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MINIREVIEWS

Endoscopy in inflammatory bowel disease: Role in diagnosis, management, and treatment

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Abstract

Endoscopy plays a fundamental role in the diagnosis, management, and treatment of inflammatory bowel disease (IBD). Colonoscopy, flexible sigmoidoscopy, and esophagogastroduodenoscopy have long been used in the care of patients with IBD. As endoscopic technologies have progressed, tools such as endoscopic ultrasound, capsule endoscopy, and balloon-assisted enteroscopy have expanded the role of endoscopy in IBD. Furthermore, chromoendoscopy has enhanced our ability to detect dysplasia in IBD. In this review article, we will focus on the roles, indications, and limitations of these tools in IBD. We will also discuss the most commonly used endoscopic scoring systems, as well as special considerations in post-surgical patients. Lastly, we will discuss the role of endoscopy in the diagnosis and management of fistulae and strictures.

Key words: Endoscopy; Inflammatory bowel disease; Crohn's disease; Ulcerative colitis; Colonoscopy; Capsule endoscopy; Dysplasia detection; Stricture dilation; Fistula management

Core tip: Although endoscopy has long been used in the diagnosis and management of inflammatory bowel disease (IBD), technologic advances have allowed for additional tools to assist in the management and treatment of IBD patients. This review article discusses the roles, indications, and limitations of endoscopy in IBD.

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INTRODUCTION

Endoscopy plays a fundamental role in the diagnosis, management, and treatment of inflammatory bowel disease (IBD). Endoscopy is essential in excluding other etiologies, establishing diagnoses, differentiating between Crohn's disease (CD) and ulcerative colitis (UC), monitoring disease activity and response to treatment, and assessing for and treating complications. Colonoscopy, flexible sigmoidoscopy, and esophagogastroduodenoscopy (EGD) have long been used in the care of patients with IBD. As endoscopic technologies have progressed, tools such as endoscopic ultrasound, capsule endoscopy, and balloon-assisted enteroscopy have expanded the role of endoscopy in IBD. This review will focus on the role, indication, and contraindication of these tools in the management of IBD.

ENDOSCOPY IN DISEASE DIAGNOSIS

Diagnostic lower endoscopy (colonoscopy, flexible sigmoidoscopy)

In patients with clinical presentations suggestive of IBD, the initial evaluation should include a colonoscopy with intubation and examination of the terminal ileum[1]. Colonoscopy with ileoscopy not only allows for direct visualization of the colon and terminal ileum, but also allows for necessary biopsies to be performed. When IBD is suspected, two biopsy specimens from five sites, including the ileum and rectum, are recommended[2]. Biopsy specimens should be obtained from both affected and normal-appearing mucosa; specimens from different locations should be labeled and submitted separately[1]. The combination of endoscopic and histologic features assists in IBD diagnosis, the differentiation of CD *vs* UC, as well as in the exclusion of other disease entities with similar presentations (*e.g.*, drug-induced colitis, infectious colitis, ischemic colitis, and segmental colitis associated with diverticulosis). Although flexible sigmoidoscopy is inadequate for a complete initial evaluation of suspected IBD, it can be useful in a few specific circumstances. Overall, colonoscopy is a safe procedure with a low rate of adverse events in patients with IBD. However, it is relatively contraindicated in patients with severe colitis and toxic megacolon. Therefore, in cases where a full colonoscopy is contraindicated, flexible sigmoidoscopy can provide a safer alternative that allows for distal bowel examination and biopsy acquisition. Additionally, flexible sigmoidoscopy can be used in patients with established IBD to assess disease activity and/or to rule out concomitant infection.

While patient presentation, history, laboratory information, and radiologic data can assist, colonoscopy is essential in differentiating UC from CD. Classically described endoscopic findings in UC include edema, loss of vascularity, erythema, mucosal granularity and friability, erosions and ulcers, and pseudopolyps. In treatment-naïve patients, these findings typically begin at the rectum and extend proximally in a continuous manner with a gradual transition to normal-appearing mucosa[3]. It is important to note that UC patients on treatment can have patchy inflammation and rectal sparing[4]. Additionally, approximately 5% of patients may also have an area of isolated peri-appendiceal inflammation, commonly known as a cecal patch, which does not have any correlation with disease activity or clinical course[5,6]. While many of the classic findings of UC can also been seen in CD, three major endoscopic findings that can aid in distinguishing CD from UC are the presence of apthous ulcers, cobblestoning, and discontinuous or "skip" lesions[7]. Although isolated involvement of the terminal ileum is highly suggestive of CD, "backwash ileitis" can occur in UC in the setting of pancolitis[8]. Mucosal biopsies with histologic examination, upper gastrointestinal (GI) and small bowel endoscopy, small bowel imaging, and serologic markers can further assist when diagnostic uncertainty remains.

Diagnostic upper endoscopy

Although upper GI tract involvement can occur in up to 16% of patients with CD[9], routine EGD is currently not recommended in adult patients suspected of having CD. However, EGD is often included in the diagnostic evaluation of suspected IBD secondary to the overlap of IBD symptoms and indications for upper endoscopy such as abdominal pain, weight loss, nausea, and vomiting. Additionally, in adults with unclassified IBD, upper endoscopy can aid in the diagnosis of CD if upper GI involvement is found. At least two biopsies should be taken from the esophagus, stomach, and duodenum during EGD for suspected upper tract IBD[10]. Endoscopic findings of upper GI CD include aphthous ulcers, strictures, fistulas, and erythema. Upper GI tract disease can present simultaneously with distal disease or later in the disease course[11]. In pediatric populations, isolated upper GI CD occurs more commonly than in adults. Thus, an EGD is recommended as part of the initial evaluation of children with suspected IBD, regardless of upper GI symptoms[12]. Upper endoscopy is also useful in evaluation for celiac disease which can have a similar presentation to IBD in both the adult and pediatric populations.

Wireless video capsule endoscopy

Wireless video capsule endoscopy (VCE), first approved in 2001, has developed into a safe and effective technology to image the small intestine. The noninvasive nature of the VCE is a significant advantage over enteroscopy, and the ability to detect early mucosal lesions allows for a greater sensitivity than radiologic studies. The diagnostic yield of VCE can be as high as 71%, depending on the clinical setting[13]. Typical findings of CD on VCE include

Table 1 Mayo endoscopic subscore

Normal (0): No inflammatory signs
Mild (1): Erythema
Moderate (2): Friability, erosions
Severe (3): Spontaneous bleeding, ulcerations

Four-grade scale (0-3)[22].

Table 2 Simple endoscopic score in Crohn's disease

Ulcer: None (0), 0.1-0.5 cm (1), 0.5-2 cm (2), > 2 cm (3)
Ulcerated surface: None (0), < 10% (1), 10%-30% (2), > 30% (3)
Affected surface: None (0), < 50% (1), 50%-75% (2), > 75% (3)
Narrowing: None (0), single passable (1), multiple passable (2), impassable (3)

Sum of five segments scores for a total score (0-56)[23].

erythema, erosions, ulcerations, and strictures[14]. VCE should not be used in patients with known or suspected strictures, as capsule retention has been described in up to 13% of patients who underwent a capsule study for CD[15]. Therefore, it is recommended that patients with known small bowel CD have small bowel imaging or a patency study prior to VCE. The aforementioned mucosal findings are not specific to CD and can be found in patients with other etiologies, including NSAID use. Therefore, an important limitation to VCE is the inability to obtain tissue for histologic diagnosis. The PillCam® SB3 is a new capsule designed to provide improved diagnostic accuracy due to better image quality and creating more images with an adaptive frame rate of 2-6 frames per second. Additionally, using the automatic mode of Rapid Reader® software version 8.0 is expected to reduce the reading time and minimize the possibility of missing lesions[16]. Given these improvements, this is being marketed for use in the evaluation of CD.

Balloon assisted enteroscopy

Given the high diagnostic yields of less-invasive modalities such as radiologic small bowel imaging and VCE, enteroscopy has a limited role in the initial evaluation of patients with suspected IBD. However, when small bowel abnormalities are identified by less invasive studies, endoscopic and histologic evaluation is often a necessary next step. When the location lies outside the reach of standard endoscopy, balloon-assisted anterograde or retrograde enteroscopy can be used to access the area of interest. Additionally, enteroscopy allows for therapeutic interventions such as hemostasis, stricture dilation, or foreign body retrieval. However, deep enteroscopy can be time consuming and technically challenging which often limits use to specialized providers and centers.

ENDOSCOPY IN DISEASE MANAGEMENT

Assessment of disease activity and response to treatment

Endoscopy allows for the visual assessment and histologic confirmation of treatment response, thus playing a critical role in the management of IBD. Clinical trials have shown that mucosal healing has been associated with improved outcomes in IBD, including sustained remission, fewer hospitalizations, and a decreased need for surgery[17,18]. Therefore, endoscopic outcomes, such as mucosal healing, are now recommended treatment goals in clinical practice[19]. In 2015, the Selecting Therapeutic Targets in Inflammatory Bowel Disease initiative set forth consensus recommendations for treat-to-target goals[19]. The international consensus group recommended that disease activity be reassessed at 6 to 9 mo by endoscopy in CD and at 3 to 6 mo after the start of therapy in UC[19]. Although no consensus exists for endoscopic disease severity scores, numerous endoscopic classification and scoring systems have been developed to standardize endoscopic assessment[20,21]. The Mayo Endoscopic Subscore for UC[22] and the Simple Endoscopic Score for CD (SES-CD)[23] are often used both in clinic trials and clinical practice and can be seen in Tables 1 and 2. Familiarity with and regular use of a disease classification and severity scoring system allows for a more standardized monitoring protocol among providers.

CRC screening and surveillance

Patients with IBD have an increased risk of developing colorectal cancer (CRC) compared to the general population[24]. Therefore, surveillance endoscopy to detect dysplasia has been recommended in patients with UC and CD with colon involvement beginning eight years after diagnosis. Additionally, surveillance colonoscopy is recommended annually, beginning at the time of diagnosis, in patients with concomitant primary sclerosing cholangitis given the high risk of CRC in this population[1,25,26].

Prior to the use of high imaging quality endoscopes, IBD-related dysplasia was thought to be an endoscopically invisible entity. Therefore, a random biopsy technique was recommended by societies and became common practice. In the era of high definition endoscopes and chromoendoscopy, most IBD-related dysplasia is now believed to be visible and endoscopically identifiable. Rather than random biopsies, a targeted biopsy sampling method is now recommended[27]. In 2015, the Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients: International Consensus (SCENIC)[28] published a consensus statement on surveillance and management of dysplasia in IBD; key recommendations can be seen in Table 3. Highlights of the SCENIC recommendations include the use of chromoendoscopy with targeted biopsy sampling rather than random biopsy sampling and the use of high-definition instead of standard-definition colonoscopes.

Along with the advances in dysplasia detection, the management of IBD-related dysplasia has also progressed. Historically, patients with dysplasia were primarily managed with colectomy. However, it is now

Table 3 Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients: International Consensus recommendations for optimizing detection and management of dysplasia in inflammatory bowel disease[28]

Detection of dysplasia on surveillance colonoscopy	When performing surveillance with white-light colonoscopy, high definition is recommended rather than standard definition
	When performing surveillance with standard-definition colonoscopy, chromoendoscopy is recommended rather than white-light colonoscopy
	When performing surveillance with high-definition colonoscopy, chromoendoscopy is suggested rather than white-light colonoscopy
	When performing surveillance with standard-definition colonoscopy, narrow-band imaging is not suggested in place of white-light colonoscopy
	When performing surveillance with high-definition colonoscopy, narrow-band imaging is not suggested in place of white-light colonoscopy
	When performing surveillance with image-enhanced high-definition colonoscopy, narrow-band imaging is not suggested in place of chromoendoscopy
Management of dysplasia discovered on surveillance colonoscopy	After complete removal of endoscopically resectable polypoid dysplastic lesions, surveillance colonoscopy is recommended rather than colectomy
	After complete removal of endoscopically resectable nonpolypoid dysplastic lesions, surveillance colonoscopy is suggested rather than colectomy
	For patients with endoscopically invisible dysplasia (confirmed by a GI pathologist) referral is suggested to an endoscopist with expertise in IBD surveillance using chromoendoscopy with high-definition colonoscopy

IBD: Inflammatory bowel disease.

Table 4 Rutgeerts score for Crohn's disease recurrence at ileocolonic anastomoses[35]

i0 no lesions in neoterminal ileum
i1 < 5 aphthous lesions in neoterminal ileum
i2 > 5 aphthous lesions with normal mucosa, skip areas with larger lesions, anastomotic lesions
i3 diffuse aphthous ileitis
i4 diffuse inflammation with ulcer, nodules, and/or stenosis

recommended that dysplasia determined to be "endoscopically resectable" be managed with polypectomy, endoscopic mucosal resection, or submucosal dissection[28]. Colectomy is now reserved for patients with "endoscopically unresectable" lesions, endoscopically invisible high-grade dysplasia despite chromoendoscopy, or multifocal dysplasia[29].

Post-surgical management

Special considerations are necessary in the care of patients who undergo an IBD-related surgery. Familiarity with post-surgical anatomy and the diagnosis and treatment of common postoperative complications are required for adequate treatment of the post-surgical patient population.

For patients with UC, ileal pouch anal anastomosis (IPAA) has become the surgical treatment of choice in patients who require colectomy. During ileal pouch endoscopy, or pouchoscopy, a gastroscope is most commonly used to examine the pouch, anastomosis, and afferent small bowel. The gastroscope allows for greater maneuverability than a colonoscope and its smaller caliber allows it to pass through a stricture or tight anastomosis more easily than the larger adult or pediatric colonoscopes. Pouchitis is the most common complication of IPAA and occurs in up to 50% of patients over 10 years of follow-up[30]. Endoscopic findings of pouchitis include mucosal erythema, edema, granularity, erosions, and ulcerations. Other possible complications after IPAA include cuffitis, pouch leakage, CD of the pouch, and pouch failure. Pouch strictures are relatively common and endoscopic therapy with balloon dilation has been found to be both safe and effective[31].

Patients with CD who undergo partial colectomy or partial ileocolectomy should have an endoscopic evaluation of the neoterminal ileum six months to one year after surgery[32,33] to evaluate for and stratify risk of recurrence. CD can recur after surgery, most commonly at the surgical anastomosis and neoterminal ileum[34]. The Rutgeerts Score[35] may be used to classify the risk of CD recurrence after ileocolonic anastomosis (Table 4). In patients who have undergone total colectomy and end-ileostomy (patients with CD, or older UC patients with poor functional outcomes after IPAA), ileoscopy can be performed to visualize the ileum and assess for disease response/recurrence.

ENDOSCOPIC THERAPY IN IBD

Stricture evaluation and management

Modern IBD medical therapies, including anti-tumor necrosis factor agents (ant-TNFs), have improved the natural history of CD. This is especially true when used before the development of irreversible fibrotic intestinal damage. Despite this, stricturing complications remain a significant cause of surgery, disability, and reduced quality of life in IBD patients[36]. Endoscopy is essential in the diagnosis and assessment of IBD-related strictures and is an evolving option for treatment.

Radiologic investigation is often an initial step when a patient with CD presents with obstructive symptoms suspicious for stricturing disease. Whether a CT scan is obtained in an emergent setting due to concern for pending small bowel obstruction, or a planned entero-

graphy is obtained prior to endoscopy, radiologic studies can provide vital information about IBD-related strictures. However, endoscopy is indispensable to allow for visual assessment of the stricture, biopsy to exclude malignancy, and to provide therapy in select cases.

In patients with CD, strictures are most often located in the terminal ileum and colon. In post-surgical patients, the site of ileo-colonic surgical anastomosis is a common location for stricturing[37]. Surgery has been a long-standing treatment option for CD-related strictures with stricturoplasty or small bowel resection. However, endoscopic balloon dilation (EBD) is increasingly used in patients with CD strictures to avoid surgery. The symptomatic benefits of endoscopic treatment can be sustained, with the ability to avoid surgery at 1, 3, and 5 years in 80%, 57%, and 52% of patients, respectively, based on a retrospective series[38]. In general, EBD is most successful in patients with a short stricture (4 cm or less) with minimal inflammation, straight angle of stricture (in line with the bowel lumen), and when there is a narrowing attributable to a single surgical anastomosis without a fistula orifice nearby[39,40]. Additionally, EBD has been found to be safe, with only a 3% rate of perforation[41]. Typically, the maximum balloon diameter used for stricture dilatation is 20 mm and stricture with fistula is classically a contraindication for endoscopic dilatation. Endoscopic balloon dilatation of ileoanal pouch strictures is safe and effective and is often recommended as the first line strategy to treat ileoanal pouch strictures[42].

Although endoscopic injection of steroids and anti-TNFs have been attempted, there is no clear evidence to support this as an adjunct to EBD. Needle-knife stricturotomy[43] and self-expanding metal stent placement[44] are additional described techniques of endoscopic stricture management. However, the indication, efficacy, and safety are still being determined and future studies will be necessary before mainstream use can be recommended. Lastly, it should be noted that a colonic stricture in UC should be considered malignant until proven otherwise. If adequate biopsies are not possible, surgery should be considered[45].

Fistula evaluation and management

Endoscopic ultrasound (EUS) has developed a role in the management of IBD, most commonly in the evaluation of perianal CD. Traditionally, surgical exam under anesthesia (EUA) or magnetic resonance imaging (MRI) were used in evaluation for suspected fistulae. However, EUS has been found to be equivalent to MRI or EUA[46] for the evaluation of perianal fistulae. EUS provides the additional benefit of being able to be performed in real-time in combination with traditional endoscopy. Endoscopic fistula treatment, including endoscopic suturing, over-the-scope clipping, endoscopic fistulotomy, and endoscopic drainage and seton placement have been described[47]. However, until recently, the treatment of fistulae refractory to medical therapy has been predominantly surgical. A recent study which included 29 consecutive patients with fistulas and IBD showed that endoscopic fistulotomy with a needle-knife appears to be safe and effective in treating IBD-related fistulas. Twenty-six patients (89.6%) achieved complete resolution of the fistula, while three patients (10.3%) had a persistent fistula and required surgical intervention[48].

CONCLUSION

Endoscopy plays an essential role in the diagnosis of IBD, differentiating between CD and UC, monitoring disease activity, assessing for and treating complications, and for colorectal cancer surveillance. New technologies and endoscopic techniques allow for an evolving role of endoscopic management of complications, such as strictures, that traditionally required surgery.

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