

Endoscopic Mucosal Resection of Early Esophageal Carcinoma—Experience of 9 Cases

Lien-Fu Lin*, Pi-Teh Huang, Ka-Sic Ho, Jai-Nien Tung

Division of Gastroenterology, Department of Internal Medicine, Tung's Taichung Metroharbor Hospital, Taichung, Taiwan, R.O.C.

Background: Early esophageal mucosal carcinoma (M1 and M2) can be treated by ablation, or by endoscopic resection such as endoscopic mucosal resection (EMR) and endoscopic submucosal dissection. Endoscopic resection enables pathologic examination of resected specimens. We hereby report our experiences with early esophageal cancer and its endoscopically observed types, chromoendoscopy with Lugol's iodine and EMR results.

Methods: Between May 2003 and July 2007, 9 patients with early esophageal carcinoma underwent EMR. The diagnosis was made by conventional endoscopy (waiting for the relaxed phase during esophageal peristalsis) followed by chromoendoscopy using 3% Lugol's iodine to stain suspected early lesions or in high-risks patients. Miniprobe endoscopic ultrasound examinations were performed in all cases except 1. EMRs were carried out with a cap-fitted endoscope (EMRC).

Results: There were 6 male and 3 female patients, with a median age of 53 years (range, 44–83 years). Six of the 9 cases had a history of smoking, 5 had a history of drinking, and 4 had a history of betel nut chewing. The endoscopic pictures of the early cancers were type 0–IIa (1 case), type 0–IIb (2 cases), and type 0–IIc (6 cases). One patient had double 0–IIc lesions. Two 0–IIb cases were detected only by chromoendoscopy using Lugol's iodine staining. The median size of the lesions was 0.85 cm (range, 0.7–2.0 cm). The final pathology reports of the endoscopically resected specimens were well-differentiated squamous cell carcinoma with free vertical and lateral margins, and no vascular or lymphatic invasion. The depths of tumor invasion were mucosal layer M1 in 7 cases, M2 in 1 case, and submucosal layer SM1 in the remaining case. There were no perforation or bleeding complications. The mean follow-up period was 13.1 months (range, 4–46 months). A M2 early esophageal cancer measuring 2 cm in diameter recurred 6 months after piecemeal EMRC. No additional adjuvant therapy was given to the SM1 case owing to her old age and bedridden condition.

Conclusion: Early esophageal cancer can be diagnosed by meticulous examination of the esophageal mucosa with conventional endoscopy, facilitated by Lugol's iodine staining, and can be treated by EMR, which is safe. Recurrence can occur after piecemeal EMR. [*J Chin Med Assoc* 2008;71(7):347–352]

Key Words: chromoendoscopy, early esophageal cancer, endoscopic mucosal resection

Introduction

Early esophageal cancers limited to M1 (also termed carcinoma *in situ*) and M2 (lamina propria) almost have no risk of lymph node metastasis, but the risk appears to be higher if the muscular mucosa layer (M3) is invaded, ranging from 0–10%.^{1–5} Compared with endoscopic ablation such as photodynamic therapy (PDT)

and argon plasma coagulation (APC),^{6,7} endoscopic resection can enable pathologic examination to assess the completeness of resection (vertical and lateral margins) and the status of vascular or lymphatic invasion. Careful endoscopic examination facilitated by Lugol's iodine chromoendoscopy^{8,9} can increase the diagnostic rate of early esophageal cancer. Endoscopic mucosal resection (EMR) techniques are divided into



*Correspondence to: Dr Lien-Fu Lin, No. 8, 11th Floor, Mei Tsun Road, Section 2, Lane 168, Taichung 402, Taiwan, R.O.C.

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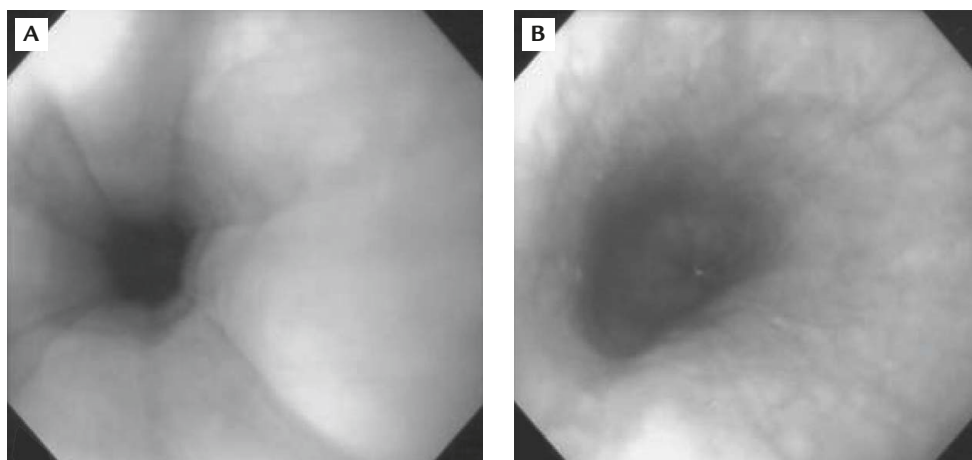


Figure 1. (A) Contracted state of esophagus. (B) Relaxed state of esophagus.

2 categories: without suction^{10,11} and with suction techniques.¹²⁻¹⁴ Inoue and Endo introduced a technique of EMR using a cap-fitted endoscope (EMRC),¹³ which is easy to perform. Herein, we report our experiences with early esophageal carcinoma and its endoscopically observed types, chromoendoscopy with Lugol's iodine and EMR results.

Methods

Between May 2003 and July 2007, a total of 9 cases of early esophageal carcinoma were reviewed. Meticulous examination of the esophagus with conventional endoscopy (Olympus GIF 240, GIF 260) was performed by a single endoscopist. Waiting for the relaxed phase during esophageal peristalsis is a key point in order not to miss early esophageal lesions (Figure 1). In cases where there was a suspicious lesion or in patients with risk factors such as history of smoking, alcoholism or betel nut chewing, staining with 3% Lugol's iodine was done using a spraying catheter. Miniprobe endoscopic ultrasound (Olympus 12 MHz) examinations were performed in all cases except for the first case. Endoscopic ultrasound (Olympus GF UM 2000) and chest computed tomography (CT) were used for detection of regional lymph nodes. Endoscopic resections were carried out with a cap-fitted endoscope using Olympus EMRC kit after positive results of well-differentiated carcinoma were reported.

The agent used for submucosal injection was 10% glycerol (100 mL of glycerol mixed with 1 mL of 2% indigocarmine and 0.5 mL of 1 in 1,000 epinephrine). The volume used for submucosal injection varied from 5 mL for small lesions to 20 mL for large lesions. If bleeding occurred, hemoclipping was done.

Table 1. Risk factors for esophageal cancers

Case	Sex	Age (yr)	Smoking*	Alcohol†	Betel nut chewing‡
1	M	50	Yes	Yes	Yes
2	M	53	No	No	No
3	F	83	No	No	No
4	M	73	Yes	Yes	Yes
5	F	70	No	No	No
6	M	44	Yes	Yes	Yes
7	M	46	Yes	Yes	Yes
8	M	48	Yes	Yes	No
9	F	56	Yes	No	No

*Smoking: 20 cigarettes/day for 20-30 years, 66.6% had smoking history;

†Alcohol: 22-55% alcohol, 200-500 mL/day for 22-50 years, 55.5% had alcohol drinking history; ‡Betel nut chewing: 10-30 nuts/day for 30-50 years, 44.4% had betel nut chewing history.

After the procedure, the patient was fasted for 1 day, and was put on liquid diet the next day. Sucralfate suspension 1 sachet was given 4 times a day. Post EMR endoscopic follow-up was performed after 1 month, 3 months and 6 months, and then yearly.

Results

The results are shown in Tables 1, 2 and 3. There were 6 male and 3 female patients, with a median age of 53 years (range, 44-83 years). Six of them had smoking history, 5 cases had alcoholic history, and 4 cases had betel nut chewing history. The endoscopic pictures of their early cancers were type 0-IIa (1 case), type 0-IIb (2 cases), and type 0-IIc (6 cases). One patient had 2 0-IIc lesions. Two 0-IIb cases were detected by chromoendoscopy using Lugol's iodine staining. The median size of the lesions was 0.85 cm (range, 0.7-2.0 cm). The final

Table 2. Results of endoscopic treatment of early esophageal mucosal cancer (1)

Case	Endoscopic type	Detection only by Lugol's iodine	Tumor size (cm)	Tumor location	Pathology	Treatment method	EMR
1	O-IIC		2	MT	WD SCC	EMRC	Piecemeal (3 pieces)
2	O-IIa		1	MT	WD SCC	EMRC	En bloc
3	O-IIC		1	MT	WD SCC	EMRC	En bloc
4	O-IIC (2 lesions)		1, 0.7	LT	WD SCC	EMRC	En bloc
5	O-IIC		0.7	MT	WD SCC	EMRC	En bloc
6	O-IIb	Yes	0.7	LT	WD SCC	EMRC	En bloc
7	O-IIC		0.7	LT	WD SCC	EMRC	En bloc
8	O-IIb	Yes	0.7	LT	WD SCC	EMRC	En bloc
9	O-IIC		1	LT	WD SCC	EMRC	En bloc

EMR = endoscopic mucosal resection; WD SCC = well-differentiated squamous cell carcinoma; EMRC = EMR with cap-fitted endoscope; MT = middle thoracic esophagus; LT = lower thoracic esophagus. Definition of location of esophageal cancer: upper thoracic is 18-24 cm from incisor teeth; middle thoracic is 24-32 cm from incisor teeth; lower thoracic is 32-40 cm from incisor teeth.

Table 3. Results of endoscopic treatment of early esophageal mucosal cancer (2)

Case	Complications*	Clipping	Blood transfusion	Final pathology	Free margin lateral/vertical	Lymphatic invasion	Depth of invasion	Additional therapy	Follow-up (mo)	Cancer recurrence	Mortality
1	None		No	WD SCC	Yes/Yes	No	M2	No	46	6 mo	No
2	None	1	No	WD SCC	Yes/Yes	No	M1	No	24	No	No
3	None		No	WD SCC	Yes/Yes	No	SM1	No	18	No	No
4	None	1	No	WD SCC	Yes/Yes	No	M1	No	7	No	No
5	None		No	WD SCC	Yes/Yes	No	M1	No	5	No	No
6	None		No	WD SCC	Yes/Yes	No	M1	No	4	No	No
7	None	4	No	WD SCC	Yes/Yes	No	M1	No	5	No	No
8	None	1	No	WD SCC	Yes/Yes	No	M1	No	5	No	No
9	None	6	No	WD SCC	Yes/Yes	No	M1	No	4	No	No

*Bleeding or perforation. WD SCC = well-differentiated squamous cell carcinoma; M1 = mucosal layer 1; M2 = mucosal layer 2; SM1 = submucosal layer 1.

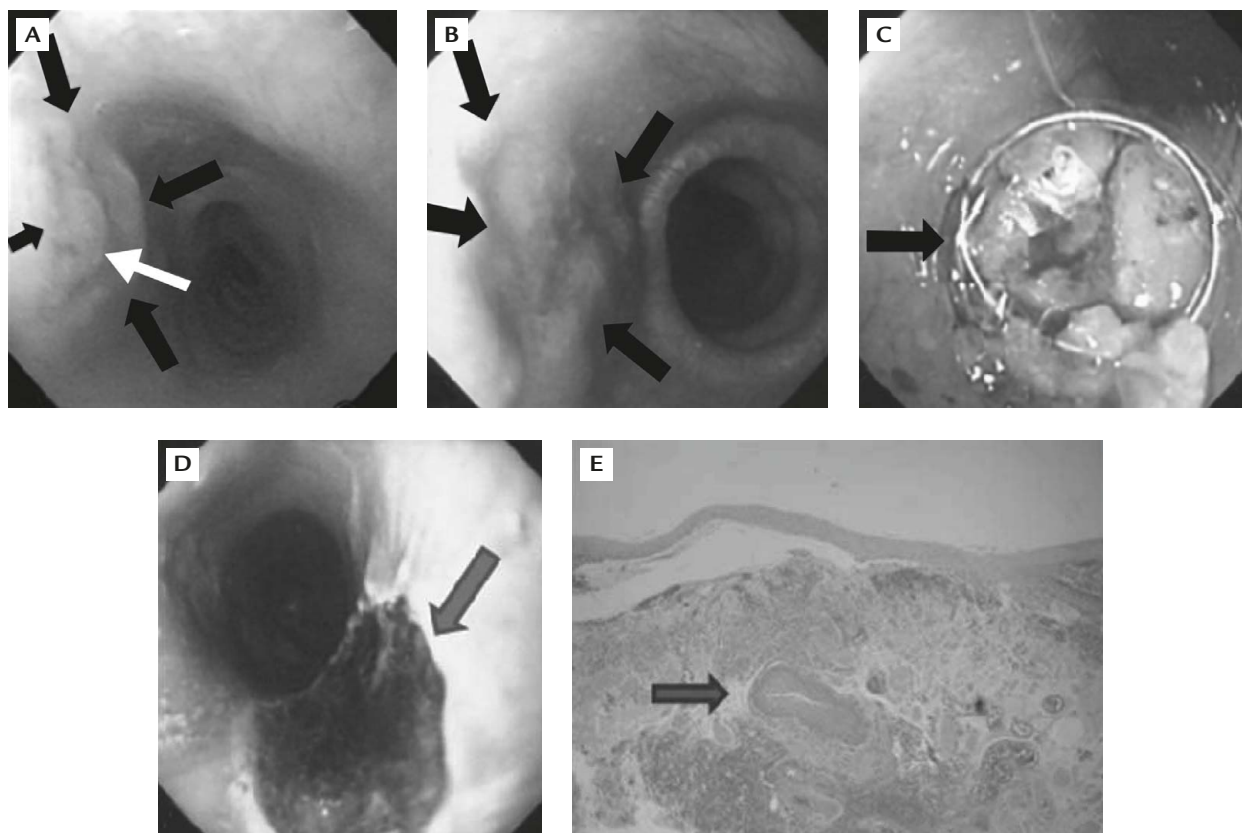


Figure 2. (A) Esophageal IIC lesion before endoscopic biopsy (black arrows), revealing a small nodular lesion in the center (white arrow). (B) Endoscopic picture post endoscopic biopsy (arrows). (C) Endoscopic mucosal resection (arrow). (D) Post endoscopic mucosal resection (arrow). (E) Histology reveals SM1 layer invasion (100 \times).

pathology reports were well-differentiated squamous cell carcinoma with free vertical and lateral margins, and no vascular or lymphatic invasion. The depths of tumor invasion were M1 (mucosal layer) in 7 cases, M2 in 1 case, and SM1 (submucosal layer) in 1 case.

Miniprobe endoscopic ultrasound was performed in 8 cases with 9 lesions. The sensitivity of miniprobe endoscopic ultrasound was 88.9%, and the accuracy in assessing the depth of invasion was also 88.9%. In the case of SM1 layer invasion (Figure 2), the patient was an 83-year-old woman with a history of right femoral neck fracture and who was bedridden. Her family refused further adjuvant therapy.

There were no complications of perforation or bleeding that needed transfusion. The mean follow-up period was 13.1 months (range, 4–46 months). An M2 case of early esophageal cancer (Case 1) measuring 2 cm in diameter recurred 6 months after piecemeal EMRC, and there was a second recurrence (metachronous esophageal cancer) 2.5 years after repeated EMR. The patient then underwent radiotherapy with poor results and finally had surgery. The pathology was submucosal cancer without lymph node invasion.

Discussion

Alcohol drinking, smoking, and betel nut chewing are risk factors for the development of esophageal carcinoma, with large-volume alcohol intake being the highest risk. The combined effect of the 3 substances is associated with a 41-fold increased risk.^{15–17} Two thirds of our patients had at least 1 of the above risk factors (Table 1).

Careful endoscopic examination with conventional endoscope can detect early esophageal carcinoma. Waiting for the relaxed phase during esophageal peristalsis can provide a clearer view of the examination field and better detection of early carcinoma. Type 0–IIC lesions are frequent among superficial esophageal cancers, with 19% reaching the submucosal layer.¹⁸ In our series, 6 of 9 cases had the 0–IIC type, and 1 of them had invaded to the SM1 layer. Most 0–IIa and 0–IIB lesions are mucosal cancers, while 90% of type 0–I lesions and 96% of type 0–III lesions are submucosal cancers.¹⁸ M1 cancer usually presents a picture of very slight depressions with a smooth surface, reddening, and sometimes fine granular changes, while in M3 or SM1 cancer, coarse granular

changes, small nodular elevations, or slightly deeper depressed areas than in M1 lesions can be demonstrated.¹⁸ The endoscopic picture of our SM1 case did show small nodular lesions in a depressed cancer, as shown in Figure 2.

Detection of early esophageal cancer can be facilitated by Lugol's iodine staining.^{8,9} But this can be complicated by allergic reaction, chest burning sensation, chemical esophagitis and acute toxic gastric mucosal injury.^{19,20} We had 2 cases of 0–IIb early cancer that were detected by Lugol's iodine chromoendoscopy. Narrow band imaging (NBI) can also be used for early esophageal cancer detection.²¹

High-resolution endoscopy,¹⁸ miniprobe endoscopic ultrasound,²² and NBI with magnifying endoscope²³ can be used to assess the depth of cancer invasion. In the literature, the accuracy to differentiate T1sm from T1m tumors was 73.5% using a 20-MHz probe,²² our accuracy was 88.9%. The difference could be due to the small number of patients in our series. The agreement of histologic depth of invasion with the pattern of intrapapillary capillary loop observed by NBI with magnifying endoscope was 83.3%.²³

EMRC was first described by Inoue and Endo.¹³ It is easy to perform, but the tumor size is usually limited to less than 2 cm.²⁴ EMR can have a 6.8% rate of severe complications such as perforation and hemorrhage.²⁵ The median tumor size in our series was small, at 0.85 cm, which was suitable for *en bloc* EMR. In the first case, the size of the tumor was 2 cm, which necessitated resection with piecemeal EMR. With piecemeal EMR, the recurrence rate can be as high as 8.3%, and 67% of the recurrences were detected within 1 year.²⁶ Metachronous esophageal cancers were found in 11% of all EMR cases and were diagnosed 1–3 years after EMR.²⁶ Our M2 esophageal cancer had local recurrence of cancer 6 months after piecemeal EMR, then metachronous esophageal cancer (cancer found lower down in the esophagus, not at initial cancer site) developed 2.5 years after a repeated EMR was done. He then received radiotherapy, but with poor results. Finally, he underwent surgery and remains alive. Endoscopic submucosal dissection can have more *en bloc* resection and less recurrence but is technically much more difficult.^{27,28} There was no recurrence in the remaining cases, but the median follow-up period was short (13.1 months).

Ota et al reported 5 cases of esophageal cancer with submucosal layer invasion after EMR—only 1 had local lymph node recurrence, with a mean follow-up period of 27.8 months.²⁹ In our case of SM1 layer invasion, the family refused any further adjuvant therapy because of her old age and bedridden condition. She remains fine.

In conclusion, early esophageal cancer can be diagnosed by meticulous examination with conventional endoscope, facilitated by Lugol's iodine staining, and can be treated by EMR, which is safe. However, recurrence can occur with piecemeal EMR.

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