

Outcome and functional prognosis of pelvic sepsis after ileal pouch-anal anastomosis in patients with ulcerative colitis

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Abstract

Purpose Restorative proctocolectomy with ileal pouch-anal anastomosis is a surgical procedure for ulcerative colitis, but pouch failure or pelvic sepsis still occurs in some patients. We conducted this study to investigate the cause of pouch failure and evaluate defecatory function after pelvic sepsis.

Methods A total of 234 patients who underwent restorative proctocolectomy were enrolled. We analyzed the cause of pouch failure, as well as defecatory function and manometric outcomes, with and without the complication of pelvic sepsis.

Results Pelvic sepsis developed in 29 (12.3%) of the 234 patients who underwent restorative proctocolectomy (pelvic sepsis group). The pelvic sepsis led to pouch failure in two of these patients (as a vaginal fistula in one and ileo-anal anastomotic leakage in one). Of the remaining majority of patients who did not suffer pelvic sepsis (control group), nine suffered pouch failure (as vaginal fistula in four, perianal abscess in two, pouch-spinal marrow fistula in one, and chronic pouchitis in two). There were no significant differences in defecatory function or manometric outcomes between the two groups. In the pelvic sepsis group, stool frequency was significantly correlated with white blood cell count ($P = 0.01$) and the duration until onset of pelvic sepsis ($P < 0.01$).

Conclusions Pelvic sepsis after restorative proctocolectomy for ulcerative colitis does not affect defecatory and

manometric function, but control of the inflammation caused by pelvic sepsis is integral for defecatory function.

Keywords Ulcerative colitis · Ileal pouch-anal anastomosis · Pelvic sepsis · Defecatory function · Pouch failure

Introduction

The technique of restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) was introduced in the early 1980s and has become the surgical procedure of choice for ulcerative colitis (UC) when proctocolectomy is required [1–3]. The IPAA procedure allows for removal of the affected colon and rectum, reconstruction of gastrointestinal continuity, and preservation of transanal defecation [4, 5]. Large series have reported excellent long-term quality of life (QOL) and functional results of IPAA [6, 7]. Although there is a high incidence of early and late post-operative complications, most can be managed without impairment of QOL [8, 9]. However, major complications, especially those accompanied by septic conditions in the pelvis, adversely affect functional outcomes and QOL.

Pelvic sepsis, including ileo-anal anastomotic leakage, pouch leakage, peri-pouch abscess formation, and pouch perianal fistula, occurs in up to 10% of patients who undergo IPAA for UC [10, 11]. In most cases, pelvic sepsis is accompanied by symptoms of fever, abdominal pain, and pelvic pain. Pelvic sepsis is diagnosed from the results of a contrast enema examination, contrast-enhanced computed tomography (CT), and endoscopy. However, if there is radiographical leakage, it is difficult to establish an early diagnosis. Treatment generally aims to control the sepsis using intravenous antibiotics, ultrasound- or CT-guided

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percutaneous drainage for pelvic abscess, or transanal drainage for fistula, and if required, relaparotomy and drainage. These treatments are usually combined with the creation of a diverting ileostomy. The outcome of treatment of these complications is improving, but there is a high rate of pouch failure if management of the pelvic sepsis fails [12]. However, even if management of pelvic sepsis is successful, its effect on defecatory function is unclear. The assessment of defecatory function and QOL is controversial, even regarding the salvage of pouch function because the spread of inflammation in the pelvis affects the pouch and sphincter muscles.

We investigated the causes of pouch failure and compared them with those in other reports. We also investigated the effect of pelvic sepsis on defecatory function and manometric outcomes by comparing patients with pelvic sepsis and successful salvage of pouch function with patients whose pouch function was preserved without pelvic sepsis. Finally, we studied the correlations between management and the degree of inflammation in pelvic sepsis with their effects on defecatory function.

Methods

Patients

The subjects of this retrospective study were 248 patients who had undergone IPAA for UC in Mie University Hospital between January, 2001 and December, 2012. Thirteen patients who were not able to be followed up and one patient who was diagnosed with Crohn's disease after IPAA were excluded. IPAA was performed as one-stage, two-stage (IPAA with diverting ileostomy and ileostomy closure), or three-stage (subtotal colectomy, IPAA with diverting ileostomy, and ileostomy closure) procedures. In 2004, we stopped performing the one-stage procedure because of the high risk of serious septic complications. In most cases ($n = 231$), we performed proctomucosectomy and hand-sewn transanal anastomosis, while in some, we performed the double-stapling technique. All of the patients provided written informed consent. The investigations were performed in accordance with the Declaration of Helsinki and approved by the Research Ethics Committee of Mie University School of Medicine, Mie, Japan.

Definitions of pelvic sepsis and pouch failure

Pelvic sepsis was defined as an infectious complication that developed in the pelvis and perianal region, including anastomotic leakage, pouch leakage, abscess formation, and pouch-related fistula, within 90 days after the one-stage

procedure, or if ileostomy closure was delayed in the staged procedure because of pelvic sepsis after IPAA. The presence of pelvic sepsis was confirmed by a combination of clinical, radiological, and operative findings. Transanal contrast enema examinations were routinely performed 5–7 days after IPAA and just before closure of the ileostomy. Patients with suspected pelvic sepsis who presented with clinical symptoms of pelvic tenderness, hyperthermia, and leukocytosis, underwent further investigations, including emergency contrast enema examination, CT scan, and transanal endoscopy. Closure of the ileostomy was scheduled for 3 months after IPAA in the absence of pelvic sepsis. Closure of ileostomy for patients with pelvic sepsis was performed only after confirmation of the healing of pelvic sepsis.

Pelvic complications occurring more than 90 days after IPAA or closure of ileostomy were considered late-phase complications separate from pelvic sepsis [3]. Therefore, late-phase complications of pouch-related fistula were not considered pelvic sepsis. Late-phase complications were also diagnosed by the above investigations if clinical symptoms appeared. Pouch failure was defined as the inability to defecate through a natural anus because of excision of the pouch or permanent diverting ileostomy.

Evaluation of defecatory function and manometric outcomes

Patients were enrolled in a routine follow-up clinic in the outpatient department every 2 months during the first 6 months and then twice a year. Patients were asked about daily stool frequency, nocturnal defecation, anal pain, soiling, the need for a pad, and the need for antidiarrheal medicine. Temporary worsening of defecation function (such as pouchitis or the late onset of anal fistula) was excluded. In most patients, manometric parameters, including maximum resting pressure, the length of the high-pressure zone, and maximal squeeze pressure, were measured just before IPAA, after IPAA just before stoma closure, and in outpatients after stoma closure, to assess sphincter function. In patients who underwent one-stage IPAA, the second manometry was performed 3 months after IPAA. We also calculated the ratio of change between pre- and postoperative data. For inflammatory evaluation at the time of pelvic sepsis, we investigated inflammatory markers [such as serum C-reactive protein levels and white blood cell count (WBC)], the duration until the onset of pelvic sepsis after a staged operation, and the duration of an elevated inflammatory reaction. WBC and C-reactive protein levels were measured at the time of diagnosis of pelvic sepsis. We investigated the relationship between stool frequency and inflammatory markers.

Statistical analyses

All statistical analyses were performed using JMP version 10 (SAS Institute, Cary, NC). Results are expressed as median values or as the mean \pm standard deviation (SD). Simple comparisons were analyzed using the Chi-squared test for categorical data and the nonparametric Mann–Whitney *U* test for continuous variables. Correlations between bowel movement and inflammatory markers were investigated using Spearman's rank correlation coefficient. Probability values less than 0.05 were considered significant.

Results

Characteristics of patients with UC

Figure 1 shows a flowchart of the patients' clinical course. A total of 234 patients were enrolled in this study. Table 1 summarizes their demographic and clinical characteristics. Pelvic sepsis developed in 29 (12.3%) patients. Pelvic sepsis developed at a higher incidence in the patients who underwent the one-stage procedures ($P < 0.001$). Other demographic and surgical factors were comparable

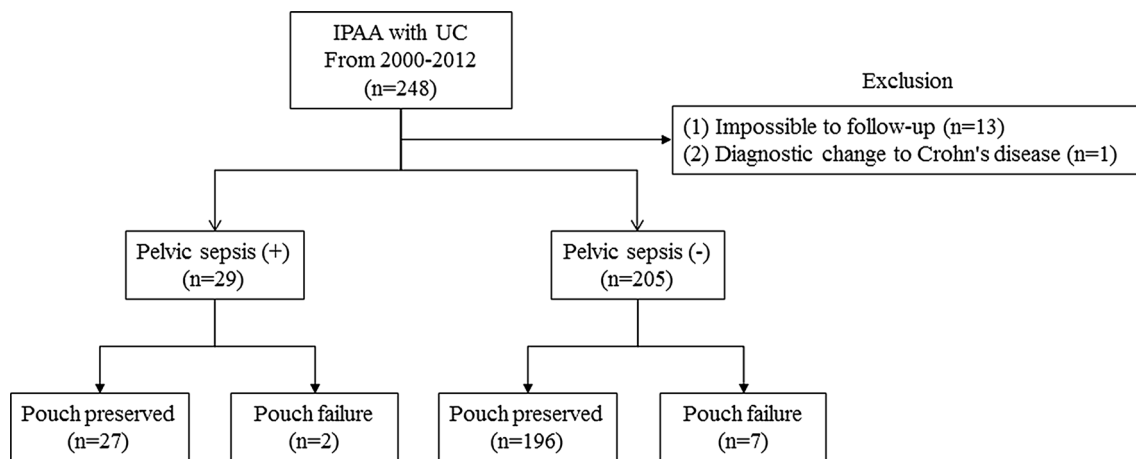


Fig. 1 Flowchart of the patients

Table 1 Characteristics of the patients who underwent ileal pouch-anal anastomosis for ulcerative colitis

	Pelvic sepsis (+) <i>n</i> = 29	Pelvic sepsis (–) <i>n</i> = 205	<i>P</i> value
Sex (male/female)	9/20	111/94	0.13
Age at operation (years)	33.2 \pm 15.2	36.1 \pm 15.5	0.41
Age at disease onset (years)	27.0 \pm 14.6	29.1 \pm 14.7	0.57
Duration of illness (years)	6.4 \pm 5.7	7.2 \pm 6.8	0.82
Disease activity (mild/medium/severe)	12/12/4	100/81/19	0.66
Extent of disease (rectum/left/total)	5/0/22	35/5/159	0.71
Total prednisolone dose (g)	15.1 \pm 20.2	13.9 \pm 17.5	0.52
Body mass index (kg/m ²)	20.1 \pm 4.0	20.2 \pm 3.6	0.86
Surgical type of procedure (1-/2-/3- stage)	6/20/3	4/140/61	<0.001*
Total operative time (min)	317 \pm 103	304 \pm 95.6	0.55
Intraoperative blood loss (ml)	509 \pm 578	442 \pm 375	0.79
Perioperative blood transfusion (yes/no)	5 (17.2)	26 (12.7)	0.50
Laparoscopic surgery (yes/no)	3 (10.3)	18 (8.8)	0.78

Values represent the number of patients (%) or the mean \pm standard deviation, except for sex, disease activity and extent of disease

* $p < 0.05$

Table 2 Causes of pouch failure

	With pelvic sepsis (<i>n</i> = 29)	Without pelvic sepsis (<i>n</i> = 205)	<i>P</i> value
Number of pouch failures	2 (6.9%)	9 (4.4%)	0.56
Cause of pouch failure	Vaginal fistula 1 Ileal-anal anastomotic leakage 1	Vaginal fistula 4 Perianal abscess 2 Pouch-spinal marrow fistula 1 Chronic pouchitis 2	

Table 3 Defecatory functional and manometric outcomes after ileal pouch-anal anastomosis for ulcerative colitis in patients with vs. those without the complication of pelvic sepsis

	Pelvic sepsis (+) <i>n</i> = 27	Pelvic sepsis (–) <i>n</i> = 196	<i>P</i> value
Stool frequency (per day)	7.0 ± 1.8	6.5 ± 2.0	0.23
Nocturnal defecation (yes/no)	8 (47.1)	49 (43.8)	0.80
Soiling (yes/no)	13 (51.2)	73 (41.0)	0.22
Anal pain (yes/no)	8 (32.0)	29 (16.7)	0.07
Using pads (yes/no)	10 (66.7)	45 (41.67)	0.07
Using antidiarrheals (yes/no)	13 (50.0)	79 (42.7)	0.48
Maximum resting pressure			
Pre (mmHg)	66.3 ± 16.0	66.0 ± 23.7	0.77
Post (mmHg)	40.3 ± 17.4	45.0 ± 17.1	0.36
Ratio of change (%)	55.3 ± 31.4	59.1 ± 40.6	0.89
Maximum squeezing pressure			
Pre (mmHg)	134.5 ± 71.9	155.4 ± 78.6	0.35
Post (mmHg)	116.2 ± 67.3	127.9 ± 66.9	0.48
Ratio of change (%)	56.0 ± 41.0	80.6 ± 95.7	0.58
Length of the high-pressure zone			
Pre (mm)	33.9 ± 10.0	33.7 ± 6.8	0.46
Post (mm)	26.0 ± 12.3	27.2 ± 13.7	0.47
Ratio of change (%)	61.1 ± 34.9	67.3 ± 36.0	0.50

Values represent the number of patients (%) or mean ± standard deviation

Pre pre-IPAA, *Post* post-IPAA

between the two groups of UC patients who were complicated by pelvic sepsis and those who were not complicated by pelvic sepsis.

Causes of pouch failure

A total of 11 patients had pouch failure, the causes of which are shown in Table 2. The causes of pouch failure complicated by pelvic sepsis were vaginal fistula and IPAA leakage. A total of nine patients suffered pouch failure because of late-phase complications. Four patients were complicated by vaginal fistula, two were complicated by

Table 4 Correlations of stool frequency and inflammatory markers

Factor	Correlation coefficient	<i>P</i> value
Serum CRP	0.26	0.3
WBC count	0.52	0.01*
Duration until onset	–0.02	0.92
Duration of elevated inflammatory reaction	0.61	<0.01*

CRP C-reactive protein, *WBC* white blood cell

* *p* < 0.05

perianal abscesses, one was complicated by pouch-spinal marrow fistula, and two were complicated by defecatory dysfunction because of chronic pouchitis. There was no significant difference in pouch failure between the two groups (*P* = 0.56).

Results of defecation function and manometric outcomes

We compared 27 UC patients complicated by pelvic sepsis with 196 patients who did not have pelvic sepsis. The 11 patients who had pouch failure were excluded. Table 3 summarizes defecatory function and manometric outcomes. There was no significant difference in defecatory function between the two groups. Preoperative manometric data (maximum resting pressure, maximal squeeze pressure, and length of the high-pressure zone) were comparable between the two groups. Postoperative manometric data were lower than those preoperatively in both groups. The ratio of change was worse in the UC patients complicated by pelvic sepsis than in those who were not, but there was no significant difference in manometric outcomes between the two groups.

Relationship between stool frequency and inflammatory markers according to pelvic sepsis

In the UC patients complicated by pelvic sepsis, stool frequency was significantly correlated with the WBC count (*P* = 0.01) and the duration of elevated inflammatory reaction (*P* < 0.01). Table 4 shows the correlation coefficients and *P* values.

Discussion

IPAA for UC can achieve excellent improvement in QOL and good function, but is associated with a 5–12% incidence of pouch failure in long-term follow-up [8, 13–15]. After pelvic sepsis, the incidence of pouch failure increases to 20–50% [16]. Complications of pelvic sepsis, including pouch–perineal fistula and pouch–vaginal fistula, are independent risk factors for pouch failure [16]. In the present series, 4.7% ($n = 11$) of patients suffered pouch failure, which is slightly better than results in other reports [3, 8]. This is because there were only two patients who suffered pouch failure among the UC patients complicated by pelvic sepsis, with no significant difference in pouch failure between the two groups. To salvage pouch function after the complication of pelvic sepsis, we treat pelvic abscess aggressively by CT-guided percutaneous drainage and early control of inflammation [17]. Furthermore, the prevention of late-phase complications is important for reducing the rate of pouch failure. In our institution, the ingenuity of the IPAA surgical technique with mucosal proctectomy below the dentate line is designed to reduce the late-phase complications of pouch-related fistula formation [18].

The long-term functional outcome of IPAA results in manageable stool frequency (approximately 6 times a day) and good fecal continence during the daytime [19]. However, assessing the functional outcome of UC patients who are complicated by pelvic sepsis after IPAA is controversial. Chessin et al. investigated the outcomes in patients who were complicated by pouch leak after IPAA and found no significant difference in the functional outcomes of those who were complicated by pouch leak and those who were not [20]. Mennigen et al. also reported that the functional outcomes of UC patients with pouch-related septic complications were not significantly inferior to those of uncomplicated controls if the pouch was salvaged [10]. In contrast, several investigators have reported that the functional outcomes of UC patients complicated by pelvic sepsis were worse than those whose clinical course was uncomplicated [3, 21, 22]. In one of these reports, Kieky et al. [3] analyzed a large number of patients over a long period of follow-up. They concluded that physicians should pay careful attention to preoperative and intraoperative planning and strategies to reduce the complications of pelvic sepsis. In our study, 12% of UC patients were complicated by pelvic sepsis after IPAA, despite which an adequate functional outcome was achieved, not significantly different from that of patients without a history of pelvic sepsis. We also analyzed manometric outcomes. In our institution, the majority of patients who underwent IPAA had mucosal proctectomy and hand-sewn anastomosis. Damage to the internal anal sphincters is greater with mucosal proctectomy than that

without mucosal proctectomy [23]. However, no reports have compared the relationship between pelvic sepsis and manometric outcomes. In our study, the manometric outcomes of UC patients with pelvic sepsis were comparable with those of UC patients without pelvic sepsis. A previous report also showed that the manometric outcome was improved after the control of inflammation in UC patients complicated by pelvic sepsis [24].

We also investigated the correlation between stool frequency and duration until onset, serum C-reactive protein levels, peripheral WBC, and the duration of an elevated inflammatory reaction in UC patients complicated by pelvic sepsis to assess the correlations between pouch function and pelvic inflammation. To our knowledge, this is the first study to evaluate the correlations between stool frequency and inflammatory markers. We found that the WBC count and the duration of an elevated inflammatory reaction were correlated with increased stool frequency, whereas C-reactive protein levels were not. This is because the blood levels were measured at the time of diagnosis of pelvic sepsis, and so, only the white blood cells were increased. The spread of inflammation in the pelvis causes a narrowed anastomosis, leading to surrounding pelvic fibrosis, pouch dysmotility, impaired pelvic floor activity, and a fibrotic, poorly compliant pouch, which does not adequately retain stool [3]. This may explain why our results suggest that early control of inflammation prevents the spread of inflammation into the pelvis and preserves functionality of the pouch. Stool frequency compromises QOL [6]. Therefore, control of inflammation after IPAA complicated by pelvic sepsis is important to preserve QOL.

This study has some limitations. The total number of patients was small, and the follow-up time was short and inconsistent. The number of responses against functional outcome also differed among patients; however, compared with previous reports on pouch failure and function after pelvic sepsis, although the total number of patients was small, our data were favorable. Ultimately, this is the first study to show that inflammation is directly linked to stool frequency.

Conclusion

The complication of pelvic sepsis after IPAA for UC does not affect defecatory or manometric function, but the control of inflammation caused by pelvic sepsis affects defecatory function. Although the frequency of pouch failure is small, control of early-phase and late-phase complications is imperative to prevent pouch failure. Further studies on larger numbers of patients are needed to refine and generalize our results.

Compliance with ethical standards

Conflict of interest Shozo Ide and his co-authors have no conflicts of interest to declare.

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