PAPER

Similar Functional Results and Complications After Ileal Pouch–Anal Anastomosis in Patients With Indeterminate vs Ulcerative Colitis

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Hypothesis: Patients who undergo ileal pouch–anal anastomosis (IPAA) for indeterminate colitis (IC) have a pouch complication and pouch loss rate only slightly higher than that associated with ulcerative colitis (UC). The functional outcome in patients with IC is no different from that in patients with UC.

Design: Retrospective review of prospectively gathered data comparing complication rates and outcomes of patients with IC vs UC who have undergone IPAA at a single institution during 19 years.

Setting: University teaching hospital.

Patients: Between July 1, 1982, and July 1, 2001, 723 patients underwent IPAA, 644 for colonic inflammatory bowel disease. A further breakdown of the latter group revealed 79 patients (12.3%) with IC and 565 (87.7%) with UC. These 2 patient populations were compared with regard to postoperative complications, pouch loss, and functional outcome.

Main Outcome Measures: Patients with IC and UC were compared with regard to pouch complications, such as J-pouch leak, fistula, cuff abscess, stricture, redo IPAA, Crohn diagnosis, and pouch loss. They were also compared with regard to 24-hour stool frequency and nighttime incontinence at 1, 3, 6, and 9 months after surgery.

Results: Approximately 98% of patients had 1 year of follow-up and 89% had long-term follow-up (mean, 78.5 months). Patients with IC were compared with those with UC with regard to pouch complications, such as cuff abscess (1.3% vs 1.6%), J-pouch leak (5.1% vs 2.3%), intra-abdominal abscess (0% vs 1.1%), stricture (7.6% vs 4.8%), and fistula (2.5% vs 1.6%). These 2 groups were also compared with regard to small bowel obstruction (6.3% vs 5.5%), pouchitis (34.2% vs 25.0%), eventual diagnosis of Crohn disease (1.3% vs 0.7%), redo IPAA (1.3% vs 0.9%), and eventual pouch loss (2.5% vs 1.2%). An evaluation of functional results revealed no significant differences between the 2 groups with regard to 24-hour stool frequency or nighttime incontinence. The pathologists classified patients with IC into 3 groups: IC but favor UC (group 1), IC but favor Crohn (group 2), and IC (group 3). Most of the postoperative complications occurred in group 1 patients, but the only pouch loss occurred in those in group 2.

Conclusions: The incidences of pouch complications after IPAA were slightly higher in the IC group compared with the UC group, but the differences were not statistically significant. Functional results were the same in both groups. Pouch loss was high in group 2 patients, but was otherwise not significantly higher in the IC group overall ($P = .36$). Most patients with IC can undergo IPAA and expect an outcome equivalent to that of patients with UC.

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SPHINCTER-SPARING surgery to treat colonic mucosal diseases has become an important addition to the surgical armamentarium since its development almost 25 years ago.[1] Extensive clinical experience reported in several large series[2-6] demonstrates that ileal pouch–anal anastomosis (IPAA) leads to good functional results and acceptable morbidity in most patients in whom it is performed for chronic ulcerative colitis (UC). It is the operation of choice when patients are confronted with a decision of sphincter-sparing vs permanent ileostomy in conditions of UC and polyposis. Conversely, patients who undergo IPAA for Crohn colitis have a different outcome, characterized by high rates of pouch complications and pouch loss, often exceeding 50%.[7-10] Crohn colitis is considered a contraindication to performing IPAA.

In approximately 10% of patients with colonic inflammatory bowel disease (IBD), pathologists are unable to distinguish between UC and Crohn colitis because the specimens contain gross and histologic features of both diseases.[11-14] Patients with pathologically ambiguous specimens are

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PATIENTS AND METHODS

In 1994, an IPAA registry was established at The University of Utah School of Medicine to include all IPAA procedures performed since 1982 and to prospectively gather data on any IPAA procedures done since the inception of the registry. Between July 1, 1982, and July 1, 2001, 723 patients underwent IPAA, 644 for colonic IBD and 79 for polyposis, collagenous colitis, or other conditions. A further breakdown of the IBD group revealed 79 patients (12.3%) with IC and 565 (87.7%) with UC. These 2 patient populations comprise the groups compared in this study. The medical charts of all patients with IC were reviewed by one of us (M.T.D.) to be certain they met the criteria for inclusion in the IC group. A pathologist specializing in gastrointestinal disease with a special interest in IBD reviewed the histologic sections of 69 (87.3%) of 79 patients with IC in the study. All specimens were viewed in real time, ie, at the time of surgery. In about 15% of patients in the combined IC and UC series, a diagnosis was made before surgery based on histologic findings from a colectomy performed before IPAA. Similarly, 26 (3.6%) of 723 patients in the combined series had gross findings intraoperatively that were suggestive of Crohn colitis and underwent a 3-stage operation. The final diagnosis in most patients was made after colectomy and IPAA. Gross and histologic characteristics of the colon that contributed to a diagnosis of IC included atypical distribution of inflammation (right-side predominance), serpiginous ulcers of the colon or rectum, skip lesions, rectal sparing, creeping fat, fistulas in the colon or perianal area, transmural inflammation, granulomas, inflammation of the terminal ileum, and focality of disease.

The IC and UC groups were then compared with regard to complications primarily affecting the J pouch as well as functional outcome, as reflected in stool frequency per 24 hours and nighttime incontinence of more than 3 episodes per week at 1, 3, 6, and 9 months after surgery. Specific complications studied included J-pouch leak, abdominal abscess, cuff abscess, anastomotic stricture, fistula, redo IPAA, surgical small bowel obstruction, and pouch loss. The IC group was divided into the 3 categories described by the pathologists for comparison: IC but favor UC (group 1), IC but favor Crohn (group 2), and IC (group 3). The patients in group 1 had gross and histologic features primarily of UC, with only a few features suggesting Crohn colitis. Similarly, those in group 2 had a preponderance of Crohn-like features and only a few features characteristic of UC. In group 3, there were equal numbers of UC and Crohn features. These 3 groups were compared with regard to complications to ascertain if one group was associated with a predominance of problems. Finally, the entire IC population was broken down according to severity to determine whether a preponderance of severe cases constituted most IC cases. Severe colitis was characterized by pseudopolyps, deep ulcerations, hemorrhage, and significant friability. Moderately severe colitis was associated with granularity, contact friability, fibrinous exudates, and mucosal edema. Mild colitis was characterized by quiescent disease, a normal vascular pattern, and pale, featureless mucosa.

Follow-up included clinic visits at 1, 3, 6, and 9 months the first year after surgery, followed by contact once a year via a mailed survey. Statistical comparisons were made using χ^2 analysis.

said to have "indeterminate colitis" (IC). Because some features of Crohn colitis are present in IC, there have been concerns that patients with IC should not undergo IPAA, because of the presumed higher risks of complications and eventual pouch loss.[15-17] This study was conducted to ascertain whether patients with IC who undergo IPAA have a higher complication rate, poorer functional results, or a higher rate of pouch loss than patients with UC in a large series involving 2 surgeons over a 19-year period at an academic medical center.

RESULTS

In this study, 79 patients (12.3%) were classified as having IC compared with 565 (87.7%) with UC. Among the 79 patients with IC, 77 (97.5%) had 1 year of follow-up and 70 (88.6%) had long-term follow-up. The mean follow-up for the combined series was 78.5 months.

Comparing the final histologic diagnosis with the preoperative diagnosis received from biopsies obtained during colonoscopy by the referring gastroenterologist or from the previous colectomy specimen, the gastrointestinal pathologist at this institution agreed with the referring pathologist's preoperative diagnosis in only 29.0% of IC cases. A review of the final histologic reports and operative reports demonstrated that 34 patients had a single finding suggestive of Crohn disease, 30 had 2 findings, and 15 had 3 findings. The most common finding was focality of inflammation, which occurred in 45.6% of patients. In descending order of frequency, 29.0% had transmural disease, 20.3% had granulomas, 17.7% had skip lesions, 13.9% had right-side predominance of inflammation and terminal ileum inflammation, 7.6% had linear ulcers, 5.0% had rectal sparing, and 3.8% had perianal fistulas. Findings demonstrated by other series[15-17] to be worrisome as predictors of an eventual diagnosis of Crohn disease occurred infrequently in this series: perianal fissures (7.6%), perianal fistulas and abscess (3.8%), and abnormal terminal ileum findings (13.9%). This reflects an effort to exclude those patients from consideration of an IPAA procedure if the findings were discovered before or during surgery.

The mean age of patients with IC was slightly higher than that of patients with UC (39 vs 37 years), and the male-female ratio was slightly different, (IC, 65%:35%; UC, 60%:40%). About 14% of patients in both groups had had a subtotal colectomy before IPAA.

Intractability was the primary indication for IPAA in 68% of patients with IC, compared with 74% of patients with UC. Preoperative prednisone was taken by 64% of patients with IC and 69% of patients with UC; 50% of patients with IC took more than 30 mg of prednisone daily, as did 49% of patients with UC. Mean preoperative total protein and albumin was 7.0 g/dL and 3.9 g/dL, respectively, in the IC group and 6.8 g/dL and 4.0 g/dL in the UC group. There were no significant differences

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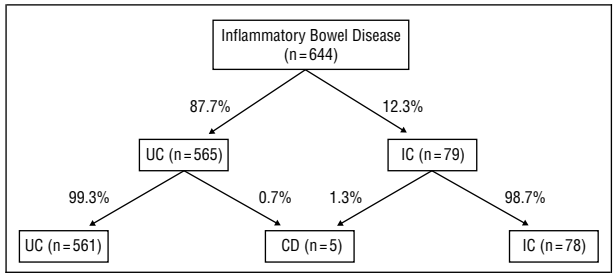
Table 1. Complications After Ileal Pouch–Anal Anastomosis (IPAA)*

Complication	Indeterminate Colitis (n = 79)	Ulcerative Colitis (n = 565)	*P* Value
Cuff abscess	1 (1.3)	9 (1.6)	.82
J-pouch leak	4 (5.1)	13 (2.3)	.15
Intra-abdominal abscess	0	6 (1.1)	.36
Stricture	6 (7.6)	27 (4.8)	.29
Pouch fistula	2 (2.5)	9 (1.6)	.55
Surgical small bowel obstruction	5 (6.3)	31 (5.5)	.76
Pouchitis	27 (34.2)	141 (25.0)	.15
Crohn diagnosis	1 (1.3)	4 (0.7)	.36
Redo IPAA	1 (1.3)	5 (0.9)	.87
Pouch loss	2 (2.5)	7 (1.2)	.36

*Data are given as number (percentage) unless otherwise indicated.



Long-term follow-up demonstrates the eventual diagnosis of the 644 patients who originally underwent ileal pouch–anal anastomosis. While 0.7% of patients (4/565) with ulcerative colitis (UC) eventually developed Crohn disease (CD), 1.3% of patients (1/79) with indeterminate colitis (IC) went on to develop CD.

between the 2 groups with regard to duration of operation, estimated blood loss, or whether a patient required blood transfusions. Patients with IC received more intraoperative intravenous fluid than did patients with UC (8209 vs 6994 mL), and their measured J pouch (at 10 cm H_2O pressure) was slightly larger (246 vs 219 mL).

Complications after IPAA and after ileostomy closure were combined, and complications in the 79 patients with IC were compared with those of the 565 patients with UC (**Table 1**). Cuff abscess, which occurred primarily after IPAA, occurred in 1 patient with IC and in 9 patients with UC (1.3% vs 1.6%, *P*=.82). J-pouch leak was diagnosed in 4 patients with IC and in 13 patients with UC (5.1% vs 2.3%, *P*=.15). Intra-abdominal abscess was detected in none of the patients with IC, while it was found in 6 patients with UC (0% vs 1.1%, *P*=.36). Stricture at the pouch-anal anastomosis developed in 6 patients with IC and in 27 patients with UC (7.6% vs 4.8%, *P*=.29). A fistula between the J pouch and vagina, urethra, bladder, or skin was seen in 2 patients with IC and in 9 patients with UC (2.5% vs 1.6%, *P*=.55).

Small bowel obstruction requiring surgery complicated the postoperative course of 5 patients with IC, while 31 patients with UC required adhesiolysis for this complication (6.3% vs 5.5%, *P*=.76). Similarly, 27 patients with IC developed pouchitis during follow-up, while 141 patients with UC had pouchitis (34.2% vs 25.0%, *P*=.15). During long-term follow-up, Crohn disease developed in 1 patient with IC, while it was diagnosed in 4 patients with UC (1.3% vs 0.7%, *P*=.36) (**Figure**).

Table 2. Functional Results After Ileal Pouch–Anal Anastomosis*

Follow-up, mo	Stool Frequency per 24 h, Mean		Nighttime Incontinence >3/wk, %	
	IC	UC	IC	UC
1	8.0	7.7	12	10
3	6.9	6.9	9	11
6	6.3	6.4	4	12
9	6.1	6.0	3	12

*IC indicates indeterminate colitis; UC, ulcerative colitis.

The most serious complications involving the J pouch resulted in redo IPAA or removal of the J pouch and placement of a permanent ileostomy. In this series, 1 patient with IC underwent redo IPAA secondary to a nonhealing fistula between the J pouch and vagina associated with an anastomotic stricture; in the UC group, 5 patients underwent redo IPAAs as a result of anastomotic disruption and pouch fistulas (1.3% vs 0.9%, *P*=.87). Among the patients with IC, 2 J pouches had to be removed (for high stool frequency and misdiagnosed Crohn disease), while 7 patients with UC had J-pouch removal for misdiagnosed Crohn disease and incontinence (2.5% vs 1.2%, *P*=.36).

When the 3 IC classifications were analyzed, 51 patients were in group 1, 11 were in group 2, and 17 were in group 3. Most of the postoperative complications occurred in group 1 patients, largely because that category had 4 to 5 times more patients than the other 2 categories. For example, the following complications occurred in patients in group 1: all 4 J-pouch leaks, the only cuff abscess, 5 of 6 strictures, 1 of 2 pouch losses, and the only redo IPAA. On the other hand, perhaps the most telling statistic in this portion of the study is that 1 of 11 patients in group 2 lost a J pouch, while only 1 of 51 patients in group 1 lost a pouch (9.1% vs 2.0%).

Pathologists recognize that in fulminant UC it is possible to "overcall" transmural inflammation caused by advanced disease. Theoretically, a large percentage of patients comprising an IC series might have fulminant UC that is incorrectly diagnosed as IC and, thus, bias the series. However, in this IC series, 27 patients had severe disease, 29 had moderately severe disease, and 23 had mild disease, demonstrating a virtually even distribution of patients in these 3 categories.

Evaluation of functional results revealed no significant differences between patients with IC and UC who were followed up long-term (**Table 2**). Stool frequency per 24 hours at 1, 3, 6, and 9 months was 8.0, 6.9, 6.3, and 6.1, respectively, in patients with IC, while similar frequencies of 7.7, 6.9, 6.4, and 6.0, respectively, were measured in patients with UC. Similarly, nighttime incontinence at 1, 3, 6, and 9 months that occurred more than 3 times a week was 12%, 9%, 4%, and 3%, respectively, in patients with IC, and 10%, 11%, 12%, and 12%, respectively, in patients with UC.

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COMMENT

The concern regarding patients with IC who undergo IPAA centers around the question of whether their disease has a natural history similar to that of Crohn colitis, as patients with Crohn colitis do poorly after IPAA. In a series by Fazio et al[18] of redo IPAA procedures, 40% of patients with Crohn colitis had excision of their J pouch because of septic and mechanical complications. Marcello and colleagues[13] documented a 37% pouch loss rate in patients with Crohn colitis, while it was only 2% in patients with UC. Other large series reveal unacceptably high failure rates in patients with Crohn colitis who undergo IPAA, including those described by Deutsch,[8] Sagar,[9] Panis,[10] and Hyman[7] and their colleagues.

However, extensive clinical experience has demonstrated that IC does not have a clinical course identical to that of Crohn colitis. The degree of increased risk of complications and pouch failure in patients with IC vs UC remains a controversial issue. Some surgeons are so concerned about the possible increased risks associated with IC that they are reluctant to offer IPAA to these patients or refuse to altogether. Marcello and colleagues[13] observed that the incidence of perineal complications and pouch failure was 23% and 2%, respectively, in patients with UC, 44% and 12% with IC, and 63% and 37% with Crohn colitis. In their series, only 3% of patients with UC eventually developed Crohn disease, compared with 13% of patients with IC. They urged caution in recommending IPAA in patients with IC. Bodzin and colleagues[16] had such high failure rates among patients with IC who underwent IPAA that they recommended ileorectal anastomosis instead of IPAA in patients known to have IC before surgery. Similarly, Atkinson et al[12] showed that patients with a pathological diagnosis of IC had a significantly worse prognosis than did patients with UC and recommended caution in performing IPAA in patients with IC.

Conversely, several series show that the risk of performing IPAA in patients with IC is only slightly higher or not increased at all. In the small series by Hyman et al,[7] 15 of 16 patients with IC and no other signs of Crohn colitis had functioning IPAA about 4 years after surgery. A study reported by Pezim et al,[19] in which they identified IC in specimens postoperatively, found no difference in the outcome of patients with IC compared with control subjects with UC. In a series of 46 patients with IC, Wells and associates[20] reported that only 1 patient was reclassified as having Crohn colitis during long-term (10 years) follow-up. A series by Deutsch et al[8] showed that Crohn colitis developed in only 3.5% of their patients. In a follow-up study to the series by Pezim et al,[19] McIntyre and colleagues[11] noted that pouch failure rates were higher in the IC group compared with the UC group (19% vs 8%), but that most patients (>80%) with IC have long-term functional results identical to those of patients with UC. A final follow-up to that series authored by Yu et al[21] determined that, during 10 years' follow-up, patients with IC had a higher incidence of pelvic sepsis (17% vs 7%), pouch fistula (31% vs 9%), and pouch failure (27% vs 11%) compared with patients with UC. In their IC group, 12 (14.6%) of 82 patients went on to have Crohn disease diagnosed, compared with 26 (1.8%) of 1437 patients with UC. They concluded, however, that patients with IC who did not develop Crohn disease experienced long-term outcomes similar to those of patients with UC.

In the present series, although there was a slight trend toward higher complication rates in patients with IC with regard to J-pouch leak (5.0% vs 2.3%), stricture (7.6% vs 4.8%), and fistula (2.5% vs 1.6%), none of these reached statistical significance. Similarly, slightly higher rates of Crohn colitis were diagnosed in the IC group (2.5% vs 1.0%), and pouch failure rates were also slightly higher (2.5% vs 1.2%), but only minimally so and at levels that were not significant. Other complication rates, such as surgical bowel obstruction and pouchitis, were also similar. An assessment of functional results revealed no differences in stool frequency or nighttime incontinence between the 2 groups.

In this series, fulminant colitis did not account for most patients diagnosed as having IC (27 severe, 29 moderately severe, and 23 mild). Therefore, one should not infer that there was a disproportionate number of IC diagnoses that were difficult to diagnose and actually were severe UC.

One observation in this series that invites caution when assessing patients with IC for IPAA was the finding that 1 (9.1%) of 11 patients in group 2 had pouch failure, compared with 1 (2.0%) of 51 patients in group 1. Although 10 of the 11 patients in group 2 have functioning pouches and have not had high complication rates, this group merits close observation because of their likely higher risk. Only 3 of the patients in this category had a preoperative diagnosis of Crohn colitis and knowingly underwent IPAA; the other 8 patients had the diagnosis made postoperatively. It is our practice to offer IPAA to this group of patients reluctantly and only after extensive counseling regarding the risk of pouch complications and pouch loss.

The surgeon who performs IPAA must do all that he or she can to make certain that this procedure is not performed on patients with Crohn colitis. Any patient with known Crohn colitis should not be offered IPAA, and patients with a diagnosis of "IC but favor Crohn" should probably not be offered IPAA as an option; ileorectal anastomosis would be a better choice. At the time of surgery, the removed colon should be opened from end to end and inspected by an experienced IBD surgeon. If atypical distribution of inflammation, skip lesions, creeping fat, bowel wall thickening, serpiginous ulcers, or cobblestoning are present, the surgeon should have frozen sections performed on the specimen to rule out Crohn disease. If the diagnosis remains unclear, performing colectomy and Brooke ileostomy and awaiting results from permanent section analysis is the safest and most prudent thing to do.

Having a pathologist who has a special interest in IBD is important in distinguishing these complex and ambiguous IBD cases. In the study by Farmer and associates,[22] the gastrointestinal specialist's diagnosis differed from the initial diagnosis of the general pathologist approximately 50% of the time. Those differences may have a profound effect on the choice of operation and eventual clinical outcome.

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In summary, this study demonstrates that most patients diagnosed as having IC can undergo IPAA and expect a good outcome. The patients with IC in this series had clinical outcomes more like those of UC than Crohn colitis. Except for those in group 2, the incidence of pouch complications and pouch loss was only slightly higher in group 3 patients, and functional results were no different. Of paramount importance in this area of complex and ambiguous IBD cases is a well-trained gastrointestinal pathologist, a thoughtful and conservative surgeon, and a patient willing to accept the recommendation of the surgical team.

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DISCUSSION

Richard C. Thirlby, MD, Seattle, Wash: The ileal pouch–anal anastomosis procedure has become the standard of care for patients with chronic ulcerative colitis, or UC, who require surgical resections. A few centers perform this procedure in patients with Crohn's disease. If this procedure is performed on patients with Crohn's, only about a third of patients will have acceptable results. About a third will actually require pouch excision, due to either severe Crohn's in the pouch or perianal fistulas or infections.

The diagnosis of Crohn's in these patients is often made years postoperatively based on obvious small bowel Crohn's. Even in retrospect, in these patients the original colectomy specimen may look like UC on gross inspection and even on rereview of pathology slides.

It was reported today by Dr Dayton and coworkers at The University of Utah that about 10% of patients undergoing IPAA procedures have indeterminate colitis on final path review. By definition, these colons have characteristics of both UC and Crohn's. Typical features of Crohn's prompting the label of indeterminate colitis include rectal sparing or other skip areas, linear ulcers, full-thickness inflammation in patients done urgently with fulminant disease, and perianal fistulas. The fear has always been that these patients would act like Crohn's patients and, with time, would develop fistulas, Crohn's in the pouch, and/or refractory pouchitis.

The purpose of the present study was to answer definitively the question: "Do patients with indeterminate colitis do less well than those with classic UC?" The answer to the question posed is a definitive no. The beauty of this study presented today is strength in numbers. Six hundred forty-four patients with a preoperative diagnosis of UC underwent IPAA. Seventy-nine had a final diagnosis of indeterminate colitis. Follow-up exceeded 1 year in virtually all patients. The data clearly show that the incidence of complications, such as pouch fistulas, anal stenoses, definite Crohn's disease, pouchitis, and pouch loss, is virtually identical in both groups.

When indeterminate colitis patients were broken down to indeterminate–favor UC vs indeterminate-favor Crohn's, it did appear that the latter group might not do as well, albeit with very small numbers. Whereas only 2% of the "favor UC" group required pouch excision, 1 of 11, or 9%, of the "favor Crohn's" group required pouch excision. Regardless, the important take-home message of this paper is clear. We can tell most of our patients with indeterminate colitis that they are going to do just fine.

However, I have several questions for Dr Dayton. The incidence of pouchitis in this series is relatively low, about 30%. Most series with long-term follow-up report pouchitis in at least 50% of patients. In our experience, if one follows a UC patient long enough and if you are honest with your data analysis, all patients eventually develop pouchitis, at least once or twice. The "Results" section of the manuscript does not state the duration of follow-up. Since the pouchitis rate is so low, my suspicion is that there is not accurate long-term follow-up on many patients.

My first question then is how many of your patients did you follow up on for longer than 3, 5, or 10 years? In addition, it would be nice to know how you document pouchitis. Some patients do not even know that they have pouchitis. Some forget what the symptoms are. I feel that a questionnaire mailed once a year with a "pouchitis yes/no" question would be an unreliable assessment of the incidence.

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Furthermore, there is pouchitis and then there is pouchitis. Some patients have trivial episodes once a year. Others are incapacitated by daily symptoms. Do you have any data on what percentage of your patients have had occasional episodes of pouchitis vs what percentage have chronic pouchitis or so-called antibiotic-dependent pouchitis? If so, are there any differences in frequencies or severities of pouchitis in your 2 groups?

Finally, recent studies suggest that ANCA [antineutrophil cytoplasmic antibody] levels predict markedly increased susceptibility to pouchitis. Many indeterminate patients are tested for ANCA prior to or just after colectomy. Do you have any data on ANCA levels in your patients and their relationship to long-term outcomes?

Fabrizio Michelassi, MD, Chicago, Ill: Dr Thirlby has asked you all of the pertinent questions; yet, you mentioned that some patients with indeterminate colitis had granulomas and/or fistulas. Those patients, in our institution, would be classified as Crohn's disease patients. We feel that granulomas are pathognomonic of Crohn's disease and fistulae are really reflective of transmural disease, which is a characteristic of Crohn's disease, rather than ulcerative colitis.

Thomas Biehl, MD, Seattle: It seems that the diagnosis of UC or Crohn's or indeterminate colitis sounds like a very difficult thing to do from a pathologist's point of view. Your pathologist seems to be well experienced. Could you comment on that pathologist's experience and how that might relate to how good your results are?

Dr Dayton: First of all, Dr Thirlby, let me spend a few moments and answer the questions that you had. You asked why the incidence of pouchitis is 30% in our series, while in some series the published rate is 50% and even higher. It all goes back to how you make the diagnosis of pouchitis. We are loathe to immediately assign a diagnosis of pouchitis to any patient who comes in with increased stool frequency, because there are a number of factors that can cause an increase in frequency, such as gastrointestinal flu, eating a meal with a high concentration of sugar, change in dietary habits, and even stress. So first of all, we start with a very careful clinical history. We ask them about constitutional symptoms, because most pouchitis patients do not have constitutional symptoms. We ask about dietary changes, etc.

The classic tetrad of symptoms in pouchitis patients is an increase in stool frequency, leakage that was not present before, a low-grade fever, and malaise. So, I think a very careful history is a very important part of establishing the diagnosis. We do not scope every single one of our patients that have a possible diagnosis of pouchitis. In this patient population, you would have time to do nothing else, because it is such a common problem. Therefore, 95% of the time, it is a clinical diagnosis, with the patient coming in with a distinct change in their bowel activity. Only in the situation of a real severe pouchitis do we scope them.

What is the duration of follow-up in our study? I am sorry I did not have that in the manuscript and I have to correct that. We have a mean follow-up of 78.5 months, so we have 6-year follow-up on these patients. It has not reached 10 years yet, but at least out this far, we think that is reasonable follow-up, and 89% of our patients fit into the category of long-term follow-up.

How many of our patients have intractable pouchitis? Approximately 25% of our patients who have pouchitis develop a severe or smoldering type that just never goes away, and you have to keep them constantly on a low dose of Flagyl or Cipro. These patients represent a real problem, for which we do not have a good answer. Approximately 5% to maybe even as high as 10% of our patients eventually get put on prednisone for their pouchitis. It works very effectively in the truly refractory pouchitis patients.

What about ANCA levels? As you may know, serum ANCA is a marker that has been identified as correlating with a high likelihood of ulcerative colitis. Corresponding to that is another serum marker called ASCA [anti-*Saccharomyces cerevisiae* antibodies] that is elevated in Crohn's disease. The only problem with these markers is that in Crohn's colitis about 20% of the patients will have a positive ANCA marker. I do not think that any of us believe that the ANCA and ASCA markers are reliable and dependable enough to make the distinction between Crohn's and ulcerative colitis yet, so we don't use those right now.

Dr Michelassi asked the question about granuloma and fissure. That is a very good question, Fabrizio. As you may have noticed in our study, most of the patients had the diagnosis of indeterminate colitis made after the colon was already out and the operation was done. Our procedure is that we take a colon out, cut it open, and look at it grossly. If there are any features that concern us, we will walk it down to the pathologist and do frozen sections. Now, our pathologist is very fond of telling us that you cannot be 100% positive with frozen sections and that permanent sections are much more dependable. In any patient who has granulomas or fissures that I identify in a specimen, which has some ambiguity grossly at the time of surgery, I would likely do a 3-stage operation and probably would not do this operation if I knew there were granulomas and fissures. That is the patient population that I worry the most about. If our pathologist says it is indeterminate colitis but he is concerned about Crohn's disease, those patients I will usually encourage to have an ileorectal anastomosis instead of a pouch operation.

Finally, Dr Biehl, what about our pathologist? There was an interesting study that was done in Louisville by Farmer and his group, in which they invited a number of general pathologists to read both colonic specimens and biopsies and then compared the results of their study with findings of a designated GI pathologist with experience in IBD. In their study, 50% of the time, the general pathologist made the incorrect diagnosis of Crohn's vs ulcerative colitis. So, I think it is very important to have a designated GI pathologist with an interest in IBD, and ultimately I think that will explain the differences in why some of the series have such a high incidence of Crohn's disease and such a high incidence of pouch loss.

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