Endoscopic Management of Nonpolypoid Colorectal Lesions in Colonic IBD

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KEYPOINTS
• Resection of nonpolypoid lesions in inflammatory bowel disease (IBD) is among the most technically demanding of endoscopic procedures.
• Inflammation and submucosal fibrosis make lesion preassessment and lifting difficult.
• En bloc excision is preferred where possible with snare or endoscopic submucosal dissection (ESD) to optimize the pathologic specimen and reduce recurrence risk.
• Close follow-up of the resection site and whole colon with dye-spray is required postresection.

INTRODUCTION
The risk of developing IBD-colitis-related colorectal cancer has been highlighted for many years. Early data suggested that the risk increased year on year with an 18% risk at 30 years1 and the initial British guidelines advocating shortening of surveillance intervals with each decade of disease.2 Subsequent data suggested the stronger influence of patient factors, including disease extent and activity, family history of colorectal cancer, endoscopic features (strictures or postinflammatory polyps) and previous dysplasia, rather than duration of disease alone, with the current generation...
of European guidelines advocating risk-based stratification. More recently, some population-based studies have suggested that previous results overestimate the risk of IBD dysplasia and cancer because of case selection from academic and tertiary centers.

Alongside risk-based stratification, a new concept emerged for the management of polypoid dysplasia in IBD, in that polypoid circumscribed lesions (adenoma like masses) even within the colitic segment, might be safely managed by endoscopic resection and close follow-up rather than by panproctocolectomy. A recent meta-analysis of 10 studies with more than 370 patients and 1700 years of patient follow-up supports this concept: 5 (95% confidence interval, 3–10) cancers developed per 1000 years of patient follow-up. The rate of dysplasia detected at subsequent colonoscopy was 65 cases per 1000 years of patient follow-up, emphasizing that close colonoscopic surveillance is mandatory. However, all the studies in this meta-analysis predate the use of chromoendoscopy. The need for proctocolectomy when dysplasia is detected in IBD is based on older data, which suggested a 19% cancer rate at immediate proctocolectomy when low-grade dysplasia was detected and as much as 42% when high-grade dysplasia was found. These data almost certainly related to a previous generation of endoscopes and endoscopists, the latter being less familiar than present-day endoscopists are with the appearances of non-polypoid colorectal neoplasms, dysplasia, and cancer in IBD and hampered by a lack of high-quality endoscopic imaging. Furthermore, these endoscopists did not enjoy the advantages of high-definition, wide-angle endoscopes and dye-spray or image-enhanced endoscopy including structure enhancement, narrow-spectrum endoscopy (narrow band imaging [NBI, Olympus, Tokyo, Japan], Fujinon intelligent chromoendoscopy [FICE, Fujinon, Tokyo, Japan], i-Scan, image-enhanced endoscopy [Pentax, Tokyo, Japan], autofluorescence, or confocal endomicroscopy (see the article on advanced imaging elsewhere in this issue). Therefore, dysplasia detected in the current era of endoscopes and endoscopists is likely to be at an early stage and can be safely managed by endoscopic resection if polypoid and circumscribed.

However, not all dysplasia detected at endoscopy in IBD is polypoid. The concept of flat dysplasia or endoscopically invisible dysplasia, detectable only by random biopsies has been commonly accepted, particularly in the prechromoendoscopy era, leading to previous generations of guidelines advocating the use of quadratic biopsies every 10 cm of colonoscopic withdrawal to detect this invisible dysplasia. This recommendation is poor for detection of early dysplasia, with one simulation paper based on colonic surface areas and dysplasia size suggesting that the standard 32 nontargeted biopsies would only detect an area of dysplasia encompassing 5% or more of the colonic surface with 80% certainty. The use of the word flat for biopsy-only-detected dysplasia is unfortunate because this word has also been used to describe non-polypoid dysplasia in the endoscopic literature as part of the Paris classification. Flat or non-polypoid in the endoscopic literature corresponds to Paris 0-IIa, flat elevated lesion; Paris 0-IIb, completely flat lesions; and Paris 0-IIc, depressed lesions. Many instances of patients diagnosed with flat biopsy-only dysplasia can be converted to circumscribed areas of dysplasia described as Paris 0-IIa, IIb, or IIc by reexamination with meticulous bowel preparation, with the patient in full remission, with an experienced endoscopist familiar with dysplasia in IBD, and with the use of high-definition endoscopes with dye-spray and image enhancement. If one accepts that circumscribed areas of flat dysplasia may be safely endoscopically resected with close endoscopic surveillance afterward, a concept that is by no means proven, then one needs to consider the special circumstances of how to safely and
comprehensively resect such lesions. The technique for endoscopic resection is the focus of this review.

APPROACH TO RESECT NONPOLYPOID DYSPLASIA IN IBD

The resection of mucosal dysplasia in the gastrointestinal tract requires a series of steps to be safe and effective, which are outlined in Box 1. Here, it is assumed that an isolated, ie, nonmultifocal, nonpolyoid (Paris 0-IIa, 0-IIb, or 0-IIc), lesion within a colitic segment has been detected; that the patient’s case has been discussed at an IBD multidisciplinary team meeting with a recommendation for attempt at endoscopic resection; and that the patient, having discussed the pros and cons of an endoscopic approach and being informed of the risks and benefits, is willing to proceed. Furthermore, it is also assumed that as far as possible the patient is in remission from colitis and that the bowel is optimally prepared. Data on approach to these lesions are scarce and predominantly based on expert end consensus opinion, extrapolation from first principles, and from experiences with resection of dysplastic lesion in noncolitic colons in situations that may mimic colitis-related fibrosis, such as scarring from previous endoscopic resection or nongranular-type laterally spreading tumors (LSTs). By definition, endoscopic resection of dysplasia in colitis is at the far end of the spectrum of difficulty of endoscopic resection and should only be attempted by experienced, usually specialist endoscopists, with appropriate experience of advanced endoscopic mucosal resection (EMR), case volume, and an

Box 1
Approach to resect nonpolyoid dysplasia in IBD

- Lesion assessment
  - Extent
  - Risk of invasion
  - Associated structures, eg, ileocecal valve
  - Scarring
  - Endoscopic access
- Lifting
  - Mucosal inflammation/scarring
  - Special lift solution, eg, hyaluronate
- Resection
  - Endoscopic mucosal resection
    - En bloc
    - Piecemeal
  - Endoscopic submucosal dissection
  - Special snares (spiral or flat band/ribbon)
- Ablation
  - Argon plasma coagulation
  - Snare tip soft coagulation
- Follow-up
  - Scar assessment
endoscopic support team with surgical backup. Such cases might usually be referred to tertiary or regional specialists.

**Lesion Assessment**

A nonpolypoid dysplastic lesion in IBD needs to first be carefully examined. Thus, before considering an attempt at endoscopic resection and weighing the associated technical risks of bleeding, perforation, and postpolypectomy syndrome, as well as the ensuing risk of cancer within the resection specimen and recurrence, the lesion characteristics must be interpreted. The first question to be addressed is lesion borders and extent. Endoscopic resection is only appropriate for lesions that have clearly defined borders (ie, circumscribed). Enhancement of the edges of these subtle lesions can be helped by the use of dye-spray or advanced imaging techniques. If a clear margin of the lesion cannot be seen, it is unlikely that endoscopic resection is appropriate because there is significant risk that residual dysplasia will be left in situ (Fig. 1). Even if a clear border can be seen, it is appropriate to perform biopsies around the lesion to look for endoscopically invisible dysplasia before committing to resection. Ideally, only a single biopsy of the lesion itself would be done to avoid welding the lesion to the submucosa even further through biopsy-associated fibrosis. The authors’ personal preference is to use a high-definition endoscope, ideally with optical magnification, and chromoendoscopy and surface enhancement for this process.

Assuming the lesion has a clear edge with no surrounding dysplasia on biopsy of macroscopically normal mucosa, the lesion should be completely clear of stool and mucus and minutely examined for risks of invasion. Suspicious aspects include a large nodule, depression and loss of pit pattern, and a masslike appearance (Fig. 2). The presence of any of these signs should lead to a careful consideration of whether endoscopic resection is appropriate. Unfortunately, these techniques, which are reasonably reliable in noncolitic colons, 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 by definition poor in colitis. Submucosal scarring impedes mucosal lift and also disrupts the mucosal layers needed to clearly assess invasion at endoscopic ultrasonography. In noncolitis cases, submucosal scarring can be seen in lesions with a previous attempt at resection, recurrence on a scar from previous EMR, or nongranular type LSTs.

![Fig. 1](image1.png)

**Fig. 1.** This endoscopic image shows a nonpolypoid flat dysplastic area in the lower region of rectum (**A**). Despite use of dye-spray, a clearly circumscribed boarder cannot be delineated (**B**). Therefore, this lesion is not suitable for endoscopic resection.
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Fig. 2. This 15-mm lesion in the rectum of a 71-year-old woman with ulcerative colitis was selected for ESD. Note that the pit pattern is difficult to interpret and that it suggests a nodule or mass lesion (Paris 0-Ia component), raising suspicion for invasion (A, B). En bloc excision was achieved with ESD; the histology showed early invasion (Kikuchi stage sm1) (C, D).

colitis cases, if the patient has a tubular colon with evidence of scarring, postinflammatory polyps, loss of vascular pattern, or active inflammation, the submucosal scarring is likely to be severe and typically involves the entire lesion.

Location of the lesion near technically difficult areas such as the appendix orifice, ileocecal valve, at a flexure, especially on the inside of the bend, and at the anal verge should also be considered. Although polyps in all these positions can be resected in noncolitic colon by experienced endoscopists, the technical difficulty is substantially increased. In combination with the other inherent challenges that colitic lesions present, this may make the likelihood of a successful resection so low that an endoscopic attempt is not appropriate.

The final stage is to consider endoscopic access. This is one of the few areas in which working in a colitic colon may have advantages because a scarred and tubular colon makes for a straight endoscope and associated accurate tip movements and a lack of haustral folds to be negotiated. Before starting, endoscopists should be satisfied that they can easily reach all areas of the lesion with submillimeter precision.

There is no specific combination of factors or scoring system that suggests that lesions are or are not safely and effectively resectable. Ultimately, at least at present, it
comes down to the experience and judgment of the assessing endoscopist. Given the fine nature of these judgments, the authors recommend that if possible the endoscopist who is going to do the resection procedure should perform the endoscopy for lesion assessment before resection.

**Lifting**

Lifting or the failure of lifting of lesions in colitis is one of the major obstacles to resection. This leads to problems with lesion assessment for invasion as outlined above, but more importantly means that the lesion cannot be safely lifted away from the underlying muscularis propria to allow a safe plane for the snare or endoscopic knife to traverse for resection. The scarring in the submucosa means that there is difficulty in finding the submucosal plane, a failure to lift, a ‘diffuse’ lift in which fluid tracks laterally rather than resulting in focal elevation, and a rapid loss of any lift achieved. Techniques to counter these problem include the use of the dynamic injection technique, 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, eg, gelofusine, or sodium hyaluronate. Other viscous solutions, eg, hypromellose or glycerol, might also be considered. Nevertheless, even with these advantages, lift in colitic lesions is often suboptimal.

**Resection**

En bloc resection of the lesion is preferable to allow precise pathologic assessment and minimize residual dysplasia or recurrence. ESD offers this possibility and is technically possible in colitis. However, the comprehensive submucosal fibrosis increases the procedural risks and reduces R0 resection rates even for superspecialist experts in ESD (Figs. 3 and 4). Use of small-caliber-tip transparent hoods can help in severe fibrosis, and there is often a need to use sharp-tipped needle knives to cut fibrotic bands, albeit at the risk of a loss of hemostatic capacity (Video 1). The adaptation of ESD concepts may offer some advantages to less-experienced Western endoscopists. Two concepts may be helpful. The first is the so-called Endoscopic Mucosal Resection with snaretip incision (SI) that can be possible for smaller lesions up to 20 mm in which submucosal scarring is not so severe and some lift is possible. Here, after lifting, the snare tip is used to make a small incision on the oral side of the lesion. This small hole is used to anchor the snare tip to allow definite edge capture and additional downward pressure with the snare in a situation of limited lift, increasing the chances on an en bloc snare resection. The second is the use of mucosal incision, the first step in full ESD. Here the use of an endoknife to carefully incise a groove around the lesion is performed before an attempt at conventional en bloc or piecemeal EMR. The edge of the snare is then placed in this marginal groove for resection. Both these concepts improve grip on the lesion edge by the snare and allow a clean resection margin at the edge of the lesion. In colitis, once resection starts, the lesion margin can be difficult to see, so marginal incision can assist here as well. This procedure is sometimes described as simplified or hybrid ESD and in some situations represents a good compromise between the time, risk, and difficulty of full ESD, yet fulfills the need for resection with a clear margin.

**Snares**

Standard snares can be used for EMR in colitis; however, as alluded to above, scarred, flat lesions with poor lift can be difficult to engage into the snare. Furthermore, if a large piece is successfully engaged, there is a risk that the scarring will pull up an area of underlying muscle leading to damage to the muscularis propria target sign or a
full-thickness perforation. Perforations are especially difficult to close in scarred mucosa. Braided or spiral snares may be used, which have an additional spiral wire around the main snare cable, to improve gripping (spiral snare 20 mm, SnareMaster, Olympus, Tokyo, Japan). An alternative is the flat band or ribbon snare (flat ribbon snare 22 m, Resection Master, Medwork, Höchstadt, Germany). This snare comprises

Fig. 3. A 20-mm nonpolypoid (Paris 0-IIa) lesion was found in the midrectum of a 53-year-old patient, with circumscribed edges after dye-spray (A). Marking was used to define the lesion edges clearly before mucosal incision. Although commonly used in ESD in the upper gastrointestinal tract, marking is rare in the colon; however, because of the subtle edges of the lesion, this may be helpful in colitis (B). A formal ESD is performed with en bloc excision (C, D) with the resected specimen showing clear margins (E). Pathology confirmed low-grade dysplasia.
Fig. 4. (A, B) A 50-mm nonpolypoid lesion in the midrectum of a patient with ulcerative colitis was scheduled for an attempt at resection by ESD. Intense fibrosis was observed in the submucosal layer (yellow-white band under mucosal flap) making resection very challenging.

Fig. 5. A 35-mm nonpolypoid (Paris 0-IIa) lesion was detected in the cecum of a patient with long-standing pancolonic IBD (A). Use of dye-spray confirms a circumscribed lesion without high-risk features (B). Narrow band imaging is used to assess the microvessel network (C). The lesion is resected in 4 fragments by piecemeal EMR with a 10-mm snare (D). All fragments are retrieved with a Roth net for pathology assessment (E). Pathology confirms a tubulovillous adenoma with low-grade dysplasia (F) (Hematoxylin and eosin, original magnification ×400). Reassessment of the scar after healing with dye-spray showed no dysplasia either macroscopically or in scar biopsies (G).
a flat band of metal to make the snare loop with the edge of the band orientated verti-

cally to the mucosa. An alternative is to use a smaller braided snare to resect small

pieces at a time, reducing the risk that too much mucosa is gathered with associated

muscle, as one might do for a scarred lesion in noncolitic colons (Fig. 5). A final option

is the use of a double-channel endoscope using a grasper to pull the mucosa into a

snare, which is in the other channel. Although this technique guarantees the ability
to grip the mucosa, the risk of perforation is significantly magnified, and experience

and extreme care are needed.

Ablation

Owing to the scarring in colitis, the nature of resection of colitic lesions often entails

piecemeal resection. Every attempt should be made to endoscopically resect any

visible part of the lesion. However, piecemeal resection coupled with significant

scaring may result in fragments or islands of dysplasia left at the resection site.

Such areas need to be definitively but safely destroyed. Argon plasma coagulation

(APC) has been commonly used for this with some evidence from the EMR literature

that it is effective in reducing recurrence.23 (Many EMR experts suggest that the

need for this in noncolitic colons is now unnecessary because the EMR technique

has improved; however, older, less-comprehensive EMR to some extent mimics the

results in colitis so the two may be comparable.) Precise use of short pulses of APC

is effective even for larger areas. Further attempts at injection before use of APC
may allow the so-called melt effect seen with the use of APC for dysplasia ablation in the duodenum.²⁴ For small fragments, the use of the tip of the snare with soft coagulation allows effective ablation without overdelivery of energy and risks of a deep mucosal burn. Ultimately, the optimum is en bloc R0 snare or ESD resection with pathologic assessment of resected tissue. Ablation should be minimized.

**Follow-Up**

After resection, which should be as complete as possible at the first attempt, careful examination of the scar should be performed at between 2 and 6 months postresection, as well as pancolonic dye-spray of the whole colon to look for metachronous lesions. The use of dye-spray and advanced imaging on the scar can be helpful here to try and detect tiny areas of recurrence. Scar biopsy should be performed even if there is no recurrence. If recurrence is suspected, and the threshold should be low, a biopsy of the site followed by the ablation methods mentioned above is appropriate, with a further examination in 2 to 6 months. Repeated recurrence despite appropriate ablation, high-grade dysplasia in recurrence biopsies, or a large area of recurrence should prompt consideration of surgical resection or ESD salvage.

**SUMMARY**

Safe and comprehensive resection of nonpolypoid dysplasia in IBD is demanding both in terms of diagnostic judgments preresection and of technical skills during the resection. Good outcomes require meticulous planning and maximizing potential technical advantages, with an aim to achieve en bloc excision where possible. The safe resection of circumscribed nonpolypoid dysplasia in IBD is possible by an appropriately trained endoscopic team and may avoid the need for colectomy.

**SUPPLEMENTARY DATA**

Video related to this article can be found online at http://dx.doi.org/10.1016/j.giec.2014.03.003.

**REFERENCES**