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Surgical management of pediatric Crohn's disease

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ABSTRACT

Management of pediatric-onset Crohn's disease uniquely necessitates consideration of growth, pubertal development, psychosocial function and an increased risk for multiple future surgical interventions. Both medical and surgical management are rapidly advancing; therefore, it is increasingly important to define the role of surgery and the breadth of surgical options available for this complex patient population. Particularly, the introduction of biologics has altered the disease course; however, the ultimate need for surgical intervention has remained unchanged. This review defines and evaluates the surgical techniques available for management of the most common phenotypes of pediatric-onset Crohn's disease as well as identifies critical perioperative considerations for optimizing post-surgical outcomes.

Introduction

Crohn's disease (CD) is a chronic inflammatory condition which manifests as progressive intestinal damage in predisposed individuals with unknown environmental exposures.[1–3] Although the exact etiopathogenesis remains elusive, there is evidence for 71 susceptibility loci on 17 chromosomes which results in intestinal immune dysfunction and abnormal interactions with typical symbiotic intestinal commensal microbiota.[1,4,5] This ultimately produces the characteristic patchy intestinal luminal inflammation which can progress to intestinal stricture, perforation and/or fistula formation, anywhere from mouth to anus.

As many as 25 % of patients diagnosed with inflammatory bowel disease (IBD) are younger than twenty years-old, and pediatric incidence is known to be increasing.[6,7] Prevalence estimates for CD range from 31 to 71 per 100,000 individuals younger than 20 years-old.[7,8] Infantile and very early onset disease, defined as onset prior to two and six years-old, respectively, are characterized by a particularly aggressive phenotype which often necessitates alternative management strategies compared to adult-onset CD.[9,10] Although adolescent-onset CD is more phenotypically resemblant of adults, there remain unique considerations due to presentation during critical development, including the impact of malnutrition, impaired growth and pubertal delay, and increased risk of psychosocial and educational challenges.[9,11] Furthermore, risk of surgical resection by the age of 30 is 43-53 % in pediatric-onset disease as compared to 12-16 % of those with adult-onset.[12]

With the development of biologic and immunomodulator therapies, research is shifting to understanding the new role of surgical therapy in this new clinical landscape.[1] Furthermore, as advances in minimally invasive surgery (MIS) are made and technique modifications introduced, it becomes increasingly important to define the breadth of surgical options available. The purpose of this review is to define surgical indications and discuss important perioperative considerations for optimizing surgical outcomes as well as to describe and appraise the surgical armamentarium available for the management of pediatric-onset CD.

Preoperative considerations

Surgical indications

In pediatric-onset CD, surgical intervention is necessitated in three principal circumstances—failure of medical therapy, growth failure, and

Abbreviations: CD, Crohn's disease; ECCO, European Crohn's and Colitis Organization; EEN, exclusive enteral nutrition; ESPGHAN, European Society of Pediatric Gastroenterology, Hepatology and Nutrition; ERP, enhanced recovery protocol; IBD, inflammatory bowel disease; IPAA, ileal pouch anal anastomosis; MIS, minimally invasive surgery; SILS, single incision laparoscopic surgery; TNF, tumor necrosis factor; UC, ulcerative colitis; VTE, venous thromboembolism.

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management of disease complications. Inadequacy of medical therapy may manifest as the escalation of symptoms despite optimized maintenance therapy or the development of antibodies to biologics rendering them ineffective. Furthermore, avoidance of long-term corticosteroid dependence is essential in children due to metabolic consequences and deleterious effects on skeletal maturation which can result in permanent growth delay.[13–16] Unique to pediatric-onset disease is the negative impact of prolonged disease activity on growth and development secondary to chronic undernutrition and prolonged exposure to proinflammatory cytokines.[13,17,18] Growth failure is best evaluated by height-for-age standard deviation (Z) scores with discrepancies in growth velocity over a period of 3-4 months.[13] Active disease during the pubertal growth spurt can diminish final adult height, and if surgical intervention for poorly controlled disease is delayed, poor catch-up growth may result.[13,19,20] As such, surgery should be considered as a means of inducing remission in early or mid-puberty for patients with growth failure.[13]

In both prospective and clinical evaluations, tumor necrosis factor (TNF) alpha inhibitors have demonstrated the ability to achieve clinical remission and mucosal healing in both luminal and fistulizing disease.[21] As biologics advance, new treatment goals include the use of early aggressive medical therapy in select patients with factors predictive of a poor prognosis.[21] In light of these advances, the disease course of pediatric CD has been dramatically altered; however, the ultimate need for surgical intervention remains consistent across an individual's disease course.[9] Representative of this, time from diagnosis to first operation has increased from 3.5 to 11.5 years. Moreover, there is a paradigm shift from control of active disease to resection of chronic strictures in terms of the most common surgical indication.[22]

Surgical optimization

As biologics are increasingly used for induction and maintenance, it is essential to understand the impact of perioperative biologic administration on post-surgical outcomes for those who warrant intervention. At present, evidence remains limited in children, although single center studies support no difference in postoperative complication rates with preoperative infliximab use.[23,24] Meta-analyses confirm these findings but are not specific to pediatric disease.[25,26] As such, current practice recommendations endorse avoiding TNF-alpha inhibitors for 4-6 weeks before elective surgery with resumption 1-3 weeks after.[27] Studies regarding the impact of newer biologics, such as vedolizumab, are power-limited but have not demonstrated significant difference in postoperative complication rates while studies regarding the impact of perioperative Ustekinumab are absent in children.[28–30] Similarly, there is conflicting and limited evidence regarding the risk of perioperative immunomodulator administration; however, it is suggested to discontinue treatment for a minimum of one week prior to surgery to reduce infection risk.[27] More defined is the dose-dependent relationship between corticosteroid use and postoperative complication risk.[31] Therefore, for patients on high-dose corticosteroids prior to surgery, a rapid taper should be performed to the lesser of 20 mg or 0.5 mg/kg daily if unable to be discontinued altogether.[30,32]

As weight loss is present in 8-23 % and poor growth is present in 7-9 % of new-onset pediatric CD, nutritional optimization is a fundamental consideration in both need for and timing of surgery.[33] Poor nutritional state at time of intervention is associated with increased risk of postoperative complications in addition to a 3.3-5.5 day increase in postoperative length of stay.[34–37] The use of exclusive enteral nutrition (EEN) not only improves a child's nutritional state but also attenuates inflammation which enables steroid-weaning and may delineate strictured bowel from that which appears narrowed due to active inflammation.[38] As 70-80 % of patients respond to initial treatment with EEN, with clinical response as vigorous as that to corticosteroid-induction therapy and with superior mucosal healing, the European Crohn's and Colitis Organization (ECCO)/European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) 2014 consensus guidelines recommend 6-8 weeks of EEN as the first line induction therapy over steroids for inflammatory intestinal luminal CD.[9,39–44] However, evidence for EEN in severe isolated pancolitis, penetrating or stricturing phenotypes, and isolated oral or perianal disease is supportive but limited.[39,45] EEN is further limited by poor tolerance in children who may necessitate temporary feeding tube placement for compliance. Furthermore, partial enteral nutrition, which allows a percentage of daily intake to remain a regular diet by mouth, has clear inferiority to EEN.[46]

Surgical management

Small bowel and ileocolonic resections

Disease activity in pediatric CD most commonly (53%) presents in a patchy distribution in both the ileum and colon while 16% have isolated ileocecal disease and only 4% have disease isolated proximal to the terminal ileum.[47] In patients with limited active small bowel or ileocolonic disease, segmental resection to grossly negative margins is sufficient, rarely requiring proximal diversion. Within the adult literature, the type of anastomosis has been found to impact short and long-term outcomes though with inconsistent results across studies.[48–55] There is little prospective evidence specific to ileocolic anastomoses in patients with CD. However, a systematic review which included patients with either CD or colorectal cancer found the stapled side-to-side anastomosis reduced anastomotic leak rates though only two studies were specific to CD and their sub-analysis was without difference in outcome.[48,56,57] A meta-analysis of 11 studies, of which 5 were prospective, and a cumulative 1113 adults with CD compared the two anastomotic approaches when performed for any intestinal anastomosis and found the stapled side-to-side to be superior to the hand-sewn end-to-end with regard to disease recurrence rates and need for reoperation; however, without difference in short term complications including anastomotic leak.[58] Even still, as many as 30% of patients have clinical recurrence within 24 months after surgery following a stapled side-to-side anastomosis creating space for outcome optimization.[59]

First described in 2011, the Kono-S anastomosis is constructed by stapling the diseased segment in such a way that the mesentery is perpendicular to the axis of the staple line. The proximal and distal bowel ends are then sutured to each other to create a supporting column for the new anastomosis at the mesenteric border. Longitudinal enterotomies on the anti-mesenteric surface on either side of the supporting column are reapproximated transversely resulting in a hand-sewn side-to-side, functional end-to-end anastomosis with a wide-diameter lumen (Fig. 1).[60] The underlying supporting column is thought to protect the anastomosis from distortion while maintaining a large luminal diameter and preventing alterations of the fecal stream which may contribute to recurrence.[61–64] Furthermore, the blood supply and innervation are preserved which promotes anastomotic healing and the isoperistaltic orientation permits ease of endoscopic surveillance. The first randomized controlled trial comparing the Kono-S to the stapled side-to-side anastomosis demonstrated lower endoscopic recurrence at 6 months and lower clinical recurrence at 24 months, and an on-going trial will compare up to 60 months postoperatively.[59,65] Meta-analysis of the nine studies published to date which compare Kono-S to conventional anastomoses supports decreased surgical recurrence and 5-year surgery-free survival but notably without any difference in endoscopic recurrence rates.[59,60,66–73]

As the first area of microscopic recurrence is typically the mesenteric aspect, the mesentery is suspected to be a major contributor to the pathophysiology of CD.[74] This lead to a new approach to ileocolonic resection where, in contrast to the Kono-S anastomosis which employs the mesentery for augmented anastomotic support, the mesentery is radically excised. Supported by a retrospective analysis demonstrating decreased surgical recurrence relative to stapled side-to-side with

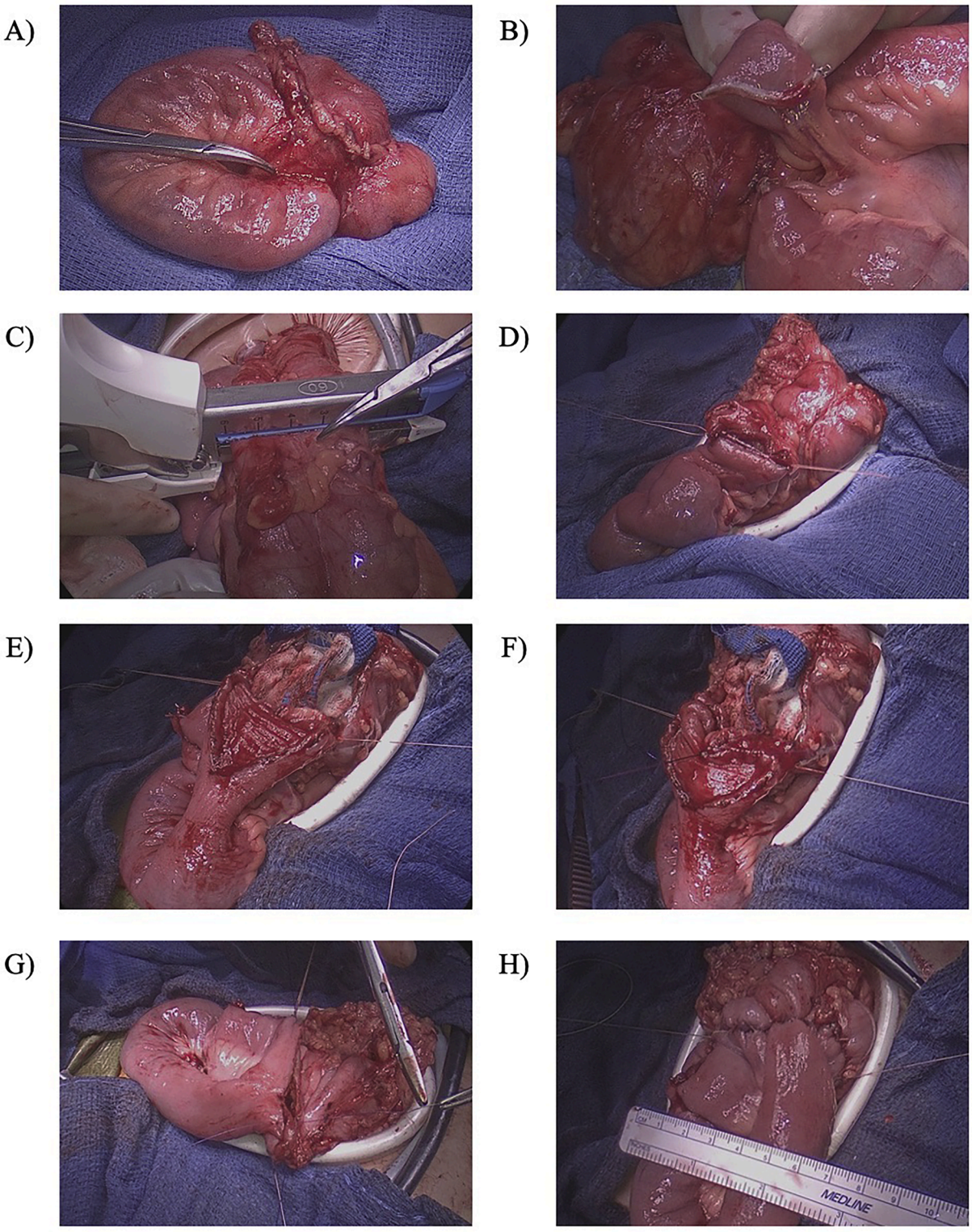

Fig. 1. Ileocectomy with Kono-S anastomosis for Crohn's ileal-ileal fistula. A) Exteriorized small bowel and cecum with instrument pointing to an ileal-ileal fistula. B) Stapled-off proximal ileal resection margin with small bowel mesentery 90 degrees to the staple line. C) Distal resection margin at the mid-ascending colon with taenia coli at mid staple line to ensure the mesentery is 90 degrees to the staple line. D) Creation of the supporting column by suturing together the stapled-off ileum and colon. E) Anti-mesenteric longitudinal enterotomies made 1 cm from the supporting column. F) Inside layer of the running-locking diamond anastomosis. G) Outside layer of the running-locking diamond anastomosis. H) Completed anastomosis with a 7 cm transverse luminal diameter.

limited mesenteric resection, a randomized controlled trial in patients aged 16-65 years-old is currently underway.[75,76] Notably, studies specific to the pediatric population which compare outcomes following the hand-sewn end-to-end, stapled side-to-side, Kono-S or radical mesenteric resection are absent and are an important area for future research.

Small bowel strictures

Stricturing intestinal disease is now the most common indication for surgical intervention in CD.[22] A systematic review encompassing 14 studies and 177 patients with stricturing pediatric-onset CD demonstrated that while 8% of patients will have a complete response to medical therapy alone, 38% undergo resection, 28 % strictureplasty and 12% endoscopic balloon dilation. However, despite no difference in postoperative complication rates, not all interventions provide equivalent outcomes. Recurrence rates associated with resection (9 %) were much less compared to strictureplasty (38 %) and endoscopic balloon dilation (47 %).[77] However, as pediatric patients have a 50 % incidence of second surgical intervention, intestinal sparing must be balanced with postoperative disease control.[9] As such, careful consideration and counseling regarding the management strategies available must be provided to each child and their caregivers.

Strictureplasty is typically performed for bowel preservation in patients with concern for short bowel syndrome, in addition to duodenal strictures, and rapidly recurrent strictures at a previous ileocolonic or ileorectal anastomosis.[78,79] Contraindications to strictureplasty include concurrent bowel perforation, malnutrition, multiple short strictures over a small length of bowel or a stricture close to an area which warrants resection.[78] Multiple approaches to strictureplasty exist with the appropriate type dictated by stricture length, number and their proximity to each other. The Heineke-Mikulicz strictureplasty is best suited for isolated, short strictures (< 10 cm) and is performed by longitudinal enterotomy along the anti-mesenteric surface centered over the strictured segment and extended proximal and distal to incorporate healthy bowel. The enterotomy is then closed transversely to widen the intestinal lumen (Fig. 2).[80,81] For medium length strictures (10-20 cm), the Finney strictureplasty is preferred and is performed by folding the involved bowel onto itself and creating an entero-enterostomy between the loop (Fig. 3); however, at the expense of leaving an area of diverticulated bowel which can serve as a reservoir for fecal stasis and disease recurrence.[78] The side-to-side isoperistaltic (Michelassi) strictureplasty was introduced to address long (>20 cm) strictured intestinal segments as well as areas of bowel with multiple strictures in close proximity—indications for intestinal resection prior to the mid 1990s.[82,83] This approach begins with mesenteric and intestinal division at the midportion of the strictured intestine with added resection of any particularly fibrotic strictured intestinal segments if indicated. The proximal intestinal segment is then brought adjacent to the distal segment so they are aligned side-to-side with seromuscular interrupted sutures. Longitudinal enterotomies on both loops of bowel with spatulation at the ends avoids blind stumps upon completion of the anastomosis (Fig. 4).[82,84,85] Since its introduction, variations of the Michelassi have been reported including the Michelassi II (the end-to-side-to-side-to-end strictureplasty) which is indicated in the albeit more rare but rather complicated, situation in which patients with three areas of stenosis are separated by two diseased segments with sequential strictures.[86]

Although results with endoscopic balloon dilation are inferior, the benefits of avoiding surgery in pediatric CD are significant. In a recent case series, advanced endoscopists placed fully-covered lumen-apposing metal stents in two patients with ileocolonic stricture and one patient with a duodenal stricture and mucosal tear. All three patients had symptom resolution with stent time in place ranging from 21-300 days.[87] In the future, it will be imperative to evaluate long-term recurrence rates following stent removal.

Colonic disease

Due to the typically aggressive nature of colonic CD, high incidence of relapse and non-essential function of the colon for nutrition, some have supported subtotal colectomy over segmental resection for all colonic disease.[9,88,89] However, with segmental resection, patients experience better anorectal function, fewer loose stools and have the potential to avoid permanent ileostomy without increasing need for future resections.[9,90] Therefore, at present the extent of resection is dependent upon disease distribution. In children it has been found that disease proximal to the left colon is suitable for segmental resection and primary anastomosis, while for disease distal to the transverse colon, outcomes are improved by subtotal colectomy or total proctocolectomy.[91] Those who have pancolitis with rectal sparing require subtotal colectomy with ileorectal anastomosis. However, an ileorectal anastomosis is predictive of anastomotic failure; therefore, these patients should receive temporary diverting ileostomy.[89] Furthermore, the presence of anorectal disease at time of ileorectal anastomosis is the best predictor of ileorectal anastomotic failure.[27,92]

If pancolitis or severe rectal disease is present, a total proctocolectomy with end ileostomy is warranted. Though, due to success experienced in ulcerative colitis (UC), discussions are emerging regarding a potential role for ileal pouch anal anastomosis (IPAA) for reconstruction in select CD patients without ileal or perianal involvement. However, CD places patients at significant increased risk for pouch failure. In a multicenter retrospective analysis performed by ESPGHAN including 111 patients with UC who underwent IPAA, 17% developed de novo CD at 3-61 months post-IPAA. Yet, only 26% of those with de novo CD ultimately required definitive ileostomy.[93] Conversely, when evaluating long-term pouch survival in patients with CD or indeterminate colitis,

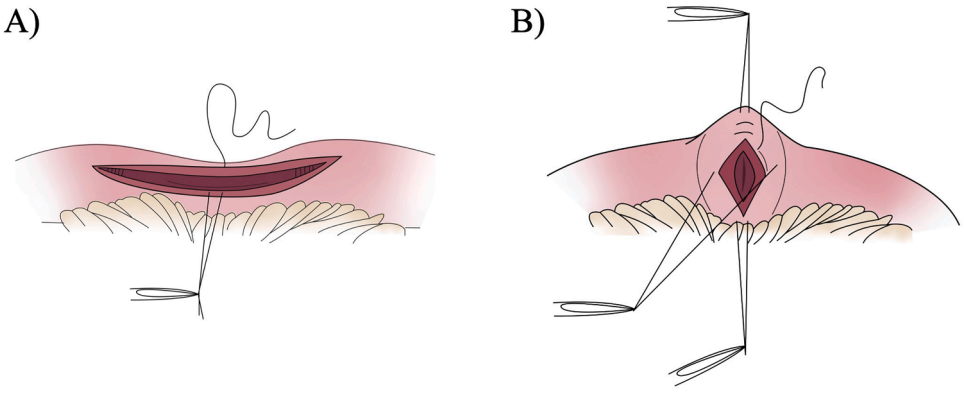

Fig. 2. Heineke-Mikulicz strictureplasty. A) An anti-mesenteric longitudinal enterotomy overlying the strictured bowel segment is performed. B) Transverse enterotomy closure widens the bowel lumen.

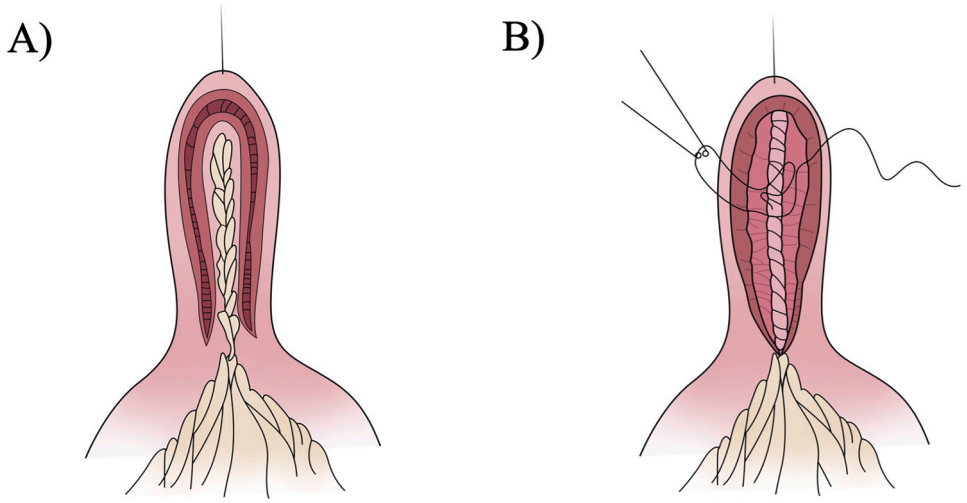

Fig. 3. Finney strictureplasty. A) The strictured bowel segment is folded back on itself. B) A side-to-side anti-peristaltic entero-enterostomy is performed between the strictured bowel loop.

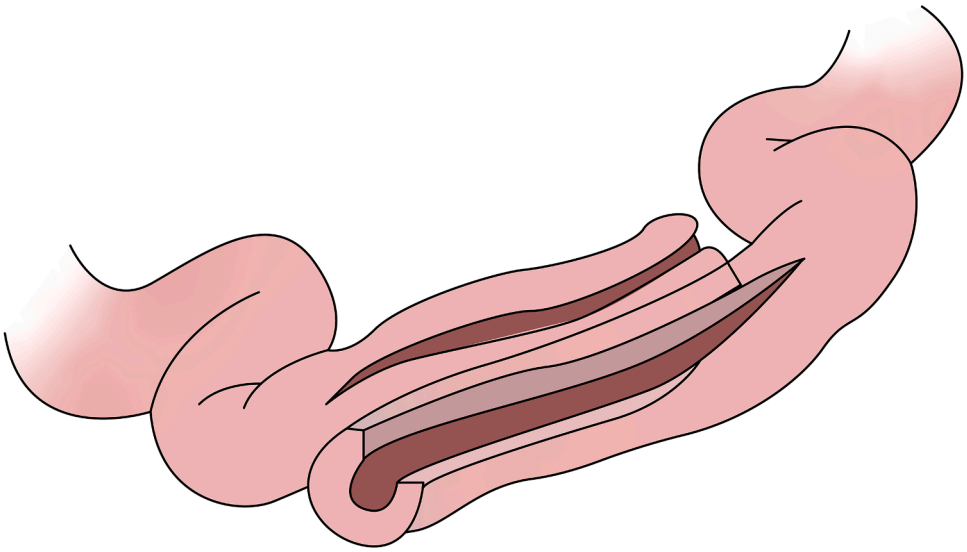

Fig. 4. Michelassi strictureplasty. Mesenteric and intestinal division is performed at the midportion of the strictured intestine with resection of fibrotic intestinal segments as indicated. The proximal intestinal segment is brought adjacent to the distal segment so they are aligned iso-peristaltic and longitudinal enterotomies are made with spatulation at the ends. A side-to-side isoperistaltic anastomosis is performed.

outcomes are increasingly inferior compared to patients with UC at five, ten and twenty years follow-up with a 61% pouch survival rate at twenty years compared to 92% for UC.[94] Furthermore, diagnosis of CD of the pouch has been associated with a five-fold increased risk of pouch failure compared to patients with IPAA without CD.[95,96] However, children rate their quality of life highly after undergoing IPAA despite experiencing complications such as increased stool frequency and urgency.[97] With the available evidence, extreme caution should be pursued if considering IPAA reconstruction in children with CD; however, the suitability of IPAA should not be excluded due to the impact on patient quality of life. With continued advancement of medical therapy, disease control may be sufficient for CD patients to undergo this procedure more routinely. Notably, as many as 13% of patients with UC who undergo IPAA develop CD-like complications, including, prepouch ileitis, perianal/internal fistula formation or proximal small bowel strictures.[98,99] Evidence supports infliximab's ability to achieve control of CD-like IPAA pouch complications with 45%-72% 12 month remission rates in adults and a successful case series in children and could potentially be useful in patients with CD who undergo IPAA.[100,101]

Minimally invasive surgery

With MIS advances and the appeal of improved cosmesis, decreased postoperative narcotic use, and shorter recovery times, laparoscopic-assisted techniques for bowel resection have become the recommended first-line surgical approach in adults.[102–106] However, slower adoption of MIS in children has prevented establishment of similar recommendations in pediatric CD. Evidence in support of laparoscopic small bowel and colonic resections in children is increasingly available.[107–114] Retrospective single-institution studies have found no difference or less postoperative complication rates alongside decreased days on intravenous narcotics, faster return to a regular diet and/or shorter postoperative length of stay.[107,112,113,115] However, it should be noted that disparities in use of laparoscopy have been demonstrated. Evaluation of the Nationwide Readmissions Database from 2010-2014, including 2,833 patients who underwent right or total colectomy, found the laparoscopic approach was more commonly employed for those with private insurance and within the highest income quartile despite no difference in hospital costs.[114]

Single incision laparoscopic surgery (SILS) has been described primarily for ileocecectomy in children.[108–110] In this technique, a wound protector and SILS port are placed through a 3 cm vertical trans-umbilical incision. Through the SILS port, three 5 mm ports are inserted. After mobilization, the bowel is eviscerated for resection and a stapled side-to-side anastomosis is created.[110] The bowel is eviscerated through the wound protector, and theoretically can reduce rates of superficial wound infections. However, only one study comparing SILS to open bowel resections has been performed for pediatric CD which demonstrated no difference in postoperative length of stay or complication rates. Furthermore, operative times were overall longer for the SILS cohort, but likely secondary to a learning curve as the more recent SILS cases were of the same duration as open.[110] As additional experience with the SILS technique accumulates, further comparisons will be necessary to open and conventional laparoscopic resections to understand if there is a role for SILS in the management of pediatric CD.

Adult colorectal surgeons have widely adopted robotic-assisted surgery due to several advantages over both open and laparoscopic surgery, particularly in individuals with a narrow pelvis who necessitate low rectal dissection. In addition, the robotic platform offers tremor reduction and a three-dimensional camera with magnification and operator control. Furthermore, the dexterity provided by the articulating instruments enables the performance of intracorporeal bowel anastomoses.[116–118] In a study comparing robotic to laparoscopic colectomy in children with IBD, 75% of robotic versus 58% of laparoscopic anastomoses were performed intracorporeal. However, postoperative intra-abdominal abscesses only occurred in patients with CD and all underwent intracorporeal anastomosis with equal distribution between laparoscopic and robotic. Furthermore, there was no difference in operative times when comparing the same colectomy type nor was there difference in postoperative length of stay while robotic colectomy resulted in increased operative costs.[118] Therefore, the benefits of robotic surgery in pediatric CD may be confined, at present, to the superior visualization and mobilization capabilities afforded in the pelvis.

Perianal Crohn's Disease

Perianal CD has wide-ranging manifestations; including benign skin tags, fistulae, abscesses, anorectal strictures, or skin breakdown; and is associated with an overall poor prognosis (Fig. 5).[119] All patients with perianal manifestations should undergo a formal exam under anesthesia, including a digital rectal exam and lower endoscopy for mucosal assessment. Magnetic resonance imaging of the pelvis/perineum has 76-100% accuracy in defining abscesses and fistulae and is important to consider prior to proceeding to the operating room.[120,121] Any abscesses present should be fully drained. If fistulous tracts are identified, their tract should be defined if able with the knowledge that they may not follow the distribution described by Goodsall's rule.[120] While asymptomatic simple fistulas can be monitored closely, for all others best results are achieved with placement of a **noncutting** seton combined with infliximab administration (Fig. 6).[122–125] Cutting setons should be avoided due to the risk of damage to the anal sphincter.[126] Delayed fistula healing has been associated with fistulotomy, fistulectomy or lesion removal while faster fistula healing is associated with treatment with anti-TNF-alpha therapy.[127] However, the use of infliximab alone does not prevent ultimate need for surgery supporting an aggressive early surgical approach.[9,128] Furthermore, fistulotomy is associated with high risk of fecal incontinence. However, a "cone-like fistula resection" has demonstrated promise in complex perianal pediatric CD when accompanied with anti-TNF-alpha therapy (Fig. 7).[129,130] In addition, direct injection of allogeneic bone marrow-derived mesenchymal stromal cells into fistulous tracts has been shown to be effective in randomized trials performed in adults, though evidence in the pediatric population is not available at present.[131–134]

For those with severe and uncontrollable disease despite maximal medical therapy and local surgical management, diverting ileostomy is warranted; however, this often results in permanent ileostomy.[27,126] In a study of complex pediatric perianal disease, of those who required ileostomy, 50 % proceeded to need additional interventions including subtotal colectomy, proctocolectomy, and complex reconstruction with perineal flap/graft.[135]

Low rectal and anal strictures can be managed with serial transanal dilations with Hegar dilators either in the operating room, office or at home pending a patient's age and tolerance. Additional conservative options include endoscopic balloon dilation, and direct injection of steroids or TNF-alpha inhibitors.[136,137] In a small cohort, augmentation of endoscopic balloon dilation with four quadrant steroid injections decreased stricture recurrence rates to 10 % from 31 %.[136] However, perforation rates as high as 10% have been reported and use is quite limited in the instance of long rectal strictures.[136] Short refractory strictures have been successfully managed with transanal anorectal Heineke-Mikulicz strictureplasty (Fig. 2) while long rectal strictures can be managed with proctectomy with proximal diversion or transanal resection with coloanal anastomosis.[27,138,139] However, in patients with low rectal strictures sphincter presentation is essential for continuity to remain an option. As such, fundamentals adapted from transanal dissection techniques for Hirschsprung disease pull-through procedures have been reported in a small case series. In three patients with low strictures, transanal sphincter preserving dissection was coupled with intraabdominal mobilization (by laparoscopy or laparotomy) and rectosigmoid resection. This was followed by pull-through for coloanal anastomosis in two and end ileostomy in the third patient; however, with anal sphincteric preservation the option of intestinal continuity remains an option for all three patients in the future.[139]

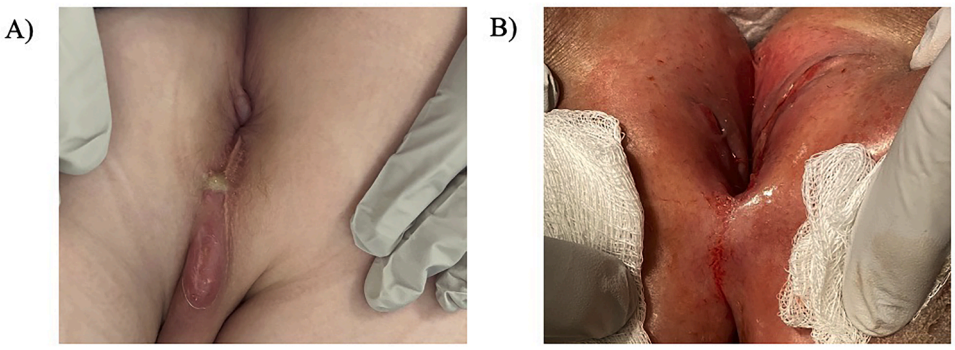

Fig. 5. Perianal Crohn's disease. A) Perianal abscess located at the anterior midline surrounded by skin denudation and a perianal skin tag at the posterior midline. B) Multiple perianal fistulas, anterior midline fissure and surrounding chronic inflammation of the perineum.

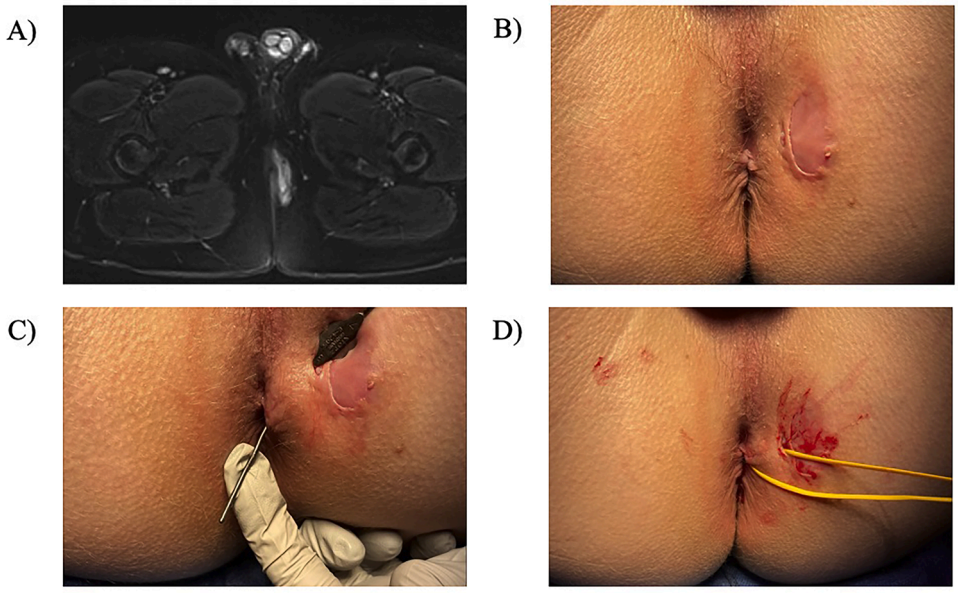

Fig. 6. Perianal fistula managed with noncutting seton. A) Magnetic resonance enterography demonstrating a perianal fistula arising from the 1:00 position of the "anal clock" and extending caudally along the natal cleft to the skin surface with inflammatory signal surrounding the fistula. B) External opening of the perianal fistula is located several centimeters from the anal verge. C) Fistula probe defining the fistula tract. D) Seton is left in place without tension to avoid damage to the sphincter complex.

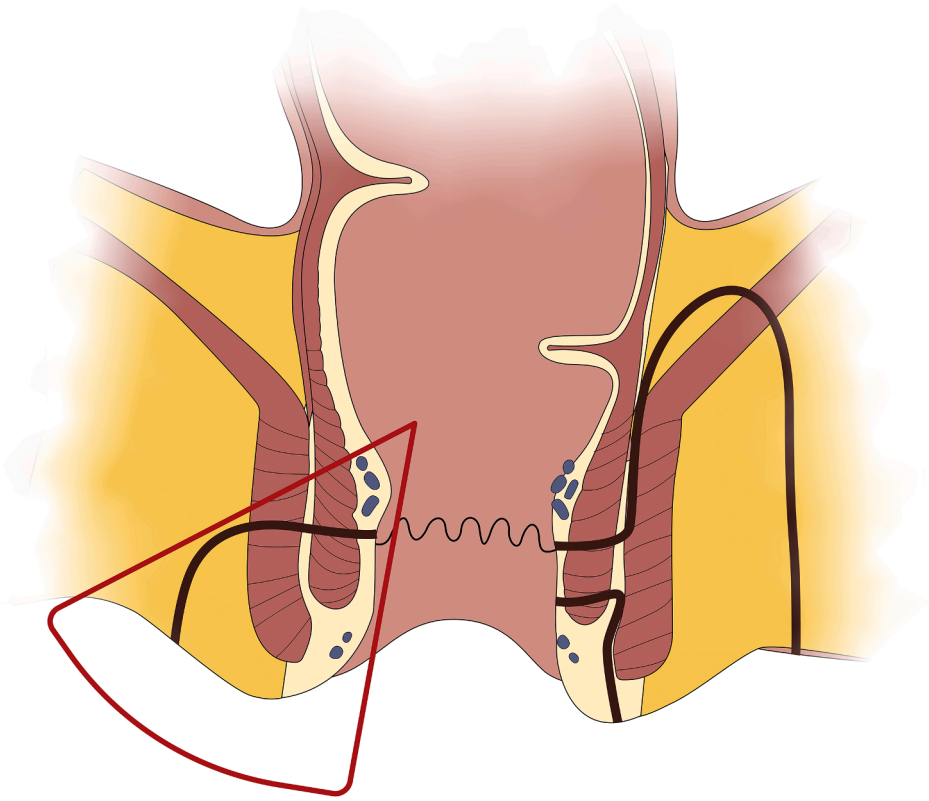

Fig. 7. Cone-like fistula resection. When combined with anti-TNF-alpha therapy, the cone-like fistula resection (red) has demonstrated promise for complex perianal fistula resection while preserving sufficient internal and external sphincter muscle to maintain fecal continence. The maroon lines demonstrate various fistulas possible: transsphincteric (left within the cone-like resection margins), suprasphincteric (right superior), and intersphincteric (right inferior). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Postoperative considerations

Enhanced recovery protocols

Enhanced recovery protocols (ERPs) are a collection of standardized interventions with demonstrated improvements in postoperative outcomes, resource utilization and patient satisfaction while expediting recovery.[140,141] Widespread adoption in adult colorectal surgery has demonstrated decreased complication rates, opioid utilization, length of stay and hospital costs; however, there is a lack of utilization of ERPs in pediatric surgery with less than 20 % of surveyed pediatric surgeons reporting full ERP implementation.[141–148] A previous study compared adults undergoing elective IBD surgery with ERP in place to pediatric patients without ERPs and demonstrated greater time to mobilization, time to a regular diet and length of stay when ERPs are not applied.[149] In addition, outcomes pre- and post-ERP implementation alongside a multidisciplinary pediatric IBD clinic demonstrated significant decreases in 30-day emergency department visits (27% to 9%) and 30-day readmissions (24% to 2%).[150] Furthermore, decreased intraoperative fluid and perioperative opioid administration, time to regular diet and length of stay has been shown post-ERP implementation for pediatric patients.[151] At present, a multi-institutional trial is underway during which a 21 element ERP for IBD elective surgery will be implemented at 18 pediatric institutions (Table 1).[152]

Venous Thromboembolism Prophylaxis

Regardless of age, pediatric patients with IBD are at significant increased risk of venous thromboembolism (VTE) relative to pediatric patients without IBD.[153] The five-year incidence of VTE in children with IBD has been shown to be 24-41 per 10,000 person years compared to 0.4-1.7 per 10,000 person years in non-IBD children.[154] VTE risk is greater for patients with active inflammation, who are hospitalized or undergoing surgery, with reduced mobility, central venous catheter in place, or underlying thrombophilia.[155] Interestingly, a protocol for VTE prophylaxis in IBD patients with acute flare and CVC was found to result in both increased doppler ultrasound performance and increased diagnosis of VTE which is a suspected result of missed VTE prior to protocol implementation.[156] Likewise, an international multidisciplinary panel convened to determine indications for VTE prophylaxis administration for hospitalized pediatric IBD patients. They determined all pediatric patients with CD and one or more risk factor for VTE should receive chemical prophylaxis while hospitalized. However, despite surgery being agreed upon as a VTE risk factor, consensus was not achieved regarding the appropriateness of the panel to determine whether VTE prophylaxis should be administered to surgical patients.[157] However, evidence in adults has demonstrated that chemical prophylaxis administration is not associated with major postoperative bleeding or other bleeding events.[158,159] In addition, a retrospective single institution study including 974 hospitalized adults with IBD found VTE prophylaxis was nearly four times more likely to be administered to a patient on the surgical service than the gastroenterology service due to the presence of established protocols for its administration for surgical patients.[159] At present, evidence evaluating the impact of thromboprophylaxis on operative bleeding and VTE incidence in surgical pediatric CD patients is non-existent. However, thromboprophylaxis is becoming more common in the perioperative care of pediatric IBD patients and will be a component of the aforementioned ERP protocol; therefore, it will be essential to delineate.[152]

Conclusion

CD can result in significant morbidity and diminished quality of life for patients of all ages; however, pediatric-onset CD demands unique considerations regarding a patient's growth, pubertal development and psychosocial function and their increased need for surgical interventions.[160] Although advances in medical therapy have significantly altered the disease course for CD, ultimate need for surgical intervention remains unchanged.[9,22] Surgical advances have been complimentary in improving rates of disease recurrence while decreasing postoperative morbidity. However, research in pediatric CD management has lingered behind their adult counterpart necessitating the extrapolation of data from adult studies. As many adult-proven advancements to the care of patients with CD are being implemented for the care of pediatric-onset CD, their expeditious evaluation is warranted.

Table 1
Preoperative, intraoperative and postoperative elements included in the enhanced recovery protocol for elective surgery for inflammatory bowel disease.[152]

Preoperative	Intraoperative	Postoperative
Patient/family education and engagement	Venous thromboembolism prophylaxis	No intraperitoneal/ perianastomotic drains
Patient Advocate Liaison (PAL)	Pre-incision antibiotic prophylaxis	Goal-directed/near-zero fluid therapy
Provider education	Standardized anesthetic protocol	Avoiding or early removal of urinary drains
Optimize medical comorbidities	Surgical procedure (i.e., minimally invasive techniques)	Prevention of ileus through gut stimulation
Avoid prolonged fasting	Prevention of nausea/ vomiting	Opioid-sparing pain regimen
Administer non-opioid analgesia	Avoid nasogastric tubes	Early oral nutrition
	Standardized hypothermia prevention	Early mobilization
		Audit protocol compliance/outcomes

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