Early gastric cancer: diagnosis, treatment techniques and outcomes

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The detection of early gastric cancer is performed by endoscopic study with or without the dye-spraying method, which is useful in detecting small lesions or surface lesions. For the diagnosis of early gastric malignancy, magnification endoscopy, narrow-band imaging and optical coherence tomography are used for histological diagnosis and research. On the other hand, endoscopic ultrasonography is used to discuss the depth of carcinoma invasion, but cannot be used to detect the malignant lesions except for the rare cases of scirrhus-type gastric carcinoma, the histological results of which are sometimes difficult to obtain by biopsy study. The role of endoscopic ultrasonography diagnosis is to assist in making a decision of therapeutic strategy. Curative endoscopic treatment of early gastric cancer is common according to the development of various endoscopic techniques and accessories. Curative treatment is feasible using these techniques. *Eur J Gastroenterol Hepatol* **18:839–845**

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Introduction

Gastric carcinoma has been detected and diagnosed by barium metal X-ray study and endoscopic study with or without biopsy study. Especially, early and minute carcinoma can be detected only by endoscopic study. According to the development and spread of endoscopy, the diagnosis of early gastric cancer is easily accomplished by endoscopic observation and biopsy study. Endoscopic detection of gastrointestinal lesions depends on the recognition of visible mucosal changes. The final diagnosis, however, is performed by histopathological study of biopsy materials. Biopsy study is still very important to obtain the correct diagnosis of the lesion as carcinoma, dysplasia, adenoma and hyperplasia, although it is sometimes possible to diagnose the lesion from the endoscopic investigation of mucosal surface detail.

Definitions of early gastric carcinoma

Early gastric carcinoma is defined as the lesion limited to the submucosal layer histologically. Although there are some problems in the histological diagnosis of early gastric malignant lesions, early gastric carcinoma limited to the mucosa becomes the indication of endoscopic curative treatment. Histological diagnosis of adenocarcinoma limited to the mucosa and adenoma is sometimes vague.

Endoscopic type of early gastric carcinoma, which is included in type 0 of Borrmann classification, was classified into types I, IIa, IIb, IIc, IIa + IIc, IIc + III, and III in Japan.

Detection of early gastric cancer

Gastric cancer can be detected by barium metal X-ray study and endoscopic examination, sometimes by conventional ultrasonography, and by computed tomography in advanced lesions.

Early and minute gastric carcinoma, however, can be detected by endoscopic study. Careful observation by endoscopy is important in detecting the small lesions. For small lesions, detecting the abnormal area and performing the biopsy study represent the effective method. In theory this is easy but, in practice, we have to learn the skills of endoscopic observation and be familiar with the small lesions.

For detecting early gastric carcinoma, endoscopists have to learn to find early cancer lesions, which have a characteristic color and an irregular mucosal pattern.

The dye-spraying method with indigo-carmine is helpful in clarifying the lesion, although it is a complementary technique and is not the absolute method. Chromo-endoscopy with indigo-carmine can be used to show surface unevenness but chromo-endoscopy with Lugol solution to detect esophageal carcinoma is a method of dye enhancement.

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Recent techniques for detecting early gastric cancer

Some endoscopic imaging modalities are used for the diagnosis of early gastric cancer, such as magnification endoscopy and narrow-band imaging (NBI). We expected histological diagnosis of gastric lesions by magnification endoscopy, NBI, or endoscopic optical coherence tomography (EOCT), which can demonstrate the cross image of gastrointestinal mucosa at a resolution 10 times higher than that of a 30-MHz ultrasound probe [1,2]. Although these tools are expected to be used for histological diagnosis, some limitations are recognized.

Magnification endoscopy

On the basis of advances in technology, high-resolution and high-magnification endoscopy with both a fiberoptic and a video imaging system has been developed and is improving. Some papers report on the diagnostic ability of high-resolution and high-magnification endoscopes. It was not easy, however, to manipulate these endoscopes in ordinary clinical examinations, especially in the upper gastrointestinal tract, because of the difficulty of focusing pictures owing to the movement of respiratory and cardiac beats and dark imaging view in magnification.

High-magnification endoscopes have a long history. The first models, which had a fiberoptic endoscope system, were developed in the late 1960s aimed at the histological diagnosis of lesions without biopsy study. Handling of endoscopes, however, had some limitations because of the dark visual field and the difficulty in focusing.

After the progress of electric endoscopes, there seems hope for the development of high-resolution and high-magnification endoscopes that can be easily manipulated. Most advanced video endoscopes for the upper tract (GF-Q240Z), which can demonstrate 80 times magnified images, can be used in the study, although the focusing of this model is not so easy in maximum magnification. Furthermore, this model provides higher-resolution pictures, easier handling and satisfactory brightness compared with former models.

We can observe the surface mucosal pattern (pits pattern) and capillary structure by using high-magnification endoscopy aimed at the histological diagnosis of the target lesion. When we investigate the lesion with a pits pattern, the dye-spraying method gives satisfactory results. Further, when we investigate the lesion from the viewpoint of a microvascular pattern, magnifying the image with NBI gives good results. On the basis of the analysis of the surface structure pattern obtained by magnification, histological changes of carcinoma, dysplasia, and adenoma might be suspected [3]. It is not easy, however, to diagnose the histological nature of the lesion from the magnified pictures. In addition, we cannot observe the whole gastrointestinal wall in the magnified image, even when we have some criteria on magnification image diagnosis. Therefore, the role of high-magnification endoscopy is to magnify the target area in which conventional endoscopy detects some abnormality in ordinary pictures.

Figure 1 shows a case of type IIa, and elevated type of gastric cancer limited to the mucosa at the posterior end of the gastric body showing the irregular pits pattern of the mucosal surface.

These pictures indicate the possibility that magnification endoscopy can judge histological diagnosis by gathering cases and analysis of images.

Endoscopic optical coherence tomography

Optical coherence tomography (OCT) is a recently developed technique for demonstrating cross-sectional images with a resolution 10 times higher than that of a 30-MHz ultrasound catheter probe. This system shows images by using broad-bandwidth illumination and recording the reflection of the illumination.

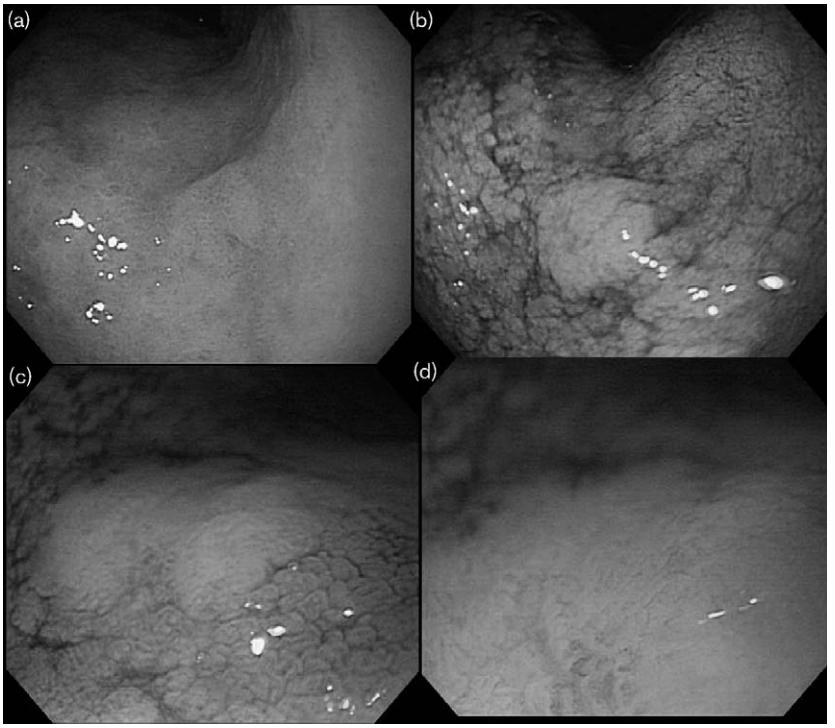
We can observe the microscopic structure of tissues by this method, but the depth of imaging penetration is limited.

We have started to evaluate the clinical application of OCT using a prototype of an OCT probe made by Olympus Co. from August 2000. This probe, which has the same aspect and same view angle of 360° as the ultrasound probe, can be used through the working channel of an ordinary endoscope; hence, we call this method EOCT. For EOCT scanning, water injection or balloon contact methods are not required, as the air does not obstruct the illumination beam.

Examined lesions were demonstrated with high resolution but poor penetration images. The depth of imaging penetration was 1.5–2.0 mm, but we were able to demonstrate the mucosal glandular structure, lamina propria, muscularis mucosa and part of the submucosa individually.

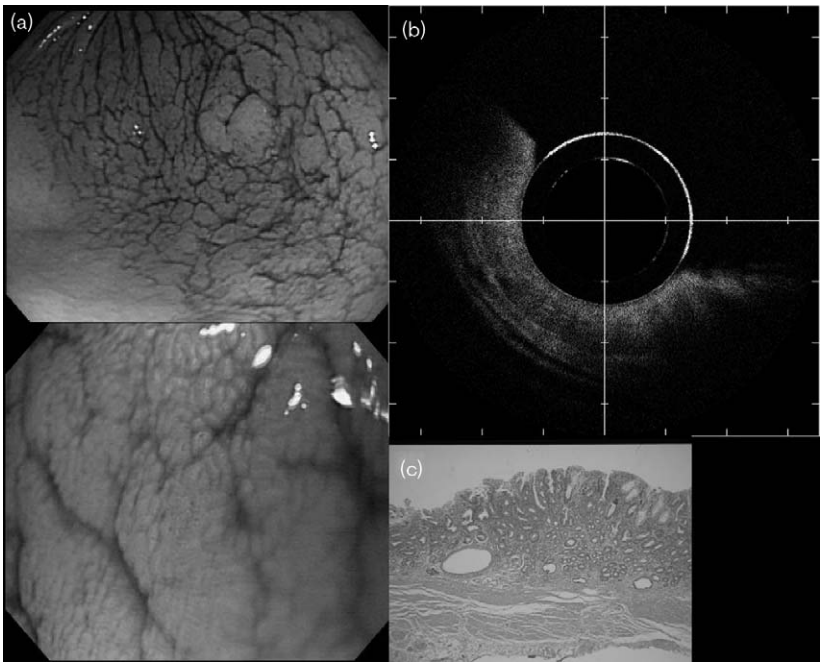
The gastric wall is also observed as a layered structure, which is different from that of the esophageal layer. The surface layer shows the gland structure, and three layers of high, low and high reflective layers behind, which are thought to be lamina propria (high reflectivity), mucosal muscle (low reflectivity) and interface layer of the submucosal layer (high reflectivity). We expected OCT to show the gland structures that can be differentiated between normal and malignant mucosa. Figure 2 shows the OCT images and mucosectomy specimen of gastric cancer. Histological diagnosis from OCT images, however,

Fig. 1



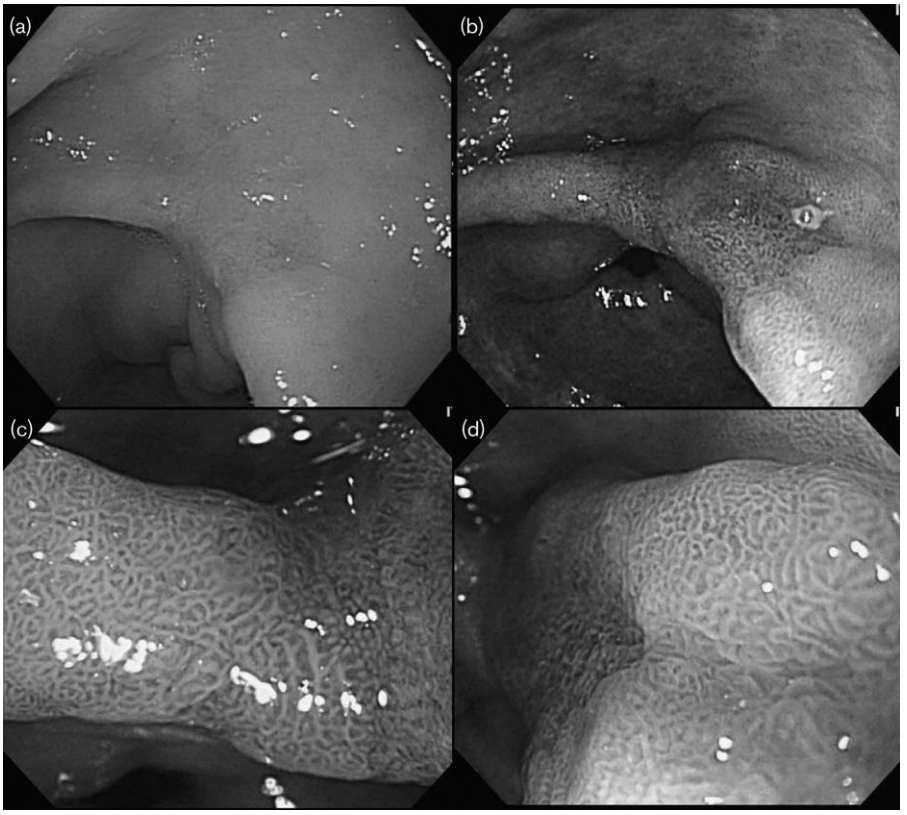
A case of type IIa, elevated type of gastric cancer limited to the mucosa. (a) Ordinary endoscopic view. (b) With dye spraying. (c and d) Magnification images of the lesion showing the irregular pit pattern of the mucosal surface.

Fig. 2



EOCT image of gastric cancer limited to the mucosa. (a and b) EOCT finding of gastric mucosal carcinoma showing the gland-like structure. (c) Endoscopic resection specimen showing the well differentiated adenocarcinoma limited to the mucosa.

Fig. 3



Narrow-band imaging of early gastric cancer type IIc. (a) Endoscopic finding type IIc early gastric cancer. (b) Narrow-band imaging of the lesion. (c and d) Magnifying image of narrow-band imaging.

seemed difficult, as we could not analyze the OCT images of the cancerous region. Further investigation should be performed in this field.

Although the resolution was much higher than that of the 30-MHz ultrasound scanner, penetration of EOCT was too poor to use this method for discussing the depth of tumor invasion. By using this particular sophisticated instrument, however, we can expect to examine the histological nature of tissues in the near future.

EOCT will be expected to be a method of optical biopsy study in the future development of this method.

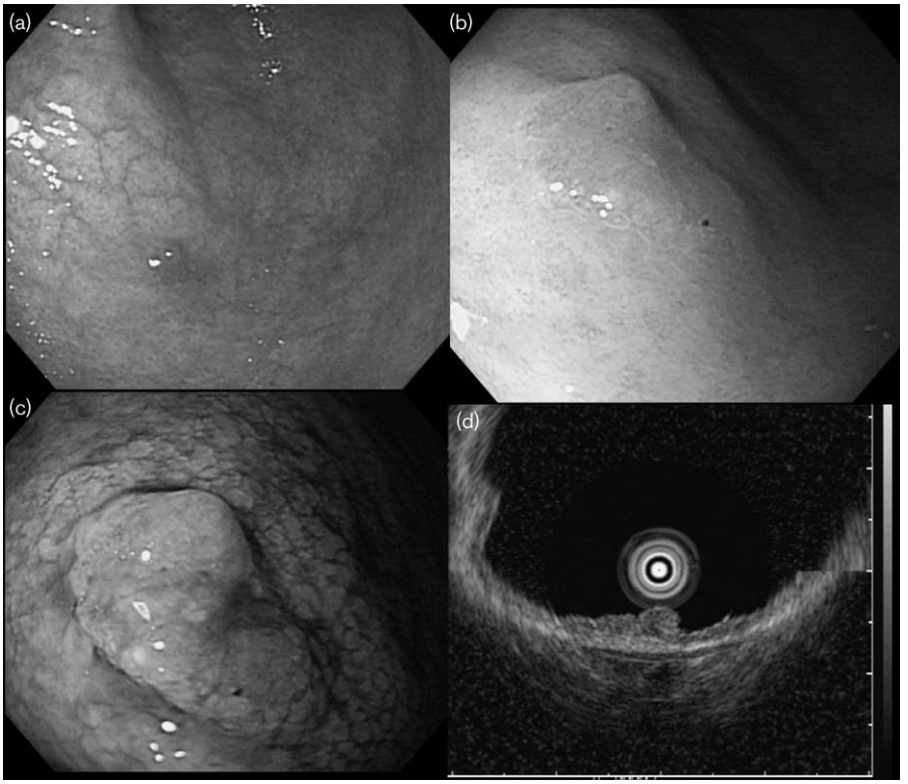
Narrow-band imaging

This system was developed to obtain the enhanced images of the video-endoscope changing the filter with narrow bands. NBI can demonstrate the enhanced mucosal pattern similar to chromo-endoscopy and the micro-vascular structure of the mucosa by the use of magnification endoscopy. Histological diagnosis of early gastric carcinoma was expected but it seems difficult, as we can expect a high possibility of the diagnosis of esophageal carcinoma to show the clearly bordered brown-colored area. Microvascular patterns could be classified into three groups, such as fine network, corkscrew, and unclassified [4]. Although the relationship of histopathological finding and classification of micro-vascular pattern is still problematic in the diagnosis of early gastric carcinoma, it seems feasible to use a combined observation with NBI and magnification endoscopy to examine the histological nature of the lesion in further investigations. Figure 3 shows a case of NBI of type IIc early gastric cancer by magnifying the image.

Endoscopic ultrasonography

Endoscopic ultrasonography (EUS) diagnosis of early gastric malignancy is a recent topic. We can demonstrate the cross section of the gastric wall ultrasonographically by using EUS. Now we have two models of EUS instruments: a conventional ultrasound endoscope with the radial scan transducer at the tip of the endoscope, and an ultrasound probe with a small radial scan transducer at the tip of the catheter, which can be used through the working channel of the endoscope. The gastrointestinal wall can be delineated as a five or more layered structure in the expanded gastrointestinal lumen by water, which is in good correspondence with histological layers. A higher

Fig. 4



Early gastric cancer, type IIa + IIc. (a) Endoscopic finding showing the redness. (b) Close view of the lesion. (c) Indigo-carmine spraying. (d) EUS pictures of gastric cancer limited to the mucosa demonstrated by a 20-MHz ultrasound probe, showing the normal submucosal layer.

frequency ultrasound scanner, such as the 20 to 30-MHz transducer, can demonstrate a more precise picture of the gastrointestinal wall.

The role of EUS is to evaluate the alteration of the gastrointestinal wall by carcinoma based on the layered structure, but we cannot detect the lesion by EUS except in the rare case of early stage of scirrhus cancer. EUS is capable of diagnosing the depth of cancer invasion, which is an important factor to choose the preferred treatment (e.g. endoscopic resection, laparoscopic surgery, or laparotomy). The diagnostic accuracy of the depth of carcinoma invasion is around 80%, when we divide the lesions into mucosal (m) carcinoma, submucosal (sm) carcinoma, carcinoma invading the muscularis propria (pm), and deeper than the subserosal layer (ss) according to our criteria, which is discussed by the three hyperechoic layers of the gastrointestinal wall [5,6].

The diagnosis of mucosal lesion, which is a good indication for endoscopic mucosectomy, is 90%. This is one of the most important diagnostic abilities of EUS to decide the indication for endoscopic treatment of the early stage of gastrointestinal malignancy. Some endoscopists insist that the EUS study before endoscopic treatment is unnecessary, but EUS reveals important information such as the presence of dilated vessels or cystic changes beneath the mucosa and gastrointestinal wall in some cases.

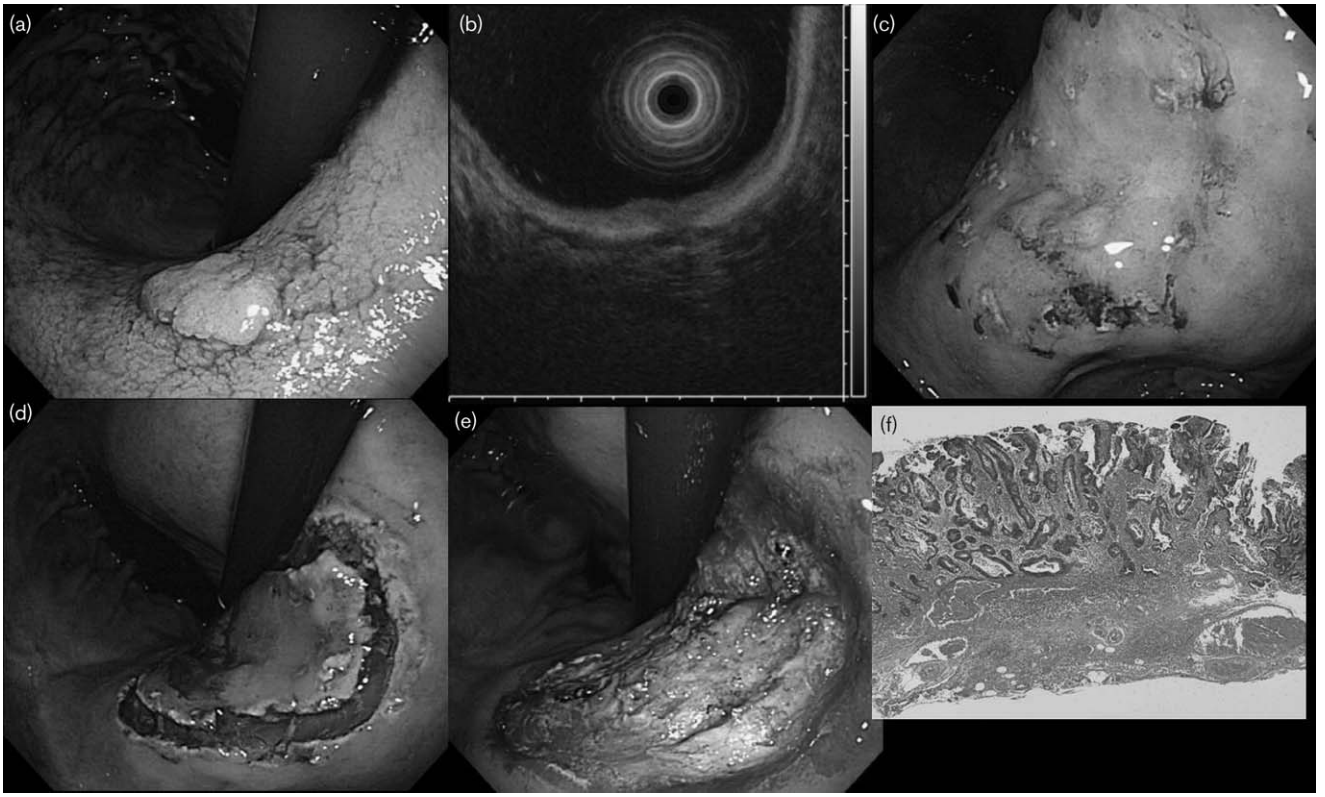
Figure 4 shows EUS pictures of gastric cancer limited to the mucosa demonstrated by a 20-MHz ultrasound probe.

Recently, three-dimensional reconstruction of EUS images obtained by a three-dimensional ultrasound probe has become possible. The significance of the three-dimensional picture is not only to demonstrate the picture that is easily understood but also to avoid overlooking the lesion. In addition, the therapeutic effect can be evaluated by measuring the mass volume using this method.

Therapeutic techniques for early gastric cancer

When early gastric carcinoma is detected endoscopically, we can discuss the indication of endoscopic curative treatment of the lesion. When the lesion limited to the mucosa without ulcerative fibrosis reached the proper

Fig. 5



A case of IIc + III early gastric cancer at angle treated by endoscopic submucosal dissection (ESD). (a) Chromo-endoscopic view of the lesion. (b) Endoscopic ultrasonography image shows the interruption of the submucosal layer (arrow). (c–e) Endoscopic resection was performed by means of ESD. (f) Resected specimen obtained by endoscopic resection.

muscle, and histological findings show well differentiated adenocarcinoma and that the size of the lesion is less than 20 mm, it is a good indication of the need for endoscopic treatment.

Endoscopic treatment of early gastric carcinoma was started by using a polypectomy technique for type I lesions. After the application of laser irradiation under endoscopic view, endoscopic laser treatment of early gastric carcinoma became popular. We could not, however, confirm the histological results on the therapeutic effect of endoscopic laser treatment [7].

Endoscopic resection was developed injecting saline beneath the lesion to perform the polypectomy-like resection. After the development of this technique, some techniques, such as the cap method or double channel mucosectomy, were developed on the basis of the original method called strip biopsy or jumbo biopsy to perform endoscopic mucosal resection of early gastric carcinoma.

Recently, a new technique named endoscopic submucosal dissection (ESD) has been developed in order to achieve a better result for curative and complete resection of the lesion [8,9]. Some instruments have also been developed for this technique. This technique requires a longer time and critical skills, and has a higher risk of perforation than former techniques; however, there is no limitation on the size of the lesion.

Endoscopic diagnosis such as chromo-endoscopy and NBI images are good methods to define the margin of the lesion, and EUS can be expected to show the depth of carcinoma invasion.

Figure 5 shows a case of early gastric cancer treated by ESD, showing the ulcerative interruption of the submucosal layer in the EUS image before treatment. By using ESD, the lesion with ulcerative change was successfully resected.

Diagnosis and treatment of early gastric cancer in the future

At present, the diagnosis of early gastric cancer is performed on the basis of endoscopic findings, which we have studied and researched. This cannot establish the universal criteria because detection and diagnosing ability depend on personal skill and experiences. Other

techniques such as blood test, gastric juice tests or gene analysis might be able to detect small gastrointestinal tract carcinoma, but there are probably some difficulties in these diagnostic methods, as we will not be able to know the position of the lesions except for direct visualization of the gastrointestinal lumen.

Future models for detecting early and small lesions should be automatically developed by the analysis of endoscopic pictures. The progress of information technology is so fast that the detection and differentiation of gastrointestinal lesions and the development of a capsule endoscope seem to be possible by auto-diagnostic endoscopy. We hope that at least therapeutic procedures for early gastric cancer will remain for endoscopists.

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