

Fate of the Pouch in 151 Pediatric Patients After Ileal Pouch Anal Anastomosis

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Background/Purpose: Ileal pouch anal anastomosis (IPAA) offers many pediatric patients a surgical cure for mucosal ulcerative colitis (MUC) with preservation of anal continence. However, some patients incur serious problems after surgery including chronic pouchitis and pouch failure. The goal of this study is to identify clinical and pathologic factors that are associated with an adverse outcome of IPAA.

Methods: A retrospective analysis of outcome was performed in 151 consecutive patients ≤ 21 years of age who underwent IPAA with a mean follow-up of 7.24 years (range, 2 to 15 years). Patients were categorized into 4 outcome groups: A, no pouchitis; B, mild, acute pouchitis; C, chronic refractory pouchitis; and D, pouch failure. Pairwise comparisons were used to test the association between the groups and clinical and pathologic variables including age, sex, duration of symptoms, perianal disease, colonoscopic histology, terminal ileitis, operation type, staged versus unstaged IPAA, colonic specimen histology, early postoperative complications defined as less than 31 days postsurgery, late postoperative complications defined as 31 or more days postsurgery, and pouch fistulae. Crohn's disease as a definitive diagnosis and indeterminant colitis, a histologic diagnosis, also were tested for association with the above variables and outcome groups.

Results: One hundred and fifty-one pediatric patients underwent IPAA utilizing mucosectomy and hand-sewn S or J (n =

44) and stapled J or S-W anastomosis (n = 107) with 0% mortality rate and outcome as follows: group A, n = 54; group B, n = 73; group C, n = 11; group D, n = 13. Variables strongly associated with poor outcome, groups C and D, were duration of symptoms ($P = .03$), perianal disease ($P = .03$), late complications ($P < .001$), pouch fistulae ($P < .001$), and Crohn's disease ($P < .0001$). Furthermore, Crohn's disease was associated strongly with female gender ($P = .01$), perianal disease ($P = .004$), early ($P = .006$) and late ($P < .001$) complications, and pouch fistula ($P < .001$). The findings of indeterminant colitis, terminal ileitis, and early postoperative complications did not show significant differences between the 4 outcome groups.

Conclusions: Crohn's disease appears to be an important determinant of postoperative complications, chronic pouchitis, and pouch failure and occurred in 15% of the authors' patients after IPAA. Indeterminant colitis and the intraoperative findings of terminal ileitis are not associated with Crohn's disease or adverse outcome after IPAA in pediatric patients. Operation type and stage do not alter the clinical course after IPAA in pediatric patients.

J Pediatr Surg 38:78-82. Copyright 2003, Elsevier Science (USA). All rights reserved.

INDEX WORDS: Crohn's disease, indeterminant colitis, ileoanal pull-through procedure, pouchitis.

ILEAL POUCH anal anastomosis (IPAA) offers many patients a potential cure for mucosal ulcerative colitis (MUC) with preservation of anal continence. However, not all patients obtain a good result after this procedure. Chronic pouchitis and pouch failure occur in 3% to 5%¹ and 5% to 10%,^{2,3} respectively, in large reports in adults. Technical problems, pelvic sepsis, pouch dysfunction, and Crohn's disease all have been

cited as potential causes of poor outcome. The aim of this study is to identify clinical and pathologic factors that are associated with an adverse outcome after IPAA in pediatric patients.

MATERIALS AND METHODS

We reviewed the medical records and conducted telephone interviews of 151 consecutive patients ≤ 21 years of age who underwent IPAA for MUC at The Cleveland Clinic Foundation between 1982 and 1999. Data were collected for a number of clinical and pathologic variables in 3 categories: preoperative, intraoperative, and postoperative. Preoperative variables included demographic information (age and sex), preoperative duration of symptoms, perianal disease, and colonoscopic histology. Intraoperative variables included colonic specimen histology, terminal ileitis, operation type, and staged versus unstaged IPAA. Postoperative variables included early postoperative complications defined as those occurring less than 31 days postsurgery, late postoperative complications, and pouch fistulae. Specific complications, both early and late, were ileoanal separation, pelvic infection, small bowel obstruction, and anal stricture. Long-term data were collected concerning the development of mild acute or chronic refractory pouchitis, pouch failure, and Crohn's disease. Pouchitis was

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Presented at the 49th Annual Congress of the British Association of Paediatric Surgeons, Cambridge, England, July 23-26, 2002.

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0022-3468/03/3801-0016\$35.00/0

doi:10.1053/jpsu.2003.50015

defined by the clinical triad of crampy abdominal pain, increased stool frequency, and bloody stools without positive stool cultures, and was confirmed in approximately one half of cases by endoscopic and histologic evaluation. Acute, mild pouchitis was defined as less than 5 total episodes, each responding promptly to antibiotic therapy. Chronic, refractory pouchitis was defined as greater than 5 episodes not responding to antibiotic therapy. Pouch failure required that an ileostomy with or without pouch excision be performed for intractable disease or poor pouch function. Crohn's disease was diagnosed definitively based on clinical, radiographic, or histologic criteria. Patients were categorized into 4 outcome groups: group A, no pouchitis; group B, acute, mild pouchitis; group C, chronic refractory pouchitis; and group D, pouch failure. Likelihood ratio χ^2 (for categorical variables) and analysis of variance (ANOVA) tests (for continuous variables) were used to test the association between all aforementioned variables including indeterminate colitis, Crohn's disease, and the 4 outcome groups. All data were entered into a computer database where it was stored and analyzed using SAS software, version 8, a product of SAS Institute Inc, Cary, NC. A significance level of $P = .05$ was used throughout the study.

RESULTS

A total of 151 patients ≤ 21 years underwent IPAA from 1982 to 1999. The mean follow-up was 7.24 years with a range of 2 to 15 years. Of 151 patients who underwent IPAA 83 were boys. The mean age at surgery was 18 years (range, 4 to 21 years). The median duration of symptoms was 2 years (range, 0 to 13 years). Preoperative colonoscopy findings were available for 125 and showed pancolitis in 76 patients (61%), left-sided colitis in 44 patients (35%), pancolitis with terminal ileal disease in 5 patients (4%), and was unavailable in 26 patients. At surgery, terminal ileitis was observed in 21 patients (14%). Histologic evaluation of the colon specimen showed ulcerative colitis in 125 patients (83%), indeterminate colitis in 16 patients (11%), Crohn's disease in 3 patients (2%), and was unavailable in 7 patients (5%). IPAA was performed in one stage in 8 patients (5%), 2 stages in 92 patients (61%), and 3 stages in 50 patients (33%). One stage procedures included total abdominal colectomy and IPAA without ileostomy. Two-stage procedures usually included first-stage total colectomy and IPAA with ileostomy and second-stage ileostomy closure. Another 2-stage strategy used in patients with severe disease or suspected Crohn's disease included first-stage total colectomy and Hartmann's pouch followed by second-stage IPAA without ileostomy. Three-stage procedures included first-stage colectomy, second-stage IPAA with ileostomy, and third-stage ileostomy closure.

IPAA was performed using several different techniques. Forty-four patients (29%) underwent mucosectomy with hand-sewn S or J pouch. Ninety-two patients (61%) underwent extramuscular dissection with stapled J pouch. Fifteen patients (10%) underwent extramuscular dissection with stapled S-W pouch.

There was no early or late mortality. Thirty-one pa-

tients (21%) incurred 39 early postoperative complications after IPAA. These include early ileoanal separation (7 patients, 5%), pelvic infection/abscess (14 patients, 9%), small bowel obstruction (15 patients, 10%), and anal stricture (3 patients, 2%). Sixty-eight patients (45%) incurred 91 late postoperative complications after IPAA. These complications include late ileoanal separation (8 patients, 5%), pelvic infection/abscess (38 patients, 25%), small bowel obstruction (18 patients, 12%), and anal stricture (27 patients, 18%).

Long-term outcome was that 54 patients (36%) had no pouchitis (group A); 73 patients (48%) had acute, simple pouchitis (group B); 11 patients (7%) had chronic pouchitis (group C); and 13 patients (9%) had pouch failure requiring ileostomy with or without pouch excision (group D). The association between these groups and clinical and pathologic variables were investigated using likelihood ratio χ^2 tests and analysis of variance (ANOVA). Results were age ($P = .80$), sex ($P = .13$), preoperative duration of symptoms ($P = .03$), perianal disease ($P = .03$), terminal ileitis ($P = .12$), colonoscopic histology ($P = .04$), colonic specimen histology ($P = .53$), operation type: mucosectomy with hand sewn S or J versus extramuscular dissection with stapled J or W ($P = .15$), one-stage versus multistaged IPAA ($P = .55$), early complications ($P = .39$), late complications ($P < .001$), and pouch fistula ($P < .001$).

Perianal disease, prolonged duration of symptoms, Crohn's disease on colonoscopic biopsy, long-term complications, and pouch fistulae all were associated with poor outcome (groups C and D). Perianal disease occurred in 3 of 11 patients (27%) in group C and 2 of 13 patients (15%) in group D versus 1 of 54 patients (2%) in group A and 3 of 71 patients (4%) in group B ($P = .03$). There is evidence that mean duration of symptoms varies by group ($P = .03$). Mean symptom duration was higher in group D (5.00 years) than in groups B (2.67 years; $P = .004$) and C (2.67 years; $P = .02$). Colonoscopic biopsies showed Crohn's Disease in 1 of 11 patients (9%) in group C and 1 of 13 patients (8%) in group D versus 0 of 54 patients (0%) in group A and 0 of 73 patients (0%) in group B ($P = .04$). Late complications occurred in 10 of 11 patients (91%) in group C and 13 of 13 (100%) in group D versus 12 of 54 patients (22%) in group A and 33 of 73 patients (45%) in group B ($P < .001$). Anal stricture was the only late complication that was not associated with a poor outcome. Finally, pouch fistulae occurred in 7 of 11 patients (64%) in group C and 8 of 13 patients (62%) in group D versus 2 of 54 patients (4%) in group A and 4 of 73 patients (6%) in group B ($P < .001$).

All patients underwent careful follow-up for signs of Crohn's Disease. These include clinical signs (oral or upper gastrointestinal [GI] ulcerations, extraintestinal

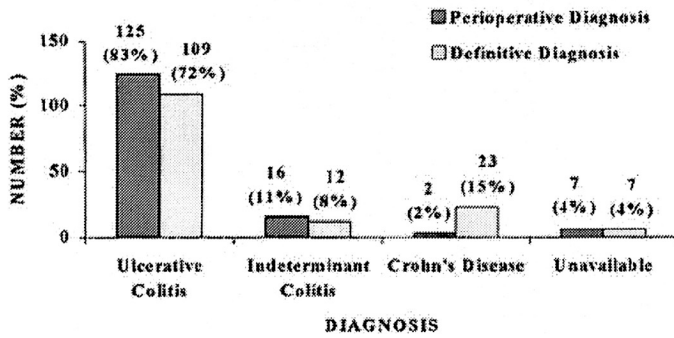


Fig 1. Diagnostic conversions.

manifestations, abdominal mass or tenderness, GI hemorrhage, weight loss, and perianal disease), radiographic signs (small bowel stricture or fistulae), and endoscopic signs (cobblestone mucosa, serpiginous ulcers, granulomas, or intestinal strictures with skip lesions). In retrospect, 2 patients were found to have histologic evidence of Crohn's disease on preoperative colonoscopic biopsy. One additional patient was found to have histologic evidence of Crohn's disease on the colonic specimen. By the conclusion of the study, an additional 20 patients were diagnosed with Crohn's yielding a total of 23 patients with a definitive diagnosis of Crohn's disease.

There were a number of diagnostic conversions during the study, all of which took place within 5 years. Seventeen of 125 patients with a perioperative histologic diagnosis of ulcerative colitis converted to Crohn's ($P = .24$), whereas 4 of 16 patients with indeterminate colitis converted to Crohn's ($P = .28$; Fig 1). Thus, there was no significant difference in conversion rate between the 2 groups. This finding is supported by outcome data summarized in Table 1.

Ten of 11 (91%) patients with chronic pouchitis (group C) and 10 of 13 (77%) patients with pouch failure (group D) were eventually discovered to have Crohn's disease. By comparison, only 2 of 11 (18%) patients in group C and 1 of 13 (8%) in group D were found to have indeterminate colitis. Overall, 20 of 24 (83%) patients in groups C and D were found to have Crohn's disease

Table 1. Affect of Crohn's Disease and Indeterminant Colitis on Outcome

	Crohn's Disease (n = 151)	P Value	Indeterminant Colitis (n = 151)	P Value
Group A				
No pouchitis	2/54		5/54	
Group B				
Mild, acute pouchitis	1/73		4/73	
Group C				
Chronic pouchitis	10/11		1/11	
Group D				
Ileostomy +/- pouch excision	10/13	<.001	1/13	.58

Table 2. Preoperative Variables Associated With Crohn's Disease and Indeterminant Colitis

	Crohn's Disease	P Value	Indeterminant Colitis	P Value
Sex				
Male	7/83		8/83	NS
Female	16/68	.01	4/68	(.39)
Age at surgery (yr)				
Mean + disease	16.35	NS	17.6	NS
Mean - disease	17.75	(.12)	17.5	(.97)
Duration of symptoms (yr)				
Mean + disease	3.83	NS	2.83	NS
Mean - disease	3.00	(.26)	3.15	(.70)
Perianal disease				
Yes	18/140		1/9	
No	5/9	.004	9/140	(.61)
Colonoscopic biopsies				
+ Disease	2/138	NS	12/138	NS
- Disease	21/138	(.17)	4/138	.17

Abbreviation: NS, Not significant.

versus only 3 of 127 (2%) patients in groups A and B ($P < .001$), whereas there were 3 of 24 (12.5%) patients with indeterminate colitis in groups C and D versus 9 of 127 (7.1%) in groups A and B ($P = .40$).

Ultimately, 23 of 151 (15%) patients had Crohn's disease after IPAA, raising the question whether clinical information or histopathology might preclude patients from IPAA who are at higher risk for Crohn's disease. Clinical and histopathologic variables were tested for possible association with Crohn's disease and indeterminate colitis. Preoperative variables are summarized in Table 2. Of all preoperative variables tested, only female gender and perianal disease were associated significantly with Crohn's disease. Intraoperative variables are summarized in Table 3. Neither terminal ileitis nor histology of the colon specimen were associated significantly with Crohn's disease. Postoperative values are summarized in Table 4. Early and late complications as well as pouch fistulae all were predictive of Crohn's disease but were not associated with Indeterminate Colitis. The only exception to this was early and late small bowel obstruction, which was not associated with Crohn's Disease.

Finally, operation type or stage had no apparent affect

Table 3. Intraoperative Variables Associated With Crohn's Disease and Indeterminant Colitis

	Crohn's Disease	P Value	Indeterminant Colitis	P Value
Terminal ileitis				
Yes	5/21	NS	0/21	
No	18/130	(.26)	12/130	.052
Specimen histology				
+ Disease	0/21	(.33)	4/11	(.02)
- Disease	3/123	(.52)	12/133	(.1)

Abbreviation: NS, Not significant.

Table 4. Postoperative Variables Associated With Crohn's Disease and Indeterminant Colitis

	Crohn's Disease	P Value	Indeterminant Colitis	P Value
Early complications				
Yes	10/31	.006	3/31	NS
No	13/120		9/120	(.70)
Late complications				
Yes	22/68	<.001	8/68	NS
No	1/83		4/83	(.12)
Pouch fistulae				
Yes	14/21	<.001	3/21	NS
No	9/128		7/128	(.18)

Abbreviation: NS, not significant.

on outcome. Mucosectomy with hand-sewn S or J pouch and extramuscular dissection and stapled J or W all produced a similar outcome ($P = .15$). Operations performed in one stage, 2 stages, and 3 stages also yielded similar results ($P = .55$).

DISCUSSION

The IPAA procedure has provided a cure for the debilitating effects of MUC and immunosuppressive therapy to many young people without the need for permanent ileostomy. Most of these former patients are completely continent of stool with an acceptable number of daily bowel movements.

Not all patients have fared so well, some incurring life threatening complications, poor pouch function, chronic pouchitis, and pouch failure. Complications of this procedure include ileoanal separation, which occurs in 2% to 6%, pelvic sepsis in 6% to 12%, pouch fistula in 6% to 10%, and anal stricture in 10% to 18% of all patients.⁴ Surgical complications occur in 30% to 66% of patients overall; however, with the exception of pelvic sepsis,⁵ these do not appear to affect pouch function long term. Pelvic sepsis significantly increases the risk of poor pouch function, which occurs in 1% to 3% of patients in this setting.⁶⁻⁸ Pouchitis occurs in 20% to 50% of all patients but responds to antibiotic therapy in 95% of patients⁹ and thus does not significantly deter quality of life. Chronic pouchitis occurs in 3% to 5% of all patients¹ and, in its most severe form, requires pouch excision in 2% of all patients.¹⁰ Finally, pouch failure occurs in 3% to 10% of all patients requiring ileostomy with or without pouch excision.^{2,5,8,9}

In addition to technical complications, another important determinant of poor outcome after IPAA is Crohn's disease. It has long been appreciated that in some cases, Crohn's colitis may be mistaken for mucosal ulcerative colitis. This has been estimated to occur in 2.5% to 5% of cases with presumed mucosal ulcerative colitis.^{2,5,11} However, in our study, with a mean follow-up of 7.24

years, it occurred in closer to 15% of cases. The explanation for this disturbing finding is unclear, but may relate in part to the length of follow-up, the patient population, and the institutional referral pattern. The mean follow-up of 7.24 years is longer than in many clinical reports. Those reports that cite a lower incidence of Crohn's disease are based on adult patients suggesting the possibility that the risk of isolated Crohn's colitis may be higher in younger compared with older patients. Many patients in this study were referred from outside the local area, and their radiologic and endoscopic evaluations were not always repeated. Whenever possible, biopsy material obtained elsewhere was reviewed by Cleveland Clinic pathologists who specialize in inflammatory bowel disease. In 2 cases, biopsy material was unavailable before IPAA and was found retrospectively to be diagnostic of Crohn's disease. In all other cases, mucosal ulcerative colitis was the favored preoperative diagnosis, and Crohn's disease was diagnosed later in the postoperative course, usually within 5 years of IPAA. Previous studies have found that Crohn's disease diagnosed after IPAA leads to pouch fistulae in 30% to 70% of cases^{2,5,11} and pouch failure in 34% to 40% of cases.^{2,5,6} In fact, pouch fistulae are the most frequent indication for rediversion, followed by pelvic infection and poor function. Pouchitis in contrast is a rare cause of pouch failure,^{1,10} and many studies have shown no association between pouchitis and Crohn's disease.^{2,12,13} Our findings appear to show that Crohn's disease is an important determinant of pouch-related morbidity including chronic pouchitis, pouch fistulae, and pouch failure in pediatric patients after IPAA. Of the 5 variables associated with poor outcome including preoperative duration of symptoms, colonoscopic biopsy, perianal disease, late complications, and pouch fistulae, all but the first 2 are significantly associated with Crohn's disease.

Our relative inability to exclude patients with Crohn's disease from IPAA and the resultant dire consequences ask the question whether any clinical or pathologic variables may be used to select the most appropriate candidates for this operation. Of the numerous preoperative variables tested, only female gender and perianal disease showed a significant association with Crohn's disease. Thus, any history of anal surgery in the past or signs of anal fissure or fistulae particularly in girls should weigh heavily against IPAA. Extraintestinal manifestations such as arthritis and primary biliary sclerosis were not addressed in this study but, according to other studies,¹⁴ are relative contraindications against IPAA.

In our study, intraoperative findings of terminal ileitis and specimen histology were not associated with Crohn's disease. Thus, it would appear that frozen section in the operating room has limited value and is not required to determine the choice of operation performed.

Although staged colectomy and subsequent IPAA may have some value in certain circumstances (ie, toxic megacolon), it would appear to have little value in excluding Crohn's disease.

In our study, 16 of 151 patients (11%) were found to have Indeterminant colitis by specimen histology—nearly twice the incidence reported in some adult series.^{2,15,16} Indeterminant colitis is a histologic diagnosis made from colonoscopic biopsies or the colon specimen that has features of both MUC and Crohn's disease. The characteristic features of indeterminant colitis include linear ulcers, fissures, and crypt abscesses similar to

MUC as well as skip areas, transmural inflammation albeit without granulomas, thickened bowel wall, creeping fat, and occasional rectal sparing similar to Crohn's disease. In the adult literature, indeterminant colitis has been found to increase incrementally the risk of pouchitis, pouch fistula, and pouch failure compared with MUC.^{2,12,16} In contrast to these reports, we found that indeterminant colitis was not associated significantly with postoperative complications, pouchitis, pouch failure, or Crohn's disease. Thus, unless clinical features raise the suspicion of Crohn's disease, the finding of indeterminant colitis alone does not contraindicate IPAA.

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