ASGE guideline: endoscopy in the diagnosis and treatment of inflammatory bowel disease

This is one of a series of statements discussing the use of gastrointestinal endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy prepared this text. In preparing this guideline, a MEDLINE literature search was performed, and additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants. When little or no data exist from well-designed prospective trials, emphasis is given to results from large series and reports from recognized experts.

Guidelines for appropriate use of endoscopy are based on a critical review of the available data and expert consensus. Further controlled clinical studies are needed to clarify aspects of this statement, and revision may be necessary as new data appear. Clinical consideration may justify a course of action at variance to these recommendations.

INTRODUCTION

Endoscopy is an important diagnostic and therapeutic modality in inflammatory bowel disease (IBD), being useful for both Crohn’s disease (CD) and ulcerative colitis (UC). Endoscopy is used to make an initial diagnosis of IBD, distinguish CD from UC, assess the disease extent and activity, monitor response to therapy, allow for surveillance of dysplasia or neoplasia, and provide endoscopic treatment, such as stricture dilation.

COLONOSCOPY WITH ILEOSCOPY

Colonoscopy with ileoscopy allows direct visualization and biopsy of the mucosa of rectum, colon, and terminal ileum. Unless contraindicated because of severe colitis or possible toxic megacolon, a full colonoscopy with intubation of the terminal ileum should be performed during the initial evaluation of patients with a clinical presentation suggestive of IBD. Because sodium phosphate–based bowel preparations and nonsteroidal anti-inflammatory drugs (NSAIDs) can cause mucosal changes mimicking IBD, these agents should be avoided before initial colonoscopy.

Patients with other colitides can have similar clinical presentations and similar endoscopic features to the patients with IBD. These colitides include infectious colitis, drug-induced colitis, ischemic colitis, and radiation colitis. The value of endoscopy alone in distinguishing IBD from non-IBD colitides is limited. However, the acquisition of the detailed information from index colonoscopy is important for the differential diagnosis of CD and UC because, once therapy is started, it may obscure discriminating features of CD from UC such as segmental colitis (patchiness) and rectal sparing. In a study of 39 patients with treated UC, 44% of patients had endoscopic patchiness and 13% had endoscopic rectal sparing; 33% had histologic evidence of patchiness and 15% had histologic sparing. At the time of colonoscopy, attention should be paid to the anal and perianal area because abnormalities are commonly seen in the setting of CD. The most useful endoscopic features (particularly the initial or index endoscopy) used to differentiate CD from UC are segmental colitis (ie, patchiness), rectal sparing, involvement of the terminal ileum, and anal or perianal disease. Other endoscopic features suggestive of CD include aphthous ulcers, discrete ulcers, serpiginous ulcers, and cobblestoning of mucosa. However, none of the endoscopic features is specific for CD or UC.

Ileoscopy is important to distinguish true CD ileitis from backwash ileitis, which occurs in up to 10% of cases of active pancolitis in UC. Features that favor CD ileitis include discrete ulcers or strictures of the terminal ileum or ileocecal valve. UC may progress proximally over time. The finding of inflammatory changes around the appendiceal orifice (cecal patch or periappendiceal patch) in the setting of UC with an otherwise normal right colon should not be confused with CD. The clinical implication of cecal patch is not clear, although a recent controlled study revealed that patients with UC with cecal patch had a similar rate of remission, relapse, and proximal extension compared with those with no cecal patch.

Endoscopy together with other diagnostic modalities can differentiate CD from UC in ≥ 85% of patients. In a prospective study of more than 350 patients with IBD followed up for more than 22 months, index colonoscopy and biopsy were accurate in distinguishing CD from UC in...
89% of cases. IBD diagnosis was revised in 4% of cases, and the diagnosis of indeterminate colitis remained in 7% of cases.\textsuperscript{14}

Mucosal biopsy is a critical component of endoscopic examination for patients with suspected IBD to differentiate IBD from other causes of colitis such as bacterial infection, ischemia, and NSAID use. Although there is no single diagnostic pathologic criterion that can definitively establish an IBD diagnosis, biopsy specimens can help differentiate CD from UC and differentiate CD and UC from other colitides. Specimens should be taken of both diseased and adjacent normal-appearing mucosa. The biopsy specimens from different locations should be separately labeled. Several features suggest chronicity (indicating IBD rather than an acute self-limited or infectious colitis) such as architectural distortion, basal plasmacytosis, increased cellularity of lamina propria, pyloric gland metaplasia, and Paneth cell metaplasia.\textsuperscript{15-17} Although the presence of granulomata suggests CD, the frequency of detection of granulomas varies from 15% to 36% of endoscopic biopsy specimens.\textsuperscript{18} Higher detection rates of granulomas can be achieved when biopsy specimens are taken from the edge of ulcers and aphthous erosions.\textsuperscript{19} Granulomas are not pathognomonic for CD and they can be found in other disease conditions such as tuberculosis, fungal and bacterial infections, diversion colitis, sarcoidosis,\textsuperscript{20} and foreign body reaction (particularly from the suture line in patients with prior bowel resection surgery).

Mucosal biopsy also helps to establish the extent of colon that is inflamed, which aids in determining prognosis, directing appropriate medical and surgical therapy, and stratifying risk for dysplasia. The extent inflammation can be classified as proctitis, left-sided colitis (inflammation up to the splenic flexure), or extensive (inflammation proximal to the splenic flexure) or pancolitis. Macroscopic proximal extension of proctitis or left-side colitis occurs in approximately one third to one half of patients.\textsuperscript{21,22} However, regression of disease to the extent of pancolitis was also common after a long duration of disease (eg, 25 years).\textsuperscript{23} The extent of endoscopic inflammation does not necessarily correlate with histologic inflammation. Colonoscopy underestimates the extent of disease compared with histology.\textsuperscript{24} The extent of colitis (pancolitis, left-sided colitis, or proctitis) should be based on histologic examination rather than on endoscopy.\textsuperscript{25}

Endoscopy is an objective tool to assess the disease activity of CD and UC, whereas subjective symptoms are not a reliable indicator of disease severity. Additionally, there is a poor correlation between symptom scores and degree of endoscopic inflammation and between clinical remission and mucosal healing.\textsuperscript{27} Endoscopy may be helpful in predicting the need for intensified medical therapy or surgical intervention.\textsuperscript{26,28} There are numerous disease activity scores that are based on clinical symptoms or endoscopic findings.\textsuperscript{24-26,30} With the use of immunomodulator and biologic therapy for IBD, objective endoscopic findings are needed to assess response to the therapy.\textsuperscript{31-33} In more recent pharmaceutical trials, the documentation of endoscopic mucosal healing has become a critical component of outcome measurement.\textsuperscript{29,34}

**FLEXIBLE SIGMOIDOSCOPY**

Under certain circumstances, flexible sigmoidoscopy may provide useful information in patients with IBD. An adequate diagnosis may be obtained, and it should be performed preferentially when colonoscopy is considered high risk (eg, fulminant colitis).\textsuperscript{35} In patients with established UC, flexible sigmoidoscopy may define disease activity and is useful in evaluating for superimposed colitides including cytomegalovirus (CMV) and Clostridium difficile infections or ischemic colitis when disease exacerbations occur.

**ESOPHAGOGASTRODUODENOSCOPY**

Esophagogastroduodenoscopy (EGD) can be a useful in the evaluation of patients with IBD. Upper gastrointestinal (GI) tract involvement (proximal to the ligament of Treitz) occurs in up to 13% of patients with CD.\textsuperscript{35,36} CD can involve the esophagus,\textsuperscript{37} stomach,\textsuperscript{38} and duodenum.\textsuperscript{39} It appears that duodenal biopsy specimens more often display granulomas (40%-68%) than do colon biopsy specimens.\textsuperscript{39-41} In patients with indeterminate colitis, upper GI tract involvement can help establish a diagnosis of CD.\textsuperscript{42} However, when the upper GI tract is involved in CD, disease is usually present elsewhere, such as the terminal ileum, colon, or perianal area. Therefore, routine EGD is not recommended in all patients suspected of having CD. Additionally, patients with UC may also have upper GI inflammation, such as diffuse duodenitis.\textsuperscript{43} Endoscopic features in these patients include edema, erythema, erosions, and thickened mucosal folds.\textsuperscript{44} Histologic examination may show active chronic inflammation with architectural mucosal distortion,\textsuperscript{44} villous atrophy, and intraepithelial lymphocytosis.\textsuperscript{45} Other applications of EGD with small bowel biopsy in patients with IBD include evaluation of concomitant celiac disease\textsuperscript{46,47} eosinophilic enteritis,\textsuperscript{48} common variable immune deficiency,\textsuperscript{49} and small bowel neoplasia.\textsuperscript{44,46} In patients with CD, symptomatic duodenal strictures may respond to endoscopic balloon dilation.\textsuperscript{49}

**ENTEROSCOPY**

Push enteroscopy has a limited role in the management of patients with IBD, especially in the era of capsule endoscopy (CE). In patients with abnormalities seen on other imaging studies that are within reach, push enteroscopy allows endoscopic and histologic evaluation and therapeutic intervention.\textsuperscript{50,51} Intraoperative endoscopy
CAPSULE ENDOSCOPY

CE allows for direct and minimally invasive visualization of small bowel mucosa. It may help identify superficial lesions not detected by traditional endoscopy and radiography. It might be useful in the initial diagnosis of CD, for detecting recurrences, for establishing extent of disease, for assessing response to therapy, and for differentiating CD from UC or indeterminate colitis. Data from retrospective studies, case series, and prospective studies have shown that CE is useful for the diagnoses of CD when small bowel follow through (SBFT) and ileoscopy are negative or unsuccessful. The diagnostic yield of CE ranges from 10% to 71% depending on the clinical setting. CE has been shown to be more sensitive in the detection of small bowel CD than is computed tomographic (CT) enterography, SBFT, and enteroclysis. In patients with mild to moderate disease and a normal SBFT, CE may allow for the detection of small bowel changes that are not within reach of push enteroscopy (PE). A recent prospective study of 42 patients compared SBFT, CT enterography, colonoscopy with ileoscopy, and CE in the assessment of small bowel CD. Of these 4 modalities, CE had the highest sensitivity (83%) with the lowest specificity (53%) and colonoscopy with ileoscopy had the highest specificity (100%) with a sensitivity of 74%. A recent study in 39 patients, the majority with known CD, reported CE sensitivity and specificity of 89.6% and 100%, respectively. Few studies have evaluated the benefit of CE in the evaluation of indeterminate colitis. One study found that 5 of 22 patients with colitis were found to have mucosal breaks in the small bowel on CE, thus changing their diagnosis to CD.

The main limitations of CE in the assessment of small bowel CD are the lack of uniform criteria for diagnosing CD, inability to allow for tissue acquisition or therapeutic intervention, and the risk for capsule retention. It is important to note that the finding of mucosal breaks in the small bowel is not necessarily indicative of CD. A variety of disease entities can cause mucosal ulcerations such as infection, ischemia, radiation injury, and drug-induced injury, particularly NSAIDs. In addition, it has been reported that up to 1% of healthy individuals had mucosal breaks and other nonspecific lesions on CE.

Capsule retention in CD patients resulting from underlying small bowel strictures is a major concern, occurring in 1% to 13% of patients with known CD. Retained capsules may require surgery in patients that may otherwise have not required surgery. A preingestion radiologic study (CT or SBFT) is recommended because asymptomatic CD strictures occur in as many as 22%. Patients with obstructive symptoms or with endoscopic and radiographic evidence of small bowel narrowing in the setting of CD should not undergo CE. Capsule retention above a CD stricture may be treated with anti-inflammatory medications, although there are no published studies.

ENDOSCOPIC ULTRASONOGRAPHY

Ultrasoundography (US) including transperineal US and endoscopic US (EUS) with a rigid scope or with flexible endoscopes has been used to assess disease activity of colitis, transmural disease, fistulae, abscess, and regional lymphadenopathy. For patients with perianal disease, EUS can accurately characterize perianal disease to reduce the risk of incomplete healing, recurrent fistula, or inadvertent sphincter injury if fistula anatomy is incorrectly delineated or an occult abscess missed at surgery. EUS has an excellent accuracy in the assessment of Crohn’s perianal fistula and abscess. EUS may be used to monitor medical and surgical therapy for CD perianal fistulae. The EUS finding of transmural disease may allow for the differentiation of CD and UC.

ENDOSCOPY IN PATIENTS WITH IBD-RELATED SURGERY

Ileal pouch endoscopy

Ileal pouch anal anastomosis (IPAA) has become the surgical treatment of choice for patients with UC who required colectomy. IPAA significantly improves health-related quality of life, although complications can occur. In addition to the immediate postoperative complications such as pouch leak and abscess, long-term inflammatory and noninflammatory complications commonly develop, including pouchitis, “cuffitis,” irritable pouch syndrome, and CD of the pouch. Pouchitis is the most common long-term complication and symptom assessment alone is not diagnostic. Endoscopic and histologic assessment allow the diagnosis of pouchitis and exclude other causes of symptoms. Pouch endoscopy is also important for the evaluation and management of CD of the pouch, cuffitis, pouch stricture, and irritable pouch syndrome. A gastroscope is easier to use than a flexible sigmoidoscope for pouch evaluation because of its smaller caliber and greater maneuverability. Endoscopic therapy such as pouch stricture dilation can be performed. Endoscopic evaluation is also useful for evaluating symptomatic patients with ileal pouch–rectal anastomoses, Kock pouches, and Brooke ileostomies.

Colonoscopy after partial colectomy or partial ileocolectomy. Recurrence of CD after partial colectomy or partial ileocolectomy is common, typically occurring at the surgical anastomosis and neoterminal ileum. Endoscopic recurrence rates range from 70% to 90% within 1 year of surgery. Endoscopic recurrence
typically precedes relapse of symptoms. Changes in the neoterminal ileum after surgery are the most prognostic factor for recurrence. Therefore, some investigators recommend postoperative colonoscopy with inspection of the neoterminal ileum 6 to 12 months after resection to identify patients who are at risk for relapse and who may benefit from appropriate medical therapy.

**ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY FOR PRIMARY SCLEROSING CHOLANGITIS**

The role of endoscopic retrograde cholangiopancreatography in patients with primary sclerosing cholangitis has been addressed in a previous document.

**CANCER SURVEILLANCE**

Individuals with long-standing UC and extensive CD colitis are at increased risk for development of dysplasia and colorectal cancer (CRC) and should undergo colonoscopic surveillance. The risk of CRC increases with longer duration and extensive severe colitis, family history of CRC, young age at onset of disease, presence of backwash ileitis, and personal history of primary sclerosing cholangitis. The presence of proctitis alone does not increase the risk for CRC. Patients with UC who have left-sided colitis or more extensive disease are at increased risk. In Crohn’s colitis, those patients with extensive disease involving more than a third of the colon also have an increased risk of CRC, similar to patients with UC. The extent of colonic involvement should be based on both endoscopic and histologic criteria, whichever reveals more extensive disease. In a case-control study of UC patients undergoing colonoscopic surveillance, there was a reduction in mortality resulting from CRC in those patients in surveillance programs.

Patients with UC or extensive Crohn’s colitis (greater than one third colonic involvement) should undergo surveillance colonoscopy every 1 to 2 years beginning 8 to 10 years after disease onset. Biopsy specimens of the colon in patients with documented pancolitis should be obtained in all 4 quadrants every 10 cm from the cecum to the rectum, to obtain a minimum of 32 biopsy samples. In patients with less extensive colitis, biopsy specimens can be limited to the microscopically involved segments. Diagnosis of dysplasia should be confirmed by a second gastrointestinal pathologist. The management of dysplastic polypoid lesions is currently evolving. The presence of high-grade dysplasia or multifocal low-grade dysplasia in flat mucosa is an indication for colectomy. The management of unifocal low grade dysplasia is controversial as to whether colectomy should be performed. Biopsy specimens should be obtained of structures, mass lesions, and macroscopic abnormalities other than pseudopolyps. Adenomatous-appearing polyps encountered should be completely removed by polypectomy and biopsy samples should be obtained from the adjacent flat mucosa to determine the presence of dysplasia. If a dysplastic polyp is identified outside an area of inflammation and there is no evidence of dysplasia in the adjacent mucosa, it can be managed as a sporadic polyp similar to polyps in individuals without UC or Crohn’s colitis. If a dysplastic polyp is in an area of active inflammation (DALM [dysplasia associated lesion or mass]) and is sessile, not amenable to endoscopic removal and there is evidence of dysplasia in the adjacent mucosa, colectomy is indicated. If a discrete polyp amenable to polypectomy is found in an area of inflammation, it should be completely removed and a biopsy specimen of the mucosa adjacent to the polypectomy site should be obtained and placed in separate jars. Tattooing of the site should also be considered. If complete removal was not possible or if there is evidence of flat dysplasia in any other sites, then a total colectomy is recommended. The finding of indefinite dysplasia requires repeat colonoscopy in 3 to 6 months and close follow-up.

There is no clear evidence that surveillance colonoscopy prolongs survival in patients with extensive colitis. However, patients in surveillance programs tend to have cancers detected at an earlier stage and have a correspondingly better prognosis, although these findings may be due to lead-time bias. There is indirect evidence that surveillance is effective in reducing the risk of death from IBD-associated CRC and is acceptably cost-effective.

Chromoendoscopy offers the potential for improved sensitivity during colonoscopic surveillance by allowing for targeted biopsies of enhanced mucosal abnormality. Prospective trials of methylene blue and indigo carmine staining reported improved detection of dysplasia in patients with UC. With chromoendoscopy using 0.1% methylene blue staining, the detection of high- or low-grade dysplasia in macroscopically normal mucosa was increased 6-fold with the number of detected flat intraepithelial neoplasia of 24 in the chromoendoscopy group versus 4 in the conventional colonoscopy group (P = .0007). In a separate study of back-to-back colonoscopy and chromoendoscopy using 0.1% indigo carmine spray, the overall detection rates of dysplasia (2% vs 7%) between the conventional colonoscopy and chromoendoscopy were not statistically different. While promising, chromoendoscopy has not yet been adopted in routine practice.

**STRUCTURE EVALUATION AND DILATION**

Colonic strictures may complicate CD, and to a lesser extent UC. In patients with CD, strictures may occur at the ileocolonic valve, terminal ileum, and ileocolonic surgical anastomosis and can be asymptomatic. In
symptomatic patients, endoscopy is indicated for assessment and biopsy to exclude possible malignancy, especially in the setting of UC, where a stricture should be considered malignant until proven otherwise. If it cannot be thoroughly examined and biopsy performed, surgical resection should be considered. The finding of a colonic stricture in the setting of CD is more likely to be benign, although complete examination with biopsy is recommended. Balloon dilation may be required to completely evaluate the stricture. Endoscopic balloon dilation has been investigated in patients with Crohn’s strictures of the small bowel, colon, and anastomosis. The majority of these studies are retrospective and the main outcome measurement is symptom relief and avoidance of surgery. Endoscopic balloon dilation may relieve symptoms. Complications include perforation and bleeding. Corticosteroid injection into the stricture at the time of balloon dilation may improve outcome.

**SUMMARY**

- Colonoscopy with ileoscopy should be performed in the evaluation of IBD and for differentiating UC from CD (B).
- Mucosal biopsy specimens are important for the diagnosis of IBD and may help differentiate CD from UC (B).
- When colonoscopy is contraindicated, or the extent of disease is limited, flexible sigmoidoscopy may provide an adequate diagnosis (C).
- EGD or enteroscopy may be helpful for diagnosing IBD when other studies have negative results and for differentiating CD from UC (B).
- CE is a less invasive technique for evaluating the small intestine for Crohn’s involvement and has been shown to be more sensitive than radiologic and endoscopic procedures for detecting small bowel lesions (B).
- In patients with CD and known or suspected high-grade strictures, CE should not be performed (C). Small bowel follow-through or CT enterography should be obtained before CE in patients with CD to assess for high-grade strictures (C).
- CRC risk is increased in both UC and extensive Crohn’s colitis and surveillance colonoscopy with multiple biopsies should be performed every 1 to 2 years beginning after 8 to 10 years of disease (B).
- The finding of dysplasia in flat mucosa, especially if multifocal, is an indication for total colectomy (B). Colectomy is indicated for colorectal cancer, high-grade dysplasia or low-grade dysplasia (particularly multifocal) in flat mucosa. A dysplastic mass lesion that cannot be removed endoscopically, or is associated with dysplasia elsewhere in the colon, is an indication for total colectomy (B).
- Dysplastic polyloid lesions may be managed as sporadic adenomas provided they are completely resected and there is no dysplasia in flat mucosa surrounding the polyp or elsewhere in the colon (B).
- EUS is highly accurate for characterizing perianal Crohn’s disease (C).
- A colonic stricture in the setting of UC should be considered malignant until proven otherwise. If adequate evaluation cannot be performed, then colectomy is indicated (C).
- Chronic benign fibrotic strictures associated with obstructive symptoms may be managed with endoscopic balloon dilation with or without steroid injections (B).

**REFERENCES**

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