Endoscopic Mucosal Resection: Best Practices for Gastrointestinal Endoscopists

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Abstract: Endoscopic mucosal resection (EMR) is an endoscopic technique used to remove sessile or flat lesions from the gastrointestinal tract. This article reviews EMR and focuses on large colorectal polyps, which constitute the most common indication for EMR. Various methods of polyp evaluation can help gastroenterologists determine whether EMR is feasible and whether referral to an advanced endoscopist may be necessary. Techniques for performing EMR include conventional hot-snare EMR with submucosal injection and electrocautery snare removal of colorectal lesions, as well as alternative EMR techniques such as cold-snare EMR and underwater EMR. Key adverse events associated with EMR include bleeding, perforation, and postpolypectomy coagulation syndrome. Finally, as residual or recurrent polyp formation is possible regardless of EMR technique, this article addresses the importance of surveillance post-EMR and the patients who are at highest risk for polyp recurrence.

Keywords

Gastrointestinal neoplasms, gastrointestinal endoscopy, adenomatous polyps, colorectal polyps, endoscopic mucosal resection

Endoscopic mucosal resection (EMR) is an endoscopic technique developed to remove sessile or flat neoplasms of the mucosa of the gastrointestinal (GI) tract. EMR can be classified a number of ways. One common means of classification is based on endoscopic technique, which includes injection-assisted EMR, cap-assisted EMR, ligation-assisted EMR, and underwater EMR (U-EMR).[1] Of these, the most frequently used technique generally is injection-assisted EMR, in which a lifting solution is injected into the submucosal space to facilitate safe and complete removal of the lesion while minimizing damage to deeper layers. The choice of solution for submucosal lift and the method for lesion removal can vary, as will be discussed.

Another common means for classifying EMR is the digestive lumen in which EMR is performed. EMR can be performed almost anywhere from the esophagus to the rectum, although the indications, techniques, and outcomes at each site may vary. EMR in the esophagus is indicated in Barrett esophagus–associated dysplasia and superficial esophageal cancer.[1-3] For superficial esophageal cancer, endoscopic submucosal dissection (ESD), a procedure in which a lesion is removed through deeper layer dissection, has generally higher en bloc resection rates and lower recurrence rates than EMR. Notably, for lesions smaller than 20 mm, there is no difference between EMR and ESD in recurrence rate, and a longer procedure time is required for ESD.[4] EMR in the stomach can be performed for early gastric cancer and type 1 gastric carcinoid, among other indications.[1] However, as with early esophageal cancer, EMR has a higher recurrence rate than ESD for both early gastric cancer[5,6] and gastric carcinoid.[7] EMR in the small intestine is most often performed for duodenal adenomas. Of note, EMR and ESD in the duodenum are considered higher risk than elsewhere, given the increased vascularity and relatively thin wall leading to higher rates of bleeding and perforation.[1]

The colon is the most frequent site for EMR; indeed, over the past decade, EMR has become a cornerstone technique for the removal of large colorectal polyps.[8-11] EMR allows for efficient and complete resection of a polyp, thereby preventing colorectal cancer–related death and avoiding risks and other drawbacks of surgery.[12] Indeed, surgical resection, which was historically standard treatment for large polyps, is associated with significant morbidity and mortality,[12] whereas EMR has been demonstrated to be both safe and effective, with high R0 (ie, complete) resection rates.[13] For large lesions, particularly in the left colon and rectum, ESD is also a highly effective option to achieve R0 resection.[14]

This article reviews EMR and focuses on large colorectal polyps. It discusses endoscopic evaluation of polyps prior to performing EMR, common EMR techniques and their respective considerations, adverse events (AEs) of EMR, and surveillance post-EMR.

Tips for General Gastroenterologists

Prior to performing EMR, the endoscopist must determine whether EMR is feasible and whether referral to an endoscopist more experienced in the removal of large polyps is appropriate. Unsuccessful resection attempts or extensive biopsying of a lesion can hinder future EMR attempts. Therefore, prior to attempted resection, careful polyp evaluation and reflection is essential.

Assessing Polyp Features and Endoscopic Mucosal Resection Feasibility

After a polyp is identified, the endoscopist must assess the appropriateness and feasibility of EMR; polyps harboring malignancy with submucosal invasion are unlikely to be completely removed by EMR, and, thus, the area adjacent to the lesion should be tattooed and referred for surgical resection or advanced endoscopic techniques (eg, ESD). Various polyp features, including size, location, morphology, and surface characteristics, can determine the likelihood of malignancy and difficulty of resection.[15]

As previously mentioned, polyp size is one of the most important risk factors for malignancy. In a large prospective study, invasive carcinoma was not found in adenomas 5 mm or smaller, although polyps 6 mm to 15 mm, 16 mm to 25 mm, 26 mm to 35 mm, and larger than 35 mm had a 2%, 19%, 43%, and 76% risk of invasive carcinoma, respectively.[16] Location also plays a role in resection difficulty, with right colonic lesions more difficult to resect owing to decreased scope mobility, higher frequency of sessile morphology, and the relative thinness of the right colonic wall. Polyp morphology provides information regarding the malignancy risk and submucosal invasion; in the Paris classification, polyps are morphologically categorized as pedunculated (Ip), sessile (Is), flat (0-IIa [slightly elevated], 0-IIb [flat], 0-IIc [slightly depressed]), or ulcerated (0-III).[17] Polyps that have a depressed component (0-IIc) or are 0-Is or 0-IIa+Is are associated with higher rates of submucosal invasive cancer.[18]

Polyp surface patterns can be classified by various means. In the Narrow-Band Imaging International Colorectal Endoscopic (NICE) classification, polyps are categorized as hyperplastic or sessile serrated polyps (type 1), conventional adenomas (type 2), or deep submucosal invasive cancer (type 3) based on color, associated vessels, and surface patterns.[19] A multicenter, prospective study found that the NICE classification identified lesions with deep invasion with a sensitivity and specificity of 58% and 96%, respectively, and had a positive predictive value and negative predictive value of 42% and 98%, respectively.[20] In the Kudo classification, polyps are classified based on the following pit patterns: round (type I), papillary/stellar (type II), small tubular or round (type III-S), large tubular or round (type III-L), gyrus/branchlike (type IV), nonstructured/amorphous (type V-I), or with a decrease of amorphous pits (type V-N). Types I and II polyps are considered benign, whereas types III through V polyps are considered as showing dysplastic changes.[21] In a prospective, multicenter study, types III and IV patterns were associated with a 4% and 5% risk of invasion, respectively; type V had a 56% risk of invasion.[22]

A composite method of assessing difficulty of polyp resection is the Size, Morphology, Site, Access (SMSA) scoring system.[23] In the SMSA system, points are given based on size (1-9 points), morphology (1-3 points), site (1-2 points), and access (1-3 points). Polyps are then assigned a total score, with corresponding levels of complexity: level 1 (4-5 points), level 2 (6-9 points), level 3

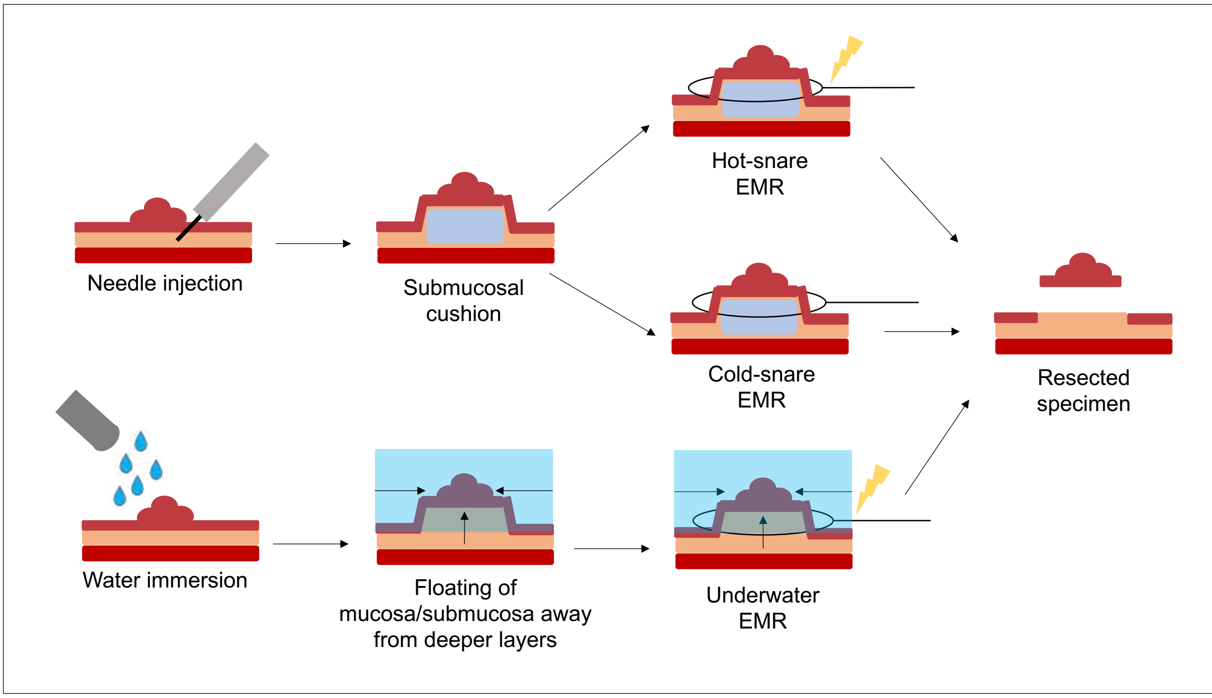

Figure. Three different endoscopic mucosal resection (EMR) methods for removal of colorectal polyps. Adapted from Yamashina et al.[73]

(10-12 points), or level 4 (>12 points). Using this scoring system and the context of his or her own EMR experience and skill set, an endoscopist can estimate polypectomy difficulty, predict which polyps are at increased risk of failed EMR, and refer a case to a more experienced endoscopist or surgeon if necessary.[24,25]

Knowing When to Refer

Once EMR is determined to be appropriate, the endoscopist must decide either to proceed with removing the polyp or to refer the case. Incomplete polyp removal is resource inefficient and makes future attempts at EMR more difficult; as a result, one should aim to completely remove a polyp on the first attempt. For this reason, for resecting polyps 20 mm or larger, the US Multi-Society Task Force (USMSTF) recommends that the endoscopist be experienced in advanced polyp resection techniques.[26] There is considerable institution-specific variability regarding whether an individual who is experienced in polyp resection techniques is an advanced endoscopist or experienced general gastroenterologist.

Endoscopic Mucosal Resection Techniques

In the colon, the 3 most common techniques for removal of large nonpedunculated polyps are hot-snare EMR (HS-EMR), cold-snare EMR (CS-EMR), and U-EMR, as shown in the Figure. Both HS-EMR and CS-EMR are variations of injection-assisted EMR wherein submucosal injection is used to create a cushion that lifts the polyp and separates it from the muscularis propria. The polyp is then removed with a snare; in HS-EMR, this is performed with electrosurgical cautery, whereas no cautery is used in CS-EMR. In U-EMR, no submucosal injection is needed. Instead, water immersion is used to float the mucosa and submucosa away from the muscularis propria.[27] Typically, the lesion is then removed by HS resection, although theoretically CS could also be used.

Submucosal Injection

Submucosal injection is performed using a retractable injection needle through the working channel of an endoscope. For large lesions, multiple injections along the perimeter of a lesion may be needed to achieve satisfactory lift.[28] A static or dynamic technique can be used for the injection; in the dynamic technique, an injection is done while the needle position is redirected.[29] Submucosal injection may be targeted to optimize visualization and resection (eg, injecting the proximal aspect of the polyp to shift its surface toward the colonoscope).

There are a variety of substances that can be used for submucosal injection, as summarized in Table 1. Normal saline (NS) is the most commonly used substance; other agents have been shown in animal studies,[30-32] retrospective studies,[33] and randomized controlled trials (RCTs)[34-40] to have benefit vs NS with regard to longer duration of

Table 1. Submucosal Agents Used During EMR

Agent	Description	Cushion Duration[a]	Advantages	Disadvantages	Efficacy (vs NS)
NS	0.9% NS in water	+	• Widely available • Inexpensive • Negligible damage to specimen • Nontoxic	• Low duration of submucosal cushion	N/A
Glycerol	Hypertonic solution (10% glycerol and 5% fructose in NS)	++	• Does not damage resected specimen • Relatively inexpensive	• Limited availability in the United States	• Longer submucosal elevation vs NS[28] • Retrospective study: EMR of 10-19 mm flat lesions with glycerol had higher en bloc resection rate and complete resection rate[33]
DW	Hypertonic solution (concentrations <15% in NS)	++	• Relatively inexpensive	• Significant tissue damage at higher concentrations • Increased risk of postpolypectomy syndrome	• RCT: EMR with 50% DW had smaller volumes, fewer injections, higher en bloc resection rate, and longer persistence of cushion[34] • Meta-analysis: DW and NS equally effective in complete resection rate and complications[43]
Hypertonic saline	3% sodium chloride	++	• Inexpensive • Widely available	• Possible tissue damage and local inflammation	N/A
Albumin	Colloidal solution	++	• Widely available	• Expensive	• Porcine study: Greater mucosal elevation with albumin vs NS[31]
SG	Colloidal solution with similar oncotic pressure to albumin	++	• Widely available • Inexpensive • Nontoxic	• Contraindicated in patients with gelatin hypersensitivity	• RCT: EMR of >20 mm polyps with SG had higher SRQ, fewer resections and injections, lower injection volume, and shorter duration[35] • Meta-analysis: SG and NS equally effective in complete resection rate. SG had a trend toward decreased postpolypectomy bleeding[43]
HPMC	Cellulose derivative with viscoelastic properties	+++	• Widely available	• Moderately expensive • Can cause antigen-antibody reactions	• Porcine study: Greater mucosal elevation with HPMC[31] • Mongrel study: Longer duration of mucosal elevation[32] • RCT: EMR of >15 mm sessile polyps showed no difference in SRQ or other outcomes[36]
FM	Solution from human coagulation proteins with high viscosity	+++	• Relatively inexpensive	• Viral contamination and associated transmission are possible	• Mongrel study: Longer duration of mucosal elevation[32] • RCT: EMR of gastric lesions with FM had no differences in en bloc resection or recurrence but FM had shorter procedure time and lower injection volume[37] • Meta-analysis: FM and NS equally effective in complete resection rate. FM had a trend toward decreased postpolypectomy bleeding[43]
HA	Glycosaminoglycan with high viscosity and water retention capability. Usually in form of 0.4% SH solution	++++	• Nontoxic • No potential antigen-antibody reaction	• Expensive • Can stimulate growth of residual tumor cells	• Porcine study: Greater mucosal elevation with HA[30] • RCT: EMR of polyps ≥20 mm with SH was associated with easier submucosal injection with similar injection time and adverse events[38] • RCT: EMR of polyps <20 mm with HA had higher rates of complete resection and longer mucosal elevation[39] • Meta-analysis: SH and NS equally effective in complete resection rate and complications[43]
HES	Colloidal volume expanding solution	++++	• Relatively inexpensive	N/A	• RCT: EMR of colorectal LST with a diameter of ≥30 mm with HES had lower injection volume, longer submucosal elevation, and shorter procedure time[42] • Meta-analysis: HES and NS equally effective in complete resection rate. HES had a trend toward decreased postpolypectomy bleeding[43]
Eleview and ORISE gel	Synthetic solutions with water, NS, bulking agent, emulsifier, oil component, and methylene blue	++++	• Convenient for clinicians • Nontoxic	• Expensive	• RCT: EMR for polyps ≥20 mm with Eleview had lower injection volumes, lower procedure time, higher SRQ, higher rate of en bloc resection, and similar adverse events[40]

DW, dextrose water; EMR, endoscopic mucosal resection; FM, fibrinogen mixture; HA, hyaluronic acid; HES, hydroxyethyl starch; HPMC, hydroxypropyl methylcellulose; LST, laterally spreading tumor; N/A, not available; NS, normal saline; RCT, randomized controlled trial; SG, succinylated gelatin; SH, sodium hyaluronate; SRQ, Sydney Resection Quotient (size of the polyp divided by the number of pieces resected and the amount of tissue per snare attempt).

[a]The number of plus signs corresponds with the length of cushion duration, with + representing the shortest duration and ++++ representing the longest duration.

submucosal cushion,[28,30-32,38,39,41] injection volume,[34,37,40,42] procedure time,[22,37,40,42] and rates of complete or en bloc resection.[22,33,34,40] However, a meta-analysis examining injection with NS, 50% dextrose water, sodium hyaluronate, succinylated gelatin (SG), hydroxyethyl starch (HES), and fibrinogen mixture (FM) showed no advantage for any single substance in terms of complete resection rate, although there was a favorable trend for HES, SG, and FM in decreasing postpolypectomy bleeding.[43] Overall, there is no compelling evidence that definitively supports the use of one solution over another, although certain advantages and disadvantages may exist in specific scenarios.

Various adjuvants in the injectate can be used. One adjuvant is diluted epinephrine (1:10,000-200,000), which can be added to reduce intraprocedural bleeding and help to maintain a clean resection field.[28] These benefits were demonstrated in a meta-analysis showing that diluted epinephrine reduced early postpolypectomy bleeding during EMR of colorectal polyps 20 mm or larger.[44] Furthermore, reduced vascular flow with epinephrine may also help delay fluid reabsorption and thus may enhance duration of the submucosal cushion. Although epinephrine may have systemic effects, they are mainly observed with higher amounts of epinephrine used for hemostasis.[28] Another adjuvant is a staining dye (eg, methylene blue or indigo carmine). These dyes allow the endoscopist to better differentiate the submucosal layer from the deeper muscle layer and identify margins during EMR.[28] If the muscularis propria is inadvertently resected, the transected surface will not be stained, leading to a target lesion that can help to identify defects.[45] Therefore, addition of a staining dye is advisable during EMR, particularly for lesions that are 20 mm or larger or laterally spreading.[46]

Whether through submucosal injection during HS-EMR and CS-EMR or through water immersion during U-EMR, submucosal lifting improves resection rates of nonpedunculated colorectal polyps.[13] The addition of an adjuvant may add further benefit in select cases.

Hot-Snare Endoscopic Mucosal Resection

In HS-EMR, injection-assisted submucosal lifting is conventionally followed by HS resection, wherein electrical current converted into heat transects the tissue where the snare is closed. This can allow for en bloc resection, ablation of polyp tissue at the margin, and cauterization of smaller blood vessels to mitigate intraprocedural bleeding.[1]

Electrical current in HS-EMR is supplied by electrosurgical generator units (ESUs). Two main types of currents are coagulation and cut currents, which differ based on voltage supplied and duty cycle. Voltage refers to the force that pushes a current through a resistance. Duty cycle refers to the percentage of total time the current is delivered. A pure coagulation current delivers a higher voltage and a low duty, interrupted cycle. This results in a slower increase in temperature, which causes cells to dehydrate without bursting. The resulting desiccation helps to coagulate vessels and prevents bleeding but may inadvertently cause deeper tissue injury. A pure cut current delivers a lower voltage and continuous, 100% duty cycle current. This leads to rapid heating of cells that burst and vaporize, resulting in cleavage of tissue along the snare.[47] Pure cut current has been associated with postpolypectomy bleeding.[48] For these reasons, blended currents with an intermediate duty cycle are often selected.[47]

The optimal ESU current setting during EMR is unknown. Retrospective analysis of blended vs pure coagulation current showed no difference in complications or bleeding rates.[49] However, with blended current, bleeding events occurred immediately or within 12 hours, whereas with pure coagulation current, bleeding 2 to 8 days later was more likely.[49] To investigate these differences, Pohl and colleagues performed an RCT of patients with nonpedunculated polyps 20 mm or larger who underwent HS-EMR.[50] Patients were randomized to either a pure coagulation current or Endo Cut Q (Erbe Elektromedizin), a proprietary combination of blended and cutting currents. There was no difference in complete removal of polyps or recurrence. Rates of severe AEs were similar in the pure coagulation and Endo Cut Q groups (7.9% vs 7.2%). Postprocedural bleeding rates also did not differ, with similar time to bleeding in both groups (2.5 vs 2 days; P=.984). Of note, the authors did find that 11% of the pure coagulation group had immediate bleeding postpolypectomy compared with 17% in the Endo Cut Q group, which was significantly different (P=.006). Overall, no clear recommendation has been made on optimal ESU current during HS-EMR. Regardless of which current is selected, clear communication with the nurse or technician during EMR is essential, as the area of tissue captured influences current density, and quicker snare closure may be important to prevent deep mural injury, particularly in the right colon.

Cold-Snare Endoscopic Mucosal Resection

Although electrocautery during HS-EMR helps with polyp removal and ablation of residual polyp tissue, there is a risk of deep mural injury. As a result, some endoscopists prefer CS-EMR, in which the polyp is removed without electrocautery after submucosal injection.

Current evidence regarding the safety and efficacy of CS-EMR, including comparisons with HS-EMR, is shown in Tables 2 and 3. Efficacy endpoints of interest include en bloc (vs piecemeal) resection, complete histologic resection, and complete macroscopic resection. Complete histologic (R0) resection refers to the absence

Table 2. Characteristics of Studies on CS-EMR and U-EMR

Study	Year	# of Patients	# of Polyps	Type of Study	Size of Polyp	Type of Polyp
CS-EMR						
Suresh et al[51]	2021	310	310	Retrospective	≥20 mm	Nonpedunculated polyps
Tutticci and Hewett[53]	2018	99	163	Prospective	≥10 mm	Nonpedunculated SSLs
Yabuuchi et al[52]	2020	72	80	Prospective	10-14 mm	Nonpedunculated adenomas
Thoguluva Chandrasekar et al[57]	2019	342+	522	Meta-analysis	≥10 mm	Nonpedunculated adenomas
CS-EMR vs HS-EMR						
van Hattem et al[58]	2021	474	562	Retrospective	≥20 mm	Nonpedunculated SSLs
Guo et al[59]	2022	256	256	Retrospective	6-9 mm	All colorectal polyps
Papastergiou et al[54]	2018	155	164	RCT	6-10 mm	Nonpedunculated polyps
Li et al[55]	2020	404	781	RCT	6-20 mm	All colorectal polyps
Thoguluva Chandrasekar et al[56]	2020	911	1137	Meta-analysis	≥10 mm	Nonpedunculated SSLs
U-EMR						
Sandhu et al[63]	2018	93	102	Retrospective	>10 mm	All colorectal polyps
Kawamura et al[64]	2018	38	64	Retrospective	6-40 mm	All colorectal polyps
Binmoeller et al[27]	2012	60	62	Prospective	≥20 mm	Nonpedunculated polyps
Wang et al[76]	2014	21	43	Prospective	8-50 mm	All colorectal polyps
Uedo et al[75]	2015	11	11	Prospective	15-25 mm	All colorectal polyps
Amato et al[67]	2016	25	25	Prospective	10-50 mm	Nonpedunculated polyps
Siau et al[68]	2018	85	97	Prospective	≥10 mm	All colorectal polyps
Schacher et al[69]	2021	24	24	Prospective	>9 mm	All colorectal polyps
U-EMR vs HS-EMR						
Schenck et al[77]	2017	75	101	Retrospective	≥15 mm	Nonpedunculated polyps
Mouchli et al[70]	2020	190	190	Retrospective	≥10 mm	Gastric/duodenal/colorectal polyps
Rodríguez Sánchez et al[71]	2019	137	162	Prospective	>15 mm	Nonpedunculated polyps
Yamashina et al[73]	2019	210	210	RCT	10-20 mm	Nonpedunculated polyps
Yen et al[74]	2020	462	255	RCT	≥6 mm	Nonpedunculated polyps
Zhang et al[65]	2020	130	142	RCT	4-9 mm	Nonpedunculated polyps
Chandan et al[66]	2021	1851	2120	Meta-analysis	≥6 mm	All colorectal polyps
Yamashina et al[72]	2021	777+	1374	Meta-analysis	≥4 mm	All colorectal polyps

Of note, in the meta-analyses by Thoguluva Chandrasekar et al[56] and Yamashina et al,[72] the number of patients was not available for some of the included studies, so the table provides the known number of patients.

CS-EMR, cold-snare endoscopic mucosal resection; HS-EMR, hot-snare endoscopic mucosal resection; RCT, randomized controlled trial; SSL, sessile serrated lesion; U-EMR, underwater endoscopic mucosal resection.

of microscopic tumor in the polyp resection site, whereas complete macroscopic resection refers to the lack of residual polyp seen endoscopically. Safety endpoints include intraprocedural or immediate postprocedural bleeding, delayed bleeding, and perforation. For CS-EMR, en bloc resection rates vary in the literature, with some endoscopists pursuing all CS-EMR in a piecemeal fashion[51] and others reporting an 83% en bloc resection rate.[52] Complete histologic resection is achieved with CS-EMR in 64% to 99% of cases.[52-55] Recurrence on surveillance colonoscopy also ranges widely, from 1% to 35%.[51,53-57] In terms of AEs, 0% to 2% of cases had intraprocedural or immediate postprocedural bleeding[51-57]; delayed bleeding or perforation is extremely rare.[52-58]

Both CS-EMR and HS-EMR have high rates of complete histologic[54,55] as well as macroscopic[58] resection.

Table 3. Current Evidence Regarding the Efficacy and Safety of CS-EMR and U-EMR

Study	En Bloc Resection	Complete Histologic or Macroscopic Resection	Recurrence	Intraprocedural or Immediate Postprocedural Bleeding	Delayed Bleeding	Perforation
CS-EMR						
Suresh et al[51]	0%	–	34.80%	1%	–	–
Tutticci and Hewett[53]	–	98.8%[a]	0.70%	1.8%	None	None
Yabuuchi et al[52]	82.50%	63.8%[a]	–	None	None	None
Thoguluva Chandrasekar et al[57]	–	99.3%[b]	4.1% (overall), 1% for SSL, and 11.1% for adenomas	1.2%	–	None
CS-EMR vs HS-EMR						
van Hattem et al[58]	–	100% vs 99%[b]	4.3% vs 4.6% at 6 months and 2% vs 1.2% at 18 months	–	0% vs 5.1%	–
Guo et al[59]	–	–	–	No difference	No difference	–
Papastergiou et al[54]	–	92.8% vs 96.3% (noninferior)[a]	–	3.6% vs 1.2% (noninferior)	None	None
Li et al[55]	–	94.1% vs 95.5% (NS)[a]	–	4.4% vs 1.9% (NS)	0.8% vs 2.6% (NS)	None
Thoguluva Chandrasekar et al[56]	–	–	0.9% vs 5% (NS on multivariate)	0.7% vs 2% (NS on multivariate)	0% vs 2.3% (NS on multivariate)	0% vs 0.3% (NS on multivariate)
U-EMR						
Sandhu et al[63]	9.80%	–	–	–	9.70%	–
Kawamura et al[64]	81%	54%[a]	–	5% (unclear if delayed or immediate)		2.6%
Binmoeller et al[27]	–	100%[b]	1.90%	–	5%	–
Wang et al[76]	–	97.7%[b]	–	–	2.30%	–
Uedo et al[75]	–	63.6%[a]	–	18.20%	None	None
Amato et al[67]	76%	100%[b]	–	8%	None	None
Siau et al[68]	45.50%	97.9%[b]	20.3% polyp recurrence, 13.6% adenoma recurrence	2.10%	2.10%	–
Schacher et al[69]	66.7%	100%[b]	–	None	None	None
U-EMR vs HS-EMR						
Schenck et al[77]	–	98.6% vs 87.1% (*P*=.012)[b]	7.3% vs 28.3% (*P*=.008)	–	6.7% vs 0% (*P*=.102)	None
Mouchli et al[70]	35.8% vs 62% (*P*<.01)	–	19.1% vs 27.1% (*P*=.215)	2.94% vs 0% (NS)	4.4% vs 4.9% (NS)	None
Rodríguez Sánchez et al[71]	49% vs 62% (*P*=.08)	100% vs 89.3% (*P*=.01)[a]	5.3% vs 17.9% (*P*=.56)	10% vs 2% (NS; unclear if delayed or immediate)		0% vs 0.9%
Yamashina et al[73]	89% vs 75% (*P*=.007)	69% vs 50% (*P*=.011)[a]	–	2% vs 2.8% (NS)	None	None

(Table continues on following page)

Table 3. *(Continued)* Current Evidence Regarding the Efficacy and Safety of CS-EMR and U-EMR

Study	En Bloc Resection	Complete Histologic or Macroscopic Resection	Recurrence	Intraprocedural or Immediate Postprocedural Bleeding	Delayed Bleeding	Perforation
U-EMR vs HS-EMR (Continued)						
Yen et al[74]	89.9% vs 90.2% (*P*=.64)	98% vs 97.1% (*P*=.91)[a]	–	2% vs 1.9% (*P*=.91)	None	None
Zhang et al[65]	94.4% vs 91.5% (noninferior)	83.1% vs 87.3% (noninferior)[a]	–	1.4% vs 1.4% (NS)	2.8% vs 0% (NS)	None
Chandan et al[66]	58.7% vs 49.7%; OR, 1.9 (95% CI, 1.1-3.34); *P*=.02	95.3% vs 81.5%; OR, 3.1 (95% CI, 0.74-12.6); *P*=.14[a]	11.3% vs 27%; OR, 0.3 (95% CI, 0.1-0.8); *P*=.01	6.7% vs 8.7%; OR, 0.8 (95% CI, 0.4-1.8); *P*=.63	2.2% vs 1.7%; OR, 1.5 (95% CI, 0.6-3.9); *P*=.41	0.6% vs 0.8%; OR, 0.9 (95% CI, 0.2-3.1); *P*=.81
Yamashina et al[72]	72.1% vs 58.2%; OR, 1.84 (95% CI, 1.14-2.96)	May result in a slight increase in R0 resection[a]	–	May result in a slight decrease in adverse events vs HS-EMR		

Efficacy endpoints include en bloc resection, rates of complete histologic and macroscopic resection, and recurrence on surveillance colonoscopy. Histologic or R0 resection refers to the lack of microscopic tumor on histopathologic specimens from the polyp resection site. Complete macroscopic resection refers to the lack of endoscopic evidence of residual polyp at the resection site. Safety endpoints include immediate or intraprocedural bleeding (within 48 hours), delayed bleeding (48+ hours after the procedure), and perforation.

CS-EMR, cold-snare endoscopic mucosal resection; HS-EMR, hot-snare endoscopic mucosal resection; NS, nonsignificant; OR, odds ratio; SSL, sessile serrated lesion; U-EMR, underwater endoscopic mucosal resection.

[a]Histologic resection findings. [b]Macroscopic resection findings.

In addition, recurrence rates are similar between the techniques.[58] Thoguluva Chandrasekar and colleagues performed a meta-analysis on large, nonpedunculated, sessile serrated lesions (SSLs) removed by EMR and found that CS-EMR was associated with lower rates of residual polyp on surveillance than HS-EMR (0.9% vs 5%), although this difference was not significant in multivariate analysis.[56] Regarding AEs, there is no reported difference in intraprocedural or immediate postprocedural bleeding.[54-56,58,59] For delayed bleeding, van Hattem and colleagues found that, for large SSLs, 5.1% of HS-EMR cases had delayed bleeding compared with none in the CS-EMR group.[58] Similarly, the meta-analysis performed by Thoguluva Chandrasekar and colleagues found lower rates of delayed bleeding with CS-EMR (0% vs 2.3% for HS-EMR), although this was not significant in multivariate analysis.[56]

Some researchers have suggested that CS-EMR may be an ideal technique for SSLs, which have little to no submucosal fibrosis and a thin mucosal layer only slightly thickened beyond the surrounding mucosa.[60] To support this, a meta-analysis evaluating outcomes after CS-EMR of nonpedunculated colorectal polyps found that the recurrence rate after CS-EMR was only 1% for SSLs compared with 11% for adenomatous lesions.[57] These findings suggest that CS-EMR may be an appropriate alternative to HS-EMR, particularly for SSLs.

Underwater Endoscopic Mucosal Resection

In some instances, submucosal injection can hinder snare capture of a flat polyp.[61] Furthermore, it could also introduce neoplastic cells into deeper wall layers.[62] For these reasons, Binmoeller and colleagues developed the U-EMR technique, in which air is aspirated and water immersion is performed.[27] This floats the mucosa and submucosa away from the deeper muscularis layer and allows for electrosurgical snare capture of the target lesion without submucosal injection.

Current evidence on the safety and efficacy of the U-EMR technique, including comparisons with HS-EMR, is shown in Table 3. The en bloc resection rate with U-EMR varies from 10% to 94%.[63-74] Complete histologic resection is observed in 54% to 100% of cases[64-66,71-75] and complete macroscopic resection is observed in 94% to 100% of cases.[27,66-69,76,77] Rates of polyp recurrence on surveillance colonoscopy range from 2% to 20%.[27,66,68,70,71,77] Intraprocedural or immediate postprocedural bleeding has been reported in 0% to 18% of cases[64-75] and delayed bleeding in 0% to 10% of cases.[27,63-66,71-74] Perforation is extremely rare; Kawamura and colleagues noted 1 perforation in a study of 38 patients (2.6%).[64]

Comparative studies show the potential advantage of U-EMR over HS-EMR. Some studies show higher rates of en bloc resection with U-EMR,[73] although others show lower rates.[70,71] Favoring the former observation, 2 separate meta-analyses found higher en bloc resection rates with U-EMR.[66,72] Of these meta-analyses, Chandan and colleagues also found higher complete macroscopic resection rates with U-EMR than HS-EMR, lower rates of recurrence on surveillance colonoscopy, and no clear difference in rates of immediate or delayed bleeding or perforation[66]; Yamashina and colleagues concluded that there may be a slightly lower risk of AEs with U-EMR.[72] In summary, U-EMR seems to be safe and effective and might allow for more complete resection than HS-EMR.

There is no single trial comparing the 3 different EMR techniques. However, Yuan and colleagues performed a meta-analysis including 36 studies and 3212 polyps comparing HS-EMR, CS-EMR, U-EMR, and other polyp removal techniques.[13] They found that resection techniques with a submucosal lift (including HS-EMR, CS-EMR, and U-EMR) had higher complete histologic resection and en bloc resection rates. Regarding safety, they found that electrocautery with HS-EMR and U-EMR was associated with higher intraprocedural bleeding than CS techniques, including CS-EMR (3% vs 0%). Delayed bleeding, perforation, and postpolypectomy syndrome were rare in all groups. Randomized trials comparing these 3 EMR techniques are needed to determine what the ideal technique may be.

Outcomes of Endoscopic Mucosal Resection

Risk of Recurrent Disease

Various techniques have been explored to mitigate incomplete polypectomy and hence polyp recurrence. As noted, CS-EMR and U-EMR may offer advantages in this regard over HS-EMR.[56] Regardless of the type of EMR pursued, targeting the resection margin may facilitate lower recurrence rates. For example, treatment of HS-EMR resection margins of polyps larger than 20 mm with thermal ablation (argon plasma coagulation or snare-tip soft coagulation) has been demonstrated to reduce adenoma recurrence by up to 50%.[78] The practice of treating resection margins with thermal ablation should be incorporated into routine practice when performing HS-EMR on laterally spreading tumors larger than 20 mm. Differences in electrosurgical settings (ie, blended vs forced coagulation) do not appear to affect polyp recurrence rate.[50] Given the complexity of this procedure, endoscopist experience and preference and individual patient considerations may ultimately determine the optimal method.[79]

Bleeding

Postpolypectomy bleeding is the most common AE after EMR, occurring in 2% to 24% of patients.[80] It is more likely to occur in patients undergoing resection of large, right-sided polyps and in patients receiving antithrombotic agents.[48,81] The EMR technique itself can also affect the risk of postprocedural bleeding. With HS-EMR, the use of electrocautery is thought to minimize intraprocedural bleeding but is also associated with a higher rate of delayed bleeding. In a study comparing CS with HS polypectomy, CS polypectomy was associated with a significantly lower rate of delayed bleeding (0.1% vs 1.1%; *P*<.001).[82] However, similar comparisons between HS-EMR and CS-EMR are not as conclusive. As noted, van Hattem and colleagues found higher rates of delayed bleeding with HS-EMR than with CS-EMR (5.1% vs 0%),[58] although other studies have found no such difference.[54,55,59] In the meta-analysis performed by Thoguluva Chandrasekar and colleagues, delayed bleeding was more common with HS-EMR in univariate analysis but not in multivariate analysis.[56] Furthermore, in a meta-analysis performed by Yuan and colleagues, the authors found no greater incidence of delayed bleeding with any technique but found lower rates of intraprocedural bleeding with CS-EMR when compared with HS-EMR.[13] Therefore, although CS-EMR is intended to decrease delayed bleeding, this benefit has yet to be conclusively demonstrated.

Clipping can be effective in reducing the risk of postpolypectomy bleeding, with an RCT showing a reduction in postprocedural bleeding from 7.1% to 3.5% with application of through-the-scope clips.[80] The benefit of clipping was particularly pronounced in patients with polyps in the right colon.

Perforation

Post-EMR perforation of colorectal lesions is rare, occurring in less than 1% of cases.[1] When the muscularis propria is resected in a perforation, the transected surface will have a white or gray central disk. When this disk is surrounded by submucosa stained by injectate containing blue dye, the resulting target appearance can be seen on both the resection surface and the underside of the specimen. When perforations are small, they can be closed endoscopically. Swan and colleagues performed a prospective study of 445 patients with colonic laterally spreading tumors 20 mm or larger.[83] Ten patients had target lesions with histologically confirmed perforations, and all were treated nonoperatively with endoscopic clips. In the case of larger perforations, urgent surgery may be required.

As mentioned, perforations are exceedingly rare in retrospective studies, prospective studies, and RCTs (Table 3). Based on large meta-analyses, no difference in perforation rate was seen among HS-EMR, CS-EMR, and U-EMR.[56,66,73]

Postpolypectomy Coagulation Syndrome

Another rare AE is postpolypectomy coagulation syndrome (PPCS). PPCS is caused by electrocoagulation injury to the colonic mucosa and underlying muscularis layer with transmural extension and concurrent peritoneal inflammation without evidence of perforation. The reported incidence of PPCS is 0.003% to 1%.[1] Larger lesion size and flatter morphology are associated with PPCS risk.[84] Patients typically present within 12 hours following colonoscopy with fever, tachycardia, and abdominal pain, although symptoms can be delayed up to 7 days postprocedure. Computed tomography showing focal thickening of the colonic wall with surrounding fat stranding without extraluminal air can be diagnostic. Treatment is supportive and involves intravenous fluids, pain control, and gradual advancement of diet, with or without antibiotics.[1] PPCS is typically self-limited and has a good prognosis.[84]

Surveillance Post–Endoscopic Mucosal Resection

Surveillance with interval colonoscopies is essential for detecting disease recurrence and metachronous colorectal polyps. Studies evaluating the recurrence rate of conventional adenomas and SSLs have noted recurrence rates from 9% to 28%.[85,86] As a result, for adenomas or SSLs 10 mm or larger removed en bloc, the USMSTF recommends a colonoscopy in 3 years.[87] However, polyps removed piecemeal require a shorter follow-up interval. A systematic review and meta-analysis found that the polyp recurrence rate after EMR was significantly higher with piecemeal resection than with en bloc resection (20% vs 3%; P<.0001).[88] Furthermore, in studies with follow-up, 76% of recurrences were detected at 3 months and 96% at 6 months, suggesting the high yield of early surveillance in cases of piecemeal resection. Owing to the increased risk of residual disease in piecemeal resections, the USMSTF recommends that a repeat colonoscopy be performed 6 months after an adenoma or SSL 20 mm or larger is resected piecemeal. A second surveillance colonoscopy performed 1 year from the first surveillance colonoscopy and a third surveillance colonoscopy 3 years from the second are also recommended.[87]

In cases of carcinoma found in an EMR specimen, the USMSTF recommends a colonoscopy 1 year after curative resection, with subsequent colonoscopies at 3 and 5 years from the initial resection, provided that prior surveillance colonoscopies are normal.[89] These recommendations are also supported by the European Society of Gastrointestinal Endoscopy and the European Society of Digestive Oncology.[90] Subsequent colonoscopies are recommended at 5-year intervals.[89] However, if the lesion was removed by piecemeal resection, a repeat colonoscopy should be performed 3 to 6 months after initial EMR.[91]

Conclusion

EMR is an important technique for removing large flat or sessile lesions throughout the GI tract. Although EMR has important applications in the esophagus, stomach, and small intestine, its most common indication is the removal of large colorectal polyps. Prior to performing colorectal EMR, the endoscopist must closely evaluate the lesion to determine whether it is amenable to EMR and whether advanced endoscopy referral is needed. HS-EMR, CS-EMR, and U-EMR are all options with their respective advantages and disadvantages and are the subject of ongoing studies. Emerging data indicate that CS-EMR is an effective option with a lower risk of AEs than HS-EMR, particularly for SSLs in the colorectum. Regardless of technique, attention should be paid to AEs of EMR, including bleeding, perforation, and PPCS. Furthermore, surveillance following EMR is important, particularly after piecemeal resection, given the risk of residual or recurrent polyps.

Disclosures

Dr Tabibian is a consultant for Olympus Corporation of the Americas. The other authors have no relevant conflicts of interest to disclose.

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