Evolving management of colorectal polyps

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***Abstract*:** Advances in endoscopic technology have led to increased success in colorectal cancer (CRC) screening and polyp management, with reduction of CRC incidence and mortality. Despite these advances, CRC is still one of the leading causes of cancer deaths, and half of all CRC develops from lesions that were missed during colonoscopy while one-fifth of CRC arise from prior incomplete resection. Techniques to improve polyp detection are needed, along with optimization of complete resection of any abnormal lesions that are found. This article will review the currently available endoscopic resection techniques and will discuss where they fit in the management of polyps of different sizes and types, such as pedunculated *versus* nonpedunculated, and those with or without suspected invasion.

Keywords: colon, EFTR, endoscopic full-thickness resection, EMR, endoscopic mucosal resection, ESD, endoscopic submucosal dissection, polyp, polypectomy

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A brief overview

Advances in endoscopic technology have positively shaped our success story in colorectal cancer (CRC) screening and polyp management.[1] These advances have manifested in the reduction of CRC incidence and mortality.[2] Despite these advances, CRC is still one of the leading causes of cancer deaths.[3] Based on a recent pooled multicohort analysis, half of all CRC develops from lesions that were missed during colonoscopy while one-fifth of CRC arise from prior incomplete resection.[4] Techniques to improve polyp detection are therefore needed, with optimization of complete resection of any abnormal lesions that are found. An ideal resection, especially for an early neoplastic lesion, is one where complete or 'en bloc' resection is achieved, with a negative histologic margin, R0. However, this can be challenging to achieve, especially when treating large (>20 mm) nonpedunculated polyps. Fortunately, for polyps that do not contain early invasion, piecemeal resection will suffice when paired with close surveillance colonoscopy to ensure no residual polyp has been left behind.

Fortunately, the majority of adenomas detected during screening colonoscopies are small, <5 mm, and almost always benign.[5] These polyps can easily be removed using a dedicated wire-loop snare without electrocautery assistance. However, more advanced techniques are required to achieve effective and safe resection of intermediate, 10–19 mm, or large, ⩾20, polyps. Larger lesions are of unique importance as the risk of cancer development increases with polyp size.[6] For nonpedunculated lesions with a diameter ⩾10 mm,[7] endoscopic mucosal resection (EMR) is generally the preferred resection modality. EMR involves the injection of fluid into the submucosal space to separate a mucosal-based lesion from the muscularis propria, followed by nonelectrocautery assisted 'cold' (Figure 1) or electrocautery assisted 'hot' (Figure 2) snare resection of the lesion. This may be done en bloc for smaller lesions and occasionally for lesions up to 20 mm. For lesions ⩾20 mm, achieving en bloc resection with EMR becomes more challenging and carries a greater risk of perforation from inadvertent trapping of the muscularis propria layer, and so they are more safely and effectively managed with piecemeal EMR. For these larger lesions, when en bloc resection is required as in the case of suspected or known invasion, the ideal resection method is endoscopic submucosal dissection (ESD), a more advanced technique where the submucosal layer is lifted similar to in EMR, but where the resection is done using an endoscopic knife to incise around the lesion and dissect through the expanded submucosal layer under the lesion (Figure 3). Although ESD can achieve

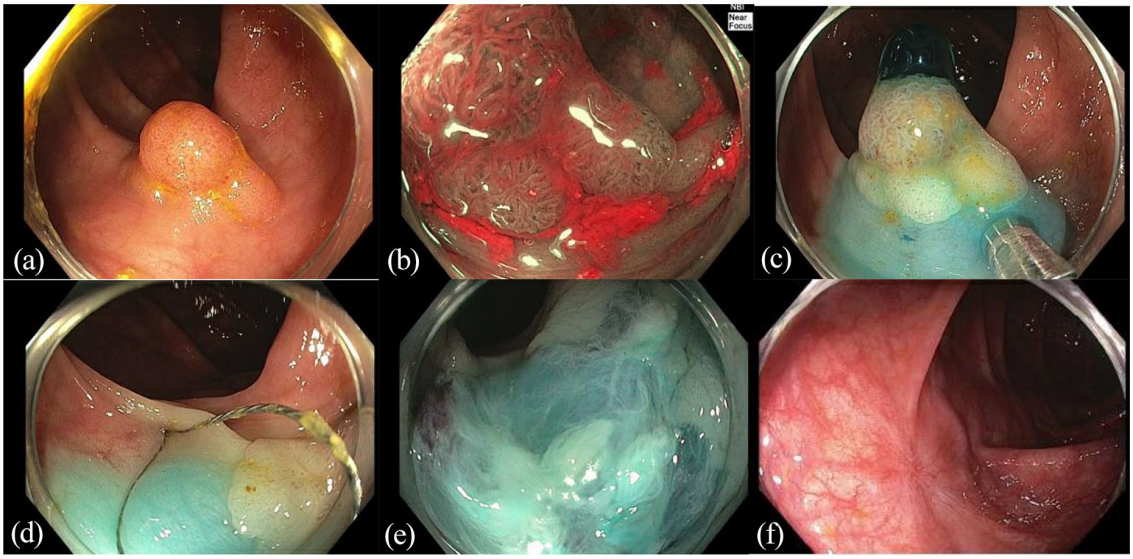

Figure 1. Cold endoscopic mucosal resection (EMR) for the management of a 22 mm transverse colon polyp in a 70-year-old male. (a, b) The colonoscope was initially advanced to the lesion site for close inspection, revealing no high-risk features. (c) Successful lifting of the polyp by injecting dilute epinephrine (1:500,000) in normal saline with methylene blue into the submucosa. (d) The lesion was resected in piecemeal with a cold snare starting at the edge of the polyp to include a wide margin of normal mucosa. (e) After removing several overlapping pieces with the cold snare and circumferential margins, the piecemeal resection was complete, with small submucosal stalks visible in the center. (f) Endoscopic view showing the post-polypectomy scar 9 months after EMR without visible recurrence.

an en bloc resection in larger and high-risk lesions, it is highly operator-dependent and requires special training. However, it is important to note that en bloc resection will allow better histopathologic evaluation and is associated with a lower recurrence rate than piecemeal resection.[8,9] It also generally takes more time to perform and carries higher risks of bleeding and perforation.

The key step with both EMR and ESD is the injection of fluid into the submucosa which should produce a visible lifting of the lesion away from deeper layers. When a polyp does not lift, producing the 'non-lifting sign,' this may be due to submucosal scarring from prior resection attempts or invasion into the submucosal layer or deeper.[10,11] A nonlifting sign in the setting of benign submucosal fibrosis may make EMR and/or ESD more technically difficult and potentially riskier and may necessitate adjuvant techniques such as the use of ablation along the scar tissue. When nonlifting represents deeper invasion, then a patient typically requires surgical excision of both the lesion as well as regional lymph nodes for a cancer beyond the deep mucosa and in some cases superficial submucosa. More recently, endoscopic full-thickness resection (EFTR) has become an option for resection of difficult residual polyps within an area of fibrosis or for resection of a mucosal or borderline cancer, particularly in a patient that may not be an optimal surgical candidate. The primary tool currently available for EFTR is the FTRD® (Full-Thickness Resection Device; Ovesco Endoscopy, Tübingen, Germany), a modified over-the-scope clip (OTSC) with built in snare that allows for a single-step, nonexposure resection of nonlifting lesions up to around 2 cm (Figure 4).[12,13]

The dramatic evolution of available tools and techniques has expanded the spectrum of polyps that we can manage endoscopically without the need for surgical intervention (Table 1). Recently published guidelines by the European Society of Gastrointestinal Endoscopy (ESGE)[14] and American Society of Gastrointestinal Endoscopy (ASGE)[15] on polyp resection are based on the robust and growing literature on the outcomes and limitations of each technique. Nonetheless, our daily practice continues to remain widely varied and influenced by other unmeasured factors, such as referral patterns and the availability of advanced resection techniques such as ESD and FTRD. In this article,

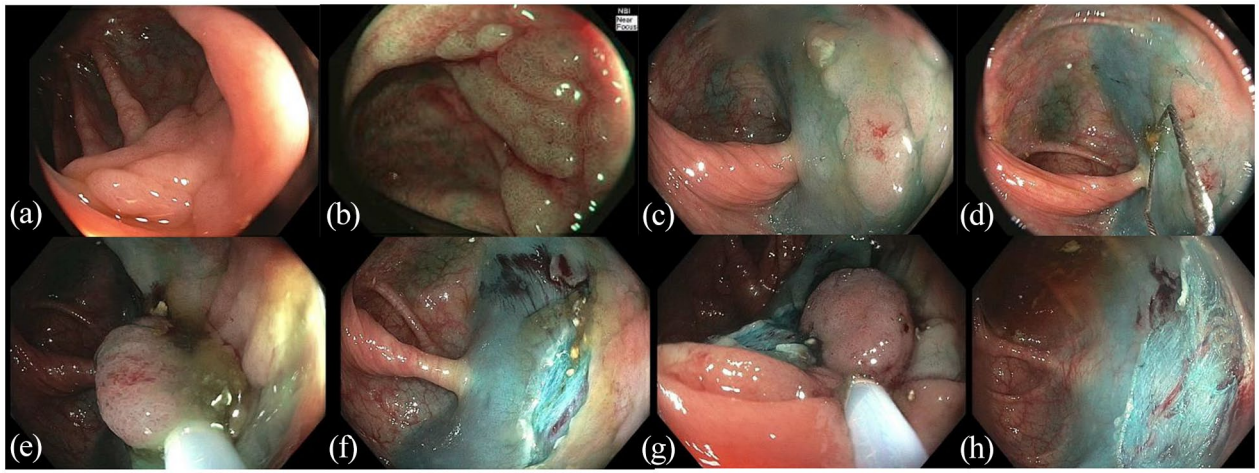

Figure 2. Hot endoscopic mucosal resection (EMR) for the management of a 35 mm laterally spreading tumor granular type (LST-G) in the transverse colon in a 69-year-old male. (a, b) The colonoscope was initially advanced to the lesion site and the polyp was extensively evaluated using HD white light and NBI with near focus imaging. No ulceration, depression, or mucosal/vascular irregularities were noted to suggest malignancy or deep invasion. (c) Successful lifting of the polyp was performed by injecting dilute epinephrine (1:200,000) in normal saline with methylene blue into the submucosa. (d, e, f, g) Piecemeal resection was carried out with a small diameter (13 mm) hot snare using EndoCut Q current, starting with a lateral margin and resecting multiple overlapping pieces. (h) The post EMR site was closely examined which did not reveal any evidence of bleeding, perforation, or residual polyp tissue.

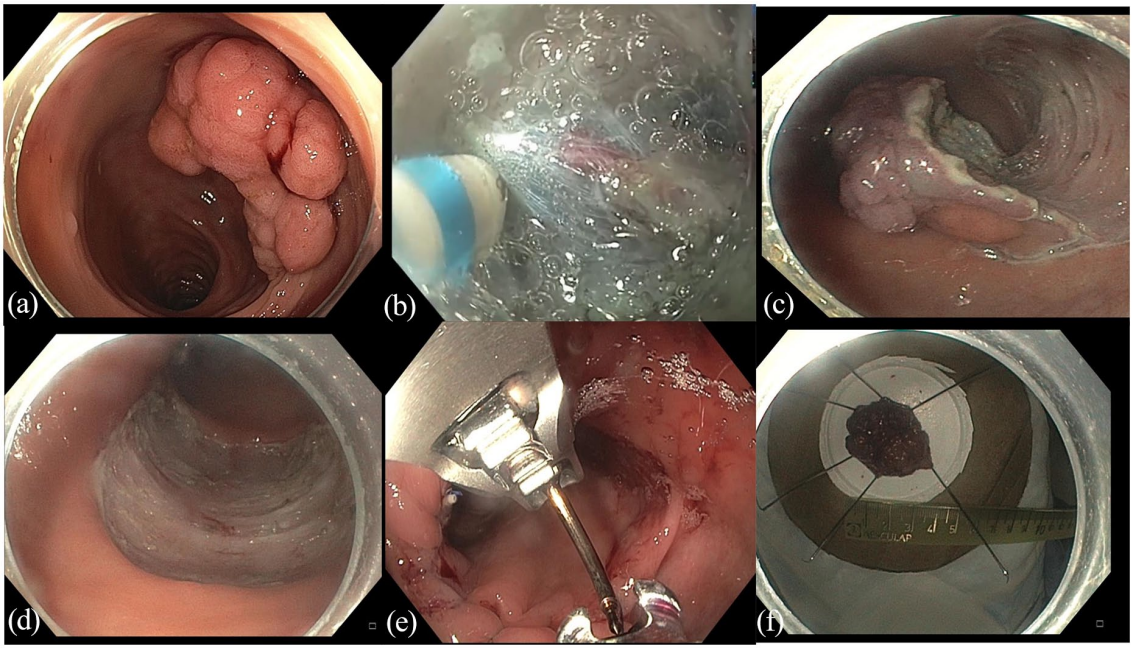

Figure 3. Endoscopic submucosal dissection (ESD) for the management of a 4 cm rectal tubular adenoma with focal high-grade dysplasia in a 64-year-old male. (a) The gastroscope was initially advanced to the site of the lesion for careful inspection, followed by submucosal injection with a colloid solution (not shown) to lift the polyp from the muscularis propria. (b) A circumferential incision was made around the polyp using an ESD knife followed by dissection through the submucosa. All encountered intervening vessels were managed by coagulation using the ESD knife or coagulation graspers. (c) The polyp was partially resected by dissecting the submucosa using the ESD knife. This was continued until the mucosal lesion was completely dissected from its submucosal base, thus achieving complete/en bloc resection. (d) Endoscopic view of the lesion site following complete/en bloc resection of the polyp. The underlying muscle layer is intact without bleeding or signs of muscle injury or perforation. (e) The submucosal defect was closed with endoscopic suturing following ESD, thus decreasing the risk of delayed bleeding and perforation. (f) The resected lesion was pinned and prepared for histopathologic examination.

we aim to review the variety of available management tools for colon polyps.

Things to look for when assessing polyps

Stratifying the lesion based on the likelihood of it harboring advanced pathology is an essential step in guiding management and choosing the optimal resection modality. In general, polyps with a diameter of ⩽5 mm have a low likelihood, 1.7%, of harboring advanced pathology. Polyps ⩾10 mm, however, have an increased incidence of harboring pre-malignant histology; 6.6% in polyps measuring 6–9 mm and 30.6% in ⩾10 mm.[16] In addition to size, morphologic characterization is another critical step that aids in differentiating an adenoma from a serrated polyp or a hyperplastic polyp, and whether the polyp is benign or malignant. One method involves assessing the pit pattern of a lesion inspected with chromoendoscopy and magnifying endoscopy, a technology not widely available in the United States, using the Kudo classification system (Supplementary Figure 1). This has shown to have a sensitivity of 89% and specificity of 85.7% in differentiating adenomatous or malignant polyps from other nonneoplastic, such as hyperplastic, polyps.[17]

Another important system in assessing a polyp is the Paris Classification, which describes the relative elevation or depression of a lesion as compared with normal background mucosa (Supplementary Figure 2).[18] As an example, a polyp with a relatively depressed surface (Paris 0-IIc) has a higher likelihood of containing invasion into the submucosa. One study found evidence of submucosal invasion in 27%–35.9% in post-resection histology evaluation of 0-IIc lesions, as opposed to 0.7%–2.4% in 0-IIa (flat, raised) lesions.[19]

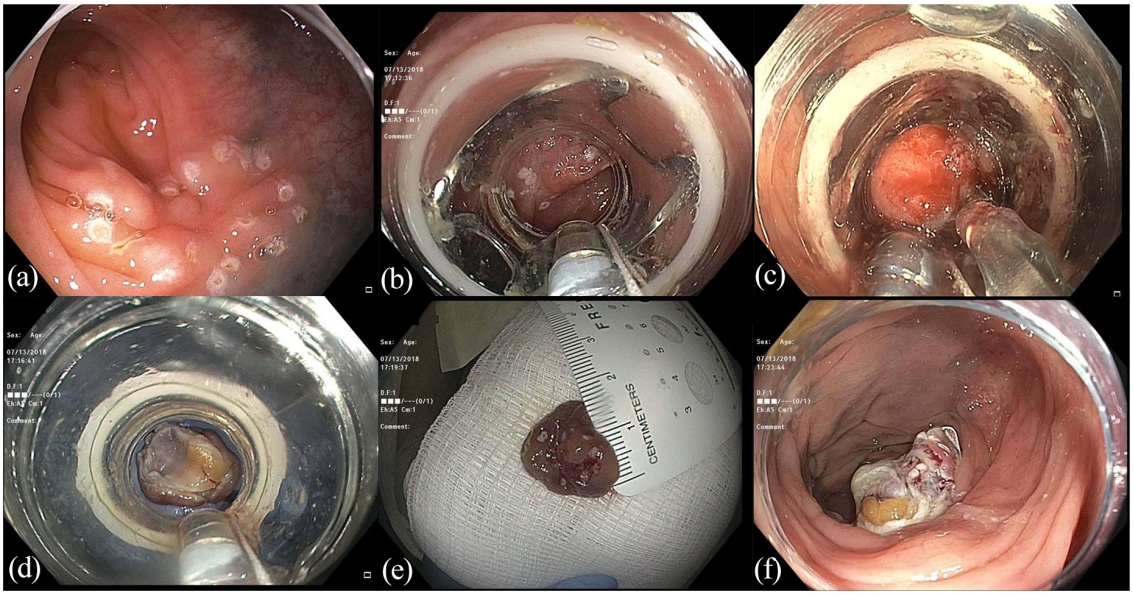

Figure 4. Endoscopic full-thickness resection of suspected residual high-grade dysplasia at the proximal transverse colon within a scarred polypectomy site in a 77-year-old male. (a) Initially, the colonoscope was advanced to the site of the lesion, and the margins of the scar/intended resection site were marked using soft coagulation current. (b) The colonoscope was removed, fitted with the full-thickness resection device (FTRD) system, and then advanced to the intended resection site. (c) The lesion was carefully grasped using the FTRD grasper and pulled into the transparent cap using rotation maneuvers and minimal suctioning until all the previously marked lesions were seen within the cap. This was followed by the deployment of the over-the-scope clip (OTSC) capturing all colonic wall layers and then resecting the lesion by tightening the snare located at the tip of the transparent cap while using EndoCut Q current. (d, e) The resected specimen was removed with the colonoscope while holding the polyp inside the cap. (f) Finally, the colonoscope was re-introduced, without the FTRD system, to examine the resection site. Correct deployment of the OTSC and complete resection of the lesion and all wall layers was appreciated, without evidence of bleeding or perforation. Pathology confirmed no cancer and no residual high-grade dysplasia.

Within the subset of polyps that qualify as laterally spreading tumors (LSTs), generally polyps with size $\geqslant$10 mm that extend laterally rather than vertically along the colon wall, the granularity of the surface is another important variable to be considered. Although more granular areas appear to be more concerning at first glance, the polyp regions more likely to harbor superficial or even deeper invasion are those that are nongranular, or smoother in appearance, particularly when paired with loss of normal vascular or pit pattern[20] (Supplementary Figure 3).

An attractive tool for Western endoscopists, especially where magnifying endoscopy and chromoendoscopy are not widely available, is the NICE (NBI International Colorectal Endoscopic) classification system (Supplementary Figure 4). The NICE system is based on the topographic characterization obtained with narrow-band imaging (NBI).[21] Based on the pit pattern, color, and vascularity as seen with NBI, a polyp is stratified as a NICE 1, 2, or 3 polyps, with an associated likely histologic assessment. In essence, a higher-risk lesion is both darker on NBI and has a more irregular pit and/or vascular pattern. This tool should be considered in the assessment of all polyps, but particularly those >20 mm, prior to attempted endoscopic resection.[21]

As with any endoscopic procedure, there will be a learning curve in attaining proficiency in the accurate assessment and real-time risk stratification of polyps. As noted previously, a nonlifting sign in treatment naïve polyps may be associated with a malignant lesion with invasion into the submucosa or deeper,[22] but often the nature of a polyp can be determined by pure visual assessment prior to lifting. Furthermore, relying on nonlifting to ascertain the presence of cancer will fail to identify mucosal cancer, where an R0 resection may spare the patient a partial colectomy. The importance of a proper polyp assessment therefore cannot be overlooked, as this step

Table 1. Summary of currently available colorectal polyp resection techniques.

	Cold forceps	Hot forceps	Cold snare polypectomy	Hot snare polypectomy	Cold endoscopic mucosal resection (EMR)	Hot endoscopic mucosal resection (EMR)	Endoscopic submucosal dissection (ESD)	Endoscopic full-thickness resection (EFTR)
Device used	Cold polypectomy forceps	Hot polypectomy forceps	Dedicated wire-loop cold snare	Dedicated wire-loop hot snare	Dedicated wire-loop cold snare	Dedicated wire-loop hot snare	Varying ESD knives available	Full-thickness resection device (FTRD)
Electrocautery involved	No	Yes	No	Yes	No	Yes	Yes	Yes
Technique	The polyp is grasped with the forceps and removed mechanically	The polyp is grasped with the forceps, cautery is applied until injury is seen at the base and then the tissue is removed mechanically	Dedicated cold snare grasps polyp and ideally a margin of normal tissue around polyp (without submucosal lift). Snare is closed and tissue is cut mechanically without the use of cautery.	Dedicated hot snare grasps polyp and ideally a margin of normal tissue around polyp (without submucosal lift). Snare is closed and tissue is cut while applying cautery.	The polyp is initially lifted by submucosal injection and the polyp is removed typically in piecemeal with mechanical closure of the snare, removing all visible polyp and a margin of normal tissue	The polyp is initially lifted by submucosal injection (or underwater) and the polyp is removed typically in piecemeal with closure of the snare, cutting tissue with the use of cautery, removing all visible polyp and a margin of normal tissue and/or coagulation of margins	The polyp is then lifted by submucosal injection, followed by incision around a lateral margin of the polyp, with dissection along the submucosal layer using a dedicated, electrocautery enhanced knife, to remove the polyp en bloc	Planned resection margins marked thermally. The FTRD system is placed onto the colonoscope. The polyp is grasped and slowly pulled into a cap loaded with a modified over-the-scope clip. The clip is deployed followed by closure of a preloaded snare at the tip of the cap, and the tissue is cut with electrocautery
Indications	Polypectomy of polyps <2 or 3 mm	Generally abandoned but previously used for polyps under 5 mm	En bloc resection for polyps up to 10 mm	En bloc resection for polyps generally up to 10 mm	Possible en bloc resection for lesions ~ 10–15 mm Typically piecemeal resection for low-risk lesions >15 mm and often >10 mm	En bloc resection for lesions~ 10–19 mm Piecemeal resection for low-risk lesions ⩾20 mm	En bloc resection for high-risk lesions, especially ⩾20 mm	En bloc resection for nonlifting mucosal polyps (scarred or polyps with deep submucosal invasion) or submucosal tumors Polyps in difficult anatomic locations

(Continued)

Table 1. (Continued)

	Cold forceps	Hot forceps	Cold snare polypectomy	Hot snare polypectomy	Cold endoscopic mucosal resection (EMR)	Hot endoscopic mucosal resection (EMR)	Endoscopic submucosal dissection (ESD)	Endoscopic full-thickness resection (EFTR)
Limitations	Only used for smaller/ diminutive polyps Limited histopathologic evaluation/ difficult to assess margins Risk of incomplete resection unless remove wide margins	Largely abandoned due to incomplete resection and residual polyp not completely ablated with cautery Limited histopathologic evaluation/difficult to assess margins Adverse events associated with the use of cautery (delayed bleeding, post-polypectomy syndrome, or perforation)	Size generally limited by small snare size and limited ability to cut through tissue larger than 10 mm Possible diminished ability of margin assessment post resection given lack of cauterized margin Depth of resection limited to mm or superficial sm, so not appropriate for resection of small cancers	Size limited due to risk of deep muscle injury if grasp too large of an area Still need to ensure a margin of normal tissue is grasped (cannot rely on cautery ablating an edge) Adverse events associated with the use of cautery (delayed bleeding, post-polypectomy syndrome, or perforation)	Not used for pedunculated polyps. Diminished effectiveness in nonlifting polyps with submucosal scaring. Diminished ability of histopathologic margin assessment post resection given no cautery margin Depth of resection limited to mm or superficial sm, so not appropriate for resection of suspected or known cancers Risk of incomplete resection requires surveillance colonoscopy at short interval (generally 6 months)	Size of individual pieces limited due to risk of deep muscle injury if grasp too large of an area, and so not ideal for en bloc resection of a larger suspected cancer Diminished effectiveness in nonlifting polyps with submucosal scaring Adverse events associated with the use of cautery (delayed bleeding, post-polypectomy syndrome, or perforation) Risk of incomplete resection requires surveillance colonoscopy at short interval (generally 6 months)	Effectiveness in dissecting nonlifting polyps with submucosal scaring Highly operator dependent, technically challenging, requires special training, and lengthy Much higher rates of perforation and bleeding Cost may be higher due to longer procedure time, cost of devices, and cost of closure of defect	Advancing the FTRD mounted colonoscope to the cecum can be challenging for proximal lesions Difficult to achieve en bloc resection for lesions >20 mm Tissue must be pulled into cap rather than suctioned, to avoid injury of extracolonic structures; more fibrotic areas may therefore be challenging Steps must be performed in rapid sequence to avoid losing grasp of tissue between deploying the clip and closing the snare Delayed adverse events may still occur despite adequate clip closure
Associated adverse events	Very low risk Virtually no delayed bleeding Essentially no perforation No post-polypectomy syndrome	Low risk May still have delayed bleeding Rare perforation May still have post-polypectomy syndrome	Very low risk Virtually no delayed bleeding Essentially no perforation No post-polypectomy syndrome	Somewhat low risk May still have delayed bleeding (but under 1%) Rare perforation May still have post-polypectomy syndrome	Very low risk Virtually no delayed bleeding Virtually no perforation No post-polypectomy syndrome	Low to medium Higher risk of delayed bleeding Higher risk of perforation Post-polypectomy syndrome	Highest risk Highest risks of immediate and delayed bleeding and perforation	Low to medium Perforation if sequential steps not performed properly or if clip later slips Clip misdeployment may affect risks and outcomes Post-polypectomy syndrome may still occur Can still have delayed bleeding Post EFTR appendicitis for polyps involving the appendix

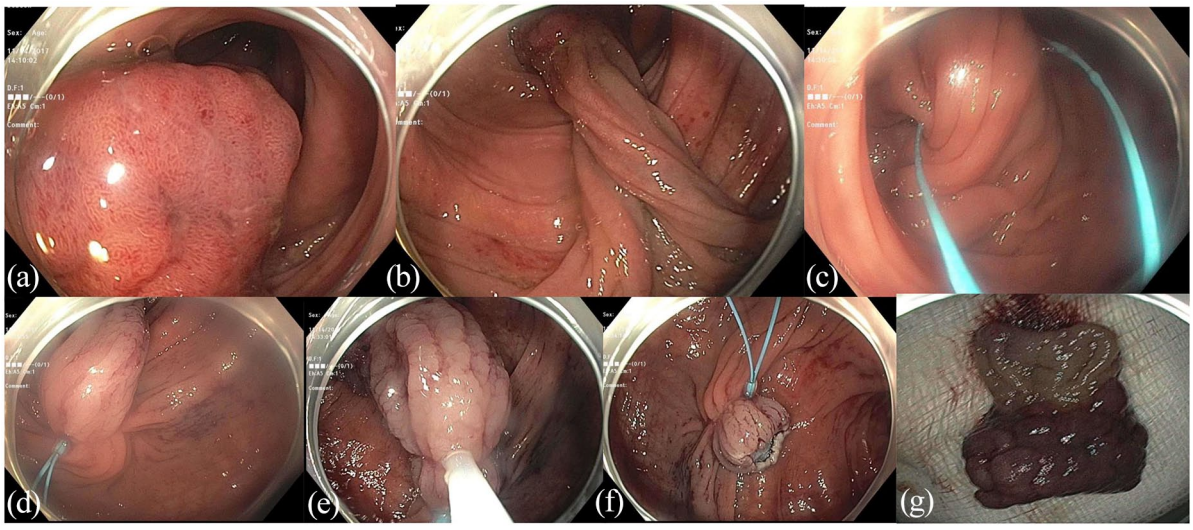

Figure 5. Resection of a 4 cm pedunculated polyp in the sigmoid colon in a 56-year-old man. (a) The head of the polyp was identified and examined and did not appear to have mucosal or vascular irregularity. (b) The stalk was identified and was long and thick, warranting ligation with resection to reduce bleeding risk. (c) The endoloop was advanced over the head of the polyp and pulled back to ensure it was fitted around the stalk and not around the head of the polyp. (d) The endoloop was secured tightly at the stalk with a large margin of normal tissue between the closed loop and the head of the polyp. (e) A large snare was placed at the stalk between the endoloop and the head of the polyp, maintaining a large margin with the actual polyp and a comfortable margin with the endoloop. (f) After snare cautery resection, the base was examined and confirmed to be clear of any residual polyp tissue, with a tightly secured endoloop in place. (g) The resected polyp was also inspected and appeared to have a wide margin of normal stalk tissue. Final pathology was 'Tubular adenoma, negative for high-grade dysplasia, completely excised.'

informs the endoscopist as to which is the optimal resection modality: piecemeal hot or cold EMR, en bloc EMR, ESD, or even referral for surgical intervention.

The evolution of endoscopic polyp resection

The optimal resection tool is one that would maximize the rate of safe and complete resection and allow a full and proper histologic evaluation. Piecemeal resection of polyps >10 mm or even >20 mm is often an acceptable mode of management. However, when dealing with lesions with high-risk features, en bloc resection becomes essential, as polyps removed en bloc allow for accurate histopathologic staging, in addition to leading to a lower recurrence rate as compared with those removed in piecemeal.[23] Furthermore, for lower-risk adenocarcinomas, including those with well-differentiated histology, those with no or only superficial submucosal invasion, <1000 μm, and in the absence of lymphovascular involvement, en bloc resection has the potential to be curative,[15] whereas surgical modalities should be considered if endoscopic en bloc resection is not achievable.[14] The choice of resection modality, particularly when it comes to more complex lesions, is nonetheless influenced by the availability of expertise in the center as well as the endoscopist's preference but should always consider whether it will lead to the best possible outcome for the patient, particularly when adenocarcinoma is suspected.

Pedunculated polyps

Very little has changed in the management of pedunculated lesions, which are removed with an electrocautery enhanced snare, or 'hot snare.' Mechanical ligation of the stalk with clips or an endoloop (Polyloop, Olympus America, Inc, San Jose, CA, USA) may be done to reduce the risk of delayed bleeding and is favored for lesions with a head diameter ⩾20 mm or stalk thickness ⩾5 mm (Figure 5).[24] The ESGE further recommended injection of dilute adrenaline in addition to the mechanical ligation of the stalk for pedunculated lesions with a head diameter ⩾20 mm or a stalk ⩾10 mm in diameter to reduce the risk of bleeding.[14]

In certain rare instances with very large pedunculated polyps, maneuvering the snare around a large head and/or a wide and long stalk might be difficult. More recently, the utilization of a scissor-type knife was introduced as a promising rescue modality for managing such difficult pedunculated lesions.[25,26]

Smaller polyps (<10 mm)

For nonpedunculated lesions, the size and polyp characteristics dictate the resection modality. Due to the high rate of incomplete resection and recurrence, the conventional use of cold forceps has been limited to lesions ⩽2 mm.[27] For polyps <10 mm, cold snare resection is in most cases the optimal method due to its high efficacy and extremely high safety profile.[28] Although hot snare has commonly been utilized for polyps <10 mm, the risk of post-polypectomy bleeding and post-polypectomy syndrome offsets any potential marginal advantage that is offered by using electrocautery in these small lesions.[29] The key to polyp resection in smaller polyps as in all polyps is to ensure that an adequate margin of normal tissue is resected around the polyp.

Intermediate polyps (10–19 mm)

In larger polyps, there is some heterogeneity regarding optimal resection modality. When dealing with nonpedunculated polyps measuring 10–19 mm, the use of simple cold or hot snare polypectomy can be considered as suggested by the ESGE;[14] however, EMR is favored by the ASGE in most polyps that are at least 10 mm in size[30] (Figures 1 and 2). In addition to creating a safety cushion to protect the deep muscle layer during hot snare resection, the submucosal injection done with EMR improves the ability to delineate the polyp's borders particularly when blue dye such as methylene blue or indigo carmine is added to the solution. This facilitates complete resection of a lesion when attempted en bloc[31] or piecemeal, by helping to identify polyp tissue that may have been inadvertently left behind during initial resection attempts. In a retrospective analysis of 251 polyps with a mean size of 15.9 ± 5.3 mm, local recurrence post EMR during a mean follow-up time of 25.5 ± 17.4 months was noted in only 3.6% of the patients.[32] The submucosal lift done with EMR may be performed with a simple and cheap saline solution, but this lift may dissipate somewhat rapidly. A longer lift time may be achieved with a colloid solution, which may then allow a higher chance of achieving en bloc resection of a polyp.[33] Finally, the addition of epinephrine in lift solutions is somewhat controversial, but the general trend is away from its use in EMR as it may mask a site that will later bleed. It is preferable to treat a bleeding site in real-time than to allow an otherwise preventable delayed bleed which has far higher morbidity. The exception to this is when performing cold snare EMR, as dilute epinephrine (we typically use 1:500,000) may keep the field clear of venous oozing, allowing a better assessment of the resection base and margins.

Larger polyps (⩾20 mm) without suspected invasion

Nonpedunculated polyps ⩾20 mm constitute a group in which endoscopic resection has gradually replaced more morbid and expensive surgical resection.[7] As opposed to lesions <20 mm, achieving en bloc resection with EMR becomes a challenge, even among the most experienced hands. The majority of neoplastic lesions are benign, and piecemeal resection using EMR, optimally taking the minimum number of pieces needed to obtain satisfactory margins, is associated with a relatively low risk of adverse events with an acceptable rate of recurrence. Therefore, EMR is the preferred method of polyp resection in this category per the latest guideline recommendations.[15,14] More recently, the need for electrocautery to assist in EMR has been challenged. Cautery is associated with the primary risks of polypectomy, including delayed bleeding, perforation, and post-polypectomy syndrome, and avoiding the use of cautery with 'cold EMR' has been demonstrated to drastically reduce and even eliminate these risks.[34,35] Studies evaluating the efficacy of cold EMR are limited but appear to show promising and reasonable complete resection rates for polyps ranging 4–9 mm.[36] There is an ongoing randomized controlled study currently ongoing comparing hot and cold EMR in polyps at least 20 mm in size that should help answer the question of relative efficacy, but multiple studies have confirmed that cold EMR is associated with virtually no adverse events.

Larger polyps (⩾20 mm) with suspected invasion

In polyps ⩾20 mm with high-risk features for early cancer such as Kudo pit pattern type IV or V_I, depressed or nongranular lesions, achieving

en bloc R0 resection becomes a necessity. Few polyps of this size and type are safely and adequately treated with EMR given its limitations. Therefore, the ESGE further recommends that en bloc EMR attempt should be limited to lesions ⩽20 mm in the colon and ⩽25 mm in the rectum.[14] In this setting, ESD is the preferred method for endoscopic resection[14,15] as it is much more likely to lead to complete en bloc and R0 resection even for much larger lesions,[37] and may therefore lead to very low post-resection recurrence rates, 0.8–2%[38] (Figure 3). Despite its substantial advantage in tackling large and advanced lesions, ESD is very challenging in the presence of submucosal fibrosis, which may be attributed to deep wall invasion, prior resection attempts or biopsies, or traction causing fibrosis. Even among experts, ESD in the presence of submucosal fibrosis is associated with increased rates of perforation and incomplete resection.[39] Of note, submucosal fibrosis similarly affects the safety and the efficacy of EMR,[40] but maybe more consequential when interfering with the complete resection of an early cancer by ESD.

Polyps unable to be resected with EMR or ESD

The last several years have seen the expansion of EFTR as a means to resect lesions that otherwise cannot be adequately treated with EMR or ESD. The FTRD device has been used for the management of subepithelial tumors as well as polyps with significant fibrosis that are otherwise not resectable.[41] Results from the first multicenter prospective trial[12] reported promising en bloc resection and R0 resection rates, 89.5%, and 84.2%, respectively. In a more recent multicenter US experience, similar en bloc (84.2%) and R0 (76.9%) resection rates were reported with FTRD for managing difficult to resect colorectal lesions.[13] The FTRD device is primarily limited by the size of the cap (21 mm diameter) (Figure 4), and therefore its efficacy in achieving complete resection declines with lesions size ⩾20 mm.[42] EFTR has additionally been proposed to manage polyps in difficult anatomic locations, such as within a diverticulum or involving the appendiceal orifice. Although EMR and ESD have been described in managing such lesions, the diminished efficacy and higher rates of adverse events have raised concerns about their utility in difficult anatomic locations.[43] A recent multicenter experience on the use of FTRD for appendiceal lesions revealed satisfactory rates of en bloc resection, 89%, and R0 histology, 93%. However, a nontrivial fraction of patients, 17% (95% confidence interval 9.4%–29%), did have post-EFTR appendicitis of which 60% required surgical appendectomies.[44] Therefore, this should primarily be considered in the setting of a multidisciplinary discussion of options, with transparency of this risk during the informed consent process. We would also argue that EFTR is not necessary for an appendiceal orifice polyp where all margins of the polyp are visible and accessible by other means of resection, such as hot or cold EMR. We have also successfully managed intra-diverticular polyps safely with the use of cold EMR, and the relative risks and benefits of EFTR *versus* cold EMR in this setting should also be considered before proceeding. One other circumstance where we have employed EFTR is in the setting of a previously resected polyp that unexpectedly contained superficial cancer, where cauterized margins were involved. EFTR in this setting informs whether there is residual tumor left behind and if so how deep it invades, to determine whether definitive surgical resection and lymph node dissection are needed.

Additional means for improving outcomes

When dealing with nonmalignant neoplastic lesions, if en bloc resection is not possible, it is important to resect all remaining visible polyp tissue with wide lateral margins preferably using the snare during the same session[14,15] to avoid leaving large areas of residual polyp that may be more difficult to remove if the patient is sent to a referral center for definitive polyp resection and to reduce the likelihood of residual microscopic polyp tissue at follow-up. This includes careful assessment and treatment of all lateral margins as well as an assessment of the base to ensure there are no remaining bridges of polyp tissue. Although this has not been updated in the ESGE guidelines, ablation of the margins of larger polyps, particularly with snare tip soft coagulation, can significantly reduce the risk of residual polyp tissue at follow-up.[15] This was previously shown in a randomized prospective trial in which patients who underwent margin ablation with snare tip soft coagulation post EMR for LSTs ⩾20 mm had a lower rate of recurrence, 5.2%, as opposed to the control group, 21%, ($p < 0.001$).[45] And when a larger polyp is removed in piecemeal, surveillance colonoscopy with enhanced imaging and systematic biopsy should be done at a short interval (typically 6 months unless there is advanced histology) to ensure there is no remaining polyp that would

then be at risk for malignant transformation as an interval cancer.[14,15,46] Smaller residual polyps at follow-up may be treated with cold or hold avulsion techniques and/or ablative techniques,[47,48] with subsequent close follow-up until clear of residual polyp. Tattoo of the site should be done for future localization unless it is in an obvious location such as the rectum or cecum.

In addition to assessing for residual polyp at the base and margins of a polyp resection, the base should be assessed for evidence of injury to the muscularis propria.[49] If present, the closure of the site is important to treat a perforation and/or prevent delayed perforation.[50,51] As noted, perforation risk may be reduced with the use of an adequate lift, possibly with a colloid solution to increase the lift time, and resection in piecemeal for polyps at least 20 mm in size, avoiding the use of a large snare and/or grasping too large an area of tissue with the snare.[52] Perforation risk may of course be drastically reduced and potentially eliminated with avoidance of cautery when it is not necessary. Similarly, delayed bleeding risk may be substantially reduced or eliminated with the avoidance of cautery when not required. When cautery is used, prophylactic clip closure may reduce the risk of delayed bleeding in polyps $\geqslant$20 mm in the right and transverse colon;[15,53,54] however, this has not yet been updated in the European guidelines.[14] In a recently published meta-analysis that included eight randomized clinical trials, placement of clips was indeed associated with a significant reduced risk of delayed bleeding post endoscopic resection of nonpedunculated polyps $\geqslant$20 mm that are located proximal to the hepatic flexure.[55]

Future perspectives and guidance

In this review, we have described varying endoscopic resection techniques for colorectal polyps, considering which tools are optimal for any given lesion (Table 1). The gap has narrowed between the indications for endoscopic and surgical resection, but this has led to increased concern about under-treating lesions that harbor advanced pathology such as low-risk adenocarcinoma when employing endoscopic resection as opposed to surgical resection. That being said, surgery is still being over-utilized for nonmalignant colorectal lesions that could otherwise have been resected endoscopically,[56,57] with some data even showing a possible uptrend in surgery in this setting.[58] As a result, the ESGE recommended that while it is appropriate to refer patients with polyps with endoscopic findings of deep submucosal invasion to surgery, those polyps without characteristics of deep submucosal invasion should not be referred for surgery without first consulting an expert center that performs advanced endoscopic resection techniques.

Despite the expansion of endoscopic tools and techniques to manage large and complex colorectal polyps, our daily routines are still influenced by patient, physician, and institutional preferences, available local expertise, and established practice and referral patterns. The hierarchy of referrals to different subspecialties has also been shown to correlate with the ultimate management modality.[59] Nonetheless, a thorough assessment of a polyp's characteristics prior to resection is a must. Prediction of a polyp's histology, including its risk for advanced histology or even deep invasion, guides all the steps that follow in its management, with lesions suspicious for mucosal invasion requiring en bloc resection and those suggesting submucosal invasion or deeper requiring biopsy, tattooing, and referral for definitive surgical management.[14,60] This is critical to sustain and improve our screening and management of colorectal polyps and CRC. In a recent innovative trend, virtual assistance in terms of artificial intelligence (AI) has been adopted in gastroenterology, particularly in the field of polyp management with evidence suggesting a promising supportive role of AI in detection as well as risk stratification of polyps.[61] Another innovative approach is the utilization of robot-assisted ESD, which was found to show promising early outcomes in terms of achieving en bloc resection with superior maneuvering powers that is reflected in shorter procedure time as compared with the conventional ESD.[62,63] The parallel advancement of endoscopic imaging and resection techniques, along with the recent integration of AI, will expectantly improve our polyp management and ultimately improve our efforts of CRC prevention.

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Supplemental material

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