Endoscopic mucosal resection

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Key Points

- Endoscopic mucosal resection (EMR) is the most accurate staging modality for assessing depth of invasion of superficial cancers.
- EMR is also a curative therapy for selected superficial cancers.
- The decision to proceed to EMR should be discussed carefully with the patient and the appropriate multidisciplinary team.
- Familiarity with different EMR techniques and equipment is vital.
- Paris type 0–III lesions and those that fail to lift following submucosal injection are not suitable for EMR.
- The risk of lymph node invasion is <5% for T1m(1–3) lesions and these are considered cured by EMR when margins are clear.
- Submucosal involvement (T1sm), discovered at EMR, carries a risk of lymph node involvement of 19–44% and is an indication for surgery in fit patients.
- With experience, perforation rates are low (1–5%).

Introduction

Endoscopic mucosal resection (EMR), also known as mucosectomy, has become an accepted curative treatment for superficial tumors of the digestive tract: benign flat or sessile lesions, high-grade intraepithelial neoplasia and superficial cancers with little or no risk of lymph node involvement in the esophagus, cardia, stomach, duodenum, ampulla of Vater, colon or rectum.

EMR allows resection of the mucosa, the muscularis mucosae and part or even all of the submucosa. It allows histological analysis of the entire lesion unlike ablative therapies such as laser or argon plasma coagulation. It also allows further treatment (surgery or radiochemotherapy) to be considered should the pathology reveal high risk features for lymphatic invasion (see below) or incomplete resection.

EMR techniques were developed originally in Japan, for the treatment of superficial cancers of the stomach and squamous esophagus. These are common in Japan and all Japanese people are offered screening endoscopy from the age of 40. As such, many superficial cancers are diagnosed and this led to the development of EMR.

These lesions are less common in Western countries but advances in endoscopic imaging and the fortuitous discovery of dysplastic lesions or superficial cancers have resulted in the adoption of these techniques. EMR has also been used for many years for colonic lesions, especially flat, sessile polyps and those larger than 2 cm.

1. Indications and limitations

The feasibility of EMR throughout the upper and lower gastrointestinal tract has been clearly demonstrated in recent years, although every lesion must be assessed on its individual merits and site-specific caveats apply in different parts of the gut (see below).

1.1. Benign lesions

For benign lesions, the limitations are essentially technical, related to difficulties in resecting very large lesions, which require piecemeal resection. Neither size nor location is a factor in the decision to consider EMR: very large lesions may be entirely benign and, conversely, small lesions may be malignant and endoscopically unresectable as a result of infiltration of the deep submucosa or muscularis propria.

1.2. Cancers

For cancers, the indications for EMR are determined by the risk of lymph node involvement which varies depending on:

- Site
- Size
- The degree of differentiation (well, moderate or poor) and
- Vertical depth of invasion.

According to the original Japanese classification and the modified ‘Paris Classification’, T1 lesions are considered resectable by EMR and may be divided into six subgroups, according to the level of invasion (Fig. 1).

- T1m1 corresponds to disease confined to the epithelium. This represents in situ cancer which does not invade the basement membrane and thus carries no risk of lymph node involvement.
- T1m2 corresponds to infiltration of the lamina propria, not involving the muscularis mucosae and with a low lymph node risk (0–2%).
- T1m3 corresponds to invasion into but not beyond the muscularis mucosae (lymph node risk up to approximately 9%).
Figure 1: Japanese classification of superficial malignant lesions of the digestive tract (T1) – *0% without lymphovascular invasion – 4.5% with lymphovascular injection.

- **T1sm1** corresponds to superficial invasion of the submucosa (upper third). These cancers are invasive and the risk of lymph node invasion is 0–19%.
- **T1sm2** corresponds to invasion of the middle third of the submucosa. The risk of lymph node invasion is 6–44% for T1sm2 and T1sm3 lesions.
- **T1sm3** corresponds to invasion of the deep submucosa. The risk of lymph node invasion is 6–44% for T1sm2 and T1sm3 lesions.
- **T2** corresponds to invasion of the muscularis propria. These cancers are advanced and not suitable for EMR, which would not be curative and also risks removing the muscularis propria and causing a perforation.

Local practices will determine whether EMR is performed under conscious sedation or general anesthesia. The latter should be considered if a long procedure is anticipated, e.g. a large lesion of the cardia, stomach or duodenum, or if an overtube is being used for multiple esophageal intubations. Relatively simple EMR procedures can be performed as a day case but more complex cases require at least overnight stay afterwards and may be best admitted the day beforehand. The patient needs to be prepared because of the risks of serious complications, although these are uncommon.

### 2. Conditions for performing EMR

Careful consultation is essential prior to EMR so that patients understand their condition, the rationale for EMR, its risks and the alternatives including minimally invasive surgery. Arrangements can be made for patients taking antiplatelet or anticoagulant therapy. Anesthetic assessment is also important in high-risk patients because it is a high-risk procedure. In many centres, EMR is performed under general anesthesia, allowing the endoscopist to concentrate solely on the complex task in hand.

### Clinical Tip

Patients with T1m1, T1m2 or T1m3 lesions may be regarded as cured by successful EMR. T1sm1, sm2 and sm3 lesions may require surgical resection or chemoradiotherapy depending on the risk of surgery which may be very high, particularly for esophageal resection.

### Warning!

Aspirin therapy can continue but warfarin (3–5 days) and clopidogrel (7–10 days) must be stopped prior to EMR.

### 3. Evaluation prior to EMR

Careful endoscopic evaluation is necessary to predict the risk of deep invasion into the submucosa or beyond as this would contraindicate EMR. The decision to proceed to EMR is based on the morphological appearances, results of endosonography and, in appropriate cases, the response to submucosal injection.

#### 3.1. Appearance on endoscopy

Size and the Paris endoscopic classification will determine with reasonable precision the risk of submucosal invasion for cancers, particularly in the stomach. The risk is virtually zero for tumors measuring less than a centimeter and low for those measuring 1–2 cm. The Paris classification (Ch. 3, Fig. 25) distinguishes between polypoid (type I), flat (type II) and ulcerated (type III) lesion types. Flat lesions may be slightly elevated (IIa), truly flat (IIb) or slightly depressed (IIc). Any combination of forms may exist, e.g. type IIa+IIc. EMR is not technically possible for type III lesions. Type I lesions are usually resectable without difficulty but site-specific factors must be considered: e.g. squamous esophageal type I lesions are associated with submucosal involvement in >90% of cases. This is not true in Barrett’s cancers, the stomach or colon. Generally the best indications for EMR are type IIa, IIb or IIc lesions, in which the risk of submucosal invasion is <10%.
3.2. Endosonography

Conventional endosonography at 7.5 and 12 MHz can differentiate between T1 and T2 stages with a diagnostic accuracy of 90%. 30 MHz catheter miniprobes can distinguish between T1 and T2 stages in almost 100% of cases in expert hands. Some studies suggest that EUS can differentiate between T1m and T1sm stages with 90% accuracy. There is a problem with overstaging as a result of peri-tumoral fibrosis and inflammation and because of this, lesions classified as T1sm by endosonography should not be automatically rejected for possible EMR.

The diagnostic accuracy of miniprobes in intramucosal tumors has been reported as approximately 95% but recent data suggests that accuracy may only be around 80%. As a result, and because EMR techniques have become easier in recent years, a ‘diagnostic’ EMR is often performed to allow more accurate and definitive pathological staging of the depth of invasion.

3.3. Submucosal injection

The response to submucosal injection (‘lifting sign’) was described by Kato and predicts deep infiltration that precludes EMR (Figs 2–4).

4. Equipment

This varies depending on whether EMR is being performed ‘freehand’ or whether cap-based methods are used (see below). Units performing EMR should have available a full range of necessary endoscopes, electrosurgical equipment and accessories and be familiar with their use (Box 1).
5. Techniques

5.1. Locating the lesion
Assessing the horizontal extent of a lesion is made easier by chroendoendoscopy and is essential for flat lesions. Lugol's iodine solution 1% (squamous esophageal lesions) and 0.2–0.4% indigo carmine (glandular mucosa) are mostly used. The margins of the lesion can be marked with electrocoagulation points using the tip of a snare or APC. This is useful only in the stomach and duodenum where staining sometimes may fail to delineate the margins for long enough, risking incomplete resection and the need for repeated sessions to clear residual neoplastic tissue.

5.2. Submucosal injection
This confirms that the lesion lifts away from the deep layers and, importantly, creates an insulating cushion that reduces the risk of perforation.

Physiological saline without epinephrine is most commonly used. Injection of epinephrine may temporarily prevent bleeding from a vessel which may subsequently begin to bleed and require repeat endoscopy for hemostasis. It is therefore preferable to detect immediate bleeding and to use clipping or thermal methods to achieve durable hemostasis. Saline is absorbed quickly and repeated injections may be necessary but there is no limit to the volume that can be used. Hyaluronic acid, 10% dextrose, 2% hydroxypropylmethylcellulose (HPMC) or other solutions have been used to allow a longer lasting injection but are generally reserved for submucosal dissection procedures (ESD).

5.3. Excision procedure
Several procedures for EMR have been described and these can be roughly divided into four types: inject and cut, pull and cut, suck and cut, simplified aspirate and cut.

5.3.1. Inject and cut (Fig. 3)
Elevation of the lesion by submucosal injection is the first step and resection removes a portion of the wall containing mucosa, muscularis mucosae, and part or all of the submucosa. To reduce the risk of perforation, it is vital to maintain sufficient lifting of the lesion throughout the procedure. This may require the injection of 10–20 mL (or up to 50 mL in some cases). Injection is undertaken at several points around the previously marked area. If there is no elevation of the lesion (‘non-lifting’), this is strong evidence of deeper than expected invasion and the procedure must be stopped. The elevated lesion is grasped in a polypectomy snare. An ‘endocut’ current or blended or pure cutting current may be used (see Ch. 1.4). The risk of perforation from deep electrocoagulation of the wall is reduced by keeping the resulting cutting plane away from the submucosal injection. This method is used mainly in the colon or rectum where it is the standard technique for small lesions, but can also be used at other sites.

5.3.2. Pull and cut
This technique requires a twin-channel endoscope. A snare passed through one channel is placed around the lesion and biopsy or grasping forceps of different size close around the apex of the lesion via the second channel. The lesion can then be pulled towards the endoscope tip before the snare is closed and resection by diathermy occurs.

5.3.3. Aspirate and cut
Several techniques have aspiration of the lesion before resection in common. Aspiration can be achieved using a plastic hood (‘cap method’, Olympus) or a band ligation device (multiband mucosectomy, ‘Duette’, Cook Medical). Some Japanese experts use an overtube in the esophagus to facilitate multiple intubations.

5.3.4. Cap method
A transparent oblique plastic cap (Fig. 5) is mounted on the endoscope. The cap has a notch that should be aligned with the instrument channel of the endoscope. The snare (a miniloop specially designed to open on contact with the inner rim of the distal end of the cap) is inserted into the cap, the lesion is aspirated into the hood and the loop is then closed, grasping the tumor. Suction is released and the loop and the tumor are pushed out of the hood. Resection is then carried out using Endo-cut mode (ERBE ICC 200 generator setting 120 W, effect 2, for 2–3 s). This technique is recommended in the esophagus and cardia. The fragile snare deforms easily and for piecemeal resections a new snare should be used for each resection.

The same technique may be used with a band ligation device (multiband mucosectomy, MBM, Fig. 6) or a diathermy snare outside the distal hood (Fig. 7). After aspirating the lesion and applying the band, resection of the pseudopolypp is carried out using a 5–7F hexagonal monofilament snare supplied with the kit. The snare should be placed below the band. This technique can be used in the stomach or esophagus and is comparable with the cap method in ease of use, outcomes and complication rates. Submucosal injection is unnecessary. The size of the resected tissue...
correlates with the amount of suction into the hood – a ‘red-out’ is needed for large lesions while less vigorous suction is necessary for small lesions. The use of a transparent plastic overtube (Fig. 8) specially designed for esophageal endotherapy has been proposed by Japanese teams and seems particularly useful for dysplasia or flat superficial cancers extending over large surface areas. It is currently unavailable in many Western countries and insertion-related perforations have been reported.

5.3.5. Simplified aspirate and cut

The use of a monofilament pediatric snare through an endoscope with a large operating channel has been suggested as an alternative to submucosal injection or suction with a cap. By using a large operating channel, there is still sufficiently powerful aspiration despite the introduction of the snare, which is progressively closed around the lesion during aspiration. This technique, which has been validated for small cancers of the esophagus, can also be considered for benign sessile colonic tumors.

**Warning!**
Submucosal injection is essential before each resection when using the Olympus cap method to avoid perforation. Injection is unnecessary in the esophagus when using multiband mucosectomy as the risk of perforation is extremely low but the risk of a complete resection is lower.

**Clinical Tip**
Handling and preparation of resected specimens
A key component of the procedure is providing the pathologist with well-oriented specimens so that accurate assessment of lateral and, more importantly, vertical depth of invasion can be performed. Tissue should be fixed on a flat cork board or wax slab using pins and placed face down in fixative.
Box 2  Practical considerations for EMR

- Extensive training is necessary for successful EMR: training courses, simulators, and animal tissue models are all available. Practice on these before undertaking cases.
- Two experienced nurses are needed to assist with EMR.
- General anesthesia is recommended so that the patient is perfectly still.
- Inject beneath all lesions, regardless of their location in the digestive tract, except when using MBM in the esophagus.
- Stain the esophagus with Lugol’s solution and the stomach and colon with indigo carmine.
- Mark the margins of gastric and duodenal lesions with the tip of a diathermy snare (20–40 W).
- Use the cap method for the esophagus and cardia.
- Have all equipment ready before starting an EMR, including epinephrine, clips and coagrasper forceps.
- Aim to resect lesions completely in a single session and preferably en-bloc.

6. Complications

Immediate bleeding is common and is part of the procedure. It should be treated during the same session, usually by clipping or coagulation with diathermy forceps (‘Coagrapers’, Fig. 9). Perforations (Fig. 10) occur in <5% and, if small and detected immediately, attempts should be made to close these with clips (Fig. 11). Perforation and haemorrhage may also be delayed (by up to 10 days for hemorrhage). Surgery is rarely required.

Very wide and particularly circumferential mucosectomies may be complicated by stenosis in up to 50% (rectum and esophagus). Dilatation is usually easy and is performed until a normal lumen has been restored. Stenoses can be avoided by performing large EMRs in two or more sessions.

7. Results

The success rate of EMR is 90–94%. Results are determined by how complete the excision is. For superficial cancers, survival rates of more than 80% have been reported, with disease-specific mortality of 2–3%. These results are equivalent to those of surgery. The recurrence rate after resection with negative margins is approximately 2% for superficial cancers of the stomach and less than 10% in the colon. Many of these recurrences are small and endoscopically treatable.
Endoscopic mucosal resection

8. Future developments

The development of surveillance and screening endoscopy targeted at patients at risk of GI cancers, advances in imaging techniques (high resolution) and education of endoscopists about the appearances of subtle abnormalities and their significance should help to increase the proportion of superficial cancers detected. It is vital that endoscopists appreciate what to look for and allow enough time for a thorough examination. New equipment will allow the resection of circumferential lesions of the esophagus, particularly dysplasia in Barrett’s esophagus, as well as extensive superficial gastric and colonic cancers. Known as endoscopic submucosal dissection (ESD) (Figs 12-14), this technique may replace some of the EMR currently performed. It has been widely adopted in Asia and is slowly emerging in other parts of the world. ESD has the advantages of complete en bloc resection of very large lesions with low recurrence rates. The procedure is at present technically challenging and time-consuming with a long learning curve. In Western countries the number of patients suitable for ESD is far smaller than in Asia and expertise should be concentrated in a small number of specialist centers.
Figure 12  Endoscopic submucosal dissection (ESD): en bloc excision of large lesions, measuring >4 cm using a dedicated knife with a ceramic insulating tip (IT-knife). (A) After marking and submucosal injection, excision starts by circumferential incision around the lesion. (B) Step by step submucosal dissection with an IT-knife. (C) Submucosal dissection for en bloc resection of the lesion.

Figure 13  Endoscopic submucosal dissection: inject and cut. (A) Staining in the esophagus and colon. (B) Marking in the stomach and duodenum only. (C) Submucosal injection. (D) Dissection using a ceramic-tipped knife. (E) Removal of the lesion as a single piece, grasped in a large snare.
9. Images

9.1. EMR of the esophagus: aspirate and cut in a single piece

Figure 15  EMR of the esophagus: aspirate and cut in a single piece. (A) Small squamous cancer of the esophagus. (B) After 1% Lugol’s solution. (C) After cap-assisted resection. (D) Follow-up image with 1% Lugol’s solution showing complete resection in a single session. (E) EMR scar at 6 months after 1% Lugol’s solution. (F) EMR scar using the FICE system (Fujinon).
9.2. Additional EMR of the esophagus

Figure 16  Additional EMR of the esophagus. (A) Follow-up of EMR at 3 months. (B) Staining with 1% Lugol’s solution with residual fragment. (C) Effective submucosal injection. (D) Difficult, limited resection (cap method). (E) Resection with a twin-channel endoscope. (F) Follow-up and further staining with Lugol’s solution.

9.3. Semi-circumferential cancer of the esophagus resected in a single session

Figure 17  Semi-circumferential cancer of the esophagus resected in a single session. (A) Semi-circumferential squamous cancer of the esophagus. (B) After 1% Lugol’s solution. (C) Submucosal injection. (D) Cap. (E) Lesion in the cap (resection in a single piece). (F) Clip to control bleeding.
9.4. EMR of the esophagus combining two techniques: aspirate and cut then pull and cut

Figure 18  EMR of the esophagus combining two techniques: aspirate and cut then pull and cut. (A) Long squamous cancer. (B) Squamous cancer after 1% Lugol's solution. (C) Submucosal injection. (D) Resection cap + EMR snare. (E) Lesion in the snare. (F) After resection. (G) Residual fragment needing resection with an endoscope with two operating channels. (H) Follow-up with 1% Lugol's solution; lesion resected whole in a single session.
9.5. Resection of extensive superficial cancer of the esophagus

Figure 19  Resection of extensive superficial cancer of the esophagus. (A) Superficial esophageal cancer. (B) After staining with Lugol’s solution, the lesion appears to be very extensive. (C) Centring the lesion in the cap. (D) Aspiration. (E) Circumferential resection. (F) Continuing the resection of the lower part of the lesion. (G) After cap resection. (H) Residual tumor tissue bridge between two resection zones – resected with a twin channel endoscope. (I) Lower end of the resection zone. (J) Middle part. (K) Upper part – resection in a single session, in total 10 cm long and 7 cm in circumference. (L) Stenosis due to scarring at 4 weeks. (M) After dilation. (N) EMR scar at 6 months. (O) Scar after 1% Lugol’s solution: no residual or recurrent lesion.

Follow-up at 4.5 years normal.
9.6. EMR of the cardia

Figure 20  EMR of the cardia. (A) Circumferential Barrett’s esophagus. (B) High-grade dysplasia on a proximal tongue of Barrett’s epithelium. (C) 1% acetic acid + electronic zoom x1.5 in the dysplastic zone. (D) 1% acetic acid + electronic zoom (x1.5) + FICE in the dysplastic zone. (E) Oblique transparent cap + special EMR snare with aspiration test on the endoscopist’s glove. (F) Aspiration of the lesion into the cap and closure of the snare. (G) Lesion outside the cap. (H) Second resection close to the first one. (I) Continued resection with an endoscope with two operating channels, the snare on the right, the forceps on the left to remove a residual fragment between two resected areas. (J) Closed snare. (K) Resection of two-thirds of circumferential Barrett’s esophagus and the tongue-like projection with the lesion. A second session will take place in 3 months for resection of the remaining Barrett’s epithelium. Treatment in two sessions to minimize the risk of stenosis.
9.7. EMR of high-grade dysplasia in Barrett’s esophagus using a band ligation device

![Image](A) High-grade dysplasia in Barrett’s esophagus. (B) 1 band placed on the edge of a previously treated area. (C) Resection by snare. (D) Resection of two-thirds of the Barrett’s segment with the lesion.

9.8A. Gastric EMR

![Image](A) Antral adenoma with high grade dysplasia. (B) After resection.

9.8B. Gastric ESD

![Image](A) Superficial gastric cancer T1m1. (B) Marking the limit of the resection. (C) ESD with Hybrid Knife T Type. (D) After resection.
9.9. Duodenal EMR

Figure 24  Duodenal EMR. (A) Small duodenal polyp. (B) Injection under the polyp. (C) Resection with the snare. (D) Confirmation of complete resection with 0.2% indigo carmine. (E) Closing with a clip to prevent secondary bleeding. (F) 2nd clip in position.

9.10. EMR of a large duodenal polyp

Figure 25  EMR of a large duodenal polyp. (A) Large duodenal polyp. (B) Submucosal injection. (C) Partial resection. (D) Oozing seen after immersion of D2 under water. (E) Clips to close the resection zone to prevent secondary bleeding. (F) Duodenal EMR scar at 3 months.
9.11. Colonic EMR: sessile lesion in the caecum

Figure 26. Colonic EMR: (A) Lateral spreading tumor (LST) in the cecum. (B) After staining with 0.2% indigo carmine. (C) Submucosal injection. (D) Partial resection with snare. (E) Resection of another fragment. (F) Active bleeding from a small vessel requiring clipping in order to continue. (G) Continuing the procedure. (H) End of the procedure.

9.12. EMR of a serrated adenoma: the only situation where marking is necessary in the colon

Figure 27. EMR of a serrated adenoma: the only situation where marking is necessary in the colon. (A) Serrated adenoma. (B) Marking necessary before resection. (C) A snare and a colonoscope with two operating channels may be useful for this type of lesion. (D) Complete resection in a single session.
9.13. EMR of a sessile rectal polyp

Figure 28  EMR of a sessile rectal polyp. (A) Staining with 0.2% indigo carmine. (B) Submucosal injection. (C) Piecemeal resection. (D) Resection of successive fragments. (E) Partial resection. (F) Follow-up showing residual adenoma at the resection margin. By using a colonoscope with optical zoom, the adenoma with elongated crypts can be clearly distinguished from normal mucosa with rounded crypts. (G) Resection of the final fragment. (H) Complete resection in a single session.


Figure 29  Perforation treated by clipping. (A) Recurrence of an incompletely resected sessile polyp. (B) After staining. (C) Intraperitoneal fatty tissue emerging through the site of perforation. (D) Closing the perforation: additional treatment with antibiotics and a fiber-free diet for 7 days before discharge.
**Further Reading**


