Endoscopic Removal of Colorectal Lesions: Recommendations by the US Multi-Society Task Force on Colorectal Cancer

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SUPPLEMENTARY MATERIAL accompanies this paper at http://links.lww.com/AJG/B415, http://links.lww.com/AJG/B416, http://links.lww.com/AJG/B420, http://links.lww.com/AJG/B421, http://links.lww.com/AJG/B431, http://links.lww.com/AJG/B432, http://links.lww.com/AJG/B422, http://links.lww.com/AJG/B423, http://links.lww.com/AJG/B424, http://links.lww.com/AJG/B425, http://links.lww.com/AJG/B417, http://links.lww.com/AJG/B426, http://links.lww.com/AJG/B427, http://links.lww.com/AJG/B428, http://links.lww.com/AJG/B429, http://links.lww.com/AJG/B418, http://links.lww.com/AJG/B433

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Colonoscopy with polypectomy reduces the incidence of and mortality from colorectal cancer (CRC).[1,2] It is the cornerstone of effective prevention.[3] The National Polyp Study showed that removal of adenomas during colonoscopy is associated with a reduction in CRC mortality by up to 50% relative to population controls.[1,2]

The lifetime risk to develop CRC in the United States is approximately 4.3%, with 90% of cases occurring after the age of 50 years.[4] The recent reductions in CRC incidence and mortality have been largely attributed to the widespread uptake of CRC screening with polypectomy.[5] The techniques and outcomes of polyp removal using colonoscopy, however, had historically remained understudied and thus, practice widely varied. Reports have shown that residual tissue after polypectomy that is judged to be "complete" by the endoscopist is common, ranging from 6.5% to 22.7%.[6] The significant variation in incomplete resection rates among endoscopists has highlighted the dependence of polypectomy effectiveness on operator technique. A pooled analysis from 8 surveillance studies that followed participants with adenomas after a baseline colonoscopy suggested that although the majority (50%) of post-colonoscopy colon cancers were likely due to missed lesions, close to one-fifth of incident cancers were related to incomplete resection.[7]

Polypectomy techniques have expanded in parallel with advances in endoscopic imaging, technology, and tools. Optimal techniques encompass effectiveness, safety, and efficiency. Colorectal lesion characteristics, including location, size, morphology, and histology, influence the optimal removal method. For example, the applications of cold snare polypectomy for small lesions, which can remove adenomatous tissue en bloc with surrounding normal mucosa, and endoscopic mucosal resection (EMR) for large and flat lesions, which utilizes submucosal injection to lift the lesion before snare resection, have evolved to improve complete and safer resection. The primary aim of polypectomy is the complete and safe removal of the colorectal lesion and the ultimate prevention of CRC. This consensus statement provides recommendations to optimize complete and safe endoscopic removal techniques for colorectal lesions (Table 1), based on available literature and experience. The recommendations from the US Multi-Society Task force (USMSTF) on the management of malignant polyps, polyposis syndromes,[8] and surveillance after colonoscopy and polypectomy[9] are available in other documents. Table 2 summarizes abbreviations and definitions of terms utilized in these recommendations.

METHODS

Process

The USMSTF is composed of 9 gastroenterology specialists who represent the American College of Gastroenterology, the American Gastroenterological Association, and the American Society for Gastrointestinal Endoscopy. We developed the guidance statements by consensus process through e-mail correspondence and multiple joint teleconferences. The final manuscript was reviewed and approval by the governing boards of the 3 respective societies.

Literature Review

We performed a systematic review of the literature based on a defined search by a medical librarian of the Ovid Medline,

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Table 1. Statements of Best Practice in This Document

Statement
Statement 1: Lesion assessment and description
The macroscopic characterization of a lesion provides information to facilitate the lesion's histologic prediction and optimal removal strategy.
• We recommend the documentation of endoscopic descriptors of the lesion, including location, size in millimeters, and morphology in the colonoscopy procedure report. (Strong recommendation, low-quality evidence)
• We suggest the use of the Paris classification to describe the surface morphology in order to provide a common nomenclature (Conditional recommendation, low-quality evidence)
• We suggest that for non-pedunculated adenomatous (Paris 0-II and 0-Is) lesions ≥10 mm, surface morphology should be also described as granular or non-granular lateral spreading lesions. (Conditional recommendation, low-quality evidence)
• We recommend photo documentation of all lesions ≥10 mm in size before removal, and suggest photo documentation of the post resection defect (Strong recommendation, low-quality evidence).
• We suggest proficiency in the use of electronic- (eg, NBI, i-scan, Fuji Intelligent Chromoendoscopy, or blue light imaging) or dye (chromoendoscopy)-based image-enhanced endoscopy techniques to apply optical diagnosis classifications for colorectal lesion histology. (Conditional recommendation, moderate-quality evidence)
• We recommend proficiency in the endoscopic recognition of deep submucosal invasion. (Strong recommendation, moderate-quality evidence)
Statement 2: Lesion removal
The primary aim of polypectomy is complete removal of the colorectal lesion, and the subsequent prevention of colorectal cancer. Endoscopists should employ the safest, most complete, and efficient resection techniques based on available evidence.
2a: Diminutive (≤5 mm) and small (6–9 mm) lesions
• We recommend cold snare polypectomy to remove diminutive (≤5 mm) and small (6–9 mm) lesions due to high complete resection rates and safety profile. (Strong recommendation, high-quality evidence)
• We recommend against the use of cold forceps polypectomy to remove diminutive (≤5 mm) lesions due to high rates of incomplete resection. For diminutive lesions ≤2 mm, if cold snare polypectomy is technically difficult, jumbo or large-capacity forceps polypectomy may be considered. (Strong recommendation, moderate-quality evidence)
• We recommend against the use of hot biopsy forceps for polypectomy of diminutive (≤5 mm) and small (6–9 mm) lesions due to high incomplete resection rates, inadequate histopathologic specimens, and complication rates. (Strong recommendation, moderate-quality evidence)
2b: Non-pedunculated (10–19 mm) lesions
• We suggest cold or hot snare polypectomy (with or without submucosal injection) to remove 10- to 19-mm non-pedunculated lesions. (Conditional recommendation, low-quality evidence)
2c: Non-pedunculated (≥20 mm) lesions
• We recommend EMR as the preferred treatment method of large (≥20 mm) non-pedunculated colorectal lesions. Endoscopic resection can provide complete resection and obviate the higher morbidity, mortality, and cost associated with alternative surgical treatment. (Strong recommendation, moderate-quality evidence)
• We recommend an endoscopist experienced in advanced polypectomy to manage large (≥20 mm) non-pedunculated colorectal lesions. (Strong recommendation, low-quality evidence)
• We recommend snare resection of all grossly visible tissue of a lesion in a single colonoscopy session and in the safest minimum number of pieces, as prior failed attempts at resection are associated with higher risk for incomplete resection or recurrence. (Strong recommendation, low-quality evidence)
• We suggest the use of a contrast agent, such as indigo carmine or methylene blue, in the submucosal injection solution to facilitate recognition of the submucosa from the mucosa and muscularis propria layers. (Conditional recommendation, moderate-quality evidence)
• We recommend against the use of tattoo, using sterile carbon particle suspension, as the submucosal injection solution. The carbon particle suspension may result in submucosal fibrosis, and can thus reduce the technical success of future endoscopic resection of residual or recurrent lesion. (Strong recommendation, low-quality evidence)
• We suggest the use of a viscous injection solution (eg, hydroxyethyl starch, Eleview, ORISE Gel) for lesions ≥20 mm to remove the lesion in fewer pieces and less procedure time compared to normal saline. (Conditional recommendation, moderate-quality evidence)
• We recommend against the use of ablative techniques (eg, APC, snare tip soft coagulation) on endoscopically visible residual tissue of a lesion as they have been associated with an increased risk of recurrence. (Strong recommendation, moderate-quality evidence)
• We suggest the use of adjuvant thermal ablation of the post-EMR margin, where no endoscopically visible adenoma remains despite meticulous inspection. There is insufficient evidence to recommend a specific modality (ie, APC, snare tip soft coagulation) at this time. (Conditional recommendation, moderate-quality evidence)
• We recommend detailed inspection of the post-resection mucosal defect to identify features for immediate or delayed perforation risk, and perform endoscopic clip closure, accordingly. (Strong recommendation, moderate-quality evidence)

Table 1. (*continued*)

Statement
• We suggest prophylactic closure of resection defects ≥20 mm in size in the right colon, when closure is feasible. (Conditional recommendation; moderate-quality evidence)
• We suggest treatment of intraprocedure bleeding using endoscopic coagulation (eg, coagulation forceps or snare-tip soft coagulation) or mechanical therapy (eg, clip), with or without the combined use of dilute epinephrine injection. (Conditional recommendation, low-quality evidence)
• We suggest that patients on anti-thrombotics who are candidates for endoscopic removal of a colorectal lesion ≥20 mm receive individualized assessment, balancing the risks of interrupting anticoagulation for colonoscopic polypectomy or mucosal resection against the risks of significant bleeding during and after the procedure. (Conditional recommendation, low-quality evidence)
2d: Pedunculated Lesions
• We recommend hot snare polypectomy to remove pedunculated lesions ≥10 mm (Strong recommendation, moderate-quality evidence)
• We recommend prophylactic mechanical ligation of the stalk with a detachable loop or clips on pedunculated lesions with head ≥20 mm or with stalk thickness ≥5 mm to reduce immediate and delayed post-polypectomy bleeding. (Strong recommendation, moderate-quality evidence)
• We suggest retrieval of large pedunculated polyp specimens en bloc to ensure ability to assess resection margins, rather than dividing polyp heads to facilitate through-the-scope specimen retrieval. (Conditional recommendation, low-quality evidence)
Statement 3: Lesion marking
• We recommend the use of tattoo, using sterile carbon particle suspension, to demarcate any lesion that may require localization at future endoscopic or surgical procedures. (Strong recommendation, low-quality evidence)
• We suggest placing the tattoo at 2–3 separate sites located 3–5 cm anatomically distal to the lesion (anal side), particularly when the purpose is to mark the lesion for later endoscopic resection. The carbon particle suspension, if injected at or in close approximation to the lesion, may result in submucosal fibrosis, and can thus reduce the technical success and increase the risk of future endoscopic resection. (Conditional recommendation, low-quality evidence)
• We suggest endoscopists and surgeons establish a standard location of tattoo injection relative to the colorectal lesion of interest at their institution. (Conditional recommendation, very low-quality evidence)
• We recommend documentation of the details of the tattoo injection (material, volume, position relative to the lesions) in the colonoscopy report, as well as photo documentation of the tattoo in relation to the colorectal lesion. (Strong recommendation, low-quality evidence)
Statement 4: Surveillance
• We recommend intensive follow-up schedule in patients after piecemeal EMR (lesions ≥20 mm) with the first surveillance colonoscopy at 6 mo, and the intervals to the next colonoscopy at 1 y, and then 3 y. (Strong recommendation, moderate-quality evidence)
• To assess for local recurrence, we suggest careful examination of the post-mucosectomy scar site using enhanced imaging, such as dye-based (chromoendoscopy) or electronic-based methods, as well as obtaining targeted biopsies of the site. Post-resection scar sites that show both normal macroscopic and microscopic (biopsy) findings have the highest predictive value for long-term eradication. (Conditional recommendation, moderate-quality evidence).
• In surveillance cases with suspected local recurrence, we suggest endoscopic resection therapy with repeat EMR, snare or avulsion method, and consider ablation of the perimeter of the post-treatment site. In such cases, subsequent examinations should be performed at 6–12 mo until there is no local recurrence. Once a clear resection site is documented by endoscopic assessment and histology, the next follow-ups are performed at 1-y and then 3-y intervals. (Conditional recommendation, low-quality evidence)
• In addition to detailed inspection of the post-mucosectomy scar site, we recommend detailed examination of the entire colon at the surveillance colonoscopy to assess for synchronous colorectal lesions (Strong recommendation, moderate-quality evidence)
Statement 5. Equipment
• We recommend the use of carbon dioxide insufflation instead of air during colonoscopy and EMR. (Strong recommendation, moderate-quality evidence.)
• We suggest the use of microprocessor-controlled electrosurgical units. (Conditional recommendation, very low-quality evidence)
Statement 6: Quality of polypectomy
The majority of benign colorectal lesions can be safely and effectively removed using endoscopic techniques. As such, endoscopy should be the first-line management of benign colorectal lesions.
• When an endoscopist encounters a suspected benign colorectal lesion that he or she is not confident to remove completely, we recommend referral to an endoscopist experienced in advanced polypectomy for subsequent evaluation and management, in lieu of referral for surgery. (Strong recommendation, low-quality evidence)
• We suggest the documentation of the type of resection method (eg, cold snare, hot snare, endoscopic mucosal resection) used for the colorectal lesion removal in the procedure report. (Strong recommendation, low-quality evidence)
• We recommend that non-pedunculated lesions with endoscopic features suggestive of submucosal invasive cancer and which are resected en bloc be retrieved and pinned to a flat surface before submitting the specimen to the pathology laboratory to facilitate pathologic sectioning that is perpendicular to the resection plane. (Strong recommendation, low quality of evidence)

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Table 1. (*continued*)

Statement
• For non-pedunculated colorectal lesions resected en bloc with submucosal invasion, we recommend that pathologists measure and report the depth of invasion, distance of the cancer from the vertical and lateral resection margin, in addition to prognostic histologic features, such as degree of differentiation, presence or absence of lymphovascular invasion and tumor budding. (Strong recommendation, moderate-quality evidence)
• We recommend that endoscopists resect pedunculated lesions en bloc, and that when submucosal invasion is present, pathologists report the distance of cancer from the cautery line, the degree of tumor differentiation, and presence or absence of lymphovascular invasion. (Strong recommendation, moderate-quality evidence)
• We recommend endoscopists engage in a local (institution-, hospital-, or practice-based) quality-assurance program, including measuring and reporting of post-polypectomy adverse events. (Strong recommendation, moderate-quality evidence)
• We suggest measuring and reporting the proportion of patients undergoing colonoscopy who are referred to surgery for benign colorectal lesion management. (Conditional recommendation, moderate-quality evidence)
• We suggest the use of polypectomy competency assessment tools, such as Direct Observation of Polypectomy Skills and/or the Cold Snare Polypectomy Competency Assessment Tool, in endoscopic training programs, and in practice improvement programs. (Conditional recommendation, low-quality evidence)

Embase, and Cochrane databases from 1946 to December 2017, as well as reviews of manual references and scientific meeting abstracts of the American College of Gastroenterology, American Gastroenterology Association, American Society for Gastrointestinal Endoscopy, and United European Gastroenterology Week from 2014–2017. The search was limited to human studies without any language restriction. We framed the search strategy using key words (Appendix 1, http://links.lww.com/AJG/B415) from formatted question statements (Appendix 2, http://links.lww.com/AJG/B416). We reviewed and synthesized high-quality studies to generate statements and, when not available, relied on lower-quality evidence and expert opinion.

Grading of Recommendations, Assessment, Development, and Evaluation Ratings of Evidence: Level of Evidence and Strength of Recommendation

The USMSTF group rated the quality of the evidence for each statement as very low quality, low quality, moderate quality, and high quality based on the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation Ratings of Evidence) methodology (Table 3).[10]

We provide a recommendation as strong or conditional according to modified GRADE criteria.[11] Wording of recommendations was based on the strength of recommendation: "recommend" was used for strong recommendations and "suggest" was used for conditional recommendations.

SECTION I: LESION ASSESSMENT

Statement 1: Lesion Assessment and Description

The macroscopic characterization of a lesion provides information to facilitate the lesion's histologic prediction, and optimal removal strategy.

- We recommend the documentation of endoscopic descriptors of the lesion, including location, size in millimeters, and morphology in the colonoscopy procedure report. (Strong recommendation, low-quality evidence)
- We suggest the use of the Paris classification to describe the surface morphology in order to provide a common nomenclature (Conditional recommendation, low-quality evidence)
- We suggest that for non-pedunculated adenomatous (Paris 0-II and 0-Is) lesions ≥10 mm, surface morphology should be also described as granular or non-granular lateral spreading lesions. (Conditional recommendation, low-quality evidence)
- We recommend photo documentation of all lesions ≥10 mm in size before removal, and suggest photo documentation of the post-resection defect (Strong recommendation, low-quality evidence).
- We suggest proficiency in the use of electronic- (eg, narrow-band imaging [NBI], i-scan, Fuji Intelligent Chromo Endoscopy or blue light imaging) or dye (chromoendoscopy)-based image enhanced endoscopy techniques to apply optical diagnosis classifications for colorectal lesion histology. (Conditional recommendation, moderate-quality evidence)
- We recommend proficiency in the endoscopic recognition of deep submucosal invasion. (Strong recommendation, moderate-quality evidence)

The macroscopic characterization of a colorectal lesion, including its location, size, and shape, combined with the real-time assessment of the suspected histopathology and estimation of the depth of invasion provides information about whether a lesion is amenable to endoscopic resection. In this document, we review key components to the macroscopic characterization of colorectal lesions. A more detailed description of the macroscopic assessment of lesions with submucosal invasion, and a decision-making guide to their optimal management is provided in separate MSTF document on Endoscopic Recognition and Management Strategies for Malignant Colorectal Polyps.

PARIS CLASSIFICATION

The Paris classification has been the most used international endoscopic classification of colorectal lesion morphology (Figure 1).[12] Although studies have shown only moderate agreement among Western experts using the Paris classification, the application of a minimal standard terminology of colorectal lesions provides the first step in stratifying which lesions are more likely to contain advanced pathology and informs their removal strategy.[13,14] In the Paris classification, there are 2 macroscopic types: (1) type 0, the superficial lesions; and (2) types 1–5, the advanced cancers.

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Table 2. Abbreviations, Terms, and Definitions

Abbreviations and terms	Definition
Abbreviation	
CRC	Colorectal cancer
EMR	Endoscopic mucosal resection
APC	Argon plasma coagulation
USMSTF	US Multi-Society Task force
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation Ratings of Evidence
SSP	Sessile serrated polyp
ESD	Endoscopic submucosal dissection
LST	Laterally spreading tumor
LST-G	Laterally spreading tumor, granular
LST-G-H	Laterally spreading tumor, granular-homogenous
LST-G-NM	Laterally spreading tumor, granular-nodular mixed
LST-NG	Laterally spreading tumor, non-granular
LST-NG-FE	Laterally spreading tumor, non-granular-flat elevated
LST-NG-PD	Laterally spreading tumor, non-granular-pseudodepressed
NICE	Narrow Band Imaging International Colorectal Endoscopic
NBI	Narrow band imaging
HSP	Hot snare polypectomy
CARE	Complete adenoma resection
ASGE	American Society for Gastrointestinal Endoscopy
ACG	American College of Gastroenterology
DOPyS	Direct Observation of Polypectomy Skills
CSPAT	Cold Snare Polypectomy Assessment Tool
Terms	
Diminutive	Lesion size ≤5 mm
Small	Lesion size 6–9 mm
Large	Lesion size ≥20 mm
Polypoid	Lesion protrudes from mucosa into lumen, includes pedunculated and sessile
Pedunculated (0-Ip)	Lesion attached to mucosa by stalk; the base of lesion is narrow
Sessile (0-Is)	Lesion not attached to mucosa by stalk; the base and top of the lesion have the same diameter
Non-polypoid	Lesion has little to no protrusion above the mucosa. Includes superficial elevated, flat, and depressed.
Superficial elevated (0-IIa)	Lesion height <2.5 mm above normal mucosa; sometimes defined as height less than one-half of the lesion diameter
Flat (0-IIb)	Lesion without any protrusion above mucosa
Depressed (0-IIc)	Lesion with base that is lower than the normal mucosa
Laterally spreading tumor (LST)	Laterally growing superficial neoplasm (instead of upward or downward growth) ≥10 mm in size
LST-granular-homogenous (LST-G-H)	LST polypoid type that corresponds to Paris subtype 0-IIa
LST-granular-nodular mixed (LST-G-NM)	LST type that corresponds to combination of Paris subtype 0-IIa and 0-Is
LST-non-granular-flat elevated (LST-NG-FE)	LST non-polypoid type corresponds to Paris subtype 0-IIa
LST-non-granular-pseudodepressed (LST-NG-PD)	LST non-polypoid type corresponds to combination of Paris subtype 0-IIa and 0-IIc
NICE type 1	Serrated class includes hyperplastic and sessile serrated lesions
NICE type 2	Adenomas
NICE type 3	Lesions with deep (>1000 μm) submucosal invasion
Cold snare polypectomy	Snare polypectomy without use of electrocautery
Endoscopic mucosal resection	Technique involving injecting solution into submucosal space to separate mucosal lesion from underlying muscularis propria; lesion can then be removed by snare
Underwater EMR	Technique involving full water immersion so that mucosa and submucosa involute as folds while muscularis propria remains circular; lesion is then resected by hot snare
Endoscopic submucosal dissection	Technique involving lifting by submucosal injectant and using ESD knife to create incision around lesion's perimeter and to dissect through expanded submucosal layer for en bloc resection
Hybrid ESD	Partial submucosal dissection followed by en bloc snare resection

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Table 2. (*continued*)

Abbreviations and terms	Definition
Endoscopic full thickness resection	Technique involving the use of a full-thickness resection device for lesions <30 mm
Cold or hot avulsion	Variant of biopsy technique for resection of fibrous residual or recurrent tissue that is non-lifting or difficult to capture with a snare. The hot avulsion technique uses endocut current (not coagulation current) and pulls the tissue away in the forceps as the current is applied.
Argon plasma coagulation	Ablative technique requiring use of ionization of argon gas by electrocautery to prevent deep tissue injury
Snare tip soft coagulation	Ablative technique requiring use of a microprocessor-controlled generator capable of delivering fixed low-voltage output, which is capped at 19 volts to prevent deep tissue injury
Chromoendoscopy	Application of dye to the colon mucosa or in the submucosal injectant for contrast enhancement to improve visualization of epithelial surface detail and resection plane
Intraprocedural bleeding	Bleeding that occurs during procedure requiring endoscopic intervention
Post-procedural bleeding	Bleeding that occurs up to 30 d after procedure requiring clinical intervention

Paris Classification Superficial Lesions, Type 0

The classification of type 0 lesions is based on the distinction between polypoid (type 0-I); and non-polypoid, (type 0-II). The polypoid type consists of pedunculated (type 0-Ip), and sessile (type 0-Is) lesions. The non-polypoid type 0-II lesions are divided by the absence (superficially elevated [type 0-IIa] and flat [type 0-IIb]) or the presence of a depression (type 0-IIc). The non-polypoid, excavated (type 0-III) lesions are rare in the colon. Although depressed (0-IIc) lesions are uncommon (1%–6% of non-polypoid lesions), their risk of submucosal invasion is the highest: the overall risk is reported to be 27%–35.9% compared with 0.7%–2.4% in flat (0-IIa) lesions. More than 40% of small (6–10 mm) depressed (0-IIc) lesions contain submucosal invasive cancer; virtually all large (>20 mm) depressed (0-IIc) lesions have submucosal invasion.[15–18]

Lateral Spreading Tumors

Non-polypoid lesions 10 mm or larger in diameter are referred to as laterally spreading tumors (LSTs). They have a low vertical axis and extend laterally along the colonic luminal wall. The morphologic subclassifications of LSTs facilitate the endoscopic removal plan, as they inform about submucosal fibrosis or the risk of submucosal invasion. Granular-type LSTs have a nodular surface and are composed of the homogeneous even-sized (LST-G-H) and mixed (LST-G-NM) nodular subtypes. Non-granular type LSTs have a smooth surface and are comprised of the flat elevated (LST-NG-FE) and pseudodepressed (LST-NG-PD) subtypes (Figure 2).[19] LST-G-H have the lowest risk (0.5%; 95% confidence interval [CI], 0.1%–1.0%), whereas LST-NG-PD have the highest risk of submucosal invasion (31.6%; 95% CI, 19.8%–43.4%).[19]

Table 3. **Grading of Recommendations Assessment, Development, and Evaluation Ratings of Evidence and Strength of Recommendations**

Rating of evidence	Definition
A: High quality	Further research is very unlikely to change our confidence in the estimate of effect
B: Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
C: Low quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
D: Very low quality	Any estimate of effect is very uncertain

NOTE. “Strength of recommendation” is determined by the balance between desirable and undesirable consequences of alternative management strategies, quality of evidence, variability in values and preferences, and resource use. Wording of recommendations was based on the strength of recommendation: “recommend” was used for strong recommendations and “suggest” was used for conditional recommendations. “Strong recommendations” are those that would be chosen by most informed patients. “Conditional recommendations” are those where patient values and preferences might play a larger role than the existence or quality of evidence.

Optical Diagnosis

Endoscopic prediction of the histologic class of a polyp may influence the resection approach to ensure complete removal. A number of studies, including several meta-analyses, have shown that optical diagnosis of colorectal lesions is feasible in routine clinical practice and comparable to the current reference standard, histopathology.[20,21] The endoscopist’s level of confidence in the optical diagnosis of a colorectal lesion is an important factor in its application to clinical practice. Although the majority of lesions have typical endoscopic features that enable a high confidence prediction of histology, in lesions that lack clear features, optical diagnosis performance may be decreased. For example, in a meta-analysis of 28 studies on optical diagnosis of colorectal lesions, the highest performance of real-time optical diagnosis of colorectal polyps was achieved when the diagnosis was made with high confidence—the area under the hierarchical summary receiver-operating characteristic curve was 0.95 (95% CI, 0.93–0.97) for polyps of any size, and 0.92 (95% CI, 0.92–0.96) for diminutive (≤5 mm) ones. This compares to the overall area under the hierarchical summary receiver-operating characteristic curve of 0.92 (95% CI, 0.90–0.94).

The Narrow Band Imaging International Colorectal Endoscopic (NICE) classification provides a validated criterion for the classification of type 1 (serrated class lesions–hyperplastic and sessile serrated lesions) and type 2 (adenomas), as well as those with deep

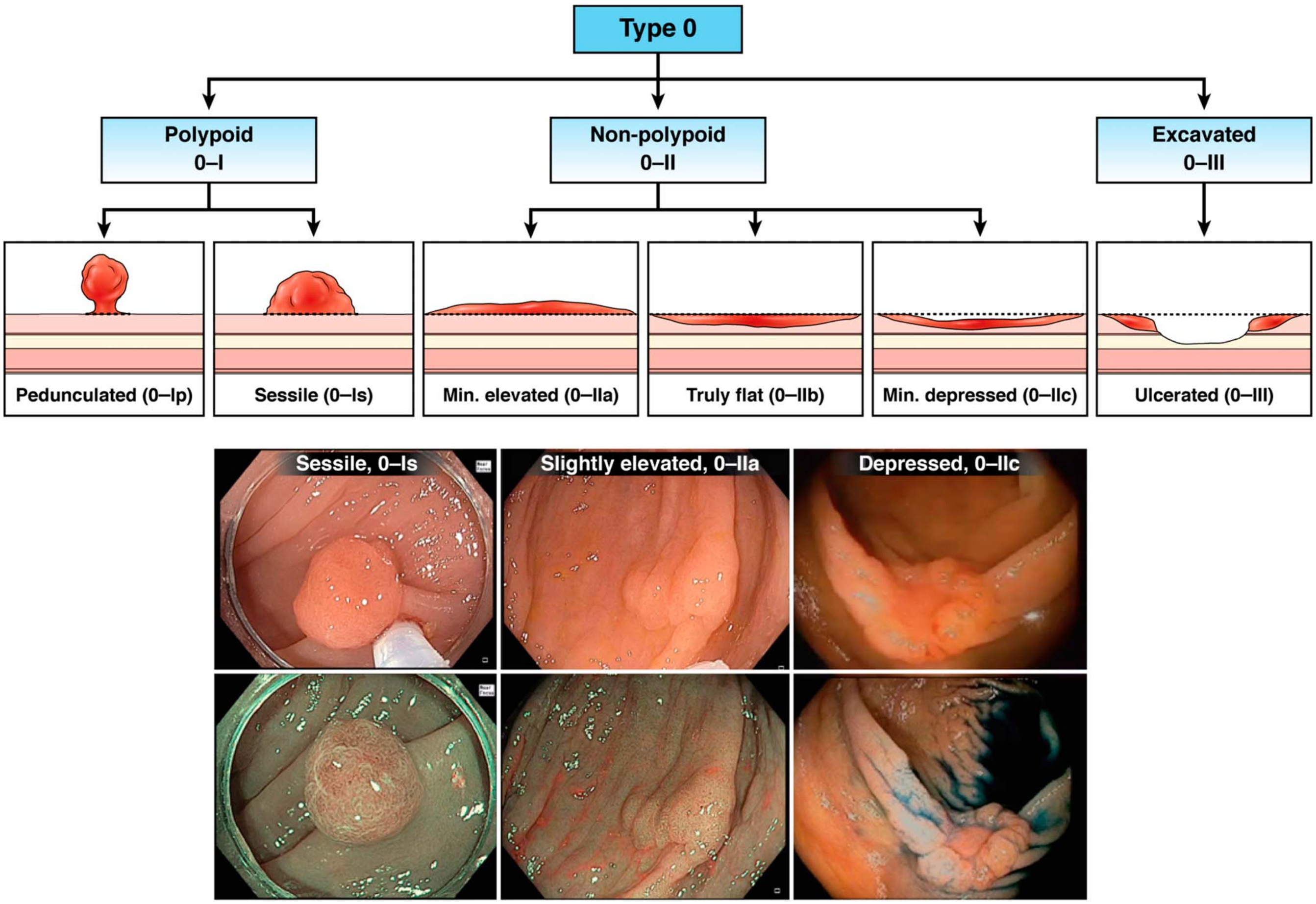

Figure 1. Paris Endoscopic Classification of superficial neoplastic lesions in the colon and rectum.

submucosal invasion (type 3), using real-time NBI during colonoscopy[22,23] (Figure 3). Its application has been shown to be useful in assessing the most clinically relevant approaches: leave hyperplastic diminutive lesions of the rectum and sigmoid colon, remove all adenomas anywhere in the colon and any serrated lesions proximal to sigmoid colon and >5 mm, and biopsy and refer to surgery lesions with deep submucosal invasion. Using this classification, experienced endoscopists have achieved 93% concordance of surveillance intervals made by real-time optical diagnosis and pathology, and a >90% negative predictive value for rectosigmoid lesions when assessments were made with high confidence.[21] A feature that has been associated with conventional adenomas is a valley in the surface topography that appears red in white light and brown in NBI relative to the rest of the polyp surface. Although insensitive (<50%), the valley sign was highly specific (>90%) for conventional adenoma in diminutive (≤5 mm) lesions, suggesting it to be a valid predictor of adenomatous histology in diminutive colorectal lesions.[24] Other endoscopic classifications of colorectal lesions using newer technologies warrant further investigation.

The subtle endoscopic appearance of large sessile serrated lesions—predominantly flat in shape with indistinct borders—has been associated with high rates of incomplete removal compared to conventional adenomas (31% vs 7.2%), with even higher rates (47.6%) in large lesions.[6] A mucous cap may be present in some sessile serrated lesions and facilitate detection. The WASP (Workgroup Serrated Polyps and Polyposis) criteria added 4 sessile serrated lesion features (ie, clouded surface, indistinctive borders, irregular shape, and dark spots inside crypts) to the NICE classification (Figure 4)[25] and showed that high confidence assessment of lesions could accurately (91%) distinguish sessile serrated lesions from non–sessile serrated lesions.[26] Within a serrated lesion, areas with a distinct surface pattern change (with NICE Type 2 features) or a nodular component are suggestive of cytologic dysplasia.[27] Identification of higher-risk lesions may influence endoscopic therapeutic strategy, pathology awareness, and surveillance recommendations.[28]

Unfavorable histologic features of colorectal lesions, such as lymphovascular invasion, tumor budding, or poor differentiation, are not feasible to endoscopically predict before resection. However, the vertical depth of invasion of submucosal cancers can be estimated based on the morphologic appearance using high-definition endoscopy without magnification. Lesion morphology, such as Paris classification 0-IIc and 0-IIa + 0-IIc, non-granular surface particularly pseudodepressed subtype, NICE type 3,[23] and Kudo pit pattern V,[29] as well as white spots (chicken skin appearance), redness, expansion, firmness, and fold convergence,[30] are associated with submucosal invasive carcinoma (Video 1, http://links.lww.com/AJG/B420, http://links.lww.com/AJG/B421). The NICE type 3 and Kudo Vn patterns are specific for deep (>1000 μm) invasion. Deep submucosal invasion in a non-pedunculated lesion is associated with a substantial risk of residual cancer in the bowel wall or

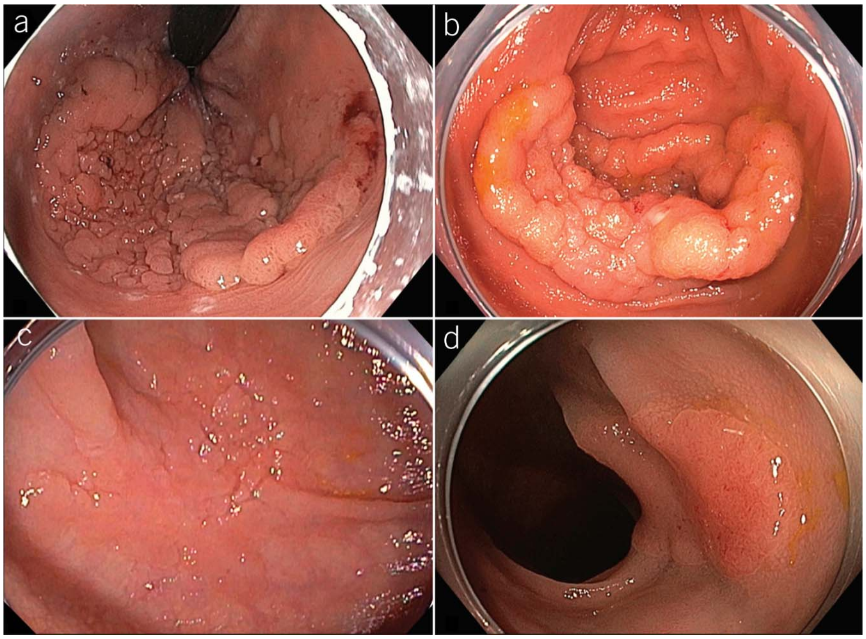

Figure 2. Lateral spreading lesions. Non-polypoid lesions ≥10 mm in diameter are referred to as laterally spreading tumors (LSTs). They have a low vertical axis and extend laterally along the luminal wall. LSTs are morphologically subclassified into granular type (LST-G) (*A, B*), which have a nodular surface, and non-granular type (LST-NG), which have a smooth surface (*C, D*). This macroscopic distinction is important to facilitate the endoscopic removal plan as it provides information about the risk of cancer or submucosal fibrosis in order to anticipate the technical ease or difficulty of the removal. Overall, LSTs were found to contain submucosal invasion (SMI) in 8.5% of the cases (95% CI, 6.5%–10.5%; I^2 86.8%; 26 studies) and high-grade dysplasia in 36.7% of the cases (95% CI 30.3%–43.2%; I^2 91.9%; 23 studies). Non-granular LSTs more often contained SMI than granular LSTs: 11.7% vs 5.9% (OR, 1.89; 95% CI, 1.48–2.42).

lymph nodes after any form of endoscopic resection. Therefore, the presence of these features should be followed by cold biopsy of the portion of the lesion demonstrating the features, tattoo of the area, and referral to surgery. Non-pedunculated lesions with superficial (<1000 μm) submucosal invasion are candidates for endoscopic resection. However, there are no endoscopic features that are sensitive in predicting superficial submucosal invasion. Non-granular morphology, particularly when associated with depression (Paris 0-IIc) or bulky (Paris 0-Is) shape, is associated with an increased risk of superficial invasion. When feasible, en bloc endoscopic resection, followed by pinning of the retrieved specimen to a flat surface (eg, cork, foam) and sectioning of the lesion perpendicular to the resection plane, allows accurate pathologic measurement of the depth of invasion. Specimens from lesions with endoscopic features suspicious for advanced histology, submucosal invasion, or cancer should be submitted in individual bottles for pathologic analysis.

SECTION II: ENDOSCOPIC REMOVAL TECHNIQUES

Statement 2: Lesion Removal

The primary aim of polypectomy is complete removal of the colorectal lesion and the subsequent prevention of CRC. Endoscopists should employ the safest, most complete, and efficient resection techniques based on available evidence.

Polypectomy techniques vary widely in clinical practice. They are often driven by physician preference based on how they were taught and on trial and error, due to the lack of standardized training and the paucity of published evidence. In the past decade, evidence has evolved on the superiority of specific methods. Although more recent practice surveys suggest an increased uptake in the use of cold snare removal techniques for diminutive and small colorectal lesions and EMR for large colorectal lesions, considerable heterogeneity in management techniques persist.[31–34] In a large survey of gastroenterologists and surgeons, physician specialty was strongly associated with management strategies. For example, surgeons were most likely to recommend surgical resection of complex benign colorectal lesions compared with gastroenterologists who were the least likely.[13]

Alarmingly, surgery for non-malignant colorectal lesions remains common practice.[35–37] In the United States, colectomy for benign colon lesions has significantly increased over the last 14 years, representing one-quarter of colectomy procedures.[38] One study showed rate increases from 6% in 2000 to 18% in 2014, for a mean (SD) lesion size of 27 (17) mm.[39] This practice trend has occurred despite professional society and guideline recommendations for endoscopic removal as the first-line treatment. Endoscopic removal of benign colorectal lesions is more cost-effective than surgery, and is associated with lower morbidity and mortality.[40,41] Data analyzed from a National Surgical Quality Improvement Program from 2011 through 2014, including 12,732 patients who underwent elective surgery for non-malignant colorectal lesions, showed a 0.7% 30-day mortality rate and 14% risk of major postoperative adverse events—with 7.8% readmissions, 3.6% redo surgeries, 1.8% colostomies, and 0.4% ileostomies.[42] By comparison, the 30-day mortality associated with endoscopic resection of large colorectal lesions was only 0.08% in a review of 6440 patients,[43] and zero in a prospective study of 1050 advanced colorectal lesions.[44]

Therefore, endoscopists should employ techniques that reflect the safest, most complete or effective, and most efficient resection

	Type 1	Type 2	Type 3
Color	Same or lighter than background	Browner relative to background (verify color arises from vessels)	Brown to dark brown relative to background; sometimes patchy whiter areas
Vessels	None, or isolated lacy vessels may be present coursing across the lesion	Brown vessels surrounding white structures**	Has area(s) of disrupted or missing vessels
Surface pattern	Dark or white spots of uniform size, or homogeneous absence of pattern	Oval, tubular, or branched white structures** surrounded by brown vessels	Amorphous or absent surface pattern
Most likely pathology	Hyperplastic and sessile serrated lesions***	Adenoma****	Deep submucosal invasive cancer

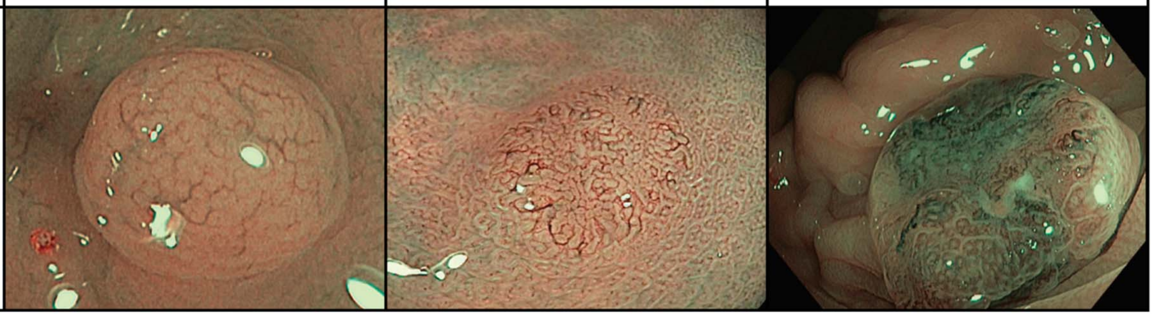

Figure 3. Optical diagnosis of colorectal lesions, NICE classification. The diagnostic criteria for colorectal lesions using NBI as recommended in the NICE classification. The use of confidence levels (high or low) in making an optical diagnosis is important in its implementation in clinical practice. *Can be applied using colonoscopes with or without optical (zoom) magnification. **These structures (regular or irregular) may represent the pits and the epithelium of the crypt opening. ***In the World Health Organization classification, sessile serrated polyp and sessile serrated adenoma are synonymous. Sessile serrated polyps often demonstrate some dark, dilated crypt orifices. ****Type 2 consists of Vienna classification types 3, 4, and superficial 5 (all adenomas with either low- or high-grade dysplasia, or with superficial submucosal carcinoma). The presence of high-grade dysplasia or superficial submucosal carcinoma may be suggested by an irregular vessel or surface pattern, and is often associated with atypical morphology (eg, depressed area).

techniques based on available evidence. A suggested management algorithm is presented in Figure 5.

2a: Diminutive (≤5 mm) and small (6–9 mm) lesions

- We recommend cold snare polypectomy to remove diminutive (≤5 mm) and small (6–9 mm) lesions due to high complete resection rates and safety profile. (Strong recommendation, moderate-quality evidence)
- We recommend against the use of cold forceps polypectomy to remove diminutive (≤5 mm) lesions due to high rates of incomplete resection. For diminutive lesions ≤2 mm, if cold snare polypectomy is technically difficult, jumbo or large-capacity forceps polypectomy may be considered. (Strong recommendation, moderate-quality evidence)
- We recommend against the use of hot biopsy forceps for polypectomy of diminutive (≤5 mm) and small (6–9 mm) lesions due to high incomplete resection rates, inadequate histopathologic specimens, and complication rates. (Strong recommendation, moderate-quality evidence)

Diminutive (≤5 mm) lesions Most colorectal lesions are diminutive (≤5 mm). At that size, they are almost always benign,[45,46] rarely harboring high-grade dysplasia or cancer (0.06%).46 Their removal using cold forceps polypectomy has been associated with high rates of incomplete resection, ranging from 9% to 61%.[47–50] Although large-capacity forceps polypectomy is superior for complete removal compared to standard forceps polypectomy, more than 1 bite is typically required (2.5 standard vs 2.2 jumbo).[48] The disruption of the mucosal surface and bleeding from the first biopsy bite may interfere with visualization and subsequent assessment of the completeness of resection thereafter. The use of enhanced imaging techniques, such as NBI, of the post-polypectomy defect has not improved completeness of resection.[51] Cold forceps resection, if necessary, should thus be limited to diminutive lesions (≤2 mm) and generally only to those when resection in a single bite is anticipated.

The risk of incomplete removal of diminutive lesions can be reduced with the use of cold snare polypectomy techniques (79%).[52] The cold snare polypectomy technique is a more complete polyp removal method because it can ensnare a few millimeters of normal mucosa around the polyp perimeter as the snare is closed (Figure 6, Video 2, http://links.lww.com/AJG/B443). This allows for en bloc lesion capture and mechanical transection of the tissue, without electrocautery risk.[53,54] A systematic review and meta-analysis of 3 prospective studies on cold resection techniques for diminutive

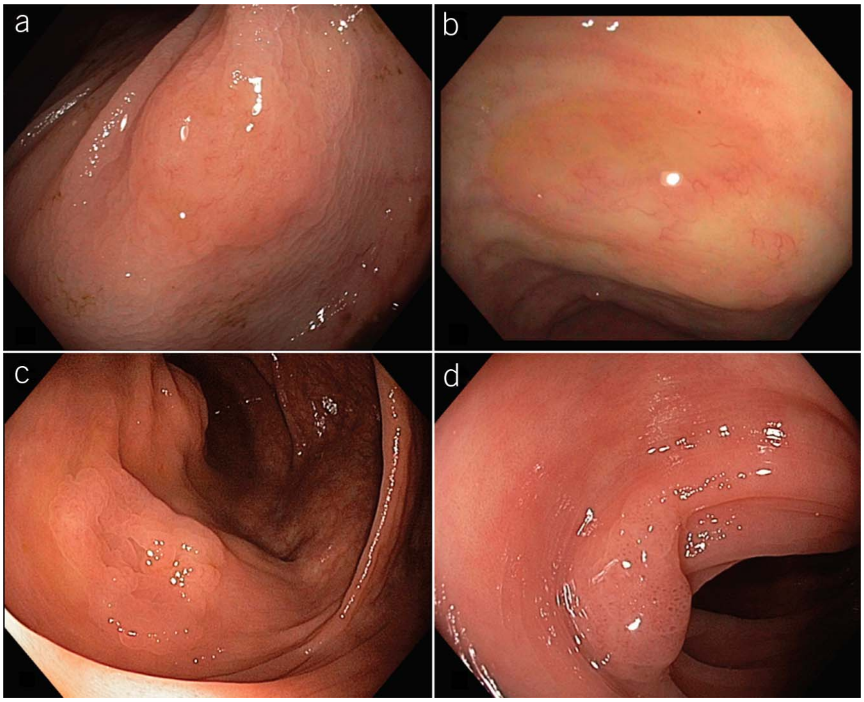

Figure 4. Morphologic features of sessile serrated lesions. Sessile serrated lesion–like features are defined as (*A*) a clouded surface, (*B*) indistinctive borders, (*C*) irregular shape, or (*D*) dark spots inside the crypts. These morphologic features are used to differentiate between sessile serrated lesions and hyperplastic lesions in the type 1 NICE polyps. The presence of at least 2 sessile serrated lesion–like features is hereby considered sufficient to diagnose a sessile serrated lesion.

(≤5 mm) lesions showed a significantly lower incomplete polyp removal rate with the cold snare compared to cold forceps polypectomy (relative risk, 0.21; 95% CI, 0.14–0.67) without heterogeneity and reported no adverse events.[52] These findings showing superiority of cold snare polypectomy to other cold polypectomy techniques have been replicated in a network meta-analysis, and are strongest for lesions ≥4 mm.[55]

Cold snare polypectomy is a safe, effective, and efficient polypectomy technique for diminutive (≤5 mm) colorectal lesions compared to hot polypectomy techniques. A recent randomized trial on 3–5 mm colorectal lesion removal showed significantly lower incomplete polyp removal rates with cold snare (19.6%) compared to hot forceps polypectomy (53.6%) ($P < .0001$).[56] No cases of perforation or delayed bleeding occurred in either group, although the rate of severe tissue injury to the pathologic specimen was higher in the hot forceps polypectomy group than cold snare polypectomy group (52.6% [71 of 135] vs 1.3% [2 of 148]; $P < .0001$). Another prospective, multicenter, randomized controlled, parallel non-inferiority trial of 796 lesions 4–9 mm in size showed complete resection rates for cold snare polypectomy (98.2%) comparable to those for hot snare polypectomy (97.4%), based on specimens obtained from the resection margin after polypectomy.[57] Post-operative bleeding requiring endoscopic hemostasis occurred only in the hot snare polypectomy group (0.5% [2 of 402 polyps]). Notably, the majority (62.7%) of the lesions studied were diminutive (4–5 mm) in size; 217 of 346 lesions in the hot snare polypectomy group and 214 of 341 lesions in the cold snare polypectomy group.

Small (6–9 mm) lesions Resection methods for small lesions have been highly variable among colonoscopists. The Complete Adenoma Resection (CARE) Study underscored the frequency of incomplete polypectomy, even for small lesions.[6] They observed a 6.8% incomplete resection rate for lesions 6–9 mm removed by hot snare technique. Cold snare and hot snare resection are distinct techniques. Cold resection methods induce less injury to the submucosal arteries than polypectomy methods using electrocautery,[58,59] and thus, decrease the risk of delayed bleeding and perforation (Video 3, http://links.lww.com/AJG/B444).[60] Prospective randomized comparisons have recently shown the efficacy of cold snare vs hot snare polypectomy for small lesions and a superior safety profile compared to hot snare polypectomy, with decreased incidence of delayed post-polypectomy bleeding and coagulation syndrome.[57,61–63] Another prospective study of patients who underwent follow-up colonoscopy 3 weeks after cold snare polypectomy for lesions <9 mm confirmed high rates of complete resection (residual adenoma rate, 0.98%) based on scar assessment and biopsy.[64] Additional studies have shown sufficient resection width and depth using cold snare polypectomy, including muscularis mucosa in the majority of specimens.[65]

Clinical trials have not defined the optimal snare choice for effective cold snare polypectomy. A study of a cold snare (0.3 mm wire, 9 mm diameter, diamond shape, stiff catheter) compared to a conventional snare (0.47 mm, 10 mm diameter oval shape, softer catheter) showed significantly higher complete resection of small lesions (≤10 mm), with dedicated cold snare vs conventional snare (91% vs 79%; $P = .015$), particularly for lesions 8–10 mm in diameter.[66] The impact of specific snare characteristics on cold snare polypectomy outcomes warrants further study.

Cold snare polypectomy has been shown to be a more efficient removal technique for lesions ranging from 3–8 mm in size compared to cold forceps or hot snare polypectomy. The total procedure time was significantly shorter using cold snare (or

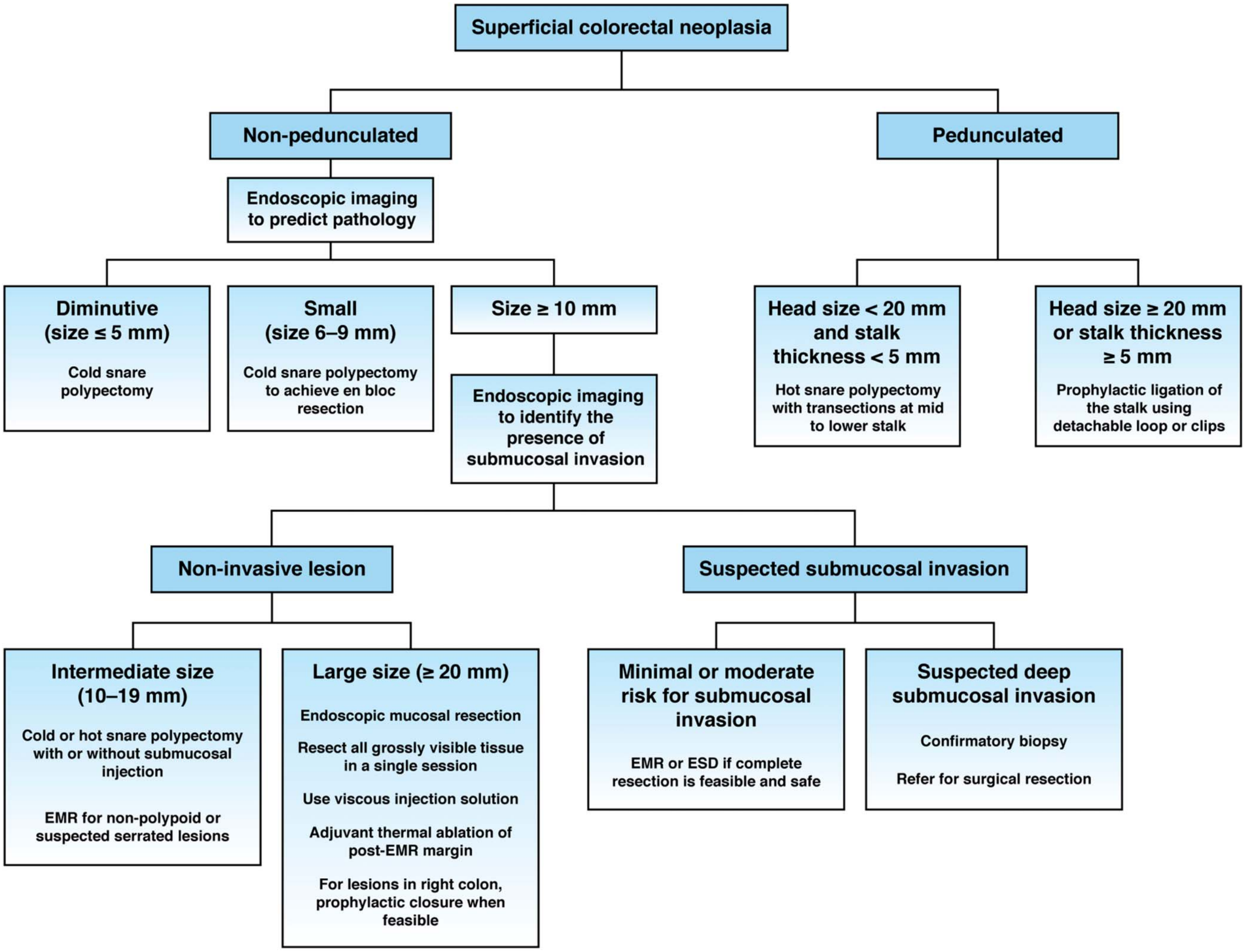

Figure 5. Algorithm for the management of colorectal lesions.

jumbo forceps) polypectomy compared to cold forceps techniques by an average of 2.66 minutes (95% CI, 0.18–5.14 minutes). Randomized trials of cold snare polypectomy have reported retrieval rates between 81% and 100%.[67–69]

2c: Non-pedunculated (10–19 mm) lesions

- We suggest cold or hot snare polypectomy (with or without submucosal injection) to remove 10–19 mm non-pedunculated lesions. (Conditional recommendation, low-quality evidence)

Optimal methods for removal of sessile lesions measuring 10–19 mm remain uncertain. However, EMR should be considered for non-polypoid and serrated lesions in the 10- to 19-mm size range. Studies have shown that using conventional polypectomy techniques for non-polypoid lesions ≥10 mm[70] and serrated lesions proximal to the sigmoid colon poses a challenge for complete endoscopic removal. The lesion borders are often indistinct, and the tissue may be difficult to capture with a snare. A recent study of 199 patients with proximal serrated lesions with a mean size of 15.9 ± 5.3 mm showed low rates of local recurrence (3.6%; 95% CI, 0.5%–6.7%) during a mean follow-up period of 25.5 ± 17.4 months when removed by EMR.[71] This is in contrast to a 31.0% incomplete resection rate reported when removed by conventional polypectomy techniques.[6]

2d: Non-pedunculated (≥20 mm) lesions

- We recommend EMR as the preferred treatment method of large (≥20 mm) non-pedunculated colorectal lesions. Endoscopic resection can provide complete resection and obviate the higher morbidity, mortality, and cost associated with alternative surgical treatment. (Strong recommendation, moderate-quality evidence)
- We recommend an endoscopist experienced in advanced polypectomy to manage large (≥20 mm) non-pedunculated colorectal lesions. (Strong recommendation, low-quality evidence)
- We recommend snare resection of all grossly visible tissue of a lesion in a single colonoscopy session and in the safest minimum number of pieces, as prior failed attempts at resection are associated with higher risk for incomplete resection or recurrence. (Strong recommendation, low-quality evidence)
- We suggest the use of a contrast agent, such as indigo carmine or methylene blue, in the submucosal injection solution to

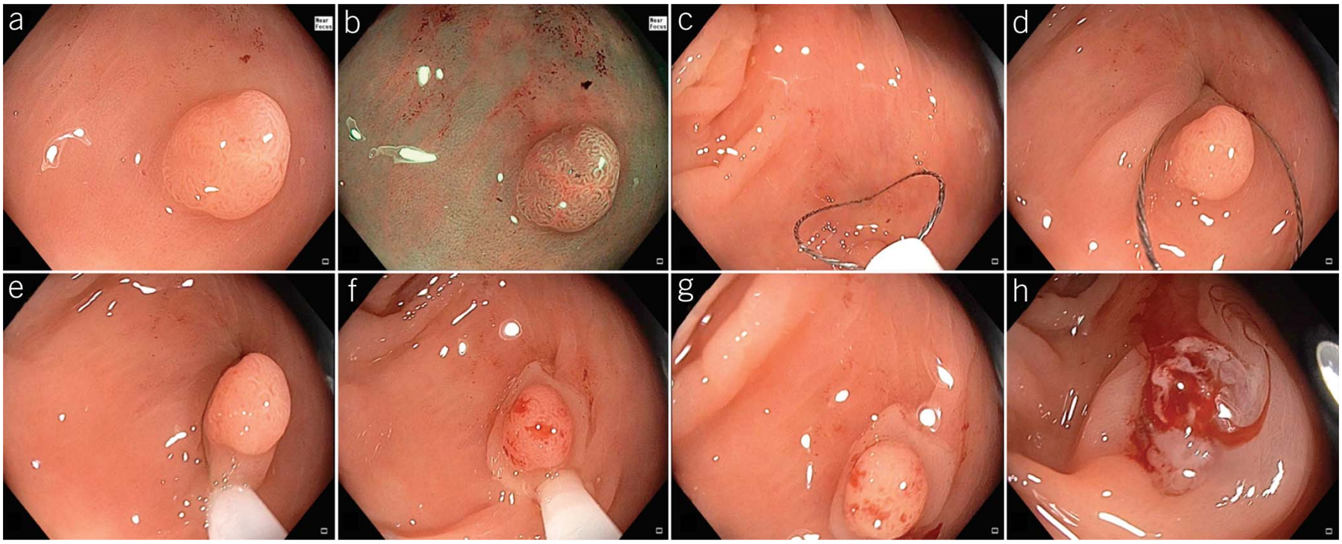

Figure 6. Cold polypectomy technique. (*A*) Diminutive colon lesion in white light. (*B*) Lesion characterization as a diminutive colon adenoma with type 2 NICE features using NBI. (*C*) Position the lesion at 5 o'clock in line with the colonoscope accessory channel. Engage the snare tip against the mucosa on the proximal side of the lesion and open slowly. (*D*) Open the snare until it has normal surrounding tissue and slightly move the endoscope distally as the snare is being opened according to the size of the lesion. (*E*) While the snare is initially "closed" in a slow and steady manner, keep the endoscope tip deflection downward to apply gentle pressure against the mucosa (the ensnared polyp should not be lifted or tented during closure). (*F*) Continue to maintain some tension on the snare catheter with gentle forward pressure during closure in order to avoid slipping of the snare upwards away from the submucosa and consequent shaving of the lesion. As the snare wire is closed, it will capture normal tissue. (*G*) Once you have secured the normal tissue, then the lesion can be "cut." The snare "close" is slow and steady, the snare "cut" is faster. The normal borders can be seen at the perimeter of the lesion in the cold snare specimen (*G*). In the 5 o'clock position, the cut polyp typically remains in place for efficient retrieval. (*H*) Minor post–cold snare oozing is expected and self-limiting.

facilitate recognition of the submucosa from the mucosa and muscularis propria layers. (Conditional recommendation, moderate-quality evidence)

- We recommend against the use of tattoo, using sterile carbon particle suspension, as the submucosal injection solution. The carbon particle suspension may result in submucosal fibrosis,

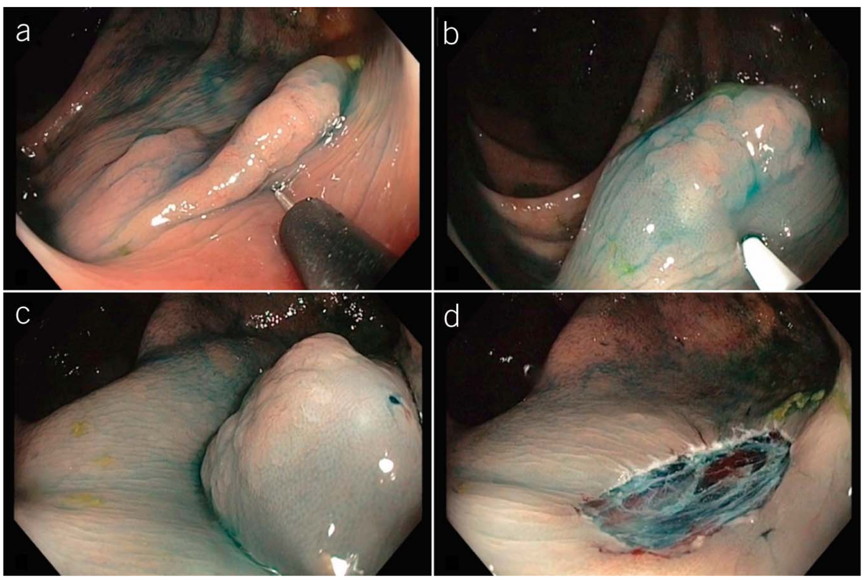

Figure 7. Inject-and-cut EMR. (*A*) We evaluate a 15-mm superficially elevated serrated–appearing lesion under white light with diluted indigo carmine solution. In preparation for resection, we ensure the targeted lesion to the 5–6 o'clock position and plan the path of injection. (*B*) We place the needle catheter next to the lesion to then expose and insert the needle into the submucosa. We rapidly inject the mixture of saline and diluted indigo carmine into the submucosa with simultaneous adjustments of the needle catheter and endoscope tip to ultimately lift the lesion upward. As the injection proceeds to the right, the direction of the injection is slightly altered to the left and then upward again in order to guide the creation of the focal submucosal bleb. (*C*) During this process, we slightly suction the lumen in order to decrease wall tension, and then are able to place a snare around the lesion, and (*D*) perform complete en bloc resection.

Table 4. Submucosal Injectants for Endoscopic Resection

Injectant name	Concentration	Unit size	Company	En bloc resection rates for lesions ≥2 cm, %	Residual lesion rates for lesions ≥2 cm, %	Price, $ (cost/MSRP)	FDA approved (available in the United States)?
ORISE Gel	—	2 × 10-mL syringe per kit	Boston Scientific	No data	No data	195 (97.50/ 10 mL)	Yes
Eleview	0.001% methylene blue	5 × 10-mL ampules per kit	Aries Pharmaceutical	18.6 (Repici et al[87])	0 18.6, adverse events (Repici et al)	462.50 (92.50/ 10 mL)	Yes
Normal saline solution	0.9% NaCl, may add dilution of indigo carmine or methylene blue	10 mL	Various	20.5–29 (Yandrapu et al[86])	13.46 (Yandrapu et al[86])	<0.01/mL	No
Succinylated gelatin	0.09 mg/mL methylene blue	10 mL	—	No data	No data	0.02/mL	No
Glyceol	10% glycerin; 5% fructose	—	Chugai Pharmaceutical	23.1 (Uraoka et al[197])	No data	0.01–0.03/ mL	No
Dextrose	50%	10-mL syringe	Various	54 (Katsinelos et al[82])	87.5 (Katsinelos et al[82])		No
Fibrinogen	1 g fibrinogen, 50 mL NS, 0.5 mL Indigo carmine, 0.5 mL 1:1000 epinephrine	—	Green Cross Corps	No data	60 (Lee et al[85]; n = 35)	0.2/mL	No
Sodium hyaluronate	0.4% sodium hyaluronate 5% indigo carmine	—	—	67 (LSTs only)	No data	50–120/mL	No

FDA, US Food and Drug Administration; MSRP, manufacturer suggested retail price; NS, normal saline.

and can thus reduce the technical success of future endoscopic resection of residual or recurrent lesion. (Strong recommendation, low-quality evidence)

- We suggest the use of a viscous injection solution (eg, hydroxyethyl starch, Eleview, ORISE Gel) for lesions ≥20 mm to removal the lesion in fewer pieces and less procedure time compared to normal saline. (Conditional recommendation, moderate-quality evidence)
- We recommend against the use of ablative techniques (eg, argon plasma coagulation [APC], snare tip soft coagulation) on endoscopically visible residual tissue of a lesion, as they have been associated with an increased risk of recurrence. (Strong recommendation, moderate-quality evidence)
- We suggest the use of adjuvant thermal ablation of the post-EMR margin, where no endoscopically visible adenoma remains despite meticulous inspection. There is insufficient evidence to recommend a specific modality (ie, APC, snare tip soft coagulation) at this time. (Conditional recommendation, moderate-quality evidence)
- We recommend detailed inspection of the post-resection mucosal defect to identify features for immediate or delayed perforation risk, and perform endoscopic clip closure, accordingly. (Strong recommendation, moderate-quality evidence)
- We suggest prophylactic closure of resection defects ≥20 mm in size in the right colon, when closure is feasible. (Conditional recommendation; moderate-quality evidence)
- We suggest treatment of intraprocedure bleeding using endoscopic coagulation (eg, coagulation forceps or snare-tip soft coagulation) or mechanical therapy (eg, clip), with or without the combined use of dilute epinephrine injection. (Conditional recommendation, low-quality evidence)
- We suggest that patients on anti-thrombotics who are candidates for endoscopic removal of a colorectal lesion ≥20 mm receive individualized assessment, balancing the risks of interrupting anticoagulation for colonoscopic polypectomy or mucosal resection against the risks of significant bleeding during and after the procedure. (Conditional recommendation, low-quality evidence)

ENDOSCOPIC MUCOSAL RESECTION FOR FLAT AND SUSPECTED SERRATED LESIONS

EMR is the preferred treatment method of large (≥20 mm) non-pedunculated colorectal lesions (Figure 7, Video 4, http://links.lww.com/AJG/B445, http://links.lww.com/AJG/B431, http://links.lww.com/AJG/B432). Used according to its indications, it provides curative resection and obviates the higher morbidity, mortality, and cost associated with alternative surgical treatment.[40,41,44,72–78] Its safety and efficacy has been shown. A systematic review of 50 studies including 6442 patients reported low risk of severe adverse events (1%) and low rates of local recurrence (14%).[43]

Recurrences were predominantly retreated with endoscopic therapy. There was a 0.3% (95% CI, 0.1%–0.4%) risk of invasive CRC at follow-up. The meta-analysis results, however, may underestimate the true post-endoscopic recurrence rate, as the main discriminator among the individual studies was the adequacy of follow-up. In 17 series it was considered inadequate, mainly due to short duration.

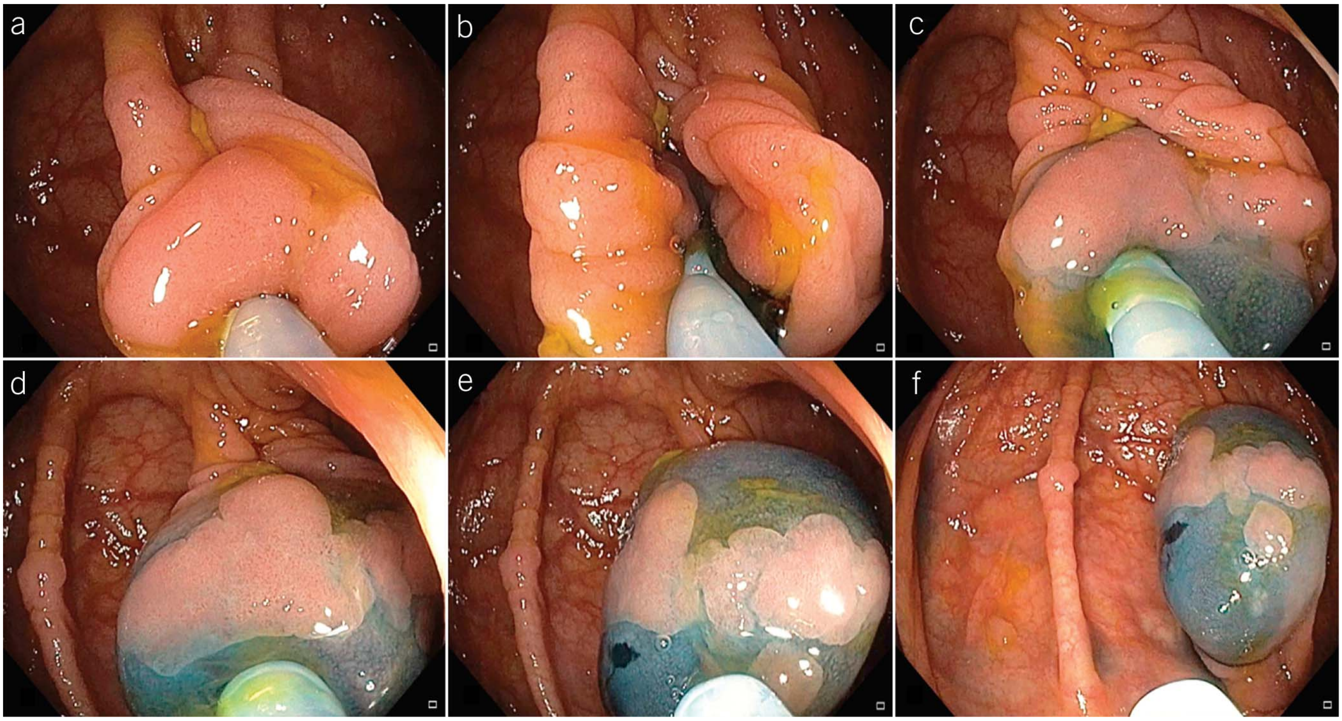

Figure 8. Dynamic submucosal injection technique. (*A*) We evaluate thickened fold under white light and can appreciate a non-polypoid, non-granular lateral spreading lesion overlying the fold. We place the needle catheter next to the lesion to then expose and insert the needle into the submucosa. (*B*) We stab the mucosa with the needle to enter the submucosal space and then rapidly inject the mixture of saline and diluted indigo carmine into the submucosa (*C*), while simultaneously pulling the needle catheter back into the endoscope and (*D*) making adjustments to the needle catheter and endoscope tip to ultimately lift the lesion upward. As the injection proceeds to the right, (*E*) the direction of the injection is slightly altered to the left and then upward again in order to guide the creation of the focal submucosal bleb. During this process, we slightly suction the lumen in order to decrease wall tension, and (*F*) then are able to ultimately create a polypoid bleb to place the snare around to capture the lesion for endoscopic resection.

Inject-and-Cut Endoscopic Mucosal Resection Technique

The inject-and-cut EMR is a simple technique that is widely used for removal of large non-pedunculated lesions.[79] Lesions <20 mm typically can be removed in a single piece (en bloc) when electrocautery is utilized, whereas lesions ≥20 mm more typically require piecemeal resection.

Submucosal injection is a key step of EMR. Many submucosal injectants are available (Table 4). The ideal submucosal injectate should be a widely available inexpensive solution that provides a sustained lift to facilitate safe and efficient piecemeal resection. Normal saline has been used most widely due its availability and low cost. Within a short time, however, saline may dissipate into the surrounding submucosal space. Thus, several colloid plasma volume-expanding solutions, such as sodium hyaluronate,[80,81] 50% dextrose solution,[82] hydroxyethyl starch,[83] succinylated gelatin,[84] and fibrinogen mixture,[85] have been investigated to facilitate resection of large lesions. A meta-analysis of 5 prospective, randomized controlled studies of colorectal EMR showed significantly higher rates of en bloc resection (odds ratio [OR], 1.91; 95% CI 1.11–3.29; $P = .02$; I^2 0%) and lower rates of residual lesions (OR, 0.54; 95% CI, 0.32–0.91; $P = .02$; I^2 0%) using a colloid solution compared to normal saline for injection of lesions >20 mm.[86] The mean polyp sizes were 20.84 mm with normal saline and 21.44 mm with a colloid solution. Notably, in the United States, hydroxyethyl starch is the only solution that is widely available at a relatively low cost.

More recently, a commercially available emulsion (Eleview; Aries Pharmaceuticals, San Diego, CA) composed of water for injection, medium-chain triglycerides as the oily phase, poloxamer 188 as the bulking/cushioning agent, polyoxyl-15-hydroxystearate as the surfactant, sodium chloride as the osmotic agent, and methylene blue as the dye, has been US Food and Drug Administration–approved for submucosal injection to lift colorectal lesions.[87] In a randomized,

Table 5. Suggested Electrocautery Setting[a]

Method	Mode	Effect	Cut duration	Cut interval	Maximum watts
Inject-and-cut EMR	Endocut Q	2/3	1	4	—
Snare tip soft coagulation	Soft Coag	5	—	—	80
Hot forceps avulsion	Endocut I	1	4	1	—
Underwater EMR	Autocut, Drycut	5	—	—	80

[a]For users of for users of other units would consult representative to identify settings that would approximate the tissue effects provided by these settings.

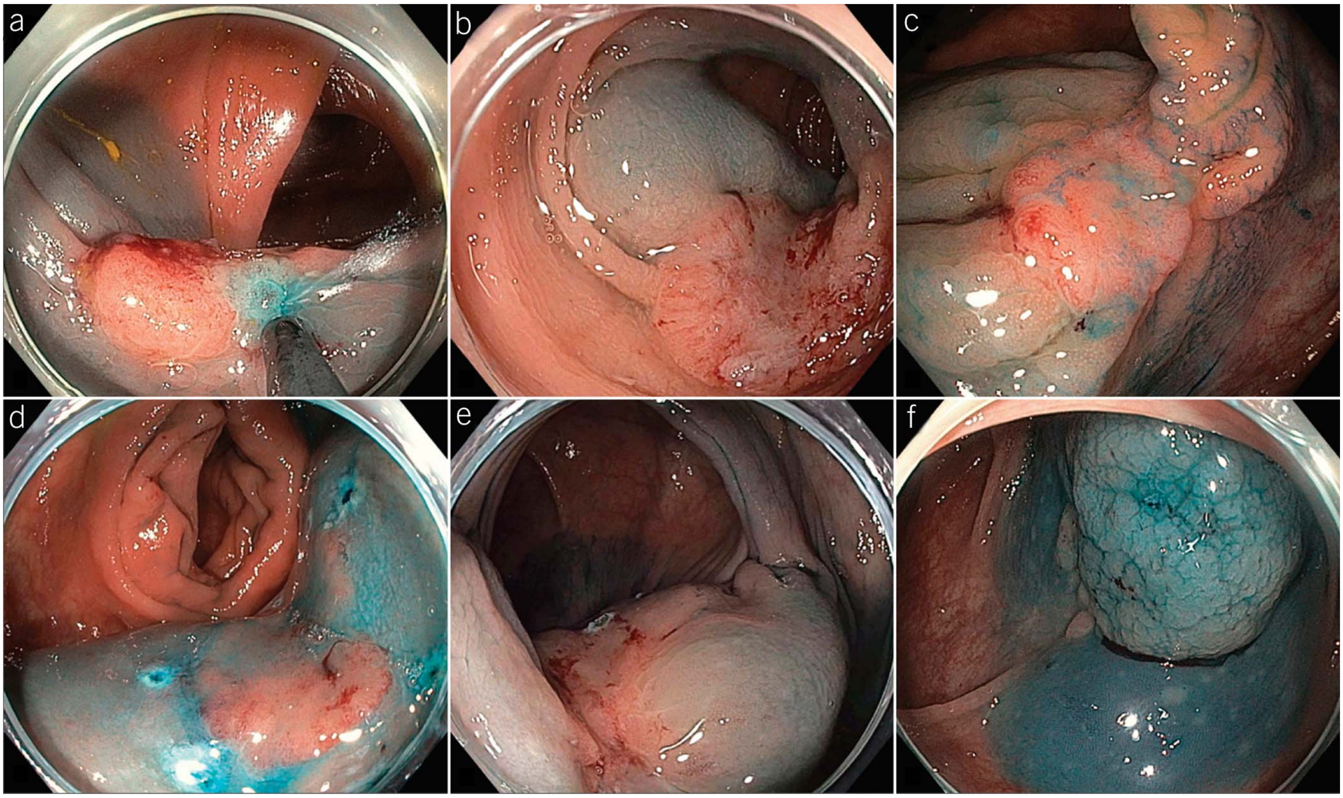

Figure 9. Non-lifting features of colon lesions. Injection of saline or viscous fluid into the submucosa beneath these lesions does not result in lifting of the lesion; instead, the lesions infold, as only the submucosa of the normal surrounding mucosa is expanded. The non-lifting sign may be due to submucosal invasion as shown in lesions (*A–C*); or underlying submucosal fibrosis in lateral spreading non-granular type lesions (*D*) or from prior polypectomy cautery (lesions *E* and *F*).

double-blind, multicenter clinical trial with parallel arms of 211 patients with a mean lesion size of 32 mm, injection with Eleview required less injection volume (16.1 mL; range of 3–41 mL vs 31.6 mL; range of 4–248 mL; $P < .001$) and had a shorter resection time 19.2 minutes, range of 1–100 minutes vs mean of 29.7 minutes, range of 2–687 minutes ($P = .326$) compared to injection using saline with methylene blue. In addition, when the commercial preparation injection was used, the lesions were removed in fewer pieces (11.9%; $P < .052$) and with more en bloc resections (58%; $P < .125$). Another commercially available viscous dyed solution (ORISE Gel, Boston Scientific, Marlborough, MA), which is prefilled into a standard Luer lock syringe, has been US Food and Drug Administration–approved for use in submucosal injection to lift gastrointestinal mucosa during endoscopic resection.

The technique of submucosal injection is a critical factor in the success of the lift and the shape and sustainability of the bleb. Dynamic submucosal injection creates a generous bulge under the lesion (Figure 8, Video 5, http://links.lww.com/AJG/B446), even when using normal saline.[88] In this technique, a small amount of solution is injected to confirm insertion into the submucosal layer, followed by rapid large-volume injection. Unlike the conventional static injection technique, in which the needle is kept stationary during the injection, dynamic submucosal injection involves a few simple maneuvers during injection to sculpt a focal bleb. During injection, the fluid is directed within the submucosa by slowly deflecting the tip of the endoscope toward the opposite wall, coupled with a slight pull back of the needle catheter and suctioning to desufflate the lumen.

A stiff snare is used to facilitate capturing of the tissue. After capturing the lesion with a snare, the lumen is insufflated with air to stretch the wall, and the snare is lifted up while the snare is slightly loosened to release any entrapped muscularis propria. The snare is then closed entirely and the lesion is then transected using microprocessor-controlled cautery. Suggested electrocautery settings are provided in Table 5.

All grossly visible tissue of a lesion should be resected in a single colonoscopy session and in the safest minimum number of pieces. Prior failed attempts at resection are associated with higher risk for incomplete resection or recurrence. Furthermore, ablative techniques, such as snare tip and APC for the ablation of residual grossly visible tissue, have been associated with an increased risk of recurrence thought to be due to incomplete treatment of deeper layers (Video 6, http://links.lww.com/AJG/B422, http://links.lww.com/AJG/B423).[89–91] Nonetheless, with piecemeal resection, ablation at the normal-appearing margins of the EMR defect using APC or snare tip soft coagulation may burn microscopic residual tissue to reduce the risk of recurrence. A small randomized trial of 21 patients with mean polyp size of 26 mm found that systematic ablation of the junction between the EMR defect and normal tissue after perceived complete snare resection resulted in a significantly lower recurrence rate ($P = .02$; OR, 0.06; 95% CI, 0–0.58, albeit the control arm had very high rates of recurrence (7 of 11).[92] A recent prospective multicenter Australian study of the application of the snare tip in the soft coagulation mode to the defect periphery and bridges also showed a significant reduction in recurrence rates (10 of 192 [5.2%])

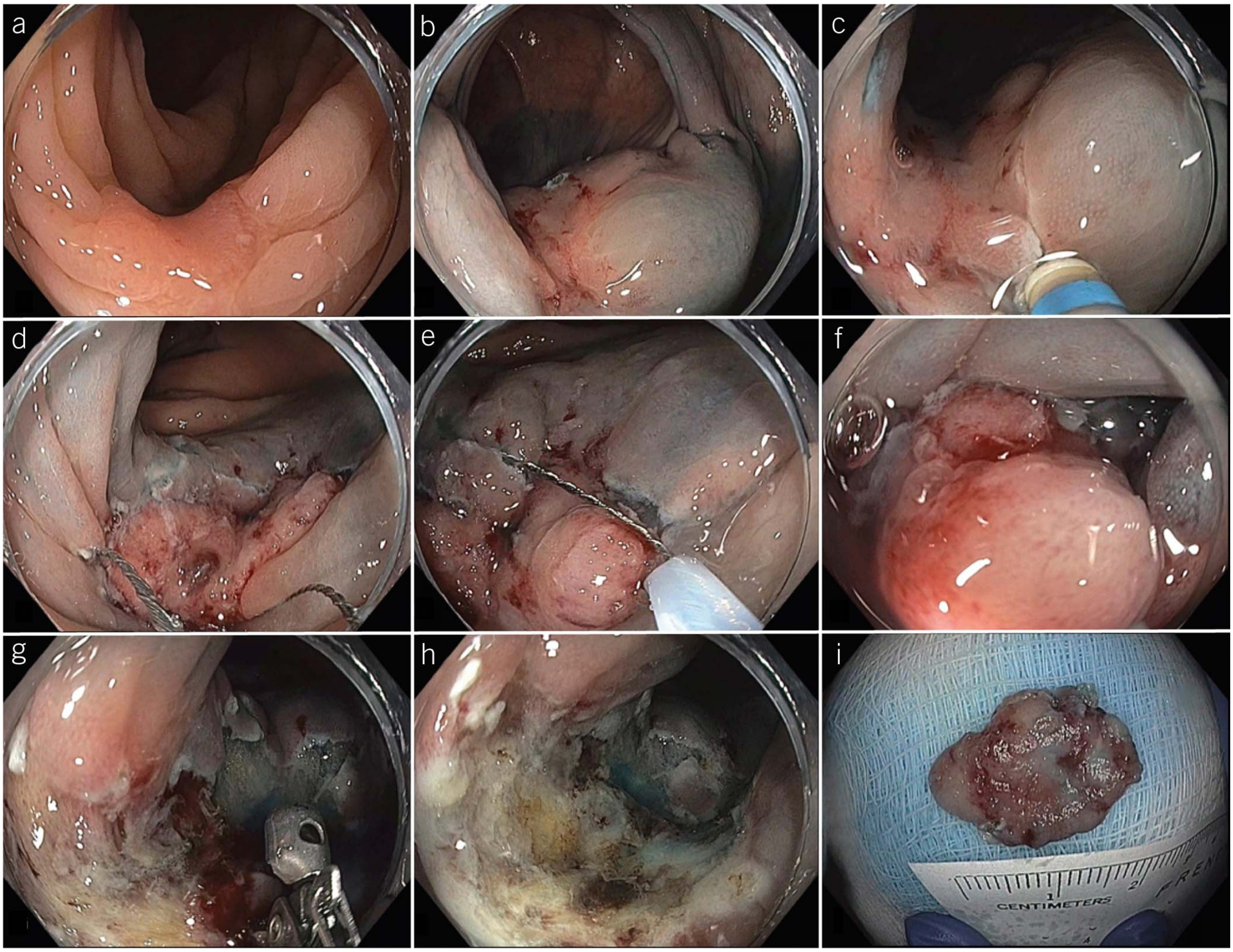

Figure 10. Hybrid ESD of prior incomplete polypectomy. (*A*) A prior incomplete polypectomy site shows macroscopically visible residual lesion within a convergence of folds. (*B*) Following submucosal injection, the lesion is non-lifting, likely due to underlying fibrosis from previous cautery. (*C*) An ESD knife is used for marginal resection of the periphery of normal mucosa surrounding the lesion. (*D*) A stiff snare tip is placed into the cut mucosa. (*E*) The snare is slowly opened using a fulcrum approach with the snare closed to fit into the cut perimeter. (*F*) The snare is then closed tightly and the lesion cut using endocut electrocautery. (*G*) Exposed bleeding superficial vessel is treated with soft coagulation using coagulation forceps. (*H*) The defect shows significant fibrosis. (*I*) The resected specimen.

compared to controls with no thermal ablation (37 of 176 [21.0%]) ($P < .001$) at first surveillance colonoscopy.[93] There has been no direct comparison of APC with snare tip soft coagulation for this purpose.

In one study using conventional hot snare polypectomy techniques, serrated lesions were nearly 4 times more likely to be incompletely resected than adenomas (31.0% vs 7.2%; $P \leq .001$), with nearly one-half of all large serrated lesions reported to be resected incompletely.[6] The incomplete resection rate was endoscopist-dependent and additionally may be due in part to the subtle appearance of sessile serrated lesions, including their flat shape and indistinct borders, but it also may reflect a suboptimal resection method. Four recent studies showed exceptional technical success and safety of inject-and-cut EMR for serrated lesions, despite their subtle morphologic features and proximal location.[71,94–96] Moreover, using inject-and-cut EMR resulted in low rates of recurrence, 3.6% (95% CI, 0.5%–6.7%) for sessile serrated lesions ≥10 mm[71] at an average 25.5 months (range, 2–74 months) and 7.0%–8.7% for serrated lesions ≥ 20 mm at an average of 12 months onward.[94,95]

Underwater Endoscopic Mucosal Resection

An alternative EMR technique, full water immersion ("underwater") EMR, has been described recently and obviates the step of submucosal injection before snare resection.[97] When the lumen is distended with water, as opposed to gas, the mucosa and submucosa involute as folds into the non-distended colon, while the muscularis propria remains circular. The segment of lumen with the lesion is completely immersed under water, the borders of the polyp are marked using APC or snare tip coagulation, and the hot snare resection is completed (Drycut, effect 5, 60W, ERBE VIO 300D). Binmoeller et al[98] reported high en bloc resection rates with underwater EMR. A study of large LSTs with a median size of 30 mm (range, 20–40 mm) showed that 55% of the lesions were removed in 1 piece using underwater EMR with a 33-mm snare. Of these 29 en bloc resections, 79% were histologically

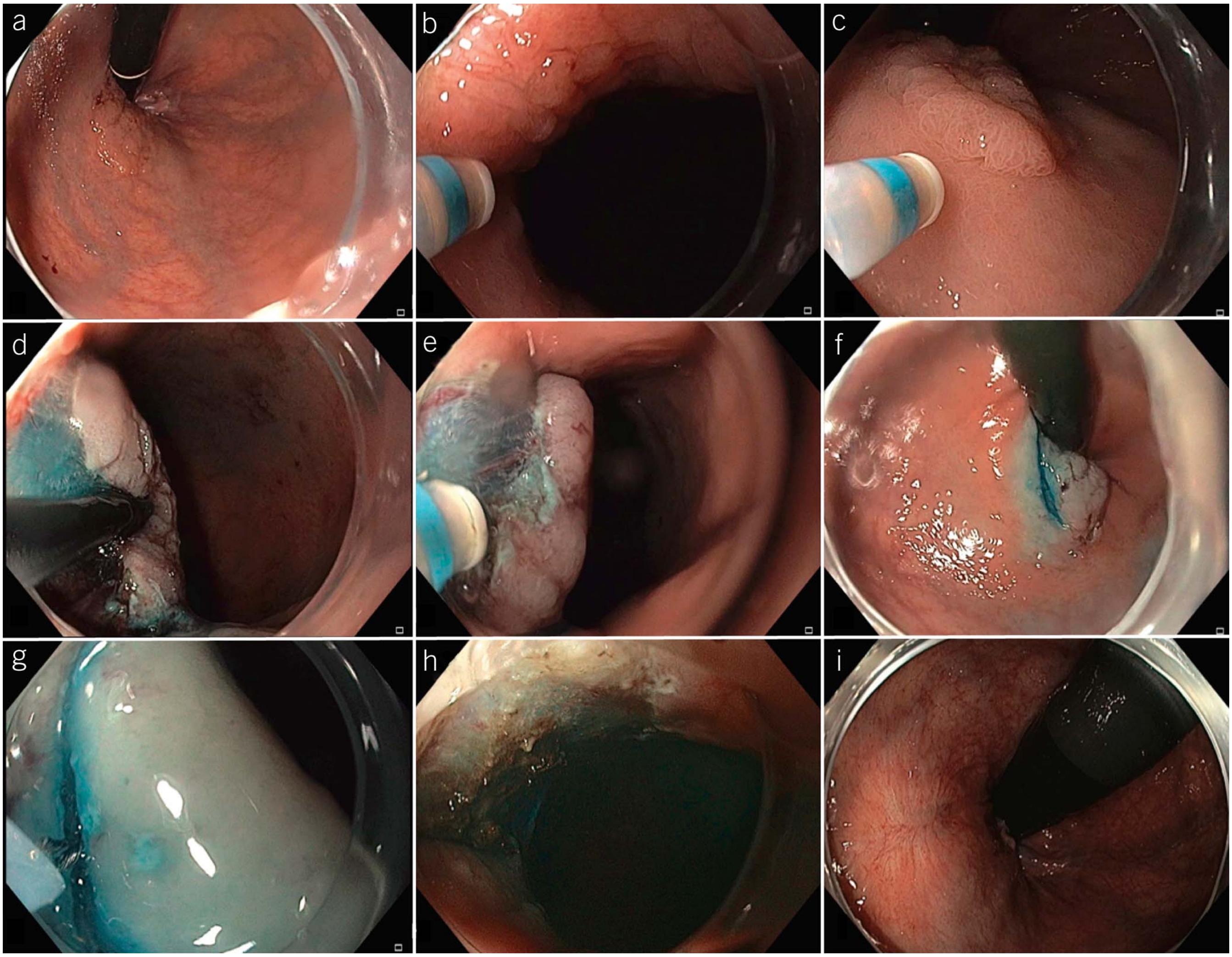

Figure 11. Hybrid ESD of distal rectal lesion involving anal canal. (*A*) A 20-mm non-polypoid lateral spreading granular-type lesion on the right wall of the distal rectum is seen in retroflexion, and (*B*) extending into the anal canal. (*C*) An ESD knife is used to mark the periphery of normal mucosa surrounding the lesion. (*D*) We lifted the lesion using dynamic submucosal injection technique and then performed circumferential incision of the normal periphery of the lesion in (*E*) antegrade and (*F*) retroflexion positions. (*G*) A stiff snare tip is placed into the cut mucosa, slowly opened to set within the cut perimeter, and then closed tightly and the lesion cut en bloc using endocut electrocautery. (*H*) The post-resection defect. The pathology was tubular adenoma. (*I*) The post resection scar site at surveillance showed no local recurrence.

verified to have free margins. Endoscopists experienced in conventional EMR report a short learning curve for the performance of the underwater EMR technique.[99–102] A prospective dual-center UK study of underwater EMR for 97 lesions (median size, 25 mm; range, 10–160 mm) by 2 experienced luminal resection endoscopists showed that submucosal lift was needed in 30% of lesions and correlated with polyp size ≥30 mm. Adenoma recurrence rates were 13.6% at a median 6 months' surveillance and were associated with female sex and difficult-to-access locations.[103] Using the technique for colon lesions ≥10 mm, studies have reported a 2%–5% delayed bleeding risk,[97,99,103] and there has been 1 case report of perforation of a proximal colon lesion removed with underwater EMR in retroflexion.[104]

Cold Snare Endoscopic Mucosal Resection

Cold snare with injection is a recently described method to remove large lesions without electrocautery to minimize the risk of delayed bleeding and perforation (Video 7, http://links.lww.com/AJG/B447, http://links.lww.com/AJG/B448).[105,106] In the technique, the submucosa is injected with a mixture of diluted epinephrine in saline with methylene blue and the lesion then snared without diathermy. A pilot study reported safe and effective use of the technique in 15 patients with a mean polyp size of 20 mm (range, 10–45 mm).[105] Various snare types were used in the small study, and in 12 of the patients cold biopsy forceps were used to remove visible residual lesion around the snared edges. No significant bleeding or perforation was observed. The same group reported their first surveillance findings using the technique for piecemeal removal of 94 lesions with a median size of 20 mm (range, 12–60 mm).[106] They followed 76.7% of the patients with colonoscopy between 2 and 10 months and found a 9.7% local recurrence rate. Two recent Australian groups independently applied the cold snare technique to sessile serrated lesions. One group of 2 endoscopists prospectively removed 163 serrated lesions ≥10 mm (median size, 15 mm; range, 10–40 mm) using an injection of succinylated gelatin and diluted methylene blue before piecemeal

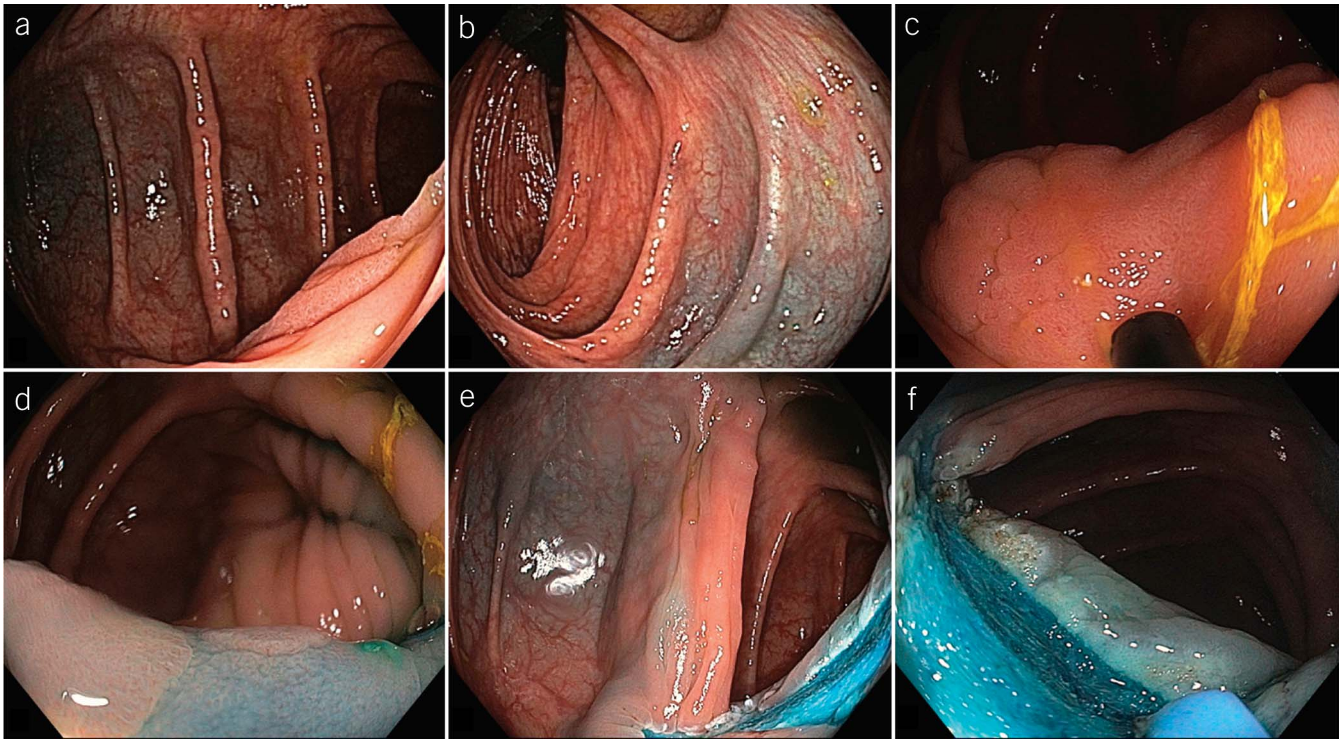

Figure 12. Use of retroflexion for complete EMR. (*A*) A non-polypoid superficially elevated lesion is seen at the hepatic flexion at a prior polypectomy site. (*B*) A tattoo is well visualized at the area in retroflexion. (*C*) Submucosal injection is performed in retroflexion. (*D*) This facilitates visualization of the lesion now in antegrade. (*E*) Endoscopic mucosal resection can then be complete. (*F*) The post-resection borders are ablated.

snare resection without diathermy. Short-term surveillance colonoscopy in 82% of the lesions (n = 134) at 6 months showed a single recurrence (0.6%).[107] For serrated lesions, the technique appears effective, despite the use of small-diameter snares and the associated increased number of pieces required for complete resection. Another group removed 41 sessile serrated polyps (median size, 15 mm; range, 10–35 mm) using cold snare polypectomy without submucosal injection. Short-term surveillance colonoscopy in fewer than one-half of the patients at 6 months showed no recurrence.[108] Long-term and comparative data are necessary to provide more robust efficacy outcomes. Generally, the need for inclusion of epinephrine in the injectate with cold EMR remains uncertain. Snare tip soft coagulation of the lesion edges and clip closure of the defect have thus far not been utilized in cold EMR.

Endoscopic Submucosal Dissection

The indications for colorectal endoscopic submucosal dissection (ESD) are relatively few, even at experienced centers, because most colorectal neoplasms are benign and can be resected using piecemeal EMR with minimal risk of recurrence. Large-sized (>20 mm in diameter) lesions that are indicated for endoscopic rather than surgical resection, and in which en bloc resection using inject-and-cut EMR is difficult, may be considered. These include lesions suspected to have submucosal invasion (ie, large depressed lesion or pseudodepressed LST-NG lesion), mucosal lesions with fibrosis, local residual early carcinoma after endoscopic resection, and non-polypoid colorectal dysplasia in patients with inflammatory bowel disease.[109]

The technique of ESD involves an endoscopic knife for cutting and submucosal injectant for lifting. After submucosal injection, a circumferential incision is performed to isolate the lesion with 3 or 4 mm surrounding normal mucosa. The submucosa under the lesion is injected further. With controlled movements under direct view facilitated with the use of a cap, the ESD knife dissects through the expanded submucosal layer to ultimately resect the lesion in 1 piece.

Hybrid Endoscopic Submucosal Dissection

The colon lumen is narrow and tortuous, and its wall is thin. As such, the risk of complication is relatively high using ESD technique compared to other removal techniques.[110–112] However, there are lesions with severe submucosal fibrosis (eg, colitis-associated dysplasia, non-granular lateral spreading lesions) or with concern for submucosal invasion, when the success of tissue capture for resection is low using a snare.[113] The technique of simplified/hybrid ESD involves partial submucosal dissection followed by en bloc snare resection of the lesion.[114] The technique provides a bridge in the safety, efficacy, and efficiency between conventional EMR and full ESD.[115]

Endoscopic Full-Thickness Resection

Endoscopic full-thickness resection in the colon and rectum is a recent approach that allows for better histologic evaluation of resection tissue, as it removes all layers of the colon wall.[116,117] Suggested indications for endoscopic full-thickness resection include lesions <30 mm, particularly non-lifting or those involving diverticulum.

The full-thickness resection device system technology is based on a proprietary over the scope clip system (Ovesco Endoscopy AG, Tübingen, Germany). It consists of a cap with a ready-to-use mounted clip and a fitted snare at its tip. The applicator cap is

Table 6. Studies of Bleeding Prophylaxis for Pedunculated Lesion Removal

First author, year	Head or stalk size included	Intervention (pre-snare)	Control (pre-snare)	Immediate bleeding rate, % (n/N)	Delayed bleeding rate, % (n/N)	Notes
Ji, 2014[140]	>10 mm head size and >5 mm stalk thickness	Clip	Loop	4.1 (4/98) vs 4.1 (4/98)	1.0 (1/98) vs 1.0 (1/98)	Loop placement failed 6.7%. Short stalk <15 mm caused slippage of loop after polypectomy. Stalk thickness >10 mm had greater risk of bleeding. Larger clips are recommended for these polyps. Loop and clip are equally safe and effective for post-polypectomy bleeding.
Luigiano, 2010[139]	>15 mm head	Clip	Loop	3 (1/32) vs 0	3 (1/32) vs 0	Head size 35–50 mm were difficult to loop. Clip-assisted resection was sufficient for these polyps.
Kouklakis, 2009[137]	>20 mm head	Epi	Loop with post-polyectomy clips	6.2 (2/32) vs 0	6.2 (2/32) vs 3.1 (1/32)	Loop with hot snare and post-snare clips significantly improved bleeding compared to adrenaline injection with hot snare.
Hogan, 2007[134]	>30 mm head	Epi	No control	0	0%	Presented 3 polyps >3 cm using epi volume reduction. Author mainly describes his personal 7-y experience with the technique and reports 0% bleeding rates.
Di Giorgio, 2004[138]	>10 mm head	Loop vs epi	Hot snare only	1.2 (2/163) vs 1.8 (3/161) vs 6.1 (10/164)	0.6 (1/163) vs 1.2 (2/161) vs 1.8 (3/164)	No reported complications using loop. Epi and loop have similar outcomes. Recommend either epi or loop for polyps >20 mm as opposed to hot snare only.
Iishi, 1996[136]	>10 mm head	Loop	Hot snare only	0 vs 2.4 (1/42)	0 vs 9.5 (4/42)	No reported complications using the loop. Loop is safe and more effective than hot snare only.
Hachisu, 1991[135]	20–40 mm head	Loop	No control	0	9.1 (10/11)	Original article presenting the loop technique "an experiment revealed that it stopped blood flow in stalks up to 5 mm in thickness."

epi, epinephrine.

mounted on the endoscope with the snare running on the outside of the scope within a sleeve. By turning the wheel, the clip is released to immobilize the target lesion tissue. The snare is then subsequently closed to cut the tissue. The technique is limited by the cap, which has an outer diameter of 21 mm. The cap size and length limits the amount of tissue that can be grasped, imposes difficulty advancing the endoscope through the colon, and impairs visibility during resection. Successful manipulation of the lesion into the cap also depends on thickness and scarring of the lesion and colonic wall.

A prospective multicenter study of 181 patients in 9 German centers demonstrated that endoscopic full-thickness resection

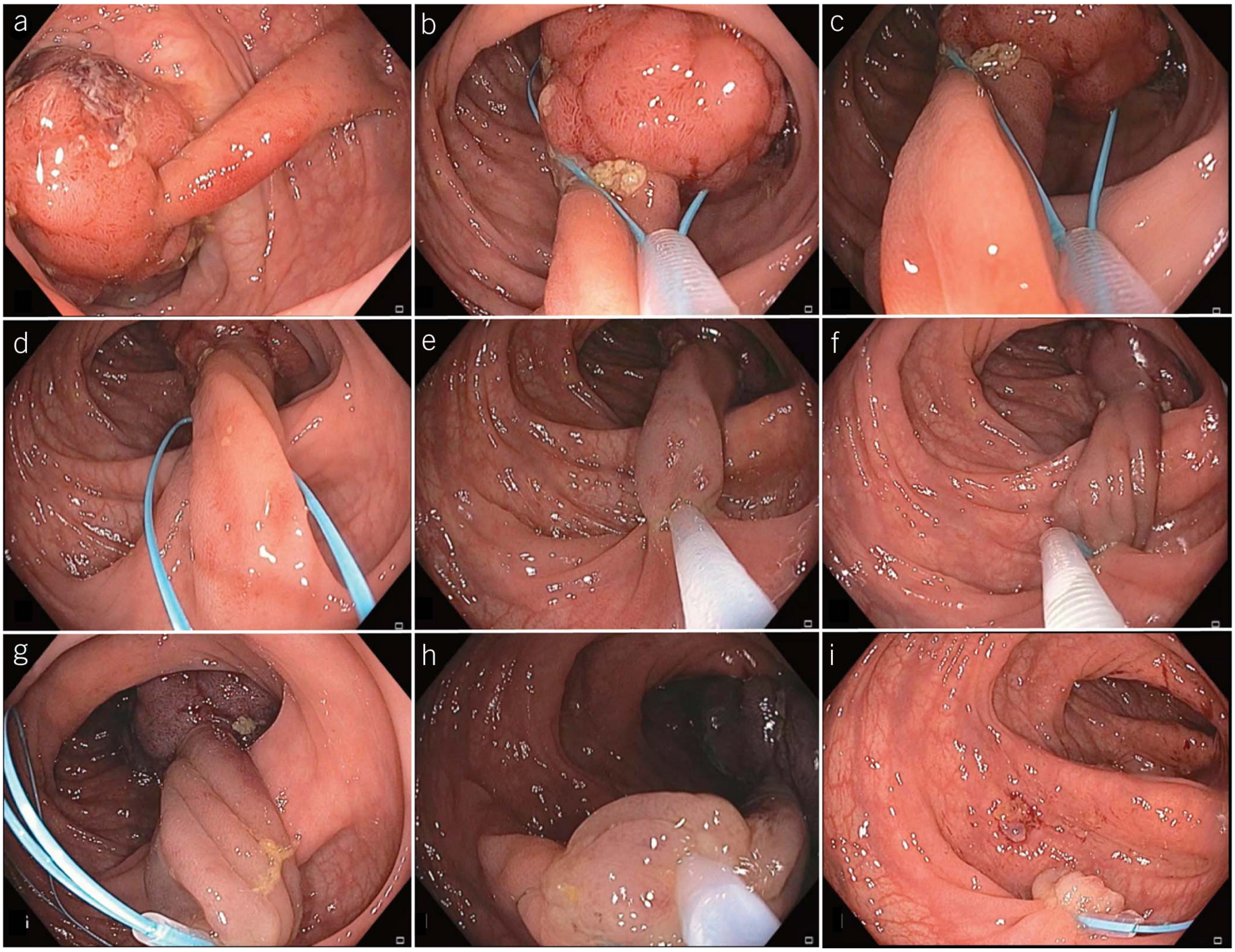

Figure 13. Pedunculated lesion with prophylactic looping. Use of the endoloop in pedunculated polyp to prevent post-polypectomy bleeding. The endoloop is used like a snare except it can be detached after its deployment at the base of the polyp. (*A*) A large pedunculated lesion is identified in the sigmoid colon. (*B*) The lesion is repositioned to facilitate the endoloop placement around the lesion head. (*C*) The loop is closed slightly as it is moved toward the base of the stalk, and (*D*) then closed further. (*E*) The loop is then closed tightly once at the base of a large pedunculated lesion to ligate the feeding vessel. The lesion starts to become ischemic, purple appearance. (*F*) Once the ischemic appearance is confirmed, the cylinder stopper of the loop is then tightened, and (*G*) released. (*H*) The electrocautery snare is placed above the loop with sufficient room to prevent the endoloop from slipping off after transection. The ideal way to snare a pedunculated polyp that has been looped is to tighten the snare as much as possible to make the snared plane smaller than the plane that has been looped. (*I*) Resection site immediately after resection. The loop remains at the base to prevent delayed bleeding.

with the full-thickness resection device was effective for difficult-to-resect colorectal lesions, such as non-lifting or challenging locations, especially for lesions $\leq$20 mm.[118] Subgroup analysis showed that R0 resection (eg, when the pathologic examination confirms that the margins of the resected specimen are free of neoplasia) decreased to 58.1% for lesions $>$20 mm vs 81.2% for lesions $\leq$20 mm (P = .0038). This may partly reflect difficulty assessing whether the lesion margin is fully contained in the cap when the lesion is fully drawn into the cap. Further outcomes studies are needed to better guide patient and lesion selection for this technique to optimize complete resection rates and safety profile.

SPECIAL FEATURES

Non-Lifting Lesions

Observation of the lesion during and after submucosal injection is a simple but important method to assess the potential for deeply invasive carcinoma.[119–121] Lesions may not lift due to submucosal invasion or because of submucosal fibrosis from prior biopsy, cautery, or tattoo (Figure 9).[122] Non-lifting areas are typically very difficult to capture in the snare. Several studies have reported the diagnostic operating characteristics of the non-lifting sign with a positive predictive value for invasive cancer to be approximately 80% in treatment-naïve lesions.[123] Difficulties encountered during attempted injection and snare resection should therefore alert the endoscopist to the possibility of deep submucosal invasion.

In the absence of invasive pathology, non-lifting fibrotic areas of lesion should be treated, but can be a challenge (Figure 10). The hot avulsion technique has recently been described for the removal of non-lifting fibrotic areas of colorectal lesions (Video 8, http://links.lww.com/AJG/B424).[124,125] The technique tears off the non-lifting tissue through grasping it with a hot biopsy forceps and then simultaneously combining low-voltage

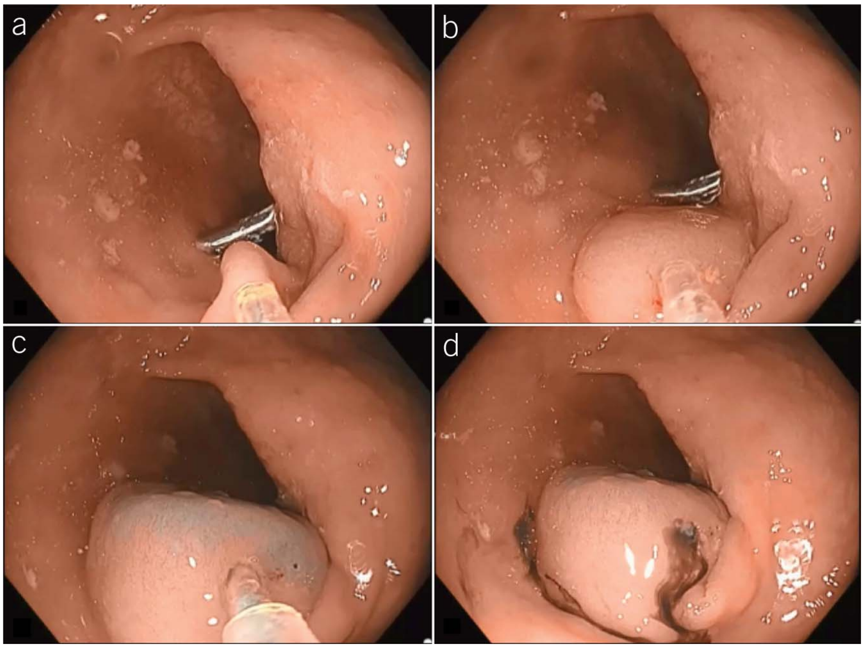

Figure 14. The bleb technique for tattooing. (*A*) A clip is visible protruding from an EMR site proximal to the visible fold. A needle is in the submucosa and tented toward the lumen so that the shape of the needle is visible. Visualization of the needle shape ensures submucosal location of the needle tip. (*B*) A small saline bleb is made and the saline bleb is seen immediately after needle withdrawal. (*C*) The tattoo-loaded needle is inserted into the saline bleb and 1-mL tattoo is injected. (*D*) The finished tattoo.

cutting current (eg, Endocut I) with mechanical traction. It is distinct from the hot biopsy polypectomy technique, which tents (rather than mechanically pulls) the tissue while burning with coagulation current, and typically has employed forced coagulation current. One retrospective study of hot avulsion in small non-lifting areas of lesions (mean [SD] size, 4.4 [3.5] mm) in 20 patients showed feasibility of the technique, with 15% recurrence rate that was successfully retreated with hot avulsion.[126] Cold forceps avulsion followed by snare tip soft coagulation or APC have been described recently.[127,128] The underwater EMR technique was also shown in one retrospective single-center study to be a useful salvage technique for non-lifting recurrent neoplasia.[129] Another retrospective single-center study showed the use of the ESD knife to dissect some of the non-lifting submucosal area to create a groove for the snare to then capture the non-lifting tissue.[130]

Difficult Locations: Appendiceal Orifice, Ileocecal Valve, Near Dentate Line, and Colitis-Associated Dysplasia

Various groups have shown success in the endoscopic removal of lesions in difficult locations, such as an anorectal lesion near the dentate line (Figure 11) or at a flexure behind a fold (Figure 12), using EMR, ESD, or hybrid methods.[113,131–133] Thus, patients with such lesions should be referred to an endoscopist with proficiency in these techniques before surgical referral.

2e: Pedunculated lesions

- We recommend hot snare polypectomy to remove pedunculated lesions ≥10 mm (Strong recommendation, moderate-quality evidence)
- We recommend prophylactic mechanical ligation of the stalk with a detachable loop or clips on pedunculated lesions with head ≥20 mm or with stalk thickness ≥5 mm to reduce immediate and delayed post-polypectomy bleeding. (Strong recommendation, moderate-quality evidence)
- We suggest retrieval of large pedunculated polyp specimens en bloc to ensure ability to assess resection margins, rather than dividing polyp heads to facilitate through the scope specimen retrieval. (Conditional recommendation, low-quality evidence)

Large pedunculated lesions should be removed by hot snare polypectomy. Transection should be at the middle to lower stalk in order to provide adequate specimen for histologic assessment of stalk invasion. En bloc resection with marking or pinning of the stalk is a key component to accurate pathologic staging to assess for the level of invasion. A case series of 3 pedunculated (≥30 mm) lesions suggested that injection of 4–8 mL of 1:10,000 epinephrine into both the polyp head and stalk may reduce polyp size and improve en bloc resection rates.[134] Prophylactic mechanical ligation of the feeding blood vessel of the stalk of large pedunculated lesions with head ≥20 mm or stalk thickness ≥5 mm may reduce immediate and delayed bleeding compared to epinephrine injection alone or no therapy (Table 6, Video 9, http://links.lww.com/AJG/B425). One prophylactic mechanical method is the application of an endoscopic loop, which is a detachable nylon loop that is applied to the base of polyp stalk to strangulate the vessel supplying the polyp (Figure 13).[135–138] Others have reported clipping of the stalk before polypectomy.[139,140] A randomized trial of pedunculated lesions ($n = 195$) with a minimum stalk diameter of 5 mm showed a similar bleeding rate after prophylaxis with placement of an endoscopic loop (5.7%) or clip (5.1%).[140] Prophylactic placement of clips for lesions with a large stalk, notably, may be difficult to achieve, and may result in thermal injury at the site of the clip. In such cases, clip placement immediately after stalk transection may be preferred. After resection, we recommend retrieval of large pedunculated polyp specimens en bloc to ensure ability to assess resection margins rather than dividing polyp heads to facilitate through-the-scope specimen retrieval. En bloc retrieval is critical to assessing completeness of resection when foci of invasive carcinoma are identified within a pedunculated polyp.

LESION MARKING

Statement 3: Lesion Marking

- We recommend the use of tattoo, using sterile carbon particle suspension, to demarcate any lesion that may require localization at future endoscopic or surgical procedures. (Strong recommendation, low-quality evidence)
- We suggest placing the tattoo at 2–3 separate sites located 3–5 cm anatomically distal to the lesion (anal side), particularly when the purpose is to mark the lesion for later endoscopic resection. The carbon particle suspension if injected at or in close approximation to the lesion, may result in submucosal fibrosis, and can thus reduce the technical success and increase the risk of future endoscopic resection. (Conditional recommendation, low-quality evidence)
- We suggest endoscopists and surgeons establish a standard location of tattoo injection relative to the colorectal lesion of interest at their institution. (Conditional recommendation, very low-quality evidence)
- We recommend documentation of the details of the tattoo injection (ie, material, volume, position relative to the lesions) in the colonoscopy report, as well as photo documentation of the tattoo in relation to the colorectal lesion. (Strong recommendation, low-quality evidence)

Colonoscopic tattooing facilitates identification of a lesion at colonoscopy or surgery.[141] Tattoos are unnecessary for lesions located in the cecum, adjacent to the ileocecal valve, or in the low rectum, where anatomic landmarks are in place and can be used as a reference. A photograph of the lesion with the anatomic landmark in view provides adequate documentation of lesion location.

Endoscopic tattooing is performed through the submucosal injection of a suspension of highly purified and fine carbon particles that are sterile and biocompatible, although not biologically inert.[142] To ensure that the tattoo injection is created safely within the submucosal space and not into the peritoneum, it is safest to first create a submucosal bleb using saline and then. once the submucosal plane is confirmed. to exchange to the tattoo injection and inject a volume of at least 0.75–1.0 mL at each site. This submucosal bleb technique of tattooing optimizes precision of the marking to avoid transmural injection that may cause clinically significant complications, such as localized peritonitis or submucosal fibrosis, from tracking at the lesion site that could increase the risk of perforation during subsequent EMR attempts.[143]

Tattoo location is dependent on the anticipated management of a lesion. For example, when marking a lesion for future endoscopic resection, then it is suggested that 2–3 separate injections at 3–5 cm distal (anal side) to the lesion should be performed (Figure 14).[144] In contrast, when marking a lesion for surgical resection, the tattoo should be targeted in line with the lesion as well as with the opposite lumen wall from the lesion to increase the likelihood that the tattoo will be seen during surgery. In all cases, the tattoo location in relationship to the lesion should be noted in the endoscopic report. Institutions should have a written standard of practice in place for tattooing and should describe and photo document in the colonoscopy report for reference.

PATHOLOGY PREPARATION AND ASSESSMENT

The benefits of polypectomy and mucosal resection can be only fully realized with high-quality pathologic assessment. Orientation of the specimen requires knowledge of the appearance of the lesion before resection. Thus, the orientation of the specimen by the endoscopist, especially in cases of serrated lesions[145] or concern for submucosal invasion, is helpful to assess the crypts at the basement membrane and submucosal glands, respectively. To aid orientation, specimens from en bloc resections are flattened and fixed at their periphery with thin needles inserted into an underlying wood or Styrofoam block before immersion into formalin. The fixed lesion is then sectioned serially at 2-mm intervals in a plane perpendicular to the endoscopic resection plane. Assessment of a non-pedunculated specimen containing carcinoma must include the depth of the lesion, neoplastic involvement of the lateral and vertical margins, histology, degree of pathologic differentiation, involvement of the lymphatics and/or blood vessels, and the presence of tumor budding. Pedunculated specimens should include the distance of the cancer from the resection margin. In the colon, involvement of the vertical margin is particularly important, more so than the involvement of the lateral margin, provided that there is no endoscopically visible lesion remaining at the conclusion of the resection. When submitting pedunculated specimens, the pathology team should be alerted to orient the specimen carefully to allow for careful assessment of the resection margin relative to any foci of neoplasia, including any focus of invasive carcinoma, if present.

Surveillance

Recommendations for surveillance after colonoscopy and polypectomy are available in a recent updated USMSTF document.[9] The current consensus document will provide further statements for surveillance after piecemeal endoscopic resection of colorectal lesions ≥20 mm.

Statement 4: Surveillance

- We recommend intensive follow-up schedule in patients after piecemeal EMR (lesions ≥20 mm) with the first surveillance colonoscopy at 6 months, and the intervals to the next colonoscopy at 1 year and then 3 years. (Strong recommendation, moderate-quality evidence)
- To assess for local recurrence, we suggest careful examination of the post-mucosectomy scar site using enhanced imaging, such as dye-based (chromoendoscopy) or electronic-based methods, as well as obtaining targeted biopsies of the site. Post-resection scar sites that show both normal macroscopic and microscopic (biopsy) findings have the highest predictive value for long-term eradication. (Conditional recommendation, moderate-quality evidence).
- In surveillance cases with suspected local recurrence, we suggest endoscopic resection therapy with repeat EMR, snare or avulsion method, and consider ablation of the perimeter of the post-treatment site. In such cases, subsequent examinations should be performed at 6–12 months until there is no local recurrence. Once a clear resection site is documented by endoscopic assessment and histology, the next

follow-ups are performed at 1-year and then 3-year intervals. (Conditional recommendation, low-quality evidence)

- In addition to detailed inspection of the post-mucosectomy scar site, we recommend detailed examination of the entire colon at the surveillance colonoscopy to assess for synchronous colorectal lesions. (Strong recommendation, moderate-quality evidence)

After piecemeal resection of non-pedunculated lesions ≥20 mm in size, a repeat colonoscopy is recommended in 6 months to assess for local recurrence and to clear the colon of synchronous lesions. There is a very high prevalence of synchronous disease in patients with lesions ≥20 mm. In a large EMR referral cohort with lesions ≥20 mm, patients had an average of 4 additional conventional adenomas; 40% had an additional advanced adenoma; 20% had an additional lesion ≥20 mm; and 0.8% had a synchronous cancer not detected by the referring physician. Of those referred for removal of a serrated lesion, 30% had unrecognized serrated polyposis.[146]

The post-mucosectomy scar site should be examined carefully; image-enhanced endoscopy techniques, such as chromoendoscopy[147] or NBI,[148] may be useful to show the presence of the innominate grooves across the scar and normal pit or microvessel patterns to ensure no local residual or recurrence. Post-resection scar sites that show both normal macroscopic and microscopic (biopsy) findings have the highest predictive value for long-term eradication.[149] However, the data supporting biopsy were largely acquired before the era of image-enhanced endoscopy, and the utility of the practice with modern instruments is currently uncertain and warrants additional study. Clip artifact has been described at the scar sites in up to one-third of post-EMR clipped defects, irrespective of clip retention. It is characterized by nodular elevation of the mucosa with a normal pit pattern, and should not be mistaken for residual neoplastic polyp in order to avoid unnecessary treatment or inappropriate surveillance interval.[150,151] The majority of EMR sites (>90%) do not have clips retained at the first 3- to 6-month surveillance colonoscopy, and moreover, residual polyp at the base of retained clips was not encountered, by either endoscopic or histologic assessment.[152]

In post-EMR surveillance cases with local neoplastic recurrence, appropriate therapy with biopsy or repeat EMR is warranted. In many cases the recurrence is on scar tissue, and EMR may be impossible. Resection of residual tissue using hot snare polypectomy or avulsion is appropriate, and many experts add ablative techniques to the margin of the resection to reduce the risk of further recurrence. Subsequent examinations should be performed at 6- to 12-month intervals, with shorter intervals used for recurrences that are large (≥1 cm) or demonstrated high-grade dysplasia. The majority of recurrences are a few millimeters in size, and the above treatment methods are highly effective, and follow-up 1 year later is adequate. Once a clear resection site is documented by endoscopic assessment and histology, the next follow-ups are performed at 1-year and then 3-year intervals. The rationale for such an intensive follow-up schedule is to treat the local recurrence, particularly after piecemeal polypectomy. Local neoplastic recurrence after endoscopic resection of large colorectal lesions has been reported in several longitudinal outcomes studies to be approximately 16%.[89,153,154] As noted above, recurrences are generally unifocal and diminutive, and can be managed endoscopically.

Although current recommendations are for close follow-up as we describe, ongoing work to better understand risk for recurrence (eg, lesion >40 mm, use of APC to treat endoscopically visible residual lesion, intraprocedure bleeding, and high-grade dysplasia) is ongoing[89,155] and future recommendations may be better tailored to baseline recurrence risk.[156]

ADVERSE EVENTS ASSOCIATED WITH COLORECTAL LESION REMOVAL

A recent systematic review and meta-analysis of population-based studies from 21 studies including 1,966,340 colonoscopies performed during the period spanning from January 1, 2001 to August 31, 2012 examined the pooled prevalence of complications after colonoscopy with polypectomy.[157] Although uncommon overall, the rate of adverse events with polypectomy appears to increase as the size and method of endoscopic removal expands. Familiarity with the endoscopic features, symptoms and signs of complications, and proficiency in the treatment of complications is a prerequisite to perform endoscopic removal of a colorectal lesion. The use of a common lexicon as a framework to measure, categorize, and report complications is important.[158]

Bleeding

Bleeding is the most common post-polypectomy–related adverse event. The American Society for Gastrointestinal Endoscopy/American College of Gastroenterology Task Force on Quality in Endoscopy recommends that the post-polypectomy bleeding rate should be ≤1/100 colonoscopies.[159,160] Pooled prevalence statistics showed colonoscopy with polypectomy was associated with a post-polypectomy bleeding rate of 9.8/1000 (95% CI, 7.7–12.1).[157] Time-trend analysis showed that post-polypectomy bleeding declined from 6.4 to 1.0/1,000 colonoscopies from 2001 to 2015. There was considerable heterogeneity in most of the analyses, and the reported incidence varies according to the definition of bleeding, and the size and type of lesions resected.

Routine endoscopic treatment of all post-polypectomy sites to prevent bleeding is not cost-effective.[161,162] A network meta-analysis of 15 randomized controlled trials with 3462 patients published until January 2016 examined the effects of prophylactic therapy for post-polypectomy bleeding, including mechanical therapy, such as endoscopic clips or detachable snare (loop), epinephrine–saline injection therapy, and coagulation therapy, compared to no prophylactic therapy.[163] The study found that prophylactic therapy with either mechanical or epinephrine–saline injection therapy compared to no prophylactic therapy decreased early post-polypectomy bleeding but did not significantly influence delayed bleeding rates. Coagulation therapy had no influence to reduce bleeding incidence. Two additional meta-analyses on prophylactic clipping showed no significant reductions in post-polypectomy bleeding rates.[162,164]

Significant risk factors for post-polypectomy bleeding include polyp size ≥10 mm, pedunculated lesions with thick stalks, LSTs, right-sided colonic lesions,[165] use of anticoagulants (Appendix 3, http://links.lww.com/AJG/B417), and patient comorbidities, such as cardiovascular or chronic renal disease.[166–168] Despite these identified risk factors, the optimal therapy to prevent bleeding after colorectal polypectomy has not been determined and moreover, the specific patient or lesion criteria in which to apply prophylactic therapy has not been defined.

Recent studies have focused on the role of bleeding prophylaxis after resection in subgroups of lesions, such as large (≥20 mm) non-pedunculated colorectal lesions.[162,169] For example, the use of a risk prediction bleeding score after endoscopic resection of large (≥20 mm) lesions has been suggested to further guide decision on prophylactic treatment.[170] Scores include size >30 mm (2 points), proximal colon location (2 points), presence of major comorbidity (1 point), and absence of epinephrine use (1 point). The probabilities of post-endoscopic resection bleeding by scores were 3.4% for low (score 0–1), 6.2% for medium (score 2–4), and 15.7% for elevated (score 5–6) risk levels. A recent US multisite randomized trial evaluating the influence of endoscopic clipping of post-polypectomy defects >20 mm found that clipping reduced the overall risk of delayed hemorrhage from 7.2% to 3.7% ($P = .02$). The benefit was confined to lesions in the proximal colon, where the bleeding risk was significantly lower when clips were applied vs not (9.8% vs 3.3%; $P < .001$).[171]

Additionally, prophylactic coagulation of visible vessels in the resection defect of large lesions removed with EMR has not been associated with decreased post-endoscopic resection bleeding. An Australian multicenter randomized trial of 347 patients with average post-endoscopic resection defect of 40 mm did not show any significant reductions in clinically significant bleeding with prophylactic treatment of visible vessel, 5.2% with prophylactic treatment using coagulation forceps (SOFT COAG at 80W Effect 4, ERBE VIO 300D) vs 8.0% no additional therapy ($P = .3$).[172]

Post-Polypectomy Coagulation Syndrome

Post-polypectomy coagulation syndrome, also called post-polypectomy syndrome or transmural burn syndrome, is thought to occur when cautery injury causes full-thickness thermal injury of the bowel wall with localized serosal inflammation and peritonitis.[173,174] Typical symptoms and signs include fever, localized abdominal tenderness (often with rebound tenderness), and leukocytosis occurring within a few hours to days of the polypectomy. Patients who are suspected to have severe post-polypectomy syndrome should be closely observed by medical and surgical teams, and receive intravenous fluids, antibiotics, and bowel rest. Most patients recover uneventfully. Abdominal radiographs and computed tomography scans may demonstrate local changes, such as air in the bowel wall but not in the abdomen in the large amounts that would be seen with perforation. In comparison to air insufflation, carbon dioxide insufflation significantly reduces post-procedure admissions and pneumoperitoneum associated with perforation at a minimal additional cost.[175,176]

Perforation

Although rare, 0.08% (95% CI, 0.06%–0.1%),[157] colonic perforation due to polypectomy remains the most serious complication. A recent meta-analysis of 50 studies that included 6779 ≥20 mm colorectal lesions reported a perforation rate with endoscopic resection of 1.5% (95% CI, 1.2%–1.7%).[43] Immediate perforation can occur when muscularis propria is included in the tissue grasped by a snare, whereas delayed perforation typically occurs as a result of a deep cut or tissue necrosis from cautery.[177] A UK study of more than 150,000 polypectomies performed within their national CRC screening program showed that cecal location of the polyp was an independent risk factor for perforation.[178] A Japanese nationwide database of 345,546 patients included 108,886 (31.5%) who underwent polypectomy, 219,848 (63.6%) who underwent EMR, and 16,812 (4.9%) who underwent ESD. Perforation was associated with male sex, renal disease (adjusted OR [adjOR], 2.6; 95% CI, 1.38–4.94); ESD; tumor size ≥20 mm (adjOR, 2.68; 95% CI, 1.61–4.44); and use of medications. including warfarin (adjOR 2.02; 95% CI, 1.10–3.70), nonsteroidal anti-inflammatory drugs (adjOR 21.5, 95% CI, 14.4–32.0), and steroids (adjOR 2.12,95% CI, 1.14–4.03).[179]

Techniques to decrease the risk of capturing the muscularis propria have been described, including adequate submucosal injection and avoidance of a large snare size. Confirmation of safe tissue capture of the submucosa can be tested by movement of the snare back and forth. If the muscularis propria is entrapped, the whole wall, as opposed to only the lesion, may be seen to move. In such a scenario, slight loosening of the snare while tenting the mucosa into the lumen and toward the endoscope may help to release potentially entrapped muscularis propria. Alternating forward and backward movements of the snare are also often performed to avoid entrapment of the muscularis propria.[79] Steps to minimize tissue injury can also be taken. Full closure of a monofilament wire snare with a distance of <1 cm between the thumb and the fingers coupled with a fast transection speed result in less tissue burn. Microprocessor-controlled electrosurgical generators sense tissue impedance and adjust power to minimize deep tissue injury.[180]

Recognition of partial or full-thickness muscularis propria resection and potential perforation is critical (Video 10, http://links.lww.com/AJG/B426, http://links.lww.com/AJG/B427, http://links.lww.com/AJG/B428). Early identification and management of perforation have correlated with reductions in surgery and morality[181] and success in endoscopic closure.[177,182] This requires careful inspection of the post-resection defect for simple exposure of the muscularis propria to full-thickness perforation.[183] The use of dyes such as indigo carmine and methylene blue avidly color the submucosal fibers and do not stain the muscularis propria. The differential staining of the submucosa and muscularis propria facilitates orientation in the safe plane of the submucosa during resection.[184] In a deep resection, the unstained muscularis propria would contrast with the blue-stained submucosa. This appearance has been described as the defect target sign to facilitate recognition of a deeper resection for endoscopic management.[185] Examination of the mucosal defect may show 2 concentric white rings of cautery, an inner ring that is the muscularis propria resection, and an outer ring that is the mucosal resection. Deep mural injury (including simple exposure of the muscularis propria without apparent injury to the muscle) has been observed in 10.2% of the EMR defect of large (≥20 mm) non-pedunculated lesions, with defect target signs and perforation observed in 3% of cases[183] and were associated with transverse colon location, en bloc resection of lesions ≥25 mm, and advanced pathology (high-grade dysplasia or submucosal invasive cancer). Endoscopic clipping techniques have been shown to be useful in cases of fresh small perforation or, prophylactically, in cases where the resection appears deep into the muscularis propria (Videos 11 and 12, http://links.lww.com/AJG/B429, http://links.lww.com/AJG/B449, http://links.lww.com/AJG/B450, http://links.lww.com/AJG/B433).[186,187] Alternative methods of closure, including endoscopic over-the-scope clips or suturing, have been described, albeit they typically require withdrawal and reinsertion of the endoscope with the equipment mounted.[188,189] After defect closure, patients without clinical signs or symptoms of peritonitis can be discharged on a conservative diet (ie, nil per os with advancing as tolerated) and a course of oral antibiotics, although this has not been studied formally. Most patients with diffuse peritonitis from colonic perforation require surgery.

EQUIPMENT AND TOOLS

Statement 5. Equipment

- We recommend the use of carbon dioxide insufflation instead of air during colonoscopy and EMR. (Strong recommendation, moderate-quality evidence.)
- We suggest the use of microprocessor-controlled electrosurgical units. (Conditional recommendation, very low-quality evidence)

Carbon dioxide Randomized controlled trials and a systematic review have demonstrated improved patient satisfaction with reduced pain scores and reduced intestinal distension on plain abdominal radiographs after routine colonoscopy with insufflation of carbon dioxide compared with insufflation of air.[190,191] The use of carbon dioxide has been shown to be even more impactful for the endoscopic resection of large colon lesions, leading to a significant reduction in the rate of post-procedure admission compared with that of air insufflation, primarily because of reduced rates of admission for pain without perforation.[176]

Cautery The majority of US endoscopists perform polypectomy using either a pure coagulating or blended current, with only a minority (3%) using pure cut current, when surveyed regarding polypectomy practices for lesions 7–9 mm in size.[192] Less is known about the applied cautery settings for larger lesions and the number of centers that have adopted modern electrosurgical units. For example, microprocessor-controlled units alternate cycles of short cutting bursts with prolonged periods of coagulation, and limit peak voltage on the basis of impedance feedback, which results in a less marked coagulating effect than the use of a non–microprocessor-controlled blended or coagulation current. Histologic specimen quality is improved as well using the microprocessor-controlled current compared to blended current.[193]

Cap The use of a soft transparent cap has been shown to facilitate colonoscopic EMR, particularly for flat lesions. It is fitted to the distal tip of the colonoscope insertion tube positioned with 3–4 mm of the cap exposed. This position stabilizes the endoscope distance in relation to the mucosa to maintain a clear, in-focus view, and can make it easier to inspect the lesion behind a fold or at a flexure.[194]

Statement 6: Quality of Polypectomy

The majority of benign colorectal lesions can be safely and effectively removed using endoscopic techniques. As such, endoscopy should be the first-line management of benign colorectal lesions.

- When an endoscopist encounters a suspected benign colorectal lesion that he or she is not confident to remove completely, we recommend referral to an endoscopist experienced in advanced polypectomy for subsequent evaluation and management, in lieu of referral for surgery. (Strong recommendation, low-quality evidence)
- We suggest the documentation of the type of resection method (eg, cold snare, hot snare, EMR) used for the colorectal lesion removal in the procedure report. (Strong recommendation, low-quality evidence)
- We recommend that non-pedunculated lesions with endoscopic features suggestive of submucosal invasive cancer and that are resected en bloc be retrieved and pinned to a flat surface before submitting the specimen to the pathology laboratory to facilitate pathologic sectioning that is perpendicular to the resection plane. (Strong recommendation, low quality of evidence)
- For non-pedunculated colorectal lesions resected en bloc with submucosal invasion, we recommend that pathologists measure and report the depth of invasion, distance of the cancer from the vertical and lateral resection margin, in addition to prognostic histologic features, such as degree of differentiation, presence or absence of lymphovascular invasion, and tumor budding. (Strong recommendation, moderate-quality evidence)
- We recommend that endoscopists resect pedunculated lesions en bloc, and that when submucosal invasion is present, pathologists report the distance of cancer from the cautery line, the degree of tumor differentiation, and presence or absence of lymphovascular invasion. (Strong recommendation, moderate-quality evidence)
- We recommend endoscopists engage in a local (institution-, hospital-, or practice-based) quality-assurance program, including measuring and reporting of post-polypectomy adverse events. (Strong recommendation, moderate-quality evidence)
- We suggest measuring and reporting the proportion of patients undergoing colonoscopy who are referred to surgery for benign colorectal lesion management. (Conditional recommendation, moderate-quality evidence)
- We suggest the use of polypectomy competency assessment tools, such as Direct Observation of Polypectomy Skills and/or the Cold Snare Polypectomy Competency Assessment Tool in endoscopic training programs, and in practice improvement programs. (Conditional recommendation, low-quality evidence)

Focused teaching is needed to ensure the optimal endoscopic management of colorectal lesions. Polypectomy competency, however, has been shown to significantly vary among colonoscopists.[195] A prospective observational study of 13 high-volume screening colonoscopists at a US academic center showed overall polypectomy competency rates ranged between 30% and 90%.[196] Moreover, polypectomy competency scores did not correlate with established quality metrics, such as adenoma detection rate or withdrawal time, suggesting that skills in adenoma detection are separate from those of adenoma resection. Given such data and the clinical implications of suboptimal polypectomy, we should direct efforts toward educating colonoscopists in polypectomy techniques. Polypectomy competency assessment tools, such as Direct Observation of Polypectomy Skills and/or the Cold Snare Polypectomy Assessment Tool, should be a standard part of endoscopic training and practice improvement programs (Appendix 4, http://links.lww.com/AJG/B418, http://links.lww.com/AJG/B419).

Ultimately, the majority of colorectal lesions can be safely and effectively removed using endoscopic techniques. The development and implementation of polypectomy quality metrics may be necessary to optimize practice and outcomes. For example, the type of resection method used for the colorectal lesion removal in the procedure report should be documented, and the inclusion of adequate resection technique as a quality indicator in CRC screening programs should be considered.[34,198] Adverse events, including bleeding, perforation, hospital admissions, and the number of benign colorectal lesions referred for surgical management, should be measured and reported. Finally, standards for pathology preparation and reporting of lesions suspicious for submucosal invasion should be in place to provide accurate staging and management.

CONCLUSIONS

Endoscopic resection of precancerous lesions reduces the incidence of CRC. Ineffective resection results in residual neoplasia and appears to be the cause of some interval cancers. There is clear evidence that endoscopic resection skills are quite variable, with a substantial need to increase the adoption of proven effective endoscopic resection techniques. Intensive investigation of resection technique in the past 2 decades has made evidenced-based recommendations possible. This report summarizes evidence- and consensus-based recommendations from the MSTF on best practices for endoscopic resection of precancerous colorectal lesions.

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Abbreviations used in this paper: adjOR=adjusted odds ratio; APC=argon plasma coagulation; CI=confidence interval; CRC=colorectal cancer; EMR=endoscopic mucosal resection; ESD=endoscopic submucosal dissection; GRADE=Grading of Recommendations, Assessment, Development, and Evaluation Ratings of Evidence; LST=laterally spreading tumor; NBI=-narrow-band imaging; NICE=Narrow Band Imaging International Colorectal Endoscopic classification; OR=odds ratio; USMSTF=US Multi-Society Taskforce.

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