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Clinical Outcomes after Ileal Pouch-Anal Anastomosis in Pediatric Patients

Christina C. Huang, BS^a, Frederick J Rescorla, MD^{a,b}, Matthew P. Landman, MD, MPH^{a,b}

^aIndiana University School of Medicine, 340 W 10th St #6200, Indianapolis, IN, USA

^bDivision of Pediatric Surgery, Riley Hospital for Children, Department of Surgery, Indiana University, RI 2500, Indianapolis, IN 46202, USA

Abstract

Background—Ileal pouch-anal anastomosis (IPAA) is the standard surgical reconstruction for patients with familial adenomatous polyposis (FAP) and ulcerative colitis (UC) who undergo total proctocolectomy (TPC). Although patients receive the same reconstruction, their postoperative complications can differ. We hypothesize that indication for TPC and other preoperative clinical factors are associated with differences in postoperative outcomes following IPAA.

Methods—A retrospective cohort of pediatric patients who underwent proctocolectomy with IPAA from 1996–2016 was identified. Preoperative, operative, and postoperative clinical variables were collected. Univariate analyses were performed to evaluate for relevant postoperative clinical differences.

Results—Seventy-nine patients, 17 with FAP and 62 with UC, were identified. FAP patients spent a mean of 1125 ± 1011 days between initial diagnosis and first surgery compared to 585 ± 706 days by UC patients ($p=0.038$). FAP patients took a mean of 57 ± 38 days to complete TPC with IPAA compared to UC patients at 177 ± 121 days ($p<0.001$). FAP and UC patients did not differ in mean number of bowel movements at their 6-month postoperative visit [4.7 ± 2.1 vs. 5.6 ± 1.9 , respectively ($p=0.134$)]. FAP patients were less likely to experience pouchitis ($p=0.009$), pouch failure ($p<0.001$), and psychiatric symptoms ($p=0.019$) but more likely to experience bowel obstruction ($p=0.002$).

Conclusion—IPAA is a safe, restorative treatment for FAP and UC patients after TPC. Based on diagnosis and preoperative course, there are differences in morbidity in IPAA patients. Clinical data such as these will allow surgeons to help families anticipate their child's pre- and post-operative course and to maximize successful postoperative outcomes.

Corresponding Author: Matthew P. Landman, MD, MPH: landman@iu.edu, Riley Hospital for Children, RI 2500, Indianapolis, IN 46202, USA.

Author Contact Information: Christina C. Huang, BS: chrhuang@indiana.edu, Indiana University School of Medicine, 340 W 10th St #6200, Indianapolis, IN, USA, Frederick J. Rescorla, MD: frescorl@iupui.edu, Riley Hospital for Children, RI 2500, Indianapolis, IN 46202, USA, Matthew P. Landman, MD, MPH: landman@iu.edu, Riley Hospital for Children, RI 2500, Indianapolis, IN 46202, USA

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CCH, FJR, and MPL developed the research question and contributed to the final manuscript. CCH and MPL abstracted data, analyzed data, and drafted the manuscript.

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Introduction

Total proctocolectomy (TPC) with ileal pouch-anal anastomosis (IPAA) is the standard restorative surgical treatment for patients with familial adenomatous polyposis (FAP) and inflammatory bowel disease (IBD), namely ulcerative colitis (UC).¹ Those diagnosed with FAP inevitably progress to colorectal cancer by age 50 without medical or surgical intervention.²³ TPC with IPAA has been shown to effectively prevent development of colorectal cancer in FAP patients while maintaining fecal continence.³ TPC with IPAA is also used to manage UC.⁴ Of patients ultimately diagnosed with UC, 25% present during childhood or adolescence.⁴ Patients who are diagnosed with FAP and UC during childhood often experience more severe phenotypes and require surgical intervention.³⁵

Management of gastrointestinal symptoms can be taxing on pediatric patients and can cause psychosocial difficulties due to frequent absences from school.⁵ While TPC with IPAA can significantly reduce cancer risk in FAP patients and debilitating symptoms in UC patients, postoperative outcomes are not consistent amongst patient cases. Restorative proctocolectomy with IPAA can be performed in either one-, two-, or three-stages (colectomy, proctectomy, then ileostomy takedown).³ The number of stages performed is often determined by preoperative factors such as steroid use and nutritional status.

The literature surrounding IPAA varies in its description of postoperative complication rates, and the association between diagnosis and postoperative outcomes are still being established. One retrospective study noted that, when compared to FAP patients, UC patients often experienced more postoperative complications such as pouchitis.⁶ This study, as with others in these patient populations, generally include small numbers. Therefore, we sought to review all TPC with IPAA patients at Riley Hospital for Children to evaluate salient preoperative factors that might predict postoperative clinical outcome. We hypothesize that indication for TPC with IPAA, amongst other preoperative clinical factors, are associated with relevant differences in surgical timing and postoperative outcomes.

Methods

Subjects

Patients who underwent TPC with IPAA at Riley Hospital for Children from 1996–2016 were identified using a search of the electronic medical record for the following CPT codes: 45119 Proctectomy, combined abdominoperineal pull-through procedure (eg, colo-anal anastomosis), with creation of colonic reservoir (eg, J-pouch), with diverting enterostomy when performed, 45113 Proctectomy, partial, with rectal mucosectomy, ileoanal anastomosis, creation of ileal reservoir (S or J), with or without loop ileostomy, 45397 Laparoscopy, surgical; proctectomy, combined abdominoperineal pull-through procedure (eg, colo-anal anastomosis), with creation of colonic reservoir (eg, J-pouch), with diverting enterostomy, when performed, 44158 Colectomy, total, abdominal, with proctectomy; with ileoanal anastomosis, creation of ileal reservoir (S or J), includes loop ileostomy, and rectal mucosectomy, when performed, and 44211 Laparoscopy, surgical; colectomy, total, abdominal, with proctectomy, with ileoanal anastomosis, creation of ileal reservoir (S or J), with loop ileostomy, includes rectal mucosectomy, when performed. Patients who underwent

the above procedures were also identified through manual review of Riley Hospital for Children weekly Morbidity and Mortality records.

Definitions of Outcome Variables—Pouch leak: evidence of leakage due to anastomotic incompetence either clinically (purulent intra-abdominal fluid found on diagnostic laparoscopy) or by imaging (contrast enema or CT scan demonstrating leak).

Superficial surgical site infection: any postoperative wound that required opening for drainage and/or oral antibiotic treatment for incisional erythema.

Deep abscess: was defined as an intra-abdominal abscess that required operative or percutaneous drainage.

Pouch failure: any pouch requiring operative revision or resection.

Pouchitis: clinical symptoms of pouch inflammation requiring oral antibiotic treatment or evidence of pouch inflammation found on diagnostic endoscopy done in response to symptoms

Bowel Obstruction: clinical symptoms and imaging signs of bowel obstruction requiring enteric decompression and/or operation for bowel obstruction.

Incontinence: soiling due to fecal incontinence uncontrolled by commonly used anti-diarrheals such as loperamide or diphenoxylate.

Bloody bowel movement: patient reported blood while wiping after bowel movement.

Postoperative anastomotic stricture at IPAA: patient with clinical symptoms of stricture that required formal dilation in the operating room.

Psychiatric symptoms: depression, anxiety, social aversion, suicidality, and stress noted by surgeons in their postoperative follow-up.

Relevant preoperative, operative, and postoperative clinical variables were collected. Institutional Review Board approval was obtained and an waiver of consent was obtained.

Statistical Analysis

Continuous variables were described as mean values with standard deviations or median with interquartile ranges. Univariate analyses with Chi-square, Fisher's exact test, or Wilcoxon-Rank Sum tests were performed to evaluate for relevant clinical differences in outcome. Statistical significance was set at 0.05. All statistical analyses were carried out with Stata version 14 (College Station, TX).

Results

A total of 80 patients were identified from the search. Seventeen patients were diagnosed with FAP, and 62 were diagnosed with UC. Patients diagnosed with indeterminate colitis (n=1) were excluded. Seventy-nine pediatric patients who underwent IPAA were analyzed.

The demographics and important preoperative clinic factors are listed in Table 1. Table 2 shows postoperative outcomes for both FAP and UC patients. Preoperatively, UC patients had more frequent abdominal pain ($p<0.001$), more preoperative hospitalizations ($p=0.002$), and lower albumin ($p<0.001$) than FAP patients. FAP and UC patients did not differ in their mean preoperative hemoglobin ($p=0.136$).

Table 2 shows time from initial diagnosis, either FAP or UC, to first surgery (stage 1 of TPC with IPAA). FAP patients spent a mean of 1125 (± 1011) days between initial diagnosis and first surgery compared to 585 (± 706) days by UC patients ($p=0.038$). Furthermore, FAP patients took significantly less time from first surgery to IPAA completion (completion of all planned procedures) with a mean of 57 (± 38) days compared to UC patients at 177 (± 121) days ($p<0.001$). FAP patients were more likely to undergo one- or two-stage procedures compared to UC patients, who were more likely to undergo two- or three-stage procedures ($p<0.001$). Within the UC patient population, there was no association between use of biologic therapy and number of stages ($p=0.302$). UC patients were more likely to have open proctectomy (33%) whereas FAP patients were more likely to have laparoscopic proctectomy (86%) ($p=0.046$). FAP and UC patients did not differ in their anastomosis type (hand-sewn vs. stapled) ($p=0.804$) nor their incidence of intraoperative complications ($p=0.465$).

At their first postoperative visit, FAP and UC patients did not differ in mean number of bowel movements [4.3 ± 2.3 vs. 6.1 ± 3.9 , respectively ($p=0.083$)]. In addition, FAP and UC patients also did not differ in mean number of bowel movements at their 6-month postoperative visit [4.7 ± 2.1 vs. 5.6 ± 1.9 , respectively ($p=0.134$)]. Postoperatively, FAP patients are significantly less likely to experience pouchitis ($p=0.009$), pouch failure ($p<0.001$), and psychiatric symptoms ($p=0.019$), but more likely to experience bowel obstruction ($p=0.002$) (Table 2). Bowel obstruction in FAP patients were due to ileostomy torsion ($n=2$), adhesions ($n=2$) and unknown etiology ($n=3$). Bowel obstructions in UC patients were due to adhesions ($n=6$) and stoma stenosis ($n=1$). Furthermore, UC patients were more likely to be prescribed anti-motility agents (88.9%) than FAP patients (66.7%) ($p=0.017$). However, there was no significant difference in daily anti-motility agent use between UC patients (74.1% used daily, 11.1% used as needed, and 14.8% did not use) and FAP patients (41.7% use daily, 16.7% used as needed, and 41.7% did not use) ($p=0.069$). Within the UC group, preoperative steroid use was associated with superficial surgical infection ($p=0.049$) but not associated with pouchitis ($p=0.872$). Furthermore, we found no association between use of laparoscopy and bowel obstruction ($p=0.39$). Analysis performed on each disease group revealed no association between use of laparoscopy and bowel obstruction within FAP patients ($p=0.92$) and UC patients ($p=0.96$). The median length of follow up for the entire cohort was 2.9 (IQR 1.1–5.2) years.

Discussion

IPAA is the standard restorative procedure after TPC for both FAP and UC. We hypothesized that, while the surgical technique is similar in both patient populations, significant postoperative differences would be noted based on the indication for surgery. In this retrospective cohort study, we identified several differences and additionally quantified

the differences in timing of surgery in both of these groups. Ultimately, we believe that, in understanding how these populations differ, surgeons will be well positioned to provide anticipatory guidance to patients and their families.

The most common complication following IPAA in patients with UC in our study was pouchitis (49%). This rate is consistent with other studies in this area. Lillehei and colleagues found UC patients had a 47% rate of at least one episode after IPAA.⁶ They note, as do we, very low rates of pouchitis after IPAA for FAP.⁶ Interestingly, Diederer et al noted 22% of their pediatric population with pouchitis postoperatively. A minority of these patients (5%) had chronic pouchitis.⁷ The differences in pouchitis rates are most likely related to the definition of pouchitis utilized in each study. We utilized a more clinically-oriented definition by including those episodes which required antibiotic therapy. Other possible pouchitis definitions may focus on more objective endoscopic and/or pathologic criteria. As other authors have noted, the rate of pouchitis following IPAA for UC is most likely related to the generalized pro-inflammatory nature of UC.

FAP patients were also less likely to experience pouch failure, psychiatric symptoms, and daily anti-motility agent use postoperatively compared to UC patients. Although psychiatric symptom was listed as a postoperative outcome because of more detailed postoperative note taking in our study, it is likely that psychiatric symptoms were present preoperatively, possibly related to stress related to managing flare-ups in UC patients. Our results agreed with Ozdemir et al, which demonstrated less frequent sepsis (FAP vs UC, 10.3% vs 10.9%), pouchitis (17.6% vs 35.7%), and pouch failure (5.9% vs 8.5%) in FAP vs UC patients.¹ In accordance with our data, Lovegrove et al also found that FAP patients were less likely to experience pouchitis (5.5%) compared to UC patients (30.1%).⁸

In this study, UC patients had a more complicated preoperative course than FAP patients and were more likely to experience abdominal pain, be hospitalized, and have lower albumin levels. These data are expected given the symptomatic course of UC which may include severe bleeding, diarrhea, obstruction, perforation, and toxic megacolon even with biologic intervention.¹ In comparison, FAP patients sometimes experience rectal bleeding from colonic adenomas, however, many patients are asymptomatic until progression to colorectal cancer in adulthood.²³ Because most of the literature focuses on postoperative outcomes, preoperative data on IPAA is sparse. Families can expect more preoperative events if their child has UC as opposed to FAP. Furthermore, preoperative use of steroids without tapering was associated with postoperative superficial surgical infection and suggests that patients should be tapered off steroids before surgery if able.

Analysis of patients' timeline to surgery revealed that FAP patients spent more time from diagnosis to first surgery (1125 ± 1011 days compared to 585 ± 706 days) but less time from first surgery to procedure completion when compared to UC patients (57 ± 38 days to 177 ± 121 days). Because of their long asymptomatic period, FAP patients expectedly undergo a longer observational period before their first surgery. In comparison, UC patients may experience complications such as refractory colitis or fulminant colitis and require urgent or even emergent colectomy.^{9,10} Furthermore, the emergent nature of some colectomies as well as preoperative deconditioning and malnutrition in some UC patients

necessitates two- or three- stage procedures thus lengthens the time from first surgery to IPAA completion. The outcome measures, “time from diagnosis to first surgery” and “time from first surgery to IPAA completion,” are important tools that can help visualize and anticipate an IPAA patient’s clinical course.

Analysis of postoperative outcomes demonstrate that FAP and UC patients did not differ in their mean number of bowel movements at neither their first postoperative visit (4.3 vs 6.1, respectively) nor their six-month postoperative visit (4.7 vs 5.6, respectively). Similarly, Ozdemir et al found no difference in mean daily bowel movements between FAP (5.4±4.4) and UC (5.3±2.6) patients.¹ However, Fazio et al demonstrated a difference in mean daily bowel movements at 1-year post-operation (FAP 6 and UC 7), but no difference in mean daily bowel movements at 5 years or 10 years post-operation.¹¹ In addition, we demonstrate that UC patients (88.9%) were more likely to be prescribed anti-motility agents compared to FAP patients (66.7%) but that there is no significant difference in anti-motility agent use between UC and FAP patients. The data offer a snapshot of anti-motility use 1-month post-operation whereas Michelassi et al demonstrate a decrease in anti-motility agent use over time for UC patients.¹² Our data suggest that many physicians may anticipate worse incontinence in UC patients compared to FAP patients when there may be no significant difference in bowel function after IPAA. Bowel function is a common concern for IPAA patients, and it is important for families and patients to be counseled on the expected number of postoperative daily bowel movements.

Interestingly, the data show that FAP patients were more likely to experience bowel obstruction. This differs from the literature where Ozdemir et al demonstrates no significance in obstruction rates between FAP (29.4%) and UC (16.6%) patients.¹ The FAP patients in this study experienced obstruction due to torsion of the ileostomy as well as from adhesions; comparatively bowel obstructions in UC patients were universally secondary to adhesions. However, long term risk of small bowel obstruction is a well-described phenomenon. In a cross-sectional study by MacLean and colleagues, 44% of their postoperative small bowel obstruction patients occurred within 30 days of their operation and 5.2% required laparotomy.¹³ Many of the postoperative bowel obstructions in our series were also in the immediate postoperative period. We do not have an explanation for the increased frequency of obstruction in FAP patients; however, many of these patients were performed in only 1 or 2 stages as opposed to the 3-stage procedure in UC. Whether this results in less intra-abdominal adhesions and an increased predilection for internal hernia or torsion around the ileostomy site is not known.

This study has several limitations. It is a retrospective study of a complex patient cohort and therefore suffers from being limited by the data present in the patient’s chart. Many of these patients, given their age, transition to providers at other institutions potentially creates missing data. Specifically, our data may underestimate postoperative episodes of pouchitis, pouch failure and small bowel obstruction. Paper charts were accessed for patients receiving procedures prior to 2008. Compared to electronic records, paper charts were more limited in their documentation and length of follow up. Furthermore, although several of our patients stay within the health system, allowing us to access their records several years after their operation, postoperative complications could be missing due to patients moving out of state

or accessing hospitals outside of the IU health system. Given the sample size, and relatively small outcome variables, we were unable to perform multivariate analyses which may have been beneficial to clarify the strength of association between outcome variables and indication for IPAA.

TPC with IPAA is a safe operative approach for patients with UC and FAP. However, it can be associated with significant morbidity, which can significantly alter a patient's, and their family's life, postoperatively. Given increased knowledge of the postoperative course after complex, many times multi-step, surgical interventions, patients and their families can better organize the logistics of care and minimize the potential anxiety that can come with major surgery. This study further contributes to the understanding of the postoperative course after TPC in light of both the indication for the procedure as well as other tangible preoperative clinical factors. These data allow for clinicians and surgeons to provide improved anticipatory guidance to this patient population.

Conclusion

In summary, this study demonstrates significant differences between preoperative, operative, and postoperative outcomes between UC and FAP patients. Measures such as “time from diagnosis to first surgery” and “time from first surgery to IPAA completion” are important data that allow surgeons to help families anticipate their child's pre- and post-operative course and to maximize successful clinical outcomes.

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Table 1

IPAA Patient Demographic and Preoperative Data

Demographics	FAP	UC	p Value
Male	11 (65%)	31 (50%)	
Female	6 (35%)	31 (50%)	
<u>Race</u>			
White	13 (76%)	48 (77%)	
African American	2 (12%)	12 (19%)	
Asian	2 (12%)	2 (3%)	
Age *	14.5 (12.2–15.8)	14.9 (12.3–16.4)	<i>NS</i>
Preoperative Complications			
# Experiencing Abdominal Pain	3 (23%)	39 (80%)	<i><0.001</i>
Average Hospitalizations One Year Preop	0	0.75 ± 0.12	<i>0.002</i>
Average Albumin	4.4 ± 0.1	3.20 ± 0.13	<i><0.001</i>
Average Hemoglobin	12.57 ± 0.45	10.92 ± 0.61	<i>0.136</i>

Values are provided in n (%) and mean (± standard deviation).

* Median with interquartile range.

Table 2**Surgical Timeline and Postoperative Complications**

Timeline	FAP	UC	p Value
Average Days from Diagnosis to Surgery	1125±1011(n=12)	585±706 (n=43)	0.038
Average Days from Stage I to IPAA completion	57±38 (n=14)	177±21 (n=53)	<0.001
Postoperative Complications			
Pouch Leak	0	2 (4%)	0.498
Superficial Surgical Infection	1 (9%)	6 (12%)	0.814
Deep Abscess	1 (8%)	3 (6%)	0.728
Pouch Failure	0	2 (4%)	<0.001
Pouchitis	1 (8%)	27 (49%)	0.009
Bowel Obstruction	7 (54%)	7 (13%)	0.002
Incontinence	0	10 (19%)	0.106
Anastomotic stricture	1 (5.9%)	8 (12.9%)	0.481
Bloody Bowel Movement	3 (25%)	13 (24%)	0.946
Psychiatric Symptoms	0	9 (17%)	0.019

Postoperative Values are provided in n (%).