Optimal Dysplasia Detection and Management in IBD: Now and in the Future

Bharati Kochar, MD, MS[1,*], Eric J. Mao, MD[2,*] and Samir A. Shah, MD, FACG[3]

KEYWORDS: Crohn's disease; ulcerative colitis; dysplasia; chromoendoscopy; colon cancer screening

Am J Gastroenterol 2023;118:1905–1908. https://doi.org/10.14309/ajg.0000000000002302

BACKGROUND

Detection of colonic dysplasia in patients with inflammatory bowel diseases (IBD) is highly variable among clinicians. We review the latest data and guidelines and offer our current approach with a look to the horizon. Risk factors of IBD-associated colonic dysplasia include history of primary sclerosing cholangitis (PSC), previous dysplasia, colonic inflammation involving ≥ one-third of the colon with disease duration >8 years from symptom onset, histologic inflammation, and family history of colorectal cancer, particularly at a younger age (younger than 50 years). These factors were reviewed recently; we summarize them in Table 1 (1,2). The risk factor with the strongest association is PSC (3). Although less studied, the macroscopic appearance of the colon, including a foreshortened colon and severe endoscopic inflammation, confers an increased risk of colon cancer (4). Surveillance colonoscopies are protective against the development of advanced colon cancer in patients with IBD (1). Reassuringly, the incidence of advanced and interval colorectal cancer in patients with ulcerative colitis is decreasing over time, possibly because of better control of inflammation, increase in high-definition (HD) colonoscopes, and the use of chromoendoscopy (5).

CURRENT STATUS

Guidelines from the American College of Gastroenterology, American Gastroenterological Association (AGA), American Society of Gastrointestinal Endoscopy, and European Crohn's and Colitis Organisation all recommend using HD colonoscopes for dysplasia screening starting 8 years after disease onset and immediately if coexisting PSC (6–11). In general, guidelines recommend dye spray chromoendoscopy (DCE). Owing to sparse evidence supporting the benefit of virtual chromoendoscopy (VCE) techniques, such as narrow-band imaging and i-scan, earlier guidelines did not recommend it. Recent studies demonstrate similar dysplasia detection rates when comparing DCE with VCE (12–14). Therefore, recent AGA and American College of Gastroenterology guidelines recommend VCE as a suitable alternative when using HD colonoscopes. Societal guidelines agree on targeted biopsies with DCE. The AGA recommends consideration for additional random biopsies in people who are at higher risk. When DCE is not available or appropriate, random and targeted biopsies are recommended by most of the societal guidelines. In Figure 1, we present lesions that are enhanced by the use of chromoendoscopy. No dye product is currently US Food & Drug Administration-approved, specifically for chromoendoscopy.

NEWER DATA

With the advent and proliferation of HD white light endoscopy (HD-WLE), the added utility of DCE was less evident. In Table 2, we summarize studies of randomized controlled trials (RCTs) assessing modes of dysplasia detection in patients with IBD. A meta-analysis of RCTs demonstrated that DCE had no additional benefit in dysplasia detection compared with HD-WLE (15). Two more recent RCTs support the ongoing use of DCE even with HD-WLE. The Swedish trial found that patients who had an examination with DCE were significantly more likely to have dysplasia detected in a macroscopic lesion. In addition, DCE was more time-efficient for the detection of dysplasia lesions, which further supports the use of DCE in clinical practice. A Chinese multicenter study noted a significant increase in detection of dysplastic lesions with DCE than HD-WLE with targeted biopsied and a trend toward a higher detection rate with DCE than

Table 1. Known risk factors for the development of colonic dysplasia in patients with inflammatory bowel diseases

Risk factor
Concomitant primary sclerosing cholangitis (PSC)
≥8 yr of colonic inflammatory bowel disease duration
≥One-third of colon inflamed historically
First-degree relative with colon cancer, younger than 50 yr
Male sex
Extensive pseudopolyposis (this has become controversial)
Shortened or tubular colon

[1]Division of Gastroenterology, Massachusetts General Hospital, Boston, Massachusetts, USA; [2]Division of Gastroenterology and Hepatology, University of California, Davis, School of Medicine, Sacramento, California, USA; [3]Division of Gastroenterology, The Miriam Hospital, Alpert Medical School of Brown University, Gastroenterology, Associates, Inc., Providence, Rhode Island, USA. **Correspondence:** Samir A. Shah, MD, FACG. E-mail: samir@brown.edu.
Received January 30, 2023; accepted April 4, 2023; published online May 4, 2023

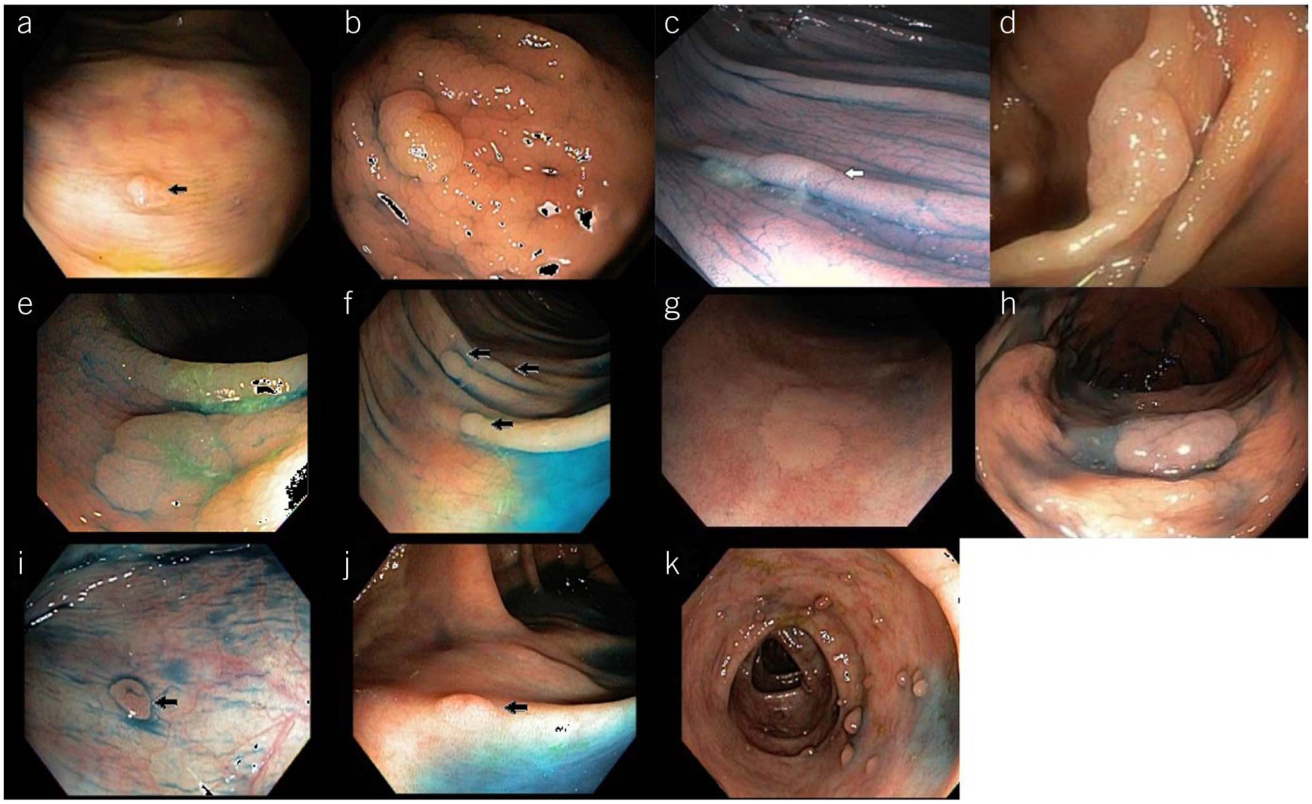

Figure 1. Polyp detection aided by dye chromoendoscopy (DCE). (**a, b,** and **c**) Polyps detected with DCE after a finding of invisible low-grade dysplasia on a random biopsy with HD-WLE. (**d, e, f, g,** and **h**) Sessile serrated adenomas detected with DCE. (**i** and **j**) Adenomatous polyps with low-grade dysplasia detected with DCE in the setting of multiple pseudopolyps as seen in (**k**).

HD-WLE with random biopsies (16). A meta-analysis updated with these 2 studies concluded that DCE remained superior even with HD-WLE and was even more significant when eliminating studies with a single endoscopist (17).

LOOKING TO THE FUTURE

The future of IBD dysplasia screening will incorporate computer-aided detection techniques and artificial intelligence, which will enhance detection rates and staging (18,19). Serologic detection of dysplastic polyps and colon cancer is under investigation, although data remain limited in patients with IBD (20).

HOW WE DO IT

Chromoendoscopy can be performed in any setting where colonoscopy can be performed. After discussing the need for the procedure with patients, we book patients in longer sessions to allow for

Table 2. Summary of studies comparing dysplasia detection between high-definition white light endoscopy (HD-WLE), dye-spray chromoendoscopy (DCE), and virtual chromoendoscopy (VCE)

Study	Location	Population	Dysplasia detection rate		
			HD-WLE	DCE	VCE
Watanabe 2016 (14)	Japan	UC n = 263	—	10.7%	11.9%
Bisschops 2018 (12)	Belgium	UC n = 131	—	21.2%	21.5%
Iacucci 2018 (13)	Canada	UC/CD n = 270	25.6%	24.4%	15.6%
Alexandersson 2020 (23)	Sweden	UC/CD n = 305	4.6%	11.1%	—
Wan 2021 (16)	China	UC n = 122	Targeted biopsy: 1.9% Random biopsy: 8.1%	Targeted biopsy: 9.7%	—

CD, Crohn's disease; UC, ulcerative colitis.

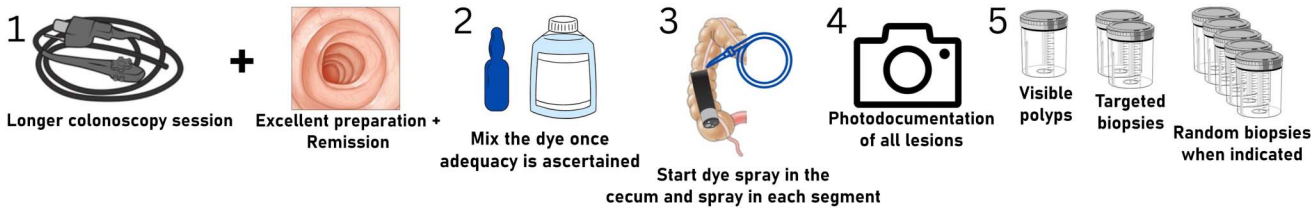

Figure 2. Summary of steps to perform chromoendoscopy.

the added time needed for the detailed examination (45 minutes in an Ambulatory Surgery Center and 1 hour in the hospital). We inform patients ahead of time that excellent preparation will be required to perform chromoendoscopy. There is no additional current procedural terminology code for chromoendoscopy that results in payment, and thus, colonoscopy with biopsy and/or polypectomy as documented are used.

During the procedure, for efficiency, we ensure that the dye of choice is in the room, but not mixed until adequate preparation to the cecum and endoscopic remission are documented. During insertion of the colonoscope, the endoscopist must wash and further clean the colon and suction residual fluid. Once adequacy, including the absence of significant inflammation, for chromoendoscopy is confirmed, request that the dye is mixed. For FD&C #2 (similar to indigo carmine), we use a 0.1% concentration (up to 0.4% is acceptable). For methylene blue, we use one 10 mL vial of 50 mg in 1,000 cc of sterile water (or 500 or 250 cc for higher concentration). We use the irrigation channel operated by the foot pedal to apply the dye, but spray catheters are also available.

We examine and photograph each segment of the colon under white light and selective narrow band imaging at the discretion of the endoscopist. Then, we spray each section with dye, aiming toward the antidependent wall and then suctioning to deflate the colon segment to promote coating of the mucosa. Once stained, one must carefully examine each area for irregularities or asymmetry in uptake of the dye and suction pools of dye to obtain complete visualization.

Chromoendoscopy confers a careful second look because it is easier to note areas where the dye did not stain. We do limited random segmental biopsies for mucosal healing (typically from the ascending and sigmoid) and label as random along with location. Any abnormal mucosa should be photographed and sampled separately as targeted biopsies with location. For high-risk situations, we recommend >32 random biopsies in addition to targeted biopsies even with DCE or VCE. If a larger lesion is seen, the endoscopist should consider whether they have the skill set to remove the lesion or whether a referral to a therapeutic endoscopist should be made for advanced resection techniques. Partial removal can result in scarring and interfere with subsequent endoscopic removal. If referring to a therapeutic endoscopist, the lesion should be untouched, described in detail including location and, if appropriate, marked with a tattoo at

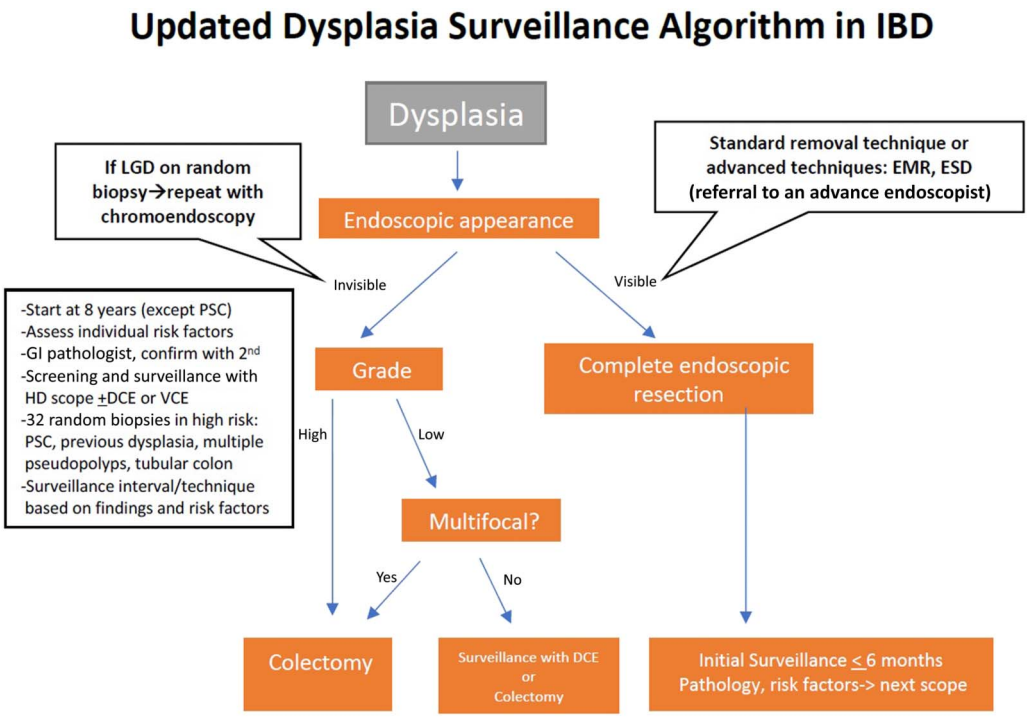

Figure 3. Updated algorithm for surveillance of dysplasia in IBD. DCE, dye-spray chromoendoscopy; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; HD-WLE, high-definition white light endoscopy; IBD, inflammatory bowel disease; LGD, low-grade dysplasia; PSC, primary sclerosing cholangitis; VCE, virtual chromoendoscopy.

least 5 cm away from the lesion. Finally, if dysplasia is detected on a random biopsy, a follow-up colonoscopy within 6 months with DCE with both targeted and random biopsies should be pursued (21,22).

Figure 2 shows the steps in performing chromoendoscopy. Patients, staff, and the endoscopist should be aware that the dye can get on to clothes. Patients are warned they may note staining, have "Smurf (blue) stools" or "Leprechaun (green) urine" for a few days after the procedure.

In Figure 3, we present an updated algorithm for dysplasia surveillance. Surveillance intervals are determined by risk factors and pathology. Patients with PSC, dense pseudopolyposis, and invisible low-grade dysplasia should remain on annual surveillance (11). Patients with limited ulcerative proctitis are not at higher risk of cancer and should be screened at the same interval as patients without IBD. As always, detailed conversations about surveillance intervals should be conducted with patients reviewing individual risk factors to ensure that both the patient and the clinician are comfortable with the chosen interval and surveillance program.

CONCLUSION

Despite the significant advances that have been made in the treatment of IBD, screening and surveillance for colon cancer remains a significant priority. The advances in endoscopes allow for better detection of subtle precancerous lesions. However, they are not sufficient, and chromoendoscopy remains part of the armamentarium for dysplasia detection. Practitioners caring for patients with IBD, in all settings, should gain comfort with this modality that can be easily implemented into routine clinical practice. Despite multimodal techniques, invisible dysplasia can still exist, and therefore, random biopsies continue to be necessary in patients at higher risk, although chromoendoscopy and in the future computer-aided detection can limit the number of random biopsies.

CONFLICTS OF INTEREST

Guarantor of the article: Samir A. Shah, MD, FACG.
Specific author contributions: All three authors worked together to outline and write the manuscript based on lectures given by S.S. on the same topic.
Financial support: None to report.
Potential competing interests: None to report.

REFERENCES

1. Wijnands AM, De Jong ME, Lutgens MWMD, et al. Prognostic factors for advanced colorectal neoplasia in inflammatory bowel disease: Systematic review and meta-analysis. Gastroenterology 2021;160(5):1584–98.
2. De Jong ME, Van Tilburg SB, Nissen LHC, et al. Long-term risk of advanced neoplasia after colonic low-grade dysplasia in patients with inflammatory bowel disease: A nationwide cohort study. J Crohns Colitis 2019;13(12):1485–91.
3. Shah SC, Ten Hove JR, Castaneda D, et al. High risk of advanced colorectal neoplasia in patients with primary sclerosing cholangitis associated with inflammatory bowel disease. Clin Gastroenterol Hepatol 2018;16(7):1106–13.e3.
4. Rutter MD, Saunders BP, Wilkinson KH, et al. Cancer surveillance in longstanding ulcerative colitis: Endoscopic appearances help predict cancer risk. Gut 2004;53(12):1813–6.
5. Choi C-HR, Rutter MD, Askari A, et al. Forty-year analysis of colonoscopic surveillance program for neoplasia in ulcerative colitis: An updated overview. Am J Gastroenterol 2015;110(7):1022–34.
6. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG clinical guideline: Management of Crohn's disease in adults. Am J Gastroenterol 2018; 113(4):481–517.
7. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG clinical guideline: Ulcerative colitis in adults. Am J Gastroenterol 2019;114(3):384–413.
8. Shergill AK, Lightdale JR, Bruining DH, et al. The role of endoscopy in inflammatory bowel disease. Gastrointest Endosc 2015;81(5): 1101–21.e13.
9. Magro F, Gionchetti P, Eliakim R, et al. Third European evidence-based consensus on diagnosis and management of ulcerative colitis. Part 1: Definitions, diagnosis, extra-intestinal manifestations, pregnancy, cancer surveillance, surgery, and Ileo-anal pouch disorders. J Crohns Colitis 2017;11(6):649–70.
10. Laine L, Kaltenbach T, Barkun A, et al. SCENIC international consensus statement on surveillance and management of dysplasia in inflammatory bowel disease. Gastrointest Endosc 2015;148(3):639–51.e28.
11. Murthy SK, Feuerstein JD, Nguyen GC, et al. AGA clinical practice update on endoscopic surveillance and management of colorectal dysplasia in inflammatory bowel diseases: Expert review. Gastroenterology 2021; 161(3):1043–51.e4.
12. Bisschops R, Bessissow T, Joseph JA, et al. Chromoendoscopy versus narrow band imaging in UC: A prospective randomised controlled trial. Gut 2018;67(6):1087–94.
13. Iacucci M, Kaplan GG, Panaccione R, et al. A randomized trial comparing high definition colonoscopy alone with high definition dye spraying and electronic virtual chromoendoscopy for detection of colonic neoplastic lesions during IBD surveillance colonoscopy. Am J Gastroenterol 2018; 113(2):225–34.
14. Watanabe K, Nishishita M, Shimamoto F, et al. Comparison between newly-developed narrow band imaging and panchromoendoscopy for surveillance colonoscopy in patients with longstanding ulcerative colitis: A prospective multicenter randomized controlled trial, navigator study. Gastrointest Endosc 2016;83:AB172.
15. Feuerstein JD, Rakowsky S, Sattler L, et al. Meta-analysis of dye-based chromoendoscopy compared with standard- and high-definition white-light endoscopy in patients with inflammatory bowel disease at increased risk of colon cancer. Gastrointest Endosc 2019;90(2):186–95.e1.
16. Wan J, Zhang Q, Liang SH, et al. Chromoendoscopy with targeted biopsies is superior to white-light endoscopy for the long-term follow-up detection of dysplasia in ulcerative colitis patients: A multicenter randomized-controlled trial. Gastroenterol Rep (Oxf) 2021;9(1):14–21.
17. Mohamed MFH, Marino D, Elfert K, et al. (2023, May 6-9). Dye Chromoendoscopy Is Superior to High-Definition White Light Endoscopy for Dysplasia Detection in Inflammatory Bowel Disease: An Updated Meta-Analysis of Randomized Clinical Trials [Poster Presentation]. DDW 2023: Chicago, IL.
18. Spadaccini M, Iannone A, Maselli R, et al. Computer-aided detection versus advanced imaging for detection of colorectal neoplasia: A systematic review and network meta-analysis. Lancet Gastroenterol Hepatol 2021;6(10):793–802.
19. Stidham RW, Takenaka K. Artificial intelligence for disease assessment in inflammatory bowel disease: How will it change our practice? Gastroenterology 2022;162(5):1493–506.
20. Heidrich I, Ačkar L, Mossahebi Mohammadi P, et al. Liquid biopsies: Potential and challenges. Int J Cancer 2021;148(3):528–45.
21. Deepak P, Hanson GJ, Fletcher JG, et al. Incremental diagnostic yield of chromoendoscopy and outcomes in inflammatory bowel disease patients with a history of colorectal dysplasia on white-light endoscopy. Gastrointest Endosc 2016;83(5):1005–12.
22. Rubin DT, Krugliak Cleveland N, Rodriquez DM. Outcomes of colitis-associated dysplasia after referral from the community to a tertiary center. Gastrointest Endosc 2016;84(6):1078–9.
23. Alexandersson B, Hamad Y, Andreasson A, et al. High-definition chromoendoscopy superior to high-definition white-light endoscopy in surveillance of inflammatory bowel diseases in a randomized trial. Clin Gastroenterol Hepatol 2020;18(9):2101–7.