be differentiated from flatus (yes or no), and if antidiarrheal agents were used. A physical examination was performed with particular attention given to a digital examination aimed at assessing the status of the anal canal, ileal pouch, and sphincter mechanism. The first colonoscopy was performed at 1 year after bowel reconstruction, and every 2 years thereafter. A total of four biopsies were performed routinely, with two parts in the ileal pouch, one part in the oral ileum, and one part in the anal transition zone.

### Statistical analysis

The Mann–Whitney *U* test was used to analyze the differences between the stapled and hand-sewn IPAA groups.  $p < 0.05$  was considered to indicate statistical significance. SPSS version 27 (IBM Corp., Armonk, NY, USA) was used for statistical analysis.

### Results

A total of 298 patients (93.1%) underwent stapled IPAA, whereas 22 patients (6.9%) underwent hand-sewn IPAA. In the stapled group, 81 of 298 patients (27.2%) had severe UC, 211 (70.8%) had intractable UC, and 5 patients (1.7%) had dysplasia/CAC, including 3 patients (1.0%) with dysplasia and 2 with CAC (0.7%). Single-stage surgery was performed in 144 patients (48.3%), two-stage surgery in 149 (50.0%), and three-stage surgery in 5 (1.7%). All five patients requiring a three-stage surgery had severe UC, developed anastomotic leakage, and further needed diverting ileostomy after the second surgery. Meanwhile, in the hand-sewn IPAA group, 1 patient (4.5%) had severe UC, 5 (22.7%) had intractable UC, and 16 (72.7%) had dysplasia/CAC. One severe case had massive bleeding from the rectum. In the five patients with intractable UC, four had refractory anal fistula, and one had a rectal-vaginal fistula. All 16 patients with dysplasia/CAC underwent a two-stage surgery. Three-stage surgery was performed on six patients with severe or intractable UC (Table 1).

Twenty-one of 320 patients (6.6%), including 5 patients who had undergone stapled IPAA and 16 patients who had undergone hand-sewn IPAA, had dysplasia/CAC. In the stapled ( $n = 298$ ) and hand-sewn IPAA ( $n = 22$ ) groups; the duration of UC (time interval from UC onset until operation) was not significantly different between patients with dysplasia/CAC and those with severe/refractory UC, but it was significantly longer than that of the total cohort ( $n = 320$ ) (severe/refractory vs dysplasia/CAC subgroups: stapled

group, 6.0 vs 8.6,  $p=0.121$ ; hand-sewn group, 12.3 vs 15.3,  $p=0.220$ ; whole cohort, 6.1 vs 13.8,  $p=0.0002$ ). There was no significant difference among the groups during the postoperative follow-up period (severe/refractory vs dysplasia/CAC subgroups: stapled group, 7.8 vs 9.5,  $p=0.383$ ; hand-sewn group, 3.0 vs 7.2,  $p=0.152$ ; whole cohort, 7.7 vs 7.7,  $p=0.650$ ). No postoperative carcinogenesis was observed in any patients in this study (Table 2).

Regarding early complications after anal-preserving surgery in the stapled group, Clavien–Dindo grade 3a complications were observed in 12 patients (4.0%) and Clavien–Dindo grade 3b in 11 patients (3.7%). Temporary ileostomy was performed in 9 of the 19 patients with anastomotic leakage. Moreover, two patients with intestinal obstruction underwent reoperation. The early complications in the hand-sewn group, Clavien–Dindo grade 3a or higher were anastomotic leakage in two patients and intestinal obstruction in two patients. Urgent surgery was required in only one case (4.5%) with surgical wound dehiscence. One patient who suffered from anastomotic leakage developed anal stricture as a late complication. The most common late complication of both procedures was ileal pouchitis, observed in 22 patients (7.4%) undergoing stapled IPAA and 4 patients undergoing hand-sewn IPAA (18.2%). Of these, two patients from each group underwent ileal pouch resection and permanent ileostomy because of intractable ileal pouchitis. Furthermore, intestinal obstruction and anastomotic stenosis were observed in a small number of patients. We also noted that both groups showed significant differences in the early complication Clavien–Dindo 3a between them (Table 3).

The frequency of postoperative bowel movement at 3, 6, 9, and 12 months was 9.4 and 8.8, 8.7 and 7.6, 8.0 and 7.8, and 7.8 and 8.4 in the stapled and hand-sewn groups,

respectively; no significant difference was observed between the two groups in any period. In terms of bowel function, soiling was observed in 27 patients (9.1%) in the stapled group and in 9 (41.0%) in the hand-sewn group (odds ratio [OR]: 0.14,  $p<0.0002$ ). Spotting was observed in 69 patients (23.2%) in the stapled group and in 14 (63.6%) in the hand-sewn group ( $OR=0.17$ ,  $p<0.0001$ ). Approximately half of the patients in the two groups had nocturnal defecation, with the difference being not significant (stapled vs hand-sewn, 152 [51.0%] vs 9 [41.0%]). One-hundred sixteen (38.9%) and 14 (63.6%) patients in the stapled and hand-sewn groups complained of difficulty in distinguishing feces from flatus; the rate was significantly higher in the hand-sewn group ( $OR=0.36$ ,  $p<0.026$ ). Approximately <70% of patients in both groups used antidiarrheal agents (Table 4).

## Discussion

Stapled and hand-sewn IPAA are typical anal-preserving procedures for UC. Ravitch et al. first reported the basis of these procedures in 1947, and Parks et al. reported a reconstruction method using the ileal pouch in 1978. Thereafter, the method was further developed and improved [8, 9]. The choice of surgical procedure depends on the postoperative bowel function, which is related to the patient's quality of life, and risk for oncogenesis, which might influence the prognosis. Furthermore, the technical and patient-related factors should be considered including body shape and narrow pelvis, and the remaining anal function in the older patients.

In our facility, stapled IPAA is performed as the standard surgical procedure. Martin et al. reported the surgical concepts for improving the bowel function in 1982. With

**Table 2** Postoperative oncogenesis ( $n=320$ )

Surgical indication at first surgery	Severe/refractory ( $n$ )	Cancer/dysplasia ( $n$ )	$p$ value
<b>Stapled IPAA (<math>n=298</math>)</b>	293	5	
Duration of UC (mean/range/years)	6.0 (0–35.4)	8.6 (0.5–21.0)	0.121
Postoperative follow-up period (average/range/years)	7.8 (1.9–15.8)	9.5 (2.8–15.8)	0.383
Postoperative oncogenesis (dysplasia/CAC/ $n$ )	0	0	–
<b>Hand-sewn IPAA (<math>n=22</math>)</b>	6	16	
Duration of UC (mean/range/years)	12.3 (3.8–17.5)	15.3 (0.3–34.3)	0.220
Postoperative follow-up period (average/range/years)	3.0 (1.9–4.7)	7.2 (1.9–12.5)	0.152
Postoperative oncogenesis (dysplasia/CAC/ $n$ )	0	0	–
<b>Total (<math>n=320</math>)</b>	299	21	
Duration of UC (mean/range/years)	6.1 (0–35.4)	13.8 (0.3–34.3)	0.008*
Postoperative follow-up period (average/range/years)	7.7 (1.9–15.8)	7.7 (1.9–15.8)	0.650
Postoperative oncogenesis (dysplasia/CAC/ $n$ )	0	0	–

*Abbreviations:* UC ulcerative colitis, IPAA ileal pouch–anal anastomosis, CAC, colitis-associated cancer

\* $p<0.05$



**Table 3** Postoperative complications ( $n = 320$ )

	Stapled IPAA ( $N = 298$ )	Hand-sewn IPAA ( $N = 22$ )	Odds ratio	$p$ value
<b>Early complications<sup>a</sup></b>				
Clavien–Dindo: Grade 1	28 (9.4%)	4 (18.2%)	0.47	0.256
Clavien–Dindo: Grade 2	68 (22.8%)	3 (13.6%)	1.87	0.430
Clavien–Dindo: Grade 3a	12 (4.0%)	4 (18.2%)	0.19	0.018*
Clavien–Dindo: $\geq$ Grade 3b	11 (3.7%)	1 (4.5%)	0.80	0.581
Anastomotic leakage	19 (9) <b>**</b> (6.4%)	2 (9.1%)	0.68	0.646
Bowel obstruction	4 (2) <b>**</b> (1.3%)	2 (9.1%)	0.14	0.057
<b>Late complications<sup>b</sup></b>				
Bowel obstruction	18 (6.0%)	1 (4.5%)	0.68	0.646
Anastomotic stricture	4(1.3%)	1 (4.5%)	1.35	0.618
Ileal pouchitis	22 (7.4%)	4 (18.2%)	0.36	0.091
Pouch failure	1 (0.3%)	1 (4.5%)	0.07	0.133
Pouch fistulae	9 (3.0%)	0 (0%)	0.53	0.807

Abbreviations: IPAA, ileal pouch-anal anastomosis

<sup>a</sup>Postoperative days  $\leq 30$

<sup>b</sup>postoperative days  $> 30$

**\*\***The patients who required surgical treatment

\* $p < 0.05$

the growing prominence of anastomotic devices and the stability of surgical manipulation, the current procedure has become ubiquitous [7, 10]. In a systematic review of 4383 patients who underwent restorative proctocolectomy reported by Lovegrove et al. the ratio of stapled IPAA was 35% ( $n = 1484$ ) and hand-sewn IPAA was 65% ( $n = 2899$ ) [11]. Uchino et al. [12] conducted a multicenter observational study on 2376 UC patients in Japan, and reported that 45% ( $n = 1076$ ) and 55% ( $n = 1300$ ) of the patients underwent stapled and hand-sewn IPAA, respectively. Meanwhile, Victor et al. reported that stapled IPAA was the basic surgical procedure for 2959 UC patients in their study conducted at a specialist center. Likewise, in our facility, stapled IPAA

was performed in 87% ( $n = 2573$ ) of patients [13]. As mentioned above, both are utilized equally as typical procedures for UC. However, the basic procedure used and its indication differ depending on the facility. The greatest advantage of stapled IPAA is that it has better postoperative bowel function than hand-sewn IPAA [7, 11, 14–18]. Our results suggested lower rates of seepage and difficulty in distinguishing feces from flatus, which was consistent with previous reports. We also appreciate the technical stability of stapled IPAA. Stapled anastomosis without anal manipulation is technically simple and controls the operation time. Furthermore, stable surgical manipulation can be achieved even if the assistant is an inexperienced practitioner. Meanwhile,

**Table 4** Comparison of postoperative anal function between patients who underwent stapled IPAA and those who underwent hand-sewn IPAA

BMs per 24 h (average/median)	Stapled IPAA ( $n = 298$ )	Hand-sewn IPAA ( $n = 22$ )		$p$ value
3 months (times)	9.4/10	8.8/10		0.799
6 months (times)	8.7/10	7.6/8		0.246
9 months (times)	8.0/8	7.8/8		0.832
12 months (times)	7.8/8	8.4/8		0.765
<b>Incontinence outcomes</b>	<b>Stapled IPAA (<math>n = 298</math>)</b>	<b>Hand-sewn IPAA (<math>n = 22</math>)</b>	<b>Odds ratio</b>	<b><math>p</math> value</b>
Soiling	27 (9.1%)	9 (41.0%)	0.14	0.0002*
Spotting	69 (23.2%)	14 (63.6%)	0.17	0.0001*
Nocturnal defecation	152 (51.0%)	9 (41.0%)	1.48	0.508
Difficulty in distinguishing feces from flatus	116 (39.9%)	14 (63.6%)	0.36	0.026*
Usage of antidiarrheal agents	206 (69.1%)	14 (63.6%)	1.28	0.636

Abbreviations: BMs bowel movements, IPAA ileal pouch-anal anastomosis

\* $p < 0.05$

hand-sewn IPAA at our facility is limited to patients with intractable anal lesions identified preoperatively or patients with dysplasia/CAC. In our study, all six patients with anal lesions had intractable anal fistulas, vaginal fistulas, and severe bleeding associated with UC. We considered that anal canal preservation would predispose those patients to the risk of postoperative complications; thus, we performed hand-sewn IPAA with a complete resection of the lesions. In addition, in patients with dysplasia/CAC, the Japanese guidelines recommend total colectomy [19]. A high risk of colorectal cancer is associated with UC, which varies across countries [20]. Moreover, the incidence of dysplasia/CAC in the postoperative anal canal increases significantly when dysplasia/CAC is observed in preoperatively or perioperatively excised specimens [21, 22]. Therefore, we also believe that hand-sewn IPAA is appropriate from the viewpoint of preventive and curative treatment for patients with dysplasia/CAC. However, it has been indicated that mucosectomy does not necessarily prevent the development of cancer [18, 21, 23]. Selvaggi et al. reported a review of pouch-related cancer in 49 patients with UC in 2014 [24]; of these, 28 (57.1%) had dysplasia (14, 28.6%) or cancer (14, 28.6%), as detected on the initially excised specimen, and they also had a significantly shorter pouch duration before cancer diagnosis ( $7.9 \pm 5.8$  versus  $14.7 \pm 7.3$  years;  $p = 0.0012$ ). In addition, they reported that the development of cancer occurred after mucosectomy in 15 of 49 patients (28.6%); they indicated that the cause of this inconsistency was due to the oncogenesis of partial residual colonic mucosa due to inadequate surgical procedures or mucinous degeneration of the small intestine in the ileal pouch. However, they suggested that avoiding mucosectomy significantly increased the risk of cancer arising from the residual mucosa (OR, 8; 95% CI, 1.3–48.7;  $p = 0.02$ ) based on the meta-analysis in their article. We performed a total colectomy in 21 patients with dysplasia/CAC. The mean duration from the onset of UC to operation was 13.8 years. Among these 21 patients, 16 (76.2%) underwent IAA, whereas 5 (23.8%) underwent stapled IPAA at their request to preserve bowel function. Of the five patients, one patient was older (age: 80 s), one patient was young (age: 30 s), and three patients had high-grade dysplasia. As mentioned above, mucosectomy can reduce the risk of postoperative cancer incidence; we leave the final choice of surgical procedure to the patient.

Anastomotic leakage has been reported as the most serious early postoperative complication that might cause ileal pouch failure [12, 25]. To avoid the risk of anastomotic leakage, two-stage surgery is performed in our institution for severe or intractable UC in patients with poor general or nutritional condition, and for those undergoing hand-sewn IPAA [5]. We used the modified two-stage surgery technique for severe/intractable cases, which involves an anastomotic procedure in the second operation. Compared with

the conventional two-stage surgery in which the anastomotic procedure is performed in the first operation, the modified approach has a similar incidence of postoperative complications. In addition, Zittan et al. reported that modified two-stage surgery is the sole preventive factor in the incidence of postoperative anastomotic site fistula [26, 27]. We performed single-stage surgery in almost half of the stapled IPAA patients ( $n = 144$  [48.3%]), comprising 139 intractable patients and 5 CAC/cancer patients. Based on our own studies on its associated risk factors, we have cautiously performed single-stage surgery in elective cases and expanded its indications. However, this is an unorthodox policy and constructing a temporary diverting ileostomy remains the standard approach. [28] Single-stage surgery should only be introduced with caution in carefully selected cases based on each institution's experience and results as well as individual patient characteristics.

Anastomotic leakage was observed in 19 patients (6.4%) in the stapled group and 2 patients (9.1%) in the hand-sewn group, totaling to 21 patients (6.6%). This was similar to the results of the multicenter meta-analysis reported by Lovegrove et al. [11] and the single-center cohort analysis reported by Fazio et al. [13]. It could be concluded that our surgical procedure selection was appropriate. Previous studies have reported that hand-sewn IPAA tends to have a higher risk of anastomotic leakage or stenosis than stapled IPAA and indicated that their causes are related to the fact that the tension placed on the mesentery of the ileal pouch is stronger than that of the stapled IPAA, and that advanced surgical skill is required for hand-sewn anastomosis [5, 25]. However, a recent meta-analysis has reported no significant difference between the two surgical procedures in terms of anastomotic leakage or stenosis [11].

Next, we will refer to the anal transitional zone (ATZ) that affects bowel function. The ATZ is anatomically located in the middle of the anal canal, covered with stratified columnar epithelium, and is the transition from the rectal mucosa to the squamous epithelium [29]. Past literature has revealed that ATZ is < 1 cm above the dentate line and contains nerve plexuses involved in temperature and perception. However, since the nerves are sparse further above the ATZ, perception is reduced. Therefore, theoretically, the sensor responsible for bowel function exists in the epithelium within 1 cm above the dentate line, and preserving this range might improve bowel function [30–32]. It has also been indicated that the cause of seepage depends on the resting pressure and the length of the anal canal [33]. Since the internal and external anal sphincters are almost entirely preserved in both stapled and hand-sewn IPAA, the resting pressure is theoretically maintained. However, in reality, the resting pressure reduces postoperatively than preoperatively, especially in hand-sewn IPAA. This may be due to damage to the sphincter muscle during anal manipulation in surgery [34]. Previously, we

examined an appropriate dissection line to eliminate the mucosa to the maximum extent in consideration of the risk of cancer and proposed partial intra-anal canal anastomosis [35]. This is a DST, wherein the resection line is set 1–2 cm above the dentate line on the anterior wall and placed on the dentate line on the posterior wall. It was shown that it is possible to maintain good bowel function equal to or better than the conventional DST. That is, ATZ does not necessarily have to be preserved all around, and if one side is preserved by even 1 cm above the dentate line, the bowel function can be sufficiently preserved. In patients who cannot excoriate via the anal canal at the deepest pelvic site due to obesity or narrow pelvis, our anastomotic technique can be performed at the dentate line on the posterior wall.

Important factors in postoperative surveillance are the presence of dysplasia/CAC in the residual mucosa within the anal canal and in the ileal pouch mucosa. As mentioned above, perfect exclusion of cancer risk is not guaranteed even after mucosectomy. Therefore, regardless of which surgical procedure was selected, we considered patients who were preoperatively diagnosed with dysplasia/CAC to be at high risk; thus, they undergo colonoscopy every year, while other patients undergo colonoscopy every 2 years. Although we have not observed dysplasia/CAC in the present study, the cumulative risk of postoperative cancer incidence is expected to be increased in the future [24]. Further studies are needed to determine the necessity and timing of surveillance by colonoscopy after both stapled and hand-sewn IPAA.

In recent years, the number of elderly UC patients has been increasing. In our study, 39 patients (12.2%) were elderly (defined as the age at surgery of  $\geq 65$  years). We chose stapled IPAA at our discretion for one very elderly patient aged 81 years with CAC because of the low remaining anal function. As in this case, the number of elderly UC patients with cancer is expected to increase in the future; thus, a surgical procedure that emphasizes the quality of life should be appropriately selected.

There are several limitations of this study. First, the number of hand-sewn cases was significantly smaller than that of stapled cases, with the shallow learning curve, and surgeon inexperience with the hand-sewn anastomosis being a major problem. In addition, the anal function of 6 patients in the IAA group who had been suffering from intractable rectal or anal problems might have been impaired preoperatively. The aforementioned issues may have contributed to the worse bowel function results observed in the hand-sewn group. If both the groups had similar number of patients, the differences might have been smaller. Secondly, the data on anal manometry are lacking, even though it was known that it is an important bowel function evaluation index. Thirdly, the postoperative cancer incidence is indicated to rise over time from 10 years or more [36], which means the observation

period in this study was insufficient to evaluate the risk of oncogenesis for each surgical procedure.

In conclusion, the indications for surgery for patients with UC are mainly severe or intractable disease and carcinogenesis, and an appropriate treatment approach and strategy should be implemented according to the patient factors. Although there was a large selection bias in comparing both stapled and hand-sewn IPAA in our study, stapled IPAA tended to contribute to improved postoperative bowel function. Meanwhile, regarding postoperative carcinogenesis, there were no patients diagnosed with dysplasia/CAC after either of the surgical procedure. However, long-term follow-up and accumulation of cases are still required. Surgeons need to fully understand the pathophysiology of UC and the characteristics of the surgical procedure, and make a comprehensive decision based on the patients' background and characteristics of each facility before selecting the surgical procedure.

**Author contribution** Conceptualization: H. Kuwabara and H. Kimura. Methodology: H. Kuwabara and H. Kimura. Formal analysis: H. Kuwabara. Project administration: Kenji K. Investigation: R.K., K.T., Kazutaka K., A.S., A.T., and I.E. Writing—original draft: H. Kuwabara. Writing—review and editing: H. Kimura. Approval of final manuscript: all authors.

## Declarations

**Ethics approval** The study protocol was approved by the Ethical Advisory Committee of Yokohama City University Graduate School of Medicine (registry as B190800050.).

**Consent to participate or consent to publish** Not applicable.

**Conflict of interest** The authors declare no competing interests.

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