Role of Fecal Diversion in Complex Crohn's Disease

John P. Burke, PhD, FRCSI^{1,2}

¹ Department of Colorectal Surgery, Beaumont Hospital, Dublin 9, Ireland

² Department of Surgery, Royal College of Surgeons in Ireland, Dublin 2, Ireland

Address for correspondence John P. Burke, PhD, FRCSI, Department of Colorectal Surgery, Beaumont Hospital, Dublin 9, Ireland (e-mail: johnburke@rcsi.ie).

Clin Colon Rectal Surg 2019;32:273–279.

Abstract

Keywords

- Crohn's disease
- ileostomy
- colostomy
- ostomy
- stoma
- fistula
- abscess
- stricture
- colitis

Crohn's disease (CD) is a chronic inflammatory condition of the gastrointestinal tract resulting in progressive tissue damage, which can result in strictures, fistulae, and abscesses formation. The triggering mechanism is thought to be in the fecal stream, and diversion of this fecal stream is sometimes required to control disease when all other avenues of medical and surgical management have been exhausted. Fecal diversion can be temporary or permanent with the indications being defunctioning a high-risk anastomosis, as a result of a surgical complication, for disease control, or due to severe colonic, rectal, or perianal disease. The incidence of ostomy formation in CD has increased epidemiologically over time. The primary indication for ostomy formation is severe perianal fistulizing disease. However, while 64% of patients have an early clinical response after diversion for refractory perianal CD, restoration of bowel continuity is attempted in only 35% of patients, and is successful in only 17%. The current review discusses the indications for ostomy creation in complex CD, strategies for procedure selection, and patient outcomes.

Crohn's disease (CD) is a chronic inflammatory disease of the gastrointestinal tract with symptoms evolving in a relapsing and remitting manner. It is a progressive condition leading to intestinal damage and any component of the gastrointestinal tract can be affected, the most common being the terminal ileum and colon. Inflammation is typically segmental, asymmetrical, and transmural but can occur synchronously at multiple sites. The sequelae of this inflammation include strictures, fistulae, and abscesses formation.¹ Current therapeutic strategies aim to induce the remission of inflammation, with the goal of preventing complications and halting the progressive course of disease, but in many, surgery is required.

The cause of CD is a combination of genetic, immunological, and microbiological factors with the triggering mechanism thought to be in the fecal stream. Diversion of the fecal stream from severely inflamed segments of bowel has long been known to decrease CD-related inflammation.² In CD patients, the restoration of the fecal stream following diversion leads to recurrent endoscopic and histological inflammation.³ Furthermore, in studies of ileum defunctioned by an ileostomy, the infusion of intestinal luminal contents induces microscopic inflammation.⁴ These con-

cepts have led to the practice of ostomy formation for disease control in patients where combined medical and surgical management has proven unsuccessful.

Fecal diversion can be temporary or permanent with the indications being defunctioning a high-risk anastomosis, as a result of a surgical complication, for disease control or due to severe colonic, rectal, or perianal disease (► **Table 1**). In the pediatric population, the formation of an ileostomy can further lead to improvements in height and weight velocities, with reduced steroid use, and hospitalization rates.⁵ An analysis of 355,239 Crohn's-related operations from 1988 to 2011 in the United States demonstrated an increased rate of stoma construction over time with an increase in ileostomy formation and a reduction in colostomy formation; weight loss and perianal fistulizing disease were most predictive of requiring stoma construction.⁶ Responders to anti-tumor necrosis factor (TNF)- α therapy are less likely to require an ileostomy or proctectomy.⁷ In contemporary practice, the majority of fecal diversion procedures can be performed laparoscopically.^{8,9}

In a series of 507 patients with colorectal CD from the prebiologic era, the cumulative risk for a permanent ileostomy was 25% at 10 years after diagnosis¹⁰ rising to 14% at 20 years¹¹

Table 1 Indications for ostomy creation in Crohn's disease

Temporary	Permanent
Defunctioning a high-risk anastomosis	APR
Postoperative complication	Proctocolectomy
Uncontrolled perianal disease	
Anorectal stricture	
Colitis or proctosigmoiditis	

Abbreviation: APR, abdominoperineal excision.

and the presence of rectal disease was associated with an increased likelihood of permanent ostomy.^{11,12} The main indication (64%) for primary stoma formation is severe perianal fistulizing disease.¹¹

The current article discusses the indications and outcomes of fecal diversion in complex CD.

Methods

PubMed was searched for articles published from January 1, 1980, to August 28, 2017, using the search terms “ileostomy” OR “colostomy” OR “stoma” AND “Crohn's.” Original studies and prior systematic reviews were examined which detailed the outcomes of patients undergoing the formation of an ostomy for the management of complex CD. All search results were combined in a reference manager database (Endnote, Version X7; Thompson Reuters, New York, NY). Reference lists of included studies were screened for additional relevant studies.

Ostomy Formation for the Defunctioning of a High-Risk Anastomosis or Postoperative Complication

Most patients with CD will require surgery at some point in their life¹³ and despite the increasing use of novel biologic agents, the incidence does not appear to be reducing.¹⁴ The most frequently performed operations include ileocecal resection for primary disease or ileocolic resection for recurrence. Anastomotic-associated complications include leak requiring reoperation, local abscess formation, and enterocutaneous fistulae. Risk factors for anastomotic complication include intra-abdominal abscess or fistula, malnutrition, steroid usage, and recurrent clinical episodes.¹⁵ In a series of 173 patients undergoing ileocolic resection for CD, an anastomotic complication rate of 11% was noted.¹⁶ Steroid usage and the presence of preoperative abscess formation were identified as independent predictors of anastomotic complication; when both factors were present, complication rates reached as high as 40%.¹⁶ Furthermore, the preoperative use of anti-TNF- α therapy has recently been identified as a predictor of anastomotic leak.¹⁷ Thus, the cautious surgeon will often defunction an ileocolic anastomosis in a malnourished patient who has a local abscess or has had a protracted period of preoperative medical treatment to avoid an anastomotic complication and its associated sequelae in this

predominantly young patient cohort. In the setting of an anastomotic leak following resection, a loop or end stoma may also be required.

Ostomy Formation for Management of Perianal Fistulating Disease

Perianal fistulae are seen in 20% of patients with CD,¹⁸ and often indicate an aggressive phenotype, with higher rates of corticosteroid dependence, surgery, and hospitalization.¹⁹ These are often our most challenging patients, in a series of 232 patients with perianal fistulating CD from the pre-biologic era (78% complex) with a median follow-up of 10 years, only 37% of complex fistulas were in remission.²⁰ Management of perianal CD requires a multidisciplinary approach with a combination of immunosuppressive therapy, antibiotics, and surgery for adequate control of sepsis and fistula management in selected cases.²¹ The advent of biologic medications has dramatically increased the options for medical management of this complex clinical presentation. In a recent series of 114 patients with septic perianal CD, there was an approximate 60% rate of healing using a combined medical and surgical approach, but 20% required a permanent stoma.²² Indeed, a small subset of patients with refractory perianal CD still require fecal diversion for control of sepsis and or symptoms. A recent survey of a UK-based expert group of colorectal surgeons and gastroenterologists listed the indications for a diverting stoma or proctectomy in the setting of perianal disease to be intractable sepsis, incontinence, and poor quality of life (QOL).²³ Furthermore, the Association of Coloproctology of Great Britain and Ireland advises, a stoma or proctectomy could be discussed earlier in a patient's treatment pathway to improve choice, as this may improve QOL.²⁴ Furthermore, the recent ECCO-ESCP position statement on the surgical management of CD advises, fecal diversion is effective in reducing symptoms in perianal CD in two-thirds of patients and may improve QOL, but only one-fifth of these patients are stoma free on the long term.²¹ Diversion is often preferable with respect to proctectomy because perianal complications, chronic pelvic sinus, or impaired healing of a perianal wound may occur. Indeed, the outcomes of local sepsis tend to be improved with abscess recurrence observed less frequently in patients with a stoma (13 vs. 60%).²⁵ However, data tend to be challenging to interpret with series describing both the pre- and post-biologic era and varying fistula complexity. For example, in one series, 49% ultimately required permanent diversion with 66% having an anal stricture and 60% of women having a rectovaginal fistula. Other series support this observation demonstrating half of the complex CD perianal fistulae required a stoma, resection, or proctectomy.²⁶ The presence of colonic disease and an anal canal stricture are independent predictors of permanent diversion.²⁷ Absence of rectal involvement is also a consistent factor associated with successful ostomy closure.²⁸

The long-term outcomes of temporary fecal diversion, including rates of attempted and successful restoration of bowel continuity and need for additional surgery such as

Table 2 Series describing defunctioning ostomy formation for perianal Crohn's disease

Author	Year	Follow-up	N	Ostomy closure
Harper et al ³⁶	1982	NR	29	17%
Orkin and Telander ⁷¹	1985	94 mo	11	0%
Grant et al ⁷²	1986	NR	12	8%
Edwards et al ³⁹	2000	54 mo	18	11%
Yamamoto et al ⁷³	2000	103 mo	31	10%
Régimbeau et al ³⁸	2001	124 mo	17	47%
Rehg et al ⁷⁴	2009	60 mo	13	23%
Hong et al ⁷⁵	2011	22 mo	21	19%
Gu et al ⁷⁶	2012	9 mo	138	22%
Uzzan et al ⁴³	2013	NR	3	0%
Sauk et al ³⁰	2014	84 mo	49	5%
Mennigen et al ⁷⁷	2015	33 mo	22	14%
Bafford et al ⁷⁸	2017	24 mo	11	25%
Martí-Gallostra et al ⁷⁹	2017	48 mo	54	19%

Abbreviation: NR, not recorded.

proctectomy, are, however, poor. Of 14 studies assessed with included patient numbers ranging from 3 to 138 and follow-up durations of 9 to 124 months, stoma closure rates of 0 to 47% were observed. However, 10 of 14 studies reported ultimate stoma closure rates of less than 20% (→ **Table 2**). A recent meta-analysis of 16 studies demonstrated that while 63.8% of patients have an early clinical response after diversion for refractory perianal CD, restoration of bowel continuity is attempted in only 34.5% of patients, and was successful in only 16.6%.²⁸ Of those in whom restoration was attempted, 26.5% required rediversion because of severe relapse. Overall, 41.6% of patients required proctectomy after failure of temporary fecal diversion. Even more disappointing, there was no difference in the successful restoration of bowel continuity after temporary fecal diversion in the prebiologic or post-biologic era (13.7 vs. 17.6%).²⁸ This must be considered in the context of the pooled efficacy of anti-TNF agents in healing of fistulizing perianal CD in randomized trials being estimated at 32.8% over 4 to 26 weeks of treatment.²⁹ However, this does not take into account novel agents such as the anti-integrins and Ustekinumab or combination immunosuppression. In studying temporal trends in rates of perianal surgical procedures, Sauk et al observed that only 10% of patients with perianal CD underwent diversion between 2009 and 2011, compared with 18% between 2000 and 2002, suggesting the increasing use of biologics may play a role in decreasing the need for diverting or surgical procedures for perianal CD.³⁰ In a series of 27 patients with CD who underwent fecal diversion (resistant proctocolitis: 17 and perianal disease: 10), the expression of I2 antibodies against a bacterial antigen of *Pseudomonas fluorescens* was highly associated with clinical response to fecal diversion.³¹

In the setting of CD-related rectovaginal fistula, a recent series of 120 patients demonstrated that the use of fecal diversion did not affect healing, but tissue interposition techniques had the highest success rates.³² In a further series of 51 patients with rectovaginal fistula, 60% of patients treated with preoperative fecal diversion healed, and 51% of patients treated with nondiverted repairs healed.³³ While anorectal stricture is often considered an indication for definitive ostomy formation, a recent series of 102 patients demonstrated stricture healing in 59% at a median follow-up period of 2.8 years with 19 patients requiring definitive ostomy.²⁰ These data conflict with an earlier series (1975–1985) of 44 patients with CD anorectal strictures where 50% required a definitive ostomy.³⁴

Despite a low likelihood of ultimate reversal, temporary fecal diversion may, however, be useful for patients who are reluctant to the idea of a permanent stoma at initial consultation, wherein temporary diversion may improve QOL and the acceptability of a stoma.

Temporary Ostomy Formation for the Management of Colonic Crohn's Disease

The formation of a defunctioning loop ileostomy is an alternative strategy for managing Crohn's colitis, which was prevalent in the prebiologic era and remains of value in certain clinical circumstances. The indications include a debilitated patient unsuitable for major resectional surgery and attempted disease control where colonic healing can be induced and patients can be weaned off steroids.^{35–37} However, despite an improvement in Crohn's colitis by fecal stream diversion, a permanent stoma is usually required.^{38,39} Published series range in the number of patients included for this indication from 10 to 102 (→ **Table 3**). In the largest series, an immediate clinical improvement was observed in 95 patients, which was sustained in 65. Thirty patients subsequently required a proctocolectomy for persistent inflammation, and 28 remained defunctioned.⁴⁰ The authors concluded that a temporary ileostomy is a safe approach producing temporary improvement in severely ill and malnourished patients with Crohn's colitis, and if subsequent resection becomes necessary, it may be less extensive.⁴⁰ While initial success rates are high, relapse rates of 33% have led other authors to recommend definitive surgery electively at an early stage after initial clinical improvement.⁴¹

Table 3 Series describing defunctioning ostomy formation for colonic Crohn's disease

Author	Year	N	Sustained improvement
Zelas and Jagelman ⁴¹	1980	79	67%
Ultee et al ⁸⁰	1981	30	19%
Harper et al ⁴⁰	1983	102	64%
Winslet et al ³⁷	1993	44	68%
Edwards et al ³⁹	2000	55	20%
Bafford et al ⁷⁸	2017	10	60%

The risk of a permanent stoma in patients with Crohn's colitis and anorectal involvement is even greater. Severe perianal disease (especially in the presence of rectal stenosis) and Crohn's colitis are strong predictors of permanent diversion.²¹ It has been suggested that combined surgical and biological treatment reduces the risk of permanent ostomy in this cohort (60.8 vs. 19.2%).⁴² However, a recent small case series demonstrated that a combination of anti-TNF- α therapy and transient ileal fecal stream diversion in severe Crohn's colitis with perianal fistula preventing definitive stoma is unsuccessful.⁴³

Abdominoperineal Excision for Crohn's Disease

Perianal CD represents a spectrum of disease including skin tags, ulcers, perianal abscess, low and high fistulae, rectovaginal fistula, anorectal strictures, and cancer. This disease can result in a significant reduction in patient QOL due to its often chronic nature which can result in persistent drainage, pain, dyspareunia, dyschezia, and anal incontinence.⁴⁴ Despite optimal medical and minimally invasive therapy, 8 to 40% will require proctectomy to control symptoms. For this reason, primary total proctocolectomy or early completion proctectomy may be considered in this subgroup of patients.²¹ In a series of 119 with anoperineal CD in the prebiologic era with a mean follow-up of 93 months, 30 patients required an APR (25%). Independent predictors of the requirement for APR included age at first anoperineal disease development, fistula as the first manifestation, and rectal involvement by CD.⁴⁵ For patients with anorectal disease and proctosigmoiditis with proximal colonic sparing which is refractory to medical management, an abdominoperineal excision is a surgical alternative to proctocolectomy with end ileostomy; however, outcomes are poor. In a recent series of 10 consecutive patients who underwent intersphincteric proctectomy with end colostomy, severe and early endoscopic recurrence in the proximal colon occurred in nine patients at a median time interval of 9.5 months.⁴⁶ Despite protracted medical treatment, completion colectomy was necessary in five patients.⁴⁶

Furthermore, there often exists difficulty in perineal wound healing,⁴⁷ with 85 and 48% unhealed at 6 and 12 months after surgery.⁴⁸ The use of myocutaneous flaps in this setting has shown promise with complete healing and control of sepsis achieved in the majority of patients reported in two series.^{49,50} Thus, patients may be considered for abdominoperineal excision in this setting but must be adequately counseled of the risks of proximal colonic recurrence and delayed perineal healing.

Fate of the Rectum following Colectomy and Terminal Ostomy for Crohn's Disease

Patients with colonic CD may undergo a sigmoid colectomy with end colostomy or a total colectomy with end ileostomy formation. The fate of the excluded rectal segment after surgery for Crohn's colitis remains a source of interest as to what is the best management strategy. An ileorectal

anastomosis can be fashioned in selected cases for sphincter preservation with one series describing its performance in 30% of cases following total colectomy.⁵¹ The incidence of completion proctectomy following total colectomy with end ileostomy formation for Crohn's colitis has been reported to be between 35 and 51%.⁵¹⁻⁵³ It appears neither initial involvement of the terminal ileum nor endoscopic inflammatory changes seen in the rectum predict eventual disease of the excluded rectal segment, but initial perianal disease is predictive of need for ultimate proctectomy.⁵² This has prompted the conclusion that should perianal disease and Crohn's colitis occur synchronously, a primary total proctocolectomy is the procedure of choice.⁵² It must be stressed, however, that the risk of colorectal adenoma or squamous carcinoma in these excluded rectal segments exists.⁵⁴ Multiple case series have highlighted this risk in this specific population,⁵⁵⁻⁵⁸ prompting the guidance that proctectomy should be performed in all patients in whom rectal preservation is not possible. Regularly scheduled interim surveillance proctoscopy should be performed every 2 years, with biopsies of macroscopically normal-appearing and abnormal-appearing rectal mucosa until proctectomy is performed.⁵⁸

Quality of Life

CD is associated with substantially impaired health-related QOL. Even in the absence of active disease, patients with CD report lower QOL, poorer function, and greater concerns, than those without disease.⁵⁹ Patients with ulcerative colitis (UC) report superior levels of health-related and disease-specific QOL than patients with CD when measured with the Inflammatory Bowel Disease Questionnaire (IBDQ) and the Hospital Anxiety and Depression scale, but this does not seem to be affected by having an ileostomy.⁶⁰ The presence of a stoma alone does not appear to be a risk factor for depression in inflammatory bowel disease.⁶¹ In a series of 21 inflammatory bowel disease patients with an ileostomy, the greatest concerns were related to intimacy, access to quality medical care, energy level, loss of sexual drive, producing unpleasant odors, being a burden, ability to perform sexually, attractiveness, and feelings about the body. Vitality was significantly reduced compared with controls.⁶² A survey of 10 members of the United Kingdom Ileostomy Association with CD reported patients with a stoma were enabled to reengage with work and social activities and helped manage Crohn's symptoms.⁶³ In contrast, in an analysis of 31 patients with CD and an ostomy, 48% of patients scored more than the cutoff for anxiety and 42% scored more than the cutoff for depression on the Hospital Anxiety and Depression Scale. However, the timing of ostomy surgery (planned vs. emergency) or ostomy type (permanent vs. temporary) was not significantly associated with anxiety, depression, or health-related impaired QOL.⁶⁴ In another survey of 69 CD patients, depressive symptoms were self-reported by 73%. Associations were found between depressive symptoms and duration of disease, prior surgery, past or present stoma, and anal stenosis.⁶⁵ Data on QOL and an ostomy for CD appear conflicting and may be related to local patient populations, but it may be concluded

that the presence of an ostomy in this patient group does not significantly worsen QOL.

Long-Term Outcomes

While ostomy formation is a common undertaking in the setting of CD, long-term complications occur with a relatively high frequency. In CD, revisional surgery for stomal complications is more common following colostomy than ileostomy (31 vs. 5%).¹¹ In patients with CD, the risk of developing an ostomy complication is 36% after 5 years and the risk of stoma reconstruction is 23% after 5 years, both of which are higher in CD than in ulcerative colitis; furthermore, the risk of stoma reconstruction is higher with a colostomy.⁶⁶ The rate of ileostomy complications necessitating reconstruction after 8 years following proctocolectomy has been shown to be 75% in CD and is higher than that in UC.⁶⁷ Ileostomy stenosis and recession are the two most common indications for reconstruction.⁶⁷ A recent systematic review of 1,438 patients who underwent total colectomy or proctocolectomy with permanent ileostomy for colonic CD demonstrated the risk of clinical disease recurrence was 24% at 5 years and 40% at 10 years. The risk of surgical recurrence was 10% at 5 years and 18.5% at 10 years. A history of ileal disease was associated with 3.2 times higher risk of disease recurrence.⁶⁸ Diagnosis at age less than 18 years and anti-TNF- α therapy before surgery have been suggested as predictive factors for overall disease recurrence.⁶⁹ Rarely, stoma adenocarcinoma can develop.⁷⁰

Conclusions

As the triggering mechanism for CD is thought to be in the fecal stream, the diversion of this fecal stream is sometimes required for disease control. Fecal diversion can be temporary or permanent with the indications being defunctioning a high-risk anastomosis, as a result of a surgical complication, for disease control or due to severe colonic, rectal, or perianal disease. The primary indication for ostomy formation is severe perianal fistulizing disease. However, while 64% of patients have an early clinical response after diversion for refractory perianal CD, restoration of bowel continuity is attempted in only 35% of patients, and is successful in only 17%. Despite a low likelihood of ultimate reversal, temporary fecal diversion may, however, be useful for patients who are reluctant to the idea of a permanent stoma at initial consultation, wherein temporary diversion may improve QOL and the acceptability of a stoma. If patients are to make informed decisions regarding fecal diversion for refractory CD, they must understand not only the likelihood of having bowel continuity restored the effect of this strategy on QOL but also its potential complications. These decisions are best made within a multidisciplinary environment, to ensure all other avenues of medical and surgical management have been exhausted.

Conflict of Interest
None to declare.

References

- Torres J, Mehandru S, Colombel JF, Peyrin-Biroulet L. Crohn's disease. *Lancet* 2017;389(10080):1741–1755
- Burman JH, Thompson H, Cooke WT, Williams JA. The effects of diversion of intestinal contents on the progress of Crohn's disease of the large bowel. *Gut* 1971;12(01):11–15
- Rutgeerts P, Goobes K, Peeters M, et al. Effect of faecal stream diversion on recurrence of Crohn's disease in the neoterminal ileum. *Lancet* 1991;338(8770):771–774
- D'Haens GR, Geboes K, Peeters M, Baert F, Penninckx F, Rutgeerts P. Early lesions of recurrent Crohn's disease caused by infusion of intestinal contents in excluded ileum. *Gastroenterology* 1998; 114(02):262–267
- Maxwell EC, Dawany N, Baldassano RN, et al. Diverting ileostomy for the treatment of severe, refractory, pediatric inflammatory bowel disease. *J Pediatr Gastroenterol Nutr* 2017;65(03):299–305
- Geltzeiler CB, Hart KD, Lu KC, Deveney KE, Herzig DO, Tsikitis VL. Trends in the surgical management of Crohn's disease. *J Gastrointest Surg* 2015;19(10):1862–1868
- Rayen J, Currie T, Gearry RB, Frizelle F, Eglinton T. The long-term outcome of anti-TNF alpha therapy in perianal Crohn's disease. *Tech Coloproctol* 2017;21(02):119–124
- Liu J, Bruch HP, Farke S, Nolde J, Schwandner O. Stoma formation for fecal diversion: a plea for the laparoscopic approach. *Tech Coloproctol* 2005;9(01):9–14
- Oliveira L, Reissman P, Nogueras J, Wexner SD. Laparoscopic creation of stomas. *Surg Endosc* 1997;11(01):19–23
- Lapidus A, Bernell O, Hellers G, Löfberg R. Clinical course of colorectal Crohn's disease: a 35-year follow-up study of 507 patients. *Gastroenterology* 1998;114(06):1151–1160
- Post S, Herfarth C, Schumacher H, Golling M, Schürmann G, Timmermanns G. Experience with ileostomy and colostomy in Crohn's disease. *Br J Surg* 1995;82(12):1629–1633
- Hurst RD, Molinari M, Chung TP, Rubin M, Michelassi F. Prospective study of the features, indications, and surgical treatment in 513 consecutive patients affected by Crohn's disease. *Surgery* 1997;122(04):661–667, discussion 667–668
- Cosnes J, Nion-Larmurier I, Beaugerie L, Afchain P, Turet E, Gendre JP. Impact of the increasing use of immunosuppressants in Crohn's disease on the need for intestinal surgery. *Gut* 2005;54(02):237–241
- Burke JP, Velupillai Y, O'Connell PR, Coffey JC. National trends in intestinal resection for Crohn's disease in the post-biologic era. *Int J Colorectal Dis* 2013;28(10):1401–1406
- Alves A, Panis Y, Bouhnik Y, Pocard M, Vicaut E, Valleur P. Risk factors for intra-abdominal septic complications after a first ileocecal resection for Crohn's disease: a multivariate analysis in 161 consecutive patients. *Dis Colon Rectum* 2007;50(03):331–336
- Tzivanakis A, Singh JC, Guy RJ, Travis SP, Mortensen NJ, George BD. Influence of risk factors on the safety of ileocolic anastomosis in Crohn's disease surgery. *Dis Colon Rectum* 2012;55(05):558–562
- de Buck van Overstraeten A, Eshuis EJ, Vermeire S, et al. Short- and medium-term outcomes following primary ileocaecal resection for Crohn's disease in two specialist centres. *Br J Surg* 2017;104(12):1713–1722
- Schwartz DA, Loftus EV Jr, Tremaine WJ, et al. The natural history of fistulizing Crohn's disease in Olmsted County, Minnesota. *Gastroenterology* 2002;122(04):875–880
- Beaugerie L, Seksik P, Nion-Larmurier I, Gendre JP, Cosnes J. Predictors of Crohn's disease. *Gastroenterology* 2006;130(03):650–656
- Molendijk I, Nuij VJ, van der Meulen-de Jong AE, van der Woude CJ. Disappointing durable remission rates in complex Crohn's disease fistula. *Inflamm Bowel Dis* 2014;20(11):2022–2028
- Bemelman WA, Warusavitarne J, Sampietro GM, et al. ECCO-ESCP consensus on surgery for Crohn's disease. *J Crohns Colitis* 2018; 12(01):1–16
- Choi CS, Berg AS, Sangster W, et al. Combined medical and surgical approach improves healing of septic perianal Crohn's disease. *J Am Coll Surg* 2016;223(03):506–514.e1

- 23 Lee MJ, Heywood N, Sagar PM, Brown SR, Fearnhead NS; pCD Collaborators. Surgical management of fistulating perianal Crohn's disease: a UK survey. *Colorectal Dis* 2017;19(03):266–273
- 24 Lee MJ, Heywood N, Sagar PM, Brown SR, Fearnhead NS; ACPGBI Perianal Crohn's Disease Group. Association of Coloproctology of Great Britain and Ireland consensus exercise on surgical management of fistulating perianal Crohn's disease. *Colorectal Dis* 2017; 19(05):418–429
- 25 Makowiec F, Jehle EC, Becker HD, Starlinger M. Perianal abscess in Crohn's disease. *Dis Colon Rectum* 1997;40(04):443–450
- 26 Bell SJ, Williams AB, Wiesel P, Wilkinson K, Cohen RC, Kamm MA. The clinical course of fistulating Crohn's disease. *Aliment Pharmacol Ther* 2003;17(09):1145–1151
- 27 Galandiuk S, Kimberling J, Al-Mishlab TG, Stromberg AJ. Perianal Crohn disease: predictors of need for permanent diversion. *Ann Surg* 2005;241(05):796–801, discussion 801–802
- 28 Singh S, Ding NS, Mathis KL, et al. Systematic review with meta-analysis: faecal diversion for management of perianal Crohn's disease. *Aliment Pharmacol Ther* 2015;42(07):783–792
- 29 Ford AC, Sandborn WJ, Khan KJ, Hanauer SB, Talley NJ, Moayyedi P. Efficacy of biological therapies in inflammatory bowel disease: systematic review and meta-analysis. *Am J Gastroenterol* 2011; 106(04):644–659, quiz 660
- 30 Sauk J, Nguyen D, Yajnik V, et al. Natural history of perianal Crohn's disease after fecal diversion. *Inflamm Bowel Dis* 2014;20 (12):2260–2265
- 31 Spivak J, Landers CJ, Vasiliauskas EA, et al. Antibodies to I2 predict clinical response to fecal diversion in Crohn's disease. *Inflamm Bowel Dis* 2006;12(12):1122–1130
- 32 Narang R, Hull T, Perrins S, Garcia JS, Wexner SD. Should immunomodulation therapy alter the surgical management in patients with rectovaginal fistula and Crohn's disease? *Dis Colon Rectum* 2016;59(07):670–676
- 33 Gaertner WB, Madoff RD, Spencer MP, Mellgren A, Goldberg SM, Lowry AC. Results of combined medical and surgical treatment of recto-vaginal fistula in Crohn's disease. *Colorectal Dis* 2011;13 (06):678–683
- 34 Linares L, Moreira LF, Andrews H, Allan RN, Alexander-Williams J, Keighley MR. Natural history and treatment of anorectal strictures complicating Crohn's disease. *Br J Surg* 1988;75(07):653–655
- 35 Oberhelman HA Jr, Kohatsu S, Taylor KB, Kivel RM. Diverting ileostomy in the surgical management of Crohn's disease of the colon. *Am J Surg* 1968;115(02):231–240
- 36 Harper PH, Kettlewell MG, Lee EC. The effect of split ileostomy on perianal Crohn's disease. *Br J Surg* 1982;69(10):608–610
- 37 Winslet MC, Andrews H, Allan RN, Keighley MR. Fecal diversion in the management of Crohn's disease of the colon. *Dis Colon Rectum* 1993;36(08):757–762
- 38 Régimbeau JM, Panis Y, Cazaban L, et al. Long-term results of faecal diversion for refractory perianal Crohn's disease. *Colorectal Dis* 2001;3(04):232–237
- 39 Edwards CM, George BD, Jewell DP, Warren BF, Mortensen NJ, Kettlewell MG. Role of a defunctioning stoma in the management of large bowel Crohn's disease. *Br J Surg* 2000;87(08):1063–1066
- 40 Harper PH, Truelove SC, Lee EC, Kettlewell MG, Jewell DP. Split ileostomy and ileocolostomy for Crohn's disease of the colon and ulcerative colitis: a 20 year survey. *Gut* 1983;24(02):106–113
- 41 Zelas P, Jagelman DG. Loop ileostomy in the management of Crohn's colitis in the debilitated patient. *Ann Surg* 1980;191(02):164–168
- 42 Coscia M, Gentilini L, Laureti S, et al. Risk of permanent stoma in extensive Crohn's colitis: the impact of biological drugs. *Colorectal Dis* 2013;15(09):1115–1122
- 43 Uzzan M, Stefanescu C, Maggiori L, Panis Y, Bouhnik Y, Treton X. Case series: does a combination of anti-TNF antibodies and transient ileal fecal stream diversion in severe Crohn's colitis with perianal fistula prevent definitive stoma? *Am J Gastroenterol* 2013;108(10):1666–1668
- 44 Rutgeerts P. Review article: treatment of perianal fistulizing Crohn's disease. *Aliment Pharmacol Ther* 2004;20(Suppl 4):106–110
- 45 Régimbeau JM, Panis Y, Marteau P, Benoist S, Valleur P. Surgical treatment of anoperineal Crohn's disease: can abdominoperineal resection be predicted? *J Am Coll Surg* 1999;189(02):171–176
- 46 de Buck van Overstraeten A, Wolthuis AM, Vermeire S, et al. Intersphincteric proctectomy with end-colostomy for anorectal Crohn's disease results in early and severe proximal colonic recurrence. *J Crohn's Colitis* 2013;7(06):e227–e231
- 47 Scammell BE, Keighley MR. Delayed perineal wound healing after proctectomy for Crohn's colitis. *Br J Surg* 1986;73(02):150–152
- 48 Chau A, Prodeau M, Sarter H, et al. Persistent perineal sinus after abdominoperineal resection. *Langenbecks Arch Surg* 2017;402 (07):1063–1069
- 49 Schaden D, Schauer G, Haas F, Berger A. Myocutaneous flaps and proctocolectomy in severe perianal Crohn's disease—a single stage procedure. *Int J Colorectal Dis* 2007;22(12):1453–1457
- 50 Brough WA, Schofield PF. The value of the rectus abdominis myocutaneous flap in the treatment of complex perineal fistula. *Dis Colon Rectum* 1991;34(02):148–150
- 51 Harling H, Hegnhøj J, Rasmussen TN, Jarnum S. Fate of the rectum after colectomy and ileostomy for Crohn's colitis. *Dis Colon Rectum* 1991;34(10):931–935
- 52 Guillem JG, Roberts PL, Murray JJ, Collier JA, Veidenheimer MC, Schoetz DJ Jr. Factors predictive of persistent or recurrent Crohn's disease in excluded rectal segments. *Dis Colon Rectum* 1992;35 (08):768–772
- 53 Sher ME, Bauer JJ, Gorphine S, Gelernt I. Low Hartmann's procedure for severe anorectal Crohn's disease. *Dis Colon Rectum* 1992; 35(10):975–980
- 54 Reynolds IS, O'Toole A, Deasy J, McNamara DA, Burke JP. A meta-analysis of the clinicopathological characteristics and survival outcomes of inflammatory bowel disease associated colorectal cancer. *Int J Colorectal Dis* 2017;32(04):443–451
- 55 Rieger N, Collopy B, Fink R, Mackay J, Woods R, Keck J. Total colectomy for Crohn's disease. *Aust N Z J Surg* 1999;69(01):28–30
- 56 Yamamoto T, Keighley MR. Long-term outcome of total colectomy and ileostomy for Crohn disease. *Scand J Gastroenterol* 1999;34 (03):280–286
- 57 Lavery IC, Jagelman DG. Cancer in the excluded rectum following surgery for inflammatory bowel disease. *Dis Colon Rectum* 1982; 25(06):522–524
- 58 Cirincione E, Gorfine SR, Bauer JJ. Is Hartmann's procedure safe in Crohn's disease? Report of three cases. *Dis Colon Rectum* 2000;43 (04):544–547
- 59 Wright EK, Kamm MA. Impact of drug therapy and surgery on quality of life in Crohn's disease: a systematic review. *Inflamm Bowel Dis* 2015;21(05):1187–1194
- 60 Nordin K, Pahlman L, Larsson K, Sundberg-Hjelm M, Löf L. Health-related quality of life and psychological distress in a population-based sample of Swedish patients with inflammatory bowel disease. *Scand J Gastroenterol* 2002;37(04):450–457
- 61 Panara AJ, Yarur AJ, Rieders B, et al. The incidence and risk factors for developing depression after being diagnosed with inflammatory bowel disease: a cohort study. *Aliment Pharmacol Ther* 2014; 39(08):802–810
- 62 Carlsson E, Bosaeus I, Nordgren S. What concerns subjects with inflammatory bowel disease and an ileostomy? *Scand J Gastroenterol* 2003;38(09):978–984
- 63 Morris A, Leach B. A qualitative exploration of the lived experiences of patients before and after ileostomy creation as a result of surgical management for Crohn's disease. *Ostomy Wound Manage* 2017;63 (01):34–39
- 64 Knowles SR, Wilson J, Wilkinson A, et al. Psychological well-being and quality of life in Crohn's disease patients with an ostomy: a preliminary investigation. *J Wound Ostomy Continence Nurs* 2013;40(06):623–629

- 65 Mahadev S, Young JM, Selby W, Solomon MJ. Self-reported depressive symptoms and suicidal feelings in perianal Crohn's disease. *Colorectal Dis* 2012;14(03):331–335
- 66 Takahashi K, Funayama Y, Fukushima K, et al. Stoma-related complications in inflammatory bowel disease. *Dig Surg* 2008;25(01):16–20
- 67 Carlstedt A, Fasth S, Hultén L, Nordgren S, Palselius I. Long-term ileostomy complications in patients with ulcerative colitis and Crohn's disease. *Int J Colorectal Dis* 1987;2(01):22–25
- 68 Fumery M, Dulai PS, Meirick P, et al. Systematic review with meta-analysis: recurrence of Crohn's disease after total colectomy with permanent ileostomy. *Aliment Pharmacol Ther* 2017;45(03):381–390
- 69 Lopez J, Konijeti GG, Nguyen DD, Sauk J, Yajnik V, Ananthakrishnan AN. Natural history of Crohn's disease following total colectomy and end ileostomy. *Inflamm Bowel Dis* 2014;20(07):1236–1241
- 70 Sherlock DJ, Suarez V, Gray JG. Stomal adenocarcinoma in Crohn's disease. *Gut* 1990;31(11):1329–1332
- 71 Orkin BA, Telander RL. The effect of intra-abdominal resection or fecal diversion on perianal disease in pediatric Crohn's disease. *J Pediatr Surg* 1985;20(04):343–347
- 72 Grant DR, Cohen Z, McLeod RS. Loop ileostomy for anorectal Crohn's disease. *Can J Surg* 1986;29(01):32–35
- 73 Yamamoto T, Allan RN, Keighley MR. Effect of fecal diversion alone on perianal Crohn's disease. *World J Surg* 2000;24(10):1258–1262, discussion 1262–1263
- 74 Rehag KL, Sanchez JE, Krieger BR, Marcet JE. Fecal diversion in perirectal fistulizing Crohn's disease is an underutilized and potentially temporary means of successful treatment. *Am Surg* 2009;75(08):715–718
- 75 Hong MK, Craig Lynch A, Bell S, et al. Faecal diversion in the management of perianal Crohn's disease. *Colorectal Dis* 2011;13(02):171–176
- 76 Gu J, Valente MA, Remzi FH, Stocchi L. Factors affecting the fate of faecal diversion in patients with perianal Crohn's disease. *Colorectal Dis* 2015;17(01):66–72
- 77 Mennigen R, Heptner B, Senninger N, Rijcken E. Temporary fecal diversion in the management of colorectal and perianal Crohn's disease. *Gastroenterol Res Pract* 2015;2015:286315
- 78 Bafford AC, Latushko A, Hansraj N, Jambaulikar G, Ghazi LJ. The use of temporary fecal diversion in colonic and perianal Crohn's disease does not improve outcomes. *Dig Dis Sci* 2017;62(08):2079–2086
- 79 Martí-Gallostra M, Myrelid P, Mortensen N, Keshav S, Travis SP, George B. The role of a defunctioning stoma for colonic and perianal Crohn's disease in the biological era. *Scand J Gastroenterol* 2017;52(03):251–256
- 80 Ultee JM, Lagaay EL, Lens J. Results of split-ileostomy in Crohn's disease of the colon. *Neth J Surg* 1981;33(04):181–185