



Endoscopic mucosal resection

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This document was reviewed and approved by the Governing Board of the American Society for Gastrointestinal Endoscopy.

The ASGE Technology Committee provides reviews of existing, new, or emerging endoscopic technologies that have an impact on the practice of GI endoscopy. Evidence-based methodology is used, by using a MEDLINE literature search to identify pertinent clinical studies on the topic and a MAUDE (U.S. Food and Drug Administration Center for Devices and Radiological Health) database search to identify the reported adverse events of a given technology. Both are supplemented by accessing the “related articles” feature of PubMed and by scrutinizing pertinent references cited by the identified studies. Controlled clinical trials are emphasized, but in many cases, data from randomized, controlled trials are lacking. In such cases, large case series, preliminary clinical studies, and expert opinions are used. Technical data are gathered from traditional and Web-based publications, proprietary publications, and informal communications with pertinent vendors. For this review, the MEDLINE database was searched for publications in English through September 2014 by using the keywords “endoscopic lesion removal,” “endoscopic resection,” “endoscopic mucosal resection,” and “EMR.”

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BACKGROUND

EMR was developed for minimally invasive, organ-sparing endoscopic removal of benign and early malignant lesions in the GI tract. This report focuses on instruments, injection solutions, and techniques currently used for EMR. This report is an update of a previous Technology Status Evaluation Report titled “Endoscopic Mucosal Resection and Endoscopic Submucosal Dissection.”¹ The topic of endoscopic submucosal dissection (ESD) is now discussed in a separate Technology Status Report.²

TECHNOLOGY UNDER REVIEW: EMR

EMR is an endoscopic technique developed for the removal of sessile or flat neoplasms confined to the superficial layers (mucosa and submucosa) of the GI tract. The commonly used techniques can be categorized as injection-, cap-, and ligation-assisted EMR. Underwater EMR is a newer technique that is useful, particularly for salvage EMR.

Proper patient and lesion selection for EMR with endoscopic and/or endosonographic evaluations is essential. Before the start of any EMR procedure, close visual inspection to delineate the margins, particularly of flat lesions, is imperative because manipulation of the lesion may obscure landmarks. It may be helpful to mark the margins of the targeted lesion with superficial cautery marks with the tip of a snare or with argon plasma coagulation (APC). Electrosurgical unit settings for polypectomy and EMR are discussed in a previous Technology committee document.³ A retrieval device may then be used to retrieve EMR specimens.

Injection-assisted EMR

Injection-assisted EMR is also often called saline solution lift-assisted polypectomy. This technique was introduced in 1955 for rigid sigmoidoscopy and then in 1973 for flexible colonoscopy.^{4,5} The procedure starts with injection of

a solution into the submucosal space under the lesion creating a safety cushion. The cushion lifts the lesion, facilitating capture and removal by using a snare while minimizing mechanical or electrocautery damage to the deeper layers of the GI wall. The lesion may be removed in a single resection or a piecemeal fashion.

Cap-assisted EMR

Cap-assisted EMR also uses submucosal injection to lift the target mucosal lesion. Dedicated mucosectomy devices have been developed that use a cap affixed to the tip of the endoscope (EMR Kit; Olympus America Inc, Center Valley, Pa) (Table 1).⁶ These single-use devices come equipped with a specially designed crescent-shaped electrocautery snare that must be opened and positioned on the internal circumferential ridge at the tip of the cap (Fig. 1). The endoscope is then immediately positioned over the target lesion, and suction is used to retract the mucosa into the cap after which the snare is closed to capture the lesion. The lesion is then resected with standard snare excision technique by using electrocautery. The available cap-assisted mucosectomy devices differ primarily in the characteristics of the cap. Caps are composed of clear plastic, which may be soft or hard. The caps are cylindrical and available with a flat circular (straight)– or oval (oblique)–shaped tip, both with outer diameters ranging from 12.9 to 18 mm.

Ligation-assisted EMR

In ligation-assisted EMR, a band ligation device (Duette Multi-Band Mucosectomy device, Cook Medical Inc., Winston-Salem, NC) is attached to the endoscope, and the banding cap is positioned over the target lesion with or without previous submucosal injection. Suction is applied to retract the lesion into the banding cap, and a band is deployed to capture the lesion, thereby creating a pseudopolyp. An electrocautery snare is then used to resect the pseudopolyp above or below the band.^{7,8} The handle of the EMR band ligator allows insertion and advancement of a snare device through the endoscope working channel without requiring removal of the banding apparatus. The kit also includes a 1.5 × 2.5-cm hexagonal braided electrocautery snare available with a 5F (for diagnostic endoscopes) or 7F (for therapeutic endoscopes) insertion sheath. In addition, the band ligation device incorporates 6 bands, allowing potential resection at as many as 6 mucosal sites without the need to change the device. Two sizes of ligating caps are available to fit endoscopes with outer diameters of 9.5 to 13 mm and 11 to 14 mm.

Underwater EMR

In the underwater EMR (UEMR) technique, luminal air is suctioned, and water is instilled to fill the GI lumen and immerse the target lesion. Water immersion allows lesion visualization without over distention of the GI tract wall. It is postulated to “float” the mucosa and submucosa

away from the deeper muscularis propria layer and allows EMR without requiring submucosal injection.⁹ This technique has the theoretical advantages of eliminating any risk of tracking neoplastic cells into deeper layers of the GI tract wall by the injection needle and making capture of flat lesions easier. This method has also been reported to be effective in managing recurrences after previous EMR, as well as patients with previous partial resections and biopsies of lesions¹⁰ because these interventions may result in submucosal fibrosis, making lifting of the lesion with submucosal injection difficult.^{11–18}

Adjunctive techniques

Additional ablative techniques are used in an organ-specific manner in addition to EMR for the ablation of residual tissue. In the esophagus, radiofrequency or cryoablation is frequently used to ablate additional Barrett’s esophagus after EMR of the dysplastic lesions. During resection of flat adenomas in the GI tract, APC or the use of hot biopsy forceps (also known as the hot avulsion technique) may be used to ablate residual adenomatous tissue at the base and edges of the resection site.^{13,19–22} However, the application of APC to ablate residual adenomatous tissue was associated with a higher risk of adenoma recurrence.²³ Use of the snare tip with soft coagulation for residual tissue that cannot be removed by snare resection in the colon is currently being evaluated in a randomized, controlled trial.

Specimen handling

Because EMR specimens are larger than biopsy samples, it is helpful for pathologic interpretation to orient and mount the specimen before submerging it in fixative. The specimen is often pinned onto a paraffin wax block and fully submerged in fixative before transporting the specimen to pathology. A paraffin wax block is beneficial because it will not float in fixative.

Submucosal injection solutions

Although submucosal injection is not essential for all EMR procedures, it is an integral part of injection-assisted EMR. Various solutions have been used for submucosal injection (Table 2). The ideal agent should be inexpensive, readily available, nontoxic, easy to inject, and provide a long-lasting submucosal cushion.^{24,25} Normal saline solution is widely available and often used for injection-assisted EMR. However, a cushion made with normal saline solution often dissipates within minutes. Multiple studies have demonstrated longer lasting cushions made with various agents including hyaluronic acid (HA), hydroxypropyl methylcellulose (HPMC), succinylated gelatin, glycerol, and a fibrinogen solution.^{26–32} Currently, there are no injection solutions that are specifically approved for EMR by the U.S. Food and Drug Administration; therefore, all solutions mentioned in this document would be considered off-label. A 0.4% solution of HA is approved as an injection solution for

TABLE 1. Commercially available devices for EMR

Mucosectomy devices	Endoscope diameter, mm	Manufacturer	Cost, US\$*	Minimum working channel size required, mm
EMR kits (include cap, needle, and 25-mm crescent snare)		Olympus America Inc, Center Valley, PA	347 each	2.0
Hard straight 13.9-mm cap	9.3-10			
Hard straight 14.9-mm cap	10-11			
Hard wide oblique 16.1-mm cap	9.3-10			
Hard wide oblique 16.1-mm cap	10-11			
Hard straight 12.9-mm cap	8.6-9.2			
Hard wide oblique 16.1-mm cap	8.6-9.2			
Soft oblique 18-mm cap	8.6-9			
Soft oblique 18-mm cap	9.1-9.8			
Soft oblique 18-mm cap	9.8-10.4			
Soft oblique 18-mm cap	10.3-11.3			
Soft oblique 18-mm cap	11.2-11.8			
Duette Multi-Band Mucosectomy device		Cook Medical Inc, Winston-Salem, NC	315 each	
DT-6	9.5-13			3.7
DT-6-5F	9.5-13			2.8
DT-6-XL	11-14			3.7

*Manufacturer list price is provided as a reference. The actual price may vary depending on specific contracts.

submucosal injection in Japan (MucoUp; Johnson & Johnson, Tokyo, Japan) and has been demonstrated to sustain mucosal lifting longer than saline solution, reducing the volume of injection solution necessary to complete an endoscopic resection.²⁸

Randomized studies evaluating HA solutions (0.4%, 0.2%, and 0.13%) used for submucosal injections in endoscopic resection demonstrate that HA solutions are more effective in maintaining mucosal elevation than saline solution.^{28,33,34} An inexpensive, over-the-counter preparation of HA (0.15% concentration) is available in the United States (Blink Contacts; AMO, Santa Ana, Calif) and was reported in a retrospective case series to be an effective agent for submucosal lifting for EMR.³⁵ HPMC has also been demonstrated to be effective in mucosal lifting for EMR.^{29,30,36} HPMC preparations are available in the United States as ophthalmic lubricants and are typically viscous solutions and must be diluted to 0.3% to 0.8% to facilitate injection. The use of succinylated gelatin as a submucosal injection solution for colonic EMR has been demonstrated to facilitate removal of large colonic lesions (>20 mm) in fewer pieces for piecemeal EMR in a randomized, double-blind trial compared with normal saline solution.³⁷ This study also demonstrated that the use of succinylated gelatin resulted in fewer resections per lesion, fewer injections per lesion, lower injection volumes, and shorter procedure duration. Glycerol (10% solution) and a solution containing fibrinogen have also been reported as effective in sustaining mucosal lifting after submucosal injection; however, the use of these agents has not been

reported in the United States.^{31,32} Tissue damage, delayed healing, and local inflammatory reaction have been reported at the injection sites when using HPMC, hypertonic sodium chloride (3.75%), and hypertonic dextrose ($\geq 20\%$) in animal models; however, the clinical significance of these findings has not been studied.^{38,39}

The volume of submucosal injection solution used during EMR varies depending on the size of the lesion and the solution used for injection. Repeated injections may be required if the cushion dissipates before complete removal of the lesion.

Dilute epinephrine (1:100,000–1:200,000) is often added to the submucosal injection fluid because of the theoretical benefits of decreased bleeding and a sustained submucosal cushion (due to delayed absorption of fluid resulting from decreased vascular flow) and is generally considered to be safe.⁴⁰ Submucosal injection of epinephrine potentially can result in systemic effects such as severe hypertension, ventricular tachycardia, and intestinal ischemia; however, case reports regarding these complications are rare and result from procedures in which the goal of therapy was hemostasis rather than EMR and during which higher concentrations of epinephrine (1:10,000) were used.⁴¹⁻⁴³ Staining dye (ie, diluted indigo carmine or methylene blue) is frequently added to the injection solution to facilitate identification of the lateral and deep margins of the target lesion before and during the resection process. The staining dye may also improve recognition of muscularis propria injury and intraprocedural perforation.^{44,45}

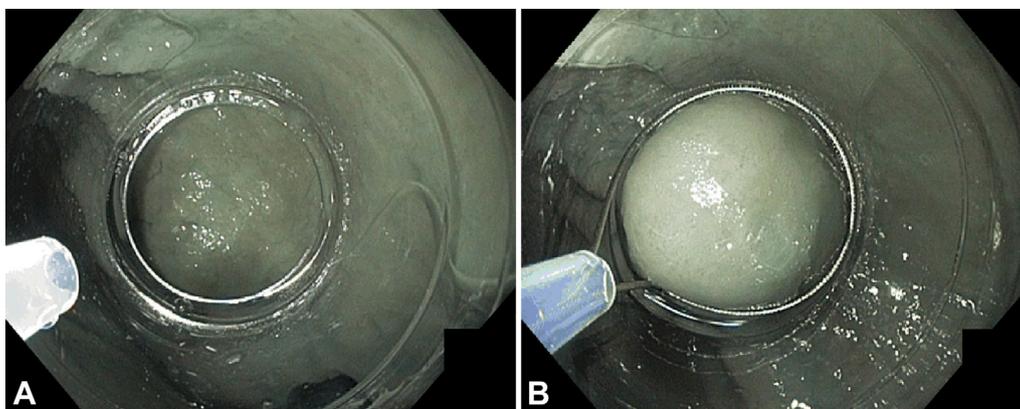


Figure 1. **A**, A clear plastic EMR cap attached to the end of an endoscope. **B**, The snare is opened and positioned on the internal circumferential ridge at the tip of the cap before suctioning the lesion into the cap. (Photographs courtesy of Olympus America, Center Valley, Pa.)

CLINICAL APPLICATIONS

EMR may be used for definitive therapy of premalignant and early-stage (T1N0) malignant lesions of the digestive tract if there is limited submucosal invasion. EUS is often used for locoregional staging before endoscopic resection. EMR can also be used to obtain larger histologic specimens (compared with the standard endoscopic tissue sampling techniques) and can provide an accurate histological T stage for these superficial malignancies.⁴⁶ These techniques can also be used to obtain a histologic diagnosis of subepithelial lesions in the GI tract located in the muscularis mucosa or superficial submucosa.^{47,48} In general, EMR should not be attempted if invasion into the deep submucosa or beyond is suspected. Nonlifting of the lesion after submucosal injection is a predictor of deep invasion and indicates that the lesion is not amenable to endoscopic removal.^{49,50} However, EMR may be attempted if the nonlifting is thought to be a consequence of submucosal fibrosis related to previous manipulation (previous biopsy or attempted/incomplete EMR) of the lesion.¹⁰ In addition, it has been shown that deep submucosal invasive cancer can be predicted with endoscopic imaging evaluation by using either the NBI international colorectal endoscopic classification or the Kudo classification (using chromoendoscopy and magnification endoscopy). Both NBI International Colorectal Endoscopic Classification type 3 lesions and Kudo type V lesions predict deep submucosal invasive carcinoma with endoscopic evaluation exhibiting areas of irregular disrupted or missing vessels along with an amorphous or absent surface/pit pattern on endoscopic evaluation.^{51,52}

EASE OF USE

EMR is essentially a variation of standard polypectomy using specialized devices. Depending on the size and location of the lesion, EMR can potentially be a technically difficult and time-consuming procedure; however, it is technically

easier to perform than ESD.^{15,53,54} For large gastric lesions, the reported mean time to complete EMR is 25.8 ± 25.9 minutes compared with 84.0 ± 54.6 minutes for lesion removal by ESD.⁵⁵

Injection-assisted EMR offers the advantages of wide availability because it does not require specialized kits. During cap-assisted EMR, the positioning of the snare within the cap before tissue capture may be challenging and a relatively unfamiliar maneuver for endoscopists and assistants. Positioning of the snare within the cap may be facilitated by lightly approximating the endoscope tip with the cap against an area of normal mucosa before attempting EMR of the target lesion. Ligation-assisted EMR is relatively easy to perform because it combines commonly used endoscopic techniques for variceal band ligation and snare polypectomy and does not require special prepositioning of the snare. In addition, multiple resections can be performed sequentially.

EFFICACY

Esophagus

EMR and ESD are indicated for treatment of superficial esophageal cancer and Barrett's esophagus-associated neoplasia (high-grade dysplasia and intramucosal carcinoma).⁵⁶⁻⁵⁸

Barrett's esophagus-associated neoplasia. EMR is commonly used for Barrett's esophagus-associated neoplasia. Techniques vary from focal EMR of nodular lesions with adjunct ablation techniques to complete EMR for eradication of the entire Barrett's segment. A randomized trial comparing cap-assisted EMR with ligation-assisted EMR for the resection of Barrett's-associated neoplasia demonstrated that ligation-assisted EMR was significantly faster than cap-assisted EMR with median procedure times of 34 minutes and 50 minutes, respectively ($P = .02$) with no differences in rates of adverse events or quality of the resection specimens.⁵⁹

TABLE 2. Solutions for submucosal injection during EMR and ESD

Solution	Cushion duration	Advantages	Disadvantages
Normal saline solution (0.9%)	+	Easy to inject, inexpensive, readily available	Dissipates quickly, short duration of mucosal lifting
Hypertonic sodium chloride (3.0%)	++	Easy to inject, inexpensive, readily available	Possible tissue damage and local inflammation at injection sites
Hyaluronic acid (0.13%-0.4%)	++++	Longest-lasting cushion	Limited availability in the U.S. Off-label use preparations available in the U.S. require further clinical evaluation
Hydroxypropyl methylcellulose (0.3%-0.8%)	+++	Long-lasting cushion, relatively inexpensive	Possible tissue damage and local inflammation at injection sites
Succinylated gelatin	++	Easy to inject, inexpensive, readily available	Contraindicated in patients with gelatin hypersensitivity
Glycerol (10%)	++	Inexpensive	
Dextrose (20%, 30%, 50%)	++	Inexpensive, readily available	Possible tissue damage and local inflammation at injection sites Increased risk of postpolypectomy syndrome
Albumin	++	Easy to inject, available in most endoscopy units	Expensive
Fibrinogen	+++	Easy to inject, long-lasting cushion	Expensive, not readily available

A single-center study of 107 patients evaluating the efficacy of complete EMR for Barrett's esophagus-associated neoplasia demonstrated that EMR was able to completely eradicate Barrett's esophagus and all associated neoplasia (high-grade dysplasia and intramucosal carcinoma) in 98.8% of patients who completed therapy per protocol without high-risk characteristics (submucosal invasion, poorly differentiated tumors, or evidence of lymphatic or vascular invasion) and in 80.4% of patients who underwent therapy with an intention to treat including those patients who had high-risk characteristics.⁵⁸ Recurrence rates for both cancer and high-grade dysplasia were 1.4%. Another multicenter retrospective study from Europe evaluated patients who had Barrett's esophagus-associated neoplasia treated with complete EMR of Barrett's esophagus and demonstrated that 58% required additional thermal ablation to eradicate residual disease.⁵⁶ Neoplasia recurred in 6.2% of patients.

EMR has also been evaluated in conjunction with radiofrequency ablation for the treatment of Barrett's esophagus-associated neoplasia, in which EMR was initially performed on any endoscopically visible abnormalities, followed by circumferential radiofrequency ablation performed at least 6 weeks after EMR.⁶⁰ After initial complete eradication of Barrett's esophagus, sustained remission of neoplasia and intestinal metaplasia was achieved in 90% of patients at 5 years of follow-up.

Superficial squamous cell cancer. A meta-analysis that included 8 studies from Asia comparing results of ESD and EMR for endoscopic resection of superficial esophageal cancer (primarily squamous cell carcinoma) demonstrated that ESD compared with EMR had a significantly higher

en bloc resection rate (97.1% vs 49.3%; odds ratio [OR] 52.76; 95% confidence interval [CI], 25.57-108.84) and a lower recurrence rate (0.3% vs 11.5%; OR 0.08; 95% CI, 0.03-0.23); however, there was no difference in recurrence rate if the lesion size was less than 20 mm (OR 0.34; 95% CI, 0.06-2.08).⁵⁷ In addition, the procedure duration was significantly longer for ESD compared with EMR.

Stomach

Early gastric cancer. Both EMR and ESD are used for the resection of early gastric cancer, and in the United States, the choice is often dictated by local availability of endoscopic and surgical expertise. Asian data indicate that ESD is associated with lower local recurrence rates than EMR, although survival rates are similar.⁶¹ A meta-analysis that included 9 retrospective studies evaluated the efficacy of ESD and EMR.⁶¹ Although the mean time for ESD was longer than EMR, the ESD group had a significantly lower local recurrence rate than EMR (0.7% vs 6.4%; OR 0.10; 95% CI, 0.06-0.18). ESD is the preferred method for removal of early gastric cancer lesions in Asia because it allows histological assessment of lateral margins that is not possible with piecemeal EMR and is associated with lower local recurrence rates.⁶² EMR may be preferred in patients with severe comorbid conditions such as liver cirrhosis or cardiovascular disease because EMR is associated with shorter procedure times and fewer adverse events.⁶³ A meta-analysis has demonstrated that proton pump inhibitors are superior to histamine type 2 receptor antagonists for the prevention of bleeding after gastric EMR.⁶⁴

Gastric carcinoids. EMR has been reported to be effective in resecting type 1 gastric carcinoids (those associated with chronic atrophic gastritis) that are less than 1 cm in diameter.⁶⁵⁻⁶⁷ EMR has been reported to be associated with a slightly lower rate of complete resection compared with ESD due to positive deep margins; however, local recurrence rates and survival are similar.^{66,67}

Duodenum

Nonampullary duodenal adenomas. Duodenal lesions not involving the major duodenal papilla can be removed with a variety of EMR techniques, but carries an increased risk of bleeding and perforation because the duodenum has increased vascularity and a thin wall. The majority of published reports on endoscopic removal of duodenal polyps originates from high-volume centers and are limited by low numbers of patients and a retrospective study design.⁶⁸⁻⁷¹ Reported success rates vary from 70% to 96% for nonampullary duodenal lesions.^{68,69,71} In addition, the technique of UEMR has been reported for resecting nonampullary duodenal adenomas with high success rates for complete resection (83% at the index session); however, adverse events included delayed bleeding, water intoxication syndrome, and stricture formation.⁷²

Colon

Injection-assisted EMR is widely used for the resection of large or flat colonic lesions. A systematic review and meta-analysis demonstrated that local recurrence after EMR occurs in 3% of cases in which the lesion is removed en bloc and in 20% of cases in which the lesion is removed in piecemeal fashion.⁷³ For recurrences that were retreated with endoscopic therapy (APC and/or EMR), the subsequent recurrence rate was 21%, with successful eradication being achieved in 91.4% of recurrences after a mean of 1.2 additional sessions. Another large multicenter prospective study with 1000 consecutive wide-field EMRs of large sessile adenomas demonstrated a 16% recurrence rate at 4 months, usually unifocal and diminutive, and a 4% recurrence rate at 16 months.²³ Recurrences were managed endoscopically in 93% of cases. If a large adenoma (>15 mm) is removed in piecemeal fashion, the patient should have a repeat colonoscopy in 6 to 12 months to evaluate for local recurrence.^{73,74} A meta-analysis comparing ESD with EMR for colorectal tumors that included 6 studies (1642 total lesions) demonstrated that ESD had a higher en bloc resection rate and lower initial local recurrence rate than EMR; however, ESD was more time-consuming and generally required hospitalization for observation after the procedure.⁷⁵

Typically, EMR in the colon is performed by using the injection-assisted EMR technique; however, UEMR without submucosal injection has also been reported.⁹ When the UEMR technique was used, the complete removal rate for recurrences was significantly higher compared with injection-assisted EMR (88.9% vs 31.8%, $P < .001$)

in a nonrandomized clinical trial.¹¹ Furthermore, the recurrence rate was significantly lower in the UEMR group than the EMR group (10% vs 39.4%, $P = .02$).

Although several studies have reported no recurrence after endoscopic removal of malignant colonic polyps, the effectiveness of EMR for the treatment of these lesions has been questioned, and EMR should not be attempted for nonlifting lesions or lesions classified as Paris II-c/III.^{15,76-78} However, nonlifting lesions that have previously been manipulated (biopsy or attempted EMR) before referral for resection are usually amenable to EMR.¹⁰

Endoscopic resection has also been reported to be successful in resecting small rectal carcinoid tumors. Technically, the procedure should be considered an endoscopic submucosal resection because a majority of rectal carcinoid tumors extend into the submucosal layer.^{79,80} The use of ligation-assisted EMR for lesions that were estimated to be less than 1 cm in diameter has resulted in resections with negative margins.⁷⁹ However, another study that compared ESD with ligation-assisted EMR for endoscopic resection of carcinoid tumors that were less than 16 mm demonstrated a higher histologically complete resection rate with ESD compared with EMR (90.3% vs 71.0%, $P = .035$), although ESD took longer to perform.⁸¹

Safety

Adverse events after EMR include bleeding, perforation, and strictures. Bleeding is the most common adverse event of EMR.

Colonic EMR. Intraprocedural bleeding rates after EMR of colorectal lesions larger than 20 mm are reported to be between 11% and 22%.^{14,82} The application of soft coagulation with the tip of a snare has been demonstrated to be both safe and effective for the treatment of intraprocedural bleeding during EMR of large colonic polyps.⁸² Other methods including hot biopsy forceps, monopolar hemostatic forceps, bicap probes, APC, and endoscopic clips can be used for achieving hemostasis. Risk factors for intraprocedural bleeding include lesion size, Paris endoscopic classification of 0-IIa + Is, tubulovillous or villous histology, and low-volume institutions.¹⁴ Bleeding rates after EMR of large colonic polyps range from 2% to 11%.¹²⁻¹⁸ The clinically significant bleeding rate after EMR of sessile colorectal polyps larger than 20 mm was reported to be 6% in a large prospective, multicenter study that included 1039 patients.¹⁴ Of the patients with clinically significant bleeding, 34% required endoscopic therapy. Prophylactic endoscopic coagulation of nonbleeding vessels by using coagulating forceps after EMR of colorectal lesions larger than 20 mm did not significantly decrease the incidence of delayed postprocedure bleeding compared with control subjects who received no additional therapy (5.2% vs 8.0%, $P = .3$). Risk factors for clinically significant postprocedural bleeding included a proximal colonic location, polyp size, and intraprocedural bleeding.¹⁴

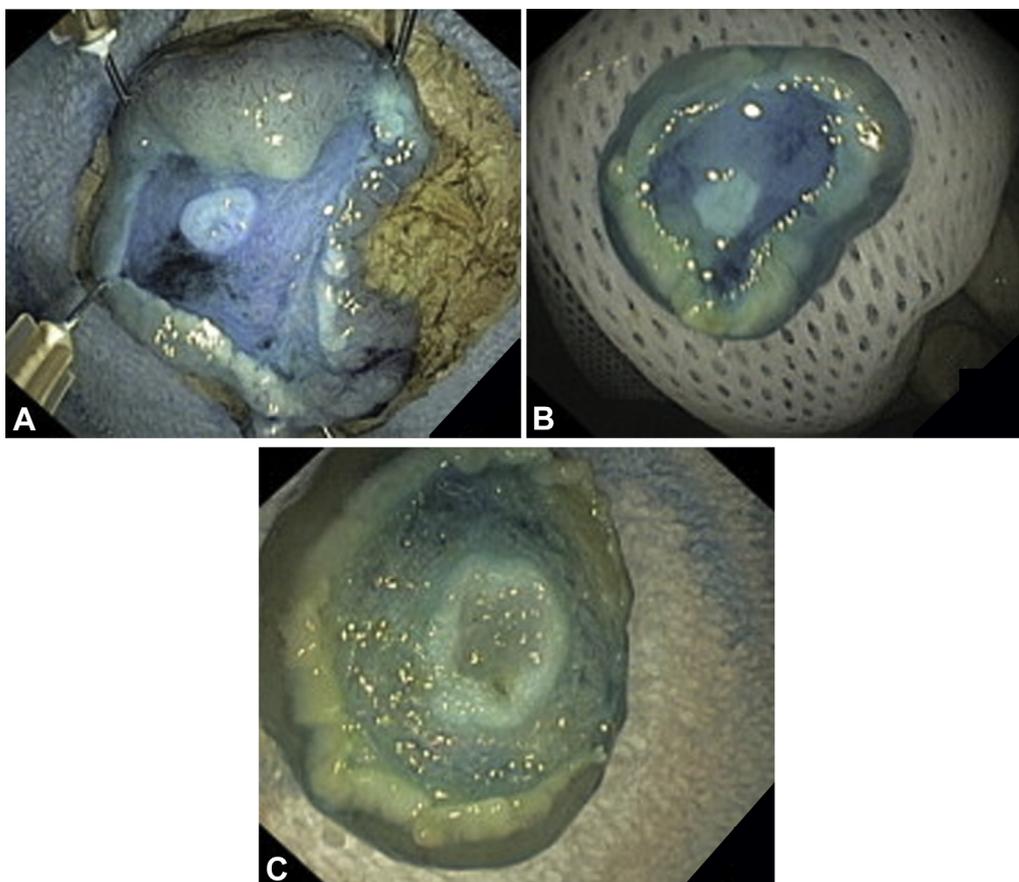


Figure 2. Three examples of a target sign in the resected specimen. All 3 figures demonstrate resected polyps with resected muscularis propria appearing as a white circular disk surrounded by blue-stained submucosa, giving the appearance of a “target.” (Reprinted with permission from Swan et al.⁸⁴)

Perforation after EMR of colonic lesions is also rare (<1%).^{15,16,76,83} A perforation can be identified by carefully examining the resection defect. Also, the transected surface of the resected specimen should be examined for a “target” sign. If muscularis propria has been inadvertently resected, the transected surface will have a white to gray central circular disk surrounded by blue-stained submucosal tissue (if the submucosal injectate contained blue dye), giving the appearance of a “target” (Figs. 2 and 3).⁸⁴ Small perforations recognized during the procedure can be successfully sealed by using endoscopic clips.⁸⁴⁻⁸⁷ Larger perforations may require urgent salvage surgery to prevent peritonitis.

Esophageal EMR. Bleeding after EMR in the esophagus is uncommon.^{21,88-92} In the largest single-center study that included 681 patients who underwent 2513 EMRs, significant bleeding requiring intervention, transfusion, or hospitalization was noted in only 1.2% of patients.⁹²

Reported perforation rates during EMR for esophageal lesions are relatively low at less than 0.5% for physicians who are experienced in performing EMR.^{53,58,92-100} However, 1 study demonstrated a perforation rate of 5% in the first 120 esophageal EMRs performed by 6 physicians who were provided with structured training.¹⁰¹ A meta-analysis comparing adverse event rates for ESD and EMR for

superficial esophageal cancers demonstrated that ESD has a significantly higher rate of perforation (OR 2.19; 95% CI, 1.08-4.47; $P = .03$).⁵⁷

Stenosis has been reported in 6% to 88% of patients after endoscopic removal of esophageal lesions.^{46,58,94,101-104} Esophageal strictures are more common after large mucosal resections and resection of multiple lesions.^{101,104} Circumferential EMR is associated with higher stenosis rates ranging from 41% to 88%.^{58,101} Esophageal strictures usually can be successfully treated by endoscopic dilation.^{58,104}

Gastric and duodenal EMR. Intraprocedural bleeding rates during gastric EMR range from 0% to 11.5% and can be managed with standard endoscopic hemostasis techniques.^{53,105,106} Delayed bleeding after gastric EMR occurs in approximately 5% of patients, with intraprocedural bleeding being the best predictor of delayed bleeding.¹⁰⁷ The risk of perforation due to gastric EMR is reported to be 1% according to a systematic review.¹⁰⁸ Intraprocedural bleeding rates for EMR in the duodenum are reported to be between 11.5% and 19.3% for lesions smaller than 3 cm⁶⁹⁻⁷¹; however, they have been reported to be as high as 57.8% for giant (>3 cm) lesions.⁷⁰ Perforations due to EMR in the duodenum are reported to be uncommon (about 2%); however, this is based on

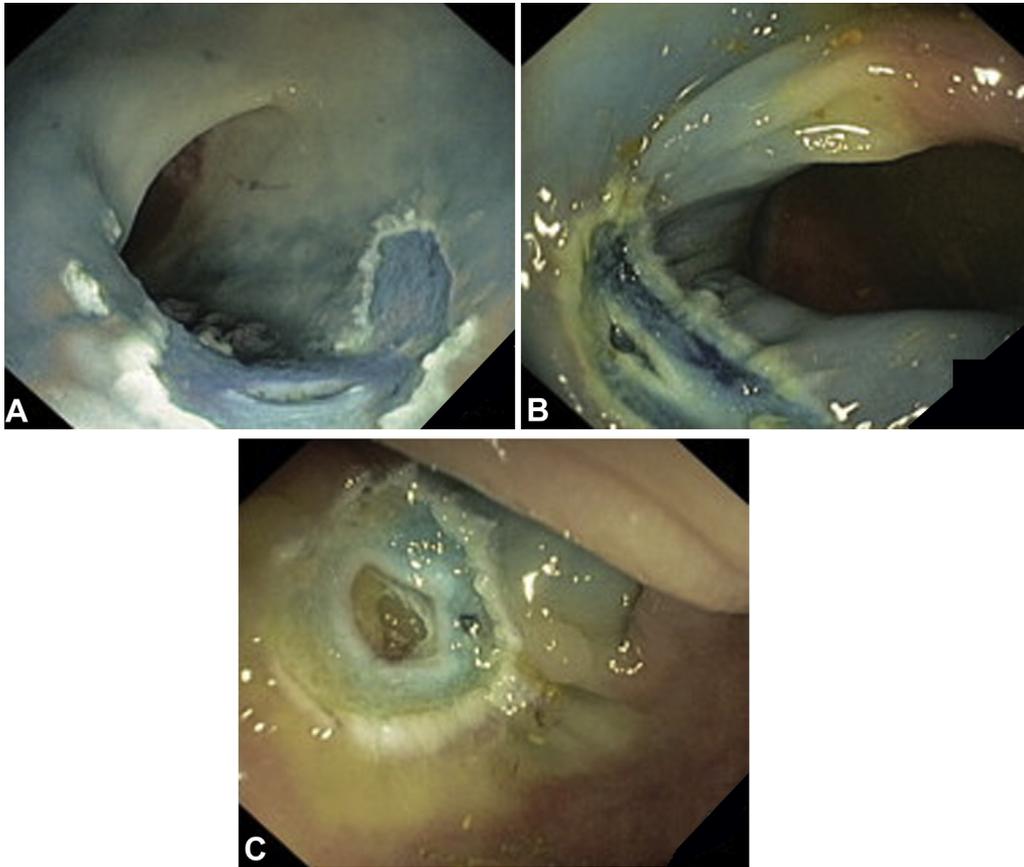


Figure 3. The resection sites corresponding to the resection specimens in Figure 2. **A**, The resection site corresponding to the resected specimen in Figure 2A. **B**, The resection site corresponding to the resected specimen in Figure 2B. **C**, The resection site corresponding to the resected specimen in Figure 2C. A defect in the muscularis propria can be seen at the center of each resection site. (Reprinted with permission from Swan et al.⁸⁴)

data from a tertiary center performing relatively a high volume of EMRs within the duodenum.⁷⁰ EMR in the duodenum should be performed with caution due to the increased risk of bleeding and perforation.

FINANCIAL CONSIDERATIONS

In 2014, new Current Procedural Terminology (CPT) category I codes for upper GI EMR were established (43211 for esophagoscopy, 43254 for EGD). These codes apply to injection-assisted, cap-assisted, and ligation-assisted techniques, including identification and demarcation of the lesion, submucosal injection, and snare resection. There are also new CPT codes for EMR in the colon for 2015: 45349 for flexible sigmoidoscopy, 44403 for colonoscopy through a stoma, and 45390 for colonoscopy (Table 3).

However, because of complexities under current review, the colon codes should not be used for the physician professional service for Medicare patients for 2015.¹⁰⁹ This reference describes the options for the physician to bill the procedure either in the same fashion as was reported in 2014 or to use a combination of codes (eg, for the colonoscopy with EMR, base code 45378 plus G6021 [CMS

designated code for the intestine unlisted service for 2015] could be reported). Use of the modifier 22 (unusual procedural services) can increase the reimbursement for the procedure, but the supportive details of how the services were substantially more extensive (describe the time and the work complexity, resources used) compared with a standard polypectomy must be documented and submitted with the procedure report.

Note that for all payers, the facility (hospital outpatient or ambulatory surgery center) should bill the 2015 colon codes even though the physician coding differs.

For all applications of the new 2015 EMR codes, biopsy of the same lesion, submucosal injection of the same lesion, snare removal, or (also new) band ligation codes should not be separately reported because these are all considered elements of EMR. In addition, if bleeding occurs as a result of the procedure, control of bleeding is not separately reported during the same session.

AREAS FOR FUTURE RESEARCH

The search for an ideal injection solution for EMR is ongoing. There is a consensus in the literature that after

TABLE 3. CPT codes for EMR in the colon

CPT 2015 code: facility Medicare or commercial or physician commercial	Description of new codes for 2015	CMS CY 2015 crosswalk for Medicare plans for physician billing
44403	Colonoscopy through stoma with EMR	44388, G6021
45349	Sigmoidoscopy with EMR	45330, G6021
45390	Colonoscopy with EMR	45378, G6021
Medicare pays these for facility, not for MD in 2015		Bill a base code for the family of codes plus the G unlisted intestine service code. Usual fee for base code. G code fee varies per schedule attached. Commercial, exchange, Medicaid billing: use 2015 codes unless told otherwise.
2014 CPT code	2015 HCPCS code: for Medicare physician billing	Long descriptor
44799	G6021	Unlisted procedure, intestine

CPT, Current Procedural Terminology; HCPCS, Healthcare Procedure Coding System.

endoscopic removal of large premalignant and early malignant lesions, patients should have endoscopic surveillance, but studies defining optimal follow-up intervals are needed. In addition, as experience in ESD grows, studies comparing piecemeal EMR with en bloc ESD of larger mucosal lesions will help to further define the indications for EMR and ESD.

SUMMARY

EMR has become an established therapeutic option for premalignant and early-stage GI malignancies, particularly in the esophagus and colon. EMR can also aid in the diagnosis and therapy of subepithelial lesions localized to the muscularis mucosa or submucosa. Several dedicated EMR devices are available to facilitate these procedures. Adverse event rates, particularly bleeding and perforation, are higher after EMR relative to other basic endoscopic interventions but lower than adverse event rates for ESD. Endoscopists performing EMR should be knowledgeable and skilled in managing potential adverse events resulting from EMR.

DISCLOSURES

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Abbreviations: APC, argon plasma coagulation; CI, confidence interval; ESD, endoscopic submucosal dissection; HA, hyaluronic acid; HPMC, hydroxypropyl methylcellulose; OR, odds ratio; UEMR, underwater EMR.

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