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CLINICAL PRACTICE UPDATE

AGA Clinical Practice Update on Endoscopic Surveillance and Management of Colorectal Dysplasia in Inflammatory Bowel Diseases: Expert Review

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Improvements in disease management, as well as endoscopic technology and quality, have dramatically changed the way in which we conceptualize and manage inflammatory bowel disease–related dysplasia over the past 20 years. Based on evolving literature, we propose a conceptual model and best practice advice statements for the prevention, detection, and management of colorectal dysplasia in people with inflammatory bowel disease. This expert review was commissioned and approved by the American Gastroenterological Association Institute Clinical Practice Updates Committee and the American Gastroenterological Association Governing Board to provide timely guidance on a topic of high clinical importance to the American Gastroenterological Association membership. It underwent internal peer review by the Clinical Practice Updates Committee and external peer review through standard procedures of *Gastroenterology*.

Keywords: Inflammatory Bowel Disease; Colorectal Cancer Screening; Chromoendoscopy; Colonoscopy.

Since its first description in 1925, colorectal cancer (CRC) has been one of the most feared complications of inflammatory bowel diseases (IBDs).[1] Not long ago, notions of imperceptible CRC development and urgent need for colectomy in the face of dysplasia dominated IBD practice. However, improvements in disease management, as well as endoscopic technology and quality, have dramatically changed the way in which we conceptualize and manage IBD-related dysplasia over the past 20 years. The proposed conceptual model and best practice advice statements in this review are best used in conjunction with evolving literature and existing societal guidelines as part of a shared decision-making process.

A summary of the Best Practice Advice statements is provided in Table 1.

Nomenclature and Reporting

Best Practice Advice 1: Precancerous colorectal lesions in inflammatory bowel disease should be described as either polypoid (≥2.5 mm tall), nonpolypoid (<2.5 mm), or invisible (detected on nontargeted biopsy), using a modified Paris Classification. The older terms *dysplasia-associated lesion or mass*, *adenoma-like mass*, and *flat dysplasia* (when referring to dysplasia detected in nontargeted biopsies) should be abandoned.

Precancerous colorectal lesions affecting people with colonic IBD (cIBD) have been described previously using terms such as *adenomatous polyp*, *adenoma-like mass* (ALM), *dysplasia-associated lesion or mass* (DALM), and *flat dysplasia* (Figure 1*A*).[2] In 2015, the international Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients consortium recommended modifying the vocabulary using an adaptation of the Paris Classification to closely match what is used for precancerous lesions in people without IBD,[3] thereby recognizing the inherent similarity of visible lesions in IBD and non-IBD colons.[4] In this system, lesions that protrude ≥2.5 mm above the mucosa should be described as polypoid (pedunculated or sessile), and lesions that protrude <2.5 mm above the mucosa should be described as nonpolypoid (flat elevated, flat, or flat depressed) (Figure 1*B*). Unique to IBD, dysplastic histology detected from nontargeted (random) biopsies should be described as "invisible" dysplasia and no longer described as flat dysplasia. The terms *DALM* and *ALM* should no longer used.

Best Practice Advice 2: Visible precancerous lesions should be described based on size, morphology, clarity of borders, presence of ulceration, location, presence within an area of past or current colitis, perceived completeness of resection, and whether any special techniques were used for visualization.

Reducing variation in reporting is important for facilitating lesion identification during follow-up colonoscopy, guiding subsequent management (resection vs surgery), and

Abbreviations used in this paper: ALM, adenoma-like mass; cIBD, colonic IBD; CRC, colorectal cancer; DALM, dysplasia-associated lesion or mass; DCE, dye spray chromoendoscopy; HD, high definition; IBD, inflammatory bowel disease; NBI, narrow band imaging; PSC, primary sclerosing cholangitis; UC, ulcerative colitis; VCE, virtual chromoendoscopy; WLE, white light endoscopy.

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Table 1. Best Practice Advice Regarding Endoscopic Surveillance and Management of Colorectal Dysplasia in Inflammatory Bowel Diseases

Best Practice Advice	Statement
1	Precancerous colorectal lesions in inflammatory bowel disease should be described as either polypoid (≥2.5 mm tall), nonpolypoid (<2.5 mm), or invisible (detected on nontargeted biopsy), using a modified Paris Classification. The older terms *dysplasia-associated lesion or mass*, *adenoma-like mass*, and *flat dysplasia* (when referring to dysplasia detected in nontargeted biopsies) should be abandoned
2	Visible precancerous lesions should be described based on size, morphology, clarity of borders, presence of ulceration, location, presence within an area of past or current colitis, perceived completeness of resection, and whether any special techniques were used for visualization.
3	Initial colonoscopy screening for dysplasia should be performed at 8–10 years after disease diagnosis in all people with colonic inflammatory bowel disease, and immediately on diagnosis of primary sclerosing cholangitis. Staging biopsies should be taken from multiple colonic segments to assess histologic disease activity and extent and to help guide future surveillance intervals.
4	Conditions and practices for dysplasia detection should be optimized, including control of inflammation, use of high-definition endoscopes, bowel preparation, careful washing and inspection of all colorectal mucosa, and targeted sampling of any suspicious mucosal irregularities.
5	Targeted biopsies should be performed where mucosal findings are suspicious for dysplasia or are inexplicably different from the surrounding mucosa. Endoscopic resection is preferred to biopsies when lesions are clearly demarcated without stigmata of invasive cancer or submucosal fibrosis. Mucosal biopsies surrounding a resected lesion are not required unless there are concerns about resection completeness.
6	Dye spray chromoendoscopy, performed by appropriately trained endoscopists, should be considered in all persons with colonic inflammatory bowel disease undergoing surveillance colonoscopy, particularly if a standard definition endoscope is used or if there is a history of dysplasia
7	Virtual chromoendoscopy is a suitable alternative to dye spray chromoendoscopy for dysplasia detection in persons with colonic inflammatory bowel disease when using high-definition endoscopy.
8	Extensive nontargeted biopsies (roughly 4 adequately spaced biopsies every 10 cm) should be taken from flat colorectal mucosa in areas previously affected by colitis when white light endoscopy is used without dye spray chromoendoscopy or virtual chromoendoscopy. Additional biopsies should be taken from areas of prior dysplasia or poor mucosal visibility. Nontargeted biopsies are not routinely required if dye spray chromoendoscopy or virtual chromoendoscopyis performed using a high-defintion endoscope, but should be considered if there is a history of dysplasia or primary sclerosing cholangitis.
9	All clearly delineated dysplastic-appearing lesions without stigmata of invasive cancer or significant submucosal fibrosis should be considered for endoscopic resection. If the resectability of a lesion is in question, referral to a specialized endoscopist or inflammatory bowel disease center is suggested.
10	A finding of invisible dysplasia should prompt repeat examination by an experienced endoscopist using high-definition dye spray chromoendoscopy under optimized viewing conditions, with extensive nontargeted biopsies in the area of prior dysplasia if no lesion is seen. A finding of unresectable visible dysplasia or of invisible multifocal or high-grade dysplasia on histology should prompt colectomy. For visible lesions that can be resected or if histologic dysplasia is not confirmed on a high-quality dye spray chromoendoscopy examination, continued endoscopic surveillance at frequent intervals is appropriate.
11	After a negative screening colonoscopy, surveillance colonoscopy should be performed every 1–5 years based on risk factors for colorectal cancer, considering current and prior burden of colonic inflammation, family history of colorectal cancer, primary sclerosing cholangitis, history of colorectal dysplasia, and frequency and quality of prior surveillance examinations.
12	Pouch surveillance should be performed at least annually in those at high risk for developing colorectal dysplasia (prior colorectal cancer or dysplasia, primary sclerosing cholangitis), as well as in those with persistent moderate to severe pouchitis and/or pre-pouch ileitis (to assess for treatment response). Surveillance intervals in those at lower risk should be individualized.
13	Targeted biopsies of representative or concerning pseudopolyps is appropriate during colonoscopy. Removal and sampling of all lesions is neither required nor practical. Surgery should be a last resort to manage colorectal cancer risk in the setting of severe pseudopolyposis. Dye spray chromoendoscopy should not be used to detect flat or subtle lesions within a field of pseudopolyps.
14	Optimal disease control with medical therapy is imperative to minimizing an individual's lifetime risk of developing colorectal cancer. There is uncertainty regarding the independent chemotherapeutic benefit of mesalamine therapy in people with colonic inflammatory bowel disease.

providing sufficient information for high-quality second-opinion consultations. Several international consortia have endorsed a standardized approach to reporting key pre-, intra-, and postprocedural quality elements, including bowel preparation; photodocumentation; extent and activity of inflammation; technique of visualization; and resection.[3,5–7] The "five S" features have been proposed to describe colonic lesions (shape, size, site, surface [Kudo pit pattern], and surrounding [mucosal activity and other lesions]).[7]

Inflammatory Bowel Disease Dysplasia Detection

When to Start Screening for Dysplasia

Best Practice Advice 3: Initial colonoscopy screening for dysplasia should be performed at 8–10 years after disease diagnosis in all people with colonic inflammatory bowel disease, and immediately on diagnosis of primary sclerosing cholangitis. Staging biopsies should be taken from multiple colonic segments to assess histologic disease activity and extent and to help guide future surveillance intervals.

Epidemiologic studies have demonstrated that CRC risk begins to rise at 8–10 years after diagnosis of cIBD.[8–10] The first screening examination performed at this interval presents an opportunity to restage macroscopic and microscopic disease activity and extent, which can be used to help guide future surveillance intervals. When performing biopsies in a segment with inflammation, targeting the most severely affected area, specifically at the edges of ulcers, if present, can be helpful.[11] Screening should begin immediately after a diagnosis of primary sclerosing cholangitis (PSC), given the well-recognized subclinical colitis that can be present for years before diagnosis.[12–14]

Foundations of Dysplasia Detection

Best Practice Advice 4: Conditions and practices for dysplasia detection should be optimized, including control of inflammation, use of high-definition endoscopes, bowel preparation, careful washing and inspection of all colorectal mucosa, and targeted sampling of any suspicious mucosal irregularities.

Colorectal dysplasia surveillance should be ideally performed when all inflammatory disease has been well controlled, as subtle precancerous findings can be obscured by inflammation and inflammation can lead to false-positive pathology findings of dysplasia.[15] Meta-analyses of studies in patients with IBD have further shown that use of high-definition (HD) endoscopes, with or without dye spray chromoendoscopy (DCE), have improved the visibility of dysplasia, such that 90% of dysplastic lesions are now visible compared with 80% with standard-definition endoscopes.[3] Most centers in North America now use HD endoscopes. Excellent bowel preparation, careful inspection of the mucosal surface, and targeted sampling of suspicious mucosal irregularities also increase dysplasia yield.[3,16–20]

Best Practice Advice 5: Targeted biopsies should be performed where mucosal findings are suspicious for dysplasia or are inexplicably different from the surrounding mucosa. Endoscopic resection is preferred to biopsies when lesions are clearly demarcated without stigmata of invasive cancer or submucosal fibrosis. Mucosal biopsies surrounding a resected lesion are not required unless there are concerns about resection completeness.

Biopsies performed during colonoscopy in patients with IBD can be categorized as targeted, nontargeted, or staging (Figure 1*F*). Targeted sampling should be performed for suspicious-appearing polypoid or flat mucosal abnormalities that are either mass-like or not clearly delineated, or for any inexplicable mucosal irregularities that might represent atypical signs of dysplasia, including changes in mucosal color or vascularity, nodularity, elevation, or ulceration.[21,22] Endoscopic resection has been shown to be safe and preferred to targeted biopsies for clearly delineated lesions without stigmata of invasive cancer or submucosal fibrosis.[23–29] Given the immense improvements in visibility with modern-day HD endoscopes, unless concerns arise regarding a lesion's borders and completeness of resection, routine biopsies of the flat mucosa surrounding a resected lesion are not needed, as they rarely demonstrate residual dysplasia.[30–32]

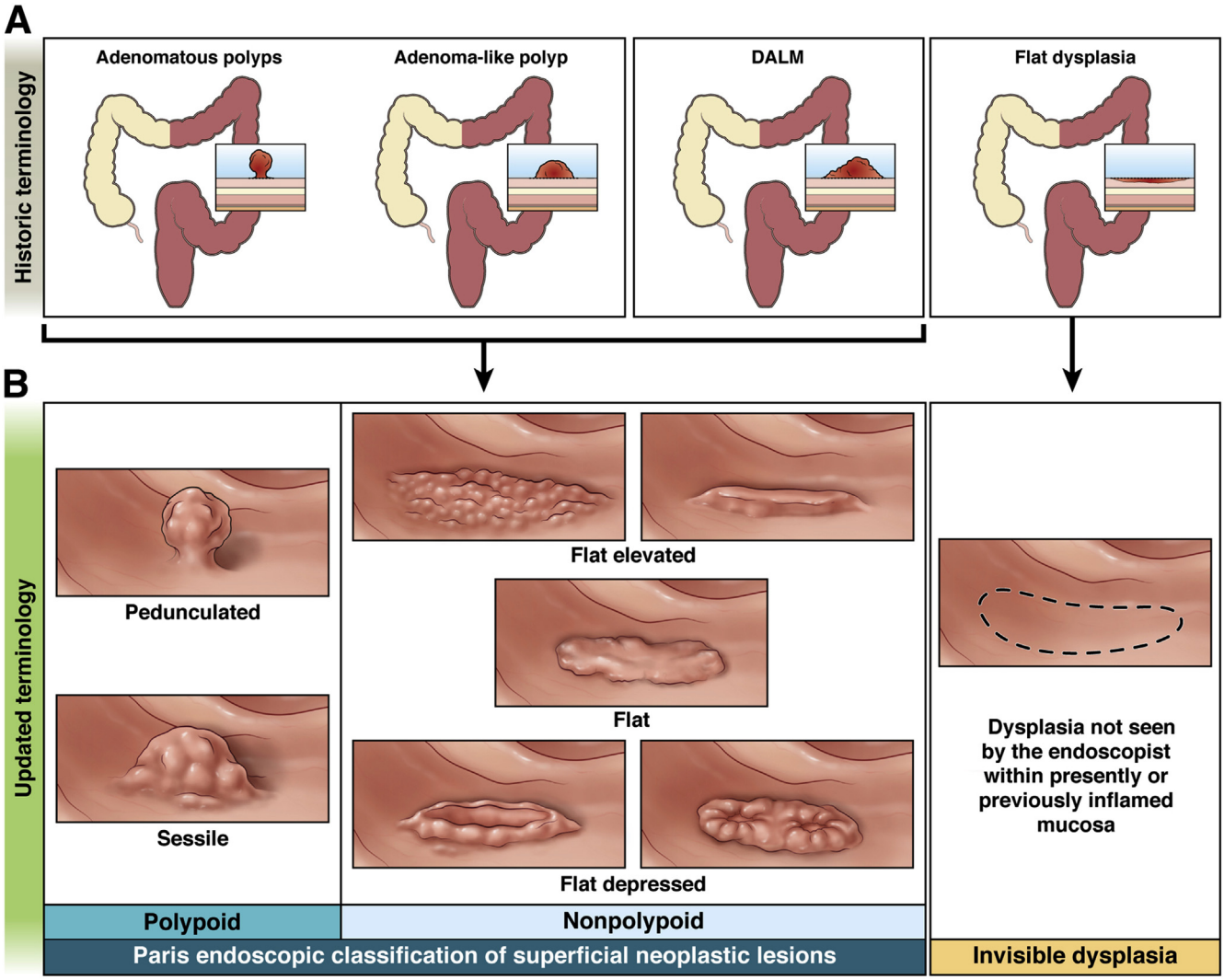
Adjuncts to Enhance Dysplasia Detection

Best Practice Advice 6: Dye spray chromoendoscopy, performed by appropriately trained endoscopists, should be considered in all persons with colonic inflammatory bowel disease undergoing surveillance colonoscopy, particularly if a standard-definition endoscope is used or if there is a history of dysplasia.

In dye spray chromoendoscopy (DCE), dilute contrast (ie, indigo carmine 0.03%–0.1%) or absorptive (ie, methylene blue 0.04%–0.1%) dyes are liberally applied over the entire colonic mucosal surface during withdrawal of the colonoscope using a spray catheter or waterjet to "unmask" dysplastic lesions by highlighting the borders and surface architecture of poorly delineated lesions.[3,33,34] Once a suspicious lesion is identified, some experts recommend spraying a more concentrated dye (indigo carmine 0.13% or methylene blue 0.2%) to further define lesion border and topography.[3] Optimal criteria for DCE have been reported.[34] Studies have demonstrated a roughly 2-fold greater dysplasia yield with DCE over standard-definition white light endoscopy (WLE),[3,18,19] and a meta-analysis of 4 randomized controlled trials (RCTs) reported a 1.6-fold greater dysplasia yield with DCE compared with HD-WLE.[19] Studies have not evaluated the impact of DCE on the long-term risks of CRC or CRC-related death.

Best Practice Advice 7: Virtual chromoendoscopy is a suitable alternative to dye spray chromoendoscopy for dysplasia detection in persons with colonic inflammatory bowel disease when using high-definition endoscopy.

Virtual chromoendoscopy (VCE) modalities, such as narrow band imaging (NBI) (Olympus; Tokyo, Japan), *i*-scan (Pentax; Tokyo, Japan), and Fuji intelligent color



In addition to Paris classification, report lesion size, morphology, border clarity, ulceration, location, if within area of colitis, completeness of resection, and any special techniques used to visualize.

C When to start screening

- 8–10 years after disease onset in all patients to stage histologic activity and extent and guide future surveillance
- At diagnosis in primary sclerosing cholangitis

D Fundamentals for dysplasia detection

- High definition colonoscope
- Quiescent disease
- Washing and careful inspection of fully visible mucosa
- Targeted biopsies of suspicious mucosal abnormalities or sites of prior dysplasia

E Enhanced dysplasia detection techniques

- Dye spray chromoendoscopy (DCE)
- Virtual chromoendoscopy (VCE)
- Non-targeted biopsies of non-suspicious areas

F Types of biopsies to obtain

Targeted		Non-targeted		Staging
Biopsies of suspicious or subtle mucosal abnormalities to rule out dysplasia	+	Biopsies of non-suspicious areas to rule out invisible dysplasia	OR	Biopsies of macroscopically inflamed and uninflamed areas to assess histologic disease activity and extent

Figure 1. Principles of CRC screening in IBD.

enhancement (Fujinon, Fujifilm; Tokyo, Japan) apply narrow wavelength spectrums of light to illuminate mucosal tissue using either selective light filters (NBI) or post-image processing techniques (*i*-scan and Fuji intelligent color enhancement), which enhance the vascular and surface architecture of mucosal lesions without the need for dye.[35] Early studies generally failed to show a benefit of VCE technologies for dysplasia detection with either standard-definition or HD endoscopes in patients with cIBD.[36–41] However, several recent studies have shown similar dysplasia detection rates when comparing HD NBI with DCE[39,42,43] or HD *i*scan with DCE,[36,39] with shorter withdrawal times favoring VCE methods. A recent meta-analysis of 11 RCTs confirmed that VCE performed similarly to DCE and HD-WLE with respect to dysplasia detection on a per-patient basis.[39]

Best Practice Advice 8: Extensive nontargeted biopsies (roughly 4 adequately spaced biopsies every 10 cm) should be taken from flat colorectal mucosa in areas previously affected by colitis when white light endoscopy is used without dye spray chromoendoscopy or virtual chromoendoscopy. Additional biopsies should be taken from areas of prior dysplasia or poor mucosal visibility. Nontargeted biopsies are not routinely required if dye spray chromoendoscopy or virtual chromoendoscopyis performed using a high-defintion endoscope, but should be considered if there is a history of dysplasia or primary sclerosing cholangitis.

The practice of taking nontargeted (random) biopsies for dysplasia surveillance in cIBD gained popularity during the 1980s and 1990s for several reasons: concerns for missed dysplastic lesions, driven by fears of multifocal and accelerated tumorigenesis due to widespread genetic aberrations within colitic mucosa ("field carcinogenesis"),[44–46] reports of high rates of synchronous and metachronous cancers within fields of invisible dysplasia,[47–51] and early recognition of unconventional growth patterns of dysplasia that mirrored inflammatory changes (ie, nodular, strictured, or ulcerated).[21,22,52] Mathematical modeling in 1 study demonstrated that 33 or more nontargeted jumbo forceps biopsies could detect dysplasia with 90% confidence,[44] leading to current recommendations.[2,33,53]

This practice was founded during a period in which visibility of the mucosa differs from today, due to use of standard-definition (or even optical) endoscopes, less effective bowel preparation solutions and regimens, and less effective medical therapies for IBD.[47,49–51,54–58] The notion of whether any dysplastic lesion is truly invisible (as opposed to just subtle) is being increasingly challenged, as is the practice of taking truly random biopsies.[3,16–20,28,59,60] Notably, a small RCT from Japan failed to show a benefit of nontargeted biopsies in patients with ulcerative colitis (UC).[61] Conversely, pooled estimates indicate that 1%–1.5% of patients with IBD undergoing surveillance with HD-WLE would not have dysplasia detected if nontargeted biopsies were eliminated.[3] Recent large series further report that up to 20% of dysplastic lesions are detected with nontargeted biopsies alone,[62,63] leading to concerns about eliminating this practice if DCE or VCE is not used. A recent study noted additional dysplasia cases detected using nontargeted biopsies, even when DCE was performed, particularly in those with a history of dysplasia, concomitant PSC, or a tubular colon.[62]

Applying Adjunctive Modalities in Routine Surveillance

The literature on enhanced dysplasia detection techniques is large and growing, but heterogeneous. Several gastroenterological societies recommend HD-DCE with targeted biopsies of suspicious lesions by appropriately trained endoscopists.[59,64–70] The American College of Gastroenterology and European Society of Gastrointestinal Endoscopy now endorse virtual chromoendoscopy as an alternative to DCE.[70] Most societies no longer recommend taking nontargeted biopsies for dysplasia detection if DCE is performed.[33,62,67,70] There is greater trepidation among experts of abandoning nontargeted biopsies if DCE is not performed.[3,71] The American Society of Gastrointestinal Endoscopy endorses nontargeted biopsies as an alternative to DCE if this expertise is unavailable or if the mucosa is poorly visualized, such as in areas of significant underlying inflammation, significant pseudopolyposis, or poor bowel preparation.[32] A Canadian multicenter RCT aims to shed further light on the utility of nontargeted biopsies for dysplasia surveillance in persons with cIBD (ClinicalTrials.gov identifier NCT04067778).

More recent network meta-analyses of RCTs have not shown any single technique to be statistically superior for detecting dysplasia (HD-WLE [with nontargeted biopsies], DCE, or NBI) although there is a trend favoring DCE.[72,73] Some studies have shown a very low incidence of advanced colorectal neoplasia in follow-up examinations when dysplasia is not identified with DCE or on consecutive negative examinations,[74–76] questioning the necessity to routinely perform frequent DCE after multiple negative high-quality examinations. Surveys in both Japan and the United States report that most gastroenterologists continue to use HD-WLE with targeted biopsies for surveillance, reserving DCE for higher-risk situations (eg, PSC and history of dysplasia).[77,78] This current document endorses HD-DCE with targeted biopsies, but acknowledges that this is an evolving area, with more recent data suggesting HD-VCE with targeted biopsies or careful HD-WLE with targeted and nontargeted biopsies also appear appropriate.

Inflammatory Bowel Disease Dysplasia Surveillance and Management

Visible Dysplasia

Best Practice Advice 9: All clearly delineated dysplastic-appearing lesions without stigmata of invasive cancer or significant submucosal fibrosis should be considered for endoscopic resection. If the resectability of a lesion is in question, referral to a specialized endoscopist or inflammatory bowel disease center is suggested.

Available data and guidelines support endoscopic resection of clearly delineated lesions, especially <2 cm, that do not harbor features of invasive cancer or submucosal fibrosis (such as mucosal depression, irregular surface architecture, radiating folds, or failure to symmetrically lift with submucosal saline injection), irrespective of lesion morphology.[3,5,28,33,79] Although more data are needed to define long-term outcomes with endoscopic resection of large (>2 cm) and/or complex dysplastic colorectal lesions, it is reasonable to consider endoscopic resection depending on lesion characteristics, local expertise, as well as current and past disease activity (Figure 2*A*). If there is uncertainty about the most appropriate management strategy, case discussion in multidisciplinary rounds or referral to a specialized IBD center for a comprehensive evaluation should be sought.

Standard polypectomy techniques should generally suffice for simpler lesions. For large and highly irregular lesions, resection using advanced polypectomy techniques, including endoscopic mucosal resection or endoscopic submucosal dissection, can be considered.[80] Excessive or deep biopsies or attempts to raise a lesion without resection should be avoided in this setting, as should unsuccessful attempts to resect a complex lesion by less experienced endoscopists, so as to limit submucosal scarring that will make the lesion more difficult to resect endoscopically in the future. When there is submucosal invasion or scarring, partial or total colectomy might ultimately be required to completely remove a lesion.[81,82] Good photodocumentation and an India Ink stain placed at least 3 cm distal to a lesion (for larger or more complex lesions) are helpful adjuncts. After endoscopic resection of a visible dysplastic lesion, the next surveillance examination should occur at 3–6 months for the highest-risk lesions and no more than 24 months after for the lowest risk,[3,33,64,67] with the latter group including simple sub-centimeter sessile or pedunculated low-grade adenomas (Figure 2*A*).[24–26,29,83]

Invisible Dysplasia

Best Practice Advice 10: A finding of invisible dysplasia should prompt repeat examination by an experienced endoscopist using high-definition dye spray chromoendoscopy under optimized viewing conditions, with extensive nontargeted biopsies in the area of prior dysplasia if no lesion is seen. A finding of unresectable visible dysplasia or of invisible multifocal or high-grade dysplasia on histology should prompt colectomy. For visible lesions that can be resected or if histologic dysplasia is not confirmed on a high-quality dye spray chromoendoscopy examination, continued endoscopic surveillance at frequent intervals is appropriate.

A finding of invisible dysplasia (indefinite, definite low-grade, or high-grade) from nontargeted biopsies, confirmed by a second expert pathologist, should prompt a repeat colonoscopy with DCE using an HD endoscope by an experienced endoscopist with the goal of unmasking invisible/subtle lesions for targeted resection (Figure 2*B*).[3,33,70] If there was active colonic inflammation during the original examination, which can sometimes lead to misdiagnosis of reactive atypia as dysplasia, measures should be taken to control the inflammation before DCE. Extensive biopsies should also be taken from the areas containing dysplasia in the original examination. If conditions for mucosal visualization are suboptimal, the DCE examination should be repeated after optimization of viewing conditions.

Modern data suggest that the risk of future CRC in the setting of unifocal low-grade dysplasia is considerably lower than in previous reports.[84,85] This is likely because of improved endoscopic visualization of early dysplastic lesions due to better inflammatory control, improved endoscope resolution, improved bowel preparation, and better overall endoscopy quality.[3,16–20] CRC rates among IBD patients have also declined substantially over time, approaching those of the non-IBD population in some centers.[9,86,87] Although the current document endorses intensive surveillance if unifocal invisible dysplasia or no dysplasia is found on extensive nontargeted biopsies in the area of prior dysplasia during a high-quality DCE, data on long-term outcomes are sparse. A risk–benefit discussion with patients, which includes assessment of disease control, as well as short- and long-term cancer risk factors, is appropriate. Discussion in multidisciplinary rounds or referral to a center with expertise in IBD care may be helpful if there is uncertainty about the most appropriate management strategy.

No Dysplasia

Best Practice Advice 11: After a negative screening colonoscopy, surveillance colonoscopy should be performed every 1–5 years based on risk factors for colorectal cancer, considering current and prior burden of colonic inflammation, family history of colorectal cancer, primary sclerosing cholangitis, history of colorectal dysplasia, and frequency and quality of prior surveillance examinations.

Although no RCTs have evaluated the efficacy of dysplasia surveillance in IBD, observational studies have suggested an earlier cancer stage at diagnosis and improved CRC-related survival.[88–92] Once initiated, dysplasia surveillance should be performed at intervals guided by established CRC risk factors, including current and historical inflammatory burden (considering endoscopic and histologic extent[9,93,94] and severity[95–98]), colitis duration,[8,9,99] family history of CRC,[100,101] PSC,[12–14] history of colorectal dysplasia,[29,84] frequency and quality of prior surveillance examinations, as well as factors that may obscure subtle dysplasia, such as chronic changes associated with severe colitis (moderate to severe post-inflammatory polyposis or extensive mucosal scarring) (Figure 2*C*).

Intervals have traditionally ranged between 1 and 3 years among US societies[2,33,70] and between 1 and 5 years among European societies.[64,67] For most patients in remission, a 2- or 3-year interval is appropriate unless additional high-risk factors are present, in which case a 1-year follow-up should be performed (Figure 2*C*). Improvements in

A Management of visible and invisible dysplasia within a colitis field*

Endoscopic assessment	Management	Next colonoscopy and comments
• < 2cm + resectable (clear border, no features of submucosal invasion or fibrosis) + no histologic features of invasive cancer	Endoscopic resection with continued surveillance	• 3–6 months: high-grade dysplasia or incomplete resection • 12 months: > 1cm, low-grade dysplasia (LGD) • 24 months: < 1cm or pedunculated, LGD
• Large (≥ 2cm) • Complex (i.e. lateral spreading, highly irregular or indistinct border) • Incomplete resection after several attempts • Local recurrence	Endoscopic resection with intensive surveillance vs surgery	• Every 3–6 months for first year (if resect) • Decision to resect based on lesion details, local expertise, disease activity
• Unresectable due to size, location, features of invasive cancer or submucosal fibrosis • Invasive cancer on histology	Surgery	
• Invisible dysplasia (non-targeted biopsy) or subtle/ poorly delineated lesion (targeted biopsy)	• Confirm histology with second pathologist • Treat inflammation • Perform dye spray chromoendoscopy (DCE)	• Use DCE to unmask subtle lesions. If no lesion seen, take extensive non-targeted biopsies in area of prior dysplasia. Use box A or B to manage.

B Management when no visible dysplasia is detected on DCE*

Histologic assessment	Management	Next colonoscopy and comments
• Persistent high-grade or multifocal invisible dysplasia	Surgery	
• Persistent unifocal low-grade invisible dysplasia	Intensive surveillance with DCE **	• 3–6 months if prior high-grade or multifocal dysplasia; 6–12 months if prior low-grade dysplasia. Continue intensive surveillance until 2 consecutive negative high quality DCE exams.
• No histologic dysplasia		

*Consider expert opinion if uncertainty; ** Although intensive surveillance proposed, long-term management is uncertain. Discuss risks and benefits of surgery vs surveillance based on current and past inflammatory burden, quality of mucosal visualization, mucosal details from where dysplasia initially detected, and other CRC risk factors.

C Timing of next colonoscopy when no dysplasia detected at present colonoscopy

Physicians should err towards the more frequent surveillance category if at least one higher risk factor exists. Timing based on past and ongoing CRC risk factors and mucosal features that may obscure dysplasia.

1 year	2 or 3 years	5 years
• Moderate or severe inflammation (any extent) • PSC • Family history of CRC in first degree relative (FDR) age < 50 • Dense pseudopolyposis • History of invisible dysplasia or higher-risk visible dysplasia < 5 years ago	• Mild inflammation (any extent) • Strong family history of CRC (but no FDR < age 50) • Features of prior severe colitis (moderate pseudopolyps, extensive mucosal scarring) • History of invisible dysplasia or higher-risk visible dysplasia > 5 years ago • History of lower risk visible dysplasia < 5 years ago	Continuous disease remission since last colonoscopy with mucosal healing on current exam, plus either of: • ≥ 2 consecutive exams without dysplasia • Minimal historical colitis extent (ulcerative proctitis or < 1/3 of colon in CD)

Note: Isolated ileal Crohn's disease without colonic inflammation should undergo CRC screening with colonoscopy same as average-risk population. Guidance for endoscopic severity, Simple Endoscopic Score for Crohn's (SES-CD) and Mayo endoscopic score for UC. Moderate-severe: SES-CD ≥ 7/ Mayo 2/3; Mild: SES-CD 3–6/ Mayo 1; No active disease: SES-CD 0–2/ Mayo 0.

Figure 2. Principles of dysplasia management and surveillance intervals in IBD.

disease control, dysplasia detection capabilities over time, and general reduction in CRC risk in society suggest that extending surveillance intervals to every 5 years in the lowest-risk patients is reasonable.[64,67,76] These patients include those with historically well-controlled disease between consecutive colonoscopies with either short-segment colonic disease (eg, isolated proctitis in UC or less than one-third of colon in Crohn's disease),[93,94,102,103] or who have had repeated examinations without dysplasia and with mucosal healing, in the absence of other inherent CRC risk factors (Figure 2*C*).[33,76] Clinicians should, however, err on the side of sooner surveillance (2–3 years) in this group if uncertainty exists regarding disease control or dysplasia risk, such as in those undergoing their first dysplasia surveillance examination ever or after many years. Patients with Crohn's disease isolated to the small bowel do not appear to harbor a greater risk of CRC than comparable non-IBD patients,[104] thus average-risk CRC surveillance recommendations appear appropriate.[105]

Special Topics

Surveillance of Ileoanal Pouch

Best Practice Advice 12: Pouch surveillance should be performed at least annually in those at high risk for developing colorectal dysplasia (prior colorectal cancer or dysplasia, primary sclerosing cholangitis), as well as in those with persistent moderate to severe pouchitis and/or pre-pouch ileitis (to assess for treatment response). Surveillance intervals in those at lower risk should be individualized.

A meta-analysis showed that IBD patients with prior colorectal dysplasia or CRC had 4.4- and 15.0-fold increased risks of pouch cancer, respectively.[106] Conversely, the cumulative incidence of cancers of the pouch and cuff (3.4% at 25 years[106]) in those without risk factors remains lower than the lifetime CRC risk in the general population. American Society of Gastrointestinal Endoscopy,[59] British Society of Gastroenterology,[64] and European Crohn's and Colitis Organisation[107] recommend annual surveillance for those at high risk of dysplasia (prior colorectal dysplasia or cancer, PSC) and those with persistent pouchitis or type C (atrophic and inflamed) mucosa. The British Society of Gastroenterology further recommends surveillance every 5 years for those without risk factors.

Pseudopolyps

Best Practice Advice 13: Targeted biopsies of representative or concerning pseudopolyps is appropriate during colonoscopy. Removal and sampling of all lesions is neither required nor practical. Surgery should be a last resort to manage colorectal cancer risk in the setting of severe pseudopolyposis. Dye spray chromoendoscopy should not be used to detect flat or subtle lesions within a field of pseudopolyps.

Acute pseudopolyps (normal mucosa within areas of ulceration, giving the impression of a polyp) and chronic post-inflammatory polyps (finger-like or sessile projections of submucosa with surface architecture similar to the surrounding mucosa on all sides) can sometimes mimic adenomas and make surveillance colonoscopy challenging, especially if present in high numbers. As these lesions are not considered precancerous,[108] their removal is not required; however, targeted sampling of representative or suspicious lesions is appropriate. Careful inspection of the flat mucosa between pseudopolyps, with or without non-targeted biopsies, might be required to identify flat or subtle lesions. Colectomy to mitigate cancer risk in the setting of extensive pseudopolyposis is rarely performed, but may be appropriate in select cases.

Chemoprevention

Best Practice Advice 14: Optimal disease control with medical therapy is imperative to minimizing an individual's lifetime risk of developing colorectal cancer. There is uncertainty regarding the independent chemotherapeutic benefit of mesalamine therapy in people with colonic inflammatory bowel disease.

Because CRC risk in IBD is primarily driven by inflammation[97] and available data do not demonstrate a clear independent chemopreventive effect of available agents, the focus of chemoprevention in IBD should be control of inflammation. Although mesalamine has been linked to multiple pathways involved in oncogenesis,[109] meta-analyses of population-based studies have yielded conflicting results regarding the chemopreventive effect of mesalamine therapy.[110–114]

Conclusions

Improvements in disease management, as well as endoscopic technology and quality, have dramatically changed the way in which we think about IBD-related dysplasia, aligning closely with how we conceptualize dysplasia in the non-IBD population. The practices of taking nontargeted biopsies and of referring patients for colectomy in the setting of low-grade or invisible dysplasia are being increasingly challenged in favor of "smart" approaches that emphasize careful inspection and targeted sampling of visible and subtle lesions using newer technologies (including HD-WLE and DCE), as well as endoscopic management of most lesions that appear endoscopically resectable. Indeed, surgery is being increasingly reserved for lesions harboring strong risk factors for invasive cancer or when endoscopic clearance is not possible. More data are required to clarify the role of nontargeted biopsies when performing an examination using HD scopes, the long-term safety of endoscopic management of large and complex dysplastic lesions, and the optimal surveillance intervals that consider an individual's lifetime inflammatory burden and other CRC risk factors. We look forward to a day when a single guideline can potentially address dysplasia surveillance and management in IBD and non-IBD patients alike. Until then, this document serves to summarize updated understanding and best practice advice for dysplasia management in IBD.

Supplementary Material

Note: The first 25 references associated with this article are available below in print. The remaining references accompanying this article are available online only with the electronic version of the article. Visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2021.05.063.

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Conflicts of interest
The authors disclose no conflicts.

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