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Postoperative and Long-Term Results of Ileal Pouch–Anal Anastomosis for Ulcerative Colitis and Familial Polyposis Coli

J.M.J.I. SALEMANS, MD, F.M. NAGENGAST, PhD, E.J.C. LUBBERS, PhD, and J.H. KUIJPERS, PhD

The immediate postoperative and long-term functional results of 51 ulcerative colitis patients and 21 familial polyposis patients who underwent ileal J-pouch–anal anastomosis were compared in this study. The incidence of postoperative complications requiring reoperation was not statistically different in both groups. The mean daily stool frequency was significantly higher in colitis patients. Pouchitis occurred in 44% of colitis patients but not in polyposis patients ($P < 0.005$). Symptoms of pouchitis included bloody diarrhea, urgency, abdominal pain, weight loss, fever, and arthritis. Six colitis patients required pouch excision because of intractable pouchitis. The overall pouch excision rate was 22% in ulcerative colitis patients and 5% in familial polyposis patients. Patient satisfaction was good in 46% of ulcerative colitis patients and 76% of polyposis patients ($P < 0.05$). Our data demonstrate that the long-term outcome of ileal pouch–anal anastomosis is more favorable in polyposis patients than in colitis patients. Pouchitis is a major long-term complication occurring exclusively in colitis patients.

KEY WORDS: ileal pouch–anal anastomosis; ulcerative colitis; familial polyposis coli; pouchitis.

Total colectomy and ileal pouch–anal anastomosis is an attractive surgical alternative for colectomy and permanent ileostomy in patients with chronic ulcerative colitis and familial polyposis coli because the entire colonic mucosa is removed while anal function can be preserved and the necessity for permanent ileostomy is eliminated (1, 2). Long-term functional results are generally gratifying as defecation frequency and degree of incontinence is acceptable in the majority of patients. Pouchitis, however, a nonspecific inflammation of the ileal reservoir, is a major long-term complication occurring in 8–44% of patients (3–15). Symptoms of pouchitis include bloody diarrhea, urgency of defecation associated with abdominal cramps, malaise, and occasionally fever and arthritis. Little is known about the pathogenesis of pouchitis. It has been suggested that pouchitis is the result of bacterial overgrowth in the ileal pouch (4–6). The generally satisfactory response to treatment with metronidazole supports this hypothesis. Bacterial overgrowth, however, is probably not the sole etiologic factor because pouchitis occurs less frequently in familial polyposis patients than in ulcerative colitis patients (4–6). Therefore several authors have suggested that pouchitis is a novel manifestation of inflammatory bowel disease persisting after total colectomy with ileal pouch–anal anastomosis (5, 16–21). Recently Lohmuller et al (5) found that patients with extraintestinal manifestations of inflammatory bowel dis-

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From the Department of Gastrointestinal and Liver Diseases, and Department of Surgery, University Hospital Nijmegen, Nijmegen, The Netherlands.

Address for reprint requests: F.M. Nagengast, Department of Gastrointestinal and Liver Diseases. University Hospital Nijmegen, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands.

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ease are at higher risk of developing pouchitis than patients who never had extraintestinal manifestations.

It is still a matter of debate whether to perform subtotal colectomy with ileorectal anastomosis or total colectomy with ileal pouch–anal anastomosis in patients with familial polyposis coli. The risk of cancer in the rectal stump after ileorectal anastomosis is approximately 10% and makes indefinite proctoscopic screening necessary (22). Still many surgeons prefer ileorectal anastomosis in familial polyposis arguing that it is less prone to complications and provides better long-term results than ileal pouch–anal anastomosis. These arguments are usually based on results achieved in series of ileal pouch–anal anastomoses performed in ulcerative colitis patients. However, results of the procedure are probably better in familial polyposis patients than in ulcerative colitis patients because polyposis patients are usually younger and in a better physical condition at the time of proctocolectomy than colitis patients. Moreover, polyposis patients are less prone to pouchitis. The aim of this study was to compare the immediate postoperative and long-term results of ileal pouch–anal anastomosis in ulcerative colitis and familial polyposis patients and to evaluate the occurrence, symptoms, and outcome of pouchitis.

MATERIALS AND METHODS

Patients. Between July 1983 and May 1990, 72 patients underwent ileal pouch–anal anastomosis for either ulcerative colitis (51 patients) or familial polyposis (21 patients) at the Nijmegen University Hospital. Forty-four of the patients were male; 28 were female. The mean age (SD) at the time of the ileal pouch procedure was 34 (13) years (range 10–61 years) in the ulcerative colitis patients and 27 (11) years (range 10–55 years) in the familial polyposis patients ($P < 0.05$). Twenty-seven (38%) patients had undergone subtotal colectomy with ileorectal anastomosis (four colitis and four polyposis patients) or ileostomy (18 colitis patients and one polyposis patient) prior to the construction of the ileal pouch. In the remaining 45 patients the initial operation included abdominal colectomy, mucosal proctectomy, and endorectal ileal pouch–anal anastomosis. All ulcerative colitis patients except those who had undergone colectomy with ileostomy (33 patients) but none of the familial polyposis patients used corticosteroids at the time of the ileal pouch procedure.

Operation. In all patients a "J" reservoir was constructed. The pouch was created by folding the terminal ileum back on to itself and anastomosing the limbs side to side. The rectal mucosa was removed from the rectal stump down to the dental line via a transanal approach. The ileal pouch was extended into the pelvis endorectally and its apex opened and sutured circumferentially to the dental line. In all patients a temporary loop ileostomy was established. At a second operation the temporary ileostomy was closed and ileal continuity reestablished. The mean interval (± SD) from construction of the ileal pouch–anal anastomosis to ileostomy closure was 6.1 ± 4.4 months in colitis patients and 4.4 ± 3.9 months in polyposis patients ($P < 0.01$).

Assessment of Results. Immediate postoperative data included mortality and morbidity requiring reoperation within 30 days after ileal pouch–anal anastomosis and ileostomy closure. Follow-up data included stool frequency, degree of incontinence, use of loperamide, occurrence of pouchitis, social functioning, and patient satisfaction. The records of all patients were studied retrospectively in June 1991. Patients with incomplete follow-up data were contacted by telephone for answers to a follow-up questionnaire. Stool frequency per 24 hr and per night was an estimate by the patients of the average number of bowel movements and was recorded 1, 3, 6, 12, and 24 months after ileostomy closure. Incontinence was defined as involuntary loss of mucus or stool requiring a perineal pad. The presence of incontinence during the day and night and use of loperamide were recorded at 12 months after ileostomy closure. Pouchitis was defined as present when episodes with abdominal cramping, bloody diarrhea, increased stool frequency, urgency, malaise, and/or fever were associated with endoscopic and histologic signs of acute inflammation. Endoscopic signs of inflammation were mucosal hyperemia with loss of vascular pattern with or without ulceration. Histological signs of acute inflammation of the ileal pouch mucosa were significant neutrophil infiltration and ulceration (18). Patients whose ileostomies were closed were asked whether they were able to work full-time or not and whether they preferred the new condition with the pouch to the ileostomy.

Statistical Analysis. Proportions were analyzed by chi-square tests with Yates's modification when appropriate. Comparisons of continuous variables were made with Student's t test or, where appropriate, with the rank-sum test. The probability of the occurrence of pouchitis in the colitis and polyposis groups was estimated with the Kaplan-Meier life-table analysis. Comparison of the two actuarial curves was made with the log-rank test. $P < 0.05$ was considered statistically significant.

RESULTS

Immediate Postoperative Results

One polyposis patient died from sepsis after the ileal pouch procedure and one colitis patient died from a cardiac arrythmia after ileostomy closure. After the initial operation, 13 (25%) ulcerative colitis patients and two (10%) polyposis patients required one or more laparotomies because of postoperative complications. After ileostomy closure 13 (30%) colitis patients and four (20%) polyposis

TABLE 1. POSTOPERATIVE COMPLICATIONS REQUIRING REOPERATION IN ULCERATIVE COLITIS (UC) AND FAMILIAL POLYPOSIS COLI (FPC) PATIENTS AFTER ILEAL POUCH PROCEDURE (IPAA) AND ILEOSTOMY CLOSURE

	IPAA			*Ileostomy closure*	
	UC ($N = 51$)	*UC* ($N = 21$)		*UC* ($N = 43$)	*FPC* ($N = 20$)
Small bowel obstruction	5 (10%)	2 (10%)	Small bowel obstruction	4 (9%)	2 (10%)
Anastomotic dehiscence	6 (12%)		Anastomotic leakage	4 (9%)	
Other	2 (4%)		Rectovaginal fistula	3 (7%)	
	13 (25%)	2 (10%)		13 (30%)	4 (20%)

patients needed reoperation (Table 1). These differences were not statistically significant. Small bowel obstruction was the most frequently encountered complication requiring relaparotomy after both the ileal pouch procedure and ileostomy closure.

Long-Term Functional Results

Analysis of stool frequency, use of loperamide, occurrence of pouchitis and of incontinence was performed in all patients whose ileostomies were taken down. In four colitis patients the pouch was removed before ileostomy closure and in three colitis patients the ileostomy was still not closed at the time of evaluation. Mean follow up after ileostomy closure in the remaining 43 colitis and 20 polyposis patients was 34 months (range 2–92) and 63 months (range 6–90), respectively. Pouch excision rate was calculated in all colitis and polyposis patients.

Stool Frequency. The mean stool frequency per 24 hr after ileostomy closure decreased gradually in both patient groups but was significantly lower in familial polyposis patients at any time after ileostomy closure (Figure 1a). Nocturnal stool frequency was significantly lower in polyposis patients one month after ileostomy closure and tended to be lower in these patients thereafter (Figure 1b). At one year eight (26%) colitis patients and one (5%) polyposis patient had more than eight stools per 24 hr. At that time five (16%) colitis patients and one (5%) polyposis patient had more than two stools during the nighttime.

Pouchitis. The overall incidence of pouchitis during follow-up was 44% in ulcerative colitis patients (19 of 43 patients) and 0% in polyposis patients ($P < 0.005$). The presence of pouchitis was confirmed by endoscopic and histological examination in all patients with symptoms compatible with pouchitis. Life-table analysis of risk of pouchitis for both ulcerative colitis and familial polyposis coli is shown in Figure 2. The probability of pouchitis occurring within five years after ileostomy closure in colitis patients is 57% versus 0% in polyposis patients ($P < 0.001$). Mean time to the first pouchitis episode was 14 months (range 1–48 months).

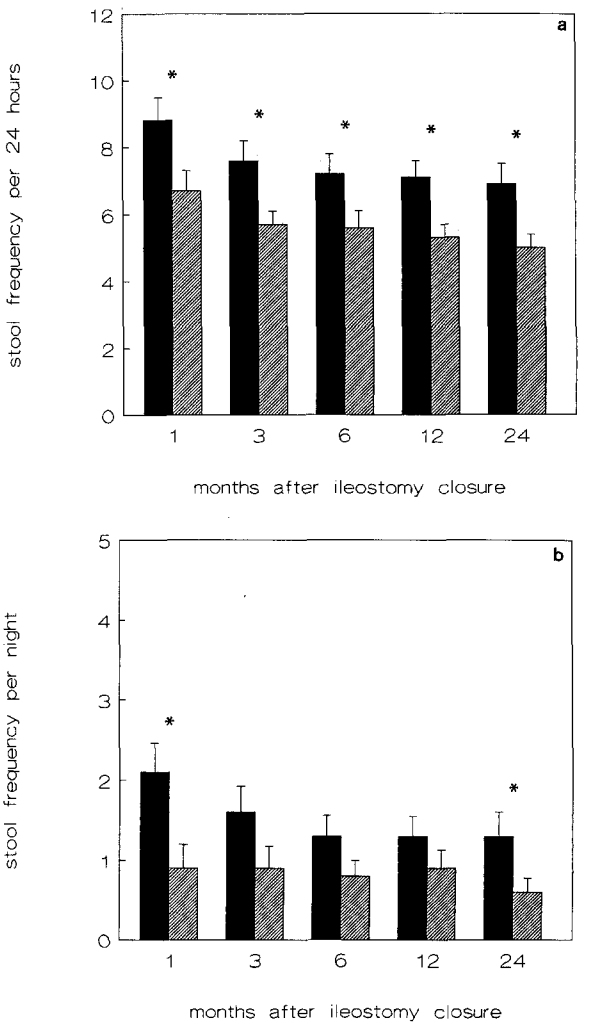

Fig 1. Twenty-four hour (a) and nocturnal (b) stool frequency (mean + SEM) 1, 3, 6, 12, and 24 months after ileostomy closure in ulcerative colitis patients (closed bars) and familial polyposis patients (hatched bars) (*$P < 0.05$).

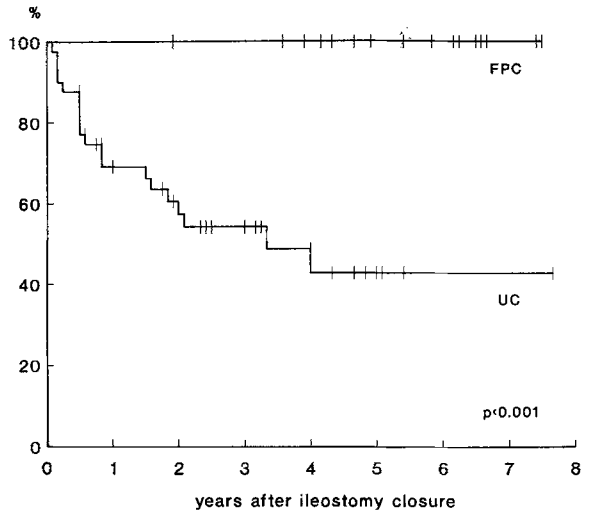

Fig 2. Life-table analysis of risk of pouchitis after ileostomy closure in ulcerative colitis patients and familial polyposis patients. Pouchitis did not occur in polyposis patients. The risk of pouchitis was significantly greater in ulcerative colitis patients.

The incidence of pouchitis was not affected by sex or age. The occurrence of pouchitis did not affect the incidence of incontinence. The number of stools per 24 hr during episodes of pouchitis was significantly higher than before pouchitis occurred (mean: 13.5 vs 7.7 stools/day, $P < 0.001$). The mean stool frequency in patients with pouchitis before the first pouchitis episode did not differ significantly from that in ulcerative colitis patients who never developed pouchitis.

Pouchitis occurred in eight of the 22 (36%) colitis patients who had undergone subtotal colectomy prior to the ileal pouch procedure and in 11 of the 29 (38%) colitis patients in whom ileal pouch–anal anastomosis was the initial procedure (NS).

Initial episodes of pouchitis were treated with metronidazole in all patients. When this treatment was unsuccessful, local or oral corticosteroids were given (13 patients). Recurrent episodes were treated in the same way. Twelve (63%) of the 19 patients with pouchitis responded favorably to medical treatment. Pouchitis occurred only once in two patients (11%). Ten (53%) patients had intermittently recurring pouchitis. The remaining seven (37%) patients developed chronic pouchitis that responded poorly to medical treatment. In six (32%) patients from the latter group the pouch was removed because of intractable pouchitis. In the seventh patient the pouch was still not removed at the time of evaluation. Histological examination of the removed pouches showed no signs of Crohn's disease.

TABLE 2. SYMPTOMS OF POUCHITIS ($N = 19$)

Symptom	*Number of patients (%)*
Increased stool frequency	13 (68)
Abdominal pain	14 (74)
Bloody stools	15 (79)
Fever	8 (42)
Weight loss	8 (42)
Fatigue	15 (79)
Arthritis	5 (26)

Symptoms of pouchitis included bloody diarrhea, urgency, increased stool frequency, abdominal cramps, fatigue, fever, and weight loss (Table 2). Five patients with pouchitis (26%) developed arthritis. Arthritis occurred concomitantly with the onset of pouchitis episodes and affected knees, ankles, elbows, and wrists. Three of these patients required permanent ileostomy because of intractable pouchitis. In all three arthritis disappeared rapidly after pouch excision. Arthritis did not occur in patients without pouchitis. The remaining two patients who developed arthritis responded favorably to oral corticosteroids.

Endoscopy showed inflammation (hyperemia, edema, loss of vascular pattern) of the ileal pouch mucosa in all pouchitis patients. Ulceration was seen in 16 (84%) patients. Mucosal biopsies from the ileal reservoir showed acute (infiltration of polymorphonuclear cells) and chronic inflammation (total or partial of villous atrophy and infiltration of lymphocytes, plasma cells and eosinophils) in all patients with pouchitis.

Incontinence. One year after ileostomy closure one ulcerative colitis patient and one polyposis patient were incontinent during the daytime. During the nighttime 16 (43%) colitis patients and six (32%) polyposis patients required a pad because of incontinence (NS).

Use of Loperamide. One year after ileostomy closure 19 (51%) ulcerative colitis patients and 12 (63%) polyposis patients used loperamide to decrease stool frequency (NS).

Pouch Excision. There was a tendency towards a lower rate of pouch excision in polyposis patients, but this failed to achieve statistical significance. In 11 (22%) of the 51 ulcerative colitis patients and in one (5%) of the 21 familial polyposis patients, the pouch was removed and a permanent ileostomy constructed ($P = 0.16$). Reasons for pouch excision were anastomotic dehiscence in three ulcerative colitis patients, pelvic abscesses in one colitis pa-

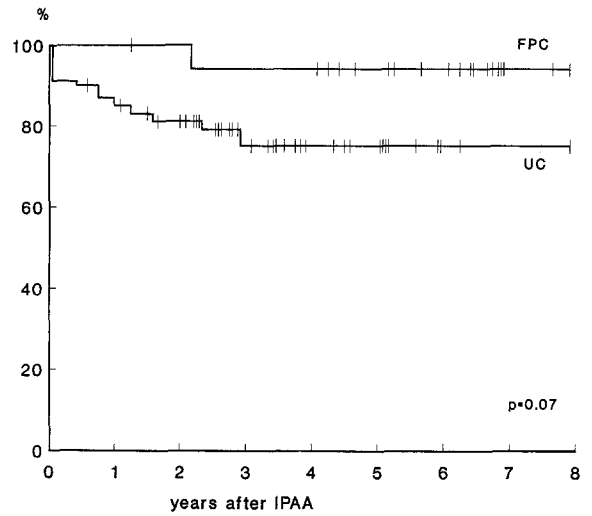

Fig 3. Life-table analysis of risk of pouch excision in ulcerative colitis patients and familial polyposis patients after ileal pouch–anal anastomosis. There was a tendency towards a lower rate of pouch excision in polyposis patients, but this failed to achieve statistical significance.

tient, intractable pouchitis in six colitis patients, incontinence in one colitis patient and unacceptably high stool frequency in one polyposis patient. Figure 3 depicts a life-table analysis of pouch excision in ulcerative colitis patients and polyposis patients. The probability of pouch excision occurring within five years after the ileal pouch procedure is 26% in ulcerative colitis patients versus 6% in familial polyposis patients ($P = 0.07$).

Ten (45%) of the 22 ulcerative colitis patients and one (20%) of the five familial polyposis patients who had undergone subtotal colectomy prior to the ileal pouch procedure required pouch excision. This difference was not statistically significant. When all patients with prior subtotal colectomy ($N = 27$) were considered as a group and compared to the patients in whom proctocolectomy with IPAA was the initial procedure ($N = 45$), the number of excised pouches was 11 (41%) and 1 (2%), respectively ($P < 0.001$).

Final Outcome. In three ulcerative colitis patients the ileostomy was still not closed at the time of evaluation. Therefore these patients were not included in the evaluation of final outcome. In the ulcerative colitis group the operation was unsuccessful in 12 patients (one postoperative death, 11 pouch excisions). The remaining 36 patients all preferred their pouch to the ileostomy. However, 14 of these patients (including seven patients with pouchitis) felt unable to work full-time because of fatigue. Therefore, at the long-term the procedure was entirely successful in only 22 ulcerative colitis patients (46%). In the familial polyposis group the procedure failed in two patients (one postoperative death, one pouch excision). The remaining 19 patients all preferred the pouch to the ileostomy. Two of these patients were not able to work full-time because of fatigue. Finally, 16 (76%) polyposis patients felt satisfied with their pouch. The difference between the two groups was statistically different at the $P < 0.05$ level.

DISCUSSION

In this study the immediate postoperative and long-term functional results of ileal pouch–anal anastomosis in 51 ulcerative colitis patients and 21 familial polyposis patients were compared. The interval between the ileal pouch procedure and ileostomy closure was longer in colitis patients than in polyposis patients. Ileostomy closure was carried out at the time that the patients were considered to be reasonably recovered from the ileal pouch procedure. Precise data demonstrating that polyposis patients are in better health at the time of the ileal pouch procedure than colitis patients are lacking in this retrospective study. Nevertheless, this is likely to be true because polyposis patients are usually operated electively whereas colitis patients undergo (procto)colectomy when severe and disabling disease is not responding to medical treatment. The majority of colitis patients but none of the polyposis patients used corticosteroids at that time. Although postoperative complications requiring relaparotomy after both the ileal pouch procedure and ileostomy closure occurred more frequently in ulcerative colitis patients than in polyposis patients, these differences did not reach statistical significance in our series.

The major long-term complication after ileal pouch–anal anastomosis is pouchitis, which occurred in 44% of ulcerative colitis patients but not in familial polyposis patients. The estimated risk of pouchitis five years after ileostomy closure in ulcerative colitis patients was 57%. As experience with the ileoanal pouch increases and follow-up lengthens, the incidence of pouchitis tends to increase (5). Even after three years of follow-up new cases of pouchitis arose in our series.

The incidence of pouchitis in our series is higher than in many other reports (3–15), where the incidence ranges from 8% to 44%. This wide range probably reflects the lack of a uniform diagnostic

standard. Moskowitz et al (18) suggested that for an unequivocal diagnosis, symptoms of pouchitis should be accompanied by endoscopic and histological features of acute inflammation. In our study all patients with clinical pouchitis fulfilled these criteria.

In some reports (9, 10, 15) colitis patients and polyposis patients were considered as one group. When colitis patients were considered separately, the rate of pouchitis would have been higher in these studies because pouchitis probably does not occur in polyposis patients. Nevertheless, the rate of pouchitis in our colitis patients is higher than in the colitis patients in the Mayo Clinic series (31%) (5). It is difficult to explain this discrepancy. In our series pouchitis was carefully looked for by endoscopy and histology, whereas in the Mayo Clinic series pouchitis was merely a clinical diagnosis.

The cause of pouchitis remains unclear. Bacterial overgrowth due to fecal stasis in the ileal pouch has been suggested as a possible pathogenetic factor. In a study by Go et al (23) ileum effluent of Kock's continent ileostomy patients showed significantly higher counts of anaerobic microorganisms (eg, *Bacteroides*) than in ileum effluent of patients with a conventional ileostomy. Nasmyth et al (17) also found greater numbers of *Bacteroides* in ileoanal pouch effluent compared with conventional ileostomy effluent. However, quantitative cultures of pouch effluent from patients with pouchitis did not reveal higher numbers of anaerobes compared with controls without evidence of pouchitis (24). These findings were confirmed by Luukkonen et al (25), who found significantly higher anaerobic counts in pouch patients compared to conventional ileostomy patients, but no specific changes in fecal bacteriology were found in patients with acute clinical pouchitis. However, since many patients respond to metronidazole, anaerobic bacterial overgrowth may contribute to the pathogenesis of pouchitis.

Several authors have suggested that pouchitis is a novel manifestation of inflammatory bowel disease after proctocolectomy (5, 16–21). In most studies pouchitis occurred exclusively in ulcerative colitis patients. Only a few cases of pouchitis in familial polyposis patients have been reported by workers from the Mayo Clinic (4, 5). These cases were poorly documented because endoscopy was not performed in these patients. However, in the Mayo Clinic population ulcerative colitis patients were at much higher risk of developing pouchitis compared to familial polyposis patients. Moreover, ulcerative colitis patients with extraintestinal manifestations of inflammatory bowel disease before proctocolectomy were at higher risk of developing pouchitis than were patients without extraintestinal manifestations. In agreement with our experience in some patients from the Mayo Clinic, a temporal relationship between flares of extraintestinal manifestations and pouchitis was observed (5). These findings support the hypothesis that pouchitis is a novel manifestation of inflammatory bowel disease persisting after proctocolectomy with ileoanal pouch anastomosis.

It has been suggested that the pouch mucosa, in an adaptive response to its new luminal environment, undergoes colonic metaplasia and thus may become vulnerable to immune damage in predisposed people (16, 19, 26–29). In a study on mucosal characteristics of pelvic ileal pouches using routine histology, mucin histochemistry, and monoclonal antibodies directed towards colonic and small bowel specific proteins (29), villous atrophy and colonic type sulphomucin was found in all pouchitis patients. However, sucrase–isomaltase, a small bowel specific disaccharidase, was present in all pouches irrespective of the presence of villous atrophy or pouchitis. It was concluded that although some ileal pouches, especially those with signs of acute inflammation, acquire certain colonic characteristics, complete colonic metaplasia does not occur.

Another factor that has been suggested to play a pathogenetic role in pouchitis is bacterial deconjugation and dehydroxylation of primary bile acids (16, 30). Under normal circumstances the greatest part of the conjugated bile acid pool is transported actively by the ileal mucosa into the portal venous system. Less than 10% of the bile acid pool passes the cecal valve and is deconjugated by the colonic bacterial flora. After deconjugation, the unconjugated primary bile acids are dehydroxylated by the colonic bacteria to secondary bile acids. Loss of hydroxyl groups makes bile acids more lipophilic than the corresponding primary bile acids (31). Under experimental conditions secondary bile acids like deoxycholic acid cause an increase of water and salt permeability in colonic mucosal cells followed by cell death (32). Therefore bacterial overgrowth in the ileal pouch probably leads to deconjugation and dehydroxylation of a great part of the bile acid pool, which may exert a toxic effect on the ileal pouch mucosa. This mechanism plays at best a supplementary role in the pathogenesis of pouchitis

because it does not explain why pouchitis does not occur in familial polyposis.

Patients who had undergone subtotal colectomy prior to the ileal pouch procedure were at high risk for pouch excision. The incidence of pouchitis was similar in the colitis patients who had undergone subtotal colectomy prior to the ileal pouch procedure and in the colitis patients in which the pouch procedure was the initial operation. This suggests that subtotal colectomy is an independent risk factor for pouch excision. In three patients the pouch was removed because of complete anastomotic dehiscence and in one patient because of pelvic abscesses, probably because of incomplete dehiscence. Traction on the pouch–anal anastomosis is often higher in patients who underwent previous intestinal surgery due to adhesions and mesenterial retraction.

In conclusion, the rate of complications requiring relaparotomy after both ileal pouch–anal anastomosis and ileostomy closure is considerable in both ulcerative colitis patients and familial polyposis patients. Long-term functional results are better in familial polyposis compared to ulcerative colitis patients since pouchitis does not occur in polyposis patients, the stool frequency is lower in polyposis patients, and patient satisfaction is better in polyposis patients. Pouchitis is a major long-term complication of ileal pouch–anal anastomosis occurring in approximately 50% of ulcerative colitis patients but not in familial polyposis patients. Pouchitis may lead to pouch excision in a considerable number of colitis patients. Many pouchitis patients show a favorable response on treatment with metronidazole, although this response is usually temporary. Patients who have undergone subtotal colectomy prior to the ileal pouch procedure are at higher risk of pouch excision compared to patients in which ileal pouch–anal anastomosis is the initial procedure.

These results have important implications for the information that should be given to ulcerative colitis patients and familial polyposis patients who are candidates for ileal pouch–anal anastomosis.

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