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## Surgical Management of Inflammatory Bowel Disease

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### Introduction

Inflammatory bowel disease (IBD) is a spectrum of inflammatory conditions, including ulcerative colitis (UC) and Crohn's disease (CD). Although IBD primarily affects the intestinal tract, extraintestinal manifestations, such as musculoskeletal, ophthalmologic, and cutaneous conditions, are common. Over 1.6 million Americans carry a diagnosis of IBD and worldwide prevalence rates continue to rise over time.<sup>1</sup> Despite major advances in medical management, surgery continues to play a supportive and complementary role in the treatment of IBD.<sup>2, 3</sup> Between 20–40% of UC patients and up to 75% of CD patients will require surgery in their lifetime, with most operations taking place due to either failure of medical management or disease complications, such as fulminant colitis, intestinal obstruction, infection/fistula, or neoplasia.<sup>3</sup> This review will focus on several advances in management of IBD from the surgical perspective.

### Trends, Indications, and Timing of Surgery in the Biologic Era

Whether or not surgery for IBD has become less common as medical management improves remains complex and somewhat unclear. Several large cohort studies appear to demonstrate a reduction in colectomy rates among UC patients over time that coincides with an increased use of immunomodulatory and biologic medications.<sup>4–6</sup> Among hospitalized patients with severe UC, infliximab has been associated with a significant reduction in the risk of colectomy in multiple randomized trials.<sup>7, 8</sup> However, several population-based studies have found both no difference in the long-term risk of colectomy and no change in emergency colectomy rates over time, suggesting that biologics may be more useful in shifting urgent procedures to elective setting rather than obviating the need for surgery altogether.<sup>9–11</sup> Interestingly, one large institutional sample and several nationwide cohort studies have demonstrated an increase in the proportion of colectomies performed for either dysplasia or cancer, again suggesting that medical management may lead to better short-term but not necessarily longer-term disease control.<sup>12–14</sup>

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Rates of surgical resection among patients with CD also appear to be decreasing over time and in conjunction with an increased use of biologic medications.<sup>9, 15</sup> Several authors note, however, that changes in surgery rates also parallel changes in other potential confounding factors, such as disease severity at diagnosis and cigarette smoking, making causal links less certain. At least one nationwide cohort study also found that, while primary resection rates dropped by nearly two-thirds, secondary resection rates remained unchanged, suggesting that some patients either remain refractory to medical therapy or experience decreasing efficacy over time.<sup>15</sup> Although multiple clinical trials have demonstrated an association between biologics and lower rates of anal fistula surgery, similar trends have not necessarily been reproduced in population-based studies.<sup>9, 16–19</sup>

The impact of biologics on surgical complication rates also remains hotly debated. Multiple retrospective, single institution studies have demonstrated mixed results, leading to confusion and conflicting recommendations.<sup>20–22</sup> Recent results from the PUCINI trial, however, finally provide some clarity, at least for anti-TNF medications. Based on a prospective cohort of patients undergoing abdominal surgery for either UC or CD at 17 U.S. centers, Cohen et al. report no difference in either overall infection or surgical site infections rates between patients with recent a exposure to anti-TNF agents (within 12 weeks of surgery) and controls.<sup>23, 24</sup> Moreover, patients with detectable anti-TNF levels appeared to have no increase in either overall or surgical site infection rates when compared to controls, calling into question prior theories regarding dose response rates. Armed with these results, many surgeons now choose to continue anti-TNF medications during the preoperative period or to time surgery based upon the medication's dosing interval. The peri-operative safety of newer biologic and small molecule therapies are still under investigation, although multiple studies on vedolizumab appear to show no clear increase in complication rates.<sup>25, 26</sup> Optimal timing for restarting patients on therapy after surgery and the associated prophylactic benefit of various therapies is less well established; most surgeons choose to restart biologic medications at 4 to 8 weeks after resection, depending on recovery and functional status.<sup>27, 28</sup>

## Enhanced Recovery Protocols

Enhanced recovery after surgery (ERAS) protocols have been a paradigm shift in perioperative management. Born out of the general colorectal field, ERAS protocols aim to promote faster recovery after surgery.<sup>29</sup> The encompassing approach focuses on preoperative counseling, nutrition optimization, standardized anesthetic regimens, multimodal pain control, and early initiation of mobilization and enteral nutrition.<sup>30</sup> As evidence has demonstrated improved outcomes in colorectal procedures, such protocols are being adopted in IBD patients.

The prehabilitation phase for scheduled procedures in IBD patients focuses on nutritional status and supplementation.<sup>31, 32</sup> The chronic inflammatory and malabsorptive state associated with IBD produces a high risk for malnutrition. Malnourished patients are at significantly higher risk for complications following surgical procedures.<sup>33, 34</sup> In elective procedures, guidelines recommend thorough assessment of nutritional status.<sup>31, 32</sup> For patients identified as being malnourished, surgery should be delayed, and nutritional

therapy initiated.<sup>31, 32</sup> Enteral therapy is generally preferred to parenteral nutrition unless contraindications exist.<sup>35</sup>

Patients in the ERAS protocol can have clear liquids up to 2 hours prior to anesthesia. Intravenous fluids are limited. Epidural analgesia is used, and premedication is withheld. Standardized multimodal pain regimens and anesthesia are used in the perioperative setting. Decompressive gastrointestinal tubes are not routinely placed, and oral intake is initiated as soon as patients recover from anesthesia. Patients are advanced to solid food as tolerated. Urinary catheters are removed on post operative day one and early ambulation is encouraged.<sup>29, 30</sup> Outcomes from ERAS protocol in ileocectomies for CD have demonstrated shorter return of bowel function, initiation of solid oral intake, and earlier discharge from the hospital.<sup>37, 38</sup>

## Minimally Invasive Surgery

Minimally invasive surgery has revolutionized intraabdominal procedures. The advantages of laparoscopic procedures in IBD has been supported in the past two decades of literature. In general, laparoscopic interventions are associated with decreased pain, ileus, and hospital stays when compared to open operations.<sup>39, 40</sup> Laparoscopic procedures have lower overall costs than open procedures in the IBD population.<sup>39</sup> Minimally invasive operations produce fewer adhesions compared to open surgeries which has increased importance for CD patients given the chronic nature of the disease and requirement for multiple operations.<sup>41</sup>

While it has been well established that the use of laparoscopy has resulted in shorter length of stay postoperatively, improved body image, decreased infertility rates, and decreased intravenous narcotic use among IBD patients, in recent years, the da Vinci robot (Intuitive Surgical, Sunnyvale, California) has become an increasingly popular and accepted modality in colorectal surgery for both benign and malignant conditions.<sup>42–48</sup> Many studies including meta-analyses have now reported equivalent safety and efficacy with a robotic approach in colorectal operations as compared to conventional laparoscopy.<sup>49</sup> The improved dexterity, visualization and ergonomics of the robotic platform have contributed to the surge in the adoption of the robotic platform. This trend of increased use has been seen in IBD surgery with many IPAA's in UC and segmental resections in CD now being performed on a robotic platform despite an increased cost and lack of haptic feedback.<sup>50–52</sup>

The most common operation performed in Crohn's disease is an ileocecal resection. A robotic approach allows the surgeon to perform an intracorporeal anastomosis (ICA), which has been associated with decreased rates of postoperative ileus and decreased incisional hernia rates since the extraction site can be moved off the midline.<sup>53–57</sup> An ICA also minimizes the amount of colon mobilization necessary, which allows the duodenum to remain in the retroperitoneum protected by the right colon and its mesentery. This is relevant in CD since most fistula to the duodenum in CD originate from recurrent ileal disease after an ileocolic resection. These can be quite difficult to treat. Thus, by avoiding mobilization of the ascending colon, rates of fistula to the duodenum may be decreased.<sup>58</sup>

While there are a limited number of published series of a robotic approach in CD, there are many more for UC given the most common operation involved a pelvic dissection, proctectomy, with IPAA. Several series have shown a robotic approach is safe with equivalent short term postoperative outcomes to a laparoscopic approach.<sup>59–61</sup> A case-matched comparison of robotic versus laparoscopic proctectomy showed no difference in postoperative complications, and a trend toward improvement in conversion rate, time to bowel function, and LOS with the robotic approach.<sup>62</sup> An observational series including 81 robotic versus 170 open IPAA from a single institution described similar short-term outcomes with improved LOS in the robotic group, but longer operative times and higher readmission rates.<sup>63</sup>

Transanal total mesorectal excision (TaTME) refers to a retrograde laparoscopic approach combined with a transabdominal laparoscopic approach to remove the rectum. This technique was initially described and mainly utilized in the treatment of low rectal cancers.<sup>64</sup> It has the advantage of improved visualization of the natural planes in the pelvis especially in the narrow male pelvis. This approach to proctectomy has been embraced by highly trained and skilled surgeons but some recent reports of CO<sub>2</sub> embolism with this technique have led to concerns with this approach.<sup>65</sup> There have been individual case reports of laparoscopic total abdominal colectomy with TaTme and ileal anal pouch for ulcerative colitis.<sup>66</sup> Although these case reports are intriguing much more data needs to be collected before this becomes a recommended approach to this complex disease and should be considered experimental at this time.

While data on robotic surgery for CD and UC continues to evolve, the current studies that a minimally invasive approach to IBD offers benefits to the patient. The robotic platform presents improved visualization, instrumentation, and dexterity.

## Anastomotic Configurations

A critical component of bowel resections is the ensuing anastomosis. In CD this new connection is commonly the site of early disease recurrence.<sup>2</sup> Recurrence at the anastomosis can be as high as 35–85% when evaluated endoscopically, and recurrence requiring surgery can be up to 50% within 20 years.<sup>3, 67, 68</sup> Surgical techniques to reduce anastomotic disease recurrence and associated complications continue to be evaluated. In the general population, surgical staplers have demonstrated comparable outcomes to hand-sewn anastomoses, with some studies demonstrating lower leak rates after ileocolic resections.<sup>69</sup> Side-to-side anastomosis (STSA) are commonly performed using a stapled technique. In the setting of IBD, particularly in CD, the STSA may create a non-peristaltic reservoir that promotes early disease recurrence.<sup>70</sup> End-to-end anastomosis (ETEA) produces a more physiologic connection. Studies have demonstrated similar recurrence rates when comparing ETEA to STSA; but ETEA may produce improved quality of life, easier endoscopic evaluation, and less health care utilization.<sup>70</sup>

The Kono-S anastomosis was initially created by Dr. Toro Kono and colleagues in Japan in 2003 in an effort to reduce anastomotic recurrence.<sup>71</sup> The basis of the technique is an antimesenteric functional end-to-end anastomosis. The anastomosis has produced promising

results with surgical recurrence-free survival rates of 98.6% over a 10-year period.<sup>72, 73</sup> Theoretical benefits of the anastomosis include a supporting column to maintain diameter limiting stenosis.<sup>72</sup> It is a functional ETEA which allows for easier endoscopic monitoring and interventions if stenosis does occur.<sup>72, 73</sup>

## Mesenteric Resection in Crohn's Surgery

A significant volume of research has been conducted to determine how to prevent postoperative recurrence of CD following an ileocolic resection. Some studies have focused on the timing of resuming postoperative medical therapy. Others have looked at surgical techniques at the time of ileocolic resection including anatomic configuration of the anastomosis and performing a stapled versus handsewn anastomosis. Interestingly, there is recent evidence to suggest that CD may be a disease of the mesentery rather than just the mucosa of the bowel alone. In CD, the transmural inflammation facilitates increased bacterial translocation into the creeping fat. These translocating antigens and activate adipocytes which are cells that have complex metabolic and immunologic functions.<sup>75</sup> Additionally, it is thought that functional abnormalities in the mesenteric structures exert an inflammatory effect: the secretion of adipokines that have endocrine functions contribute to immunomodulation through a response to afferent signals, neuropeptides, and functional cytokines; mesenteric nerves are involved in the pathogenesis through neuropeptides; and lymphatics in the mesentery may obstruct, remodel, and impair contraction, contributing to the irregularly thickened mesentery seen in CD. Interestingly, the interaction between neuropeptides, adipokines, and vascular and lymphatic endothelia leads to adipose tissue remodeling. This makes the mesentery an active participant in CD, seemingly as much as the bowel itself.<sup>76</sup> However, the mesentery is typically spared, or left *in situ*, during resection for CD, unlike resections for adenocarcinoma of the colon where a high ligation is performed.

Findings from a retrospective review by Coffey et al spearheaded momentum to consider performing a high ligation in CD at the time of an ileocecal resection.<sup>77</sup> In this study, those patients who underwent a high ligation (n=34) compared to those with a mesenteric sparing approach (n=30) had a significantly lower rate of surgical recurrence (40% vs 2.9%; p=0.003). The mesenteric disease activity in this study predicted surgical recurrence, underscoring the relevance of the mesentery in driving disease recurrence.<sup>77</sup> This has prompted the initiation of several international multicenter randomized control trials to study this particular question of whether a high ligation at the time of ileocecal resection can reduce rates of disease recurrence following an ileocecal resection.

## Segmental Colectomy in CD

Although medically refractory Crohn's colitis has traditionally been treated with either subtotal colectomy (STC) or total proctocolectomy (TPC), there is growing interest in performing more limited resections, at least for select patients. Compared to STC or TPC, segmental colectomy (SC) allows for preservation of bowel length and function as well as, potentially, a lower likelihood of stoma formation. On the other hand, these benefits must be weighed against the risk and timing of disease recurrence as well as the possibility of higher rates of surgical complications, including anastomotic leak.

Multiple observational studies have compared SC to STC, including two systematic reviews. Tekkis et al. 2006 found no difference in overall or surgical recurrence, although patients undergoing SC required reoperation an average of 4.4 years earlier than those undergoing STC.<sup>78</sup> Angriman et al. 2017 performed an updated review, including a total of 11 studies and 1436 patients.<sup>79</sup> Again, there was no difference in overall or surgical recurrence between the groups even when limiting the analysis to studies performed during the biologic era. Interestingly, however, patients undergoing SC had a significantly lower rate of any stoma (OR 0.26,  $p=0.001$ ) and permanent stoma formation (OR 0.52,  $p=0.001$ ).<sup>79</sup> Overall, recurrence rates appear to vary between 40–60% depending on the population and follow-up period.<sup>80–83</sup>

Although neither review specifically commented on anastomotic leak, Kiran et al. 2011 found no difference in anastomotic leak (2% vs. 3%,  $p=1.0$ ), abdominal abscess (4% vs. 2%,  $p=0.59$ ), or 30-day readmissions rates (16% vs. 7%,  $p=0.13$ ) in a large, retrospective series of patients undergoing either SC or STC for Crohn colitis.<sup>84</sup> Angriman and colleagues did find a higher rate of post-operative complications among patients undergoing SC when compared to STC, however, they provided no additional information regarding the type or severity of the complications they identified.<sup>79</sup>

As with many decisions in IBD, the choice between SC and STC in the setting of Crohn's colitis should be individualized. Surgeons need to weigh the risks and benefits of surgery, including how well a patient would tolerate a major complication and how likely a patient will be to adhere to ongoing surveillance. After safety concerns are met, quality of life becomes paramount. SC offers better bowel function, on average, than STC or TPC without an apparent difference in the likelihood of recurrence. For that reason, select patients with segmental inflammation that either does not respond to medical management or results in a local complication (e.g., fistula or stricture) are increasingly being offered SC and continued surveillance rather than STC or TPC.

## Surgical Considerations for Dysplasia

Dysplasia of the colonic mucosa remains a controversial topic. There are two major classifications of this disease process associated with ulcerative colitis. The first is the histologic presence of dysplasia obtained by random biopsies at the time of surveillance colonoscopy, referred to as invisible dysplasia. The other is visible dysplasia best described using the Paris Classification combined with Kudo pit pattern. Both pathologic classifications have gone through significant evolution over the past 20 years and have resulted in changes in recommendations of treatment.

Visible lesions were (previously sometimes referred to as DALMs) considered aggressive and the presence warranted a total proctocolectomy. The term DALM (Dysplasia Associated Lesion or Mass) is no longer used and instead, lesions should be described according to the Paris Classification. Recent studies support colon preservation if the lesion can be endoscopically removed in its entirety and without evidence of malignancy.<sup>85</sup> Some lesions require advanced endoscopic skills for proper removal and endoscopists should appropriately refer to a colleague with those skills for endoscopic mucosal resection (EMR)

or endoscopic submucosal dissection; in that setting, the best approach is to leave the lesion alone but mark near it (4–5 cm distal) with India Spot. Manipulation of the lesion with even biopsy can result in scarring that makes complete endoscopic removal technically more difficult. Long term outcomes demonstrate that 50–65% of patients will develop metachronous adenomas similar to rates seen in non-UC adenoma cohorts. With close endoscopic surveillance many of these patients can avoid colectomy without a significant risk of malignancy.<sup>86</sup>

The finding of invisible dysplasia has been considered a predictor of developing a future malignancy and the presence of co-existent cancer. The nomenclature has been simplified to indefinite for dysplasia (IND), low grade dysplasia (LGD) and high grade dysplasia (HGD) with noted significant interobserver variability.<sup>87</sup> Patients with HGD, defined as severe nuclear changes and the nuclei extending to the upper third of the cell, should undergo total proctocolectomy. The decision of colectomy vs. continued surveillance in patients with LGD, defined as cells having enlarged hyperchromatic nuclei limited to the lower two thirds of the cell, is still controversial. Historically, most surgeons and gastroenterologists agreed that surveillance in these patients is acceptable with low risk of malignancy. However, some recent studies advocate for colectomy in these patients due to 9–20% of patients progressing to carcinoma in an average of 6 years.<sup>88</sup>

## Perianal Fistulizing Disease

Perianal fistulas are a major source of morbidity in Crohn's disease with 17–50% of patients experiencing fistula during the duration of their disease.<sup>89</sup> Rates of fistula closure have improved with the use of biologic medical therapies.<sup>18, 19</sup> Newer surgical techniques for complex fistula, such as ligation of the intersphincteric fistula tract (LIFT), have aimed to improve healing while preserving fecal continence.<sup>90</sup> Rates of healing after the LIFT procedure have been shown to be 40–60% with low rates of sphincter compromise.<sup>90, 91</sup> In addition to intrabdominal surgery, minimally invasive methods have been developed for fistula procedures. Video-assisted anal fistula treatment (VAAFT) is a sphincter sparing technique with improved visualization of the internal opening of the fistula tract.<sup>92</sup> In addition to sphincter sparing, advantages of this novel method include faster healing and earlier return to work when compared to traditional seton techniques.<sup>93</sup> Given high recurrence rates and surgical morbidity, there has been an interest in augmented healing of fistula with various products such as plugs, glues, and other biomaterials. Adipose derived mesenchymal stem cells (ADSC) have shown promise in a phase III randomized control trial where healing rates were 50% versus 34% in the placebo arm.<sup>94</sup> There has yet to be a definitive approach to management of challenging fistula in the setting of CD. The vast array of techniques and therapeutic adjuncts allow the surgeon to tailor the approach to the individual patient.

## Telemedicine in the Surgical Patient

Telemedicine and its rapid evolution have much to offer IBD surgery; it will play an increasing role in IBD surgical care. Telemedicine has been present in healthcare since 2000 and rapidly expanded with advances in telecommunication capabilities. The COVID

pandemic transformed the landscape for telemedicine and rapidly advanced physician and patient awareness and acceptance.<sup>95</sup> Currently, 15–20% of outpatient visits are conducted using telemedicine at a national level.

Due to the complexity of IBD patients, their care is typically conducted in a multi-disciplinary approach including several non-surgical teams. Telemedicine enables these teams to coordinate care and come together using video conferencing.<sup>96</sup> Telemedicine fundamentally enables patients and physicians to access patients at a distance. This has implications for diversity, equity, and inclusion for the IBD care of all patients.

## Conclusion

The ever-changing landscape of IBD treatment presents a unique balance of medical and surgical co-management. IBD practitioners must be well versed in advances in the entire field of these inflammatory conditions to provide optimal patient care. A multidisciplinary approach involving the surgeon, gastroenterologist, pathologist, radiologist, nutritionist, and others with patient engagement is critical to optimal patient management and outcomes.

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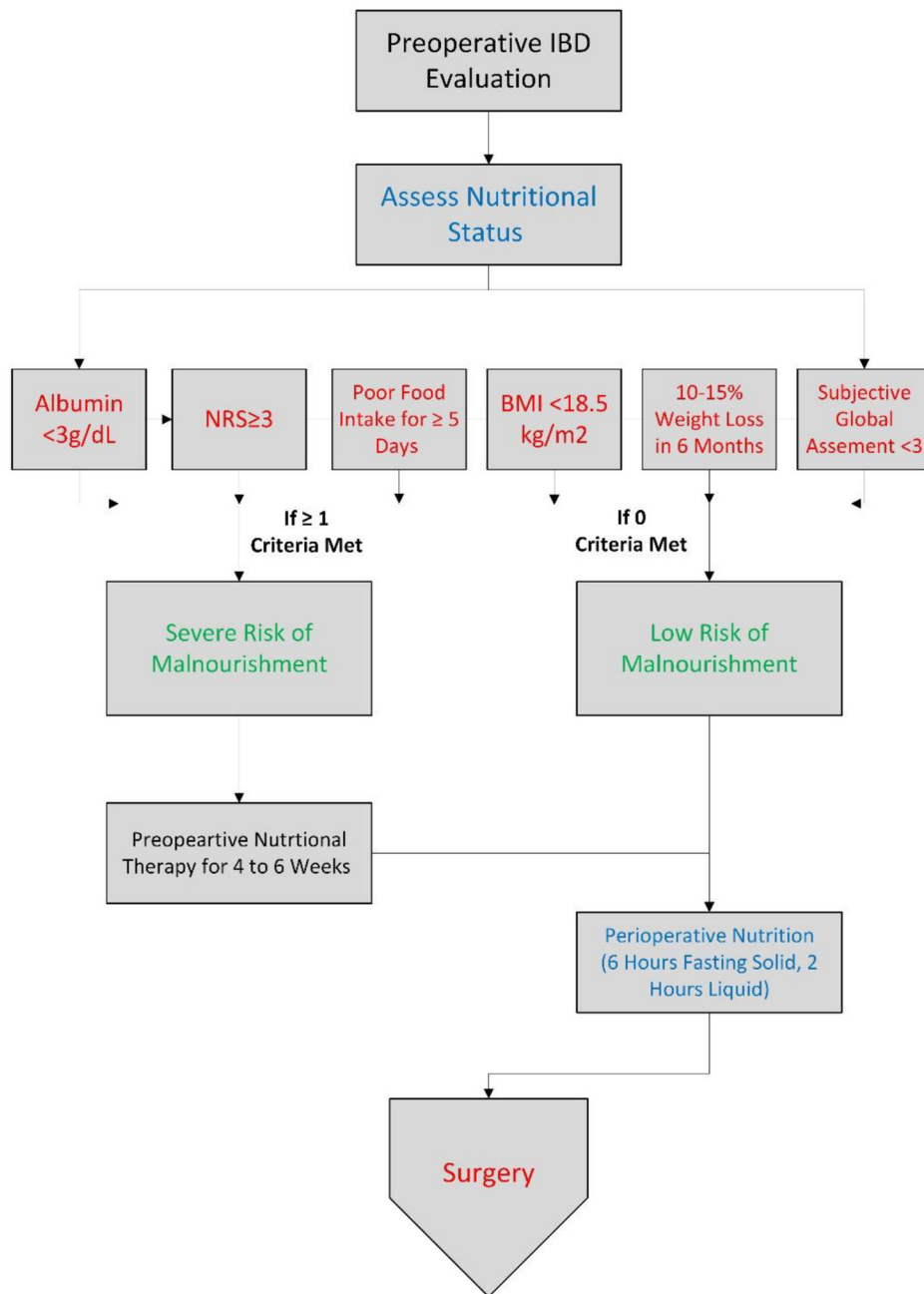
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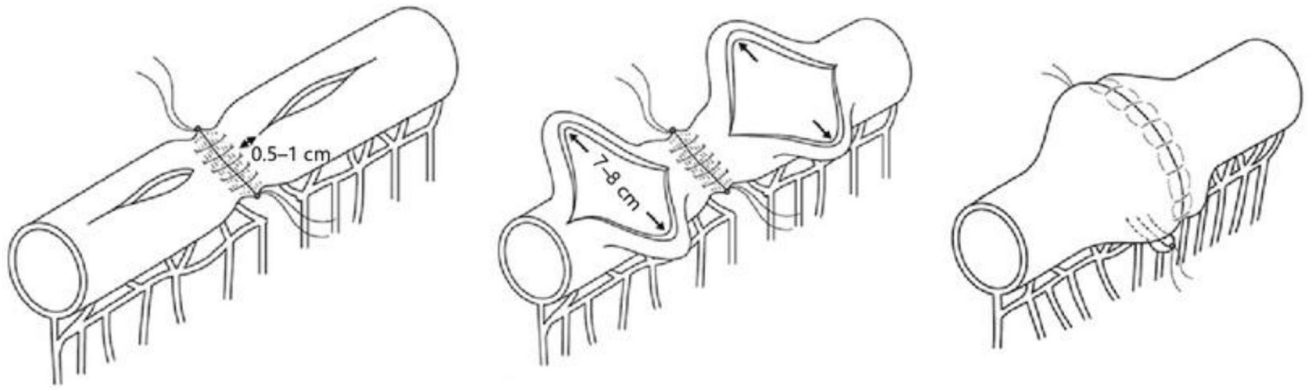
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**Figure 1.** Perioperative nutritional assessment and optimization in IBD patients. Adapted from *da Silva et al.* 2021 and European Society for Clinical Nutrition and Metabolism guidelines.<sup>31</sup>, 36



**Figure 2.** Schematic diagram of the Kono-S anastomosis, adapted from *Luglio and Kono 2021*.<sup>74</sup> Licensed by Creative Commons <https://creativecommons.org/licenses/by-nc/4.0/>