Clinicopathologic Characteristics and Outcomes of Early Gastric Cancer Treated with Endoscopic Submucosal Dissection at the gastric angle

Qiaoyan Wu  
Ningbo City First Hospital  https://orcid.org/0000-0002-0917-9516

Haizhong Jiang  
Ningbo City First Hospital

Shuanglin Xie  
Ningbo City First Hospital

Xiaoyun Ding (✉ dyyyding@126.com)  
Ningbo City First Hospital  https://orcid.org/0000-0002-3731-3508

Research article

Keywords: Early gastric cancer, Endoscopic submucosal dissection, Location, Gastric angle, Severe submucosal fibrosis

DOI: https://doi.org/10.21203/rs.3.rs-36168/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Background

None studies have been reported focused on Early gastric cancer (EGC) at the gastric angle although EGCs have been commonly found in this region in Chinese patients. We attempted to discover the characteristics of EGC patients treated Endoscopic submucosal dissection (ESD) at the gastric angle that have not yet to be reported.

METHODS

We reviewed the medical records of patients with EGC treated with ESD from January 2010 to December 2018, and investigated and analyzed clinicopathologic features and ESD outcomes of EGC patients.

RESULTS

In all 444 EGC patients receiving ESD treatment, the second most common anatomic site was the gastric angle (23.0%), following the gastric antrum (55.6%). Compared to the other gastric parts, the EGC at the gastric angle had a relatively higher percentage of the flat or depressed lesions (67.7%) (P=0.05). The rate of severe submucosal fibrosis was significantly higher in the gastric angle lesions (15.69%) than those in the gastric body (4.5%), cardia (3.9%), antrum (1.21%) (P < 0.001). Among EGCs at the gastric angle there were lower rates of en bloc resection, complete resection and curative resection, as well as higher perforation rate and longer procedure time in the severe submucosal fibrosis group (P<0.05).

CONCLUSIONS

The gastric angle is the second most common location of EGCs resected with ESD. There is a higher rate of severe submucosal fibrosis in EGCs at the gastric angle, which suggests more attention should be paid to patients with EGCs at the gastric angle referred for ESD.

Background

Gastric cancer is a common malignant tumour all over the world, especially in the eastern Asia. EGC is defined by tumor invasion confined to the mucosa or submucosa, irrespective of the presence of lymph node metastases[1]. With rapid advances in endoscopic technology and endoscopic screening[2], the detection rates of EGC have increased up to 57.6% in South Korea and more than 70% in Japan[3,4], resulting in lower mortality and a better 5-year survival rate. Endoscopic resection (ER) such as Endoscopic mucosal resection (EMR) and ESD, had been recommended as a standard therapy for EGC without lymph node metastasis (LNM), which can achieve almost same long-term survival with the benefits of less invasiveness and preservation of a better life quality[5].

It would be helpful to diagnose and treat EGC more accurately and efficiently if EGC features at different locations can be determined. As one study indicated that tumors in the gastric cardia had some particular
features: higher proportions of EGCs originated in the cardiac mucosa with slightly elevated gross patterns and intestinal adenocarcinoma histology, and the risk for lymph node metastasis in this location was significantly lower than that in the distal stomach[6]. However, no study has reported EGC features at the gastric angle, although EGCs have been commonly found in this small region in Chinese patients. Therefore, we conducted a retrospective study to evaluate the incidence and characteristics of EGC treated by ESD at the gastric angle. In addition, we compared the different factors of EGC at the gastric angle related to their managements.

**Methods**

**Patients**

A total of 504 consecutive patients with EGCs who underwent gastric ESD in a single center were reviewed from January 2010 to December 2018. The patients were enrolled according to the Japanese Gastric Cancer Treatment Guidelines 2010[7].

Of these, 60 patients were excluded: 46 patients did not meet the criteria, 8 had lesions arising in a remnant stomach, and 6 had received a gastric tube after esophagectomy. Finally, a total of 444 patients with EGC in different gastric locations were analyzed in the present study (Fig. 1 and Fig. 2). The retrospectively analyzed medical records included clinical data, endoscopic findings, ESD procedure and pathology. Written informed consent was obtained from all patients before ESD. The study was approved by the Ethics Committee of the institution that belongs to our hospital.

**ESD procedures**

Endoscopy, Endoscopic ultrasonography and abdominal Computer Tomography, Ultrasonography examinations were carried out before ESD to evaluate the lesions and determine whether they met the indications. All patients were sedated under general anesthesia, and airway intubation was performed. The patients’ cardiorespiratory functions were monitored during the procedure. ESD was performed by experienced GI endoscopists. A standard single accessory-channel endoscope (GIF-Q260J; Olympus Optical Co, Ltd, Tokyo, Japan) was used to perform ESD procedures. The lesions of EGC were identified and their lateral demarcations were determined by using white-light endoscope, chromoendoscopy with indigo-carmine solution, narrow-band imaging, magnifying endoscopy or a combination of these techniques. The typical ESD procedure was as follows: 1) a transparent cap was attached to the tip of the endoscope, and marking dots were made outside the lesion margin by electrocoagulation; 2) normal saline solution and epinephrine mixture (1:10,000) with methylthionine chloride (0.2 ml) was injected with a 23-gauge needle into the submucosal layer to lift the mucosa; 3) one or two of various knives was used to cut the circumferential mucosa outside the marking dots including Dua-knife (Olympus), insulated-tip-knife (Olympus), and Hook-knife (Olympus). 4) the submucosa under the lesion was dissected until the whole lesion was cut off. During the whole procedure, we performed endoscopic hemostasis either with the knife itself or with hemostatic forceps (FD-410LR; Olympus) whenever active bleeding was noticed. Because of the resulting artificial large gastric ulcer after ESD, all patient were administered a proton
pump inhibitor by intravenous injection for 5 days and continuously given an oral proton pump inhibitor and a mucoprotective agent for approximately 2 months.

**Histopathological Evaluation and Therapeutic outcomes**

After ESD, the resected specimen was stretched and fixed on plate, cut into 2-mm-thick slices after formalin fixation. The histological type, size, depth of invasion, lateral and vertical margins, and lymphatic-vascular invasion were assessed according to the Japanese Classification of Gastric Carcinoma[8]. When the final pathological diagnoses of gastric lesions did not meet endoscopic curative resection criteria, surgical rescue resection was recommended. “En bloc resection” was defined as resection in a single piece without fragmentation. “Complete resection” was defined as an en bloc resection with lateral and vertical tumor-negative margins. “Curative resection” was defined as a complete resection with an absence of lymphovascular invasion and meeting absolute or expanded indications[9]. “Delayed bleeding” was defined as the occurrence of clinical symptoms and laboratory changes that indicated GI bleeding after ESD. “Perforation” was diagnosed by direct endoscopic observation of mesenteric fat or the presence of free air on an abdominal radiograph or abdominal computed tomography scan. “Stenosis” was judged as a complication when it was symptomatic and needed endoscopic or surgical intervention.

**Statistical analysis**

All data analyses were conducted using statistical software (SPSS version 19.0; SPSS Inc., Chicago, Ill). Quantitative data were presented as the means and SDs in the form “mean ± SD” or the medians and ranges. Categorical data were presented as the rate, proportion, and ratio. Comparisons among the different groups of gastric regions were performed using one-way analysis of variance, Pearson’s chi-square test or Fisher’s exact test. A univariate analysis was carried out to evaluate the factors related to severe submucosal fibrosis at the gastric angle using an independent-samples t test or Pearson’s chi-square test/Fisher’s test. \( P \text{ values } \leq 0.05 \) were considered statistically significant.

**Results**

In 444 EGC patients the mean age was 62.6 ± 8.8 years, and 302 patients (68.0%) were male. The predominant locations of all lesions were the antrum and the angle of stomach (55.6% and 23.0%, respectively). According to macroscopic appearance, type flat and depressed lesions were a little more common in 248 patients (248/444, 55.9%). Submucosal cancer and undifferentiated cancer account for 6.8% and 5.6% respectively in all included cases. Severe submucosal fibrosis was found in 23 cases (23/444, 5.2%) during ESD procedures. The results of ESD pathological examination showed 2.0% of positive lateral margin, 1.8% of positive vertical margin, and 1.1% of positive Lymphovascular invasion. The rates of en bloc resection, complete resection and curative resection were 98.9%, 95.3%, 90.3%, respectively.

Additional radical surgical treatments were performed in 26 (5.9%) of 43 noncurative resection patients, and one had lymph node metastases in these 26 patients. The remaining 17 patients did not
undergo surgery because of refusal to undergo surgery, comorbidities, and advanced age. Although the prevailing procedure-related complication was delayed bleeding with 5.4% in all patients (24/444), only one case with delayed bleeding required blood transfusion and underwent emergency surgery because the bleeding could not be controlled endoscopically. Perforation occurred in 6 cases (1.4%) during ESD, which were all managed successfully by endoscopic clipping. There was no delayed perforation in our case series (Table 1).
| Characteristic                                      | Number (%) |
|---------------------------------------------------|------------|
| Male, n (%)                                       | 302 (68.0) |
| Age (yr), mean ± SD                               | 62.6 (8.8) |
| Location, n (%)                                   |            |
| Cardia                                           | 26 (5.9)   |
| Fundus                                           | 2 (0.5)    |
| Body                                             | 67 (15.1)  |
| Angle                                            | 102 (23.0) |
| Antrum                                           | 247 (55.6) |
| Macroscopic type, n (%)                           |            |
| Elevated                                         | 196 (44.1) |
| Flat or depressed                                 | 248 (55.9) |
| Severe submucosal fibrosis, n (%)                 | 23 (5.2)   |
| Depth of invasion, n (%)                          |            |
| Mucosal lesion                                    | 414 (93.2) |
| Submucosal invasion                               | 30 (6.8)   |
| Resection margin involvement, n (%)               |            |
| Lateral margin (+)                                | 9 (2.0)    |
| Vertical margin (+)                               | 8 (1.8)    |
| Lymphovascular invasion, n (%)                    | 5 (1.1)    |
| Histology, n (%)                                  |            |
| differentiated                                    | 419 (94.4) |
| undifferentiated                                  | 25 (5.6)   |
| En bloc resection, n (%)                          | 438 (98.6) |
| Complete resection, n (%)                         | 423 (95.3) |
| Curative resection, n (%)                         | 401 (90.3) |
| Complications, n (%)                              |            |
|                          | number(%) |
|--------------------------|-----------|
| Perforation              | 6 (1.4)   |
| Delayed bleeding         | 24 (5.4)  |
| Additional gastrectomy, n (%) | 26(5.9)   |
| Procedure time (min), mean ± SD | 69.3(37.6) |

In all enrolled cases, the lesions larger than 2 cm were more common at the gastric body (43.2%) and angle (40.2%) than at the antrum (23%) and cardia (19.2%) ($P = 0.04$). There was a relatively higher percentage of the flat or depressed lesions at gastric angle (67.7%) ($P = 0.05$) compared to the other gastric parts. The rate of severe submucosal fibrosis was significantly higher in the lesions of gastric angle (15.69%) than in those of gastric body (4.5%) and antrum (1.21%) ($P < 0.001$), and a lower rate of en bloc resection of the lesions at gastric angle was also observed (95.1%, $P = 0.02$). In addition, perforation during ESD occurred in 3 cases (2.9%) at the gastric angle, 2 cases (3%) at the gastric body, and no case at the antrum and cardia, but there was no statistical difference. Similarly, no difference was observed in delayed bleeding among the different gastric parts. (Table 2).
Table 2
Clinicopathological Characteristics of EGC among the Different Locations

| Variables                        | Cardia (n = 26) | Fundus† (n = 2) | Body (n = 67) | Angle (n = 102) | Antrum (n = 247) | P value |
|----------------------------------|-----------------|-----------------|---------------|-----------------|------------------|---------|
| Male sex, n(%)                  | 21 (80.8)       | 2 (100.0)       | 53 (79.1)     | 68 (66.7)       | 158 (64.0)       | 0.05    |
| Age (yr), mean ± SD              | 66.3 (9.2)      | 59.5 (10.6)     | 63.8 (8.9)    | 63.6 (8.1)      | 61.5 (9.3)       | 0.01    |
| Tumor size (mm)                  | 0.04            |                 |               |                 |                  |         |
| < 20 mm, n(%)                    | 21 (80.8)       | 0 (0.00)        | 38 (56.7)     | 61 (59.8)       | 173 (70.0)       |         |
| ≥ 20 mm, n(%)                    | 5 (19.2)        | 2 (100.0)       | 29 (43.2)     | 41 (40.2)       | 74 (23.0)        |         |
| Macroscopic type, n(%)           |                 |                 |               |                 |                  | 0.05    |
| Elevated                         | 11 (42.3)       | 1 (50.0)        | 31 (46.3)     | 33 (32.4)       | 120 (48.6)       |         |
| Flat or depressed                | 15 (57.7)       | 1 (50.0)        | 36 (53.7)     | 69 (67.7)       | 127 (51.4)       |         |
| Severe submucosal fibrosis, n(%) | 1 (3.9)         | 0 (0.0)         | 3 (4.5)       | 16 (15.7)       | 3 (1.2)          | < 0.001 |
| Depth of invasion, n(%)          |                 |                 |               |                 |                  | 0.08    |
| Mucosal lesion                   | 23 (88.5)       | 1 (50.0)        | 59 (88.1)     | 95 (93.1)       | 236 (95.5)       |         |
| Submucosal invasion              | 3 (11.5)        | 1 (50.0)        | 8 (11.9)      | 7 (6.9)         | 11 (4.5)         |         |
| Resection margin involvement, n(%)|                 |                 |               |                 |                  |         |
| Lateral margin(+)                | 1 (3.9)         | 0 (0.0)         | 4 (6.0)       | 2 (2.0)         | 2 (0.8)          | 0.04    |
| Vertical margin(+)               | 1 (3.9)         | 0 (0.0)         | 1 (1.5)       | 2 (2.0)         | 4 (1.6)          | 0.67    |
| Lymphovascular invasion, n(%)    | 0 (0.0)         | 0 (0.0)         | 2 (3.0)       | 2 (2.0)         | 1 (0.4)          | 0.14    |
| Histology, n(%)                  |                 |                 |               |                 |                  | 0.08    |
| differentiated                   | 25 (96.2)       | 1 (50.0)        | 61 (91.0)     | 93 (91.2)       | 239 (96.8)       |         |
| undifferentiated                 | 1 (3.9)         | 1 (50.0)        | 6 (9.0)       | 9 (8.8)         | 8 (3.2)          |         |
| En bloc resection, n(%)          | 26 (100.0)      | 2 (100.0)       | 66 (98.5)     | 97 (95.1)       | 246 (99.6)       | 0.02    |
| Complete resection, n(%)         | 25 (96.1)       | 2 (100.0)       | 61 (91.0)     | 95 (93.1)       | 240 (97.2)       | 0.10    |

†Because two cases in the gastric fundus were too few to analyze, features of other gastric parts were compared in the Table 1 except gastric fundus features.
| Variables                                      | Cardia (n = 26) | Fundus† (n = 2) | Body (n = 67) | Angle (n = 102) | Antrum (n = 247) | P value |
|-----------------------------------------------|-----------------|-----------------|---------------|-----------------|-----------------|---------|
| Curative resection, n(%)                      | 22 (84.6)       | 2 (100.0)       | 53 (79.1)     | 91 (89.2)       | 233 (94.3)      | < 0.05  |
| Complications, n(%)                           |                 |                 |               |                 |                 |         |
| Perforation                                   | 0 (0.0)         | 0 (0.0)         | 2 (3.0)       | 3 (2.9)         | 1 (0.4)         | 0.10    |
| Delayed bleeding                              | 1 (3.9)         | 0 (0.0)         | 3 (4.5)       | 8 (7.8)         | 12 (4.9)        | 0.71    |
| Additional gastrectomy, n(%)                  | 2 (7.7)         | 0 (0.0)         | 7 (10.4)      | 7 (6.8)         | 10 (4.0)        | 0.16    |
| Procedure time (min), mean ± SD              | 85.6(45.0)      | 105.0(35.6)     | 84.0(44.5)    | 80.1(39.6)      | 58.9(34.4)      | 0.32    |

†Because two cases in the gastric fundus were too few to analyze, features of other gastric parts were compared in the Table 1 except gastric fundus features.

Among the patients with EGC at the gastric angle, there were significantly higher rates of tumor size larger than 2 cm (P = 0.01) and undifferentiated lesions (P < 0.001) on pathological evaluation in the cases with severe submucosal fibrosis. We also found that there was a higher incidence of ulcerative lesions in the severe submucosal fibrosis group than in no severe submucosal fibrosis group (4/16, 25.0% vs 5/86, 5.8%, p = 0.03). The univariate analysis showed that there were lower rates of en bloc resection, complete resection and curative resection, a higher rate of additional gastrectomy, and longer ESD procedure time in the severe submucosal fibrosis group. Perforation during ESD procedure occurred more commonly in the lesions with severe submucosal fibrosis (18.8% vs 0%, P < 0.001). There was a relatively higher rate of delayed bleeding in the severe submucosal fibrosis group, but with no statistical difference (18.8% vs 5.8%, P = 0.08). (Table 3).
Table 3
Univariate Analysis of Factors Anticipated to be Associated with Severe Submucosal Fibrosis in EGCs at
the Gastric Angle

| Variables                                | Severe submucosal fibrosis (n = 16) | No severe submucosal fibrosis (n = 86) | P value |
|------------------------------------------|------------------------------------|--------------------------------------|---------|
| Male sex, n(%)                           | 13 (81.3)                          | 55 (66.0)                            | 0.18    |
| Age (yr), mean ± SD                      | 65.9(8.2)                          | 63.9(8.2)                            | 0.36    |
| Tumor size(mm)                           |                                    |                                      | 0.01    |
| < 20 mm, n(%)                            | 5 (31.3)                           | 56 (65.1)                            |         |
| ≥ 20 mm, n(%)                            | 11 (68.7)                          | 30 (34.9)                            |         |
| Macroscopic type, n(%)                   |                                    |                                      | 0.49    |
| Elevated                                 | 4 (25.0)                           | 29 (33.7)                            |         |
| Flat or depressed                        | 12 (75.0)                          | 57 (66.3)                            |         |
| Depth of invasion, n(%)                  |                                    |                                      | 0.08    |
| Mucosal lesion                           | 13 (81.2)                          | 82 (95.3)                            |         |
| Submucosal invasion                      | 3 (18.8)                           | 4 (4.7)                              |         |
| Resection margin involvement, n(%)       |                                    |                                      |         |
| Lateral margin(+)                        | 1 (6.3)                            | 1 (0.0)                              | 0.29    |
| Vertical margin(+)                       | 1 (6.3)                            | 2 (0.0)                              | 1.0     |
| Histology, n(%)                          |                                    |                                      | < 0.001 |
| differentiated                           | 10 (62.5)                          | 83 (96.5)                            |         |
| undifferentiated                         | 6 (37.5)                           | 3 (3.5)                              |         |
| En bloc resection, n(%)                  | 11 (68.8)                          | 86 (100.0)                           | < 0.001 |
| Complete resection, n(%)                 | 11(68.8)                           | 84 (97.7)                            | < 0.05  |
| Curative resection, n(%)                 | 9 (56.2)                           | 82 (95.3)                            | < 0.001 |
| Complications, n(%)                      |                                    |                                      |         |
| Perforation                              | 3 (18.8)                           | 0 (0.0)                              | 0.00    |
| Delayed bleeding                         | 3 (18.8)                           | 5 (5.8)                              | 0.08    |
Discussion

It has been recognized that promotion of endoscopic screening is important to improve the diagnosis rate of EGC[10]. Many studies have also provided suggestions on how to improve the accuracy and effectiveness of detecting EGC[11,12]. In recent years Well-qualified endoscopic screening has began to become available in China, as a result more EGCs have been found and treated with ER[13,14]. We investigated the clinical data and endoscopic findings of EGC treated with ESD in our center, and compared the characteristics of EGC in different gastric parts in order to elucidate their own particular features of the lesions according to anatomical sites, which will be much beneficial for us to diagnose and treat EGC more efficaciously and accurately afterwards. In this study we especially focused on EGC at gastric angle as its particular anatomy. This is also the first report to characterize EGC at the gastric angle treated with ESD[15].

In our case series we found that the gastric angle was the second most common location of EGCs treated by ESD, accounting for twenty-three percent of all patients. The gastric angle is a bending area on the lesser curvature, comprising the boundary between the gastric body and the antrum. Although it is a small area, there is a high percentage of gastric diseases such as gastric ulcer and cancer arising from this region in Chinese patients. Most studies reported the distributions of gastric cancer according to the lower third, middle third, and upper third of the stomach. Feng et al.[16] reported that EGC lesions were found 318 patients (63.2%) in the lower third, 98 patients (19.5%) in the middle third, and 87 patients (17.3%) in the upper third of the stomach respectively in 503 patients of Chinese ethnicity. However, we believe that it is better to evaluate the distributions of EGC according to gastric antrum, angle, body, fundus, and cardia, which would be more helpful to our targeted endoscopic observation of different parts, and improve the early diagnostic efficiency of early gastric cancer. Therefore, as to a second common site of EGC, we should pay more attention to observing gastric angle region endoscopically.

With a more detailed investigation on the EGC features at the different anatomical regions where EGC occurs, we found there were higher rates of larger lesions in size at gastric angle and body, and a higher rate of flat-depressed lesions at gastric angle according to endoscopic gross type. It was also unexpectedly noticed that severe submucosal fibrosis was more commonly found in the lesions of EGC located at the gastric angle than those at other gastric parts during ESD procedure. In our opinion it may be the reasonable explanations for this result that gastric ulcers are prone to occur at the gastric angle region and there is the higher rate of flat-depressed EGC lesions at gastric angle. Oi et al[17] have put forward the double-regulation theory to explain why peptic ulcer disease often occurred in the gastric
angle and why the ulcer often recurs at the same or adjacent parts of previous ulcers. Mechanical tension and exposure to high concentrations of acid in the pyloric gland area may lead to these findings. Ulcer recurrence may lead to the abnormalities of the scar and severe submucosal fibrosis In result of repeated ulcer healings. Furthermore, in addition to more flat-depressed EGC lesions at the gastric angle, in our study we also found that more ulcerative lesions were observed in the severe submucosal fibrosis group at the gastric angle. Isozaki et al.[18] reported that the depressed EGC lesions with ulcer can lead to the severe submucosal fibrosis that occurs in the submucosa of EGC lesions, which sometimes can be misdiagnosed as advanced gastric cancer.

It has been considered that the location of EGC lesions at the gastric angle was one site of difficult ESD because the submucosal dissection plane at the gastric angle is much difficult to manipulate. Furthermore severe submucosal fibrosis also imposes great difficulty for endoscopic submucosal dissection because submucosal injections normally fail to raise the lesion[19], leading to a higher non-en bloc resection rate, a longer procedure time and higher risk of perforation in our study. In addition, Nagata et al[20] reported that the density of fibrotic changes in the lesion affects ESD procedure time. Therefore, a challenge lies in cleaving fibrotic submucosal tissue beneath scars (severe submucosal fibrosis to achieve higher en bloc resection rate and lower procedure time, as well as avoid perforation. Traction-assisted endoscopic submucosal dissection using dental floss and a clip has been reported to be useful for shortening the duration of the ESD procedure and reducing the risk of intraoperative perforation, which would be more helpful for managing the lesions with severe submucosal fibrosis, especially for the lesions located at the gastric angle[21].

Some reports have suggested that severe submucosal fibrosis is a risk factor of microperforation during ESD[22]. When fibrosis is present beneath the lesion, the thin submucosal cushion due to lifting failure and hard fibrotic tissue probably lead to surgical error through improper positioning of the knife. Though the patients have microperforations, surgical treatment can be avoided by immediately closing the hole with endoclips. The rapid closure of openings minimizes gastric content leaks. A recent result suggests that the small size of the defect in patients with microperforations after closure and the low level of bacterial contamination from the gastric contents due to gastric acidity prevented contamination of the peritoneal cavity and reduced the need for nasogastric drainage[23].

Our study has several limitations. First, it was a retrospective study in a single academic center. The data from multicenter and prospective studies may be more accurate for research. In addition, this retrospective study didn’t include patients who underwent surgical resection or untreated patients with EGC. Therefore, because of its retrospective nature and selection bias, the data in this study cannot be generalized. Second, because of the small number of patients with severe submucosal fibrosis at the gastric angle, multivariate analysis for determining independent predictors of severe submucosal fibrosis was not performed.

Conclusions
The second most EGCs resected by ESD were detected at the gastric angle despite being a small area. There was a significantly higher rate of severe submucosal fibrosis in the EGC lesions at the gastric angle, which suggests more attention should be paid to patients with EGC at the gastric angle referred for ESD.

**Abbreviations**

EGC: Early gastric cancer; ESD: Endoscopic submucosal dissection

**Declarations**

**Ethics approval and consent to participate**

The research was approved by the ethical standards of the Institutional Ethics Committee of Ningbo City First Hospital (No. 2020-R152).

**Consent for publication**

Not Applicable

**Availability of data and materials**

The datasets generated and/or analyzed during the current study are not publicly available due individual privacy but are available from the corresponding author on reasonable request.

**Competing interests**

The authors declare that they have no competing interests.

**Funding**

This work was funded by Ningbo Municipal Bureau of Science and Technology (2014C51001), Department of Health of Zhejiang Province (2018ZH025). This funding body played roles in the collection data.

**Authors' contributions**

All authors assisted with manuscript preparation and revisions. QY W and XY D planned and conducted the study. QY W, HZ J, SL X and XY D analyzed and interpreted the data. QY W, and DX Y drafted and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

**Acknowledgements**
References

1. Murakami T. Early cancer of the stomach. *World J Surg.* 1979;3:685-92.
2. Reavis KM, Melvin WS. Advanced endoscopic technologies. *Surg Endosc.* 2008;22:1533-46.
3. Rahman R, Asombang AW, Ibdah JA. Characteristics of gastric cancer in Asia. *World J Gastroent erol.* 2014;20:4483-90.
4. Hosokawa O, Miyanaga T, Kaizaki Y, et al. Decreased death from gastric cancer by endoscopic screening: association with a population-based cancer registry. *Scand J Gastroenterol* 2008;43:1112-5.
5. Kim SG, Ji SM, Lee NR, et al. Quality of Life after Endoscopic Submucosal Dissection for Early Gastric Cancer: A Prospective Multicenter Cohort Study. *Gut Liver.* 2017;11:87-92.
6. Huang Q, Li R, Xu GF, Zhou D, Fan XS, Zou XP. Emerging evidence supports grouping by location of early gastric carcinoma for appropriate clinical management in Chinese patients. *J Dig Dis.* 2018;19:730-36.
7. Sano T. Evaluation of the gastric cancer treatment guidelines of the Japanese Gastric Cancer Association. *Gan To Kagaku Ryoho.* 2010;37:582-6.
8. Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma: 2nd English edition. *Gastric Cancer.* 1998;1:10-24.
9. Ono H, Yao K, Fujishiro M, et al. Guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer. *Dig Endosc.* 2016;28:3-15.
10. Khanderia E, Markar SR, Acharya A, Kim Y, Kim YW, Hanna GB. The Influence of Gastric Cancer Screening on the Stage at Diagnosis and Survival: A Meta-Analysis of Comparative Studies in the Far East. *J Clin Gastroenterol.* 2016;50:190-7.
11. Sumiyama K. Past and current trends in endoscopic diagnosis for early stage gastric cancer in Japan. *Gastric Cancer.* 2017;20:20-27.
12. Zhenming Y, Lei S. Diagnostic value of blue laser imaging combined with magnifying endoscopy for precancerous and early gastric cancer lesions. *Turk J Gastroenterol.* 2019;30:549-556.
13. Zhang X, Li M, Chen S, et al. Endoscopic Screening in Asian Countries Is Associated With Reduced Gastric Cancer Mortality: A Meta-analysis and Systematic Review. *Gastroenterology.* 2018;155:347-354.
14. Chen Q, Yu L, Hao CQ, et al. Effectiveness of endoscopic gastric cancer screening in a rural area of Linzhou, China: results from a case-control study. *Cancer Med.* 2016;5:2615-22.
15. Huang Q, Fang C, Shi J, et al. Differences in Clinicopathology of Early Gastric Carcinoma between Proximal and Distal Location in 438 Chinese Patients. *Sci Rep.* 2015;5:13439.
16. Feng F, Sun L, Xu G, et al. Is it reasonable to treat early gastric cancer with mucosal infiltration and well differentiation by Endoscopic Submucosal Resection? *J Gastrointest Surg.* 2015;19:2111-9.
17. Oi M, Oshida K, Sugimura S. The location of gastric ulcer. Gastroenterology. 1959; 36: 45-56.
18. Isozaki H, Okajima K, Yamada S, Nakata E, Takeda Y. Endoscopic evaluation of the depth of invasion of the depressed type early gastric cancer and apparently early advanced cancer in cases of a peptic ulcer within the cancer lesion. Gastroenterol Jpn. 1993; 28: 201-8.
19. Kim JH, Nam HS, Choi CW, et al. Risk factors associated with difficult gastric endoscopic submucosal dissection: predicting difficult ESD. Surg Endosc. 2017; 31: 1617-26.
20. Nagata S, Jin YF, Tomoeda M, et al. Influential factors in procedure time of endoscopic submucosal dissection for gastric cancer with fibrotic change. Dig Endosc. 2011; 23: 296-301.
21. Yoshida M, Takizawa K, Suzuki S et al. Conventional versus traction-assisted endoscopic submucosal dissection for gastric neoplasms: a multicenter, randomized controlled trial (with video). Gastrointest. Endosc. 2018; 87: 1231–40.
22. Yoo JH, Shin SJ, Lee KM, et al. Risk factors for perforations associated with endoscopic submucosal dissection in gastric lesions: emphasis on perforation type. Surg Endosc. 2012; 26: 2456-64.
23. Bittinger M, Messmann H. Is nonsurgical management safe and effective for patients with microperforation caused by EMR? Nat Clin Pract Gastroenterol Hepatol. 2007; 4: 134-5.

Figures
Patients with EGC resected by ESD were reviewed \((n=504)\) from January 2010 to December 2018

**Exclusion criteria**
- Did not meet the criteria \((n=46)\)
- Lesions in a remnant stomach \((n=8)\)
- Received a gastric tube after esophagectomy \((n=6)\)

**Locations of EGCs \((n=444)\)**

- Cardia \((n=26)\)
- Fundus \((n=2)\)
- body \((n=67)\)
- Angle \((n=102)\)
- Antrum \((n=247)\)

**Figure 1**

Study flow chart
Figure 2

Patients Distribution of EGC