

Restorative Proctocolectomy with Ileal Pouch-Anal Anastomosis for Ulcerative Colitis and Familial Adenomatous Polyposis: Twenty Years Follow-Up in 174 Patients

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Abstract

Background: Restorative proctocolectomy with ileal pouch-anal anastomosis has become the surgical procedure of choice for patients with ulcerative colitis and familial adenomatous polyposis.

Objectives: To evaluate the long-term functional outcome of patients who underwent this surgical procedure.

Methods: We performed this observational study in 174 consecutive patients: 146 with UC and 28 with FAP. The patients, 91 males and 83 females with a mean age of 34.1 ± 10.6 years (range 6–67 years), underwent the procedure between January 1984 and January 2004 (mean follow-up 64.8 months, range 1–240 months). The indications for surgery were intractable disease in 124 patients (71%), dysplasia in 36 (21%), severe bleeding in 8 (5%), and perforation in 6 (3%).

Results: A protective ileostomy was performed in 140 patients (96%) with UC and 12 (43%) with FAP. An urgent three-stage procedure was necessary in 14 patients (8.4%). A mucosal proctectomy was performed in 94 (54%), and a double stapling technique in 80 (46%). Mean length of hospital stay was 9.4 ± 6.6 days (range 5–34 days, median 8). Complications included pelvic sepsis in 7 patients (4.2%), anastomotic leakage in 8 (4.8%), bowel obstruction in 22 (13.2%), incisional hernia in 12 (7.2%), anastomotic stenosis that usually responded to manual dilatation in 46 (27.6%), pouchitis in 106 (61%), recto-vaginal fistula in 3 (1.8%), retrograde ejaculation in 3 (1.8%), and impotence in 2 (1.2%). There was no mortality in this group of patients. The median number of bowel movements per 24 hours was six in UC patients and five in FAP patients, with at least one bowel movement during the night. Complete daytime and night-time continence was documented in 124 patients (71%). Overall satisfaction was 95%.

Conclusions: Restorative proctocolectomy with ileal pouch-anal anastomosis confers a long-term good quality of life to both UC and FAP patients, and the majority of patients are fully continent with five to six bowel movements per day.

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Restorative proctocolectomy with ileal pouch-anal anastomosis has become the procedure of choice for the surgical treatment of patients with ulcerative colitis and familial adenomatous polyposis. This procedure combines the goals of removing the affected colon and rectum, reducing the risk of cancer, and maintenance of gastrointestinal continuity, transanal defecation and continence. Although most patients enjoy a significant improvement in quality of life, with good functional outcomes, IPAA surgery can be

associated with a significant number of complications leading to pouch excision or permanent diversion [1–3].

Several studies have examined the short- and long-term reasons for ileal pouch failure and found that unrecognized Crohn's disease [4], pelvic sepsis [5], mucosal proctectomy [6], and fistula formation [7] may contribute to poor functional outcomes requiring re-division of the bowel, or pouch excision [8]. Although several studies have concluded that short-term functional results are very satisfactory and remain constant [9], others have suggested that functional results deteriorate over time [10]. The present study was conducted to evaluate the early and late complications and the long-term functional outcome and quality of life in patients who underwent restorative proctocolectomy with ileal pouch-anal anastomosis for ulcerative colitis or familial adenomatous polyposis during the past 20 years of follow-up.

Patients and Methods

Between January 1984 and January 2004, 174 consecutive patients underwent restorative proctocolectomy with IPAA for a preoperative diagnosis of UC in 146 patients and FAP in 28 patients. The surgical procedures were performed at the Hadassah Medical Center in Jerusalem and the Carmel Medical Center and Rambam Medical Center in Haifa. The senior author participated in all surgical procedures.

The majority of patients underwent the procedure under elective circumstances. A protective temporary loop ileostomy (two-stage technique) was fashioned in 140 patients (96%) with UC and in only 12 patients (43%) with FAP. Early in our experience, a hand-sewn mucosal proctectomy was performed in 94 patients (54%), while lately 80 patients (46%) underwent the double stapling technique. Early in our experience the reservoir design was the S-type in 64 patients, and in the last 110 patients a J-type pouch was fashioned. The mean length of hospital stay was 9.4 ± 6.6 days (range 5–34 days, median 8). Closure of the ileostomy was performed 31–352 days after pouch construction (mean 121 ± 68 days). Closure of the temporary stoma was always preceded by radiographic examination and digital examination with finger dilatation of the ileo-anal anastomosis whenever necessary. In 14 patients (8.4%) a three-stage technique was performed under emergency conditions.

We assessed the patients' outcome by review of hospital records, telephone interview or direct approach during routine office examination according to a structured questionnaire. The questionnaire comprised a list of questions aimed at assessing the use of medications, dietary restrictions, frequency of bowel movements,

UC = ulcerative colitis

FAP = familial adenomatous polyposis

IPAA = ileal pouch-anal anastomosis

and continence during daytime and night-time. It also related to the ability to distinguish flatus from stool, the ability to defer bowel movements, the presence of major or minor leakage, the incidence of perineal rash, and the use of protective pads. Quality of life was assessed by questions regarding physical function, social function, emotional problems, and general health perception. During office follow-up a physical examination was performed with particular attention to digital examination aimed at assessing the status of the IPAA, anal canal, pouch, stricture, and sphincter mechanism. When symptoms of pouchitis were suspected a rigid anoscopy with biopsy was added, and when ileoanal stenosis was detected immediate digital dilatation was performed.

Statistical analysis

Functional outcome results were compared using the Yates-corrected chi-square test. A value of $P < 0.05$ was considered statistically significant.

Results

In the 20 year period 1984 to 2004, the mean follow-up in the 174 patients was 64.8 ± 10.6 months (range 1–240 months). Perioperative data were available for all patients [Table 1], but long-term follow-up data by telephone interview or office questionnaire was obtained only in 131 patients (75.3%). The early and late postoperative complications are summarized in Tables 2 and 3.

There was no early or late mortality in this group of patients. The most significant early complications were anastomotic leakage and pelvic sepsis. These complications were particularly prevalent in UC patients with longstanding disease, malnutrition and chronic steroid therapy. A one-stage restorative proctocolectomy (without ileostomy) was performed within a short period in both UC and FAP patients. This procedure was associated with a high incidence of pouch failure and pelvic sepsis, particularly in UC patients under steroid therapy [11]. Therefore, the one-stage procedure was lately abandoned in most UC patients and has been reserved for FAP patients only. In patients with FAP, mucosal proctectomy and a hand-sewn ileo-anal anastomosis were usually performed in order to resect a maximal number of polyps. When few or no polyps were detected in the distal segment of the rectum the double stapling technique was also used. Peroneal nerve palsy occurred early in our series in extremely obese patients with extended operation time when mucosal proctectomy and a hand-sewn S-type anastomosis were used. Lately, use of the double stapling technique and formation of a J-type pouch by the stapler have considerably shortened the operating time. Also, in obese patients special care is taken in padding the patient's feet before the procedure.

Mechanical intestinal obstruction was rare in the immediate postoperative period and usually responded to conservative treatment, while intestinal obstruction after discharge from the hospital developed in 22 patients (12.6%). In 10 of these patients laparotomy was necessary for release of adhesions or resection of a segment of bowel stricture (4 patients). The most prevalent late postoperative complication was pouchitis. This complication was usually mild, with increased frequency of bowel movements, abdominal colic, tenesmus, partial loss of continence, with malaise

Table 1. Indications for surgery in 174 patients

	Ulcerative colitis (n)	Familial adenomatous polyposis (n)	Total
Intractable disease	124	–	124 (71%)
Dysplasia	10	26	36 (21%)
Severe bleeding	6	2	8 (4.8%)
Perforation	6	–	6 (3.6%)

Table 2. Early postoperative complications (within 30 days)

	UC (n)	FAP (n)	Total
Pelvic sepsis	5	2	7 (4.2%)
Anastomotic leakage	6	2	8 (4.8%)
Wound infection	14	2	16 (9.6%)
Peroneal nerve palsy	3	–	3 (1.8%)
Intestinal obstruction	5	1	6 (3.6%)
Ileostomy dysfunction	8	2	10 (6%)
Mortality	–	–	–

Table 3. Late complications (after 1 month)

	UC (n)	FAP (n)	Total
Pouchitis	99	7	106 (61%)
Severe pouchitis	15	1	16 (9.6%)
Intestinal obstruction	20	2	22 (13.6%)
Anastomotic stricture			
Mild	40	6	46 (27.6%)
Severe	9	1	10 (6%)
Anastomotic fistula	7	1	8 (4.8%)
Pouch-vaginal fistula	3	–	3 (1.8%)
Retrograde ejaculation	2	1	3 (1.8%)
Impotence	2	–	2 (1.2%)
Reversal of ileostomy	6	–	6 (3.6%)
Pouch removal	4	–	4 (2.4%)
Mortality	–	–	–

and mild temperature. Antibacterial treatment, usually with a combination of cyprofloxacin and metronidazole, and conventional treatment with 5-ASA and steroids was followed by resolution of symptoms within a few days in most cases. In 9.6% of these patients the disease was severe, recurrent and led to significant morbidity, which necessitated reversal of the ileostomy in five patients and removal of the pouch in four. A mild anastomotic stricture that usually responded to finger dilatation was a frequent finding in 46 patients, while a severe stricture, which needed at least one mechanical dilatation under anesthesia, developed in 10 patients. The most crippling complications of the procedure were impotence in 2 males (1.2%) and pouch-vaginal fistula in 3 females (1.8%). Impotence and retrograde ejaculation developed only in patients who underwent the double stapling technique but were not detected early in our experience in patients

Table 4. Long-term results (response to questionnaire)

	UC	FAP	Total
No. of patients	114 (78%)	17 (61%)	131 (75.2%)
Medications	20	2	22 (16.7%)
Diet restrictions	74	10	84 (64.1%)
Median no. of bowel movements	6	5	–
Median no. of bowel movements at night	1	1	–
Full continence			
Day time	92 (80.7%)	14 (82.3%)	106 (80.9%)
Night-time	84 (73.7%)	11 (78.6%)	95 (72.5%)
Continence			
Major leakage	7 (6.1%)	2 (11.8%)	9 (6.9%)
Minor leakage	14 (12.3%)	3 (17.6%)	17 (12.9%)
Use of pads	14 (12.2%)	2 (11.7%)	16 (12.2%)
Perineal rash	15 (13.1%)	3 (17.6%)	18 (13.7%)
Quality of life			
Better	96 (84.2%)	5 (29%)*	101 (77.1%)
Much better	85 (74.5%)	2 (11.8%)*	87 (66.4%)
Overall satisfaction			
Good	110 (96%)	14 (82%)	124 (94.6%)
Excellent	100 (88%)	10 (59%)*	110 (84%)

* $P < 0.01$ between UC and FAP patients

in whom a hand-sewn mucosal proctectomy was used, most probably because resection of the rectal mucosa was performed from inside the rectum.

Long-term follow-up information is available for 114 of the UC patients (78%) and 17 of the FAP patients (61%) [Table 4]. The median number of bowel movements in UC patients was 6/24 hours, and 5/24 hours in FAP patients, with one at night in both groups. All patients defecate spontaneously. Dietary restrictions were common in both groups (64.1%), mainly to alter the time of their meals in order to avoid bowel movements at inappropriate times (social activities, night-time, etc.). Continence was judged by the ability to defer a bowel movement until convenient, and to distinguish flatus from stool, the presence of major or minor leakage, perineal rash and the use of pads. Full continence during daytime was detected in 80.9% of the patients, while full continence at night was only experienced by 72.5%, with a major leakage in 6.9%, use of pads in 12.2%, and perineal rash in 13.7%. There was no significant difference in continence between UC and FAP patients.

The patients' subjective assessment of quality of life shows overall satisfaction and adjustment with the lifestyle imposed by the procedure. The UC patients judged quality of life as better in 84.2% of the cases, while only 29% of the FAP patients assessed that their quality of life was improved by the operation ($P < 0.01$). Overall satisfaction and adjustment was judged as good in 96% of UC patients and in only 82% of FAP group, and excellent in 88% vs. 59% ($P < 0.01$) [Table 4].

Discussion

Restorative proctocolectomy with ileal pouch-anal anastomosis has been shown to be an effective and safe surgical therapy for patients

with UC or FAP. This procedure was described in the late 1970s as an alternative to total colectomy with Brook's ileostomy, continent ileostomy or ileorectal anastomosis, and has been our treatment of choice for UC and FAP since 1984. Because of the complexity of the operation and the relatively high rate of early and late complications, the indications for this type of surgery were initially conservative. Improvements in the surgical management of these patients have helped to reduce the complication rate of this surgical procedure and have led to improved functional outcome and quality of life. Techniques such as use of the circular stapler to perform the ileo-anal anastomosis without the need for dilating retractors to place sutures by hand, avoiding a long muscular cuff after mucosal proctectomy, a short efferent limb of the S-type pouch, preservation of the anal transitional zone, and increasing use of salvage surgery have all helped to reduce the rate of pelvic sepsis and have contributed to improved functional outcome [12,13]. With these improvements in surgical management, and increasing experience with the use of the double-stapled J-pouch and preservation of the anal transitional zone, the indications for surgery were extended to higher risk patients, including patients older than 50 years, with satisfactory functional results [14].

A meta-analysis of 8,500 patients who have undergone ileo-anal surgery over the last 20 years in 20 major centers [8] suggested that the overall worldwide pouch failure rate was about 6%, while reports from the last 5 years show that the failure rate has dropped considerably to 2%. This was attributed to more careful patient selection, more definitive preoperative diagnosis, more experienced surgeons with better surgical techniques, improved postoperative care, and intensive patient follow-up and education. The major causes for adverse outcomes with pouch failure were associated either directly with Crohn's disease or with Crohn's-associated complications, including fistulas, perianal sepsis, sinus tracts, etc. Pelvic sepsis is almost always due to some degree of breakdown of the ileo-anal anastomosis. In females this complication may lead to pouch-vaginal fistula. In the present study, 4.2% of the patients developed early postoperative sepsis, and 4.8% developed anastomotic leakage, all of which responded to conservative therapy. The causes for reversal of ileostomy in six patients in our study were severe recurrent pouchitis, which did not respond to conservative therapy in five patients, and incontinence of the anal sphincter in one patient.

Pouchitis is the most common complication of IPAA for UC. Diagnosis of the disease depends mainly on symptoms, endoscopy and histology. An 18-point pouchitis disease activity index was recently developed and later simplified by omitting the histologic evaluation with similar sensitivity and specificity [15]. Mild pouchitis is a long-term complication that occurred cumulatively in up to 61% of our patients, with severe pouchitis that did not respond to conservative therapy in 9.6%. Mild pouchitis occurred with a similar incidence in UC and FAP patients, while severe pouchitis with complications was more frequently observed in UC patients [Table 3]. This is probably due to the inflammatory nature of UC compared with FAP. The etiology of pouchitis is unclear, and studies have been undertaken of bacteriology, inflammatory cellular infiltrates, platelet-activating factor, emptying of the reservoir,

ischemic changes, short-chain fatty acids, bile acids and others. It is quite possible that pouchitis represents yet another manifestation of idiopathic inflammatory bowel disease.

Postoperative quality of life has become an important measure of the functional result of restorative proctocolectomy in UC and FAP patients. Functional outcome has been reported to significantly correlate with quality of life following IPAA [16–18]. A significant number of patients with UC who underwent surgery have been found to enjoy a significant improvement in postoperative quality of life with scores sometimes comparable to those of the general population, while functional outcome in FAP patients is usually considerably worse in comparison to preoperative function and to the general population [18–20].

We previously compared the functional outcome and complications in patients who underwent IPAA, or total proctocolectomy with Brook's ileostomy, Kock's pouch, or ileorectostomy [21]. Social behavioral function in eight categories of daily functions (social, home activities, work, travel, diet, sexual function, body image, and skin problems) was assessed during four periods of life: before the disease, before surgery, post-surgery with ileostomy, and after closure of ileostomy. Summation of these functions in a social behavioral functional index showed that 91% of the patients reported an improvement after closure of ileostomy, and 91% responded that they would be happy to undergo their surgery again and would recommend it to others.

Delaney et al. [22] presented a univariate and multivariate analysis of data on the functional outcome and quality of life in 1,895 patients who underwent IPAA. Only 4.1% of the patients developed failure of their IPAA because of long-term complications of surgery or poor function. Functional results were not as good in patients in the older groups. This was manifested by a slight reduction in the percentage of perfect continence, and an increase in the number with seepage of stool at night. Daytime and nighttime stool frequencies were similar between various age groups. Only minimal differences in quality of life between permanent ileostomy and IPAA were observed, even though maintenance of continence was the primary concern of colitis patients preoperatively. Between 95% and 100% of patients under the age of 65 stated they would undergo the surgery again, compared to 89–100% of patients older than 65 at the time of surgery.

Carmon and colleagues [23] studied the correlation between quality of life and functional outcome in 77 of 99 patients (78%) who underwent IPAA for ulcerative colitis using the Short-Form 36 (SF-36) for scoring and the Global Assessment of Function Scale to evaluate functional outcome. They found that the quality of life in patients after IPAA was excellent, with scores equal to published norms for the general Israeli population. Functional outcome correlated strongly with quality of life, and older age was associated with lower scores in both functional outcome and quality of life scales.

In the present study only 131 of the 174 patients (75.2%) who underwent IPAA responded to our questionnaire. During the 20 years of follow-up since the first operated patient, no significant difference between patients with UC or FAP was found in the long-term use of medications, dietary restrictions or median number of

bowel movements during daytime or night-time. Although we could not detect a significant difference in the long-term functional results between the two groups, judgment of quality of life as better was significantly higher in UC patients compared to FAP patients (84.2% vs. 29.0%, $P < 0.01$). This is readily explained by the fact that most FAP patients were usually asymptomatic or had minimal symptoms preoperatively and normal bowel habits, and the indication for surgery was most frequently detection of multiple polyposis, or genetic counseling.

Overall satisfaction from the surgical procedure was also significantly better in the UC group of patients.

Conclusion

Restorative proctocolectomy with IPAA provides a very satisfactory quality of life and functional outcome for patients with UC or FAP. Pouchitis is still the most common complication, occurring in 61% of the patients, with severe pouchitis occurring in 9.6%. This procedure was followed by a significant number of complications, but the number and severity of complications have been reduced in recent years, with better functional outcome, a median of five to six bowel movements per day, and significant improvement in quality of life, particularly in UC patients.

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Any man under 30 who is not a liberal has no heart, and any man over 30 who is not a conservative has no brains

Winston Churchill

Everywhere I go, I'm asked if I think the university stifles writers. My opinion is that they don't stifle enough of them

Flannery O'Connor (1925-64), American writer, particularly acclaimed for her stories which combined the comic with the tragic and brutal. She belonged to the Southern Gothic tradition that focused on the decaying South and its damned people.

Capsule

JC virus exploits a serotonin receptor

JC virus (JCV) is a common human polyomavirus responsible for the fatal demyelinating disease, progressive multifocal leukoencephalopathy (PML), in immunocompromised individuals. About 5% of AIDS patients develop this currently untreatable fatal disease. Typical and atypical antipsychotic drugs inhibit JCV infection of glial cells. Elphick et al. found that the cellular

receptor for JCV on glial cells is a serotonin receptor. These findings contribute to the understanding of the pathogenesis of PML in AIDS patients and suggest that therapy based on existing serotonin receptor inhibitors may be feasible.

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E. Israeli

Capsule

Bone marrow contribution to gastric cancers in mice

Although the cellular origin of epithelial cancers, such as gastric cancer induced by *Helicobacter pylori* infection, remains to be established, a prevailing assumption is that they derive from resident epithelial stem cells. In contrast to this theory, Houghton and associates found that gastric cancers caused by experimental *Helicobacter* infection in mice were of bone marrow, rather than epithelial cell, origin. Bone marrow-derived cells from donor mice were tracked in chronically infected

recipients and predominated in the gastric mucosa where they displayed features of neoplastic progression, eventually forming epithelial cancers. If an equivalent contribution of bone marrow-derived cells to epithelial cancers could be established in humans, this finding would significantly revise the understanding of the origin and progression of malignancy.

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