Indeterminate Colitis

Long-Term Outcome in Patients After Ileal Pouch-Anal Anastomosis

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Uncertainty persists concerning the long-term results of ileal pouch-anal anastomosis performed for indeterminate colitis. PURPOSE: This study was designed to compare functional outcomes of ileal pouch-anal anastomosis in patients with typical chronic ulcerative colitis and indeterminate colitis. METHOD: Seventy-one ileoanal pouch patients were identified with a diagnosis of indeterminate colitis. Mean follow-up was 56 months. Outcomes were compared with 1,232 chronic ulcerative colitis patients after ileal pouch-anal anastomosis. Mean follow-up was 60 months. RESULTS: (mean ± SD) There was no difference in the frequency of daily bowel movements (indeterminate colitis, 7 ± 3, *vs.* chronic ulcerative colitis, 7 ± 2). Daytime and nighttime incontinence rates were likewise similar. Prevalence of pouchitis was identical (33 percent). However, failure rate was higher in the indeterminate colitis group (indeterminate colitis, 19 percent, *vs.* chronic ulcerative colitis, 8 percent; ($P = 0.03$)). CONCLUSIONS: At a mean of nearly five years after surgery, failure appears to occur more frequently in patients with indeterminate colitis than in patients with chronic ulcerative colitis. However, the great majority of indeterminate colitis patients (>80 percent) have long-term functional results identical to those of patients with chronic ulcerative colitis. [Key words: Indeterminate colitis; Ileal pouch-anal anastomosis; Long-term outcome; Ulcerative colitis; Crohn's disease]

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Ileal pouch-anal anastomosis (IPAA) is associated with acceptable long-term functional outcomes in most patients requiring surgical management of chronic ulcerative colitis (CUC).[1] Controversy persists, however, about the results of IPAA performed in those patients with so-called atypical ulcerative colitis or what has come to be known as indeterminate colitis (IC). Indeterminate colitis is defined generally as colitis with histologic features in the excised specimen, suggestive of *both* Crohn's disease and ulcerative colitis (UC).

Although a firm diagnosis of Crohn's disease precludes ileoanal anastomosis, in 5 to 10 percent of patients the pathologist cannot distinguish UC from Crohn's colitis reliably. In a previous study from the Mayo Clinic,[2] ileoanal anastomosis performed in patients with a diagnosis of IC was shown to have similar outcomes as those performed in patients with a definitive diagnosis of UC. A more recent study from the Lahey Clinic[3] reported a much higher rate of late complications and failures in pouch patients with IC.

To help resolve this controversy, outcomes of all patients with a diagnosis of IC who had undergone IPAA at the Mayo Clinic were evaluated, including those previously reported; a larger group of IC patients thus was followed for a longer period of time.

PATIENTS AND METHODS

Between January 1981 and September 1992, more than 1,400 IPAA operations for UC and familial polyposis were performed at the Mayo Clinic. Pathologic reports of all excised specimens were reviewed. Colectomy in 10 percent of patients had been performed elsewhere, but specimens had been reviewed by Mayo Clinic pathologists before surgery. Seventy-one patients were identified with a diagnosis judged as IC, including 25 previously reported.[2] Charts of these patients were reviewed to insure that there was no *preoperative* suspicion of Crohn's disease, which by our definition excludes a diagnosis of IC. Definition of IC at Mayo is the unequivocal diagnosis of CUC preoperatively but inconclusive histology on examination of the pathologic specimen intraoperatively.

There were six predominant pathologic findings suggesting the diagnosis of IC (Fig. 1): 1) an abnormal distribution with varying degrees of inflammation; 2) creeping serosal fat; 3) submucosal neuronal proliferation; 4) retention of mucous-secreting cells; 5) deep linear ulceration or fissuring; 6) the presence of focal transmural inflammation in the absence of toxic colitis.

A registry of all pouch patients at the Mayo Clinic is

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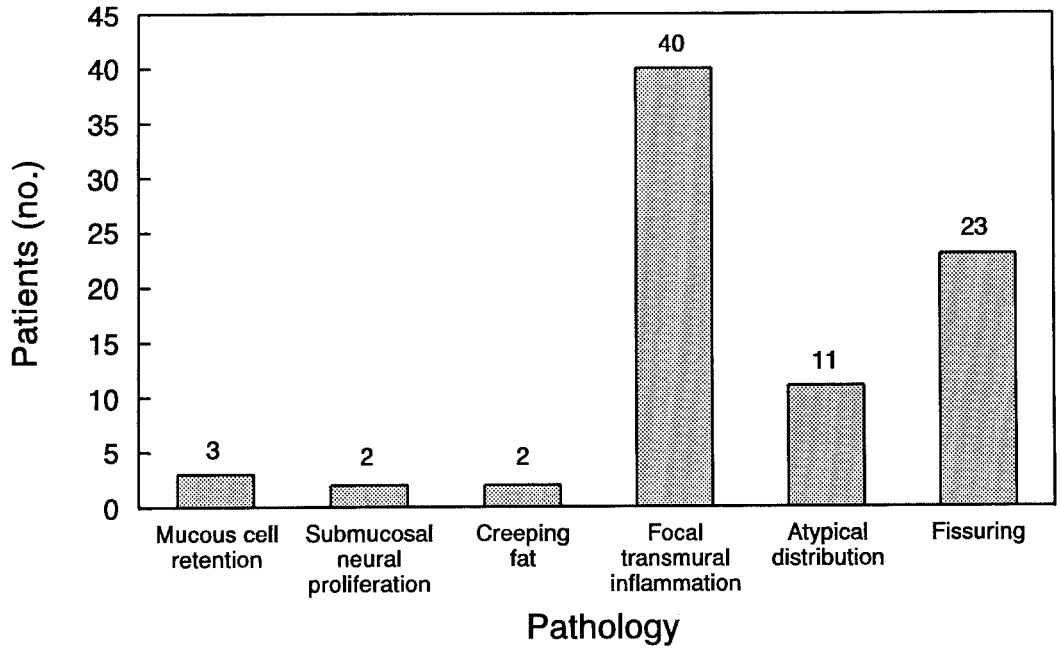

Figure 1. Frequency distribution of atypical pathologic findings suggesting the diagnosis of indeterminate colitis.

kept by an independent data clerk as part of an annual follow-up program. Data on the most recent functional parameters of the IC group, as well as complications, were recorded. No surgeon conducted any part of the follow-up. Results in 1,232 typical UC patients who had undergone an ileoanal anastomosis before October 1992 were also assessed. Comparisons of complications and failure rates between the two groups were analyzed using the chi-squared test. Differences in functional outcome were analyzed using the Wilcoxon's rank-sum test.

RESULTS

The IC and CUC groups were comparable in terms of age, sex, and time of follow-up (Table 1). Median interval between pouch construction and ileostomy closure was two months in both groups. Follow-up in patients with indeterminate pathology ranged between 1 and 120 (mean, 56) months following stoma closure and was similar to the UC group. One patient in the IC group was lost to follow-up, as were 20 patients in the much larger UC group.

Perioperative complications occurred at the same rate in the two groups, with small bowel obstruction being the most frequent problem (Table 2). The prevalence of pouchitis, identified as a syndrome manifest by frequent watery, often bloody stools, urgency, incontinence, abdominal cramping, and malaise or fever, was likewise identical at 33 percent.

Outright failure in the IC group, however, occurred at a higher rate than in the UC group (19 percent *vs.* 8 percent; $P = 0.03$). Failure was defined as the need for a permanent ileostomy with or without pouch excision. Of 13 IC failures occurring between 2 and 80 (mean, 35) months, 9 had perianal disease, 3 of which had a definite diagnosis of Crohn's disease. The four other failures were related to operative complications. Although late failures did occur in the UC group (range, 0–108 months), mean time to failure was shorter (25 months), with only 30 percent having evidence of perianal disease.

Five additional patients from the IC group have subsequently been diagnosed with gross and histologic changes typical of Crohn's disease involving the

Table 1.
Comparability of "Indeterminate" and "Ulcerative" Colitis Patient Populations

Type of Colitis	Number	Age (range)	% Women	Mean Follow-up (mo) (range)*
Indeterminate	71	31 (15–58)	56	56 (1–120)
Ulcerative	1,232	32 (13–64)	47	60 (0–139)

All differences = not significant.
* Following ileostomy closure.

Table 2.
Complications in Indeterminate and Ulcerative Colitis Patients

Type of Colitis	Complication n (%)			
	Obstruction	Pelvic Sepsis	Pouchitis	Failure
Indeterminate	10 (14)	5 (7)	22 (33)	13 (19)*
Ulcerative	183 (15)	66 (5)	351 (33)	98 (8)

* $P = 0.03$.

pouch. At the present time, pouch function remains satisfactory in all of them, with no evidence of perianal disease to date.

Two additional failures had occurred in the group of 25 subjects reported by Pezim *et al.*[2]; increased follow-up of this original group of IC patients resulted in a 16 percent failure rate as opposed to the originally reported 8 percent rate. In addition, three patients from this study, including one who originally had been lost to follow-up, are included in the group of patients with Crohn's disease and satisfactory pouch function to date. Functional results of patients with IC and CUC are listed in Table 3 and are similar between groups.

DISCUSSION

Although medical management of CUC and Crohn's disease is often similar, it is important to distinguish the two when surgical management is contemplated; poor results occur frequently in patients with a clinical diagnosis of Crohn's disease who undergo IPAA.[4]

Since the first descriptions of Crohn's disease,[5,6] difficulties have arisen in distinguishing this entity from UC when the clinical picture is similar. Problems are encountered because of frequent overlapping histologic features of the two diseases.[7,8] Ulcerative colitis, although never discontinuous, may appear as such grossly if variable intensities of the inflammation are present. Fissuring and longitudinal ulceration, accepted as features of Crohn's disease, may occasionally be seen with UC. However, retention of goblet cells favors a diagnosis of Crohn's disease; with lesser degrees of inflammation this feature may be seen in UC as well. Transmural involvement, usual for Crohn's disease, is often seen in fulminant cases of UC. When only a single focus of inflammation is found, one cannot exclude an intensely diseased area of UC as the cause rather than Crohn's disease. Granulomas, a reliable means of distinguishing Crohn's disease, are frequently not found in colonic specimens at all.

An experienced pathologist should be able to distinguish UC and Crohn's colitis in the majority of patients, particularly if the clinical history is known. Ultimately, in about 5 to 10 percent of patients, diagnosis will remain obscure, and pathology will be labeled "indeterminate."

Our practice has been to proceed with ileoanal anastomosis in those patients labeled indeterminate at the time of surgery, *if there is nothing present preoperatively to suggest Crohn's disease.* With further sectioning and analysis over time, some patients may be labeled later as having Crohn's disease. Even under these circumstances, however, Hyman *et al.*[4] have shown that, with *no* preoperative clinical features of Crohn's disease present, results at a mean follow-up of 38 months were quite good. Results from a smaller study[9] have shown similar acceptable pouch function at three years in three of five patients judged by histologic criteria to have Crohn's disease when there was no clinical or operative findings to initially suggest the diagnosis.

Table 3.
Long-Term Functional Results in Indeterminate and Ulcerative Colitis Patients

Type of colitis	n	Stools (No./24 hr)	Incontinence (%)*				
			Daytime			Nighttime	
			N	O	F	None	Spotting
Indeterminate	55	7 ± 3	60	33	7	30	70
Ulcerative	1,006	7 ± 2	68	27	5	38	62

N = never; O = occasional staining; F = frequent staining that can interfere with activities. $P > 0.05$ between all groups.

Literature is conflicting as to the outcome of IC. In 1966, Lewin and Swales[10] concluded that "atypical" UC behaved as UC, with no evidence of small bowel recurrence. Wells *et al.*[11] have concluded that IC patients are unlikely to show features of Crohn's disease over the long term. The previous study from this institution[2] agrees with this finding. A study from the Lahey Clinic,[3] however, reported opposite findings; there was a high incidence of late perineal complications following ileoanal anastomosis, presumably on the basis of recurrent Crohn's disease.

Although failure rates were higher as a result of perianal disease, presumably related to Crohn's disease, our results indicate that the majority (>80 percent) of these indeterminate cases *do not* develop recurrent Crohn's disease and do experience satisfactory pouch function over the long term. At our institution, frozen section examination of all specimens is performed. If frozen section is not available, it may be wise to avoid immediate pouch construction if the diagnosis is insecure. If rectal disease is minimal with no dysplasia, ileorectal anastomosis may suffice as a temporary measure, avoiding a stoma.

Importantly, if the patient has evidence of indeterminate pathology and has a clinical suspicion of Crohn's disease present *before* the operation, we do not favor IPAA but proceed with proctocolectomy or ileorectal anastomosis (if the rectum is spared) in the belief that the patient has Crohn's disease.

CONCLUSION

Results of this study indicate that "indeterminate colitis," as defined by a pathologist *at the time of operation* with no clinical suspicion of Crohn's disease preoperatively, can be treated by IPAA with an excellent chance of long-term success.

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