Is There a Role for Ileal Pouch Anal Anastomosis in Crohn's Disease?

Nicole E. Lopez, MD¹ Karen Zaghyian, MD¹ Phillip Fleshner, MD¹

¹Division of Colon and Rectal Surgery, Cedars-Sinai Medical Center, Los Angeles, California

Address for correspondence Nicole E. Lopez, MD, Division of Colon and Rectal Surgery, Cedars-Sinai Medical Center, 8787 Beverly Blvd, Suite 101, Los Angeles, CA 90048 (e-mail: naoli.lopez@gmail.com).

Clin Colon Rectal Surg 2019;32:280–290.

Abstract

Keywords

- Crohn's disease
- indeterminate colitis
- ileal pouch anal anastomosis
- de novo Crohn's disease
- ileorectal anastomosis

Traditionally, surgical interventions for colonic Crohn's disease (CD) have been limited to total abdominal colectomy and ileorectal anastomosis, or total proctocolectomy with end ileostomy if there is rectal involvement. However, improved understandings of the biology of CD, as well as the development of biologic therapies, have enabled more limited resections. Here, we review the indications for, and limitations of, specific procedures aiming to preserve intestinal continuity in colonic CD.

The standard surgical treatment for medically refractory Crohn's disease (CD) of the colon is total abdominal colectomy with ileorectal anastomosis (IRA), or, in cases of concurrent rectal disease, total proctocolectomy with end ileostomy.

Though maintaining intestinal continuity is a priority, patients with CD of the rectum have not typically been considered to be candidates for restorative procedures such as ileal pouch anal anastomosis (IPAA). Instead, it has generally been accepted that patients with CD who have undergone IPAA experience unacceptably high rates of Crohn's-related pouch complications, including fistulas, strictures, and abscesses. In these circumstances, medical and surgical therapies can be used to salvage the pouch. However, ultimately some patients may require either pouch excision or permanent diversion, commonly referred to as pouch failure.^{1–9}

In the early 1990s, reports of inferior pouch outcomes among patients with CD emerged, recounting pouch failure rates of 30 to 45%.^{1–4} Since that time, it has commonly been accepted that IPAA should be avoided in patients with CD. Literature investigating pouch outcomes in patients with CD is retrospective and, given the tendency to avoid IPAA in known CD, is primarily composed of patients with a preoperative diagnosis of UC who underwent IPAA and present in a delayed fashion with symptoms and/or complications typical of CD^{1,2,4–9} (►Table 1). These patients, identified as having

developed *de novo Crohn's*, have increased pouch-related complications, as might be expected with persistence/recurrence of clinically symptomatic disease. As such, patients with *de novo Crohn's* should be recognized as clinically distinct from patients with *primary CD*. This distinction calls to attention the importance of understanding the evolution of disease and the importance of timing of diagnosis relative to IPAA on implications for pouch-related outcomes. Specifically, in relation to IPAA, CD can be diagnosed (1) preoperatively (*intentional IPAA*); (2) immediately after IPAA, based on pathologic examination of tissue specimens (*incidental IPAA*); or (3) months to years after the primary surgical intervention, when symptoms occur (*delayed presentation after IPAA*). The first two time points represent *primary CD*, whereas the final time point would be identified as *de novo CD*.

These principles are critical to understanding the nuances in the surgical treatment of colorectal CD and will be the subject of the following paragraphs.

What Is the Role of Restorative Pouch Procedures in Primary Crohn's Disease?

Studies examining selected subsets of patients with primary CD—those with no ileal or perianal disease and those with CD found incidentally on pathologic specimen at the time of TAC/

Table 1 Outcomes of IPAA in patients with Crohn's disease

Year	Author/Hospital	Design	Study years	Patients	Risk of CD-related complications	Pouch failure in CD	Follow-up
1991	Hyman et al ¹ Cleveland Clinic	Retrospective review	1983–1989	IBD undergoing IPAA, <i>n</i> = 362 Preoperative diagnosis of UC, later diagnosed with CD, <i>n</i> = 25 CD incidental, <i>n</i> = 16 CD delayed, <i>n</i> = 9 (2.4%)	36%	32% CD incidental: 6% CD delayed: 89%	38.1 mo
1991	Deutsch et al ² University of Toronto	Retrospective review	1982–1989	UC undergoing IPAA, <i>n</i> = 272 CD, <i>n</i> = 9 CD incidental, <i>n</i> = 5 CD delayed, <i>n</i> = 4 (1.5%)	66%	44% CD incidental: 40% CD delayed: 50%	NR
1993	Grobler et al ³ Queen Elizabeth Medical Centre, University of Birmingham	Retrospective review	1983–1990	IBD undergoing IPAA, <i>n</i> = 81 CD, <i>n</i> = 10 CD incidental, <i>n</i> = 9 CD delayed, <i>n</i> = 1 (1.2%)	60%	30%	48 mo (15–86)
1995	Fazio et al ³⁰ Cleveland Clinic	Retrospective review	1983–1993	IBD undergoing IPAA, <i>n</i> = 933 CD incidental, <i>n</i> = 67 (7.2%)	NR	CD incidental: 26%	35 mo
1996	Sagar et al ⁴ Mayo Clinic	Retrospective review	1981–1995	IBD undergoing IPAA, <i>n</i> = 1,509 CD, <i>n</i> = 37 (2.5%) CD incidental, <i>n</i> = 6 CD delayed, <i>n</i> = 31 (2%)	38%	73%	10 y (3–14)
1996	Panis et al ¹⁰ Hospital Lariboisiere	Case-control	1985–1992	UC, <i>n</i> = 71 CD intentional, <i>n</i> = 32	29%	2 of 21 (10%) at 5 y	5 y
2000	Peyrègne et al ⁵ Centre Hospitalier Lyon-Sud, France	Retrospective review	1985–1997	UC undergoing IPAA, <i>n</i> = 54 CD, <i>n</i> = 7 (13%) CD incidental, <i>n</i> = 3 CD delayed, <i>n</i> = 4 (7.4%)	71%	43% CD incidental: 0% CD delayed: 60%	7 y
2001	Mylonakis et al ⁶ Queen Elizabeth Hospital, UK	Retrospective review	NR	UC undergoing IPAA developed CD, <i>n</i> = 23 CD incidental, <i>n</i> = 12 CD delayed, <i>n</i> = 11	NR	52% CD incidental, 33% CD delayed, 64%	10.2 y
2001	Regimbeau et al ¹¹ Hospital Lariboisiere	Retrospective review	1985–1998	CD, <i>n</i> = 41 CD intentional, <i>n</i> = 26 CD incidental or delayed, <i>n</i> = 15	27%	7%	113 ± 37 mo
2003	de Oca et al ⁵⁷ Ciudad Sanitaria y Universitaria de Bellvitge, Hospital del Llobregat, Barcelona, Spain	Retrospective review	1985–2000	IBD undergoing IPAA, <i>n</i> = 112 CD incidental, <i>n</i> = 12 (11%)	42%	17%	76 mo (12–72)

(Continued)

Table 1 (Continued)

Year	Author/Hospital	Design	Study years	Patients	Risk of CD-related complications	Pouch failure in CD	Follow-up
2004	Braveman et al ⁵⁸ Lahey Clinic	Retrospective review	1980–2002	IBD undergoing IPAA, <i>n</i> = 726 CD, <i>n</i> = 32 (4.4%) CD incidental, <i>n</i> = 19 (2.6%) CD delayed, <i>n</i> = 13 (1.8%)	93%	28%	153 (13–253) mo
2004	Hartley et al ⁷ Cleveland Clinic	Retrospective review	1983–1999	IBD undergoing IPAA, <i>n</i> = 1,883 CD, <i>n</i> = 60 (3.2%) CD incidental, <i>n</i> = 47 CD delayed, <i>n</i> = 13	Symptomatic, <i>n</i> = 21 (35%) Median time to symptom onset 46 m (5–108)	CD overall, <i>n</i> = 7 (12%) CD symptomatic, 7 of 21 (33%)	46 (4–158) mo
2005	Brown et al ⁸ Mount Sinai Hospital	Retrospective review	1982–2001	IBD undergoing IPAA, <i>n</i> = 1,192 CD, incidental or delayed, <i>n</i> = 36	64%	56%	83 ± 65 mo
2005	Tekkis et al ⁹ St Mark's St. Mary's Middlesex	Retrospective review	1978–2003	IBD undergoing IPAA, <i>n</i> = 1,652 CD incidental or IC favoring CD; <i>n</i> = 26 (1.6%)	Pelvic sepsis/leak, stricture, fistula, hemorrhage, and pouchitis <i>p</i> = NS	58%	4.7 y
2008	Melton et al ¹² Cleveland Clinic	Retrospective review	1983–2007	IBD undergoing IPAA, <i>n</i> = 2,834 CD, <i>n</i> = 204 (7.2%) CD intentional, <i>n</i> = 20 (10%) CD incidental; <i>n</i> = 97 (47%) CD delayed, <i>n</i> = 87 (43%)		61 (30%) CD intentional or incidental 15% CD delayed 51%	7.4 y
2010	Shen et al ¹³	Case-Control	2002–2008	CD intentional, <i>n</i> = 11 UC, <i>n</i> = 44	64%	1 (9.1%)	5 y
2013	Le et al ¹⁴	Retrospective review	1994–2010	CD intentional, <i>n</i> = 17 UC, <i>n</i> = 261	24%	1 (6%)	60 (range, 17–159) mo

Abbreviations: BD, inflammatory bowel disease; CD, Crohn's disease; IPAA, ileal pouch anal anastomosis; UC, ulcerative colitis.

IPAA for UC—indicate that these patients may have acceptable outcomes after IPAA.^{10–14} In a case–control study published in 1996, Panis et al were the first to specifically address pouch outcomes in patients with primary CD in absence of ileal and perianal disease. They found a pouch failure rate (10%) was not significantly different from that in patients with UC. Functional outcomes were also similar.¹⁰ Several groups have confirmed these findings.^{1,5,7,11–14} However, when considering IPAA in patients with primary CD, it is important to note that in comparison to patients with UC, patients with a preoperative diagnosis of CD may be at significantly increased risk of developing CD of the pouch (15.9 vs. 63.5%, $p = 0.003$ reported by Shen et al and 11 vs. 41%, $p = 0.002$ described by Le et al).^{13,14} As such, CD-related pouch complications are relatively common (29–64%).^{7,11–14} Even so, pouch failure is infrequent (6–15%)^{7,11–14} (► **Table 1**).

Based on these data, carefully selected patients with CD who require rectal resection and have no preoperative suggestion of small bowel or perianal disease appear to have reasonable outcomes with IPAA. Therefore, in patients who are motivated to maintain intestinal continuity with clear understandings of the increased risk of recurrent disease, increased pouch-associated morbidity, the risk of short bowel in the event of pouch failure requiring excision, and an understanding that creation of a second pouch after excision is not practical may be considered for IPAA.

What Is the Role of Restorative Pouch Procedures in Indeterminate Colitis?

In contrast to CD, where IPAA should be considered only in highly selected individuals, IPAA is the standard operative treatment in UC. As described, accurate diagnosis has important implications for outcomes after IPAA; therefore, it is imperative to be as precise as possible in differentiating CD from UC. This distinction is generally made using a combination of clinical, radiologic, endoscopic, pathologic, and occasionally serologic or genetic findings. However, 10 to 20% of patients have either overlapping features of disease or insufficient evidence to conclusively characterize disease.^{15,16}

Various terminologies (*uncertain colitis*, *idiopathic chronic colitis*, *IBD-NOS* and *IBD-unknown etiology*, *IBD-unclassified* and *indeterminate colitis [IC]*) have been used to describe disease in these circumstances, leading to confusion surrounding the matter.¹⁷ In 2005, the Montreal Working Party aimed to clarify the subject, recommending that the term “indeterminate colitis” “*be reserved only for those cases where colectomy has been performed and pathologists are unable to make a definitive diagnosis of either Crohn's disease or ulcerative colitis after full examination.*” The term “inflammatory bowel disease, type unclassified” (IBDU) should be used when, after ruling out infectious causes for colitis, “*there is evidence on clinical and endoscopic grounds for chronic inflammatory bowel disease affecting the colon, without small bowel involvement, and no definitive histological or other evidence to favor either Crohn's disease or ulcerative colitis.*”¹⁸ Given the heterogenous nature of studies with respect to timing of diagnoses, this will be simplified for the purposes

of this discussion and the term “indeterminate colitis” will be used to collectively refer to IBDU and IC.

Refining the terminology is an important first step to improving our understanding of IC; however, it is fundamentally a placeholder term, used until more certain diagnosis is possible. Therefore, diagnostic ambiguity is inherent. This is exacerbated by a lack of consensus among pathologists regarding the pathologic findings and clinical implications associated with IC.¹⁵ The difficulty in obtaining pathologic certainty can be confounded, especially in the setting of fulminant colitis, where pathologic specimens from patients with UC commonly display findings consistent with CD.¹⁶ While most patients presenting with fulminant colitis have underlying UC, Crohn's-like pathologic findings such as rectal sparing and transmural inflammation are common in this setting.^{15,19} Finally, to some extent, the capacity to make accurate pathologic diagnoses is dependent on the experience of the pathologist. This is best illustrated by a study where general pathologist interpretations of histology were compared with those of a gastrointestinal (GI) pathologist. The GI pathologist's diagnoses differed from the diagnoses by a general pathologist in 45% of surgical specimens and 54% of biopsy specimens, highlighting the role of experience in diagnostic accuracy.¹⁵

Variability in nomenclature, shifting of disease course, depth of individual pathologist experience, and a lack of clear pathologic definition of IC result in an inherent heterogeneity in studies investigating pouch outcomes in patients with IC. Inconsistencies resulting from these limitations make interpreting the data difficult. While some studies have suggested poorer pouch outcomes among patients with IC in comparison to those with UC,^{20–24} more recent reports have indicated outcomes similar to those seen in UC.^{8,25–29} In particular, these studies show that IC does not appear to have a significant effect on pouch failure rates.^{8,26,27,29} Similarly, many studies reveal comparable functional outcome.^{22,24,26,27,29} Still, some argue that patients with IC may be at increased risk of developing pouch-related complications,^{8,27,29} perhaps related to an increased risk of developing CD of the pouch in this population.^{23,24,27}

Intuitively, many would agree with the assertion made by McIntyre et al that patients with IC who do not develop CD of the pouch have more similar outcomes to patients with UC.²² It therefore becomes pertinent to ascertain whether patients with IC have an increased risk of developing CD in comparison to those with UC. Several studies have revealed an increased incidence of evolution to CD among patients with IC in comparison to those with UC.^{23,24,27,29} However, others show no difference in rates of developing CD^{26,28} (► **Table 2**).

In a unique study investigating the likelihood of developing CD based on either preoperative clinical diagnosis or postoperative pathologic diagnosis of IC, our group showed no difference in development of CD, regardless of timing of diagnosis, despite a significant number of changed diagnoses based on postoperative pathology. However, in comparison to other studies on the subject, this group found a higher rate of IC (29%), based on both preoperative and postoperative criteria.²⁸ This higher rate of IC may indicate that the population includes patients who might otherwise be

Table 2 Outcomes of IPAA in patients with indeterminate Colitis

Year	Author/ Hospital	Design	Study years	Patients	Risk of complications	Pouch failure	Follow-up	Diagnosis changed to Crohn's
1989	Pezim et al ²⁵ Mayo Clinic	Retrospective review	1981–1986	Postoperative pathologic diagnosis UC, n = 489 IC, n = 25 (4.8%)	Risk of reoperation UC, n = 71 (14%) IC, n = 5 (20%) p = NS	UC, n = 17 (4%) IC, n = 2 (8%) p = NS	38 ± 18 mo	NR
1991	Koltun et al ²⁰ Lahey	Retrospective review	1980–1989	Postoperative pathologic diagnosis UC, n = 235 IC, n = 18 (7%) CD, n = 6 FAP, n = 29	UC, 8 of 235 (3.4%) IC, 9 of 18 (50%) CD	UC, 0.4% IC, 28%	40 mo (range, 6–109 mo)	UC and IC, incidental and delayed, n = 6 (2%)
1994	Atkinson et al ²¹ UBC	Retrospective review	1984–1992	Postoperative pathologic diagnosis UC, n = 158 IC, n = 16 (10%)	Fistulas (1 vs. 25%) and pelvic infections (1 vs. 25%) were more common in IC	UC, n = 8 (5%) IC, n = 3 (19%) p < 0.05	NR	NR
1995	McIntyre et al ²² Mayo Clinic	Retrospective review	1981–1992	Postoperative pathologic diagnosis UC, n = 1,232 IC, n = 71 (5.4%)	Obstruction, pelvic sepsis or pouchitis p = NS	UC: 8% IC: 19% p = 0.03	60 mo	UC, 0% IC, 11.3%
1997	Marcello et al ²³ Lahey	Retrospective review	1980–1994	Preoperative diagnosis UC, n = 499 IC, n = 42 (8%) CD, n = 2 Postoperative pathologic diagnosis UC, n = 479 IC, n = 40 (7%) CD, n = 11	Perineal complications UC: 23% IC: 44% CD: 63% p = 0.005	UC, 2% IC, 12% CD, 37% p = 0.013	NR	UC, 3% IC, 13% p = 0.006
2000	Yu et al ²⁴ Mayo Clinic	Retrospective review	1981–1995	Postoperative pathologic diagnosis UC, n = 1,437 IC, n = 82 (5%)	Any complication (48 vs. 63%; p = 0.04), pelvic sepsis (7 vs. 17%; p ≤ 0.001) and pouch fistula (9 vs. 9%; p < 0.001) were more common in IC	UC, n = 122 (11%) IC, n = 19, (27%) p < 0.001	UC, 83 (range, 1–167) mo IC, 83 (range, 1–193) mo	UC, 2% IC, 15% p < 0.001
2002	Dayton et al ²⁶ University of Utah	Retrospective review	1982–2001	Postoperative pathologic diagnosis UC, n = 565 IC, n = 79 (12%)	No differences in abscess, leak, fistula, stricture, bowel obstruction; p = NS	UC, n = 7 (1.2%) IC, n = 2 (2.5%) p = NS	78.5 mo	UC, n = 4 (0.7%) IC, n = 1 (1.3%) p = NS

Table 2 (Continued)

Year	Author/ Hospital	Design	Study years	Patients	Risk of complications	Pouch failure	Follow-up	Diagnosis changed to Crohn's
2002	Delaney et al ²⁷ Cleveland Clinic	Retrospective review	1983–1999	Postoperative pathologic diagnosis UC, n = 1,399 IC, n = 115 (7%)	Pelvic abscess (8.7 vs. 2.2%; $p < 0.01$) and perianal fistula (7.0 vs. 1.7%; $p < 0.05$) were more common in IC	UC: 3.5% IC: 3.4% $p = NS$	UC, 5.5 ± 3.4 y IC, 3.4 ± 3.0 y	UC, 1.3% IC, 6% $p < 0.01$ Pathologically proven UC, 0.4% IC, 4.3% $p < 0.05$
2002	Rudolph et al ⁵⁹	Retrospective review	1991–1999	Postoperative pathologic diagnosis UC, n = 71 IC, n = 35 (32%) CD, n = 14	Fistulas (10 vs. 26%; $p = 0.02$) were more common in IC	UC, n = 6 (8%) IC, n = 0 (0%) CD, n = 14 (100%)	54 mo	NR
2003	Alexander et al ³⁷ Cleveland Clinic	Retrospective review	1982–1999	UC, n = 125 IC, n = 16 (11%) CD, n = 3		IC, n = 0 (0%) CD, n = 0 (0%)	7.2 (range, 2–15) y	NS
2004	Pishori et al ⁶⁰ Cleveland Clinic Florida	Retrospective review	1998–2000	Postoperative pathologic diagnosis UC, n = 285 IC, n = 13 (4.2%) CD, n = 5	UC, n = 107 (37.7%) IC, n = 4 (30.7%) CD, n = 3 (60%) $p = NS$	UC, 2.1% IC UC, n = 6 (2.1%) IC, n = 0 (0%) CD, n = 0 (0%) $p = NS$	40 mo	UC and IC, n = 0 (0%)
2005	Brown et al ⁸ Mount Sinai Hospital	Retrospective review	1982–2001	Postoperative pathologic diagnosis UC, n = 1135 CD ^a , n = 36 IC, n = 21 (1.7%)	UC, 22% CD, 64% IC, 43% $p < 0.005$	UC, n = 63 (6%) IC, n = 2 (10%) CD, n = 20 (56%) $p < 0.005$ (IC is different from CD but not UC; CD is different from UC)	UC 98 ± 4 mo IC 59 ± 62 mo CD 83 ± 65 mo	NR
2009	Murrell et al ²⁸ Cedars-Sinai	Retrospective review	1997–2007	Preoperative diagnosis UC, n = 237 IC, n = 97 (29%) Postop pathologic diagnosis UC, n = 226 IC, n = 98 (29%)	NR	NR	26 (range, 3–492) mo	Pre-op UC, n = 24 (10%) IC, n = 16 (16%) $p = NS$ Post-op UC, n = 26 (11%) IC, n = 14 (14%) $p = NS$
2017	Jackson et al ²⁹ Cleveland Clinic	Case control	1985–2014	Postoperative pathologic diagnosis UC, n = 224 IC, n = 224	Fistula (15.6 vs. 8%; $p = 0.01$) and was more common in IC	UC, 4.9% IC, 5.8% $p = NS$	UC, 115 ± 76 mo IC, 121 ± 84 mo	UC, 2.7% IC, 5.8% $p = 0.04$

Abbreviations: CD, Crohn's disease; FAP, familial adenomatous polyposis; IBD, inflammatory bowel disease; IC, indeterminate colitis; IPAA, ileal pouch anal anastomosis; N/A, not applicable; NR, not reported; UC, ulcerative colitis.

^aCD diagnoses: 1 incidental, 35 delayed.

recognized as having UC, perhaps diluting the negative effects that other authors attribute to IC.

The largest and perhaps most well-designed study, by Jackson et al in 2017, used case-matched analysis to show that while patients with IC undergoing IPAA develop CD at higher rates than their UC counterparts, their pouch outcomes including morbidity, function, and pouch failure rates are comparable.²⁹

While the evidence is somewhat conflicting with regard to whether there may be an increased incidence of CD of the pouch among patients with IC undergoing IPAA, it appears certain that patients with IC can be considered for IPAA with satisfactory outcomes that may be similar to those in UC.

What Is the Outcome of Pouches that Were Made for UC but Turned Out to Be Crohn's?

Patients undergoing IPAA for UC generally have excellent outcomes with good quality of life, and low pouch failure rates (5–10%).^{30–33} However, patients subsequently developing CD, referred to as *de novo Crohn's*, experience increased pouch-associated morbidity with associated pouch failure rates ranging from 33 to 89%.^{1,2,4–8,12}

De novo Crohn's occurs in 0.7 to 15.9% of patients after IPAA performed for UC.^{13,14,26,28,34} Differences in reported prevalence are likely related to dissimilarities in diagnostic criteria, length of follow-up, and regional practice patterns. As such, the true prevalence of CD of the pouch is unknown. The most significant risk factors for developing CD of the pouch appear to be preoperative diagnosis of CD, long duration of having the pouch, smoking, and family history of CD.^{27,34–36} Whether preoperative diagnosis of IC is associated with increased risk of *de novo Crohn's* is yet to be determined, as some studies have suggested a clear association between preoperative diagnoses of IC and the development of pouch CD, while others have shown none.^{23,24,26–28,37–40}

CD of the pouch can affect the afferent limb, the pouch, or the anal transition zone and patients present with a variety of symptoms. They may experience abdominal pain, diarrhea, increased frequency of stool, urgency, and incontinence, making it difficult to distinguish from more common causes of these symptoms such as surgical complications, cuffitis, or pouchitis.⁴¹ Yet these symptoms, in the presence of smoking, family history of CD, persistent nausea and vomiting, weight loss, anemia, and fistulas that cannot be attributed to technical problems from surgery, should prompt suspicion of CD.^{35,36,38}

CD of the pouch can lead to pouch fistulas, septic complications, and pouch failure. Like primary CD, *de novo Crohn's* can be medically managed with antibiotics, steroids, immunomodulators, and biologics, and many will likely need these therapies for life. Often, these therapies must be used in conjunction with endoscopic and surgical interventions.⁴¹

Prior to the era of biologic therapy, pouch failure rates in patients developing CD of the pouch were up to 89%.^{1–6,8,42} There are limited data regarding treatment of CD of the pouch. However, in an early study investigating the utility of anti-tumor necrosis factor therapy in the treatment of CD of the pouch, Colombel et al reported 62% complete response

after induction with 33% pouch failure after median follow-up of 21.5 months.⁴³ Similar results have been reported in more recent studies^{44–50} (–Table 3).

When biologic therapies are ineffective in symptom management, proximal diversion should be considered. Careful decision making must be made with regard to pouch resection, especially in the era of rapidly evolving biologic therapies offering a constant possibility of new effective therapies.

Ileorectal Anastomosis

By removing all colonic and perianal disease, total proctocolectomy with end ileostomy results in the lowest rates of recurrence and reoperation for colonic CD.⁵¹ However, these benefits come with an increased risk of perineal wound complications, the possibility of damage to the pelvic autonomic nerves controlling urinary continence and sexual function, and the need for a permanent ileostomy.^{52–54} Patients and surgeons alike have strong inclinations to maintain bowel continuity. As such, many have sought more conservative options.

As discussed, in select patients, with no small bowel or perianal disease, IPAA may be an option for maintaining intestinal continuity in patients with Crohn's colitis. Still, this procedure is controversial in CD secondary to a presumed increase in pouch complications. Furthermore, it requires proctectomy and its associated risks, leaving a desire for more conservative options.

Rectal preservation through subtotal colectomy (STC) with IRA offers a third option and has been associated with good outcomes among patients with extensive colonic disease but no rectal, anal, or perineal involvement. However, this approach has been criticized for its increased risk of rectal or anastomotic recurrence. Of 131 patients undergoing IRA for CD, Longo et al reported on 118 who maintained intestinal continuity after surgery. At 9.5 years, 72 (61%) maintained a functioning IRA. The mean duration of pouch function was 9.2 years. Eighty-five patients (65%) developed recurrent CD and 64 (49%) required further surgery.⁵⁵ Similarly, O'Riordan et al described a cohort of 76 patients with CD undergoing IRA with 72% maintaining functional IRA at 10 years and 28 (37%) requiring repeat operative intervention.⁵³ A meta-analysis published in 2017 supported these findings, showing significantly higher risk of recurrence (odds ratio [OR]: 3.53, 95% confidence interval [CI]: 2.45–5.10, $p < 0.0001$) and reoperation (OR: 3.52, 95% CI: 2.27–5.44, $p < 0.0001$) with IRA in comparison to TPC. However, with regard to postoperative complications, the analysis favors IRA (OR: 0.19, 95% CI: 0.09–0.38, $p < 0.0001$).⁵⁴

These data suggest that IRA is a feasible option for maintaining intestinal continuity among patients with colonic CD and relative rectal sparing as long as the patient can accept increased risks of disease recurrence and need for further operative intervention.

Is There a Role for Pouch-Rectal Anastomosis?

There may be a subset of patients with CD of the colon and upper rectum, but distal rectal sparing, in whom a resection of

Table 3 Impact of biologic therapy on pouch outcomes in *de novo* Crohn's disease

Year	Author/ Hospital	Design	Drugs	Study years	Patients	Follow-up	Response	Pouch failure
2003	Colombel et al ⁴³ Mayo	Retrospective review CD diagnosed by either prepouch ileitis or fistulizing pouch disease	IFX	1998–2002	<i>n</i> = 26 Complex perianal or pouch fistulizing disease, <i>n</i> = 14 (54%) Prepouch ileitis, <i>n</i> = 5 (19%) Both, <i>n</i> = (27%)	21.5 (range 3–44) mo	Short-term (median 13.4 wk): <i>n</i> = 26 Clinical improvement, <i>n</i> = 22 (85%) Complete response, <i>n</i> = 16 (62%) Partial response, <i>n</i> = 6 (23%) Long-term (21.5 mo): <i>n</i> = 24 Good or acceptable function <i>n</i> = 14 of 24 (67%) 11 of 14 (79%) still on infliximab	<i>n</i> = 8 of 24 (33%)
2009	Shen et al ⁴⁶	Retrospective review CD of the pouch who failed medical therapy	ADA	2007–2008	<i>n</i> = 17 Inflammatory, <i>n</i> = 10 Fibrostenotic, <i>n</i> = 2 Fistulizing, <i>n</i> = 5	4 wk and 8 wk	4 wk Clinical improvement: Partial, <i>n</i> = 6 (35%) Complete, <i>n</i> = 7 (41%) Endoscopic improvement: Partial, <i>n</i> = 4 (29%) Complete, <i>n</i> = 7 (50%) 8 wk Clinical improvement: Partial, <i>n</i> = 4 (23%) Complete, <i>n</i> = 8 (47%)	<i>n</i> = 3 (18%)
2010	Ferrante et al ⁴⁷ Belgian IBD Research Group	Retrospective review Refractory pouchitis and <i>de novo</i> CD receiving IFX	IFX	NR	<i>n</i> = 28 Pouchitis and/or pre-pouch ileitis, <i>n</i> = 25 Pouch fistula, <i>n</i> = 7 Both, <i>n</i> = 4	10 wk 20 mo	10 wk Clinical response: 88% (<i>n</i> = 16; 14 partial, 8 complete) Fistula response: 86% (<i>n</i> = 6; 3 partial, 3 complete). PDAI decreased from 9.0 (IQR 8.0–10.0) to 4.5 (IQR 3.0–7.0) points (<i>p</i> < 0.001). 20 (range, 7–36) mo Clinical response: 56% Fistula response: 43% (<i>n</i> = 3, complete) 13 patients (52%) were still on IFX	<i>n</i> = 5 (18%)
2011	Haveran et al ⁴⁸ Hershey Medical Center	Retrospective review CD like complications	Total IFX, <i>n</i> = 13 IFX only, <i>n</i> = 4 AZA/6-MP only, <i>n</i> = 8	1990–2009	Fistulizing, <i>n</i> = 21 Strictureing, <i>n</i> = 13 Severe pouchitis, <i>n</i> = 6	97 ± 11.8 mo	“Successful treatment” <i>n</i> = 7 of 13 (54%) Fistulizing 6 of 12 (50%)	<i>n</i> = 6 of 13 treated with IFX (46%; all with fistulizing disease)

(Continued)

Table 3 (Continued)

Year	Author/ Hospital	Design	Drugs	Study years	Patients	Follow-up	Response	Pouch failure
2012	Li et al ⁴⁹ Cleveland Clinic	Retrospective review CD of the pouch which failed routine medical therapy	Both IFX/ (AZA)/(6-MP), n = 9	2006–2011	n = 48 Inflammatory disease, n = 15 Fibrosenotic disease, n = 8 Fistulizing disease, n = 25	8 wk Median: 25.1 mo	Strictureing 1 of 1 (100%) Severe pouchitis None treated with IFX Clinical response, n = 34 (71%) 8 wk Partial, n = 10 (21%) Complete, n = 24 (50%) 25.1 mo Partial, n = 10 (21%) Complete, n = 16 (33%)	n = 9 (19%)
2017	Robbins et al ⁵⁰ Cedars-Sinai	Retrospective review IPAA who developed <i>de novo</i> CD	Anti-TNF: IFX, ADA, and CZP	1993–2014	n = 38	4.4 (range, 0.7–12) y	"Successful treatment" n = 28 (74%)	n = 10 (26%)

Abbreviations: ADA, adalimumab; AZA, azathioprine; CD, Crohn's disease; CZP, certolizumab pegol; IFX, infliximab; IPAA, ileal pouch anal anastomosis; NR, not reported; PDAL, perianal disease activity index; 6MP, 6-mercaptopurine.

the colon and upper rectum would result in a short rectal stump. This anatomy, when fashioned into a straight ileorectal anastomosis, would be expected to have poor functional outcomes. Therefore, in these patients, Kariv et al suggested that creating a small ileal pouch (12.3 ± 3.1 cm) with a rectal anastomosis (IPRA) might be advantageous in comparison to IPAA in that it circumvents the need for low pelvic dissections, reducing the risk of nerve damage and associated morbidities, but maintains improved functional results associated with the pouch reservoir.⁵⁶ The group reports on 23 patients who underwent IPRA for colorectal CD. They found high rates of disease recurrence (64%) and reoperation (42%), as well as increased nighttime seepage and need for pads in comparison with standard IRA. Conversely, the group described a relatively low rate of pouch failure (9%). Additionally, all patients appeared to be satisfied with their outcomes, stating they would undergo the procedure again.⁵⁶ Further literature supporting this approach is scarce to nonexistent; however, in motivated patients who have a full understanding of the risks associated with the procedure (high risk of disease recurrence and reoperation, potential pouch failure, and loss of small bowel associated with pouch failure), this may be an acceptable option for providing bowel continuity. Nevertheless, the authors cautioned that patients must be carefully selected, with minimal small bowel and rectal involvement, as well as adequate small intestinal length serving as prerequisites to consideration for IPRA.⁵⁶

Conclusion

According to surgical dogma, the standard surgical interventions for colonic CD are total abdominal colectomy and ileorectal anastomosis, or total proctocolectomy with end ileostomy if there is rectal involvement. However, improvements in understanding the chronology of disease as well as the development of biologic therapies that can reduce symptoms and perhaps slow the course of disease have increased our ability to provide more limited resections, expanding opportunities for maintaining intestinal continuity. Still, both patient selection and patient participation in decision making are imperative for optimizing outcomes.

References

- Hyman NH, Fazio VW, Tuckson WB, Lavery IC. Consequences of ileal pouch-anal anastomosis for Crohn's colitis. *Dis Colon Rectum* 1991;34(08):653–657
- Deutsch AA, McLeod RS, Cullen J, Cohen Z. Results of the pelvic-pouch procedure in patients with Crohn's disease. *Dis Colon Rectum* 1991;34(06):475–477
- Grobler SP, Hosie KB, Affie E, Thompson H, Keighley MR. Outcome of restorative proctocolectomy when the diagnosis is suggestive of Crohn's disease. *Gut* 1993;34(10):1384–1388
- Sagar PM, Dozois RR, Wolff BG. Long-term results of ileal pouch-anal anastomosis in patients with Crohn's disease. *Dis Colon Rectum* 1996;39(08):893–898
- Peyrègne V, Francois Y, Gilly FN, Descos JL, Flourie B, Vignal J. Outcome of ileal pouch after secondary diagnosis of Crohn's disease. *Int J Colorectal Dis* 2000;15(01):49–53

- 6 Mylonakis E, Allan RN, Keighley MR. How does pouch construction for a final diagnosis of Crohn's disease compare with ileoproctostomy for established Crohn's proctocolitis? *Dis Colon Rectum* 2001;44(08):1137-1142, discussion 1142-1143
- 7 Hartley JE, Fazio VW, Remzi FH, et al. Analysis of the outcome of ileal pouch-anal anastomosis in patients with Crohn's disease. *Dis Colon Rectum* 2004;47(11):1808-1815
- 8 Brown CJ, Maclean AR, Cohen Z, Macrae HM, O'Connor BI, McLeod RS. Crohn's disease and indeterminate colitis and the ileal pouch-anal anastomosis: outcomes and patterns of failure. *Dis Colon Rectum* 2005;48(08):1542-1549
- 9 Tekkis PP, Heriot AG, Smith O, Smith JJ, Windsor AC, Nicholls RJ. Long-term outcomes of restorative proctocolectomy for Crohn's disease and indeterminate colitis. *Colorectal Dis* 2005;7(03):218-223
- 10 Panis Y, Poupard B, Nemeth J, Lavergne A, Hautefeuille P, Valleur P. Ileal pouch/anal anastomosis for Crohn's disease. *Lancet* 1996;347(9005):854-857
- 11 Regimbeau JM, Panis Y, Pocard M, et al. Long-term results of ileal pouch-anal anastomosis for colorectal Crohn's disease. *Dis Colon Rectum* 2001;44(06):769-778
- 12 Melton GB, Fazio VW, Kiran RP, et al. Long-term outcomes with ileal pouch-anal anastomosis and Crohn's disease: pouch retention and implications of delayed diagnosis. *Ann Surg* 2008;248(04):608-616
- 13 Shen B, Patel S, Lian L. Natural history of Crohn's disease in patients who underwent intentional restorative proctocolectomy with ileal pouch-anal anastomosis. *Aliment Pharmacol Ther* 2010;31(07):745-753
- 14 Le Q, Melmed G, Dubinsky M, et al. Surgical outcome of ileal pouch-anal anastomosis when used intentionally for well-defined Crohn's disease. *Inflamm Bowel Dis* 2013;19(01):30-36
- 15 Farmer M, Petras RE, Hunt LE, Janosky JE, Galandiuk S. The importance of diagnostic accuracy in colonic inflammatory bowel disease. *Am J Gastroenterol* 2000;95(11):3184-3188
- 16 Odze RD. A contemporary and critical appraisal of 'indeterminate colitis'. *Mod Pathol* 2015;28(Suppl 1):S30-S46
- 17 Geboes K, Colombel JF, Greenstein A, et al; Pathology Task Force of the International Organization of Inflammatory Bowel Diseases. Indeterminate colitis: a review of the concept-what's in a name? *Inflamm Bowel Dis* 2008;14(06):850-857
- 18 Silverberg MS, Satsangi J, Ahmad T, et al. Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. *Can J Gastroenterol* 2005;19(Suppl A):5A-36A
- 19 Swan NC, Geoghegan JG, O'Donoghue DP, Hyland JM, Sheahan K. Fulminant colitis in inflammatory bowel disease: detailed pathologic and clinical analysis. *Dis Colon Rectum* 1998;41(12):1511-1515
- 20 Koltun WA, Schoetz DJ Jr, Roberts PL, Murray JJ, Collier JA, Veidenheimer MC. Indeterminate colitis predisposes to perineal complications after ileal pouch-anal anastomosis. *Dis Colon Rectum* 1991;34(10):857-860
- 21 Atkinson KG, Owen DA, Wankling G. Restorative proctocolectomy and indeterminate colitis. *Am J Surg* 1994;167(05):516-518
- 22 McIntyre PB, Pemberton JH, Wolff BG, Dozois RR, Beart RW Jr. Indeterminate colitis. Long-term outcome in patients after ileal pouch-anal anastomosis. *Dis Colon Rectum* 1995;38(01):51-54
- 23 Marcello PW, Schoetz DJ Jr, Roberts PL, et al. Evolutionary changes in the pathologic diagnosis after the ileoanal pouch procedure. *Dis Colon Rectum* 1997;40(03):263-269
- 24 Yu CS, Pemberton JH, Larson D. Ileal pouch-anal anastomosis in patients with indeterminate colitis: long-term results. *Dis Colon Rectum* 2000;43(11):1487-1496
- 25 Pezim ME, Pemberton JH, Beart RW Jr., et al. Outcome of "indeterminant" colitis following ileal pouch-anal anastomosis. *Dis Colon Rectum* 1989;32(08):653-658
- 26 Dayton MT, Larsen KR, Christiansen DD. Similar functional results and complications after ileal pouch-anal anastomosis in patients with indeterminate vs ulcerative colitis. *Arch Surg* 2002;137(06):690-694, discussion 694-695
- 27 Delaney CP, Remzi FH, Gramlich T, Dadvand B, Fazio VW. Equivalent function, quality of life and pouch survival rates after ileal pouch-anal anastomosis for indeterminate and ulcerative colitis. *Ann Surg* 2002;236(01):43-48
- 28 Murrell ZA, Melmed GY, Ippoliti A, et al. A prospective evaluation of the long-term outcome of ileal pouch-anal anastomosis in patients with inflammatory bowel disease-unclassified and indeterminate colitis. *Dis Colon Rectum* 2009;52(05):872-878
- 29 Jackson KL, Stocchi L, Duraes L, Rencuzogullari A, Bennett AE, Remzi FH. Long-term outcomes in indeterminate colitis patients undergoing ileal pouch-anal anastomosis: function, quality of life, and complications. *J Gastrointest Surg* 2017;21(01):56-61
- 30 Fazio VW, Ziv Y, Church JM, et al. Ileal pouch-anal anastomoses complications and function in 1005 patients. *Ann Surg* 1995;222(02):120-127
- 31 Foley EF, Schoetz DJ Jr, Roberts PL, et al. Rediversion after ileal pouch-anal anastomosis. Causes of failures and predictors of subsequent pouch salvage. *Dis Colon Rectum* 1995;38(08):793-798
- 32 Meagher AP, Farouk R, Dozois RR, Kelly KA, Pemberton JH. J ileal pouch-anal anastomosis for chronic ulcerative colitis: complications and long-term outcome in 1310 patients. *Br J Surg* 1998;85(06):800-803
- 33 Michelassi F, Lee J, Rubin M, et al. Long-term functional results after ileal pouch anal restorative proctocolectomy for ulcerative colitis: a prospective observational study. *Ann Surg* 2003;238(03):433-441, discussion 442-445
- 34 Hahnloser D, Pemberton JH, Wolff BG, Larson DR, Crownhart BS, Dozois RR. Results at up to 20 years after ileal pouch-anal anastomosis for chronic ulcerative colitis. *Br J Surg* 2007;94(03):333-340
- 35 Shen B, Fazio VW, Remzi FH, et al. Risk factors for diseases of ileal pouch-anal anastomosis after restorative proctocolectomy for ulcerative colitis. *Clin Gastroenterol Hepatol* 2006;4(01):81-89, quiz 2-3
- 36 Shen B, Remzi FH, Hammel JP, et al. Family history of Crohn's disease is associated with an increased risk for Crohn's disease of the pouch. *Inflamm Bowel Dis* 2009;15(02):163-170
- 37 Alexander F, Sarigol S, DiFiore J, et al. Fate of the pouch in 151 pediatric patients after ileal pouch anal anastomosis. *J Pediatr Surg* 2003;38(01):78-82
- 38 Shen B, Fazio VW, Remzi FH, et al. Risk factors for clinical phenotypes of Crohn's disease of the ileal pouch. *Am J Gastroenterol* 2006;101(12):2760-2768
- 39 Melmed GY, Fleshner PR, Bardakcioglu O, et al. Family history and serology predict Crohn's disease after ileal pouch-anal anastomosis for ulcerative colitis. *Dis Colon Rectum* 2008;51(01):100-108
- 40 Zaghayan K, Kamiński JP, Barmparas G, Fleshner P. De novo Crohn's disease after ileal pouch-anal anastomosis for ulcerative colitis and inflammatory bowel disease unclassified: long-term follow-up of a Prospective Inflammatory Bowel Disease Registry. *Am Surg* 2016;82(10):977-981
- 41 Shen B. Crohn's disease of the ileal pouch: reality, diagnosis, and management. *Inflamm Bowel Dis* 2009;15(02):284-294
- 42 Tekkis PP, Purkayastha S, Lanitis S, et al. A comparison of segmental vs subtotal/total colectomy for colonic Crohn's disease: a meta-analysis. *Colorectal Dis* 2006;8(02):82-90
- 43 Colombel JF, Ricart E, Loftus EV Jr, et al. Management of Crohn's disease of the ileoanal pouch with infliximab. *Am J Gastroenterol* 2003;98(10):2239-2244
- 44 Viscido A, Habib FI, Kohn A, et al. Infliximab in refractory pouchitis complicated by fistulae following ileo-anal pouch for ulcerative colitis. *Aliment Pharmacol Ther* 2003;17(10):1263-1271

- 45 Calabrese C, Gionchetti P, Rizzello F, et al. Short-term treatment with infliximab in chronic refractory pouchitis and ileitis. *Aliment Pharmacol Ther* 2008;27(09):759–764
- 46 Shen B, Remzi FH, Lavery IC, et al. Administration of adalimumab in the treatment of Crohn's disease of the ileal pouch. *Aliment Pharmacol Ther* 2009;29(05):519–526
- 47 Ferrante M, D'Haens G, Dewit O, et al; Belgian IBD Research Group. Efficacy of infliximab in refractory pouchitis and Crohn's disease-related complications of the pouch: a Belgian case series. *Inflamm Bowel Dis* 2010;16(02):243–249
- 48 Haveran LA, Sehgal R, Poritz LS, McKenna KJ, Stewart DB, Koltun WA. Infliximab and/or azathioprine in the treatment of Crohn's disease-like complications after IPAA. *Dis Colon Rectum* 2011;54(01):15–20
- 49 Li Y, Lopez R, Queener E, Shen B. Adalimumab therapy in Crohn's disease of the ileal pouch. *Inflamm Bowel Dis* 2012;18(12):2232–2239
- 50 Robbins L, Zaghiyan K, Melmed G, et al. Outcomes with anti-tumour necrosis factor-alpha therapy and serology in patients with de novo Crohn's disease after ileal pouch anal anastomosis. *J Crohn's Colitis* 2017;11(01):77–83
- 51 Yamamoto T, Keighley MR. Proctocolectomy is associated with a higher complication rate but carries a lower recurrence rate than total colectomy and ileorectal anastomosis in Crohn colitis. *Scand J Gastroenterol* 1999;34(12):1212–1215
- 52 Yamamoto T, Bain IM, Allan RN, Keighley MR. Persistent perineal sinus after proctocolectomy for Crohn's disease. *Dis Colon Rectum* 1999;42(01):96–101
- 53 O'Riordan JM, O'Connor BI, Huang H, et al. Long-term outcome of colectomy and ileorectal anastomosis for Crohn's colitis. *Dis Colon Rectum* 2011;54(11):1347–1354
- 54 Angriman I, Pirozzolo G, Bardini R, Cavallin F, Castoro C, Scarpa M. A systematic review of segmental vs subtotal colectomy and subtotal colectomy vs total proctocolectomy for colonic Crohn's disease. *Colorectal Dis* 2017;19(08):e279–e287
- 55 Longo WE, Oakley JR, Lavery IC, Church JM, Fazio VW. Outcome of ileorectal anastomosis for Crohn's colitis. *Dis Colon Rectum* 1992;35(11):1066–1071
- 56 Kariv Y, Remzi FH, Strong SA, Hammel JP, Preen M, Fazio VW. Ileal pouch rectal anastomosis: a viable alternative to permanent ileostomy in Crohn's proctocolitis patients. *J Am Coll Surg* 2009;208(03):390–399
- 57 de Oca J, Sánchez-Santos R, Ragué JM, et al. Long-term results of ileal pouch-anal anastomosis in Crohn's disease. *Inflamm Bowel Dis* 2003;9(03):171–175
- 58 Braveman JM, Schoetz DJ Jr, Marcello PW, et al. The fate of the ileal pouch in patients developing Crohn's disease. *Dis Colon Rectum* 2004;47(10):1613–1619
- 59 Rudolph WG, Uthoff SM, McAuliffe TL, Goode ET, Petras RE, Galandiuk S. Indeterminate colitis: the real story. *Dis Colon Rectum* 2002;45(11):1528–1534
- 60 Pishori T, Dinnewitzer A, Zmora O, et al. Outcome of patients with indeterminate colitis undergoing a double-stapled ileal pouch-anal anastomosis. *Dis Colon Rectum* 2004;47(05):717–721