Refresher Course

Endoscopic Mucosal Resection (EMR) : A Review

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INTRODUCTION

Endoscopic mucosal resection (EMR), which represents a major advance in therapeutic endoscopy, has come to play an increasingly important role in the treatment of early cancer in the gastrointestinal tract. EMR has recently been widely used in countries such as Japan and Korea[1,2]. It has gained increasing popularity for the treatment of early esophageal cancer in Western countries[3,4]. Most importantly, long-term studies have demonstrated EMR outcomes similar to those of surgery which has led to the acceptance of EMR as a standard procedure[5]. Ultimately, the treatment of early gastrointestinal cancers by EMR may obviate the need for surgical therapy in selected patients.

TECHNIQUES

Various EMR techniques have been described. Many of these techniques utilize standard endoscopic equipment such as snares, grasping forceps, injection needles and a transparent cap. These EMR techniques could be broadly divided into three categories: techniques without suction, techniques with suction and modified techniques (Table 1).

Table 1. Classification of techniques of endoscopic mucosal resection (EMR). Modified from Shim CS: Endoscopic Mucosal Resection: An overview of the value of different techniques[22].

Technique	Author
Techniques without suction	
Injection and cut	Tada et al. 1993[9]
Injection, lifting and cut	Takekoshi et al. 1994
Injection, precut and cut	Yamamoto et al. 1999
Lift and cut method using an overtube	Inoue & Endo 1990
Techniques with suction	
Esophageal EMR or Makuuchi tube method	Makuuchi 1996
Modified Makuuchi tube method	Kawano et al. 1991
Endoscopic mucosal resection with cap	Inoue et al. 1990[12]
Endoscopic mucosal resection with ligation	Shim 1999
Simple suction	Soehendra et al. 1997[3]
Modified techniques	
Percutaneous traction-assisted EMR (PTA-EMR)	Ono et al. 2000
EMR with three-channel outer tube and multiple forceps	Mukai et al. 2001
EMR with insulated-tip diathermic knife (IT-EMR)	Ohkuwa et al. 2001

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In 1973, Dehle and colleagues first recommended submucosal injection with physiological saline as a technique for raising sessile polyps in the colon to facilitate snare excision (*injection and cut technique*)[6]. In this technique, the diseased mucosa raised off the muscularis propia by the creation of a submucosal bleb was strangulated by a snare, and was cut by application of electrocautery. Most EMR techniques incorporate a submucosal injection to separate the lesion from the mucularis propia and thereby minimizes the risk of perforation. Normal saline solution with or without epinephrine is commonly employed. However, saline diffused quickly, and the use of other solutions such as hypertonic saline, 10% glycerol/5% fructose, 50% dextrose, and sodium hyaluronate have been reported. Initial injection of the distal aspect of the lesion has been advocated to optimize visibility and facilitate excision. Injection volumes generally range from 2 to 30 ml and can be repeated during the procedure as necessary. Inability to lift the lesion may be due to an incorrect injection technique or may indicate malignant invasion into deeper layers which is a contraindication to EMR[7].

The lift-and-cut technique was described for biopsy of a submucosal lesion by Martin et al. in 1976[8]. In 1993, Tada and colleagues were the first investigators to use this technique to completely excise an early gastric cancer using a double-channel endoscope[9]. The technique is generally performed with the special endoscope using a forceps and a snare. An opened snare is inserted through one of the accessory channels and placed around the elevated lesion; the forceps is passed through the second channel and used to grasp and simultaneously lift the lesion into the snare which is then excised with standard electrocautery and retrieved.

In 1990, *the EMR with cap technique* was first used by Inoue et al. for resection of esophageal mucosal lesions[10]. This technique was applied later as a treatment for mucosal lesions of the esophagus, stomach and colon in 1993. The tip of the endoscope is covered with a specially designed transparent endoscope cap. A small size snare is inserted through the biopsy channel of the endoscope and opens inside the cap fitted on the tip of the scope. Before resection, more than 10 ml of normal saline solution (with or without epinephrine) is injected into the submucosal layer around the target mucosal lesion in order to lift the lesion. After injection of saline, the SD-221L-25 snare (Olympus Inc.) is passed down the biopsy channel and opened inside the rimmed cap. Under full endoscopic suction, the lesion is tightly packed inside the cap of the endoscope and snared. The snare is then advanced out of the cap so that the extent of the captured mucosa can be confirmed prior to resection. Finally resection is performed with high-frequency electrocautery[11,12]. This technique is a simpler and easier refinement of EMR method but still needs to use a specialized tube. This technique has the disadvantage that piecemeal resection is needed to deal with lesions larger than 1.5 cm in diameter. Complete excision may not be possible using the cap attachment, either because the lesion does not fit into the cap, or suction is inadequate for drawing it completely into the cap.

The simple suction technique was introduced by Soehendra et al. in 1997[3]. The polypectomy snare is made of monofilament stainless steel wire with a diameter of 0.4 mm which provides the stability required for snaring the lesion. When opened, the snare measures 3x5 cm (Figure 1). A large-channel therapeutic endoscope is used to provide adequate suction alongside the inserted snare. Prior to EMR, the tumor is positioned at six-o'clock by rotating the endoscope to optimize access for EMR (Figure 2; A,B,C). Without prior saline injection, the polypectomy snare is then positioned around the lesion. When the snare is being pressed against the mucosa, it is closed while applying gentle aspiration to draw the tumor bearing mucosa into the snare. Resection is carried out using a pure coagulation current (30-40 W). This method is a relatively simple and easy EMR technique.

EMR may not be completed in one session, particularly when the lesion is large. It is very important to resect the entire tumor for a definitive pathologic examination[13]. When piecemeal resection is carried out, the residual portion between the first and second resected areas must not be left because it can easily develop local recurrence. Divided resection is gradually gaining general support in Japan, although it is still controversial.

The various EMR methods are applicable to all early cancers in the gastrointestinal tract. However the most important points are the endoscopist's experience and the advantages and disadvantages of the various EMR methods.

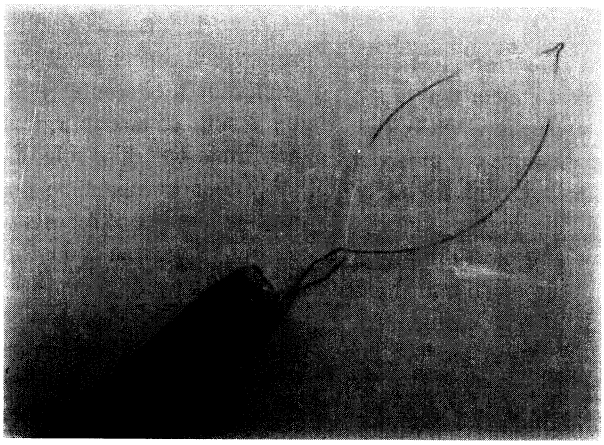
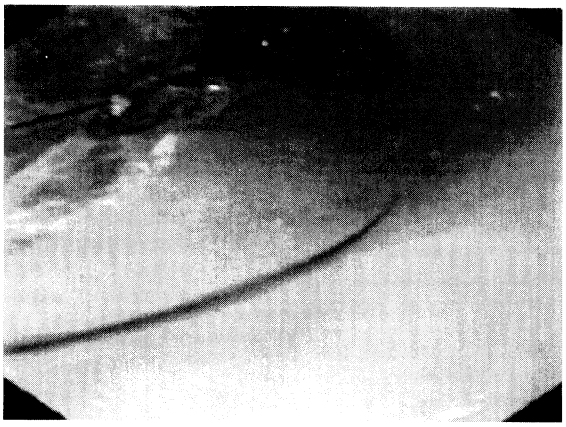


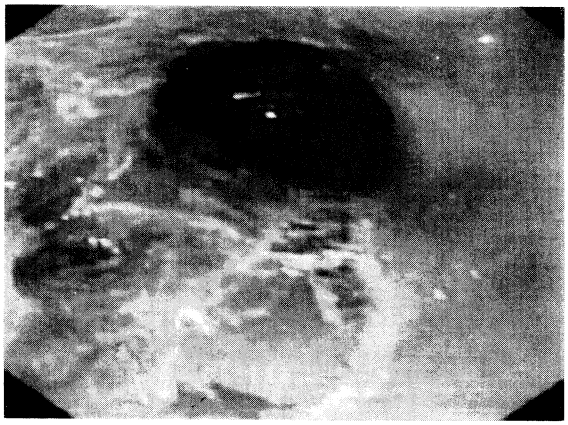
Figure 1. The polypectomy snare measures 3x5 cm.



A



B



C

Figure 2. Technique of simple EMR. **A**, The snare is placed around the lesion and firmly pressed against the mucosa. **B**, To draw the mucosa into the snare, gentle aspiration is applied while the snare is closed. **C**, Resection is then carried out using pure coagulation current.

INDICATIONS

Endoscopic mucosal resection (EMR) is indicated for removal of mucosal cancer that is not associated with lymph node metastasis. EMR is useful, not only as a therapeutic measure for mucosal cancer, but also as a diagnostic approach for polypoid mucosal lesions.

To examine the depth of tumor infiltration and to detect regional lymph node metastasis, high resolution endosonography (EUS) is recommended. In most of the early esophageal cancer studies, 20 MHz miniprobes were used. However, attempting to distinguish intramucosal from submucosal carcinoma is difficult, both endoscopically and ultrasonographically.

General indication for EMR includes

1. Lesion limited to mucosa
2. Without lymph node metastasis
3. Well-differentiated carcinoma.

In the esophagus, EMR is indicated for superficial cancer lesions (m1, m2), less than 2 cm, excluding a circumferential lesion. This is base on the results of large surgical series with histological confirmation[14]. The role of EMR in the treatment of early adenocarcinoma is not yet clear because of the limited number of reports published to date.

Japanese endoscopists are expertised in assessing the depth of invasion of gastric cancers purely on the basis of endoscopic features (Figure 3). The limitations of EMR in the treatment of gastric adenocarcinoma are based on a large database of more than 10,000 surgically resected cases collected at the Cancer Institute Hospital in Tokyo[15] and from other studies[16,17]. EMR is appropriate for elevated-type lesions less than 2 cm in diameter and for depressed-type lesions less than 1 cm in diameter without ulceration (Table 2).

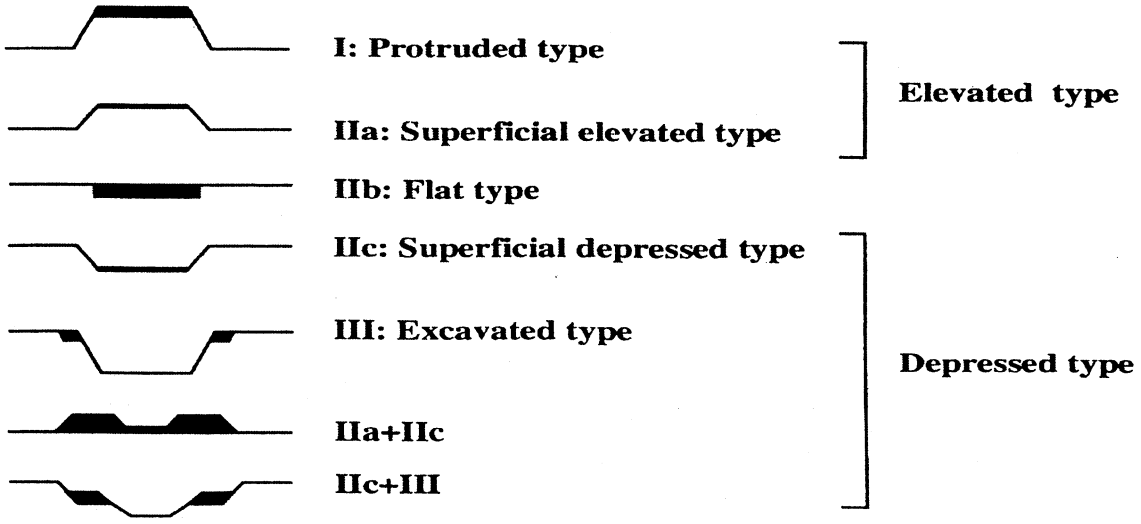


Figure 3. Macroscopic classification of superficial early gastric cancer.

OUTCOME

Complications

The main complications of EMR are bleeding and perforation. Most cases of bleeding can be managed endoscopically by injecting the bleeding site with low concentration adrenaline/saline, treating the bleeding point with argon plasma coagulation, or by applying endoscopic clips.

Table 2. Indication for EMR in superficial early cancers of the gastrointestinal tract[5].

Cancer	Organ		
	Esophagus	**Stomach**	**Colon**
Pathology	Squamous cell	Well differentiated	Well differentiated
T stage	m1, m2	Any m	Any m, sm1
Size and type	Exclude circumferential	IIa: up to 2 cm, or IIb and IIc: up to 1 cm without ulcer or ulcer scar	No limitation

Perforation

Submucosal injection is considered to be a useful tool for avoiding perforation when performing EMR. Large experience in the esophagus and stomach have seemingly proved the effectiveness of this additional method[16,17]. EMR in the esophagus, however, is a quite safe procedure, probably because of the particular structure of the muscle layers of the wall that makes perforation with EMR unlikely. This has been observed for many years in the rubber band ligation therapy for esophageal varices. Perforation due to EMR in the esophagus, however, is usually small and can be successfully managed with clipping.

Recurrence

Local recurrence after EMR is another important issue. Nomura et al. reported that the rate of local recurrence after EMR in patients with solitary esophageal cancer was 4%, while the recurrence rate for multiple lesions was 40%[18]. This may be attributed to the fact that squamous cell carcinoma of the esophagus is often associated with multiple synchronous lesions. In a study of 54 patients with squamous cell carcinoma, Pesko et al.[19] found histologic evidence of multiple lesions independent of the main tumor in the resected esophagus in 31% of patients. They proposed the concept that the entire esophagus may be considered a single field for carcinogenesis. However, it is unknown whether these multiple esophageal carcinomas occur simultaneously. A study of Shimizu et al.[20] suggested that considerable time may be required for the formation of additional lesions; more than 2 years were required on average for formation of a second lesion after resection of an initial lesion.

In recent Japanese series, the following results have been given. The 5-year survival rate after EMR varies between 95 and 100 % with a recurrence rate of 3-7%[21].

EMR of early cancer and high-grade dysplasia (HGD) in Barrett's esophagus (BE)

The appropriate management of patients with BE with HGD or early adenocarcinoma is controversial because patients with HGD are at the highest risk for developing esophageal cancer and there is a high likelihood of coexisting invasive cancer in these patients. Thus, accurate nonsurgical methods for staging malignancy in patients with BE are needed. EMR is extremely useful for the staging as well as treatment of superficial lesions in BE. EMR helps confirm the nature of the lesion and may be a sufficient local treatment. One of its advantages is that it can be used as treatment for patients with comorbid illnesses who cannot tolerate esophagectomy. In addition, EMR provides tissue specimens for a better diagnosis including the confirmation of clear margins. Thus, EMR is not only therapeutic but also diagnostic in these patients. However, prospective long-term randomized studies of these patients are lacking at this time.

SUMMARY

EMR is an important addition to therapeutic endoscopy and has got the potential to become useful over the coming years. EMR is being used increasingly as an alternative to surgery in patients with early-stage esophageal carcinoma because it is

minimally invasive and maintains a good quality of life. EMR is an organ-preserving therapeutic option and thereby avoids many of the problems associated with surgery.

Proper patient selection and improved diagnostic methods such as magnifying endoscopes and fluorescence spectroscopy are likely to identify more patients with premalignant and malignant lesions confined to the mucosa where EMR can be used as a curative therapy.

REFERENCES

1. Matsushita M, Hagiro K, Okazaki K, et al. Endoscopic mucosal resection of gastric tumors located in the lesser curvature of the upper third stomach. Gastrointest Endosc 1997; **45:** 512-15.
2. Takeshita K, Tani M, Inoue H, et al. Endoscopic treatment of early esophageal or gastric cancer. Gut 1997; **40:** 123-27.
3. Soehendra N, Binmoeller KF, Bohnacker S, et al. Endoscopic snare mucosectomy in the esophagus without any additional equipment: a simple technique of resection of flat early cancer. Endoscopy 1997; **29:** 380-83.
4. Giovannini M, Bernardini D, Moutardier V, et al. Endoscopic mucosal resection (EMR): Results and prognostic factors in 21 patients. Endoscopy 1999; **31:** 698-701.
5. Soelikno RM, Inoue H, Chang KJ. Endoscopic mucosal resection. Gastrointest Endosc Clin N Am 2000; **10:** 595-617.
6. Dehle P, Largiader F, Jenny S, et al. A method for endoscopic electroresection of sessile colonic polyps. Endoscopy 1973; **5:** 38-40.
7. Uno Y, Munakata A. The non-lifting sign of invasion colon cancer. Gastrointest Endosc 1994; **40:** 485-89.
8. Martin TR, Onstad GR, Silvis SE, et al. Lift and cut biopsy technique for submucosal sampling. Gastrointest Endosc 1976; **23:** 29-30.
9. Tada M, Murakamai A, Karita M, et al. Endoscopic resection of early gastric cancer. Endoscopy 1993; **25:** 445-50.
10. Inoue H, Endo M. Endoscopic esophageal mucosal resection using a transparent tube. Surg Endosc 1990; **4:** 198-201.
11. Inoue H, Takeshita K, Hori H, et al. Endoscopic mucosal resection with a cap-fitted panendoscope for esophagus, stomach, and colon mucosal lesions. Gastrointest Endosc 1993; **39:** 58-62.
12. Tada M, Inoue H, Yabata E, et al. Colonic mucosal resection using a transparent cap-fitted endoscope. Gastrointest Endosc 1996; **44:** 63-65.
13. Lambert R. Endoscopic treatment of esophagogastric tumors. Endoscopy 1998; **30:** 80-93.
14. Kodama M, Kakegawa T. Treatment of superficial cancer of the esophagus: A summary of responses to a questionnaire on superficial cancer of the esophagus in Japan. Surgery 1998; **123:** 432.
15. Nakagima T. Tabular analysis of 10,000 cases of gastric cancer in CIH. Jpn J Cancer Chemother 1994; **21:** 1813.
16. Makuuchi H, Kise Y, Shimada H, et al. Endoscopic mucosal resection for early gastric cancer. Semin Surg Oncol 1999; **17:** 108.
17. Noda M, Kodama T, Atsumi M, et al. Possibilities and limitations of endoscopic resection for early gastric cancer. Endoscopy 1997; **29:** 361.
18. Nomura T, Boku N, Ohtsu A, et al. Recurrence after endoscopic mucosal resection for superficial esophageal cancer. Endoscopy 2000; **32:** 277-80.
19. Pesko P, Rakie S, Milicevic M, et al. Prevalence and clinicopathologic features of multiple squamous cell carcinoma of the esophagus. Cancer 1994; **73:** 2687-90.
20. Shimizu Y, Tukagoshi H, Fujita M, et al. Metachronous squamous cell carcinoma of the esophagus arising after endoscopic mucosal resection. Gastrointest Endosc 2001; **54:** 190-94.
21. Suzuki H, Masuda K, Fujisaki J, et al. Endoscopic treatment of gastrointestinal cancers-indication and limitation. Jpn J Clin Med 1996; **54:** 1699-704.
22. Shim CS. Endoscopic mucosal resection: an overview of the value of different techniques. Endoscopy 2001; **33:** 271-75.