

Ileal Pouch–Anal Anastomosis—A Surgical Perspective

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Despite aggressive medical management, approximately 50% of patients with inflammatory bowel disease will require surgery during the clinical course of their disease. For ulcerative colitis, surgery offers the chance for cure, with ileal pouch anal anastomosis as the procedure of choice in elective cases. In this article, we review the development, indications, and recent advances in ileal pouch anal anastomosis surgery and the remaining controversies regarding surgical technique and staging of surgery in the modern era of biological medical therapy.

Semin Colon Rectal Surg 23:110-116 © 2012 Elsevier Inc. All rights reserved.

Despite recent advances in medical therapy, surgery remains a prominent and valuable alternative in the treatment algorithm for inflammatory bowel disease (IBD), with approximately 50% of patients requiring surgery during the course of their disease.^{1,2} While surgery offers only palliation from symptoms in the case of Crohn's disease (CD), it offers the chance for cure in patients with ulcerative colitis (UC) by elimination of the chronically inflamed colon and rectum, thus reducing the risk of recurrent flares and in the long run of neoplastic degeneration. Up to the early 1980's, the only surgical treatment for UC was a total proctocolectomy with permanent ileostomy. Although this still remains a viable option in a selected group of patients, restorative procedures such as a proctocolectomy with ileal pouch–anal anastomosis (IPAA) has become the procedure of choice since its first description by Parks et al³ in 1980. Restorative procedures combine the goal of removing the colon and rectum with the additional benefit of maintaining gastrointestinal continuity, preserving the anal sphincter complex and allowing for continence through the normal route of defecation. Patients report an improved quality of life after IPAA, with a recent report demonstrating substantial functional durability in 92% of patients at 20 years.⁴⁻⁶ The surgical aspects of restorative UC surgery have changed dramatically during the past 30 years, secondary to advances and innovations in surgical technology, with the aim of improving functional outcome and decreasing morbidity. This article will provide an overview of the results of IPAA surgery along with recent ad-

vances in the field, and highlight remaining controversies with regard to surgical technique and timing of surgery.

Indications for Surgery

UC is a chronic inflammatory disease characterized by diffuse mucosal inflammation that always involves the rectum and progresses in a continuous manner to involve the colon. Clinical presentation is that of a relapsing clinical course marked by exacerbation and remission with the cardinal symptom of bloody diarrhea. Patients may also present with abdominal pain, increased frequency of bowel movements, urgency, or tenesmus. However, a subset of patients may present with more severe symptoms and signs of systemic illness, including fever, weight loss, and malnutrition. Regardless of presentation, medical therapy is the mainstay in management successfully inducing remission in a majority of patients with or without the inclusion of immunomodulators and/or biological agents, such as cyclosporine (CsA) and infliximab (IFX), respectively. However, despite their demonstrated short-term benefit, controversy remains over the ability of either IFX or CsA to reduce the long-term colectomy rate: approximately 30% of patients require surgery after 10 years of disease,⁷ with failure of medical management remaining the number one indication for surgery.

Indications for operative intervention can be categorized as either emergent or elective, each requiring a completely different and patient-specific surgical approach. The most common emergent indication is acute fulminant colitis, with or without progression to potentially life-threatening complications, such as toxic megacolon, intractable bleeding, or perforation. In the absence of peritonitis, which may be difficult to appreciate in immunocompromised patients, the

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treatment is hospital admission with fluid resuscitation, bowel rest, and aggressive medical therapy, which includes intravenous steroids with or without CsA or IFX as rescue therapy for steroid refractory disease.^{8–11} Patients with persistent or progressive symptoms despite this regimen should undergo operative intervention with a subtotal colectomy and end ileostomy as the procedure of choice. Although restorative proctocolectomy and IPAA in the acute setting has been reported,¹² the general consensus is that proctectomy and/or IPAA are not recommended in these patients because of concerns over increased complication rates, including impaired healing of both the perineum and the pouch anastomosis. Indeed, in a recent article by Heuschen et al,¹³ looking at postoperative complications after IPAA reconstruction for UC, they showed an increased incidence of pouch-related complications in patients with severe preoperative disease, on high-dose steroids (>40 mg/d), or with significant anemia—all typically present in patients hospitalized with acute fulminant colitis. After removal of the acutely inflamed colon, patients can often be weaned off steroids with an associated improvement in their nutritional status and anemia. At this point, the patient may undergo a staged completion proctectomy with IPAA, and it is our practice both in the severely acute phase as well as in patients receiving IFX to wait a minimum of 3–6 months to perform this second stage of the operation.¹⁴

Elective indications for surgery include medical intractability, the development of dysplasia or carcinoma, and disabling extracolonic manifestations of UC. For patients undergoing elective surgery, IPAA is the procedure of choice. Failure of medical management, generally defined as an inability to wean steroids or immunosuppressive therapy for 12 months without recurrence of symptoms, remains the most common indication for elective surgical intervention. Development of colorectal cancer is not an uncommon problem in chronic UC, with an overall prevalence of 3.7% and an incidence approaching 1% per year for each year after 10 years of disease.^{15,16} In patients diagnosed with metastatic carcinoma, IPAA is not indicated, and often an abdominal colectomy with an ileorectal anastomosis is the palliative procedure of choice, unless the cancer is located in the rectum. Several reports have shown the safety and feasibility of IPAA in patients with curable colon cancer, and IPAA has been shown to be safe with a favorable oncological prognosis and functional outcome.^{17–19} However, in the setting of locally advanced rectal cancer, where neoadjuvant therapy is indicated, IPAA should be avoided because of the long-term sequelae of pelvic radiation on the anal sphincter, resulting in worse functional outcomes.²⁰ Lastly, surgical intervention for disabling extracolonic manifestations of disease is rare, with postoperative improvement seen only in disease-associated arthritis and skin lesions, specifically pyoderma gangrenosum.

Contraindications to IPAA include fecal incontinence and poor anal sphincter function. Although a full comprehensive preoperative manometric evaluation is rarely performed, a detailed history, paying particular attention to previous vaginal deliveries, pregnancies, and previous anorectal operations, together with a thorough anorectal examination must

be obtained to avoid poor postoperative function. As expected, higher preoperative resting anal sphincter pressures >40 mm Hg have been associated with improved postoperative pouch function and quality of life; however, the opposite does not hold true.²¹ Similarly, advanced age, which was previously thought to be a relative contraindication to IPAA because of the higher incidence of anal sphincter dysfunction with increasing age, especially in multiparous women, has been reevaluated. Recent data suggest that with appropriate patient selection, IPAA can be successfully performed with acceptable functional outcomes even in septuagenarians.^{22,23}

Ileal Pouch–Anal Anastomosis

The first description of the IPAA by Sir Alan Parks was that of an “S” pouch, characterized by an ileal reservoir attached directly to the anus with a long efferent limb created to avoid incontinence. In reality, the long efferent limb often created issues with pouch emptying. Since then, other configurations have emerged in an effort to decrease complications and improve outcomes, such as the quadruple-loop W pouch and lateral isoperistaltic H pouch. The most common pouch performed today is the double-loop J pouch owing to ease of creation and good functional results.²⁴ In a large prospective study conducted at our institution evaluating 391 consecutive patients who underwent IPAA J pouch for either UC or indeterminate colitis, we found a 96% overall patient self-reported “excellent” or “good” satisfaction rate at long-term 15-year follow-up.²⁵ Specifically, after an initial postoperative adjustment period, patients averaged 6 bowel movements every 24 hours, and this frequency remained constant over time with a concurrent decrease in antidiarrheal drug use. Approximately 73% of patients demonstrated continence at 5 years with most episodes of leakage occurring at night. Interestingly, our data further demonstrate that patients who established continence early after surgery maintained continence at 5 years unless jeopardized by pouchitis. This is consistent with other published reports, documenting an association of pouchitis with worse long-term functional outcomes.²⁶

Pouchitis is the most common complication after IPAA surgery, with a cumulative incidence of approximately 40% of patients at 10 years. Clinical presentation typically includes abdominal/pelvic pain, fever, an increase in stool frequency, and a preoperative history of smoking and/or steroid therapy. Moreover, patients with primary sclerosing cholangitis are also known to have an increased frequency of pouchitis after IPAA.²⁷ As mentioned earlier, even after appropriate treatment and resolution of symptoms, an episode of pouchitis portends a worse long-term functional outcome demonstrated by an increase in incontinence.²⁶ Other complications after IPAA surgery include small bowel obstruction, anastomotic stricture, sexual dysfunction or infertility, as well as anastomotic leak and pelvic sepsis. Pelvic sepsis is the most severe complication after IPAA surgery, with data confirming worse functional outcomes and increased pouch failure rates.^{28,29} In response, some surgeons routinely perform a diverting and protecting loop ileostomy at the time of

IPAA. Although this does not prevent an anastomotic leak, proponents argue that it decreases the rate of pelvic sepsis and associated pouch failure. However, others argue that creation of an ileostomy is a source of extra morbidity secondary to an increased rate of associated small bowel obstruction as well as the need for a subsequent hospitalization to perform an ileostomy takedown, and quote published reports demonstrating similar complication rates and functional outcomes in those without diverting ileostomy versus those managed with a diverting ileostomy.^{30,31} In a recent meta-analysis comparing IPAA with and without diverting loop ileostomy, there was no difference in functional outcomes; however, there were noted differences in perioperative complication rates.³² In the non-stoma group, there was a slightly increased rate of stricture, which is in contrast to the data from our institution where the increased stricture rate in the stoma group was attributed to the tension on the anastomosis that prompted the surgeon to perform a diverting stoma.²⁵ Also, there was a statistically significant increase in the incidence of an anastomotic leak and subsequent pouch-related sepsis in the group that did not receive a diverting ileostomy.³² It is tempting to postulate that these data advocate for the use of a diverting ileostomy at the time of IPAA. Nonetheless, this topic remains controversial, and in our practice, construction of a diverting loop ileostomy is performed at the surgeon's discretion based on intraoperative and patient-related conditions, including blood loss, anastomotic tension, nutritional status, obesity, and preoperative steroid or IFX therapy. Regardless of diversion, anastomotic leak and pelvic sepsis often occur early after surgery. Late presentation may be atypical and present as a smoldering abscess or fistula; however, any evidence of late pelvic inflammation and/or sepsis should also raise the suspicion of CD.

Controversies

Laparoscopic Versus Open IPAA

Since its introduction to the surgical community, laparoscopic surgery has gained widespread popularity. The advantages of laparoscopy, such as faster recovery, less pain, less use of pain medications, less adhesion formation, and better cosmesis, are appealing to the young IBD patients. Despite that, the adoption of laparoscopy has been slow,³³ secondary to the concern over the complexity of these operations, both in CD and in UC. Specifically, laparoscopic surgery in UC requires advanced surgical skills because of the need to access multiple quadrants of the abdomen during resection and involves handling and resection of friable tissue with foreshortened mesentery. The early reports, in fact, quoted conversion rates for laparoscopic colectomy up to 20%, even in experienced laparoscopic hands.³⁴

Although data on long-term functional results of laparoscopic IPAA are lacking, the short-term benefits are clear. The majority of studies comparing laparoscopic IPAA with conventional open surgery demonstrate an improvement in patient-reported body image and cosmesis, as well as a decrease

in narcotic usage, faster return of bowel function, and decreased hospital stay.³⁵ Even though there is often an increased operative time with laparoscopic surgery and, in some instances, an increase in cost, studies do not demonstrate any significant difference in perioperative complications.³⁶⁻³⁸ However, these studies are limited in that they are small, often single-institution experiences with short follow-up. In a recent Cochrane analysis comparing laparoscopic versus open IPAA surgery for either UC or familial adenomatous polyposis, there was no difference in perioperative mortality or postoperative complications between the 2 groups.³⁹ However, with the exception of improved cosmesis, when the authors examined factors involved in postoperative recovery, that is, narcotic use, return of bowel function, length of operation, no significant differences were found, thus leaving the issue still unresolved. To further evaluate the role for laparoscopic IPAA, we identified 179 patients at our institution who underwent either laparoscopic or open IPAA for UC and monitored them in a prospective manner for short- and long-term outcomes for >5 years.⁴⁰ Our data demonstrate excellent functional results with laparoscopic IPAA. There was no identifiable difference in postoperative complications between the laparoscopic and open groups; however, consistent with previous reports, there was a trend toward decreased narcotic usage in the laparoscopic group. Interestingly, compared with previously mentioned studies, there was no difference in operative time or hospital stay. Although this was only an observational study and not a randomized trial, our data support the findings of previous articles demonstrating a trend toward benefit in the use of laparoscopy in patients with UC undergoing IPAA, and as a result, laparoscopy is currently the technique of choice in our practice.

There is no absolute contraindication to laparoscopic IPAA other than underlying cardiopulmonary disease that precludes the safe use of pneumoperitoneum. That said, laparoscopic IPAA can be technically challenging in obese patients who have a thick and foreshortened mesentery that does not reach the pelvic floor. Although there are surgical "tricks" that can be used to lengthen the bowel, such as selective scoring of the mesentery with or without vessel ligation, obesity is becoming more prevalent in our Western society and, thus, a more prominent problem in the daily practice of IBD surgeons. In a retrospective analysis performed at the Cleveland Clinic comparing the complication rate and functional outcomes of IPAA in obese (body mass index >30) and nonobese patients (body mass index <30), there was no difference in long-term outcomes.⁴¹ Furthermore, the incidence of perioperative pouchitis, pelvic sepsis, or pouch failure in both groups was similar, despite the slightly increased incidence of anastomotic leak in the obese population. Therefore, most surgeons conclude that laparoscopic IPAA is still an accepted procedure in the obese population with minimally increased morbidity, albeit with increased technical difficulty. In recent years, it has been our practice in the super-obese population to perform a hand-assisted total abdominal colectomy, leaving a Hartman pouch and end ileostomy in the upper quadrants where, typically, the abdominal

wall is not as thick. The second stage of the procedure is then postponed until significant weight loss is achieved.

Handsewn Versus Stapled IPAA

The original description of the IPAA involved leaving a long rectal sleeve with complete stripping of the rectal mucosa proximal to the dentate line both transabdominally and transanally, with the goal of eradicating disease by complete mucosectomy, and was followed by a subsequent handsewn anal anastomosis with the pouch ‘pulled through’ the long rectal sleeve.⁴² This was indeed a time-consuming procedure associated with significant blood loss. Also, it made it impossible to survey any residual island of rectal mucosa that would be covered by the pouch. Subsequently, similar to surgical advances in laparoscopy, the introduction of a stapled anastomosis significantly simplified the construction of the IPAA, and with better understanding of anorectal physiology and the changes associated with this procedure, the long rectal sleeve became obsolete. More stapled IPAA have been performed since the 1990’s, and the long-term fate of the residual rectal mucosa/anal transition zone (ATZ) has created controversy and led to concerns over residual disease, chronic inflammation, and risk of cancer.⁴³

The exact length and location of the ATZ has been extensively studied with conflicting results based on the methodology used.^{44,45} Fenger first described the ATZ using an Alcian dye technique. This technique stains the ATZ macroscopically with the columnar epithelium looking dark blue, the squamous epithelium does not stain, and the ATZ looks pale blue.⁴⁴ With this technique, the margins of the ATZ spanned from 6 mm below to 20 mm above the dentate line.⁴⁴ Further studies by Thompson-Fawcett et al⁴⁵ demonstrated that the Alcian dye technique overestimates the length of the ATZ when compared with computer mapping of the histological results.⁴⁵ Using computer histological mapping, the median span was 0.45 cm versus 0.73 cm by the Alcian dye technique. Significantly, columnar epithelium has been mapped lower in the anorectal canal and will be retained when a stapled technique is used, with potential long-term consequence after restorative proctocolectomy IPAA.⁴³

When compared with mucosectomy and handsewn anastomosis, a double-stapled IPAA is performed above the dentate line, thus preserving the ATZ. Preservation of the ATZ by stapled anastomosis is appealing with data from several large studies demonstrating improved functional outcomes when compared with handsewn IPAA.⁴⁶⁻⁴⁸ Specifically, stapled IPAA is associated with improved continence and higher resting anal pressures, likely because of less damage to the anal sphincter complex during the construction of the anastomosis, as well as decreased rates of pelvic sepsis and pouch failure. Data from our institution support these observations with maintenance of continence in long-term follow-up plus an additional trend toward a shorter hospital stay if stapled.²⁵ However, the functional benefit seen with stapled IPAA anastomosis must be balanced by the concern for recurrent disease or development of dysplasia in the remaining rectal epithelium.

Retained rectal mucosa after a stapled anastomosis for IPAA is potentially affected by recurrent or persistent inflammation, malignancy, or both. In a recent prospective study, the incidence of postoperative inflammation after IPAA was significant with only approximately 10% of patients demonstrating histologically normal biopsies of the ATZ.⁴⁹ Of the remaining patients included in the study, approximately 5% of patients developed acute inflammation, whereas approximately 85% were found to have chronic inflammation. Interestingly, inflammation was not associated with worse functional outcome or quality of life. The progression from inflammation to dysplasia and carcinoma is known, with the incidence of dysplasia after stapled IPAA estimated at 4.5%.⁵⁰ Conversely, in a published report by Branco et al,⁵¹ development of dysplasia after IPAA was independent of the type of anastomosis (stapled vs handsewn). Still, because of the risk of developing dysplasia or cancer in the retained rectal mucosa after stapled IPAA, it is our practice to follow a conservative selective approach in patient selection. Specifically, patients who are identified preoperatively as having either dysplasia or cancer are not offered stapled anastomosis, regardless of the location of preoperative disease, and instead, a complete mucosectomy with handsewn anastomosis is preferred.⁴³ Irrespective of the protocol and/or policy followed, colectomy with IPAA does not completely abolish the risk for long-term neoplastic degeneration of the ATZ and/or pouch, with cumulative incidences at 5, 10, 15, 20, and 25 years of 0.9%, 1.3%, 1.9%, 4.2%, and 5.1%, respectively,⁵² and a pooled cumulative prevalence of 1.13%.⁵³ Long-term postoperative surveillance of the ATZ and the pouch is, therefore, warranted.

IPAA and Biologic Therapy

As mentioned previously, pelvic sepsis is not an infrequent complication of IPAA surgery with a reported incidence of as high as 10%,⁵⁴ regardless of the anastomotic approach or the presence of a protective ileostomy. Often caused by a leak from the pouch itself, pelvic sepsis can be difficult to treat and is associated with a subsequent increase of pouch failure.^{28,29} Since the introduction of biological therapy for UC patients with steroid refractory disease in 2005,¹¹ recent studies have demonstrated contradictory results regarding an increased risk of postoperative complications after IPAA (Table 1). The 2 larger studies available to date showed that at least in the short term, patients undergoing IPAA, treated preoperatively with IFX, had an increase in postoperative pouch-related and infectious complications. This did not seem to differ with respect to the timing of last dose of IFX (either < or >2 months before surgery).^{55,57} In particular, patients treated preoperatively with IFX experienced increased rates of wound infections and anastomotic leak; however, the increased rate of anastomotic leak was not associated with an increase in pelvic abscesses likely owing to the use of a diverting loop ileostomy. On the contrary, Ferrante et al⁵⁸ reported that preoperative treatment with steroids and IPAA without diverting ileostomy, as opposed to preoperative IFX and IPAA with diversion, was an independent predictor of

Table 1 Effect of Preoperative IFX Therapy on Postoperative Complications After Surgery for UC

Author	Year (Study duration)	Study Design	% IFX patients (# IFX/non-IFX)	Follow-up	Two-Stage Operation (%)*	Complications (%) IFX/non-IFX	P Value or OR†
Selvasekar et al ⁵⁵	2007 (2002-2005)	Retrospective	15.6% (47/254)	30 Days	IFX (89%) Non-IFX (83%)	Infectious‡: 28%/10%	OR = 3.5 (1.6-7.5)
Schluender et al ⁵⁶	2007 (2000-05)	Retrospective	11% (17/134)	30 Days	IFX (88%) Non-IFX (69%)	IFX specific: 17%/n/a Overall: 33%/31% IFX + CsA vs IFX–CsA: 80%/29%	n/a P > 0.05 P = 0.04
Mor et al ⁵⁷	2008 (2000-06)	Retrospective Case matched	50% (46/46)	Early: <30 days Late: >30 days	IFX (100%) Non-IFX (100%)	Early overall: 35%/15% Pelvic sepsis: 22%/2% Late overall: 52%/37%	P = 0.027 P = 0.016 P = 0.23
Ferrante et al ⁵⁸	2009 (1998-2008)	Retrospective	15.6% (22/119)	30 Days	IFX (32%) Non-IFX (42%)	Pouchitis: 39.1%/15.2% Infectious: 9%/24%	P = 0.037 P = 0.161
Yang et al ⁵⁹	2010	Meta-analysis (5 articles)	706, total patients	Short term	Variable	Pouch specific§: 0%/15% Overall Infectious Noninfectious	P = 0.076 1.80 (1.12-2.87) 2.24 (0.63-7.95) 0.85 (0.50-1.45)

#, number; CI, confidence interval; IFX, infliximab; IPAA, ileal pouch anal anastomosis; OR, odds ratio; n/a, not applicable; CsA, cyclosporine; UC, ulcerative colitis.

*2-stage: IPAA and diverting ileostomy as first stage followed by ileostomy takedown.

†Parentheses are 95% CI.

‡Infectious defined by authors includes anastomotic leak, pelvic sepsis, and wound infection.

§Pouch-specific complications defined by authors include anastomotic leak and pelvic abscesses.

postoperative infectious complications. Others have reported an increase in postoperative complications with the combination of IFX and CsA but not IFX alone; however, in these studies, perioperative complications have not been reported in patients treated with CsA alone.^{56,60} To help resolve this conflicting data, a meta-analysis published by Yang et al⁵⁹ confirmed an increase in overall short-term postoperative complications in patients who underwent IPAA for UC and received preoperative IFX. However, this same association was not seen in relation to short-term postoperative infectious complications in the subgroup analysis limited by statistical power.

Similar to patients who present with acute fulminant colitis, the patients requiring biological therapy for steroid refractory disease and have not responded, are often malnourished and expectedly immunosuppressed at surgical presentation. As mentioned previously, staging in the setting of fulminant colitis allows for patients to be weaned off medication, restore nutritional status, and optimize overall medical status in an effort to decrease post-IPAA complications, and this paradigm applies even more to this compromised group of patients. Because of the concern over higher postoperative complication rates after IPAA in patients who previously received IFX, this staged surgical approach has been advocated. In a recent retrospective review, 118 consecutive patients who underwent IPAA for UC for elective reasons were divided in a nonrandomized manner into 2 groups: 2-stage IPAA (1st = proctectomy with IPAA and diverting ileostomy, 2nd = ileostomy takedown) and 3-stage procedure (1st = subtotal colectomy with end ileostomy, 2nd = proctectomy with IPAA and diverting ileostomy, 3rd = ileostomy takedown).¹⁴ Group selection was done at the surgeon's discretion. Of the patients in the 3-stage group, 96% were on steroids and 43% were on biological therapy compared with 67% and 16%, respectively, in the 2-stage group. Additionally, the 3-stage group had more complex and acute disease. However, despite the increased preoperative risk profile and concurrent drug regimen, the incidence of intraabdominal abscess formation and septic complications was significantly decreased in the 3-stage group. These data suggest that a more conservative, 3-stage approach portends better outcome in patients with severe disease on aggressive medical therapy.

Although further studies are required to confirm the relationship between biological therapy and postoperative infectious complications in UC, it is our practice to perform a 3-stage procedure in patients receiving aggressive medical therapy, including biologics, before surgery in an effort to minimize postoperative complications potentially exacerbated or caused by biological therapy.

Conclusions

The field of IPAA surgery for UC continues to advance in conjunction with progress in medical management. However, several controversies remain to be solved, with the issue of postoperative complications associated with biological therapy having significant clinical decision-making implica-

tions. IBD surgeons will be confronted with these clinical questions, as more and more biologics will be introduced in medical protocols.

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