

# Controversies in the diagnosis and management of early gastric cancer

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Early diagnosis and treatment is the key to improving the prognosis of gastric cancer. The past decades have witnessed the rapid advances in the diagnosis and management of early gastric cancer (EGC): endoscopy has played an increasingly important role, whereas laparoscopic techniques have also been introduced for EGC treatment. In China, the proportion of EGC is gradually increasing, and this condition will soon become a hot research topic. In this article, we will elucidate some major controversies in the diagnosis and management of EGC.

## Ambiguities in the diagnosis of EGC

### *Ambiguity of definition*

According to the Japanese Gastric Cancer Association, EGC is defined as a lesion of the stomach confined to the mucosa and/or submucosa, regardless of its area or the lymph node metastatic status (1). According to their morphological appearance under endoscope, EGC has been classified as type I (protruded), type II (superficial), type III (excavated), and the mixed type, among which the type II lesions are further subdivided into IIa (elevated), IIb (superficial spread), and IIc (depressed) (2). Obviously, the Japanese classification of EGC is an endoscope-based clinical diagnosis.

Currently, the most commonly used staging system for gastric cancer remains the TMN system, which is based on the post-operative pathology. The TNM system, however, does not define EGC. The EGC in the Japanese “gastric cancer” classification is roughly equal to the T1 gastric cancer in the TNM system. The prognosis of EGC and the treatment decision-making should be based on the post-operative pathology. In other words, the diagnosis of EGC need to be based on both clinical diagnosis and pathological staging.

### *Differences in diagnostic criteria*

The criteria for the pathological diagnosis of EGC differ between China and Japan. In China, the Vienna classification of gastrointestinal epithelial neoplasia was applied, i.e., a gastric cancer is diagnosed only when the tumor at least invades deeper than the lamina propria mucosae. In Japan, in contrast, the gastric cancer is diagnosed based on cellular

atypia or structural atypia rather than the depth of invasion. Therefore, some of the EGC cases diagnosed in Japan may be the atypical hyperplasia or high-grade adenoma/dysplasia in China. Thus, special attention must be paid when citing relevant literature authored by our Japanese colleagues.

### Accuracy of clinical staging

Treatment decision-making depends on the tumor stage. Currently we are unable to accurately determine the EGC. Before the initiation of endoscopic treatment, the infiltration of EGC [localized within the mucosa layer (T1a) or has already invaded the submucosa layer (T1b)] as well as the lymph node metastatic status must be accurately identified.

#### *T staging: accurate staging by endoscopic ultrasonography and high-resolution CT*

In recent years, along with the rapid advances in endoscopic treatment, particularly the optimization of endoscopic submucosal dissection (ESD), the indications of ESD for EGC has extended from T1a to some of T1b cases (3,4). Endoscopic ultrasonography remains the most reliable technique for T staging; however, its accuracy rate (roughly 80%) is still not satisfactory (5).

#### *N staging: lymph node metastatic status*

The lymph node metastatic status varies greatly among EGC patients due to the difference in the depth of tumor invasion. The lymph node metastasis rate was 3% if the tumor was localized within the mucosa layer but could reach 20% when the tumor invaded the submucosa layer (6). Identification of the lymph node metastatic status for pre-operative staging is particularly challenging and currently no satisfactory method has been available. Multiplanar reformation (MPR) has an accuracy rate of 78% for lymph node staging in gastric carcinoma patients (7); for EGC, the accuracy rate can be even lower.

The accuracies of sentinel lymph node (SLN) detection in identifying EGC were diverse and therefore its role is highly debatable (8,9). Notably, its false-negative rate (FNR) reached 15-20% in literature (10,11). Therefore, SLN detection can not be a standard technique for the screening of EGC.

### Various treatment options

EGC can be cured by standard radical surgery, with the

5-year survival rate exceeding 90%. However, the radical surgery will inevitably impair the quality of life. How to minimize the surgical scope and improve quality of life has become a hot research topic in this field. Up to now endoscopic resection and modified radical surgery have been listed as the standard treatment.

#### *Endoscopic resection*

Endoscopic resection has become the standard treatment for EGC. Endoscopic mucosal resection (EMR) is feasible for differentiated mucosal cancer sized <2 cm and without any ulcer. On the contrary, ESD enables the en bloc resection of the lesion, has larger resection scope, and can be applied in patients with ulcer(s). Therefore, ESD is superior to EMR (12). In 2000, Gotoda *et al.* analyzed the clinical data of 5,265 surgically treated EGC patients and found that the risk of lymph node metastasis were low under the following conditions: there was an extremely low risk of lymph node metastasis in cases that were (I) differentiated intramucosal cancers without ulcer findings, irrespective of tumor size, (II) differentiated intramucosal cancers less than 3 cm in size with ulcer findings, and (III) differentiated minute invasive submucosal cancers less than 3 cm in size (13). Notably, endoscopic resection of EGC should be based on pre-operative examinations and post-operative pathology, during which the lymph node metastatic status, depth of lesion invasion, and size of tumors can be identified. All the postoperative specimens should undergo continuous slicing and histopathologic examinations, which are helpful to judge whether the lesion has been completely removed. Salvage surgery may be performed for patients with vascular infiltration and invasion as well as those with lymph node metastasis.

In most EGC patients, the metastatic lymph nodes are localized within the group 1 lymph nodes. About 5% of submucosal gastric cancers may be associated with the metastasis in the group 1 lymph nodes, mainly in lymph nodes 7, 8a, and 9 (14,15). Therefore, for EGC patients who are not eligible for endoscopic resection, dissection of the above lymph node stations are reasonable, and often can achieve good outcomes (16).

#### *Laparoscopic surgery*

The role of laparoscopic treatment for EGC has progressively been recognized. A multicenter prospective

phase III clinical study has demonstrated that the laparoscopic procedures were better than the early gastric cancer surgery. As a safe and feasible technique, its short-term efficacy is better than the open surgery (17). In fact, laparoscopic wedge resection (LWR), pylorus-preserving distal gastrectomy (PPG), and vagus nerve-preserving gastrectomy have been applied in EGC patients without any risk of lymph node metastasis.

The laparoscopy-endoscopy cooperative surgery has also been applied for the treatment of EGC. It combines the endoscopic submucosal dissection with laparoscopic gastric wall resection, which prevents excessive resection and deformation of the stomach after surgery.

### Challenges associated with new techniques

The proportion (about 10%) of the diagnosed EGC remains low in China. Both laparoscopy and endoscopy have high technical requirements, and the training of medical professionals in this regard often takes a long period of time. Endoscopic or laparoscopic treatment is highly dependent on accurate clinical staging and judgment, with the ultrasonic endoscope being the required equipment for the clinical diagnosis of EGC. Without ultrasonic endoscope and experienced endoscopy specialists, these new procedures could not be introduced. Also, we can not simply copy the Japanese experience, because the diagnostic criteria used in Japan and China are somehow different. Investigations on the new techniques for EGC should only be performed in major hospitals, in which some relevant clinical trials may be conducted. Finally, the implementation of these new techniques for EGC calls for the close cooperation among medical staff from the departments of endoscopy, pathology, and surgery.

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