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Original Articles

Long-term outcomes of ileal pouch-anal anastomosis for pediatric chronic ulcerative colitis☆,☆☆,★

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ABSTRACT

Background: Ileal pouch-anal anastomosis (IPAA) is the surgical treatment of choice for patients with chronic ulcerative colitis (CUC). In the pediatric population, short-term outcomes of IPAA are excellent but long-term data limited. The purpose of this study is to report long-term functional and quality of life outcomes of IPAA in pediatric patients. Methods: Functional outcomes and quality of life (QoL) following IPAA in patients ≤18 years of age were prospectively assessed by survey over a 30 year period. Preoperative information, chronic pouchitis and pouch loss were retrospectively reviewed. Results: Over 30 years, 202 children with CUC underwent IPAA. Questionnaires were returned by 87% and median (range) survey follow-up was 181.5 (7.8–378.5) months. Postoperative day and night-time stool frequency did not increase over time though incontinence increased slightly. Quality of life (QoL) was generally excellent and stable over time. Crohn's disease (CD) was diagnosed in 33 (16%) patients during the follow-up period. Chronic pouchitis occurred in 22 patients and pouch failure in 13 patients. Kaplan Meier estimates of pouch survival at 20 years were 61% for patients with CD and 92% for CUC. Conclusions: Ileal pouch-anal anastomosis has long-term durability as a cure for pediatric chronic ulcerative colitis, with most patients reporting stable bowel function and QoL. Chronic pouchitis and pouch failure affect a minority of patients and require further study.

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Chronic ulcerative colitis (CUC) is a highly morbid disease of the colon and rectal mucosa that impacts pediatric and adult patients. While most adults have disease limited to the rectum and left colon, children are more likely to have pancolonic disease [1]. Medical therapy ranges from aminosalicylates for mild disease to corticosteroids for disease flares to anti-TNFα antibody therapy for severe disease. Nearly one third of patients, however, will ultimately require surgical treatment for CUC and children are more likely to require surgery than adults [2,3]. Surgical indications include medication intolerance, medically refractory disease, neoplasia, and fulminant disease. Initially described in 1978 by Parks and Nicholls, ileal pouch-anal anastomosis (IPAA) is the procedure of choice for patients with CUC, including children [4–6].

Long-term outcomes following IPAA in adults with CUC are satisfactory; however, data on long-term outcomes in children are limited [7,8]. Short-term outcomes are excellent, with quality of life following IPAA comparable to age-matched healthy children [9,10]. A recent study of children who underwent IPAA with mean follow-up of 9 years demonstrated that outcomes remain satisfactory in the intermediate term, with most of the 339 children with CUC reporting that they would undergo IPAA again [11]. Since children undergoing IPAA are expected to live with their pouch for many years and failure rates of IPAA increase with time, additional data on long-term pouch performance are needed [12]. This study aims to determine the long-term functional and quality of life (QoL) outcomes of IPAA for pediatric CUC.

1. Patients and methods

This study was approved by the Mayo Clinic Institutional Review Board. Children (≤18 years of age) who underwent IPAA between January 1, 1980 and December 31, 2009 were identified using a previously established, prospectively maintained colon and rectal surgery database of patients who consented to participating in the database. This database was cross-referenced with billing data at our institution to ensure that the study was comprehensive of all pediatric patients undergoing IPAA. Patients were mailed an internally standardized, previously

Abbreviations: CUC, chronic ulcerative colitis; IPAA, ileal pouch—anal anastomosis; QoL, quality of life; CD, Crohn's disease; SD, standard deviation; OR, odds ratio; PSC, primary sclerosing cholangitis.

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published questionnaire on a yearly basis to determine quality of life and functional outcomes prospectively [7]. All patients without follow-up within the last year were administered the same annual questionnaire by mail in June of 2011 following the end of the study period. Patients' medical records were reviewed to obtain demographic information, preoperative clinical information, operative technique, and postoperative clinical information.

Preoperative data obtained retrospectively from patients' medical records included age, gender, duration of CUC prior to IPAA, preoperative stool frequency, corticosteroid administration within 4 weeks of IPAA, use of anti-TNFα biologic agents, and preoperative albumin and hemoglobin levels. Anti- TNFα biologic agents have been approved for CUC since August, 2005. Patients underwent IPAA as part of a one, two, or three stage procedure. A two stage IPAA was defined as a total proctocolectomy with IPAA and diverting ileostomy, followed by ileostomy takedown at a later date. A three stage procedure was defined as total or subtotal colectomy with ileostomy followed by completion proctectomy, IPAA at a second operation, and closure of ileostomy at a third operation. IPAA was completed by rectal mucosectomy with hand sewn pouch to anal anastomosis or stapled anastomosis which preserved the anal transition zone.

Postoperative outcomes studied were functional information, change in diagnosis to Crohn's disease (CD), chronic pouchitis, and pouch loss. Functional information, including postoperative stool frequency and incontinence, and QoL were evaluated prospectively by the questionnaire. The questionnaire asked patients to enumerate their daily stool frequency. Patients were determined to have increased day and night-time stools if they exceeded the overall cohort's mean stool frequency plus two standard deviations. The questionnaire asked patients to report the frequency of incontinence; frequent incontinence was defined as ≥1 episode per week and could include day- or night-time leakage. Additionally, use of pads and anti-motility agents was collected. Quality of life was measured in the questionnaire by asking patients to report if specific QoL measures were improved, unaffected, mildly restricted, or severely restricted following IPAA. These measures were: ability to work, family life, sexual life, social life, athletics, and travel. Patients had the option to choose "not applicable" for each QoL measure. For patients who returned multiple questionnaires, the results of the most recent questionnaire were reported. Thus, if a patient responded with "not applicable" to a QoL measure in one questionnaire then responded differently on a later questionnaire, the most recent response was used.

Ideally, results from individual patients would have been compared over time. Because of variable return of questionnaires, however, we opted to report patients' most recent questionnaire results. Responses to questionnaires about postoperative stool frequency, incontinence, use of pads or medications, and QoL were compared between 5, 10, 15, 20, and 30 year postoperative time points. Responses to questionnaires returned within 1 year of the time point were included (5 year data included results of patients whose most recent questionnaires were returned from 4 to 6 years postoperatively and 10 year data included results of questionnaires returned from 9–11 years postoperatively). Since the individual patients that returned questionnaires at each time point were not static, only descriptive analysis of these outcomes were performed.

The outcomes of postoperative diagnosis of CD, development of chronic pouchitis, and pouch loss were obtained by retrospective chart review. Crohn's disease was determined using pouch biopsy results or a documented change in diagnosis from CUC to CD in patients' medical record. Chronic pouchitis was defined as >4 weeks of combination antibiotics or rotating antibiotic therapy [13,19], or immunosuppression with oral corticosteroids or anti-TNF alpha agents. Pouch loss was defined as permanent ileostomy with or without pouch excision.

1.1. Statistics

Descriptive statistics were reported using mean (SD) or median (range) for continuous variables and frequency (percent) for categorical variables. Since duration of follow-up was variable for individual patients, development of chronic pouchitis and pouch loss were assessed using Kaplan Meier estimates rather than single percentages. Multivariable analysis was used to control for differences in operative technique including number of stages of IPAA and stapled vs. hand-sewn anastomosis. Logistic regression models were used to evaluate the impact of these factors on functional outcomes and QoL. Cox proportional hazards regression was used to determine the impact of operative approach on time-dependent outcomes of chronic pouchitis and pouch failure. Logistic regression was used to assess the association of functional outcomes (postoperative day and night-time stool frequency) with QoL. When postoperative stool frequency was a significant predictor of restricted QoL, results were presented as odds ratio (OR) per stool, meaning that each additional stool conferred the stated odds of the quality of life outcome. Demographic analyses included all patients; however, patients that did not return questionnaires were excluded from analysis of outcomes identified by questionnaire. The alpha-level was set at ≤0.05 for statistical significance.

2. Results

We identified 202 children who underwent IPAA at our institution for CUC from 1980 through 2009. Of the 175 (87%) patients who returned at least one questionnaire, 102 patients returned >1 questionnaire, 55 returned ≥10 questionnaires, and 13 returned ≥20 questionnaires (Table 1). Median (range) length of questionnaire follow-up was 182 (8–379) months. The cohort's demographic information and preoperative clinical characteristics are in Table 2. Most patients underwent a two stage procedure (78.7%) with a hand sewn IPAA (77.6%) and J pouch configuration (95.1%). Primary sclerosing cholangitis (PSC) was diagnosed in 12 patients (5.9%) and CD was diagnosed in 33 (16.3%) patients during the follow-up period.

2.1. Stool frequency and incontinence

Changes in postoperative stool frequency over time were small and clinically insignificant. From 5 to 30 years postoperatively, mean daytime stool frequency increased from 5.5 to 6.8 stools and mean night-time stool frequency from 1.4 to 1.7 stools (Table 3). At each 5 year interval, 4% or fewer patients experienced increased stool frequency (greater than the mean plus two standard deviations, or 11 stools per day and 4 stools per night). No patients reported increased

Table 1
Number of postoperative questionnaires returned by patients ($N = 202$).

Number of surveys returned	Patients (n)	%[a]
0	27	13.4
1	73	36.1
2	8	4.0
3	9	4.5
4	5	2.5
5	5	2.5
6	3	1.5
7	3	1.5
8	6	3.0
9	8	4.0
10	8	4.0
11	5	2.5
12	5	2.5
13	7	3.5
14	1	0.5
15	6	3.0
16	4	2.0
17	1	0.5
18	2	0.9
19	3	1.5
≥20	13	6.4

[a] Sum to 100.3% owing to rounding.

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