Endoscopic Mucosal Resection (EMR)

INTRODUCTION/BACKGROUND

Removal of large colon polyps can put patients at risk for procedure complications and inadequate resection of the lesion. Endoscopic mucosal resection (EMR) is a well-described technique that is safe and predominantly used for removal of larger lesions (> 1cm) of the gastrointestinal tract, which are limited to the superficial layers such as the mucosa and submucosa. EMR can be used to remove benign, premalignant, and early (T1N0) malignant lesions, which can prevent the need for surgical intervention. To perform EMR, patient selection is critical for optimal outcomes. Patients should be selected if concern for an invasive lesion is low, based on lesion size, and if polyp features are of low complication risk. Also, patients who do not meet these criteria but are poor surgical candidates may also benefit from EMR. There are several EMR techniques, each with their own indications, risks, and benefits. Lesions may either be taken out whole (i.e. en bloc) or by removing them in segments (i.e. piecemeal). It has been studied that lesions greater than 1.5 or 2 cm should be removed piecemeal to reduce the risk of perforation.1-5

Techniques

There are three main techniques for EMR: injection, cap, and band ligation. Underwater EMR is a more recent technique, which also is performed by some endoscopists.

Injection-assisted EMR is a technique that involves injection of a substance under the mucosa to separate the mucosa from the submucosa to allow for resection of the lesion without penetration into the deeper layers of the GI tract in an attempt to decrease the risk of perforation. This also allows for removal of lesions en bloc, depending on the size of the lesion. It is important to inject and lift the (continued on page 40)
proximal side of the lesion first as if this is not done, the lesion may be distorted into a position that is away from the endoscope obstructing visualization and placing it in an unfavorable position for resection. Nonlifting of a lesion can be a predictor of deeper invasion and is not indicated for removal through EMR.\textsuperscript{1,6-8} However, nonlifting can also occur if the lesion has previously manipulated or intervened upon. If nonlifting is thought to be due to prior manipulation of the lesion, EMR may be attempted.\textsuperscript{9}

After the lesion is adequately lifted, resection is then performed using a snare with electrocautery. (Figure 1) If the lesion size is not amenable to removal en bloc, it may be removed piecemeal by systematically beginning at one margin and working across the entire lesion. The endoscopist must take great care to ensure islets of residual tissue are not left as these may become difficult to remove. Prior to removal of each portion of the polyp, the portion to be ensnared should be lifted away from the mucosa to further help prevent injury to the muscularis propria. Resection should be continued until the muscularis propria has been exposed. Remnants of adenomatous tissue can be removed with conventional methods for polypectomy such as forceps or snares, however the remnant tissue may also be treated with argon plasma coagulation (APC), alternative forms of monopolar coagulation, or may be fulgurated.

The cap-assisted technique also begins with injection of a solution in the submucosal space similar to the injection-assisted technique. However, a cap is placed at the end of the endoscope to allow for suction of the entire lesion or portion of the lesion into the cap. An electrocautery device, such as a hot snare, is placed in position prior to the retraction of the lesion into the cap and is used to resect the retracted portion of the lesion. There are caps available, which include an electrocautery device, most commonly a snare, attached to them. This process is repeated until the lesion is fully resected. The caps that are available are plastic and are cylindrical in order to fit on the end of the endoscope similar to caps used for variceal band ligation.\textsuperscript{10}

Ligation-assisted EMR is a technique that does not require an injection into the submucosal

\textbf{Figure 1.} EMR of a large colonic polyp via injection and hot snare. 
\textit{All images courtesy of Douglas G. Adler, MD}

\textbf{Figure 1a.} Colonic polyp prior to resection.

\textbf{Figure 1b.} The lesion is lifted by submucosal injection using saline.

\textbf{Figure 1c.} Final appearance of the lesion after snare resection and application of endoclips.

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space. As in cap assisted, a cap is placed over the end of the endoscope. However, the cap used with this technique is equipped with band ligation. The lesion is retracted into the cap by the use of suction. A band is then deployed onto the lesion to ligate the portion to be resected. An electrocautery device is subsequently used to resect the ligated area.\textsuperscript{11,12} The EMR band ligator allows for passage of a snare through the working channel of the endoscope without removal of the band ligating cap. The cap is typically equipped with six bands. (Figure 2)

The underwater technique is performed by filling the GI tract with water, which theoretically allows the lesion to elevate itself or float. It has been hypothesized that this enables the lesion to separate itself from the deeper layers of the GI tract and therefore theoretically allow for resection with less risk of injury or perforation.\textsuperscript{13} This method however has been thought to have a decreased risk of seeding malignant cells into the deeper layers of the mucosa after resection. Furthermore, it has been postulated that this technique may also decrease the fibrosis formation at the resection area making recurrent lesions easier to manipulate.\textsuperscript{9} As fibrosis makes lifting a lesion much more difficult, the underwater technique has been found to be valuable and beneficial in treating lesions which have been previously manipulated.\textsuperscript{6,14-20}

**Injectable Solutions**

Several solutions are available for injection into the submucosal space to help prevent injury to the deeper layers of the GI tract with EMR. Normal saline is the most commonly used solution, is readily available, and is inexpensive, however, it dissipates after only a few minutes. Dissipation of the lift can be managed with repeating the injection, which is a common occurrence, especially when removing large lesions. Solutions such as hyaluronic acid, hydroxypropyl methylcellulose, succinylated gelatin, glycerol, and fibrinogen containing solutions have all been found to last longer than normal saline.\textsuperscript{21-27} Hyaluronic acid is also inexpensive but is not readily available in the U.S. In several trials with which have compared hyaluronic acid to normal saline, it has been concluded that hyaluronic acid sustains a more effective lift. Hyaluronic acid has been found to

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**Figure 2.** EMR of two gastric carcinoids by the cap/band method.

**Figure 2a.** 2 gastric carcinoids seen on EGD

**Figure 2b.** 7.5MHz EUS image of one of the carcinoids prior to removal.

**Figure 2c.** EMR cap device in place. Note a band has been placed around the base of one of the lesions.
be the solution that sustains a lift for the longest duration of all currently available solutions.\textsuperscript{28} Hydroxypropyl methylcellulose however is a readily available solution and has a good duration of lift but has been found to have a risk of tissue damage at the injection site.\textsuperscript{29,30} Succinylated gelatin is readily available and inexpensive but is mainly used for colonic lesions $> 20$ mm as it has been found to assist in removing lesions in piecemeal fashion.\textsuperscript{31}

Other endoscopic tools and techniques are available to further assist the endoscopist to identify the lesion margins. Chemoendoscopy is one modality, which involves staining the colonic mucosa with a topical solution to help delineate the lesion in its entirety. Solutions that have been used include methylene blue, toluidine blue, Lugol’s solution, Congo red, phenol red, and indigo carmine. Another tool that can be used is narrow band imaging (NBI) which is a mode that most high definition endoscopes are now equipped with and which enhances the mucosal surface without the need for dyes. The wavelengths that make up white light have been found to have different penetration abilities. Blue light has been shown to penetrate only the superficial layers of the colon while red light penetrates into the deeper layers. NBI therefore uses blue light wavelengths to reveal the superficial vasculature of the mucosa, which helps identify the lesion easier.\textsuperscript{32} Along with these tools, other helpful solutions may be added to the solution used to lift the lesion to be resected. Epinephrine (1:100,000 - 1:200,000) is sometimes added to the solution to theoretically decrease the risk of post polypectomy bleeding by means of vasoconstriction of the feeding vessels. However, this has the potential side effects of epinephrine use, such as severe hypertension, tachycardia, arrhythmias, and intestinal ischemia, which are all rare complications but are well documented when epinephrine is absorbed systemically.\textsuperscript{33-36} Other very helpful additives to a solution are methylene blue and indigo carmine. These additives significantly assist in delineating the margins of the lesion as it stains the underlying mucosa blue without affecting the color of the lesion itself, highlighting the margins. This staining may also help identify the muscularis propria and therefore can help prevent perforation.\textsuperscript{37,38}

Efficacy

In the esophagus, EMR can be used for removal of superficial malignancies as well as Barrett’s associated high-grade dysplasia and intramucosal carcinoma.\textsuperscript{39-41} For Barrett’s associated neoplasia, EMR may be used as a solitary modality to remove neoplastic lesions or may be used in conjunction with ablative techniques to remove large segments of Barrett’s. A recent study which evaluated the efficacy of complete resection of Barrett’s and its associated neoplasia through EMR, found that neoplasia with high risk characteristics, such as submucosal invasion, poor differentiation, lymphatic or vascular infiltration, was completely eradicated in 98.8% of patients.\textsuperscript{41} Recurrence rates in this study were found to be very low (1.4%) for both neoplastic and highly dysplastic lesions. Studies have compared cap-assisted and ligation-assisted techniques for removal of Barrett’s associated neoplasia and it has been shown that the ligation-assisted technique slightly decreases the time of the procedure, however both techniques were found to be equally efficacious and had similar rates of adverse events.\textsuperscript{42}

Studies that have evaluated EMR with radiofrequency ablation for Barrett’s have shown remission of neoplasia and metaplasia in 90% of patients 5 years after treatment. In these prospective studies, EMR was first performed on the visible abnormalities and was followed up by circumferential radiofrequency ablation 4-6 weeks after the initial treatment.\textsuperscript{43}

EMR can also be used to remove superficial squamous cell carcinoma (SCC) in the esophagus. Many studies have evaluated the efficacy of EMR on SCC, which have seen a recurrence rate of as low as 0.3% in lesions smaller than 20 mm.\textsuperscript{40}

In the stomach, endoscopic submucosal dissection, or ESD, is most commonly used for gastric cancer as it has been found to be associated with lower recurrence rates when compared to EMR (0.7% vs 6.4% respectively), however, EMR and ESD for early gastric cancer have been found to have similar overall survival rates.\textsuperscript{44} Due to the lower recurrence rate, ESD is the preferred method for removal of gastric cancer, when available, as it also carries the benefit of histologic evaluation of the margins of the removed lesion\textsuperscript{45} (ref 45). EMR does not have this benefit, especially when lesions
are removed piecemeal. Gastric carcinoids that are less than 1 cm can also be resected with EMR, however ESD again is the preferred modality as it has also been shown to reduce local recurrence rates in this setting.\(^{46,47}\)

Several non-ampullary lesions have been resected with EMR, however in the duodenum, the risk of bleeding and perforation are the highest due to its thin walls. There are several studies that have quoted success rates of up to 96% in removal of these lesions, however as previously mentioned, many of these studies have reported a higher risk of complications.\(^{48-51}\)

The colon is largely the most common area of the gastrointestinal tract where EMR is used and is typically performed using the injection-assisted technique. One recent study has shown that local recurrence rates for removal of flat lesions are as low as 3% when removed en bloc but up to 20% when removed in piecemeal.\(^{52}\) After endoscopic retreatment of these areas, with APC, EMR, or both, recurrence rate was 21%, however eradication rate of 91.4% was eventually achieved with an average of 1.2 retreatment sessions. Another large study revealed a recurrence rate of 16% at 4 months and a 4% recurrence rate at 16 months.\(^{52}\) The majority of recurrences in these patients were managed endoscopically and through the results, a timeframe for follow-up colonoscopy after a lesion was removed via EMR was proposed. It was proposed that patients with lesions greater than 15 mm and removed piecemeal, should have colonoscopy repeated in 6-12 months to evaluate for recurrence.\(^{51,53}\) Interestingly, when injection-assisted EMR has been compared to under water EMR, it was found that recurrent lesions were removed significantly better by using the underwater technique (88.9% vs 31.8%).\(^{14}\) A prospective study with polyps ranging from 20 – 100 mm removed via en bloc or piecemeal had an overall recurrence rate of 4.2% after a mean of 30 months. Recurrence was most commonly seen in patients with polyps greater than 40 mm.\(^{18}\) However, in another recent study with a mean polyp size of 30mm, invasive adenocarcinoma was found in 6 polyps (3.4%), 5 of which were successfully treated with EMR.\(^{20}\)

As previously mentioned, colonic lesions that do not lift with injection into the submucosal

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space should not be lifted as this likely indicates invasion into the deeper layers of the bowel wall. However, if a lesion's inability to lift is thought to be due to fibrosis secondary to a previous intervention, it has been found that these lesions are amenable for removal via EMR.

As in the esophagus, other techniques may be used as an adjunct to EMR for removal of colonic adenomatous lesions. Several other techniques have been used with EMR, such as biopsy forceps or snare to ablate or remove residual tissue. Interestingly, this adjunctive technique has been found to increase the risk of recurrent lesions.

**Adverse Events**

The most common adverse events associated with EMR are bleeding, perforation, and strictures. The most common overall complication is bleeding. Clinically significant bleeding rates can be seen in 11-22% of cases with removal of colonic lesions greater than 20mm. About one third of these patients may need endoscopic intervention to establish hemostasis. Conventional endoscopic methods for hemostasis are used in this setting. Risk factors for clinically significant post-EMR bleeding include size of the lesion, Paris classification (0-IIa and IIs), and tubulovillous or villous histology. Luckily, colonic perforation with EMR is rare and occurs in less than 1% of cases. Signs of injury to the muscularis propria include a whitish or grey central circular area surrounded by the blue staining of the submucosal layer (if a staining additive has been used). This is also known as the “target” sign. As with perforations in the colon through other methods, small defects may be controlled with the use of endoclips, however larger perforations often require surgical intervention.

Bleeding secondary to gastric EMR can be seen in up to 11.5% of cases and is also managed through conventional hemostatic techniques. Bleeding rates in the duodenum have similar risk as in the stomach for lesions less than 3cm but have been reported in up to 58% of cases with larger lesions. The risk of perforation in the stomach is low (<1%) likely due to the increased thickness of the stomach wall. Few studies have been performed which have evaluated the risk of perforation in the duodenum and report a risk of less than 2%, however the risk is believed to be higher given the thin duodenal walls, therefore it is advised that EMR in the duodenum should be performed with caution.

In the esophagus, adverse events are overall much lower than in the colon. Unlike the colon, the most common adverse effect in the esophagus is stenosis and can widely range between 6-88% of cases according to several studies. Strictures can occur after removal of large mucosal resections, circumferential resections, or resection of multiple lesions but can be treated similarly to strictures of any alternative etiology with esophageal dilation. Bleeding can also occur in the esophagus and has been observed in about 1.2% of patients. Perforation in the esophagus is also seen less often and has been reported as low as less than 0.5% in the setting of an experienced endoscopist who routinely uses EMR. In comparison to ESD, EMR has been associated with a significantly lower rate of perforation.

**CONCLUSION/SUMMARY**

EMR is a very helpful and safe endoscopic technique for removal of larger premalignant and early-stage malignant lesions of the gastrointestinal tract. Prior to the consideration of EMR, it is critical that the lesion selection is appropriate. Close endoscopic evaluation to delineate lesion margins, size (>1 cm), and identification of lesion depth are imperative. EUS can be used, if needed, to stage the lesion and further identify the depth of mucosal involvement. Many endoscopists have found it helpful to lift the lesion with a staining solution or mark the periphery of the lesion with cautery such as argon plasma coagulation or with the tip of a hot snare to further define the lesion margins and extent to be resected. Adjunctive techniques may be used along with EMR to further remove or ablate residual tissue. Lesions greater than 1.5 or 2 cm should be removed piecemeal. However, close follow-up colonoscopy, especially if the lesion is removed piecemeal as this poses a higher risk for
recurrence. The most common adverse event is bleeding and if the lesion is deemed to be high risk, preventative measures or conventional hemostatic methods should be taken if post-resection bleeding occurs. Endoscopists performing EMR should be knowledgeable and skilled in treating possible adverse events associated with EMR.

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Answers to this month’s crossword puzzle: