

Large Early Gastric Cancers Treated by Endoscopic Submucosal Dissection with an Insulation-tipped Diathermic Knife

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It is difficult to remove a large early gastric cancer (≥ 3 cm) in one-piece resection using conventional endoscopic mucosal resection. We tried to use an insulation-tipped (IT) diathermic knife to dissect these lesions. IT-endoscopic submucosal dissection (ESD) was performed in four aging patients with gastric malignancy. All lesions could be removed in one-piece resection by IT-ESD, although three of them exhibited remarkable fibrosis and ulceration. Three cases experienced curative treatment with IT-ESD after the pathologic evaluation, but it was not curative in one case because the pathology showed angiolymphatic invasion. This patient refused additional surgery in consideration of existing major systemic diseases. At 3 months to 1 year of follow-up, endoscopy showed no evidence of residual cancer. IT-ESD is effective in the treatment of large early gastric cancer and is an alternative treatment for early gastric cancer patients who are at risk for major operation. [*J Formos Med Assoc* 2007;106(3):260–264]

Key Words: endoscopic mucosal resection, endoscopic submucosal dissection, gastric cancer

Early gastric cancer (EGC) was defined in 1962 by the Japanese Research Society as gastric cancers that are limited to the mucosa or submucosa regardless of the presence of lymph node metastasis.¹ In Japan, the 5-year survival rate of patients with EGC is more than 90% after gastrectomy with complete removal of the primary and secondary lymph nodes.^{2,3} The incidence of nodal metastasis of intramucosal and submucosal EGCs has been reported to be 3% and 20%, respectively.⁴ Endoscopic mucosal resection (EMR) for EGC was first performed in Japan in 1983. The original strip biopsy technique was advocated by Tada et al.⁵ Modifications in EMR by using a transparent cap (EMR-C) were developed by Inoue et al.⁶ and were commonly used for treatment of

early gastroesophageal tumors. However, it is difficult to remove gastroesophageal cancers larger than 2 cm and those with ulceration or submucosal fibrosis using the strip biopsy method and EMR-C. In Taiwan, EMR for EGCs is not frequently used because most gastric cancers are diagnosed in an advanced stage. We previously reported EMR-C for an EGC with focal submucosal invasion in a patient with decompensated liver cirrhosis.⁷ Hosokawa developed a new endoscopic knife, an insulation-tipped diathermic knife (IT-knife), which has a ceramic ball at the top of the incising needle to prevent leakage of electricity toward the deeper layer of the stomach.⁸ The device was introduced into clinics in 1994.⁸ Hosokawa and Yoshida provided a better

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method for *en bloc* resection of gastric neoplasms larger than 30 mm in size.^{9,10} The indication for endoscopic submucosal dissection (ESD) of EGCs has been expanded in the National Cancer Center Hospital in Japan according to Gotoda et al's report.¹¹ ESD with an IT-knife has rarely been reported in Taiwan. Here, we report four patients with large (≥ 3 cm) EGCs or high-grade dysplasia who were successfully treated by IT-ESD.

Patients and Methods

Case 1

A 67-year-old man with parkinsonism for 13 years under medical control complained of epigastric pain for 5 months. Upper gastrointestinal

(UGI) endoscopy was performed and revealed a gastric ulcer at the lesser curvature of the gastric antrum. After 2 months of proton pump inhibitor (PPI) therapy, the ulcer healed. However, an erythematous depressed area with central scarring and irregular margin at the previous location of the ulcer was found (Figure A). Chromoendoscopy demonstrated the lesion more prominently after using 0.2% indigo carmine (Figure B). Biopsies showed severe dysplasia. In addition, endoscopic ultrasound (EUS) (UM-2R; Olympus Optical Co. Ltd., Tokyo, Japan) showed only thickening of the first and second layer of the gastric wall and no evidence of perigastric lymph nodes. Because the lesion was larger than 3 cm and had central scarring, it would have been difficult to resect it in one piece using conventional EMR. Under general

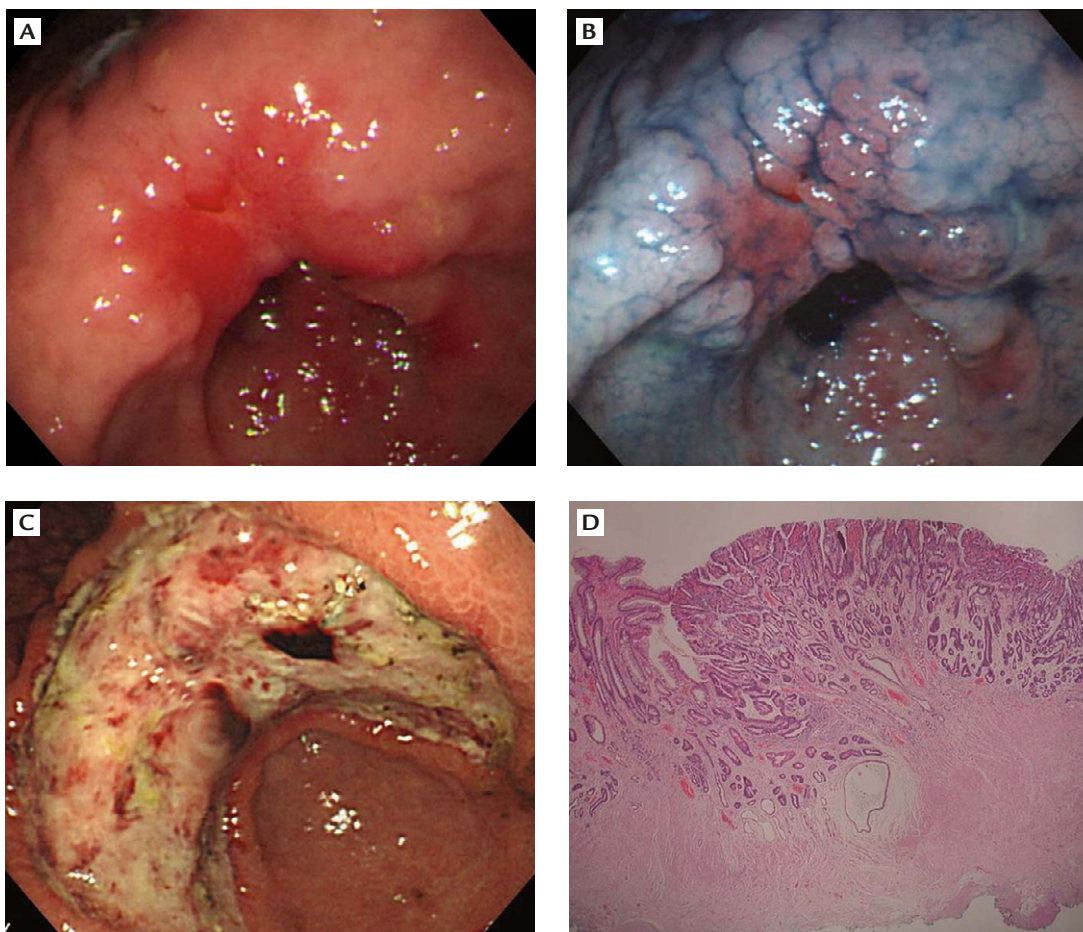


Figure. (A) An erythematous depressed area with central scarring and irregular margin at the lesser curvature of the gastric antrum. (B) Chromoendoscopy shows the lesion more prominently after using 0.2% indigo carmine. (C) A large active ulcer is found after IT-ESD in case 1. (D) Microscopically, the greatest extent of the mucosal depressed area shows a picture of an intramucosal adenocarcinoma. Remarkable fibrosis in the submucosa can be seen (hematoxylin & eosin, 40 \times).

anesthesia, we first marked the margin of the tumor with a needle knife (KD-1L; Olympus Optical Co. Ltd.) to ensure a cancer-free margin and complete resection. Then we injected 1–4 mL of normal saline plus indigo carmine into the submucosa to lift the lesion. Circumferential incision was done initially, then ESD was smoothly performed with the IT-knife (KD-610L; Olympus Optical Co. Ltd.). The electrosurgical unit (PSD-60; Olympus Optical Co. Ltd.) was used and the Endocut mode (80W, Effect 3) was set. A large active ulcer was found after IT-ESD (Figure C). The characteristics of the tumor are shown in the Table. All surgical margins were free of the carcinoma. Remarkable fibrosis in the submucosa was also seen (Figure D). At the 3-, 6-, 9-, and 14-month follow-ups, endoscopy showed no evidence of residual cancer or local recurrence after the biopsies were displayed.

Case 2

A 77-year-old man with diabetes mellitus, chronic renal insufficiency, and ischemic heart disease for years under medical control complained of

epigastric pain for 2 months, which could sometimes be relieved with antacids. UGI endoscopy was performed and revealed an ulceration with irregular nodular margin at the posterior wall of the gastric antrum. Endoscopic biopsies showed severe dysplasia. Repeat UGI endoscopy and biopsy proved a moderately differentiated adenocarcinoma. Abdominal CT scan and EUS showed no evidence of distant metastasis and no enlarged lymph nodes. This patient refused subtotal gastrectomy because of major systemic diseases. IT-ESD was performed smoothly. The characteristics of the tumor are shown in the Table. The tumor extended into the submucosa and was very close to the deep surgical margin. In addition, lymphatic-capillary permeation was frequently seen. Obviously, this procedure was not curative for him. We suggested additional surgery but he and his family refused again due to chronic renal insufficiency and ischemic heart disease. At the 3-month follow-up, endoscopic biopsy showed no evidence of residual cancer or local recurrence. Unfortunately, he died of acute myocardial infarction and congestive heart failure 6 months after ESD.

Table. Characteristics of patients who underwent endoscopic submucosal dissection for early gastric cancer or high-grade dysplasia

Patient	Age (yr)/gender	Macroscopic type/tumor location	Tumor size (cm)/resected specimen size (cm)	Pathologic diagnosis	Time needed for operation (hr)/blood loss (mL)	Curative treatment	Cancer-free interval (mo)
1	67/male	Ilc/gastric antrum	2.6 × 2.2/4 × 3.3	Well-differentiated adenocarcinoma, intramucosa	3/50	Yes	18
2	77/male	Iia + Ilc/gastric antrum	3 × 1.8/5.2 × 4.9	Moderately differentiated adenocarcinoma, submucosa	2.5/50	No (cut margin free of cancer but with lymphatic-vascular invasion)	3
3	72/male	Ilc/gastric angle	2.5 × 1.5/4 × 3.5	Moderately differentiated adenocarcinoma, intramucosa	2.5/30	Yes	6
4	60/male	Iia/gastric antrum	3.5 × 2.8/4.8 × 3.8	High-grade dysplasia, intramucosa	3.5/150	Yes	3

Cases 3 and 4

IT-ESD was performed smoothly for these two patients. The basic data of the patients and the characteristics of the tumors are shown in the Table. There was no evidence of residual cancer and local recurrence on follow-up endoscopy.

Discussion

Surgery has been considered the gold standard treatment for EGC. However, the surgical treatment of EGC is associated with substantial costs as well as risks. Gastrectomy has an operative mortality rate of between 1% and 6.5%.^{12,13} A Dutch study reported a 10% mortality rate and a 43% complication rate.¹⁴ Even after curative surgery, the quality of life may be reduced because of early fullness during eating, dysphagia, reflux symptoms, abdominal discomfort, diarrhea, vomiting, postprandial sweating, and fatigue.¹⁵⁻¹⁷ For the past 20 years, EMR for EGC has been widely performed as a standard method in Japan. The empirical indication for EMR is intestinal-type mucosal cancers without ulcerative findings, ≤ 2 cm in size if elevated or ≤ 1 cm in size if depressed or flat. The Japanese Gastric Cancer Association issued the first version of their gastric cancer treatment guidelines in 2001, which stated that endoscopic resection was indicated for intestinal-type mucosal cancers without ulcerative findings, ≤ 2 cm in size, regardless of tumor morphology.¹⁸ These criteria were determined by considering two aspects: being free of lymph node metastasis and probability of successful *en bloc* resection. The technique of EMR has improved and ESD can dissect a larger lesion. Therefore, the indication for EMR for EGC could be expanded to all those tumors that have been described as node-negative tumors including superficial submucosal invasion.^{11,19}

In our cases, endoscopic biopsies from an ulcerative tumor provided a limited pathologic finding such as severe dysplasia. It is better to treat these lesions with PPI for 1–2 months. After the ulcer has healed, it is easier to obtain an accurate pathology from endoscopic biopsies. Moreover,

invasive cancer can be understaged as severe dysplasia without complete resection of the tumor. Therefore, we consider that EMR is indicated for those with a pathology disclosing severe dysplasia.

With conventional EMR methods including the strip biopsy method and EMR-C, it is difficult to remove gastroesophageal cancers larger than 2 cm and those with ulceration or submucosal fibrosis. When performing EMR, *en bloc* resection is the optimal method, because it is often difficult to reconstruct an entire lesion from multiple specimen fragments; multiple specimen fragments do not contribute to accurate histopathologic evaluation of resected margin and angiolymphatic invasion.¹⁰ Therefore, we treated these four patients suffering from large early gastric tumors (≥ 3 cm) with or without central ulceration and fibrosis by IT-ESD rather than by conventional EMR. We also carried out one-piece resection in these four patients. In Ohkuwa et al's⁸ study, the one-piece (*en bloc*) resection rate for tumors between 11 mm and 20 mm in size was lower at 29% (5/17), compared with a rate of 75% (12/16) for similarly sized lesions treated with IT-ESD. One-piece resection can reduce the local recurrence rate of gastric cancer after EMR.^{9,10}

IT-ESD is one kind of advanced EMR with a relatively high risk of bleeding and perforation. In addition, IT-ESD is more time-consuming than conventional EMR. From Hamanaka et al's report, it took more than 2 hours to dissect the EGC with IT-ESD in 14% of the patients they treated. Furthermore, major complications such as perforation and bleeding occurred in 4% and 2%, respectively.²⁰ In our studies, the operation time was around 2–3 hours. Meanwhile, neither major bleeding nor perforation was encountered in these four patients. Although these four patients had large early gastric tumors and three of them had central ulcer and fibrosis, we were able to dissect and exfoliate the ulcerative and fibrotic part with the IT-knife without difficulty.

In conclusion, our preliminary experience revealed IT-ESD to be effective for large EGC with central fibrosis and ulceration and for those who are at high risk for major operation or those who

refuse surgery. But it is not recommended for inexperienced endoscopists considering the high level of skill needed and a relatively higher risk of complications.

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