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Review Article

Review Article

Interventional endoscopy in inflammatory bowel disease: a comprehensive review

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Abstract

Interventional endoscopy can play a key role in the multidisciplinary management of complex inflammatory bowel disease (IBD) as an adjunct to medical and surgical therapy. The primary role of interventional IBD (IIBD) includes the treatment of Crohn's disease-related stricture, fistula, and abscess. Endoscopic balloon dilation (EBD), endoscopic stricturotomy, and placement of endoscopic stents are different forms of endoscopic stricture therapy. EBD is the most widely used therapy whereas endoscopic stricturotomy has higher long-term efficacy than EBD. Fully covered and partially covered self-expanding metal stents are useful in long and refractory strictures whereas lumen-apposing metal stents can be used in short, and anastomotic strictures. Endoscopic fistula/abscess therapy includes endoscopic fistulotomy, seton placement, endoscopic ultrasound-guided drainage of rectal/pelvic abscess, and endoscopic injection of filling agents (fistula plug/glue/stem cell). Endoscopic seton placement and fistulotomy are mainly feasible in short, superficial, single tract fistula and in those with prior surgical seton placement. Similarly, endoscopic fistulotomy is usually feasible in short, superficial, single-tract fistula. Endoscopic closure therapies like over-the-scope clips, suturing, and self-expanding metal stent should be avoided for *de novo*/bowel to hollow organ fistulas. Other indications include management of postoperative complications in IBD such as management of surgical leaks and complications of pouchitis in ulcerative colitis. Additional indications include endoscopic resection of ulcerative colitis-associated neoplasia (by endoscopic mucosal resection, endoscopic submucosal dissection, and endoscopic full-thickness resection), retrieval of retained capsule endoscope, and control of bleeding. IIBD therapies can potentially act as a bridge between medical and surgical therapy for properly selected IBD patients.

Keywords: Crohn's disease; ulcerative colitis; stricturotomy; endoscopic balloon dilation; endoscopic mucosal resection; endoscopic submucosal dissection

Introduction

Structural complications of Crohn's disease (CD) like stricture, fistula, and abscess occur after the initial 4–5 years of disease [1]. At this juncture, in the absence of effective anti-fibrotic therapy in inflammatory bowel disease (IBD), interventional IBD (IIBD), and surgery are the mainstays of treatment. These structural complications occur in a specific sequence: chronic inflammation leads to stricture formation which leads to fistula in the upstream bowel with abscess. Endoscopic stricture therapy depends on basic principles of dilatation (with balloon), cutting (stricturotomy), and stent placement [self-expanding metal stents (SEMS)] [2]. Endoscopic treatment of fistula initially includes initial treatment of associated stricture (with aforementioned techniques) and drainage of abscess if any. Then chronic fistula can be treated with cutting (fistulotomy), filling (with glue/plug/stem cell), or closure (with SEMS/sutures/clips) [3]. Apart from CD, stricture/fistula/abscess can occur in ulcerative colitis in the postoperative scenario such as after ileal pouch-anal anastomosis (IPAA).

Understanding the natural history of IBD and indications of IIBD

Untreated or partially treated chronic inflammatory process in IBD especially CD leads to fibrogenesis and stricture formation after initial 4–5 years of disease [1]. Early diagnosis and optional treatment of inflammation can prevent such complications of IBD. After stricture develops, there can be formation of fistula above the stricture site due to the formation of high-pressure zone proximally which can lead to abscess formation. This sequence of chronic inflammation, stricture, fistula, and abscess is seen in majority of the cases in the natural history of IBD complications. The positive predictive value of stricture is 86.2% for the presence of fistula in CD [4]. Once these mechanical complications develop (up to one-third over the first 5 years), medical treatment options are limited given the lack of effective anti-fibrotic therapy. At this point, the treatment options are surgical resection or interventional endoscopic therapies. Although the risk of first intestinal surgery (33.3% at 5 years and 46.6% at 10 years) is decreasing with current medical therapy, the rate of

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Table 1. Indications of interventional IBD.

Type of IBD	Crohn's disease	Ulcerative colitis
Indications	Stricture	Colitis-associated neoplasia
	Fistula/abscess	Pouch complications
	Post-surgical complications (leaks)	Bleeding control
	Retrieval of retained capsule endoscope	
	Bleeding control	

IBD = inflammatory bowel disease.

second surgery has not decreased in the last 3 decades [5, 6]. Hence, IIBD is an alternative, effective option to surgery which should be discussed with patients albeit with a higher risk of recurrence and mild risk of complications [7]. IIBD can also be helpful to delay up to 6.5 years as shown in a retrospective study [8]. Moreover, IIBD can be helpful to manage post-surgical complications. Thus IIBD can be used as a bridge between surgery and medical therapy (Table 1).

In long-standing UC, colorectal cancer develops which can be managed with endoscopic resection. Moreover, after IPAA, pouch complications can be managed with IIBD to avoid pouch excision [9, 10].

Management of IBD strictures

Classification of IBD strictures

To understand the treatment of IBD strictures, it is important to understand the different types of strictures so that the appropriate patient can be selected for endoscopic therapy. Based on etiology, IBD strictures can be classified into those due to CD, UC, or post-surgical [11]. The risk of colorectal neoplasia can be as high as 33% in UC. Symptomatic strictures, proximal to splenic flexure in long-standing disease (>20 years) are risk factors for developing neoplasia. Extensive biopsies (false negative biopsy 3.5%) are required prior to endoscopic therapy in UC-associated strictures followed by yearly surveillance. The threshold for surgical resection should also be low in this scenario.

Among post-surgical strictures, anastomotic strictures are the best candidates for endoscopic therapy. *De novo* strictures in CD are also candidates for endoscopic therapy. Although the risk of colorectal cancer is lower compared with UC (up to 6.8%), biopsies should be taken prior to endotherapy especially for small bowel strictures [11].

From the endoscopist perspective, strictures can be ulcerated, fibrotic, or mixed (partly ulcerated and fibrotic based on the presence of ulceration). Fibrotic and mixed strictures are candidates for endoscopic therapy. Basically, all strictures have 3 components histologically: inflammation, fibrosis, and muscular hypertrophy/hyperplasia [12]. Advanced therapies in IBD target only inflammation and hence endoscopic therapy or surgical resection is warranted to treat IBD strictures.

Morphologically strictures can be web-like or spindle-shaped. It is important to recognize that endoscopic therapy for spindle-shaped strictures is associated with higher risk of complications compared with web-like strictures [13].

Approach to endoscopic management of CD strictures

Several factors need to be considered before endoscopic stricture therapy in CD (Figure 1). Clinical history such as fistulizing disease, surgical history, and anti-tumor necrosis factor (anti-TNF) exposure should be explored. Inflammatory markers in blood and stool could help indicate an inflammatory phenotype. Before endoscopic stricture therapy, cross-sectional imaging is essential to evaluate number, length, and location of strictures along with the extent of pre-stenotic dilation which is central to the management of strictures. Long (>4–5 cm), multiple strictures (>4) with significant pre-stenotic dilation (>5 cm) warrant surgery [2, 14]. BACARDI risk model (B3-stricturing disease—1 point, anti-TNF exposure—1 point, NOD2/CARD15 risk allele—1 point, pre-stenotic dilation—2 points, inflammatory marker C-reactive protein >11 mg/L—1 point) can predict the risk of surgery in ileal stricturing CD (Figure 1) [15]. Inflammatory strictures should be treated with medical therapy. Mixed/fibrotic, short strictures (≤4 cm) are candidates of endoscopic stricture therapy. Usually ≤4 strictures are considered feasible for endoscopic therapy, however, any number of strictures can be treated endoscopically if technically feasible [16].

Principles of endoscopic stricture therapy

There are 3 basic principles of endoscopic stricture therapy: (i) dilation, (ii) cutting, and (iii) stenting (Figure 2). Irrespective of stricture location, endoscopic balloon dilation (EBD) is feasible in any location of the gastrointestinal tract. Endoscopic stricturotomy (ES) involves incising the stricture circumferentially in the non-ulcerated areas in all quadrants with or without cutting the intervening fibrous tissue (radial incision and cutting). ES is feasible in small bowel with deep enteroscopy although can be technically challenging [17]. ES is more preferable in distal bowel, esophagus, and stomach as endoscope shaft main straight and tip remains under control (Table 2).

Endoscopic balloon dilation

Outcomes of EBD

EBD is the most widely used technique for endoscopic stricture therapy. EBD is associated with high technical (74%–100%) and clinical success with low complication rates (0%–10.6%) (Table 3) [18]. However, recurrence symptoms occur in half and about two-third require re-dilation or surgery at a follow-up over 20–144 months [19]. Based on a systematic review and meta-analysis, the technical success, clinical success, and major complication rates in small bowel strictures due to CD were 94.9%, 82.3%, and 5.3%, respectively. During follow-up, almost half (48.3%) had recurrent symptoms and two-thirds required re-intervention (38.8% re-dilatation and 27.4% surgery) [19]. For ileo-colonic strictures, technical success, clinical success, recurrent symptoms, and complication rates were 90%, 80.8%, 47.5%, and 2.8%, respectively. Recurrent symptoms were more frequent in gastro-duodenal strictures (70.5%) although technical success, clinical success, and complication rates were 100%, 87%, and 2.9%, respectively. Surgery was required in 30.8% [19].

Comparison of EBD with other techniques

EBD vs surgery

Retrospective study have shown that EBD can delay surgery for up to 6.5 years. On intermediate follow-up (median 2.1 years), 45.3% required subsequent surgery. In those with long-term follow-up (5 years), only 15.4% were surgery-free. In comparison, 21.7% of patients require reoperation after ileo-cecal resection in 21.7% of cases [8]. A recent prospective, propensity-matched analysis of CD strictures (<5 cm, ≤3 in number) with 1-year follow-up showed that the cumulative probability of symptoms recurrence/treatment escalation/re-surgery was not different between those who underwent EBD and those who underwent surgery. However, the rate of re-intervention was higher in the EBD group [7].

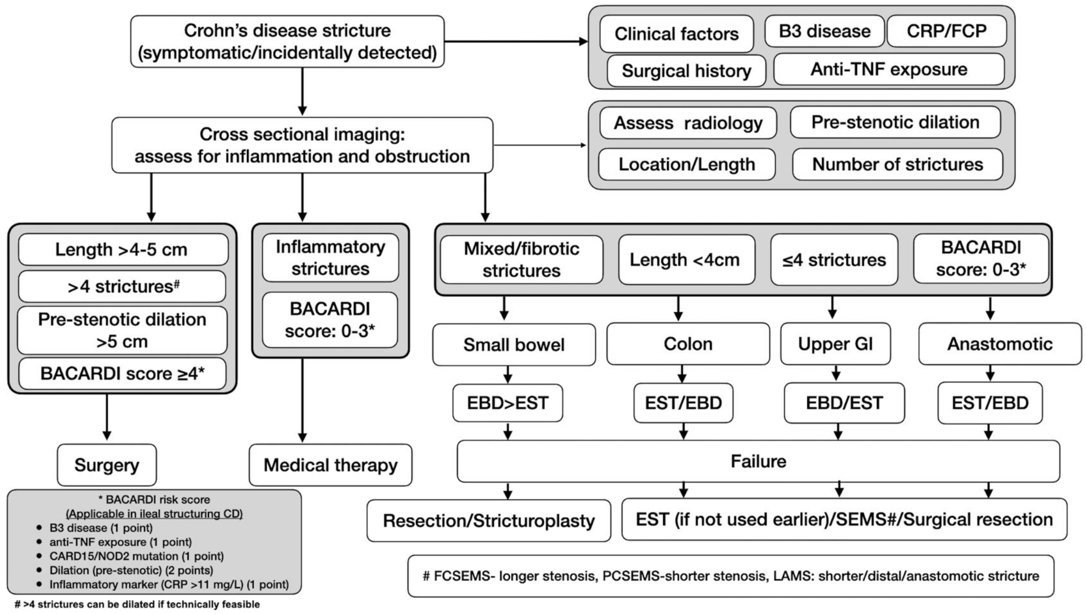

Figure 1. Approach to endoscopic therapy in Crohn's disease strictures. B3 = fistulizing disease, CRP = C-reactive protein, EBD = endoscopic balloon dilation, EST = endoscopic stricturotomy, FCP = fecal calprotectin, FCSEMS = fully covered self-expanding metal stents, LAMS = lumen-apposing metal stents, PCSEMS = partially covered self-expanding metal stents, TNF = tumor necrosis factor.

Figure 2. Endoscopic stricture therapy. (A) Endoscopic balloon dilation. (B) Endoscopic stricturotomy for rectal stricture. (C) Lumen-apposing stent placed for refractory pylori stricture fixed with suturing.

Table 2. Basic differences between EBD and ES.

Item	ES	EBD
Training	Extensive and advanced	Advanced
Location	Distal bowel/esophagus/stomach-endoscope shaft straight and tip under control (can control depth and location)	Anywhere in the gastrointestinal tract
Length	<3 ideal	<5 ideal
Shape	Symmetric or asymmetric	Symmetric
Use for angulated stricture	No	May be attempted
Use for multiple stricture	No	May be attempted
Immediate efficacy	++	++
Short-term efficacy	+++	++
Long-term efficacy	++	+
Bleeding	6%–10%	2%–3%
Perforation	1%	1%–5%
Specific indication	Refractory/fibrotic/distal bowel strictures, can avoid ulcerated area in mixed stricture/inflammation	Angulated/inflammatory

EBD = endoscopic balloon dilation, ES = endoscopic stricturotomy.

Table 3. Summary of major, large studies on EBD in IBD/CD strictures.

Study, year of publication	No. of patients	Type of strictures, location,	Technical success	Clinical success	Recurrence rates	Complications	Repeat dilation	Surgery on follow-up	Median follow-up period, months
Andujar *et al.* (2010)	187	Anastomotic; pouch, ileo-colonic	79.5%	55.3%	–	1.3%	49.7%	20.9%	40
Van Assche *et al.* (2010)	138	Ileal; ileo-colonic	97%	–	55.8%	5.1% per patient analysis	46%	24%	69.6
Gustavsson *et al.* (2012)	178	Anastomotic; upper gastrointestinal, small bowel, ileo-colonic	89%	77%	66.4%	5.3%	66%	36%	144
Atreja *et al.* (2014)	128	*De novo* and anastomotic; ileo-colonic	83%	–	73.4%	3.1%	58.6%	32.8%	21.6
Bhalme *et al.* (2014)	79	Anastomotic; upper gastrointestinal, small bowel, ileo-colonic	95%	43%	66%	4%	66%	23%	26.8
Lian *et al.* (2015)	185	Anastomotic; ileo-colonic	91%	–	–	1.1%	–	35.7%	46.8
Sunada, 2016	85	Small bowel	–	–	–	5.9%	75.3%	24.7%	41.9
Lian *et al.* (2017)	176	Anastomotic; ileo-colonic	90.3%	–	–	8.8%	–	51.7%	21.6
Reutmann *et al.* (2017)	135	*De novo* and anastomotic; ileo-colonic	74%	–	–	0.7%	–	28.1%	41.7
Shivashankar *et al.* (2018)	273	Anastomotic; entire gastrointestinal tract, pouch, anastomosis	91.3%	91.3%	41.8%	2.1%	41.8%	30%	31.2
Sivasailam *et al.* (2021)	99	Anastomotic; ileo-colonic	75%	–	52%	3.3%	52%	33%	62

EBD = endoscopic balloon dilation, IBD = inflammatory bowel disease, CD = Crohn's disease.

Comparative studies between EBD, ES, and stenting are discussed in subsequent sections.

Predictors of EBD efficacy

The common theme in all kinds of strictures with EBD is high recurrence rates requiring re-interventions. Negative predictors of EBD efficacy are long stricture, Asian race, high body mass index, proximal small bowel (jejunal/proximal ileal stricture), *de novo* stricture, and pre-stenotic dilation. Positive predictors are colonic strictures, graded dilation, use of proton pump inhibitor, and anti-TNF [19]. Length of stricture ≤5 cm is an important predictor of surgery-free survival. The risk of surgery increases by 8% with each 1-cm increase in the length of stricture [20]. Inflamed stricture was negatively associated with efficacy [21]. Dilation diameter ≥15 mm was associated with successful EBD [21]. A diameter of 14–15 mm had a similar surgery-free survival compared with 16–18 mm dilation, but the interval of dilations was longer in the latter [22]. Results with intra-lesional steroid/anti-TNF injection are conflicting with two meta-analyses showing no incremental benefit over EBD alone [20, 23, 24]. Medications at the time of EBD combined with anti-TNF and thiopurine therapy were associated with lower risk of repeat EBD (hazard ratio: 0.23) [25]. On the contrary, another large study has shown that the outcome of EBD is not influenced by concurrent medical therapy or the degree of inflammation [26]. Upper gastrointestinal strictures, especially gastro-duodenal strictures, are associated with a higher risk of recurrent symptoms and repeat dilation [19, 27].

Outcomes for anastomotic strictures with EBD were better compared with *de novo* strictures [28, 29]. In ileo-colonic anastomotic strictures, 5-year surgery-free survival after EBD can be predicted based on a nomogram (developed based on a retrospective study) that includes disease duration, duration from time of surgery, pre-stenotic dilation, and presence of symptoms [30]. In stricturing ileal CD, the BACARDI risk model can help guide appropriate therapy. A BACARDI risk score of 4–6 predicts failure of medical/endoscopic therapy (Figure 2) [15].

In conclusion, EBD for strictures in IBD demonstrates significant short-term efficacy but carries a notable risk of recurrence during subsequent follow-ups, often necessitating further dilation or surgical intervention. Complications are relatively infrequent, occurring in fewer than 10% of cases.

Endoscopic stricturotomy

ES presents a viable alternative, boasting superior long-term effectiveness and reduced rates of re-intervention compared with EBD [31–33]. ES entails incising the stricture, albeit it demands specialized expertise and may pose an increased risk of bleeding (6%–10%) [31–33].

Patient selection for ES

ES is indicated for short (≤4 cm), predominantly fibrotic/mixed strictures as a primary therapy or as salvage therapy in refractory strictures. Ileo-cecal/rectal/pyloric strictures are considered ideal for ES, whereas complications due to ES in small bowel/anal strictures can cause significant morbidity [34]. Small bowel ES can be technically challenging but feasible [17]. Complications after duodenal and esophageal ES can be life threatening [34]. ES has better outcomes for anastomotic strictures than *de novo* strictures probably because the former is often due to surgical ischemia rather than chronic inflammation in IBD [32, 33].

Method of ES

In ES, stricture is cut open by doing radial incision of stricture with or without circumferential cutting of fibrotic tissue with or without placement of spacer clips (i.e. stricturoplasty: clips act as spacers to prevent re-approximation and also delayed bleeding) [35]. ES is done with either needle knife (length 5–7 mm) or insulated tip knife (length 3.5 mm with 1.7 mm ceramic tip). The ceramic tip in the insulated tip knife offers added safety benefits, yet its use can be restricted in small bowel strictures as they could not be passed through the narrow channel of the balloon enteroscopes. The length of the knives served as a reference to determine the depth of incision, which was carefully regulated to not exceed the submucosa. The recommended electrocautery settings for ES is Endocut-I 3-1-3 (effect-3, cut duration-1, cut interval 3), which helps to minimize the risk of bleeding, a concern known to be elevated with ES [2].

A distal cap can help to enhance stability during ES although it limits vision. ES is technically easier with strictures accessible by therapeutic gastroscope due to its straight shaft facilitating control over the cutting's depth and location. For right colonic and ilea-cecal strictures, a colonoscope can be utilized. For small bowel strictures, either a pediatric colonoscope or double-balloon enteroscope can be used to reach the stricture. ES in small bowel strictures is technically challenging and complications are difficult to manage if they occur [17].

Outcomes of ES

ES is associated with high technical (92%–100%) and variable clinical success (42.3%–100%) based on indication of ES. The need for re-interventions was not infrequent (8%–61.9%); however, the need for subsequent surgery was definitely lower than what is reported with EBD (9%–22.5%). While ES had a lower reported perforation rate (∼1%) compared with EBD (1%–5%), it posed a higher risk of bleeding requiring transfusion (6%–10%, EBD: 3%–5%) [31–33].

Comparison of ES with other techniques

ES vs surgery

Lan *et al.* conducted a comparative study between ES and ileo-colonic resection for primary distal ileal strictures in CD. They found that ES offered similar surgery-free survival rates (subsequent surgery 15.4% vs 18.8% after ileo-colonic resection) with fewer postoperative complications compared with resection. However, the median follow-up was only 1.5 years (ES arm, 1.8 years ileo-colonic resection arm) [33]. Long-term comparative studies are warranted (Table 4).

ES vs EBD

In another retrospective study comparing ES ($n = 40$) with EBD ($n = 160$) for ileal pouch strictures, both techniques were deemed safe and effective, although ES was associated with a higher incidence of bleeding and EBD with perforation [36]. In a retrospective comparative study, ES was significantly better than EBD for anastomotic strictures in terms of stricture-related emergency visit and subsequent surgery (ES: 9.5%, EBD: 33.5%) although bleeding requiring transfusion was higher in the ES arm [32]. ES demonstrated superior short-term clinical and long-term efficacy compared with EBD, resulting in lower rates of re-intervention or surgery (9%–22.5%) [31–33, 35–39] (Table 4).

Table 4. Summary of major studies on ES in IBD/CD strictures.

Study, year of publication	Patients	Technical success	Clinical success of ES	Recurrence rates	Complications	Repeat interventions	Surgery on follow-up	Median/mean follow-up (months)
Lan *et al.* (2017)	85 [Ileal pouch ($n = 50$), CD ($n = 35$)]	100%	54.7% (29/53)	60.6%	3.7% (bleeding 3.3%, perforation 0.4%)	60.6%	15.3%	11
Lan *et al.* (2018)	185 anastomotic strictures (ES 21, EBD 164)	100%	72.7% (vs 45.4% EBD)	61.9%	14.3% (bleeding requiring transfusion)	61.9%	9.5%	9
Zhang *et al.* (2020)	49 IBD	100%	67.6%	34.7%	4.7% (bleeding)	49% additional ES, 20.4% additional EBD	12.2%	11
Mohy-Ud-Din *et al.* (2020)	11 IBD (including pouch)	92%	92%	–	9% (self-limiting bleed)	8% repeat ES	9%	5
Lan *et al.* (2020)	CD primary distal ileal strictures [ES ($n = 13$) vs ICR ($n = 32$)]	100%	50.0% (vs 90% ICR)	38.5%	6.9%	15.4% (surgery)	15.4%	21
Lan *et al.* (2021)	40 pouch strictures [ES ($n = 40$) vs EBD ($n = 160$)]	100%	42.3% (vs 13.2% EBD)	44.4% (vs 41.3% EBD)	4.7% (bleeding) (vs 0.8% EBD)	22.5%	22.5% (vs 20.6%)	7
Herman *et al.* (2024)	24 anorectal or anopouch non-passable strictures	100%	–	–	0%	67%	11%	12.8

ES = endoscopic stricturotomy, CD = Crohn's disease, IBD = inflammatory bowel disease, ICR = ileocecal resection, EBD = endoscopic balloon dilation.

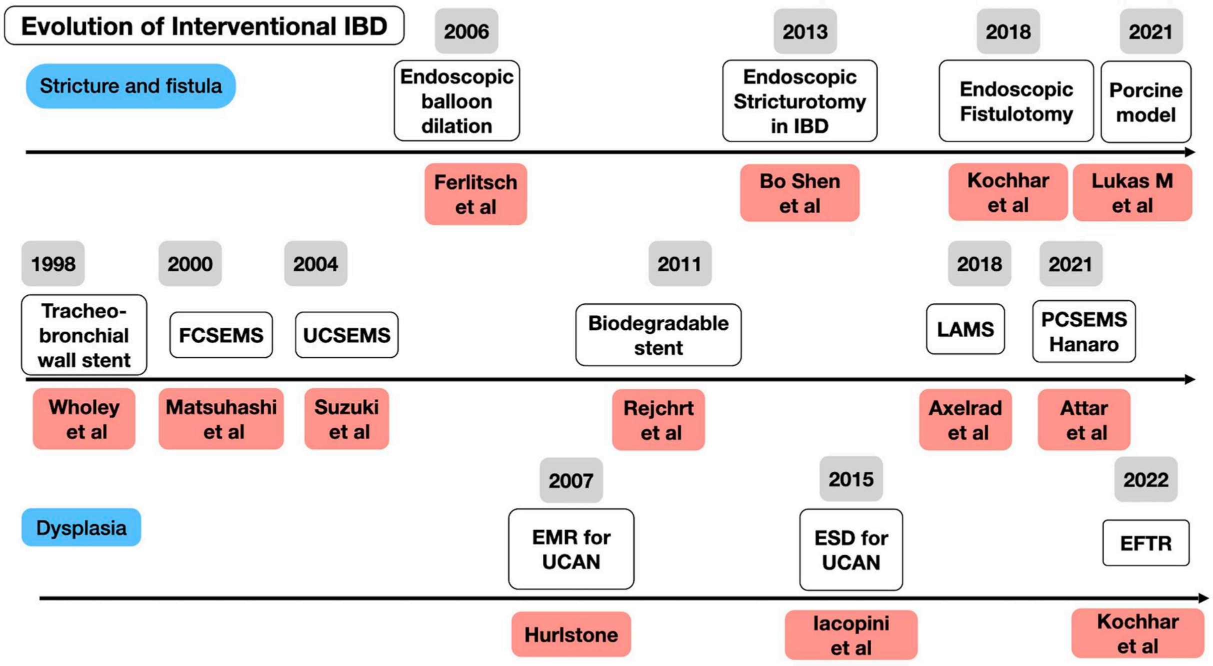

Figure 3. Evolution of interventional IBD therapies. EFTR = endoscopic full-thickness resection, EMR = endoscopic mucosal resection, ESD = endoscopic submucosal dissection, FCSEMS = fully covered self-expanding metal stents, IBD = inflammatory bowel disease, LAMS = lumen-apposing metal stents, PCSEMS = partially covered self-expanding metal stents, UCSEMS = uncovered self-expanding metal stents.

Endoscopic stenting

Indications and types

The earliest endoscopic treatment for IBD strictures was the use of using stents. Wholey *et al.* [40] used trachea bronchial stent for colonic CD. This was followed by the use of fully covered SEMS (FCSEMS), uncovered SEMS (UCSEMS), biodegradable stents, lumen-apposing metal stents (LAMS), and partially covered SEMS (PCSEMS) [41–45] (Figure 3).

For refractory strictures in IBD, endoscopic stenting can be done following unsuccessful attempts with EBD or ES. In appropriately selected patients, stenting may also be used as primary therapy. While long strictures (3–5 cm) are considered optimal for endoscopic stenting using FCSEMS such as the Niti S enteral colonic covered stent, shorter strictures can be managed with PCSEMS like the HANARO stent, which exhibits lower migration rates than FCSEMS. LAMS is effective in treating short anastomotic strictures, characterized by their short delivery catheters initially designed for draining pancreatic fluid collections. Hence, LAMS is unsuitable for stenoses not reachable by therapeutic gastroscope. Additionally, biodegradable stents like the SX-ELLA-BD stents, composed of polydioxanone, gradually degrade within 10–12 weeks and may be utilized for IBD-related strictures, although they are not yet recommended for routine clinical application. It is worth noting that these stents are not introduced through the scope (Table 5) [46].

Technical tips for endoscopic stenting in IBD

The initial step in stent selection involves choosing a stent that is at least 1.5 cm longer than the stricture on each side, considering that stents can potentially foreshorten (5%–40%). To assess the length of the stricture, radiographic contrast material is injected through the catheter or balloon after a hydrophilic soft guidewire is passed through the stricture. After stent placement, it needs to be fixed by thought-the-scope clips, over-the-scope clips (OTSC), or endoscopic suturing. LAMS can be placed using similar principle used for pancreatic fluid collections. It is essential to note that the duration of stenting should not exceed 4 weeks for FCSEMS and 1 week for PCSEMS to avoid tissue ingrowth [47].

Results of endoscopic stenting

The pooled technical and clinical success rates for CD stricture with endoscopic stenting are 93% and 61%, respectively, according to a meta-analysis. Common problems with stents include frequent migration (up to 43.9%, proximal migration: 6.4%), abdominal pain (18%), and perforation (3%) (Table 6) [40–46, 48–64]. Long-term follow-up studies are warranted as the follow-up time varied from 3 to 69 months.

Comparison of stenting with other techniques

Stenting vs EBD

In the only randomized controlled trial (RCT) (ProtDilat) in interventional IBD, endoscopic stenting was less effective than EBD in terms of the need for re-intervention at 1 year (FCSEMS: 49%, EBD: 20%, odds ratio: 3.9). The results of this RCT suggested that EBD is superior to stenting and therefore stenting is not currently recommended for IBD stricture management as primary therapy. Despite these discouraging outcomes, endoscopic stenting might still hold promise in managing refractory, long, and prolonged strictures associated with IBD/CD [65]. Innovative designs of endoscopic stents specifically for IBD/CD are warranted.

The result of endoscopic treatment (SEMS/EBD) vs surgery (ENDOCIR study, multicenter RCT, NCT04330846) is eagerly awaited.

Endoscopic management of fistula and abscesses

Prior to performing endoscopic treatment of fistula and abscess in IBD, it is important to understand various types of fistulae. They can be classified based on etiology, underlying disease, symptoms, organs involved, length/depth, concurrent stricture,

Table 5. Summary of studies on endoscopic stent placement in IBD/CD strictures.

Author, year of publication	No. of patients	Length	Stent type	Technical success	Clinical success	Recurrence	Adverse events/ migration	Repeat intervention	Duration of Stenting, weeks	Surgery	Follow-up, months
Attar *et al.* (2021)	46 CD (post-EBD: 36)	Mean 3.9 cm (all <5 cm)	PCSEMS (Hanaro stent)	100%	58.7%	6.5%	15.2% (4 pain, 3 proximal migration)	34.8%	1	17.3%	26
Loras-Andujar *et al.* (2022)	39 CD	Mean 4 cm (all <9 cm)	FCSEMS	92.3%	51%	–	7.7% (2 proximal migration, 1 perforation)	49%	<1	–	12
Das *et al.* (2020)	21 CD	<6 cm	PCSEMS	95.8%	54.2%	12.5%	21.7% (2 pain, 3 migration)	9.5% restenting	1	–	3–50
Loras *et al.* (2012)	17 CD (post-EBD: 14)	2–6 cm	PCSEMS/FCSEMS	94.1%	64.7%	31%	5.9% spontaneous migration, 52% migration	–	4	43.7%	12
Wholey *et al.* (1998)	1 colon CD	–	Tracheo-bronchial Wallstents	100%	100%	–	–	100%	3	Bridge to surgery	0.75
Matsuhashi *et al.* (2000)	2 colon, ileo-colonic anastomosis, post-EBD	–	FCSEMS	100%	100%	0%	100% (migration)	0%	4 and 22	0%	54
Suzuki *et al.* (2004)	2 colon	–	USCEMS	Yes	Yes	Yes	Fistula in 1	Surgery and repeat stenting	3 and 104	1/2	3 and 26
Rejchrt *et al.* (2011)	11 CD (post-EBD 7)	1.5–5	Polydioxanone biodegradable stent	90%	63%	36.3%	27% early stent migration	–	16	–	16
Axelrad *et al.* (2018)	1 rectal-colon anastomosis (post-EBD)	1 cm	LAMS	Yes	Yes	0%	No	–	8	–	3
Attar *et al.* (2012)	11 CD (post-EBD 9)	1–4 cm	FCSEMS	90%	36%	63.6% (1 year); 90% (total)	10 % proximal migration, 70% migration	18.2%	<4	18.2%	26

EBD = endoscopic balloon dilation, FCSEMS = fully covered self-expanding metal stents, UCSEMS = uncovered self-expanding metal stents, PCSEMS = partially covered self-expanding metal stents, ES = endoscopic stricturotomy, LAMS = lumen-apposing metal stents, CD = Crohn's disease.

Table 6. Summary of various stents used in IBD/CD strictures.

Name of stent	Diameter, mm	Length, cm	Stent type	Specifics
Axios stent	10, 15, 20 (21–29 for flanges)	1 (saddle length)	LAMS	Short delivery catheter (not for stenosis unreachable by therapeutic endoscope)
Niti S enteral covered stent	18–22	6–15	Fully covered enteral stent	High migration rates
HANARO stent	20 (26 at ends)	2.4, 5.4, 7.4 (6, 9, 11)	PCSEMS	Lower migration rates compared with FCSEMS
SX-ELLA biodegradable stents	18, 20, 23, 25	6, 8, 10	Biodegradable stent	Polydioxanone, through the scope stents, degraded in 10–12 weeks

IBD = inflammatory bowel disease, CD = Crohn's disease, LAMS = lumen-apposing metal stent, CSEMS = partially covered self-expanding metal stents, FCSEMS = fully covered self-expanding metal stents.

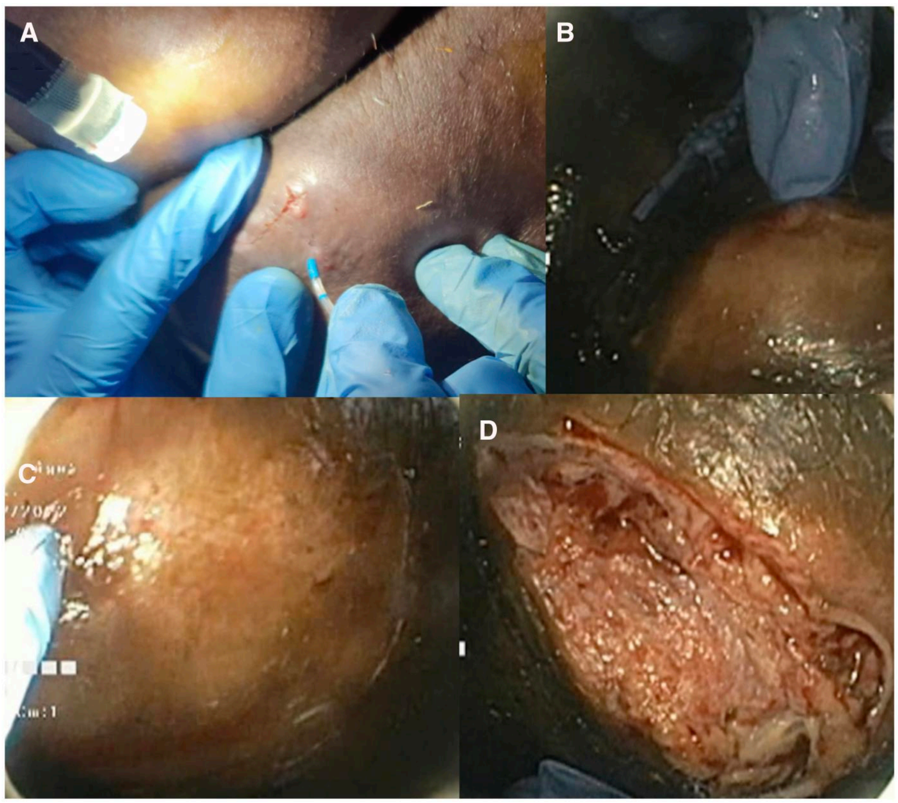

Figure 4. Endoscopic fistulotomy for perianal fistula. (A) Freehand technique using hand-held needle knife. (B) Pus pointing out perianal area at prior surgical fistulotomy site on biologic therapy. (C) Incision through needle knife through the scope. (D) Post-fistulotomy.

complexity, and malignant potential. Two-third of fistulae are external among which perianal fistulae are the most common phenotype.

The principles of fistula/abscess therapy are primarily as follows: (i) drain any abscess (endoscopic knife/endoscopic ultrasound: endoscopic ultrasound-guided pigtail stent placement/ seton); (ii) cut open chronic fistula; (iii) fill fistula cavity with glue, plug, sclerosant, or stem cell; and (iv) close the feeding side of the fistula/acute leak. Associated stricture should be treated endoscopically prior to fistula/abscess treatment.

Endoscopic drainage

Incision and drainage

Endoscopic drainage for abscess associated with CD-related fistula can be achieved using a needle knife for perianal fistula management. In cases of perianal fistula, complete fistulotomy can be performed for short and superficial fistulas outside the external anal sphincter. However, partial fistulotomy is typically reserved for long fistulas (Figure 4) [3].

Endoscopic seton placement

Endoscopic seton placement is feasible for simple, short, superficial perianal fistula as primary therapy or for recurrence after surgical seton placement. It is usually done by passing a guide wire through the external opening, which is grabbed by a forceps inside rectum which is pulled out and then a draining seton is railroaded over to secure the seton in place (Figure 5) [66]. Endoscopic seton placement for complex perianal fistula has been described with the use of fistuloscopy using ultra-thin endoscope which is usually a challenge given the tortuous course of the fistula [67].

Endoscopic ultrasound-guided drainage

When intra-abdominal or pelvic abscesses are inaccessible for drainage via interventional radiology due to bowel overlay,

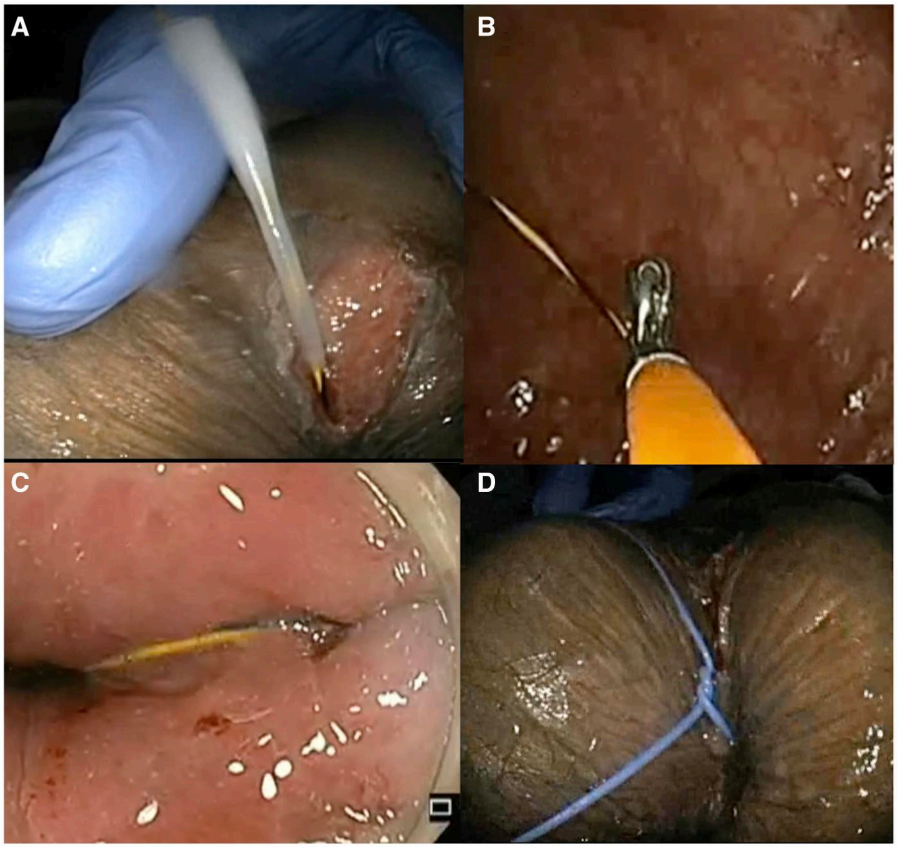

Figure 5. Endoscopic seton placement. (A) Guidewire placed through external opening. (B) Guidewire grabbed by forceps. (C) Guidewire coming out through internal opening at anal verge. (D) Endoscopic seton placed.

endoscopic pigtail drainage becomes a viable option. This procedure can be conducted with or without endoscopic ultrasound guidance (Figure 6) [3].

Endoscopic fistulotomy

Endoscopic fistulotomy is a viable treatment option for various types of fistulas associated with IBD: bowel–bowel/pouch–pouch fistulas, perianal, and primary ileo-cecal fistulas. It is particularly suitable for short (<2 cm), superficial fistula in the distal bowel. The effectiveness of fistulotomy has been demonstrated in perianal/tip of J fistula and pouch-to-pouch fistula, etc as shown in a series of 29 patients [68]. High rates of fistula resolution (89.6%) and clinical success (75.8%) have been reported, with minimal complications such as post-procedural bleeding. Following fistulotomy, placement of endoclips can help prevent the re-approximation of the fistula tract. However, it is important to exercise caution and avoid fistulotomy in cases of long, deep fistulas, those near sphincters, or those close to anterior rectal nerves, especially due to their proximity to urogenital structures.

Injection of filling materials

Glue

Glue injection can be done endoscopically around the internal opening of the fistula. The data for glue injection are conflicting. Supplementary fibrin glue alongside anal advancement flap for intricate anal fistula repair, did not show any benefit over flap alone in an RCT [69]. Comparison of glue injection to observation alone following seton removal for low anal fistulas revealed superior fistula healing (38% vs 16%), particularly for simple fistulas [70]. A large retrospective study ($n = 119$) showed that fibrin glue injection achieved complete fistula remission in 45.4% at 1 year, with even higher rates (63%) in individuals on combined immunomodulators and biologic therapy [71].

Anal fistula plug

It is worth noting that anal fistula plu (AFP) placement is typically performed in the operating theater by surgeons, although it can also be conducted under endoscopic guidance. In a prospective study of 20 patients with Crohn's anorectal fistula, AFP successfully closed 80% of cases and 83% of fistula tracts, particularly effective in simple fistulas [72]. However, another trial found no added benefit of AFP over seton removal alone [73]. A long-term follow-up study reported an overall healing rate of 38%, with no extra advantage after using three fistula plugs [74].

Stem cells

Similar to fistula plug, endoscope stem cell injection is possible. Injection of adipose tissue-derived allogeneic stem cells (120 million cells) into fistulas effectively induced clinical and radiologic remission at 24 weeks, with remission rates of 51% compared with 36% with placebo. This effect was sustained at 52 weeks with remission rates of 56.3% vs 38.6% with placebo in complex perianal fistulas refractory to conventional and biologic therapy in CD [75, 76].

Sclerosing agents

A case report demonstrated that injecting 10 mL of 50% dextrose along with doxycycline into a chronic non-healing sinus in the rectal stump post J pouch surgery over three sessions induced fibrosis and promoted healing [77].

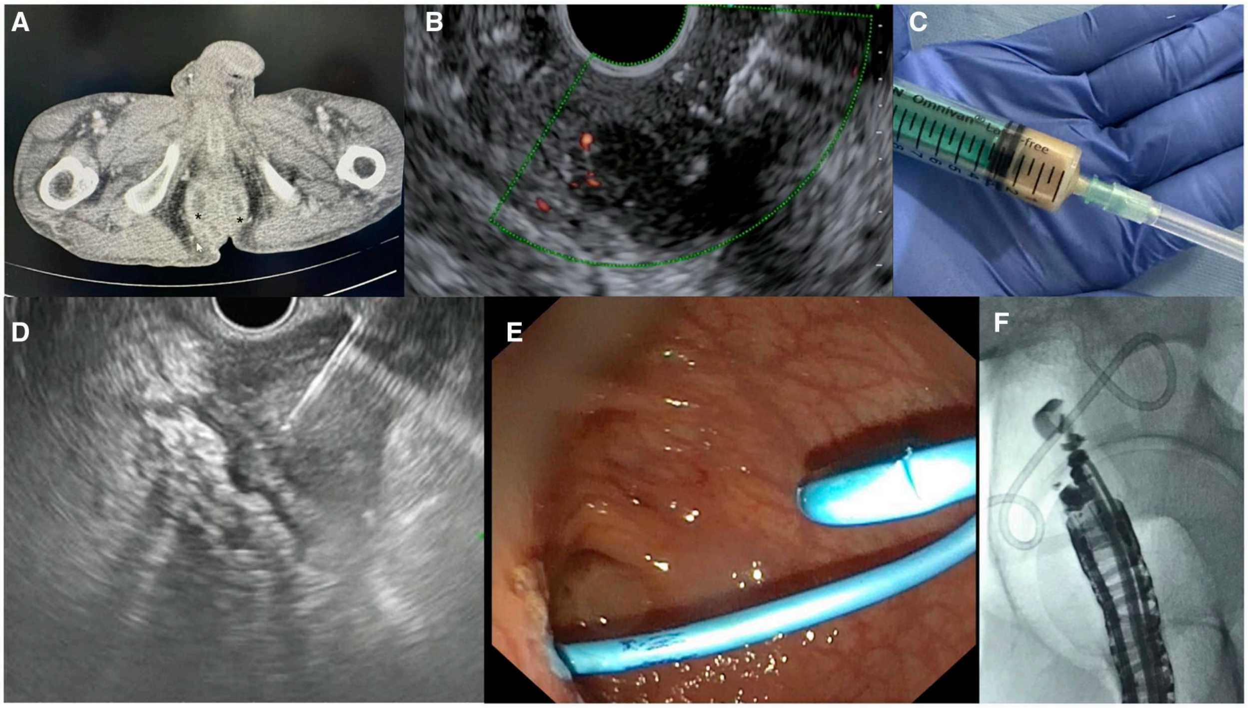

Figure 6. EUS-guided abscess drainage. (A) Perianal fistulae (*) on computed tomography. (B) Needle punctured. (C) Pus aspirated. (D) Larger pelvic abscess. (E) Pigtail placed under EUS guidance. (F) Echoendoscope and pigtail stent seen after EUS-guided drainage on fluoroscopy. EUS = endoscopic ultrasound.

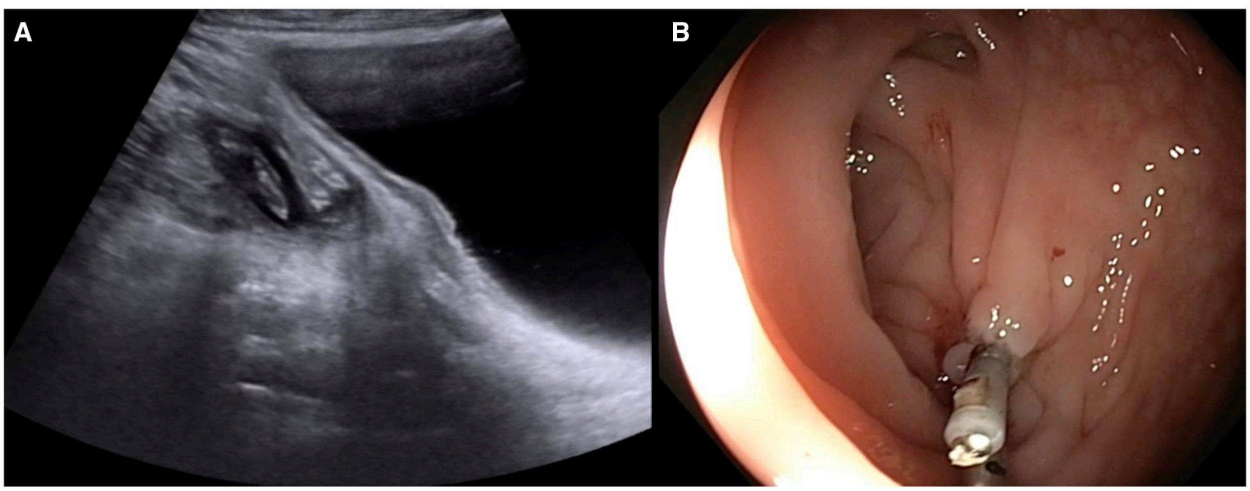

Figure 7. Endoscopic clip placement (B) for vesico-sigmoid fistula seen on intestinal ultrasound (A).

Endoscopic closure

Endoscopic clipping

OTSC, designed for gastrointestinal defect closure, outperforms thought-the-scope clips for IBD surgery-related anastomotic leaks, with higher efficacy in leaks and perforations than fistulas. Reports show OTSC effectively treated leaks at the tip of J and perianal fistulas (nearly 70% overall technical success) [78, 79]. However, OTSC is not recommended for CD-related primary fistulas or bowel-to-hollow organ fistulas due to suboptimal success rates and potential worsening (Figure 7). For enterocutaneous fistulas, OTSC can be used for intestinal feeding, but results are limited. OTSC is best suited for closure of surgery-related leaks/perforations with single tracts and minimal inflammation [3].

Endoscopic suturing

While endoscopic suturing is utilized for non-IBD fistulas, there are no reported series on its application for IBD-related fistulas. However, it is not advised for bowel-to-hollow organ fistulas (recto-vaginal and pouchovaginal) or proximal bowel fistulas due to technical challenges. Suturing may find utility in closing large perforations or fixing SEMS in IBD endoscopic procedures (Figure 2C) [3].

Endoscopic stenting

FCSEMS have been employed for post-surgical strictures and CD-related fistulas, as evidenced by three cases in a total of 20 case series. Nevertheless, stent migration poses a significant challenge and the long-term efficacy remains uncertain [80].

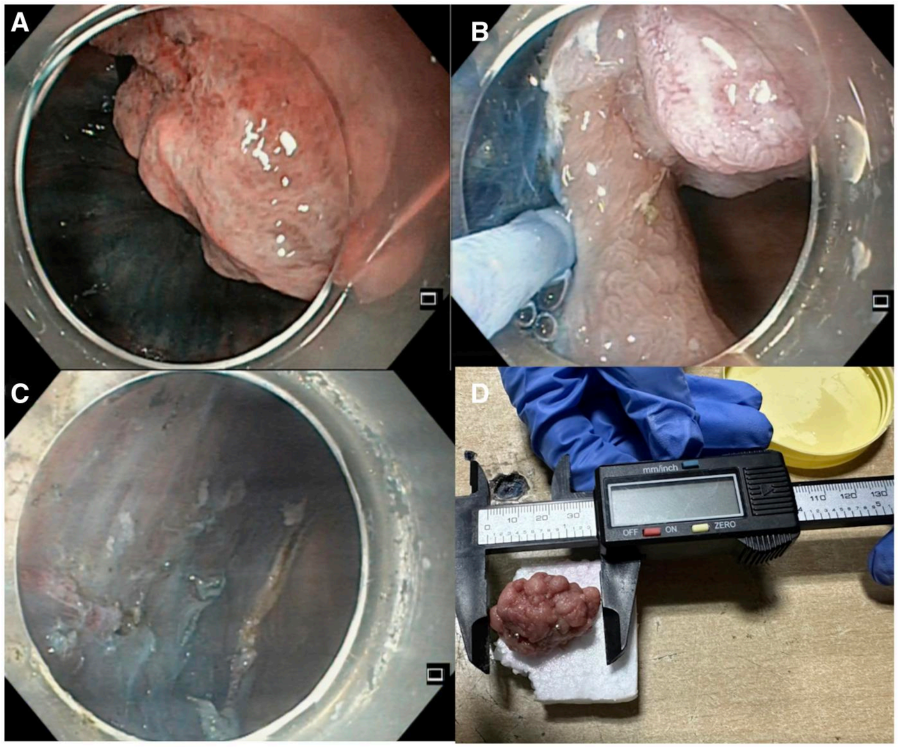

Figure 8. ESD for rectal lesion in ulcerative colitis. (A) Pre-ESD; (B) During ESD. (C) Post-ESD. (D) Specimen post-resection. ESD, endoscopic submucosal dissection.

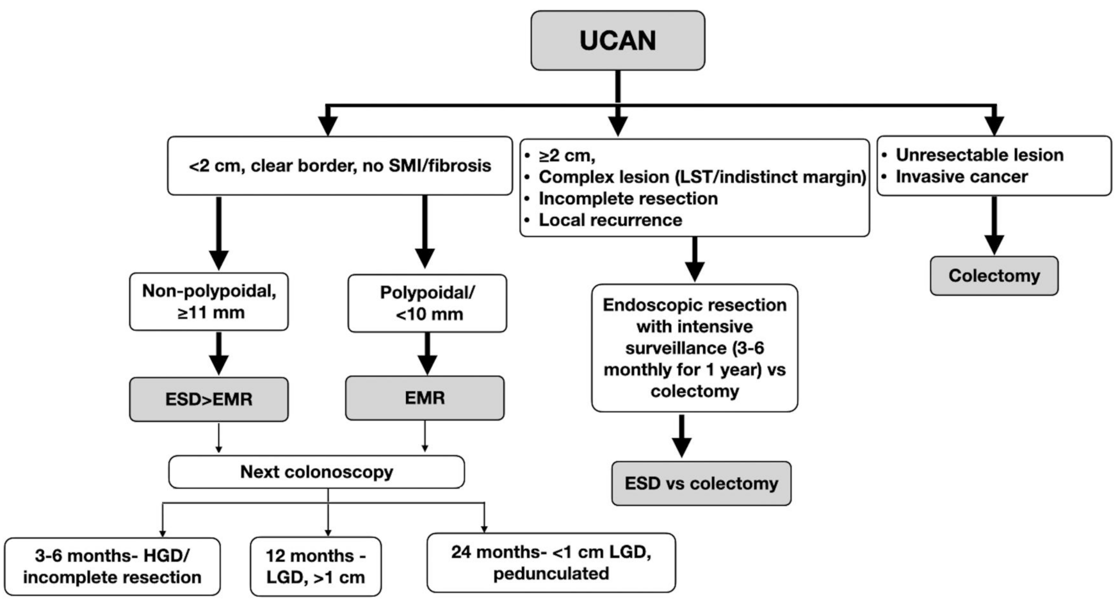

Figure 9. Endoscopic management of UCAN. ESD = endoscopic submucosal dissection, EMR = endoscopic mucosal resection, HGD = high-grade dysplasia, LGD = low-grade dysplasia, LST = laterally spreading tumor, SMI = submucosal invasion, UCAN = ulcerative colitis-associated neoplasia.

Colitis-associated neoplasia

Previously, colectomy was the standard approach for any grade of dysplasia. However, it was later recognized that endoscopic resection for polypoidal high-grade dysplasia or endoscopically visible dysplasia, formerly known as dysplasia-associated lesion or mass, along with surveillance, could circumvent the need for colectomy. Studies have shown comparable outcomes between polypectomy and proctocolectomy for polypoidal lesions, but vigilant surveillance is essential for detecting metachronous lesions [81].

Endoscopic mucosal resection

Similar to polypectomy for polypoidal lesions, flat dysplasias can be safely managed with endoscopic mucosal resection (EMR) [82]. Underwater EMR is particularly advantageous for resecting ulcerative colitis-associated neoplasia (UCAN) compared with conventional EMR, especially in areas of scarring and severe submucosal fibrosis that hinder lifting of the lesion [83]. Underwater EMR has demonstrated safety, efficacy, and time-saving benefits, effectively removing large polyps in ulcerative colitis with SMF through the 'heat-sink' and 'floating' effects [84].

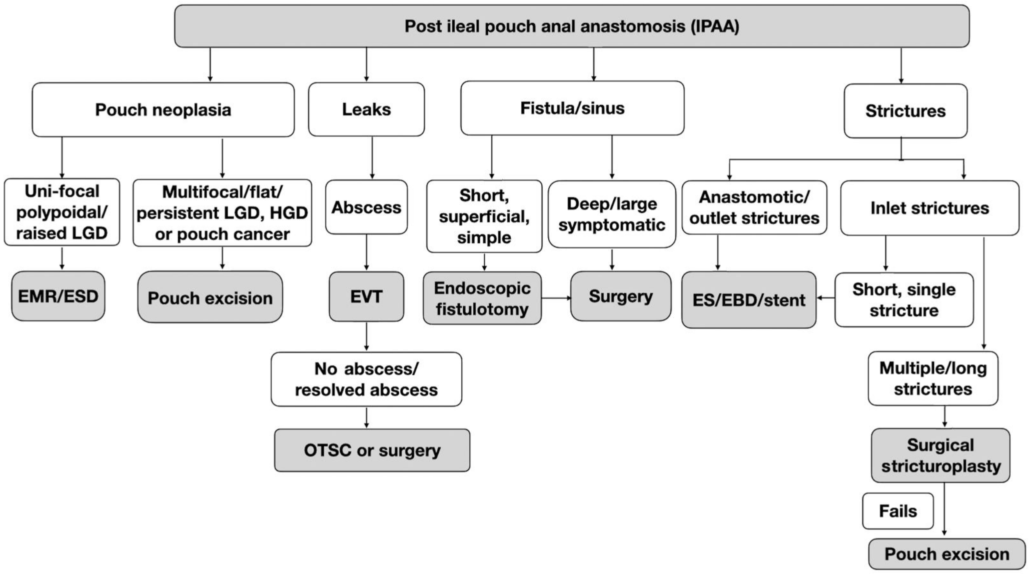

Figure 10. Algorithm for endoscopic management of pouch-related complications. EBD = endoscopic balloon dilation, EMR = endoscopic mucosal resection, ES = endoscopic stricturotomy, EVT = endoscopic vacuum therapy, HGD = high grade dysplasia, LGD = low grade dysplasia, OTSC = over the scope clip.

Endoscopic submucosal dissection

Endoscopic submucosal dissection (ESD) offers en-bloc and R0 resection rates of 83% and 67% for colitis-associated neoplasia. Long-term follow-up reveals up to 70% may develop metachronous UCAN, potentially requiring colectomy or re-ESD [85]. ESD's advantage lies in total excision biopsy (Figure 8), though technical challenges from scarring and submucosal fibrosis affect nearly 40% of cases [86]. Analysis underscores the importance of surveillance colonoscopy, revealing 21% of lesions being endoscopically invisible [86]. Techniques like multi-traction with clips address recurrence of high-grade dysplasia [87]. Water pressure-assisted ESD shows promise for faster procedures [88]. Meta-analyses reported high en-bloc and R0 resection rates, with ESD efficacy linked to lesion characteristics like invasiveness and surface features [89]. ESD for non-polypoidal UCAN yields inferior outcomes due to submucosal fibrosis [90–92]. Prior to ESD-era, approaches like EMR and argon plasma coagulation were utilized for challenging large, poorly lifting adenomas [93].

Choice of endoscopic resection technique for UCAN

The decision between ESD and EMR for UCAN can be guided by recent findings indicating higher R0 resection rates with ESD for lesions ≥11 mm (94% vs 55%) and non-polypoidal lesions (100% vs 55%). EMR may be preferable for lesions ≤10 mm (Figure 9). However, ESD carries a 10% risk of intra-procedural perforation and 3% of patients may develop metachronous high-grade dysplasia [94]. Another study suggests EMR for small lesions without fibrosis and ESD for large lesions with fibrosis [95]. Notably, both techniques aid in preventing colectomy by removing large UCAN [96]. As opposed to UCAN, the risk of progression is lower in sporadic adenoma in the non-colitic segment in UC. Hence, polypectomy or EMR could be an acceptable option in sporadic adenoma as compared with UCAN [81].

Alternative modalities to EMR or ESD

Hybrid resection combining ESD and full-thickness resection device can be effective for lesions with severe submucosal fibrosis, particularly in large laterally spreading tumors [97]. ESD-assisted EMR, dating back to 2008, demonstrated an en-bloc resection rate of 78% with an R0 resection rate of 94% in patients undergoing en-bloc resection [98]. Recently, full-thickness resection device was successfully used in a case of long-standing UC for a non-lifting, fibrotic adenoma in the descending colon [99].

Risk of recurrence

Following endoscopic resection of polypoid dysplasia in UC, the recurrence rates for cancer and any dysplasia are 5.3 cases/1,000 patient-years and 65 cases/1,000 patient-years, respectively [100].

Role of IIBD in postoperative pouch complications in UC

Endoscopic therapy holds a pivotal role in addressing postoperative pouch complications in UC. Pouch strictures, among other issues like floppy pouch complex or anastomotic leaks, are often manageable through endoscopic means (Figure 10).

Pouch strictures

Pouch outlet strictures related to sealed ileal pouches have been effectively managed using wire-guided stricturotomy with an insulated tip knife. Additionally, both inlet and outlet pouch strictures have shown successful outcomes with controlled radial expansion balloon dilation, improving symptoms and quality of life for patients, particularly those with CD of the pouch [101].

EBD has demonstrated a clinical success rate of 66.7%, with pouch inlet/afferent limb strictures effectively treated using both EBD and ES. However, ES carries a higher risk of bleeding (4.7% vs 0% with EBD), while EBD poses a higher risk of perforation (0.8% vs 0% with ES). Factors such as stricture length (>5 cm) and pouchitis are predictive of subsequent surgery [36].

Studies have emphasized EBD as the preferred initial treatment for pouch strictures, with high technical (98%) and clinical success (95%) rates reported without major adverse events. Long-term follow-up studies have shown favorable outcomes, with a

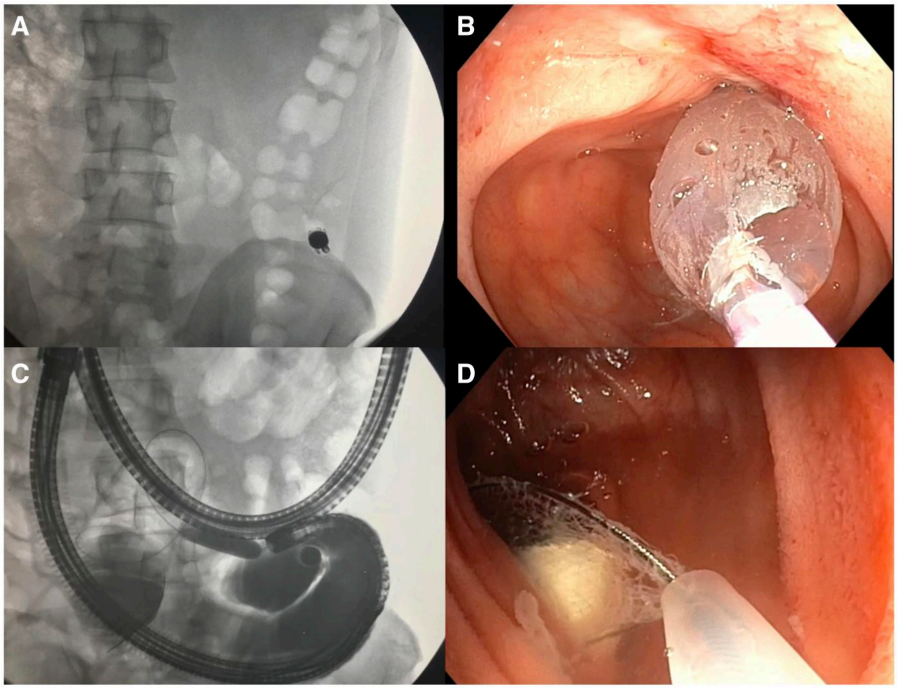

Figure 11. Device-assisted enteroscopy-guided removal of impacted capsule endoscope. (A) Fluoroscopy showing radiopaque capsule. (B) Endoscopic balloon dilation of the stricture. (C) Fluoroscopic visualization of balloon. (D) Removal of the capsule endoscope using motorized spiral enteroscope.

majority of patients (87.3% over 10 years) retaining their pouches over extended periods [102].

For pouch-anal strictures, a systematic review recommends bougie dilation followed by balloon dilation as primary modalities before considering surgical options. Endoscopic therapy, particularly EBD, is crucial for managing fibrotic strictures, while inflammatory strictures may require medical treatment. Surgical stricturoplasty is preferred over pouch excision for mid-pouch strictures [103].

Pouch leaks

Pouch leaks, particularly from the 'tip of the J', have been effectively managed using two OTSCs, resulting in successful closure in approximately two-thirds of patients with one or two sessions. However, subsequent procedures, either with OTSC clips or endoscopic suturing, were needed in 50% of cases, and ultimately, one-third of patients required surgery [104].

For anastomotic leakage post-IPAA, a short period of endoscopic vacuum therapy (EVT) with periodic sponge changes has demonstrated efficacy in facilitating early surgical closure. In one study, 100% secondary anastomotic healing was achieved in the early closure group compared with 52% in the conventional treatment group, with median healing times of 48 and 70 days, respectively [105]. Another series documented complete healing of leaks within a median of 2 months [106]. Therefore, EVT can be considered for managing anastomotic leaks post-IPAA, while OTSC should be reserved for leaks without abscess formation [107].

Pouch fistula

Endoscopic fistulotomy is effective for short, superficial, simple fistulas like pouch-to-pouch, perianal, and ileo-cecal types [107]. In IBD-related cases, it achieves a 90% success rate, with 10% requiring surgery [68]. Comparing with redo-surgery, it shows superior healing rates (78.4% complete healing) with lower subsequent surgery and adverse events [108]. Clipping combined with fistulotomy effectively heals pouch-to-pouch fistulas [109].

Pouch sinus

Endoscopic sinusotomy is an effective treatment for chronic pouch anastomotic sinus following IPAA in UC, with a moderate healing rate (53.2% complete, 15.3% partial). Compared with redo surgery, which initially achieves a higher complete healing rate of 94%, endoscopic sinusotomy demonstrates lower morbidity (2.5% vs 43.5%). Recurrence rates and the need for further surgery are not significantly different between endoscopic and surgical closure approaches [110].

Similarly to pouch fistulas, EVT can help manage anastomotic leaks post-IPAA to prevent the development of chronic presacral sinuses [111]. For refractory sinus post-IPAA, multiple sessions of endoscopic sinusotomy guided by Doppler ultrasound, along with topical doxycycline injection, have been utilized. However, surgery may be necessary for large, deep symptomatic sinuses, as endoscopic therapy is typically reserved for small sinus tracts [112].

Studies investigating factors influencing sinus healing and pouch survival have identified CD of the pouch as a negative predictor of healing, while higher body mass index and longer intervals between sinusotomies are positive predictors [113]. Conversely, excess body mass index gain post-sinusotomy has been associated with recurrent sinuses [114]. Factors influencing surgery-free survival include acute anastomotic leak, toxic megacolon, and longer or delayed sinusotomy, with protective factors including longer intervals between sinusotomies and concurrent use of 50% dextrose and doxycycline [113].

Endoscopic hemostasis for severe bleeding in diverted ileal pouches can be achieved with hypertonic saline spray containing 50% dextrose [115]. Multiple endoscopic sinusotomies increase the chances of sinus healing, while delayed diagnosis and complex sinuses negatively impact success rates [116].

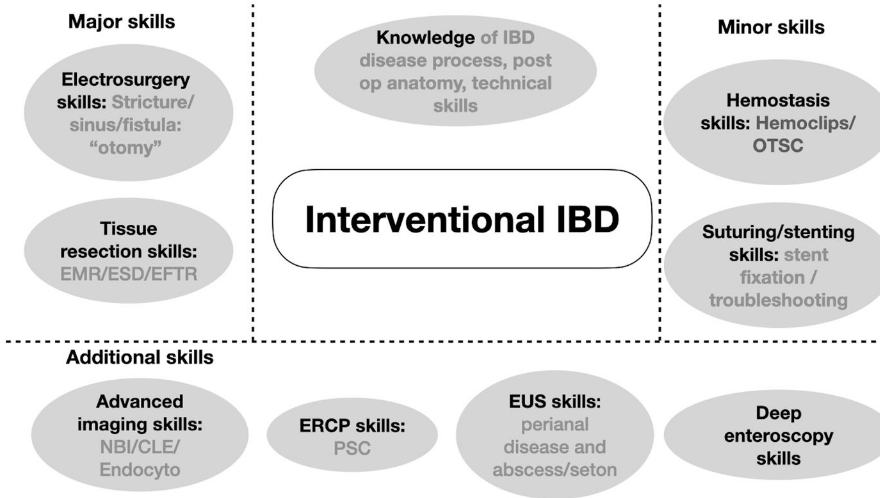

Figure 12. Skills required for interventional IBD therapies. CLE = confocal laser endomicroscopy, EFTR = endoscopic full-thickness resection, EMR = endoscopic mucosal resection, ERCP = endoscopic retrograde cholangiopancreatography, ESD = endoscopic submucosal dissection, IBD = inflammatory bowel disease, NBI = narrow band imaging, OTSC = over the scope clip, PSC = primary sclerosing cholangitis.

Floppy pouch complex

In managing floppy pouch complex, lifestyle modifications should be initially attempted, such as avoiding excessive straining. If unsuccessful, endoscopic ligation or plication can be considered [117].

Pouch neoplasia

Pouch neoplasia, including low-grade dysplasia, high-grade dysplasia, adenocarcinomas, and squamous cell carcinomas, can develop after IPAA. Established risk factors such as pre-colectomy cancer or dysplasia, along with proposed factors like primary sclerosing cholangitis, family history of colon cancer, chronic pouch inflammation, long-standing UC, and type 'C' mucosa (atrophic mucosa with chronic inflammation), indicate the risk of pouch neoplasia and necessitate regular pouch surveillance [118].

Annual pouchoscopy with biopsies from specific sites is recommended for individuals with established risk factors, while those with proposed risk factors may undergo surveillance pouchoscopy every 1–3 years [119]. Patients without risk factors should have surveillance pouchoscopy every 3 years. Early detection through surveillance is crucial as pouch neoplasia carries a poor prognosis, and prompt intervention can salvage the pouch.

Following endoscopic resection of uni-focal polypoidal or raised low-grade dysplasia, surveillance should occur every 3 months for 2 years. Resection should be en-bloc, regardless of the method used (polypectomy, EMR, or ESD), with extensive biopsy of adjacent mucosa (Figure 10). Multifocal, flat, or persistent low-grade dysplasia, high-grade dysplasia, or pouch cancer may require surgical intervention such as excision, mucosectomy, or pouch advancement. Individuals with established risk factors may ultimately require complete proctectomy [118].

Endoscopic retrieval of retained capsule endoscope

Endoscopic retrieval of retained capsule endoscope has been described with double balloon enteroscopy and motorized spiral enteroscopy with or without EBD of small bowel strictures (Figure 11) [120, 121]. The success rate could be as high as 80%–92% with double balloon enteroscopy [122, 123].

Bleeding control

Focal bleeding from visible vessel can be stopped using hemoclips in UC or CD [121].

Future directions and research gaps

Despite advancements in interventional endoscopy for IBD, significant research gaps persist, particularly in long-term efficacy and safety data, comparative effectiveness of treatments, standardization of protocols, and development of innovative endoscopic technologies tailored for IBD. Additionally, there is a need for predictive biomarkers to guide personalized treatment, prediction of treatment success, studies on combined endoscopic and surgical approaches, and an emphasis on patient-reported outcomes and quality of life. Addressing these gaps through comprehensive, long-term, and comparative studies will refine the role of interventional endoscopy in IBD management, leading to optimized patient care.

Conclusions

Treating complications of IBD with endoscopic therapy presents challenges. The bowel is frequently inflamed, fibrotic, and affected by the transmural nature of the disease. Additionally, altered bowel anatomy, suboptimal bowel preparation, compromised nutritional status, and concurrent use of biologics or steroids further complicate the process. Interventional endoscopy for IBD needs multifaceted approach and training (Figure 12). However, IIBD has the potential to delay or prevent surgery and help manage postoperative complications. IIBD is a bridge between medical and surgical therapy. Stricture, fistula, abscess, and neoplasia can be treated with IIBD therapies prior to surgery. Post-surgical recurrence of complications can be managed by IIBD. Future controlled studies with long-term follow-up are warranted to position these therapies in the current management algorithm.

Authors' Contributions

P.P. was responsible for conceptualization, literature review, original draft writing, illustrations, proofreading, and critical review.

D.N.R. was responsible for proofreading and critical review. Both authors read and approved the final version of the manuscript.

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Conflicts of Interest

None declared.

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