Clinical and Physiological Aspects of Ileal Pouch-Anal Anastomosis

J. M. J. I. SALEMANS & F. M. NAGENGAST
Dept. of Medicine, Division of Gastroenterology and Hepatology, University Hospital Nijmegen, Nijmegen, The Netherlands

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Proctocolectomy with ileal pouch-anal anastomosis is the surgical treatment of choice for severe 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. Long-term functional results are generally gratifying, as defecation frequency and degree of incontinence are acceptable in most patients. Pouchitis, however, a non-specific inflammation of the ileal reservoir, is a major long-term complication occurring in a considerable number of patients. The etiology of pouchitis is unknown. Since pouchitis occurs more frequently or even exclusively in ulcerative colitis patients it is assumed that pouchitis is a novel manifestation of inflammatory bowel disease. However, bacterial overgrowth in the ileal pouch may also play a pathogenetic role. Chronic inflammation and villous atrophy of varying severity is found in virtually all pouches. Acute inflammatory changes and ulceration are associated with pouchitis.

Key words: Familial polyposis; ileal pouch-anal anastomosis; pouchitis; ulcerative colitis

J. M. J. I. Salemans, M.D., Geert Grooteplein Zuid 8, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands (fax: +31 80 540103)

Total colectomy with ileal pouch-anal anastomosis has been accepted as the treatment of choice for severe ulcerative colitis and familial polyposis coli. The main advantages of the procedure are that it obviates the need for a permanent ileostomy, it preserves anal continence, and it removes all disease-prone mucosa. This review discusses the immediate postoperative and long-term functional results after ileal pouch-anal anastomosis, recent surgical developments in pouch surgery, pouchitis and histologic alterations in the ileal-pouch mucosa, and physiological changes after pouch surgery.

POSTOPERATIVE COMPLICATIONS AFTER ILEAL POUCH-ANAL ANASTOMOSIS

Although the mortality of proctocolectomy with ileal pouch-anal anastomosis is remarkably low, there is a substantial postoperative morbidity. The commonest major postoperative complications include anastomotic stricture, perianal abscess, fistula, intra-abdominal abscess (pelvic sepsis), and small bowel obstruction.

Anastomotic stricture

The risk of anal stricture following ileal pouch-anal anastomosis has been reported to be between 8% and 14% (1,2). Most of the strictures will respond favourably to a single dilatation. However, repeated dilatations may result in fibrosis or incontinence. Recurrent strictures may increase the risk of pouchitis (3).

Pelvic sepsis

The incidence of pelvic sepsis following ileal pouch-anal anastomosis varies between 5% and 20% (2,4–8). Pelvic sepsis may result from anastomotic dehiscence or disruption of the suture or staple line. Cuff abscess was the most common cause of pelvic sepsis at the time surgeons used to leave a rectal cuff through which the pouch was pulled down. Since the introduction of a stapled ileal pouch-anal anastomosis, which does not involve a rectal cuff, this complication has been eliminated. Pelvic sepsis is the commonest cause of pouch failure and results in pouch excision in approximately 5–10% of all pouches (2,7,9,10).

Small bowel obstruction

Small bowel obstruction is the most common early complication occurring in approximately 15–20% of patients undergoing ileal pouch anal anastomosis (4,5,10–13). Approximately half of these patients require surgical intervention (14). The majority of episodes of small bowel obstruction occur after closure of the temporary ileostomy.

LONG-TERM RESULTS AFTER ILEAL POUCH-ANAL ANASTOMOSIS

The largest series with the longest follow-up to date on the quality of life after ileal pouch-anal anastomosis has been reported by Kohler et al. (15) from the Mayo Clinic. They randomly selected 240 patients from 971 patients with chronic ulcerative colitis who had undergone ileal pouch-

anal anastomosis between 1982 and 1989 (30 patients each year) for an assessment of their long-term functional results and quality of life. One-hundred-and-sixty patients undergoing cholecystectomy during each of the same years served as controls (20 patients per year). Ileal pouch-anal anastomosis patients had more frequent stools and more fecal spotting than cholecystectomy patients. In spite of the altered bowel habits, 90% of ileal pouch-anal anastomosis patients had an excellent overall quality of life and 91% had good performance scores in the areas examined. Results were similar to patients who had undergone cholecystectomy. Moreover, quality of life and bowel habits remained steady in both groups of patients during the 8-year follow-up.

Several studies have compared the postoperative and long-term functional results of the ileal–anal pouch anastomosis procedure in ulcerative colitis and familial polyposis patients (3, 10, 11, 16, 17). Table I summarizes the frequency of postoperative complications, the stool frequency at one-year follow-up, the percentage of patients with night-time soiling, and the incidence of pouchitis in both patient groups in these studies. Colitis patients tend to have a higher overall complication rate and more pouch-related septic complications, but these differences are generally not statistically significant. In most studies the long-term functional results are better in polyposis patients. However, Tjandra et al. (17) found very similar functional outcomes after ileal pouch-anal anastomosis in polyposis patients and ulcerative colitis patients. They studied 39 pairs of patients, individually matched for surgeon, types of ileal pouch, technique of ileal pouch-anal anastomosis, duration of follow-up after pouch construction, age, and gender. The major difference between both groups was that pouchitis occurred more frequently in the colitis group than in the polyposis group.

INFLUENCE OF POUCH DESIGN ON FUNCTIONAL OUTCOME

Nicholls and Pezim (18) compared functional outcome in 88 colitis and polyposis patients who had undergone restorative proctocolectomy with three different pouch designs (58 triplicated (S), 12 duplicated (J) and 18 quadruplicated (W) pouches). Stool frequency was significantly higher in patients with J pouches compared to those with W pouches or S pouches. Overall, there was an inverse relationship between reservoir volume and defecation frequency. J pouches were significantly smaller than the other two designs. All patients with J or W pouches defecated spontaneously, while only 41% of those with S pouches did so. Sagar et al. (19) compared functional outcome between S and W pouches and found that the mean stool frequency in patients with W pouches (3.5 per day) was significantly lower compared to those with S pouches (6.0 per day). Patients with W pouches were found to have greater efficiency of evacuation and their pouches were more capacious compared to those with S pouches. In conclusion, stool frequency after ileal pouch-anal

Table I. Comparison of postoperative and long-term functional results of the ileo-anal pouch anastomosis operation for ulcerative colitis (UC) and familial polyposis coli (FPC)

Study (reference)	No. of patients FPC vs UC	Postoperative complications (%) FPC vs UC	Stool frequency (per 24 h) FPC vs UC‡	Nighttime incontinence (%) FPC vs UC	Pouchitis (%) FPC vs UC	Conclusions, comments
Becker and Raymond (11)	22/78	Overall: 13	4.4 vs 5.8†	?	0 vs 30†	Long-term results are better in FPC patients
Dayton et al. (16)	38/239	Similar in FPC and UC patients	4.2 vs 6.0†	5 vs 25†	0 vs 19†	Long-term results are better in FPC patients
Dozois et al. (3)	94/758	26 vs 29*	4.5 vs 5.8†	26 vs 40†	7 vs 22†	Long-term results are better in FPC patients, sepsis requiring reoperation more common in UC patients
Tjandra et al. (17)	39/39	21 vs 28*	6 vs 6*	51 vs 51*	10 vs 33†	FPC and UC patients have similar functional outcomes, but pouchitis is more common in UC
Salemans et al. (10)	21/51	10 vs 25*	5 vs 7†	32 vs 43*	0 vs 44†	Long-term results are better in FPC patients

* Not significant.
† $p < 0.05$.
‡ Usually at 1 year follow-up after ileostomy closure.

anastomosis appears to be inversely related to pouch capacity. The majority of patients evacuate spontaneously after ileal pouch-anal anastomosis, and catheter evacuation has only been reported in patients with S pouches.

SUBTOTAL COLECTOMY BEFORE ILEAL POUCH-ANAL ANASTOMOSIS

In patients with ulcerative colitis, ileal pouch-anal anastomosis can be performed either at the time of colectomy or as a delayed procedure after subtotal abdominal colectomy and ileostomy. There has been debate as to whether delayed ileal pouch-anal anastomosis results in superior functional results, since patients are frequently steroid-free and have little evidence of active disease. Galandiuk et al. (20) analyzed 95 patients who had undergone subtotal colectomy prior to ileal pouch-anal anastomosis. Postoperative complications were compared with those of 776 ulcerative colitis patients who underwent ileal pouch-anal anastomosis at the time of colectomy. Delayed ileal pouch-anal anastomosis was associated with a significantly higher rate of septic complications (11% versus 5%), but a lower incidence of postoperative obstruction (7% versus 15%) compared to ileal pouch-anal anastomosis at the time of colectomy. Functional results were similar in both groups. In our experience (10), patients who had undergone subtotal colectomy prior to the ileal pouch procedure were at high risk for pouch failure. When all patients who had undergone subtotal colectomy prior to ileal pouch-anal anastomosis ($n = 27$) were compared to the patients in which proctocolectomy with ileal pouch-anal anastomosis was the initial procedure ($n = 45$), the number of excised pouches was 11 (41%) and 1 (2%), respectively ($p < 0.001$). In contrast to these studies, Penna et al. (21) found lower rates of pelvic sepsis and postoperative small bowel obstruction in patients who had undergone subtotal colectomy with ileostomy prior to the pouch procedure compared with patients who underwent the classical two-stage procedure. The functional outcome was similar in both groups.

SURGICAL PROCEDURES: RECENT DEVELOPMENTS

Handsewn versus stapled pouch-anal anastomosis

The originally introduced pelvic pouch procedure (22, 23) involved transanal mucosectomy, a long rectal muscular cuff and a handsewn ileoanal anastomosis. In order to improve functional outcome and to reduce the incidence of postoperative anastomotic complications the stapled ileal pouch-anal anastomosis was introduced (24). This procedure avoids the difficult and time-consuming mucosal proctectomy, but leaves 1–2 cm of rectal mucosa behind proximal to the dentate line to facilitate the stapled anastomosis. The risk of cancer in this small segment of remaining rectal mucosa does not seem to be very high. However, persisting disease activity, dysplasia, and cancer in the remaining rectal mucosa have

Table II. Studies comparing clinical outcome of ileal pouch-anal anastomosis with and without temporary diverting ileostomy

Study and year of publication	Type of study	No. of patients with vs without diverting ileostomy	Type of operation with vs without diverting ileostomy	Use of steroids with vs without diverting ileostomy	Incidence of pouchitis with vs without ileostomy	Anastomotic leaks and pelvic sepsis with vs without ileostomy	Conclusions, comments
Jarvinen & Luukkonen (93) 1991	Retrospective, non-randomized	15 vs 16	HSA/HSA	?	20% vs 5% (NS)	0% vs 6% (NS)	Incidence of complications and functional results similar in both groups, hospital stay shorter without ileostomy
Cohen et al. (31) 1992	Retrospective, non-randomized	71 vs 87	SA/SA	?	?	7% vs 18% ($p < 0.05$)	Higher incidence of anastomotic leaks in patients without ileostomy and in those taking steroids
Grobler et al. (29) 1992	Prospective, randomized	23 vs 22	SA/SA	Patients on steroids were excluded	9% vs 23% (NS)	4% vs 5% (NS)	Incidence of complications and functional results similar in both groups, hospital stay shorter without ileostomy
Sagar et al. (30) 1992	Retrospective, non-randomized	28 vs 30	SA/SA	29% vs 33%	?	10% vs 11% (NS)	Incidence of complications similar in both groups, hospital stay shorter in patients without ileostomy
Sugerman & Newsome (37) 1994	Retrospective non-randomized	63 vs 68	HSA/SA	? vs 63%	28% vs 31% (NS)	33% vs 15% ($p < 0.05$)	Incidence of complications and functional results similar in both groups, hospital stay shorter without ileostomy
Tjandra et al. (36) 1993	Non-randomized	50 vs 50	SA/SA	40% vs 40%	18% vs 22% (NS)	4% vs 14% ($p < 0.05$)	Higher incidence of anastomotic leaks in patients taking steroids, functional results similar in both groups

HSA = handsewn ileal pouch-anal anastomosis with mucosectomy; SA = stapled ileal pouch-anal anastomosis without mucosectomy; ? = not stated; NS = not significant.

been documented (25, 26). Several groups have compared the clinical outcome of handsewn ileoanal anastomosis with mucosectomy versus stapled ileoanal anastomosis without mucosectomy (6, 9, 27). Wettergren et al. (9) studied 144 consecutive patients who underwent either handsewn ($n = 96$) or stapled ($n = 48$) J-pouch ileoanal anastomosis. The percentage of anastomotic leaks was similar in both groups (13% versus 15%), as was the percentage of pouches that had been removed because of postoperative complications (5% versus 6%), but the incidence of anastomotic stenosis was significantly higher in patients with a handsewn anastomosis (23% versus 6%).

Two prospective, randomized studies (6, 27) comparing the complication rate and functional outcome after handsewn ileal pouch-anal anastomosis with mucosectomy or stapled ileoanal anastomosis without mucosectomy showed a similar complication rate and similar functional results in both groups. The authors of both articles concluded that double-stapled ileoanal anastomosis does not offer any functional or technical advantage over hand-sutured anastomosis, and they preferred full mucosectomy since removal of disease is complete.

Schmitt et al. (28) studied the incidence of inflammation and dysplasia in retained mucosa after double-stapled ileoanal reservoir ulcerative colitis. They evaluated 56 patients who had undergone double-stapled ileal pouch-anal anastomosis with a mean of 1 cm of rectal epithelium left above the dentate line. No evidence of dysplasia was found in any of the biopsy specimens just above the dentate line, and the distal resection line revealed active ulcerative colitis in 19 (35%) patients. Only one of these patients experienced any symptoms referable to active colitis.

Temporary diverting ileostomy

Until recently, a temporary defunctioning loop ileostomy has been employed routinely in patients undergoing ileal pouch-anal anastomosis to lessen the risk of anastomotic leak and pelvic sepsis. However, the ileostomy itself and its closure may be a source of significant complications (10, 29–35). Moreover, ileostomy closure prolongs total hospital stay (29, 30).

Table II summarizes a number of studies comparing clinical outcome of ileal pouch-anal anastomosis with and without temporary diverting ileostomy. Cohen et al. (31) compared the surgical complication rate and outcome of 483 consecutive patients who had undergone ileal pouch-anal anastomosis performed with or without loop ileostomy. Three-hundred-and-twenty-five patients had a handsewn anastomosis with ileostomy, 87 had a stapled ileal pouch-anal anastomosis with ileostomy, and 71 patients had a stapled anastomosis without ileostomy. The rate of anastomotic leakage was significantly reduced in patients with a stapled ileal pouch-anal anastomosis with ileostomy compared with those with a handsewn anastomosis and ileostomy. The omission of the ileostomy was associated with a higher incidence of anastomotic leaks, but spontaneous healing occurred in almost all patients. Patients on steroids and patients who had undergone a true one-stage procedure had a greater risk of developing an anastomotic leak. Functional results were excellent in all groups, even in the patients who had had an anastomotic leak.

In a prospective randomized study, Grobler et al. (29) assessed the role of temporary ileostomy in patients receiving a stapled ileal pouch-anal anastomosis. Patients using steroids were excluded. The incidence of anastomotic leaks, pelvic sepsis, bowel obstruction, and pouchitis was similar in patients with or without ileostomy. Approximately half of the patients in the ileostomy group developed ileostomy-related complications and total hospital stay was longer with ileostomy.

In a non-randomized way, Sagar et al. (30) similarly compared the clinical outcome after stapled ileal pouch-anal anastomosis with or without temporary ileostomy. The use of high-dose corticosteroids was no contraindication to ileostomy omission. The decision for or against an ileostomy was made during the procedure based on urgency, toxaemia, anastomotic tension, and integrity of anastomoses. The avoidance of the ileostomy did not lead to an increased incidence of pelvic sepsis. The total length of stay in the hospital (included the hospitalization for ileostomy closure) was significantly reduced in the group of patients without an ileostomy.

In a study by Tjandra et al. (36), anastomotic leakage, pelvic abscess, and septic complications requiring relaparotomy were more common after ileal pouch-anal anastomosis without ileostomy, compared to a carefully matched control group of patients with ileostomy. Patients using high-dose corticosteroids had an increased risk of complications. Functional results were similar in both groups. Sugerman and Newsome (37), however, found fewer acute complications and better stool control in patients with a stapled ileal pouch-anal anastomosis without ileostomy compared to a control group of patients with mucosectomy, handsewn ileal pouch-anal anastomosis, and temporary ileostomy.

In conclusion, omitting a temporary loop ileostomy probably does not lead to an increased number of pouch failures, not at least in a group of selected patients. In general, functional results are similar in patients who are operated without ileostomy compared to those without ileostomy. Whether the use of corticosteroids at the time of surgery increases the risk of anastomotic leaks is not clear, since data are scarce and conflicting. A temporary loop ileostomy itself is associated with a high incidence of complications and a prolonged hospital stay.

ILEAL POUCH-ANAL ANASTOMOSIS IN CROHN'S DISEASE

Ileal pouch-anal anastomosis is generally considered contraindicated in patients with Crohn's disease because of the high

Table III. Incidence of pouchitis

Study	No. of patients	Pouchitis	Diagnosis		
			Clinical	Endoscopy	Biopsy
Rauh et al. (69)	215	30(14%)	+	+	–
Becker & Raymond (11)	100	18(18%)	+	+	–
de Silva et al. (68)	61	13(21%)	+	+	+
Metcalf et al. (49)	188	15 (8%)	+	–	–
Pemberton et al. (4)	390	55(14%)	+	–	–
Lohmuller et al. (41)	734	212(29%)	+	–	–
McMullen et al. (94)	73	11(15%)	+	–	–
Schoetz et al. (95)	104	7 (7%)	+	–	–
Fonkalsrud et al. (96)	145	34(23%)	+	–	–
Telander et al. (97)	114	29(25%)	+	+	+
Salemans et al. (10)	72	19(30%)	+	+	+
Penna et al. (98)	41	(0%)[1]			
Tjandra et al. (17)	78	17(22%)	+	–	–
Dayton et al. (16)	277	45(16%)	+	–	–

[1] This study included only familial polyposis coli patients.

risk of pelvic sepsis, fistulas (pouch-anal and pouch-vaginal), and pouchitis. However, distinction between ulcerative colitis and Crohn's colitis may be difficult, if not impossible. The outcome of ileal pouch-anal anastomosis in patients who were operated upon for presumed ulcerative colitis but subsequently were found to have Crohn's disease has been described by several groups. Hyman et al. (38) reviewed the records of 362 ileal pouch patients with a preoperative diagnosis of ulcerative colitis and analyzed the outcome of 25 (7%) patients who were postoperatively proven to have Crohn's disease. Sixteen patients had a functioning pouch, seven had required pouch excision, one was diverted, and one had died. In a subgroup of 9 patients in which there was a clinical feature suspicious for Crohn's disease preoperatively, 8 patients had their pouch removed ($p < 0.01$). Deutsch et al. (39) reported on 9 (3.5%) out of 272 patients who appeared to have Crohn's disease. Four patients (44%) eventually had their pouches removed, and five patients had functioning pouches: three with no complications and two with persistent perianal disease. Grobler et al. (40) found a marginally higher complication rate in 20 patients with pathological features of Crohn's disease. Pouch excision or a persistent stoma was necessary in 30% of patients with Crohn's disease compared to 15% in patients with definite ulcerative colitis ($p = 0.23$). However, functional results were acceptable if the pouch could be retained. These data demonstrate that patients with Crohn's colitis have an increased risk of complications and pouch failure. Therefore, ileal pouch-anal anastomosis should not knowingly be performed in these patients.

POUCHITIS

Ileal pouch inflammation or pouchitis is one of the major long-term complications of ileal pouch-anal anastomosis. Clinically, pouchitis is characterized by increased stool frequency, bleeding, abdominal pain, and systemic symptoms such as fever, arthralgia, fatigue, and weight loss. There is much confusion surrounding pouchitis because the syndrome has not been tightly defined. The reported incidence of pouchitis varies widely between 7% and 42% (3, 4, 10, 11, 41–49). This variation can partly be explained by whether or not endoscopic and histologic confirmation was required to establish a diagnosis of pouchitis (Table III). Therefore, it has been proposed by several authors that the definition of pouchitis should include endoscopic (increased vascularity, bleeding, ulceration) and histopathological (acute inflammation, ulceration, chronic changes) criteria (50–52). Moreover, the incidence of pouchitis tends to increase with more prolonged follow-up, as can be seen in successive reports from the Mayo Clinic (4, 41, 49).

The etiology of pouchitis is unknown. It has been suggested that pouchitis is the result of bacterial overgrowth, particularly of anaerobic bacteria, secondary to stasis in the ileal pouch (53–56). The generally satisfactory response to treatment with metronidazole supports this hypothesis. However, bacterial overgrowth alone is probably not sufficient to explain pouchitis, since virtually all pouches have bacterial overgrowth compared to normal ileum or terminal ileostomies. Moreover, quantitative cultures of pouch effluent from patients with pouchitis did not reveal differences in bacterial counts compared with patients without pouchitis (53, 57, 58).

Ruseler-van Embden et al. (59) recently investigated the composition of ileal reservoir microflora in patients with and without pouchitis. An increased number of aerobes and a decreased ratio of anaerobes to aerobes in patients with pouchitis was found compared to those without pouchitis. Since anaerobes are largely responsible for the production of short-chain fatty acids, this microbial imbalance may explain the markedly decreased amounts of short-chain fatty acids in output from patients with pouchitis (60). Short-chain fatty acids, especially butyrate, are considered to be the major source of energy for colonic epithelium. Since the pouch epithelium can undergo colonic metaplasia (48, 57), lack of

Table IV. Incidence of pouchitis related to diagnosis

Study	No. of patients UC/FPC	Pouchitis (%) UC/FPC
de Silva et al. (68)	56/4	23/0
Becker & Raymond (11)	78/22	23/0
Pemberton et al. (4)	390/0	14/–
Penna et al. (98)	0/41	–/0
Dayton et al. (16)	239/38	19/0
Tjandra et al. (17)	39/39	33/10
Lohmuller et al. (41)	668/66	31/6
Salemans et al. (10)	51/21	44/0

short-chain fatty acids might result in damage of the mucosa of the pouch. Irrigation of the pouch with short-chain fatty acids has been shown to be beneficial in patients with pouchitis (61).

Several authors have suggested that pouchitis is a novel manifestation of inflammatory bowel disease persisting after total colectomy with ileal pouch-anal anastomosis (41, 48, 50, 62–64). In most large series (3, 41) pouchitis is more common in patients with ulcerative colitis than in those with familial polyposis, and indeed may well be restricted to colitis patients (10, 11) (Table IV). Only a few cases of pouchitis in familial polyposis patients have been reported by the Mayo Clinic (3, 41), but these cases were poorly documented since endoscopy was not performed. The presence of backwash ileitis in ulcerative colitis patients does not predispose to later development of pouchitis, and an inflamed terminal ileum does not seem to be a contra-indication for ileal pouch-anal anastomosis in ulcerative colitis patients (65).

Pouchitis is associated with the development of conditions such as arthritis, iridocyclitis, erythema nodosum, and pyoderma gangrenosum, which are characteristic extracolonic manifestations of ulcerative colitis (41, 62, 66). Lohmuller et al. (41) found that patients with extraintestinal manifestations of inflammatory bowel disease are at higher risk of developing pouchitis than patients who never had extra-intestinal manifestations. These findings suggest that immunological mechanisms play a role in the pathogenesis of pouchitis and may have implications for the selection of patients with ulcerative colitis for ileal pouch-anal anastomosis.

Transient mucosal ischemia may cause oxygen-derived free radical production by xanthine oxidase, precipitating pouchitis after ileal pouch-anal anastomosis. Therefore, Levin et al. (67) studied the effect of allopurinol, a xanthine oxidase inhibitor, in patients with acute and chronic pouchitis. Acute pouchitis resolved promptly in four of eight patients. Seven of the 14 patients with chronic pouchitis responded completely with no recurrence of symptoms during treatment. Allopurinol either terminated an episode of acute pouchitis or prevented pouchitis from recurring in 50% of patients. These data support a role for mucosal ischemia and oxygen-free radical production in the etiology of pouchitis.

Pouchitis usually responds favorably to treatment with metronidazole orally or rectally. However, recurrence rates are as high as 60% (41, 68). Successful treatment of pouchitis with sulfasalazine (69), topical 5-aminosalicylic acid (70), topical or systemic steroids (68, 69), and short-chain fatty acids irrigation (61) has been reported in patients who do not respond to metronidazole. However, until now, no controlled trials comparing different treatments have been performed.

In conclusion, pouchitis is a major long-term complication after ileal pouch-anal anastomosis. Since pouchitis is confined to ulcerative colitis patients, it is likely that ulcerative colitis and pouchitis is a novel manifestation of inflammatory bowel disease. Immunological, luminal, and microbiological factors probably play a supplementary pathogenetic role.

HISTOPATHOLOGICAL ALTERATIONS IN ILEAL POUCHES

Shepherd et al. (48) studied mucosal biopsy specimens from the ileal reservoirs of 92 patients who had undergone restorative proctocolectomy. Chronic inflammation (infiltration with lymphocytes and eosinophils) was found in almost all, as was villous atrophy of varying severity. Acute inflammatory changes (infiltration with polymorphs) and ulceration were associated with pouchitis. The severity of acute inflammation was increased in ulcerative colitis patients compared with those with familial polyposis and pouchitis was present only in patients who had had ulcerative colitis. Although the mucosa of some ileal pouches acquire certain colonic characteristics, complete colonic metaplasia does not occur (71). The proportions of epitheloid cells and tingible body macrophages have been found to be increased in pouches with pouchitis compared with pouches without pouchitis or normal ileum (72). Since an increase of these macrophage subpopulations is characteristic of inflammatory bowel disease, their presence in pouchitis suggests that ulcerative colitis and pouchitis have similar pathogenetic mechanisms.

BILE ACID METABOLISM

The fecal bile acid output is increased in ileal pouch patients compared to healthy, non-colectomized volunteers (73, 74). Retention of ^{75}Se-taurohomocholate (SeHCAT) is decreased in these patients compared to non-operated colitis patients (75) or healthy controls (76, 77). Postprandial conjugated bile acid levels increase to a lower extent in ileal pouch patients compared to healthy subjects (78). Therefore, reabsorption of bile acids is impaired after ileal pouch anal anastomosis. Bile acid malabsorption might be expected in these patients for several reasons. First, the mucosa of ileal pouches show histologic signs of inflammation in the vast majority of patients (50). Second, reabsorption of bile acids may be impaired, since the relative mucosal surface of the terminal ileum is smaller after construction of a reservoir. Finally,

stasis in the ileal pouch may lead to deconjugation of bile acids as a result of bacterial overgrowth. Bile acid malabsorption may lead to alterations in bile composition and saturation index. Therefore, the risk of gallstone formation may be increased in ileal pouch patients. To assess the influence of colectomy on bile composition and saturation index Harvey et al. (79) collected bile samples at the time of abdominal surgery in patients with ulcerative colitis before or after colectomy. The precolectomy group comprised 17 patients who were sampled at the time of colectomy. The postcolectomy group comprised 11 patients who had undergone (sub)total colectomy previously (and were operated upon for conversion from conventional ileostomy to a pelvic pouch or for other reasons). The bile composition in the precolectomy group was similar to control patients without gallstones, and few had crystals in their bile. In the postcolectomy group, cholesterol concentrations were very high, all biles were supersaturated, and almost all patients had cholesterol crystals in their bile. However, to date, there is still no evidence that patients with an ileal pouch are at greater risk for cholelithiasis.

WATER AND ELECTROLYTE BALANCE

Changes in water and sodium balance after ileal pouch-anal anastomosis are similar to those after conventional ileostomy. Santavirta et al. (80) studied water and electrolyte balance in 30 patients with ileal pouch-anal anastomosis, 10 patients with conventional ileostomy, and 9 non-operated patients with quiescent ulcerative colitis. Daily urinary excretion of sodium in non-operated patients was significantly higher than in patients with an ileal pouch or conventional ileostomy. Daily fecal weight, urinary volume, and urinary excretion of sodium were similar in patients with ileal pouch-anal anastomosis and conventional ileostomy. Using tritiated water and a bromide dilution technique, Christie et al. (81) showed that the body content of water and extracellular fluid are normal in patients with ileal pouch-anal anastomosis.

MALABSORPTION

Hylander et al. (82) found moderate steatorrhea in approximately 30% of patients 3 months after ileostomy closure, but fecal fat excretion normalized with time. The absorption of carbohydrates, amino acids, and bile acids by the ileal pouch mucosa after proctocolectomy with ileal pouch-anal anastomosis has been found to be markedly decreased compared to normal ileum (83). Impaired intestinal absorption of D-xylose and low serum iron levels have been reported in ileal pouch patients. Nevertheless, clinical signs of malnutrition or malabsorption are rare in these patients (77). Low vitamin B_{12} levels and decreased Schilling tests have been found in patients with ileal pouch-anal anastomosis (57,74,82). Bacterial overgrowth in the pouch may contribute to vitamin B_{12} malabsorption, since some microbial species utilize dietary vitamin B_{12} from the host.

MOTILITY OF THE SMALL INTESTINE

Soper et al. (84) found that small bowel transit is markedly slowed in most patients after proctocolectomy with ileal pouch-anal anastomosis compared to conventional ileostomy or healthy non-colectomized subjects. However, gastric emptying of liquids is not altered in these patients (84). Installation of oleic acid in the ileal pouch slows gastrointestinal transit and increases plasma levels of peptide-YY, neurotensin, and enteroglucagon (85). These hormones are believed to play a relevant role in the adaptive response after large bowel resection. Basal and postprandial plasma levels of peptide-YY have been reported to be increased after ileal pouch-anal anastomosis compared to healthy controls (86). Infusion of peptide-YY induces a dose-related inhibition of mouth to caecum intestinal transit time and of the rate of gastric emptying (87). Results of these studies suggest that peptide-YY may play a major role in the adaptive response of the intestine to proctocolectomy with pouch construction.

Fasting and postprandial plasma cholecystokinin levels are elevated and fasting gallbladder volumes are decreased after proctocolectomy with ileal pouch-anal anastomosis in humans (88). These findings suggest that the colon contains a factor that inhibits the release of cholecystokinin.

SEXUAL FUNCTION AND PREGNANCY

The most common complication in males is retrograde ejaculation, which occurs in 1–10% of men undergoing restorative proctocolectomy, whereas impotence has been reported in up to 1.5% of the male population undergoing ileal pouch-anal anastomosis (11, 45, 89, 90).

Sexual function in women after restorative proctocolectomy has been studied by Metcalf et al. (91), who interviewed 100 women who had undergone proctocolectomy with a Kock pouch ($n = 50$) or an ileo-anal anastomosis ($n = 50$) regarding their preoperative and postoperative sexual function. Frequency of intercourse increased and the incidence of dyspareunia decreased after operation in both groups. Only one patient in each group reported a postoperative disturbance in ability to achieve orgasm. Overall, the majority of women in this study experienced enhanced sexual function after operation, which they attributed mainly to improved health. Nelson et al. (92) described 20 women who underwent ileal pouch-anal anastomosis and subsequently had at least one successful pregnancy and delivery. Eleven deliveries were vaginal with episiotomy, and nine were cesarean sections. No maternal deaths occurred. The frequency of nocturnal stooling increased in the ileal pouch-anal anastomosis patients during pregnancy, and the increase persisted for 3 months after delivery. In contrast, the frequency of daytime

stools and the incidence of incontinence were not greatly altered by pregnancy or delivery. Moreover, postpartum pouch function was not influenced by the type of delivery. Ileal pouch-anal anastomosis appears to be compatible with normal childbearing postoperatively. The route of delivery should be individualized in these patients.

GENERAL CONCLUSIONS

Proctocolectomy with ileal pouch-anal anastomosis has become the treatment of choice for severe ulcerative colitis and familial polyposis coli. The procedure should not knowingly be performed in patients with Crohn's colitis. The procedure carries a low mortality but a considerable morbidity. The surgical procedure has become less complicated and less time-consuming since the introduction of new stapling devices. However, the complication rate has not declined apparently. Without mucosectomy some rectal mucosa is left behind and uncertainty remains whether these patients are at risk of dysplasia and cancer. Using the stapling techniques, omission of the temporary loop ileostomy probably does not increase the number of pouch failures, at least in a group of selected patients. Pouchitis, occurring in as many as 40% of ulcerative colitis patients, is the most frequent late complication and may lead to pouch excision.

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