Advanced Endoscopic Resection of Colorectal Lesions

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5.1 Introduction

Advanced endoscopic resection techniques are important to ensure adequate removal of complex or large colorectal polyps. Mounting evidence suggests endoscopic resection as a safer, more cost-effective modality [1–3], compared to surgical resection. Multiple society guidelines now recommend endoscopic resection as the first step for the management of complex benign colon polyps. In this article, we will discuss the assessment and technical aspects of advance resection for the management of complex colorectal polyps.

5.2 Polyp Assessment

Determination of submucosal invasion is critical to assess if endoscopic resection is appropriate. Optical diagnosis with macroscopic and microscopic assessment in conjunction with findings such as non-lifting is key to ensuring complete resection.

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5.2.1 Macroscopic Appearance

Originally described in 2002, the Paris classification categorizes lesion into superficial and advanced types, with type 0 being superficial neoplasms and type 1–5 reserved for advanced carcinoma [4]. Types 0, or superficial neoplasms, are further subclassified into polypoid and non-polypoid lesions (Fig. 5.1). Types 0–I are pedunculated (0-Ip) or sessile (0-Is) in appearance. Type 0-II lesions may be slightly elevated (0-IIa_, flat (0-IIb) or depressed (0-IIc) [4, 5]. Types 0–III are ulcerated lesions.

Morphologic classification is an important step to facilitate lesion management. The risk of submucosal carcinoma is higher for non-polypoid lesions (Paris type 0-II) compared to polypoid lesions [6, 7]. Flat lesions greater than 10 mm are termed laterally spreading tumors (LST) (Fig. 5.1). Granular LSTs (LST-Gs) have a nodular surface appearance as opposed to non-granular LSTs (LST-NGs), which are smooth. LST-Gs with uniform nodules have a <2% submucosal invasion regardless of size. LST-Gs with nonuniform nodules and LST-NGs have higher risk of submucosal invasion [6]. Depressed lesions greater than 20 mm have been found to have a 87.5% risk of submucosal cancer [8].

5.2.2 Microscopic Diagnosis

Real-time optical diagnosis has been found to be highly accurate and effective for the histologic prediction of small colorectal polyps [9]. The Kudo classification describes pit patterns in five categories, using chromoscopy and magnification [10]. Types I and II are nonneoplastic, whereas types III and IV are adenomatous patterns, and type V is cancerous [8]. Narrowband imaging (NBI) can enhance visual assessment of polyps. The NBI International Colorectal Endoscopic (NICE) classification incorporates tissue color, vascular, and surface pattern to differentiate serrated class lesions from adenomatous. It has also been validated for the prediction of submucosal invasion with a 92% sensitivity and negative predictive value [11]. For example, NICE type I lesions are hyperplastic, type II are adenomatous, and type III are concerning for containing deep submucosal cancer [11].

Work by Moss and colleagues has also found that polyps with Paris 0-II a-c morphology, non-granular surface and Kudo pit pattern V were at high risk for submucosal invasion [12]. Additionally, the NICE criteria have a 92% sensitivity and negative predictive value for prediction of submucosal carcinoma [11]. Type 3 lesions are associated with submucosal invasion.

The non-lifting sign is an indicator if the surrounding submucosal tissue lifts, but the lesion does not with injection. Lesions may not lift due to submucosal invasion or because of submucosal fibrosis from prior biopsy, cautery, or tattoo (Fig. 5.1). Studies have demonstrated that the presence of the non-lifting sign is associated with a positive predictive value for invasive cancer to be approximately 80% [13]. Additional signs of submucosal invasion include converging folds, chicken skin appearance, expansive appearance, and firm consistency [14].

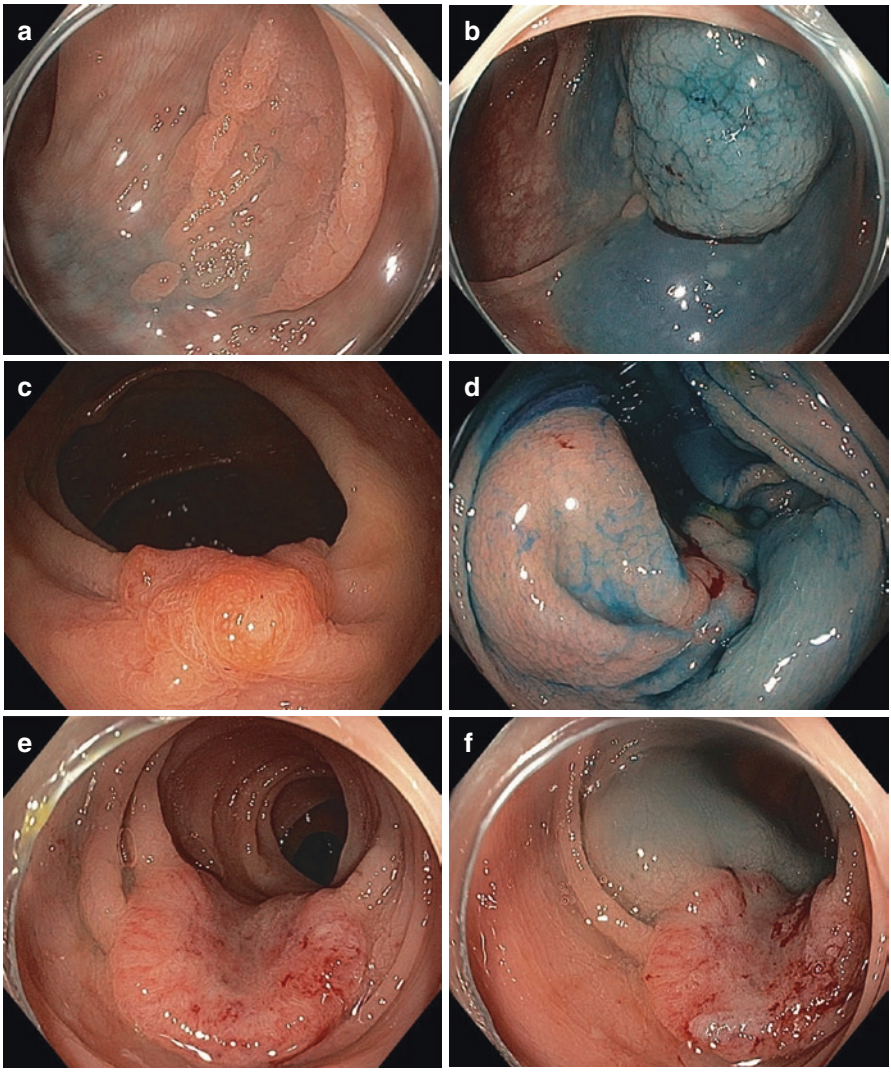

Fig. 5.1 The non-lifting sign

5.3 Resection Technique

Advanced endoscopic techniques include the standard inject-and-cut endoscopic mucosal resection (EMR) as well as endoscopic submucosal dissection (ESD). Adjunctive EMR techniques such as EMR with cap, underwater EMR, and EMR with cold snare have been more recently applied and studied. En bloc or R0 resection is ideal, though in lesions >20 mm this may not be feasible, and the goal should be to remove the lesion in as few pieces as safely possible.

5.3.1 Instruments and Equipment

Personnel should have familiarity with the range of equipment used and the technical aspects of the procedure. We recommend the use of a high-definition adult colonoscope with a water-jet channel and CO2 insufflation in most cases. A therapeutic upper endoscope may be an alternative for left-colon lesions. Additionally, we prefer the use of conscious sedation over deep sedation with propofol [14].

5.4 EMR Techniques

5.4.1 Inject-and-Cut

The inject-and-cut EMR is a simple technique that is widely used for removal of large flat or sessile lesions. Submucosal injection is a key step of EMR. In this technique, saline is injected into the submucosal space of the colon wall. Injection in the submucosal layer is first confirmed using a small amount of solution, followed by rapid large-volume injection. We recommend the use of the dynamic injection technique to create a sufficient bleb under the lesion (Fig. 5.2). Unlike in static injection, the tip of the endoscope is slightly directed to the opposite wall coupled with a slight pull back of the needle catheter and simultaneous gentle suctioning [15]. Using this maneuver, the needle tip is maintained in the superficial submucosa, and a localized bleb can be easily created. This mound of fluid creates a cushion for resection as well as brings the lesion into the lumen toward the colonoscope.

Saline is the most commonly used solution though it may quickly dissipate. Viscous solutions such as hydroxyethyl starch, sodium hyaluronate solution, 50% dextrose, and succinylated gelatin are alternatives to improve maintenance of submucosal cushion. A 2016 systematic review compared normal saline to sodium hyaluronate, 50% dextrose,

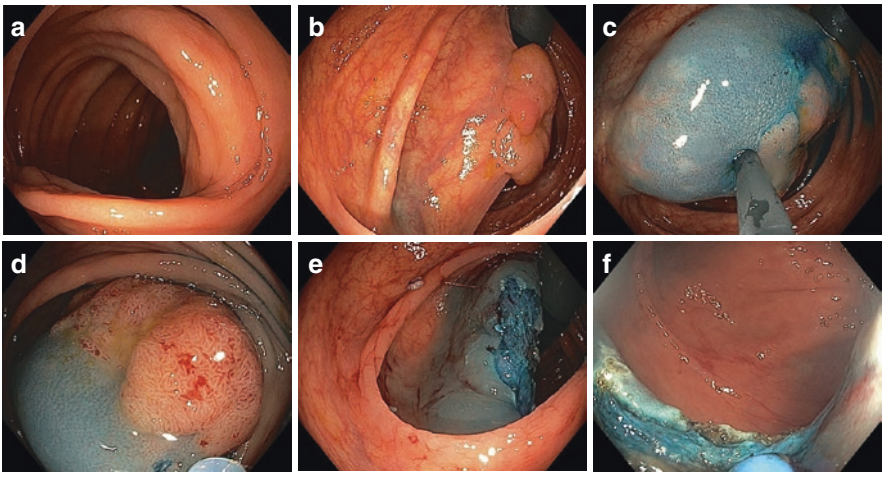

Fig. 5.2 Dynamic submucosal injection

hydroxyethyl starch, and fibrinogen and found no difference in complete resection (OR 1.09, CI 0.82–1.45) and only limited data on the efficacy of the other viscous solutions [16]. A 2017 systematic review pooled the results of viscous solution and found that viscous solution increased en bloc resection (OR 1.91, CI 1.11–3.29) and decreased risk of residual lesions (OR 0.54, CI 0.32–0.91) compared to normal saline [17]. Therefore, if available, the use of viscous solutions should be considered. Succinylated gelatin is not available in the USA. Sodium hyaluronate, the most studied solution in three randomized controlled trials, is relatively expensive.

A stiff snare can then be used to capture the lesion of interest to perform EMR. After snare capturing of the lesion, carbon dioxide insufflation will expand the wall, and slight loosening of the snare with up tip deflection will release any entrapped muscularis propria. The snare is then closed entirely almost to the hub, and the lesion is transected using electrosurgical current (ERBE, Endocut Q Effect 3, Duration 1, Interval 4) [14]). Microprocessor control units use alternate cycles of short-cutting bursts with interval periods of coagulation and limit peak voltage with impedance feedback (Figs. 5.3 and 5.4).

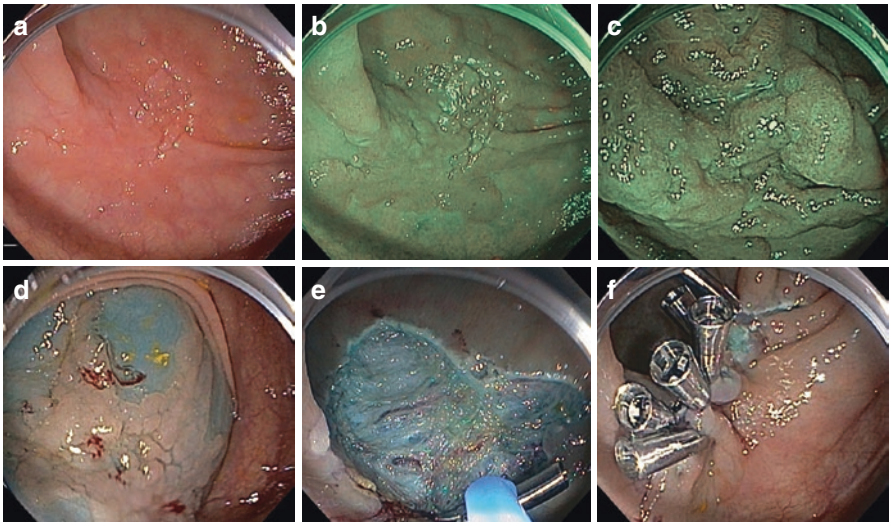

Fig. 5.3 Inject and cut endoscopic mucosal resection of nongranular lateral spreading lesion

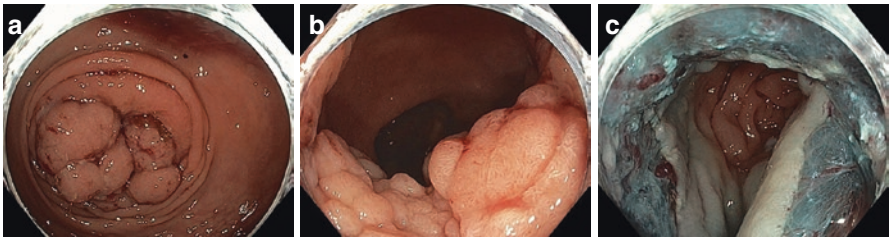

Fig. 5.4 Inject and cut endoscopic mucosal resection of granular lateral spreading lesion.

All visible neoplastic tissue should be resected in a single session. For lesions <20 mm, en bloc resection is recommended, particularly for LSL-NG lesions. Piecemeal EMR may be necessary for lesions larger than 20 mm. Due to the risk of submucosal invasion in the dominant nodule in an LSL-G, the dominant nodule should be resected and submitted to pathology separately. Ablative techniques, such as the use of snare tip soft coagulation and argon plasma coagulation (APC) on residual tissue, have been associated with an increased risk of local recurrence [18]. Once all neoplastic tissue has been removed, data suggests lower local recurrence rates when ablative therapies, such as APC or snare tip soft coagulation, are applied to the resection margin. A recent randomized controlled trial applying the snare tip in the soft coagulation mode to the defect periphery and bridges showed a significant reduction in recurrence rates. Recurrence outcomes using argon plasma coagulation versus snare tip soft coagulation have not been compared.

5.5 Alternative EMR Techniques

5.5.1 Cap-Assisted EMR

The use of a plastic cap during EMR can be useful to help deflect surrounding tissue during standard inject-and-cut EMR. Dedicated cap and snare devices can also be used for cap-assisted EMR in the rectum. Neoplastic tissue is suctioned into the cap, which can then be snared.

5.5.2 Underwater EMR

Underwater EMR was first described by Binmoeller et al. [19]. In underwater EMR, the water substitutes air insufflation. Injection is not necessary making this an alternative for fibrotic lesions. In his initial study of 60 patients, Binmoeller and colleagues demonstrated that the technique was safe with no perforation or post-polypectomy syndrome. Follow-up study by Curcio and colleagues in 2014 demonstrated complete resection at 3 months' follow-up in an additional 72 patients [20].

5.6 Cold Snare EMR

Cold snare EMR, whereby no electrosurgical cautery is applied, has been demonstrated to be feasible for lesions >1 cm. However, thus far evidence has been limited to single-center retrospective studies [21, 22].

5.7 ESD

Endoscopic submucosal dissection (ESD) is an alternative resection technique in the colon and particularly rectum. It is a technique mainly considered for complex lesions such as non-granular-type lateral spreading lesions with Vi pit pattern or those with concern for adenocarcinoma, with underlying fibrosis or with residual lesion after prior incomplete resection attempts (Table 5.1). Compared to EMR, ESD allows for en bloc resection of lesions (79% versus 34%); however, there is a higher risk of perforation (4.9% versus 0.9%) and need for surgery (7.8% versus 3.0%) [23] and significantly longer procedure time. Several studies have shown the safety and efficacy of EMR in the management of complex colorectal lesions, including those of large size, granular- and non-granular-type lateral spreading lesion morphology, and sessile serrated polyp histology [24].

5.7.1 Technique

ESD begins with marking the normal mucosa surrounding the lesion. Submucosal injection is then done to lift the lesion. The circumference of the lesion is then incised using a needle-type ESD knife, and the submucosal layer is then dissected. The resected en bloc can then be pinned and submitted to pathology. Attempts to simplify ESD technique have been described such as "precutting EMR," whereby the circumference of the lesion alone is incised by using a knife for ESD, and then the lesion is snared without submucosal dissection. Likewise, hybrid ESD is a technique in which an ESD knife dissects some of the submucosal layer, and then the lesion is snared (Fig. 5.5).

Table 5.1 Indications for ESD for colorectal tumors[a]

Lesions for which endoscopic en bloc resection is required
1. Lesions for which en bloc resection with snare EMR is difficult to apply
• LST-NG, particularly LST-NG (PD)
• Lesions showing a VI-type pit pattern
• Carcinoma with shallow T1 (SM) invasion
• Large depressed-type tumors
• Large protruded-type lesions suspected to be carcinoma[b]
2. Mucosal tumors with submucosal fibrosis
3. Sporadic localized tumors in conditions of chronic inflammation such as ulcerative colitis
4. Local residual or recurrent early carcinomas after endoscopic resection

EMR endoscopic mucosal resection, *ESD* endoscopic submucosal dissection, *LST-G* laterally spreading tumor granular type, *LST-NG* laterally spreading tumor non-granular type, *PD* pseudo-depressed, *SM* submucosal

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[a]Partially modified from the draft proposed by the Colorectal ESD. Standardization implementation working group

[b]Including LST-G, nodular mixed type

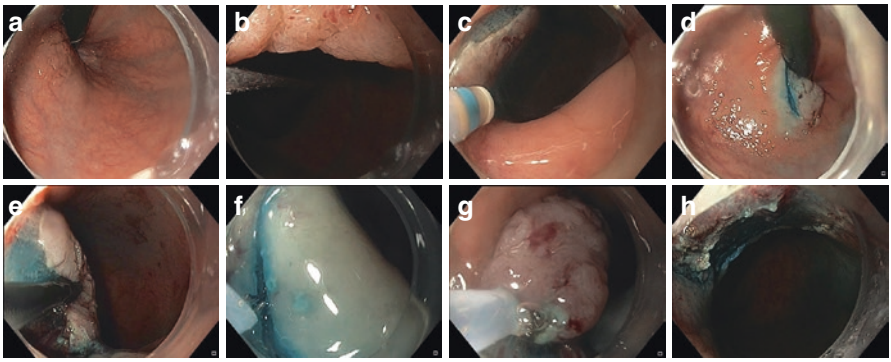

Fig. 5.5 Hybrid ESD of rectal lesion

5.8 Special Considerations

5.8.1 Scar

Previous treatment, such as biopsy, snaring, EMR, or tattoo, can cause submucosal scarring. Submucosal injection may be ineffective in formation of a submucosal bleb. The lesion may be difficult to snare, and inadvertent slippage of the snare can lead to perforation. Furthermore, pathology of the scarred tissue may be difficult to interpret. Avulsion of scarred or residual neoplastic tissue with biopsy forceps and high-frequency cutting current is a recently promising method for non-lifting tissue that is difficult to capture and resect using a snare [25]. A single-center retrospective study showed significantly lower recurrence rate in such non-lifting areas using hot avulsion compared to APC (OR 0.079, $p < 0.001$) [26].

5.8.2 Pedunculated Polyps

Pedunculated polyps are supplied by multiple blood vessels, and resection should take into account reducing the risk of bleeding. Options include the use of a detachable snare (Endoloop), clipping, or epinephrine injection to ligate the vasculature in the stalk of the pedunculated polyp. A randomized control trial in 2004 compared epinephrine injection versus detachable snare and found that both significantly decreased the risk of bleeding from 15.1% to 2.7% and 2.9%, respectively, but that there was no significant difference between epinephrine injection and detachable snare [27]. Whereas studies have shown a 5.4% risk of bleeding with hemoclip use [28].

Regardless of technique, the patient should be positioned, so the polyp attaches at the 12 o'clock position, and the colonoscope is rotated, so the stalk is at the 6 o'clock position. The endoloop or clips should be placed at the stalk so that the

lesion turns dark red indicating that the polyp has been appropriately strangulated. Snare resection can then take place. Epinephrine has been described for polyp size reduction. It is to be injected into the head of the polyp to reduce polyp volume and allow for snaring. This may take up to 8 mL of 1:10,000 epinephrine [14].

5.9 Complications

The most common complications after endoscopic resection include bleeding and perforation.

The risk of perforation after EMR is 1–2% and 5–10% after ESD. Delayed perforation is thought to result from mural injury at the time of resection and recognition at the time of resection can decrease the risk of mortality and need for surgery. The target sign, the appearance of a white central circular disk representing the muscularis propria, surrounded by stained submucosa and a white cauterized, is an early indication of perforation [29]. More subtle signs of deep mucosal injury include focal loss of the submucosal plane raising concern MP injury. Prophylactic clipping is recommended to prevent clinically significant perforation [30].

Bleeding after endoscopic resection can occur immediately or be delayed. There is a 7–9% risk of bleeding after endoscopic resection [3]. Various methods such as soft-tip snare coagulation, coagulation forceps, or clip can be used to treat immediate bleeding at the time of resection. A 2014 study found that clinically significant post-endoscopic bleeding as defined by emergency department visit, hospitalization, or need for intervention occurs after 6.3% of EMRs for lesions >20 mm and is associated with proximal colon location, the use of electrosurgical cautery without a microprocessor unit but not lesion size, or comorbidities [31]. Fifty-five percent of these bleeds resolved spontaneously, and only 33% required endoscopic therapy [32].

5.10 Recurrence and Surveillance

Risk of recurrence in EMR is higher than ESD and is estimated to be 16% at the initial colonoscopy and 4% late colonoscopy. Due to the risk of recurrence, careful surveillance is recommended. The initial follow-up endoscopic exam is recommended at 6 months. Risk factors for recurrence include LSL $\geq$ 40 mm, bleeding during procedure, and high-grade dysplasia. Tate and colleagues proposed the Sydney EMR recurrence tool (SERT) scoring system based on these risk factors and suggest that those with a SERT score of 1 or more should have surveillance at 6 and 18 months, whereas those with a SERT score of 0 could safely undergo first surveillance at 18 months [33].

We recommend standard performance of surveillance colonoscopy at 6 months with a high-definition colonoscope. Careful inspection of the scar should be performed with white light and NBI to assess for evidence of macroscopic recurrence.

A prospective single-center study found that white light with NBI has a 94% (CI 89.6–99.6%) accuracy compared to 91.3% (86.3–94.6%) with white light alone [34]. Biopsies should be taken of the scar site even if no macroscopic recurrence is detected. We recommend repeat EMR or ESD for recurrence and continued surveillance at 6 month until clear and then 1 year and then 3 years.

Conclusion

Endoscopic resection should be the treatment of choice for complex colon polyps. Advanced resection techniques should be used to safely accomplish resection of such lesions. Complications of perforation and bleeding should be recognized and can be managed endoscopically. Continued surveillance with colonoscopy at 6 months after index procedure is important to detect and treat recurrences.

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