



## Long-term follow up of ileal pouch anal anastomosis in a large cohort of pediatric and young adult patients with ulcerative colitis



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### ABSTRACT

**Aim:** The study's aim is to determine long-term outcomes in a large cohort of pediatric and young adult patients who underwent proctocolectomy with ileal pouch anal anastomosis (IPAA) for ulcerative colitis (UC).

**Methods:** Patients diagnosed with UC in childhood or adolescence (age  $\leq 21$  years) who underwent IPAA in childhood, adolescence, or young adulthood between 1982 and 1997 were contacted to determine pouch history, complications, and quality of life.

**Results:** Data were obtained from 74 patients out of a previously reported cohort. Median age at diagnosis of UC was 15 years and at surgery was 18 years. Median follow-up was 20 years. Complications during follow-up were pouchitis (45%), strictures (16%), fistulae (30%), obstruction (20%), and change of diagnosis to Crohn's (28%). Twenty-three percent reported no complications. Fourteen percent had pouch failure, with Crohn's and fistulae reported to be the most frequent complications. Seventy-nine percent reported being very satisfied at 20 years follow-up.

**Conclusion:** To our knowledge, this study represents the largest cohort with the longest follow-up of pediatric and young adult patients undergoing IPAA for UC. Change in diagnosis to Crohn's and development of fistulae are risk factors for pouch failure. Despite reported complications, IPAA remains an excellent option for pediatric patients with UC.

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Approximately one third of patients with ulcerative colitis (UC) will ultimately require surgical management for optimal control of their disease or to lessen the risk of malignancy [1]. Proctocolectomy and ileal pouch anal anastomosis (IPAA) have emerged as the procedures of choice in patients with UC in this era. Over time the incidence of complications associated with IPAA increases, including pouchitis, fistulae formation, and change in the diagnosis to Crohn's disease. The purpose of this study was to report long-term outcome data in a pediatric and young adult population and to determine the incidence of complications associated with IPAA, including the frequency of change in diagnosis from UC to Crohn's disease.

### 1. Materials and methods

Between 1982 and 1997, 176 children and adolescents diagnosed with ulcerative colitis at age 21 or younger underwent colectomy with IPAA at our institution. Pouch outcome in this cohort, whose age at surgery ranged from 3 to 29 years with three patients older than the age of

21, was initially evaluated and reported at 2 and 5 years postoperatively [2,3]. An unpublished survey conducted in 2002 reached 157 of these patients. From November 2010 through August 2011 attempts were made to contact that cohort of 157 patients by telephone. Seventy-four patients were able to be contacted. Data for analysis were obtained via telephone interviews and subsequent supplemental information was obtained via review of patient charts. We did consider limiting our cohort to only those children who underwent IPAA in childhood (age  $\leq 21$  years of age), however, to evaluate cohort progression, we continued with the same cohort as prior studies.

#### 1.1. Telephone interview

During the telephone interview, performed solely by the primary investigator, patients were asked about their medication history and current medication use, stooling frequency, and presence of fecal incontinence. Additional questions were asked about complications related to their pouch, identification of dysplasia of the pouch, a change in their diagnosis from UC to Crohn's disease, and difficulty with conception or pregnancy. Patients were also asked about their overall satisfaction with the pouch surgery on a 5-point scale, with 1 = very

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dissatisfied, 2 = somewhat dissatisfied, 3 = no opinion, 4 = somewhat satisfied, and 5 = very satisfied. (See Appendix for full questionnaire.)

### 1.2. Chart review

For each patient, demographic information was recorded. Indication for surgery was recorded for all patients if this information was available. Surgical information for patients included whether the patient underwent a 1-, 2-, or 3-stage procedure, whether the pouch-anal anastomosis was hand-sewn or stapled, and configuration of the pouch.

### 1.3. Statistical analysis

All information was entered into a secure computer database (RED-Cap) for statistical analysis. The data were described using quartiles for continuous variables, and counts and percentages for categorical variables. Groups defined by demographic and clinical characteristics were compared on complication rates and other categorical variables using chi-square and Fisher's exact tests as appropriate, and on continuous variables using Wilcoxon rank sum tests. The incidence of pouch failure over time was analyzed using the Kaplan–Meier method. All tests were two-tailed and performed at a significance level of 0.05. SAS 9.2 software (SAS Institute, Cary, NC) was used for all analyses.

#### 1.3.1. Ethical considerations

The study was approved by the Institutional Review Board at the Cleveland Clinic Foundation, Cleveland, OH.

## 2. Results

Between November 2010 and August 2011, 74 out of 176 patients who underwent IPAA for UC at Cleveland Clinic Foundation over a 15-year period between 1982 and 1997, and who had been contacted previously for 2- and 5- year follow-up studies, were able to be successfully re-contacted by mailed letter and subsequently telephone call. These patients were contacted for the purpose of providing self-reported follow-up information regarding the long term outcomes of the IPAA procedure. Demographic information, including gender, age at UC diagnosis age at time of IPAA, as well as age at time of survey and years since surgery can be found in Table 1. In addition, type of anastomosis,

number of stages of procedure, as well as type of pouch can be found in Table 1.

The most common indication for surgery was failure of medical management, occurring in 59 patients (80%) for whom this information was available. Failure of medical management was defined as persistent symptoms unresponsive to medical therapy, including bleeding requiring frequent transfusions, unacceptable side effects of medication, or poor nutritional status. Other indications for surgery included toxic megacolon (10%), dysplasia (1.5%) and colonic perforation (1.5%).

At the time of our follow-up interview, 8% of patients reported currently being on biologics, 3% were on immunomodulators, 9% were on 5-ASA products, 19% were on antibiotics, and 4% were on steroids. Some patients were on one or more IBD medications at the same time. Forty-four percent of patients reported that they were on medications to control stooling frequency. The drugs most commonly used were loperamide and diphenoxylate.

Sixty percent of the cohort reported having children, and 25% of the total cohort reported that they had problems conceiving. The group of 25% who reported having problems conceiving was comprised of women only; no men reported having had any problems conceiving. Of the women, 21 out of 35 (60%) reported having children. Of these 21 women, 10 (48%) reported having some difficulty during their pregnancy or delivery. No standard definition for “problems conceiving” was used. Answers were recorded as provided by the patients based on their understanding of the term. Problems conceiving were not associated with age at diagnosis or surgery, type of procedure, or type of pouch (data not shown).

Table 2 lists the specific pouch complications reported. The most frequent complication reported was pouchitis (defined as intermittent episodes of pouchitis or chronic pouchitis), occurring in 33 patients (45%). Fistulae development (enterocutaneous, perianal, or both) was the second most common complication, occurring in 22 patients (30%). Obstruction and strictures were reported in 20% and 16% of patients, respectively. Seventeen patients (23%) reported that they had no complications associated with the pouch. Sixty-five of the 74 (88%) reported undergoing endoscopic exam of the pouch and biopsy. There were no reports of dysplasia. Of those who had undergone endoscopic exam of the pouch, only a portion had routine endoscopic exams while others had random or infrequent endoscopic exams of the pouch. There were no significant complication differences between genders with the exception of females reporting higher rates of obstruction ( $p = 0.02$ ) (Table 2). Further analysis did not reveal any statistical significance

**Table 1**  
Demographics of IPAA cohort.

| Factor  | Total (N = 74) |
|---|----------------|
| Gender, No. (%)                                     |                |
| • Female  | 35 (47)        |
| • Male  | 39 (53)        |
| Current age, median (min, max)                      | 38 (21,50)     |
| Age at IBD diagnosis, median (min, max)             | 15 (3,21)      |
| Age at time of surgery, median (min, max)           | 18 (3,29)      |
| Type of anastomosis*, No. (%)                       |                |
| • Handsewn  | 21 (30)        |
| • Stapled   | 48 (70)        |
| Type of procedure*, no. (%)                         |                |
| • 1 stage   | 2 (3)          |
| • 2 stage   | 39 (56)        |
| • 3 stage   | 29 (41)        |
| Type of pouch*, no. (%)                             |                |
| • J pouch   | 48 (67)        |
| • S pouch   | 24 (33)        |
| Indications:  |                |
| Failure of medical therapy, no. (%)                 | 59 (80)        |
| Toxic megacolon, no. (%)                            | 7 (10)         |
| Perforation, no. (%)                                | 1 (1)          |
| Dysplasia, no. (%)                                  | 1 (1)          |
| None recorded, no. (%)                              | 6 (8)          |
| Years of follow-up since surgery, median (min, max) | 20 (15,28)     |

\* Data not available for all subjects. Missing values: Type of anastomosis = 5, type of procedure = 4, type of pouch = 2.

**Table 2**  
Long-term complications in IPAA cohort by gender.

| Factor                                    | Total (N = 74) | Female (N = 35) | Male (N = 39) | p-value            |
|---|----------------|-----------------|---------------|--------------------|
| No. of complications experienced, no. (%) |                |                 |               | 0.038 <sup>1</sup> |
| • None                                    | 17 (23)        | 7 (20)          | 10 (26)       |                    |
| • 1                                       | 24 (32)        | 7 (20)          | 17 (44)       |                    |
| • 2                                       | 14 (19)        | 9 (26)          | 5 (13)        |                    |
| • 3                                       | 9 (12)         | 4 (11)          | 5 (13)        |                    |
| • 4                                       | 9 (12)         | 7 (20)          | 2 (5)         |                    |
| • 5                                       | 1 (1)          | 1 (3)           | 0 (0)         |                    |
| Pouch complications:                      |                |                 |               |                    |
| Stricture, no. (%)                        | 12 (16)        | 8 (23)          | 4 (10)        | 0.14 <sup>2</sup>  |
| Fistula, no. (%)                          | 22 (30)        | 13 (37)         | 9 (23)        | 0.19 <sup>2</sup>  |
| Obstruction, no. (%)                      | 15 (20)        | 11 (31)         | 4 (10)        | 0.024 <sup>2</sup> |
| Pouchitis, no. (%)                        | 33 (45)        | 13 (37)         | 20 (51)       | 0.22 <sup>2</sup>  |
| Other infection, no. (%)                  | 8 (11)         | 6 (17)          | 2 (5)         | 0.14 <sup>3</sup>  |
| Diagnosis changed to Crohn's*, no. (%)    | 20 (28)        | 13 (37)         | 7 (19)        | 0.084 <sup>2</sup> |
| Pouch taken down*, no. (%)                | 10 (14)        | 6 (17)          | 4 (11)        | 0.51 <sup>3</sup>  |

p-values: 1 = Wilcoxon Rank Sum test, 2 = Pearson's chi-square test, 3 = Fisher's Exact test.

\* Data not available for all subjects. Missing values: Has diagnosis changed to Crohn's = 2, has pouch been taken down = 1.

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