



Endoscopic detection and resection of dysplasia in inflammatory bowel disease-techniques with videos

Sameen Khalid¹ · Aamer Abbass¹ · Neelam Khetpal¹ · Bo Shen² · Udayakumar Navaneethan³

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Abstract

Background Patients with ulcerative colitis and Crohn's colitis have an increased risk of developing dysplasia and colorectal cancer as compared to the general population; surveillance colonoscopy is recommended in this patient population.

Methods This review of the published literature aimed to assess the published evidence.

Results Detection of dysplasia requires examination of mucosa with targeted biopsies of the visible lesions as well as random biopsies to detect invisible lesions. Newer endoscopic techniques, in particular chromoendoscopy, increase the yield of identifying dysplastic lesions. The surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients International Consensus (SCENIC) guidelines recommends that colonoscopy using chromoendoscopy is the optimal endoscopic surveillance strategy to detect dysplasia. Once dysplastic lesions are discovered on surveillance endoscopic examination, careful and meticulous descriptions of lesions is mandatory to aid in further decision making. Management of dysplastic lesions in inflammatory bowel disease patients depends on endoscopic (morphological) and histologic findings and patient characteristics such as age, general condition of the patient, and patient preferences. Endoscopic mucosal resection, endoscopic submucosal dissection, and surgery are different therapeutic options for colonic dysplastic lesions detected in the setting of inflammatory bowel disease.

Conclusions In this review, we discuss the various techniques for endoscopic resection of dysplasia in patients with inflammatory bowel disease. Further research is required to determine the optimal approach to diagnosis and management of dysplasia in patients with inflammatory bowel disease.

Keywords Chromoendoscopy · Dysplasia · Endoscopic mucosal resection · Inflammatory bowel disease · Ulcerative colitis

Introduction

Patient with inflammatory bowel diseases (IBDs), including ulcerative colitis (UC), and Crohn's colitis (CC) have an increased risk of developing dysplasia and colorectal cancer [1–8]. This risk has been estimated to be 2 to 5 times higher as compared to

the general population of the same age group [2, 8–11] and increases with increased disease duration, extensive colitis, family history of colorectal cancer, presence of concomitant primary sclerosing cholangitis, and severity of microscopic or endoscopic inflammation [8, 9, 12–14]. Most cases of colorectal cancer arise from dysplasia; hence, surveillance colonoscopy is recommended in this disease population [1, 2]. Surveillance colonoscopy and polypectomy has shown to reduce the incidence of colorectal cancer by 80% and mortality of colorectal cancer by 50% in the general population [15–17]. It is believed that the rate of progression from dysplasia to colorectal cancer in patients with IBD is more rapid than in general population [12]. The main aim of surveillance colonoscopy in the past was to identify dysplasia and refer for colectomy in a timely manner.

Surveillance colonoscopy is recommended yearly in IBD patients with extensive colitis starting 8 to 10 years after the diagnosis is established [6, 9, 12, 18–21]. In the past, detection of dysplasia required examination of mucosa by targeted biopsies of the visible lesions as well as random or nontargeted

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✉ Udayakumar Navaneethan
udhaykumar81@gmail.com

¹ Department of Internal Medicine, Advent Health, Orlando, FL, USA

² Department of Gastroenterology, Cleveland Clinic, Cleveland, OH, USA

³ Center for Interventional Endoscopy, Advent Health, University of Central Florida College of Medicine, 601 E Rollins Street, Orlando, FL 32803, USA

biopsies to detect invisible lesions. It was suggested that a minimum of 33 random biopsies need to be collected from all colonic segments from cecum to rectum by obtaining 4 quadrant biopsies every 10 cm, in addition to the targeted biopsies, using white-light standard-definition colonoscopy at each surveillance [1, 3, 6, 9, 12, 22–25]. Despite this intensive regimen, sampling error is a known limitation of this approach in patients with IBD. Other limitations include poor physician adherence, poor sensitivity, increased procedure time, and cost [26, 27]. If dysplasia was detected on these biopsies, the patient was traditionally referred for colectomy. To overcome the limitation of sampling error, newer endoscopic techniques have been developed. With the advent of newer advanced endoscopic techniques such as chromoendoscopy, most dysplastic lesions are visible and less number of biopsies is required, making surveillance less cumbersome for both patients and the physicians.

Dysplastic colonic lesions detected using advanced imaging techniques can be managed successfully by either endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) or surgery depending on the morphology and depth of invasion. In this review, we discuss the techniques for endoscopic resection of dysplasia in patients with IBD.

Tumorigenesis of colitis-associated neoplasia

Colitis-associated neoplasia (CAN) shares some of the steps of tumorigenesis with sporadic CRC but also has some distinct features from sporadic CRC. It usually follows an inflammation–dysplasia–carcinoma sequence without involvement of a distinct adenoma formation which is a characteristic of sporadic CRC.

As compared to sporadic cancer where dysplasia arises in one or two focal regions of colon, CAN is frequently associated with two or more primary synchronous cancers, and this multifocality is due to the broader “field effect” of mucosal inflammation of colon in IBD that gives rise to neoplasia [28].

The natural history of dysplasia in colitic mucosa progresses from no dysplasia to indefinite for dysplasia to low-grade dysplasia (LGD) to high-grade dysplasia (HGD) and eventually invasive cancer. This is an important factor underlying surveillance of CRC in IBD patients [28]. It is possible for CRC in IBD to sometimes arise in the absence of dysplasia or without the progression of LGD to HGD. Nevertheless, dysplasia of any grade in IBD is associated with a high risk of synchronous or metachronous CRC.

Detection of dysplasia

Detection of dysplasia requires an understanding of the lesion characteristics, characterization of dysplasia using various techniques including high-definition white-light endoscopy and chromoendoscopy.

Characterization of dysplasia

One of the first priorities for complete endoscopic resection is to characterize the dysplastic lesions. Dysplasia in IBD tends to be subtle in the form of a slight elevation, focal friability, obscure vascular pattern, uneven redness, villous mucosa, or irregular nodularity and has not been well defined. In patients with IBD, dysplasia is sometimes classified as flat or raised. Flat dysplasia is an endoscopically invisible lesion that is detected microscopically in random biopsy specimens. Detection of these lesions requires adequate sampling of the mucosa and is prone to sampling error. Raised dysplastic lesions in the past were called by various terminologies including dysplasia-associated lesions or masses (DALMs) or adenoma-like mass or dysplasia (ALMs) [9, 12]. The SCENIC consensus statement recommends that terms such as DALM, adenoma-like, and nonadenoma-like should be not be used [1]. The consensus document recommends using the terminology visible and invisible dysplasia. The SCENIC document uses a modification of the Paris classification to describe dysplasia. Visible dysplasia is the one identified on targeted biopsies from a lesion that is seen during colonoscopy. It may be polypoid or nonpolypoid. Polypoid or protruded lesions are defined as the lesions protruding from the mucosa of the colon into the lumen. These lesions rise > 2.5 mm above the surrounding mucosa. These are further classified as pedunculated (attached to mucosa by a stalk, Ip), subpedunculated (attached to mucosa by a very small stalk, Isp), or sessile (not attached to mucosa by a stalk, Is). Nonpolypoid lesions are defined as lesions with little or no protrusion above the mucosa of the colon. These lesions rise < 2.5 mm above the surrounding mucosa. These are further classified as flat elevated lesions and flat lesions. Flat elevated lesions include superficial elevated (protruded but are less than 2.5 mm above the mucosa, 0-IIa), flat elevated lesions with central depression (0-IIa+c), or flat elevated lesions with raised broad-based nodule (0-IIa+Is). Flat lesions include flat mucosal change (not protruded above the mucosa, 0-IIb), depressed (depressed below the level of the mucosa, 0-IIc), or excavated (deep depression below the level of the mucosa, 0-III) [15]. Table 1 describes the various terminology used in describing lesions in IBD patients, and Figs. 1, 2, 3, 4, and 5 show the various lesions described in the table.

Other descriptors such as location within or outside an area of known colitis, borders (distinct or indistinct), and presence of ulceration should also be noted. These features are different from the usual Paris classification which is used in non-IBD patients. In addition, visible dysplasia should be classified as endoscopically resectable or endoscopically unresectable. The SCENIC guidelines define the term “endoscopically resectable” as a lesion in which distinct margins are identified, a lesion that appears to be completely excised on visual inspection after endoscopic

Table 1 Various terminology used in describing lesions in IBD patients

Lesion definition	Description
Polypoid	Lesion protruding from the mucosa into the lumen > 2.5 mm
Pedunculated	Lesion attached to the mucosa by a stalk
Sessile	Lesion not attached to the mucosa by a stalk: entire base is contiguous with the mucosa
Nonpolypoid	Lesion with less than 2.5 mm protrusion or no protrusion above the mucosa
Superficial elevated	Lesion with protrusion but less 2.5 mm above the lumen
Flat	Lesion without protrusion above the mucosa
Depressed	Lesion with at least a portion depressed below the level of the mucosa
Ulcerations	Ulceration within the lesion
Borders	Lesion's border is discrete or indistinct

resection, complete resection is confirmed by the histological examination of the resected specimen, and histologic examination of the mucosa adjacent to the resection site is dysplasia-free [1]. Invisible dysplasia is the one identified on random or nontargeted biopsies without a visible lesion in spite of using advanced endoscopic imaging [1].

Lesion assessment

Careful endoscopic assessment of the lesions is of paramount importance. This careful assessment has two components: overview or global assessment of the lesion followed by focused assessment of any suspicious areas. Lesions with a risk of submucosal invasion should undergo en bloc resection. Focal assessment for the presence of disrupted mucosal pit pattern should be assessed on the basis of Kudo system and are examined using white-light endoscopy. We routinely use Kudo pit pattern for assessment of lesions. However, it is controversial whether the Kudo pit pattern can be used to predict histology of colonic IBD lesions, especially in the presence of inflammation-associated regenerative pattern. The use of other classifications systems such as Sano, NBI International Colorectal Endoscopic and Japanese NBI Expert Team has not been studied in IBD patients. However, their utility in lesion evaluation in the setting of IBD has not been studied.

In the general population, majority of sessile lesions are 0-IIa or 0-IIa+1s and carry a low risk of submucosal invasion. In a large study, presence of distal 0-Is or 0-IIa+1s nongranular

lesion was associated with up to 15.3% risk of submucosal invasion. Additionally, 0-IIa+c lesions have the highest risk of submucosal invasion [29]. Lesions with depression (0-IIc, 0-IIa+c, 0-Is+c) have increased risk of submucosal invasion. These global assessment tools allow overall estimation of submucosal invasion risk in colonic lesions. However, these have not been studied in IBD patients and may not be applicable.

Detection of dysplasia by novel endoscopic techniques

Newer endoscopic techniques such as chromoendoscopy increases the yield of identifying dysplastic lesions in IBD patients and may lead to reduced need for random biopsies by allowing targeted biopsies to be taken for histological evaluation.

Chromoendoscopy

Chromoendoscopy is an advanced endoscopic technique that has been implemented recently for use in cancer surveillance in patients with IBD. In conventional chromoendoscopy, different dye solutions, classified as either absorptive or contrast agents, are applied to the mucosal surface [21, 30]. These dye solutions provide contrast enhancement to improve visualization of epithelial surface. Absorptive agents include 0.1% methylene blue and 0.05% cresyl violet [9]. Different cells absorb these absorptive agents to different degrees, highlighting distinct cell types. Contrast agents include 0.03 to 0.5%

Fig. 1 Low-grade dysplastic sessile lesion with regular margin

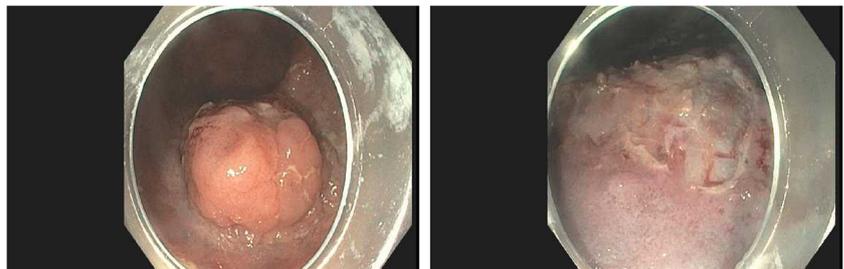
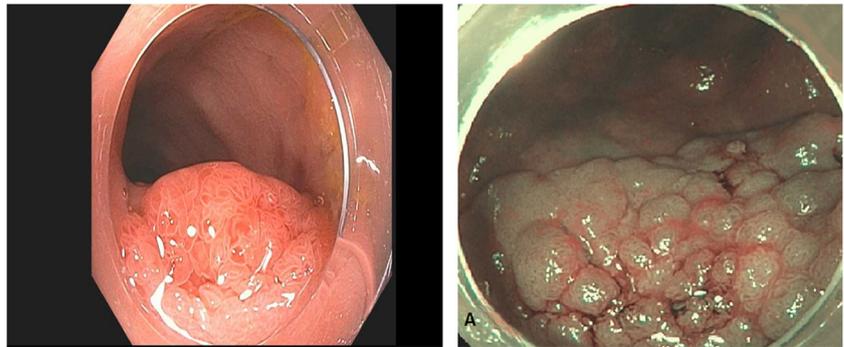


Fig. 2 Low-grade dysplastic superficial elevated lesion with regular margin



indigo carmine [3]. These contrast agents coat colonic mucosal surface, highlighting tissue architecture. Good bowel preparation is very important for evaluation of mucosal surface. The colonoscope is inserted to the cecum using high-definition white-light endoscope. The colonic mucosa is sprayed using dye solution while withdrawing the colonoscope. During withdrawal, each colonic segment is sprayed and carefully inspected. Either a spray catheter or a foot wash pump can be used for spraying. Indigo carmine is spray diluted (~0.03%). For best visualization, we prefer the foot wash pump and the spray is targeted to the antigravity wall of the colon. Any excess dye that pools is suctioned. When a spray catheter is used, the spray catheter is inserted through the biopsy channel until its tip protrudes 2 to 3 cm, and dye is sprayed throughout the mucosa while the colonoscope is being withdrawn [31]. When suspicious lesions are visualized, a more concentrated indigo carmine (0.13%, 5 mL ampule of indigo carmine with 25 mL water) is applied with a syringe via the biopsy channel to better delineate the lesion extent and the mucosal detail (Video 1). This technique enhances surface markings of the colonic mucosa and helps in improving the detection of subtle lesions, increasing the sensitivity of endoscopic examinations [32, 33]. It also aids in better characterization of the lesion once it is detected, increasing the specificity of the endoscopic examinations. It allows differentiation of neoplastic from nonneoplastic lesions by enabling characterization of crypt architecture through evaluation of pit pattern

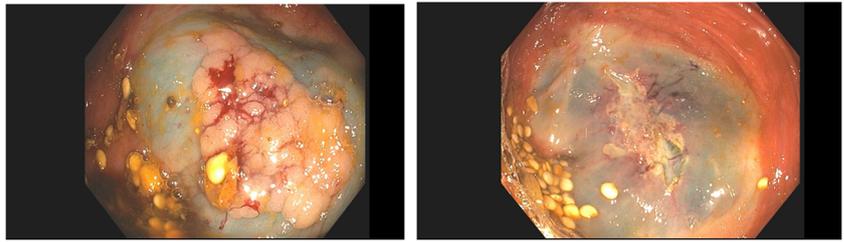
[3, 9, 12]. Lesions that are endoscopically resectable should undergo EMR or ESD or tattoo and referral to an endoscopist with expertise in these procedures [1]. Lesions that are not endoscopically resectable should undergo targeted biopsies. In cases where no lesions are identified, at least 2 biopsies from each colonic segment should be obtained to determine the histologic extent and disease severity [34–41]. In a recent meta-analysis, the difference in the diagnostic yield between chromoendoscopy and white-light endoscopy for detecting dysplasia in patients with IBD was 7% (95% CI 3.2 to 11.3%) [42]. By allowing meticulous mucosal examination and targeted biopsies of suspicious lesions, this technique has been reported to be more effective method of surveillance as compared to obtaining numerous nontargeted biopsies. It has also deemed to be more cost-effective as compared to the standard white-light endoscopy in a recent cost-effectiveness analysis [43]. Use of chromoendoscopy leads to a 15% increase in the overall dysplasia detection rate and a 51% increase in the detection of endoscopically visible dysplasia as compared with standard white-light endoscopy, and a 12% increase in the overall dysplasia detection rate as compared with high-definition white-light colonoscopy.

The SCENIC consensus and the European Crohn's and Colitis Organization consensus statement recommend the use of chromoendoscopy to obtain targeted biopsies and stated that chromoendoscopy is superior to random biopsies in the detection of neoplasia [4, 44, 45]. Guidelines by British Society of Gastroenterology, Crohn's and Colitis Foundation, American Gastroenterological Association, European Society of Gastrointestinal Endoscopy, and the European Society of Gastrointestinal Endoscopy also endorse chromoendoscopy with pan colonic dye spraying and targeted biopsies by appropriately trained endoscopists [4, 18, 44, 45]. We had demonstrated that endoscopic features including pseudopolyps especially on standard-definition white-light colonoscopy did not appear to reliably predict the development of colitis-associated neoplasia leaving room for image-enhanced endoscopy such as chromoendoscopy for surveillance [46]. In a retrospective analysis of data from two large independent surveillance cohorts, pseudopolyps were associated with greater severity and extent of colon inflammation



Fig. 3 Low-grade dysplastic superficial elevated lesion with mixed Kudo pit pattern 0-IIa IIIIL with regular margin

Fig. 4 Flat, low-grade dysplastic lesion with regular margin



and higher rates of colectomy; however, pseudopolyps were not associated with development of any degree of colon neoplasia [47]. Thus, the presence of pseudopolyps although makes chromoendoscopy less accurate should not discourage endoscopists from performing chromoendoscopy.

It was initially thought that random biopsies are unnecessary when chromoendoscopy is used. However, a recent large French multicenter study demonstrated that random biopsies yielded neoplasia in 0.2% per-biopsy (68/31865), 1.2% per-colonoscopy (12/1000) but 12.8% per-patient with neoplasia (12/94). Despite their low yield, the authors recommended that random biopsies should be performed in association with chromoendoscopy in patients with IBD with a personal history of neoplasia, concomitant primary sclerosing cholangitis, or a tubular colon during colonoscopy [48].

Role of pathology

One of the critical steps in the continued surveillance of dysplasia in IBD is pathologist's interpretation of biopsy specimens as well as effective communication with endoscopist to interpret histological evidence in the context of endoscopic findings. There is a considerable intra-observer and inter-observer variability in the interpretation of dysplasia in IBD patients with overall agreement between experts ranging from 42 to 72% [12].

Highest level of agreement is usually seen for two ends of spectrum which is negative for dysplasia and HGD and lowest degree of agreement is seen for indefinite for dysplasia and

LGD [12, 49, 50]. Intra-observer and inter-observer variability can be optimally improved if strict and validated diagnostic criteria are followed for the interpretation of dysplasia.

The US Multi society Task Force on Colorectal Cancer guidelines and SCENIC International Consensus Statement strongly recommend that if any of the biopsies are positive for indefinite for dysplasia, LGD in flat mucosa or HGD; it should be confirmed by a second pathologist expert in dysplasia in IBD before proceeding to further surveillance and therapeutic interventions [6, 51, 52].

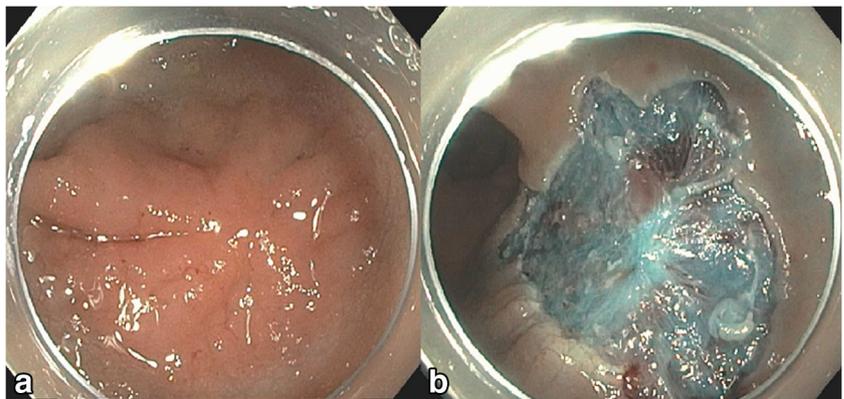
Management

Endoscopic reconfirmation

Management of dysplastic lesions in IBD patients depends on endoscopic and histologic findings and patient characteristics such as age, general condition of the patient, and patient preferences. EMR, ESD, and surgery are different therapeutic options for colonic lesions detected in the setting of IBD.

The SCENIC guidelines recommend that if the visible dysplastic lesion is deemed endoscopically resectable, en bloc EMR should be performed [1]. Other options for endoscopic resection include hybrid EMR and ESD. It is recommended that biopsies be performed of the flat mucosa surrounding the resection site to ensure that the lateral margins are free of dysplasia [3, 5, 43, 53]. Tattooing or photodocumentation of the area to facilitate future surveillance or treatment should

Fig. 5 High-grade dysplastic depressed lesion with irregular margin



also be performed [53]. Endoscopically unresectable visible dysplastic lesions are indications for colectomy. Features of the lesions that are not amenable to endoscopic resection include ill-defined margins, submucosal invasion, asymmetrical lift, ulcerations or large depressions, and flat neoplastic change with distorted pit patterns adjacent to the lesion [3, 5, 32]. Unfortunately, these features, which are reasonably reliable in non-IBD patients perform less well in colitis, because the scarring may lead to pseudodepression and inflammation distorts pit patterns. The nonlifting sign, which in combination with macroscopic appearance gives a good estimate of likely invasion in the assessment of noncolitis-associated lesions, is poor in colitis.

For endoscopically invisible dysplastic lesions detected by random biopsies, confirmation with two gastrointestinal pathologists is recommended [3, 6, 44, 53]. Once dysplasia is confirmed by both pathologists, repeat colonoscopy using high-definition colonoscopy with chromoendoscopy by an endoscopist with expertise in IBD surveillance is recommended by the SCENIC guidelines [1, 3]. If a visible dysplastic lesion is found in the same site of the colon as the previous random biopsy showing invisible dysplasia, then the lesion should be characterized according to the Paris classification and classified as endoscopically resectable or unresectable and managed accordingly [54]. If a visible dysplastic lesion is not located, then management should be individualized according to the degree of dysplasia [53]. Patients with unifocal low-grade invisible dysplasia may choose to have continued intensive surveillance colonoscopy while patients with high-grade invisible or multifocal dysplasia should undergo colectomy [3, 53].

EMR is commonly used for the resection of polypoid lesions and nonpolypoid lesions with clear margins. ESD is indicated for nonpolypoid lesions.

Endoscopic mucosal resection

Microprocessor-controlled electrosurgical generators that deliver alternating cycles of high-frequency cutting and prolonged coagulation currents are used when EMR is performed. Return electrode sends signals through which tissue impedance is sensed and adjustment of power output is done to avoid deep tissue injury [15].

Once a lesion is identified and deemed endoscopically resectable, submucosal injection between mucosa and muscularis propria creates a fluid cushion that avoids unintentional deep tissue injury and perforation. Normal saline is inexpensive and easy to prepare and inject but does not provide sustained mucosal elevation. Colloidal solutions have shown better outcomes in terms of fewer injections, fewer resections, and less time to complete EMR as compared to normal saline [54, 55]. Because of the presence of submucosal fibrosis, the use of thinner-bore injection needles (25 G rather

than 21 G or 23 G), and the use of more viscous and longer-lasting injection solutions including colloids such as gelofusine, sodium hyaluronate, or hydroxyethyl starch may be useful. In our practice, 80 mg of indigo carmine blue per 500 mL solution of hydroxyethyl starch is used. This biologically inert blue dye is avid for the submucosal loose areolar connective tissue and demarcates the boundary of the lesion. It also outlines the extent of the submucosal cushion, thus allowing safe resection margins. Irrigation with injection fluid of the nonstained areas within the EMR defect can be confirmed as submucosa as the dye is avidly taken up by the connective tissue of the submucosa. This allows reassurance of complete resection or prompts need for intervention. Epinephrine (1:100,000) is injected to maintain bloodless resection field and decreases the chance of post-procedural bleeding [15].

Different types of snares are available such as serrated, oval, thin wire, mini-hex, mini-oval, and microsnares. Their utilization depends on the lesion size, morphology, and location. These snares come in different sizes (10–30 mm) and configurations (oval, round, and hexagonal). Serrated snares are the snares most commonly used for large en bloc resection or wide field piecemeal EMR [15].

Endoscopic mucosal resection technique

Positioning of the patient and endoscopic orientation to maximize the lesion access is of paramount importance. In some case, retroflexion may be required to fully resect or access the lesion, and in some cases, a thinner caliber endoscope such as pediatric colonoscope or gastroscope may be useful.

The first step involves submucosal injection to create well-circumscribed mucosal elevation. The needle tip is tangentially placed against the mucosal surface and the fluid is injected simultaneously as the needle tip goes into the mucosa (Fig. 6 and Video 2). This elevates the mucosal lesion into the lumen allowing it to be accessed for EMR. A sequential inject and resect technique is utilized for wide field piecemeal EMR (> 40 mm). Poor mucosal elevation can be due to invasive disease, submucosal fibrosis which is common in patients with IBD or aggressive biopsy [15]. A poorly lifting lesion is not an absolute contraindication for EMR, but this factor should be taken into account during the therapeutic process [15]. Elevating the entire lesion at once should be avoided as it limits grasp of the snare and decreases the size of the sequential resections by the snare. It is preferred to perform en bloc or limited piecemeal resections if feasible as they allow more accurate histological assessment and may decrease the risk of recurrence as compared to lesions removed in multiple pieces. En bloc resection should be considered for lesions up to 20 mm in the right colon and 25 mm in the left colon particularly the rectum [15].

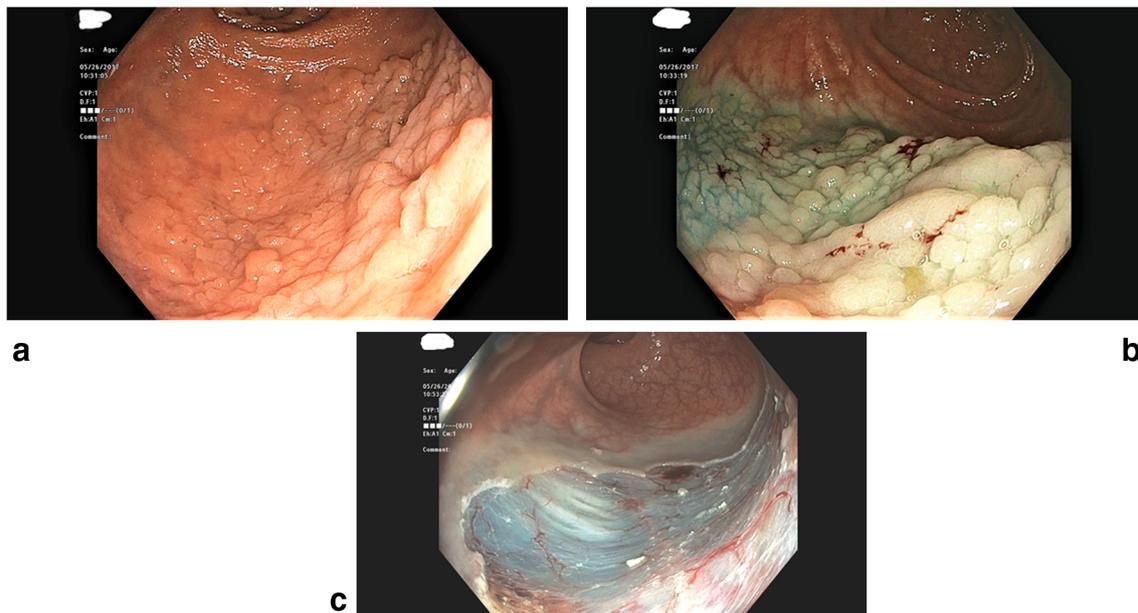


Fig. 6 Endoscopically resectable visible polypoid dysplastic lesion removed using endoscopic mucosal resection. **a** Polypoid superficial elevated lesion. **b** The lesion lifts after dynamic submucosal injection with a mixture of diluted indigo carmine, hydroxyethyl starch, and epinephrine and the lesion resection using a stiff snare. **c** Inspection of

the postresection defect shows no residual dysplasia. The EMR lesion specimen is diagnosed tubular adenoma (low-grade dysplasia, and the biopsy of the periphery confirmed chronic active inflammation without dysplasia

Place the lesion in 6 o'clock position and resect the most difficult portion first while including 2–3 mm of the normal mucosal margins. Work from the point of first entry into the submucosal plane in a sequence, using the edge of the defect as the base for snare attachment. To perform large en bloc resection, align the longitudinal axis of the snare with the longitudinal axis of the lesion in order to maximize the tissue capture. Open the snare fully, then angle down over the submucosal cushion while aspirating air to reduce the tension in colonic wall and maximize tissue capture. Then, tightly close the snare to avoid muscularis propria in the captured tissue. It is not possible to transect lesions of more than 10-mm diameter without the use of diathermy in cases where serrated snares are used. These maneuvers are used to confirm safe tissue capture: checking the movement of ensnared tissue by moving the snare catheter quickly back and forth; if the ensnared tissue moves independently to the underlying colonic wall, this is an indication of safe tissue capture. Another method is to make sure the snare closes fully with minimal puckering of the surrounding tissue [15]. Snare is kept closed while the foot pedal is pressed. Transect the tissue with the help of microprocessor-controlled electrosurgical generator using alternating cycles of high-frequency short-pulse cutting with more prolonged coagulation current. Transection should be fast. If it is prolonged, it raises concerns for muscularis propria entrapment or deeper invasion of neoplasia. The defect is washed and examined after each resection to evaluate for residual adenoma or evidence of deep injury. All the specimens are sent to pathology in formalin. (Video 2).

Once endoscopic resection is performed, biopsies should be obtained around the resection site to ensure that there is no invisible dysplasia and complete endoscopic resection has been accomplished.

A recent systematic review and meta-analysis of ten studies that included a total of 376 IBD patients with resected polypoid (Paris 0-Ip and 0-Is) dysplasia with 1704 years of follow-up reported an annualized incidence for CRC of 0.5%. The pooled incidence for colorectal cancer was 5.3 cases (95% CI, 2.7–10.1 cases), advanced lesions were 7 cases (95% CI, 4–12.4), and any dysplasia were 65 cases (95% CI, 54–78 cases) per 1000 years of follow-up [8]. Another study of 45 IBD patients had 50 adenomatous dysplastic lesions that were treated with EMR [56]. The average lesion size was 14.4 mm (range 6–40 mm). The majority (72%) had complete resection with no major adverse events. On average follow-up of 28.8 months, there was one local recurrence that was successfully retreated with EMR. No patients required surgery or developed colitis-associated cancer. Effectiveness data of endoscopic resection for nonpolypoid dysplasia is more limited. Though recent advances in endoscopic imaging have improved the recognition of nonpolypoid lesions in patients with IBD, their natural history and outcomes for complete endoscopic resection are less known, and much is extrapolated from the endoscopic removal of non-IBD nonpolypoid lesions. In a study from our center, employing EMR following chromoendoscopy, resection of polypoid (Paris 0-Ip and 0-Is) dysplasia was

accomplished in 100% of patients ($n = 23$). Recurrence was identified in 2 patients, which was managed endoscopically [57].

Complications of EMR include postprocedural pain, serositis, delayed bleeding, and perforation [15]. Careful postresection examination of the EMR mucosal defect is important in identifying high-risk patients so that early recognition and prompt management can be performed.

Endoscopic submucosal dissection

ESD is a significant advancement in therapeutic endoscopy as it can achieve a higher en bloc resection rate by performing submucosal dissection using a special electrosurgical knife. This technique results in both more accurate histopathological assessment and enhanced curability.

ESD is not as widely performed in the colorectal lesions compared with gastric lesions because of greater technical difficulty in particular in IBD patients due to submucosal fibrosis [2]. In a recent study of 32 UC patients who underwent ESD for resection of dysplasia, more than 94% of patients had nonpolypoid lesions which were resected with a median size of 33 mm (range 12–73 mm) [58]. Submucosal fibrosis was observed in 31 (97%) lesions resected. En bloc resection was possible in 29/32 lesions (91%). Pathology showed LGD in 19 (59%), HGD in 7 (22%), and cancer in 4 (13%). Four patients, including two with T1 cancer, one with invisible dysplasia, and one with LGD who preferred to undergo surgery, subsequently underwent proctocolectomy. Recurrence was observed in only one patient (after a median of 33 months [range 6–76 months]). Similar successful outcomes in patients with UC who underwent ESD for nonpolypoid lesions in UC have been reported in a prior study [59].

Unfortunately, western gastroenterologists have less experience with ESD as compared to EMR. In our practice, ESD is rarely performed for IBD patients.

Colectomy is reserved for patients who have endoscopically unresectable lesions or endoscopically invisible high-grade dysplasia despite chromoendoscopy examinations or multifocal dysplasia. Features of lesions not suitable for endoscopic resection include poorly circumscribed lesion, indistinct borders, and depressed or amorphous surface with loss of surface details suggesting invasive cancer. Such lesions are endoscopically “nonresectable.” Figure 7 highlights our algorithm in approaching patients with dysplasia in the setting of IBD.

Endoscopic full-thickness resection which has been studied in non-IBD patients provides options to remove colonic lesions which may not be removed with EMR or ESD because of presence of submucosal fibrosis [60]. It has not been studied in IBD patients; however, it could have a potential greater role in removing lesions in IBD patients.

Surveillance after index resection

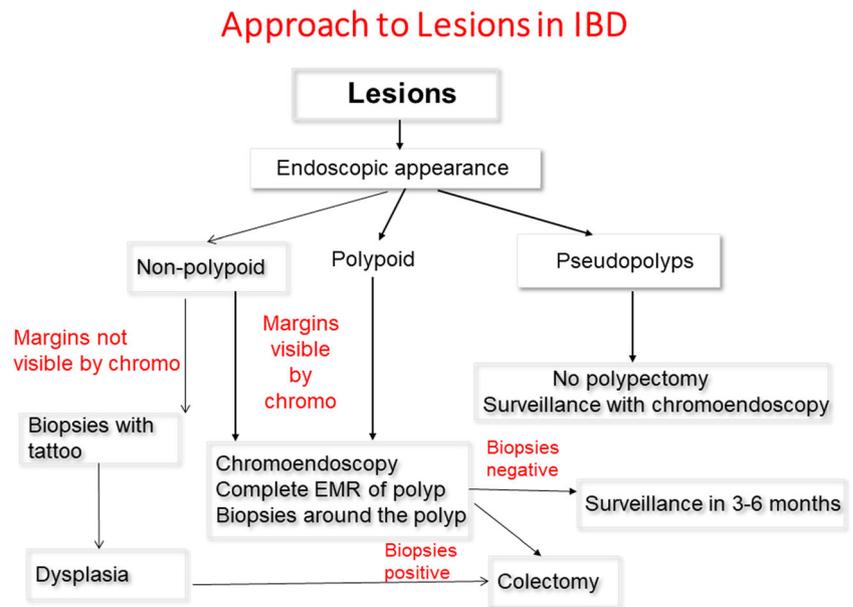
Optimal surveillance intervals after endoscopic resection of polypoid and nonpolypoid dysplastic lesions in IBD patients have not been established. The SCENIC guidelines recommend surveillance colonoscopy to be performed within 3 to 6 months followed by repeat colonoscopy at 12 months after the index resection and biopsies should be obtained of the resection site to document removal of all dysplastic tissue. Annual surveillance should be performed thereafter [3].

Surgical approach

The standard surgical approach for UC associated dysplasia or carcinoma not amenable to endoscopic resection is restorative proctocolectomy with ileal pouch anal anastomosis (IPAA). The two most common techniques for reconstruction include mucosectomy and creation of hand-sewed ileal pouch anal anastomosis in which rectal mucosa is completely removed theoretically versus stapled technique to create ileal pouch anal canal anastomosis in which a cuff of rectal mucosa and anal transition zone is retained. Stapled IPAA is technically easier and less time consuming than hand-sewn IPAA [61]. Also, preservation of anal transition zone in stapled IPAA is associated with better nocturnal continence [62]. Procedures such as total abdominal colectomy (TAC) with ileorectal anastomosis (IRA) and end ileostomy with blind Hartmann’s pouch are less preferable due to increased risk of carcinoma in retained rectum. Total abdominal proctocolectomy with end ileostomy is usually performed in patients who cannot undergo IPAA either due to multiple comorbidities, preexisting anal incontinence, high risk of pouch failure and are willing to have permanent stoma. It also does not require any surveillance after the procedure as compared to IPAA where surveillance is needed to detect recurrence of dysplasia-carcinoma in ileal pouch and rectal cuff [63]. Proctocolectomy for CAN requires extensive lymph node resection and mobilization of mesentery which can be safely achieved with less procedural time with hand-assisted laparoscopic surgery as compared to conventional laparoscopy [59].

CD-associated neoplasia poses great challenges in surgical decision making due to the nature of the disease itself including patchy inflammation and skipped lesions, frequent anal involvement, rectal sparing, risk of small bowel carcinoma, and malignant transformation of fistulae. Total proctocolectomy is usually preferred by surgeons as CD poses the risk of synchronous and metachronous dysplasia similar to UC. IPAA reconstruction is rarely seen in CD as it requires absence of perianal and small bowel disease. Total proctocolectomy is usually done with end ileostomy in CD patients [63].

Fig. 7 Algorithm for management of dysplastic lesions in IBD



Recurrence of neoplasia after colectomy with ileal pouch

Proctocolectomy substantially decreases the risk of colorectal carcinoma in IBD patients, but IPAA retains the risk of recurrence of dysplasia and cancer in pouch as well as rectal cuff. Given the field effect of mucosal inflammation and dysplasia in IBD, mucosectomy and hand-sewn anastomosis theoretically eradicates the risk of future development of anorectal cuff carcinoma [64]. A recent systematic review reported a total of 49 pouch-related cancers reported to date. Two thirds of the cases occurred in anal transition zone and one third in ileal pouch. Cumulative incidence of carcinoma developing in ileal pouch or rectal cuff/anal transition zone after IPAA is found to be 0.33% at 20-year follow-up. The strongest risk factor for the development of ileal pouch or cuff cancer is the presence of dysplasia or cancer in the operative specimen. Surveillance should begin within 2 years after IPAA, and yearly surveillance is recommended. Several articles have debated the cost-effectiveness of surveillance after IPAA given low risk of pouch/anal cuff cancer. Abdominoperineal resection of the pouch should be considered for patients who are found to have persistent anorectal cuff HGD or pouch-related adenocarcinoma [65].

Recent developments

Iacucci et al [66] developed and validated a new endoscopic classification, FACILE (Frankfurt Advanced Chromoendoscopic Ibd LEsions), using all imaging

modalities for diagnosis of dysplasia in IBD. Presence of a flat lesion, irregular surface, vascular pattern, and sign of inflammation predicted dysplasia. Also, Sugimoto et al. [67] classified the morphological features of the HGD using the SCENIC consensus. The authors found 84.6% of HGD lesions were nonpolypoid in appearance (superficial elevated, flat, and depressed). Superficial elevated lesions were associated with Kudo pit pattern IV–V gyrus-like villous, and flat lesions associated with Kudo pit pattern IIII-large tubular or roundish using magnification endoscopy.

Conclusion

Newer endoscopic techniques, including chromoendoscopy, increase the yield of identifying dysplastic lesions. The SCENIC guidelines recommend that colonoscopy using chromoendoscopy is the optimal endoscopic surveillance strategy to detect dysplasia. Once dysplastic lesions are discovered on surveillance endoscopic examination, careful and meticulous descriptions of lesions is mandatory to aid in further decision making. Once found, dysplastic lesions should be described by the modified Paris classification and should be characterized as endoscopically resectable or nonresectable. Endoscopic resection with close surveillance is recommended over colectomy for endoscopically visible and resectable lesions. EMR, ESD, and surgery are different therapeutic options for colonic dysplastic lesions detected in the setting of inflammatory bowel disease. Future efforts should focus on ways to facilitate the implementation of the optimal endoscopic detection and management.

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Paper preparation and revisions—S Khalid, N Khetpal, and A Abbass

Compliance with ethical standards

Conflict of interest Udayakumar Navaneethan and Bo Shen are consultants for AbbVie. Udayakumar Navaneethan is on the speaker bureau for Takeda, AbbVie, Pfizer, and Janssen. None of the other authors declared financial conflict of interest.

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