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RETROSPECTIVE STUDY

# Impact of tumor location on clinical outcomes of gastric endoscopic submucosal dissection

Ji Young Yoon, Choong Nam Shim, Sook Hee Chung, Wan Park, Hyunsoo Chung, Hyuk Lee, Sung Kwan Shin, Sang Kil Lee, Yong Chan Lee, Jun Chul Park

Ji Young Yoon, Choong Nam Shim, Sook Hee Chung, Wan Park, Hyunsoo Chung, Hyuk Lee, Sung Kwan Shin, Sang Kil Lee, Yong Chan Lee, Jun Chul Park, Department of Internal Medicine, Institute of Gastroenterology, Yonsei University College of Medicine, Seoul 120-752, South Korea

Author contributions: Yoon JY and Shim CN contributed equally to this work; all the authors participated in this study.
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Correspondence to: Jun Chul Park, MD, Assistant Professor, Department of Internal Medicine, Institute of Gastroenterology, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-752, South Korea. junchul75@yuhs.ac
Telephone: +82-2-22282272 Fax: +82-2-3936884
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## Abstract

**AIM:** To determine whether there is a correlation between the location of the lesion and endoscopic submucosal dissection (ESD) outcome.

**METHODS:** From January 2008 to December 2010, ESD of 1443 gastric tumors was performed. *En bloc* resection rate, complete resection rate, procedure time and complication rate were analyzed according to the tumor location.

**RESULTS:** The rates of *en bloc* resection and complete resection were 91% (1318/1443) and 89% (1287/1443), respectively. The post-ESD bleeding rate was 4.3%, and perforation rate was 2.7%. Tumors located in the upper third of the stomach were associated with a longer procedure time and significantly higher rates of incomplete resection, piecemeal resection, and perforation than tumors below the upper third of the stomach. Posterior wall lesions had significantly longer procedure times and higher rates of incomplete resection and piecemeal resection than lesions in other locations. In multivariate analysis, posterior wall lesions and upper third lesions were significantly associated with incomplete resection and perforation, respectively. In post-ESD bleeding analysis, location was not a significant related factor.

**CONCLUSION:** More advanced endoscopic techniques are required during ESD for lesions located in the upper third or posterior wall of the stomach to decrease complications and improve therapeutic outcomes.



**Key words:** Endoscopic submucosal dissection; Gastric neoplasm; Location; Complication; Outcomes

**Core tip:** Location of the tumor is one of the most important clinical factors for complete resection and complications of endoscopic submucosal dissection (ESD) for early gastric cancer. Nonetheless, few studies have evaluated clinicopathologic outcomes of ESD according to the subdivision of tumor location. Based on our data, posterior wall lesions and upper third lesions were significantly associated with incomplete resection and perforation, respectively. Therefore, endoscopists should recognize the need for more advanced endoscopic techniques when performing ESD for lesions located in the upper third or posterior wall of the stomach to decrease the rate of serious complications and improve clinical outcomes.

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## INTRODUCTION

Advances in diagnostic technology and the increasing prevalence of screening programs have increased the rate of early gastric cancer (EGC) detection. EGCs that are confined to the mucosa and lack lymph node metastasis can be cured by endoscopic resection, such as endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD)[1-4]. Compared with EMR, ESD may achieve complete resection not only of larger lesions but also of ulcerative lesions. In addition, ESD allows for a precise histological assessment of resected specimens and may reduce the risk of residual disease and local recurrence[5].

The factors affecting successful ESD include several characteristics of lesions such as location, presence of ulceration and histology[6,7]. In a recent multicenter study, scarred lesions, undifferentiated lesions and lesions located in the upper third required more advanced ESD techniques, because the complete resection rate is lower with these lesions than with other lesions[7]. In addition, the location of the tumor is one of the most important clinical factors for whether or not complete resection is possible or whether or not complication occurs. However, few studies have evaluated clinicopathologic outcomes of ESD according to the subdivision of tumor location in the longitudinal portions of the stomach and cross-sectional circumference divided into four equal parts. Therefore, we conducted this study to evaluate the level of difficulty of the procedure and clinicopathologic outcomes according to the tumor location.

## MATERIALS AND METHODS

### Patients

We analyzed 1319 patients with 1443 lesions who underwent ESD for gastric tumors at Yonsei University Health Care Center between January 2008 and December 2010.

Endoscopy with standard upper gastrointestinal endoscopes (GIF Q260 and H260, Olympus, Japan), chromoendoscopy with indigo carmine, and biopsies of the lesions with standard biopsy forceps (FB-21K-1; Olympus, Japan) were initially performed to determine the feasibility of ESD. Endoscopic ultrasonography (EUS) with radial scanning echoendoscopes (EG-3679URK, Pentax, Japan and GF-UE260, Olympus, Japan) was performed in case of carcinoma to evaluate the depth of invasion. Patients with lesions confirmed to be gastric cancer underwent abdominal computed tomography (CT) scans to determine if lymph node or distant metastasis was present. For this study, the endoscopic findings of EGC were classified as elevated (types Ⅰ or Ⅱa), flat (type Ⅱb), depressed (types Ⅱc, Ⅱc+Ⅲ, or Ⅱa+Ⅱc) or mixed (types Ⅱa+Ⅱb, Ⅱb+Ⅱc, Ⅱa + Ⅱc, Ⅲ+Ⅱa or Ⅲ+Ⅱb).

Gastric tumor lesions were classified according to their location in the upper, middle, and lower thirds of the stomach, and also to location in the cross-sectional circumference divided into four equal parts (anterior wall, posterior wall, lesser curvature or greater curvature).

Eligibility criteria for ESD were as follows: (1) differentiated adenocarcinoma (well- to moderately-differentiated tubular adenocarcinoma) or dysplasia confirmed histologically by forceps biopsy; (2) depth of invasion limited to the mucosa or submucosa (≤ 500 μm penetration into the submucosa) as determined by EUS; (3) lesions without ulceration, regardless of size, or 30 mm or less in size with ulceration; or (4) undifferentiated adenocarcinoma or intramucosal cancer without ulcer findings ≤ 20 mm in size[8].

### Endoscopic resection

All procedures were performed by an attending gastroenterologist, and five attending physicians were involved in the procedures. All ESDs were performed under conscious sedation using intravenous propofol or midazolam. Vital signs were continuously monitored during the procedure. After identifying the target lesion, marking dots were made circumferentially about 5 mm lateral to the margin of the lesion using a needle knife (KD-10Q, Olympus, Japan) or argon plasma coagulation (ERBE Elektromedizin, Germany). Epinephrine (1:10000 dilution) was then injected submucosally around the lesion, and an initial short incision was made in the mucosa with a needle knife to allow submucosal insertion of the tip of an insulation-tipped (IT) knife (KD-611L, Olympus, Japan). Circumferential mucosal cutting was performed outside the marking dots, and an additional submucosal injection was carried out. Finally, direct dissection of the submucosal layer was performed, and endoscopic hemostasis with specialized hemostatic forceps (FD-410LR, Olympus, Japan) was performed when needed.

### Histologic evaluation of resection efficacy

All resected specimens were systematically sectioned at 2 mm intervals centered on the part of the lesion closet to the margin and the site of the deepest invasion. Histological assessment was based on the Vienna classification[9].

Final pathologic diagnoses were classified as low grade dysplasia (LGD), high grade dysplasia (HGD), differentiated EGC, and undifferentiated EGC.

### Outcome measures

Patient data, including patient age, gender, previous medication history, the size, number and location of lesions, procedure start and end times, endoscopic findings, pathology, and complications, were collected.

Complete resection of *en bloc* resected tumors was defined as the lateral and vertical margins being free of tumor cells on histologic examination. Complete resection of tumors resected in a piecemeal fashion was defined as complete removal of the entire lesion, including sufficient tumor-free margins after perfect reconstruction of all pieces.

Procedure time was defined as the time from marking to complete removal, including the time required

**Table 1 Baseline characteristics of gastric tumors *n* (%)**

| Characteristic | Value |
|---|---|
| Gender (female:male) | 1:2.18 (454:989) |
| Age, yr, mean ± SD | 63.0 ± 9.4 |
| Tumor size, mm | |
| < 20 | 1034 (71.7) |
| ⩾ 20 | 409 (28.3) |
| Macroscopic appearance | |
| Elevated | 310 (21.5) |
| Flat | 128 (8.9) |
| Depressed | 90 (6.2) |
| Mixed | 915 (63.4) |
| Ulcer | 71 (4.9) |
| Invasion depth | |
| Mucosa | 612 (42.4) |
| Submucosa | 106 (7.3) |
| Location Ⅰ | |
| Lower third | 1233 (85.4) |
| Middle third | 112 (7.8) |
| Upper third | 98 (6.8) |
| Location Ⅱ | |
| Anterior wall | 294 (20.4) |
| Lesser curvature | 481 (33.3) |
| Posterior wall | 405 (28.1) |
| Greater curvature | 263 (18.2) |
| Histology | |
| Low grade dysplasia | 534 (37.0) |
| High grade dysplasia | 176 (12.2) |
| Differentiated EGC | 655 (45.4) |
| Undifferentiated EGC | 78 (5.4) |
| Procedure time, min | 61.8 (± 47.0) |
| Curability | |
| Complete resection | 1287 (89.0) |
| Incomplete resection | 156 (11.0) |
| Resectability | |
| *En bloc* | 1318 (91.3) |
| Piecemeal | 125 (8.7) |
| Perforation | 39 (2.7) |
| Post-ESD bleeding | 63 (4.3) |

EGC: Early gastric cancer; ESD: Endoscopic submucosal dissection.

for hemostasis. Complication data included whether a complication occurred and details regarding bleeding, perforation and other factors related to the type of complication.

### Clinicopathologic evaluation

To identify factors affecting the success of ESD, we analyzed lesion characteristics, procedure, and the procedure result. Analyzed lesion characteristics included the presence of ulceration, macroscopic morphology, size and location of the tumor.

Procedure results were analyzed for curability. Resection was deemed complete when removal was achieved with tumor-free lateral and vertical margins and there was no lymphovascular involvement or lymph node metastasis. Incomplete resection was defined as any resection that did not meet the curative criteria described above.

### Follow-up

Endoscopic surveillance by esophagogastroduodenoscopy (EGD) was performed 3, 6, 12, and 24 mo after ESD for EGC to exclude local recurrence, as well as synchronous, and metachronous lesions. After 24 mo, EGD was carried out annually. Moreover, abdominal CT scans were performed every 6 mo for the first year and annually thereafter, to detect lymph node or distant metastasis. In cases with adenomas, endoscopic surveillance by EGD was scheduled for 3, 12, and 24 mo after ESD.

### Statistical analysis

The data were analyzed using Pearson's $\chi^2$ test, unpaired *t*-test, Fisher's exact test, and the Mann-Whitney *U* test. *P* values < 0.05 were considered significant. To identify related risk factors for complications and complete resection, predictors with *P* values < 0.05 in the univariate analysis were included in a backward, stepwise multiple logistic regression model. All data analyses were conducted using a statistical software package (SPSS version 18.0, Chicago, IL, United States).

## RESULTS

### Gastric tumor characteristics

During the study period, ESD was performed in 1319 patients with 1443 gastric tumors. Baseline clinicopathologic characteristics of the gastric tumors and the clinical outcomes of ESD are shown in Table 1. Mean age was 63.0 ± 9.4 years. The lesions consisted of 733 (50.8%) EGCs and 710 (49.2%) dysplastic lesions. Submucosal invasion occurred in 7.3% of cases. Mixed-type endoscopic morphology was the most common (63.4%). With respect to size and location, tumors less than 20 mm in size (71.7%), those located in the lower third (85.4%) and those located in the lesser curvature (33.3%) were most common. The mean tumor size was 15.72 ± 8.81 mm. The mean procedure time was 61.8 ± 47.0 min. The complete resection rate was 89% (1287/1443), and the *en bloc* resection rate was 91.3% (Table 1). The post-ESD bleeding rate was 4.3%, and the perforation rate was 2.7%. Most cases of bleeding (60/63) were treated by endoscopic hemostasis such as hemoclipping, argon plasma coagulation or epinephrine injection. Two cases were treated by angiographic embolization. Only one case required surgery for bleeding control.

Around half of all perforation cases (20/39) were minute or micro-perforations, while the remaining ones were overt perforations. Only two such cases required surgery. All other cases were treated by conservative care. There was no mortality in the present study.

### Endoscopic outcomes according to the location

We compared the clinical outcomes of ESD in relation to detailed tumor location. Upon division into upper third and other lesions, the upper third lesion group had significantly higher percentages of incomplete resections (19.4% *vs* 10.2%, $P = 0.005$) and piecemeal resections (15.3% *vs* 8.2%, $P = 0.015$) compared with other tumor locations. Additionally, upper third lesions required a longer procedure time (90.51 min *vs* 59.71 min, $P < 0.001$) and were associated with a higher perforation rate (9.2%

**Table 2 Comparison of the upper third and non-upper third groups *n* (%)**

| | Upper third | Non-upper third | *P* value |
|---|---|---|---|
| Tumor size, mm | | | |
| < 20 | 70 (71.4) | 964 (71.7) | 0.520 |
| ⩾ 20 | 28 (28.6) | 381 (28.3) | |
| Ulcer | 2 (2.0) | 69 (5.1) | 0.172 |
| Pathology | | | |
| Dysplasia | 45 (45.9) | 665 (49.4) | 0.501 |
| Carcinoma | 53 (54.1) | 680 (50.6) | |
| Curability | | | |
| Incomplete resection | 19 (19.4) | 137 (10.2) | 0.005 |
| Complete resection | 79 (80.6) | 1208 (89.8) | |
| Resectability | | | |
| *En bloc* | 83 (84.7) | 1235 (91.8) | 0.015 |
| Piecemeal | 15 (15.3) | 110 (8.2) | |
| Procedure time, min, mean ± SD | 90.51 ± 58.06 | 59.71 ± 45.46 | < 0.001 |
| Perforation | 9 (9.2) | 30 (2.2) | < 0.001 |
| Post-ESD bleeding | 4 (4.1) | 57 (4.2) | 0.600 |

ESD: Endoscopic submucosal dissection.

**Table 3 Comparison of the posterior wall and non-posterior wall groups *n* (%)**

| | Posterior wall | Non-posterior wall | *P* value |
|---|---|---|---|
| Tumor size, mm | | | |
| < 20 | 278 (68.6) | 756 (72.8) | 0.065 |
| ⩾ 20 | 127 (31.4) | 282 (27.2) | |
| Ulcer | 21 (5.2) | 50 (4.8) | 0.771 |
| Pathology | | | |
| Dysplasia | 216 (53.3) | 494 (47.6) | 0.053 |
| Carcinoma | 189 (46.7) | 544 (52.4) | |
| Procedure time, min, mean ± SD | 69.41 ± 52.55 | 58.84 ± 44.39 | < 0.001 |
| Curability | | | |
| Incomplete resection | 60 (14.8) | 96 (9.2) | 0.002 |
| Complete resection | 345 (85.2) | 942 (90.8) | |
| Resectability | | | |
| *En bloc* | 358 (88.4) | 960 (92.5) | 0.013 |
| Piecemeal | 47 (11.6) | 78 (7.5) | |
| Perforation | 14 (3.5) | 25 (2.4) | 0.27 |
| Post-ESD bleeding | 17 (4.2) | 44 (4.2) | 0.552 |

ESD: Endoscopic submucosal dissection.

*vs* 2.2%) (Table 2). There was no significant difference in the frequency of post-ESD bleeding.

After dividing location according to posterior wall and other lesions, the posterior wall lesion group had a significantly longer procedure time (69.41 min *vs* 58.84 min, $P < 0.001$) and higher rates of incomplete resections (14.8% *vs* 9.2%, $P = 0.002$) and piecemeal resections (11.6% *vs* 7.5%, $P = 0.013$) than lesions in other locations (Table 3). There was no significant difference in the frequency of post-ESD bleeding or perforation between the two groups.

### *Factors related to incomplete resection and complications*

We analyzed the factors associated with complete resection complications of ESD such as perforation or bleeding. In univariate analyses, lesion size larger than 20 mm, upper third location, posterior wall location, carcinoma and procedure time longer than 60 min were significantly related to incomplete resection. In multivariate analysis, lesion size larger than 20 mm, posterior wall location, carcinoma and procedure time longer than 60 min were significantly related to incomplete resection (Table 4).

**Table 4 Multivariate analysis for incomplete resection**

| | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | OR (95%CI) | *P* value | OR (95%CI) | *P* value |
| Tumor size, mm | | | | |
| < 20 | 1 (reference) | | | |
| ⩾ 20 | 2.144 (1.526-3.011) | < 0.001 | 1.846 (1.283-2.654) | 0.001 |
| Ulcer | | | | |
| - | 1 (reference) | | | |
| + | 1.210 (0.589-2.485) | 0.604 | | |
| SM invasion | | | | |
| - | 1 (reference) | | | |
| + | 1.828 (0.811-4.119) | 0.146 | | |
| Location | | | | |
| Non-upper third | 1 (reference) | | | |
| Upper third | 2.12 1(1.247-3.607) | 0.006 | 1.576 (0.882-2.814) | 0.124 |
| Location | | | | |
| Non-posterior wall | 1 (reference) | | | |
| Posterior wall | 1.707 (1.208-2.410) | 0.002 | 1.687 (1.163-2.449) | 0.006 |
| Pathology | | | | |
| Dysplasia | 1 (reference) | | | |
| Carcinoma | 4.921 (3.240-7.475) | < 0.001 | 4.675 (3.049-7.166) | < 0.001 |
| Procedure time, min | | | | |
| < 60 | 1 (reference) | | | |
| ⩾ 60 | 2.494 (1.772-3.509) | < 0.001 | 1.648 (1.142-2.379) | < 0.001 |

SM: Submucosa.

In addition, univariate predictors of perforation were lesion size larger than 20 mm, upper third location, procedure time longer than 60 min and piecemeal resection. In multivariate analysis, upper third location, procedure time longer than 60 min and piecemeal resection were statistically significantly related to perforation (Table 5).

Moreover, univariate predictors of post-ESD bleeding were lesion size larger than 20 mm, procedure time longer than 60 min and piecemeal resection. In multivariate analysis, procedure time longer than 60 min and piecemeal resection were statistically significantly related to post-ESD bleeding (Table 6).

## DISCUSSION

ESD has been widely accepted as an effective and safe treatment for gastric tumors[5,10]. To summarize previous studies, it is believed that the location of a lesion affects both the completeness of resection and whether complications are likely to occur[6,7,11-14]. These previous studies analyzed tumor location which is anatomically divided

**Table 5 Multivariate analysis for perforation**

| | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | OR (95%CI) | *P* value | OR (95%CI) | *P* value |
| Tumor size, mm | | | | |
| < 20 | 1 (reference) | | | |
| ⩾ 20 | 2.470 (1.304-4.678) | 0.006 | 1.574 (0.807-3.071) | 0.183 |
| Ulcer | | | | |
| - | 1 (reference) | | | |
| + | 1.637 (0.492-5.451) | 0.422 | | |
| SM invasion | | | | |
| - | 1 (reference) | | | |
| + | 1.041 (0.238-4.550) | 0.957 | | |
| Location | | | | |
| Non-upper third | 1 (reference) | | | |
| Upper third | 4.433 (2.042-9.623) | < 0.001 | 2.783 (1.138-6.803) | 0.025 |
| Location | | | | |
| Non-posterior wall | 1 (reference) | | | |
| Posterior wall | 1.451 (0.746-2.820) | 0.272 | | |
| Pathology | | | | |
| Dysplasia | 1 (reference) | | | |
| Carcinoma | 1.755 (0.905-3.405) | 0.096 | | |
| Procedure time, min | | | | |
| < 60 | 1 (reference) | | | |
| ⩾ 60 | 8.143 (3.390-19.561) | < 0.001 | 4.985 (1.978-12.565) | < 0.001 |
| Curability | | | | |
| Complete resection | 1 (reference) | | | |
| Incomplete resection | 1.842 (0.799-4.248) | 0.152 | | |
| Resectability | | | | |
| *En bloc* | 1 (reference) | | | |
| Piecemeal | 7.352 (3.748-14.423) | < 0.001 | 4.029 (1.987-8.170) | < 0.001 |

SM: Submucosa.

**Table 6 Multivariate analysis for post-endoscopic submucosal dissection bleeding**

| | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | OR (95%CI) | *P* value | OR (95%CI) | *P* value |
| Tumor size, mm | | | | |
| < 20 | 1 (reference) | | | |
| ⩾ 20 | 1.938 (1.151-3.362) | 0.013 | 1.523 (0.886-2.619) | 0.128 |
| Ulcer | | | | |
| - | 1 (reference) | | | |
| + | 1.377 (0.485-3.909) | 0.547 | | |
| SM invasion | | | | |
| - | 1 (reference) | | | |
| + | 0.807 (0.276-2.358) | 0.695 | | |
| Location | | | | |
| Non-upper third | 1 (reference) | | | |
| Upper third | 1.621 (0.957-2.745) | 0.072 | | |
| Location | | | | |
| Non-posterior wall | 1 (reference) | | | |
| Posterior wall | 0.990 (0.559-1.754) | 0.972 | | |
| Pathology | | | | |
| Dysplasia | 1 (reference) | | | |
| Carcinoma | 1.633 (0.963-2.770) | 0.069 | | |
| Procedure time, min | | | | |
| < 60 | 1 (reference) | | | |
| ⩾ 60 | 2.804 (1.636-4.807) | < 0.001 | 2.120 (1.185-3.793) | 0.011 |
| Curability | | | | |
| Complete resection | 1 (reference) | | | |
| Incomplete resection | 1.259 (0.587-2.698) | 0.555 | | |
| Resectability | | | | |
| *En bloc* | 1 (reference) | | | |
| Piecemeal | 3.771 (2.040-6.971) | < 0.001 | 2.749 (1.433-5.276) | 0.002 |

SM: Submucosa.

into three portions (upper, middle, and lower thirds) as a factor related to the clinical outcomes of ESD. Many studies reported that upper third location was associated with incomplete resection, longer procedure time and a higher rate of perforation[7,11,12]. However, even among tumors located in the same thirds of the stomach, the difficulty of the procedure and the clinical outcomes may be different according to the cross-sectional circumference, which is divided into four equal parts.

In our study, after dividing the upper third lesions from other lesions, it was found that the upper third lesion group had significantly higher percentages of incomplete resections (19.4% *vs* 10.2%) and piecemeal resections (15.3% *vs* 8.2%), longer procedure time (91 min *vs* 60 min) and a higher perforation rate (9.2% *vs* 2.2%). Furthermore, we analyzed clinical outcomes between posterior wall lesions and non-posterior lesions. The posterior wall lesion group had significantly longer procedure times and more frequent piecemeal and incomplete resections, which are likely explained in part by the difference in technical difficulty and poor visual field.

In previous studies, procedure time during ESD became longer as tumor locations became higher[7,15]. In addition, longer procedure time was needed for tumors located in the posterior wall[15]. These findings were consistent with our study results. As longer procedure times have been shown to be associated with increased risks of complications[16,17], we attributed the relationship between tumor location and complications to the longer procedure time of ESD for gastric tumors in the upper-third or the posterior wall of the stomach. As mentioned above, prolonged procedure time in cases involving the upper-third or the posterior wall location was caused primarily by technical difficulties and a poor visual field. During ESD for gastric tumors in the upper-third of the stomach, endoscopists cannot let the knife encroach on the submucosal layer beneath the tumor, and cannot control the direction and depth well adhering to the dissection plan[7]. Along these lines, the worse outcomes after ESD for those lesions in this study were also consistent with earlier studies that demonstrated lower rates of *en bloc* and curative resections in lesions of the upper portion of the stomach[6,7,12].

It is very important that we determine the factors related to complete resection, because clinically complete resection is the ultimate goal of ESD, and it is closely related to tumor recurrence rate after ESD[18,19]. We analyzed incomplete resection rates according to the tumor location, and independent factors related to incomplete resection. In multivariate analysis, lesions larger than 20 mm, posterior wall location, carcinoma and procedure time longer than 60 min were statistically significantly associated with incomplete resection. Interestingly, the significant factor of location for incomplete resection was being in the posterior wall in our study. The posterior wall location makes it technically difficult to use a knife during ESD in comparison with the anterior wall or lesser curvature locations. Furthermore, in this study, almost all cases of endoscopic resection were performed using a single channel endoscope and because this endoscope's accessory channel opening is oriented at the 7 o'clock position, which is the opposite direction needed for posterior wall dissections, and makes ESD of posterior wall lesions difficult.

During the ESD procedure, serious complications such as bleeding or perforation may occur. Risk factors for perforation were identified in a recent study by Yoo *et al*[20], who proposed that risk of perforation is associated with age, depth of invasion and length of the procedure. In our study, the perforation rate was significantly associated with upper third location. This may be due to the fact that lesions in the lower third are easily approached and manipulated by endoscopy, and thus it is technically easier to perform ESD and there is a lower chance of applying sufficient tension on the gastric wall to cause perforation. Another possible reason is that the lower or the mid-portion of the gastric wall is thicker than the upper portion of the stomach.

Previous reports showed that bleeding occurred more frequently in the corpus than in the antrum[11,21]. Okada *et al*[22] demonstrated that having a tumor located in the mid-third of the stomach was an independent risk factor for post-ESD bleeding. However, the relationship between tumor location and post-ESD bleeding remains controversial to date. In our post-ESD bleeding analysis, location was not a significant factor for post-ESD bleeding. Besides tumor location, various factors such as the patient's underlying medical and drug history, the endoscopist's experience and preventive coagulation of visible vessels in the resection area after ESD may affect post-ESD bleeding. A recent study demonstrated that post-ESD bleeding depends on how meticulously coagulation of visible vessels is performed after dissection[23]. Regrettably, we could not analyze the effect of underlying disease or anti-platelet agents on post-ESD bleeding because we had relatively few patients with chronic disease such as chronic renal failure or cirrhosis, and all the patients in our study who underwent ESD discontinued anti-platelet agents prior to the procedure.

Limitations of this study include the fact that it was a retrospective single-center study with a limited follow-up duration. Therefore, there may be a bias according to the endoscopist who performed the ESD. In addition, we did not include long-term follow-up data concerning recurrence, disease-free survival, and overall survival, which are important for evaluating the effect of risk factors on outcomes. Nevertheless, this study focused on outcomes after ESD for gastric tumors with reference to therapeutic efficacy and complications according to lesion location. Although we did not address long-term outcomes, this study revealed that the two main components for the feasibility of ESD, acceptable complete resection and complication rates, change according to the location of gastric tumors. In addition, the clinical implications of tumor location were based on large-volume data. Accordingly, we suggest that attention to gastric tumor location, particularly in the upper third or posterior wall, during ESD is needed to avoid incomplete resection and complications. We should also explain the possibility of further surgical treatment after ESD to patients with such lesions. Nonetheless, further investigations with long-term follow-up data concerning the clinical significance of tumor location are needed to support our recommendations.

In conclusion, ESD for gastric tumor is an effective and safe therapy. However, endoscopists should recognize the need for more advanced endoscopic techniques when performing ESD for lesions located in the upper third or posterior wall of the stomach in order to decrease the rate of serious complications and improve clinical outcomes.

## COMMENTS

### Background

Advances in diagnostic technology and the increasing prevalence of screening programs have increased the rate of early gastric cancer (EGC) detection. EGCs that are confined to the mucosa and lack lymph node metastasis can be cured by endoscopic resection, such as endoscopic mucosal resection and endoscopic submucosal dissection (ESD).

### Research frontiers

Previous studies analyzed tumor location which is anatomically divided into three portions (upper, mid, and lower thirds) as a factor related to the clinical outcomes of ESD.

### Innovations and breakthroughs

In this study, the perforation rate was significantly associated with upper third location. This may be due to the fact that lesions at lower third are easily approached and manipulated by endoscopy, and thus it is technically easier to perform ESD and there is a lower chance of applying sufficient tension on the gastric wall to cause perforation.

### Applications

ESD for gastric tumor is an effective and safe therapy. However, endoscopists should recognize the need for more advanced endoscopic techniques when performing ESD for lesions located in the upper third or posterior wall of the stomach in order to decrease the rate of serious complications and improve clinical outcomes.

### Peer review

This is an interesting study regarding on the technical aspect of gastric ESD, focused on the tumor location. The number of the subjects is large and the analysis is simple with clear results.

## REFERENCES

1 **Cho WY**, Cho JY, Chung IK, Kim JI, Jang JS, Kim JH. Endoscopic submucosal dissection for early gastric cancer:

quo vadis? *World J Gastroenterol* 2011; **17**: 2623-2625 [PMID: 21677830 DOI: 10.3748/wjg.v17.i21.2623]
2 **Chun HJ**, Keum B, Kim JH, Seol SY. Current status of endoscopic submucosal dissection for the management of early gastric cancer: a Korean perspective. *World J Gastroenterol* 2011; **17**: 2592-2596 [PMID: 21677825 DOI: 10.3748/wjg.v17.i21.2592]
3 **Lee JH**, Hong SJ, Jang JY, Kim SE, Seol SY. Outcome after endoscopic submucosal dissection for early gastric cancer in Korea. *World J Gastroenterol* 2011; **17**: 3591-3595 [PMID: 21987605 DOI: 10.3748/wjg.v17.i31.3591]
4 **Lee JH**, Kim JJ. Endoscopic mucosal resection of early gastric cancer: Experiences in Korea. *World J Gastroenterol* 2007; **13**: 3657-3661 [PMID: 17659722]
5 **Oka S**, Tanaka S, Kaneko I, Mouri R, Hirata M, Kawamura T, Yoshihara M, Chayama K. Advantage of endoscopic submucosal dissection compared with EMR for early gastric cancer. *Gastrointest Endosc* 2006; **64**: 877-883 [PMID: 17140890 DOI: 10.1016/j.gie.2006.03.932]
6 **Imagawa A**, Okada H, Kawahara Y, Takenaka R, Kato J, Kawamoto H, Fujiki S, Takata R, Yoshino T, Shiratori Y. Endoscopic submucosal dissection for early gastric cancer: results and degrees of technical difficulty as well as success. *Endoscopy* 2006; **38**: 987-990 [PMID: 17058162 DOI: 10.1055/s-2006-944716]
7 **Chung IK**, Lee JH, Lee SH, Kim SJ, Cho JY, Cho WY, Hwangbo Y, Keum BR, Park JJ, Chun HJ, Kim HJ, Kim JJ, Ji SR, Seol SY. Therapeutic outcomes in 1000 cases of endoscopic submucosal dissection for early gastric neoplasms: Korean ESD Study Group multicenter study. *Gastrointest Endosc* 2009; **69**: 1228-1235 [PMID: 19249769 DOI: 10.1016/j.gie.2008.09.027]
8 **Gotoda T**, Yanagisawa A, Sasako M, Ono H, Nakanishi Y, Shimoda T, Kato Y. Incidence of lymph node metastasis from early gastric cancer: estimation with a large number of cases at two large centers. *Gastric Cancer* 2000; **3**: 219-225 [PMID: 11984739]
9 **Schlemper RJ**, Riddell RH, Kato Y, Borchard F, Cooper HS, Dawsey SM, Dixon MF, Fenoglio-Preiser CM, Fléjou JF, Geboes K, Hattori T, Hirota T, Itabashi M, Iwafuchi M, Iwashita A, Kim YI, Kirchner T, Klimpfinger M, Koike M, Lauwers GY, Lewin KJ, Oberhuber G, Offner F, Price AB, Rubio CA, Shimizu M, Shimoda T, Sipponen P, Solcia E, Stolte M, Watanabe H, Yamabe H. The Vienna classification of gastrointestinal epithelial neoplasia. *Gut* 2000; **47**: 251-255 [PMID: 10896917]
10 **Goto O**, Fujishiro M, Kodashima S, Ono S, Omata M. Outcomes of endoscopic submucosal dissection for early gastric cancer with special reference to validation for curability criteria. *Endoscopy* 2009; **41**: 118-122 [PMID: 19214889 DOI: 10.1055/s-0028-1119452]
11 **Jeon SW**, Jung MK, Cho CM, Tak WY, Kweon YO, Kim SK, Choi YH. Predictors of immediate bleeding during endoscopic submucosal dissection in gastric lesions. *Surg Endosc* 2009; **23**: 1974-1979 [PMID: 18553202 DOI: 10.1007/s00464-008-9988-7]
12 **Ohnita K**, Isomoto H, Yamaguchi N, Fukuda E, Nakamura T, Nishiyama H, Mizuta Y, Akiyama M, Nakao K, Kohno S, Shikuwa S. Factors related to the curability of early gastric cancer with endoscopic submucosal dissection. *Surg Endosc* 2009; **23**: 2713-2719 [PMID: 19357917 DOI: 10.1007/s00464-009-0473-8]
13 **Goto A**, Nishikawa J, Okamoto T, Hamabe K, Nishimura J, Nakamura M, Kiyotoki S, Saito M, Miura O, Sakaida I. Outcomes of endoscopic submucosal dissection for early gastric cancer and factors associated with incomplete resection. *Hepatogastroenterology* 2013; **60**: 46-53 [PMID: 22975584 DOI: 10.5754/hge12533]
14 **Mannen K**, Tsunada S, Hara M, Yamaguchi K, Sakata Y, Fujise T, Noda T, Shimoda R, Sakata H, Ogata S, Iwakiri R, Fujimoto K. Risk factors for complications of endoscopic submucosal dissection in gastric tumors: analysis of 478 lesions. *J Gastroenterol* 2010; **45**: 30-36 [PMID: 19760133 DOI: 10.1007/s00535-009-0137-4]
15 **Ahn JY**, Choi KD, Choi JY, Kim MY, Lee JH, Choi KS, Kim do H, Song HJ, Lee GH, Jung HY, Kim JH. Procedure time of endoscopic submucosal dissection according to the size and location of early gastric cancers: analysis of 916 dissections performed by 4 experts. *Gastrointest Endosc* 2011; **73**: 911-916 [PMID: 21296348 DOI: 10.1016/j.gie.2010.11.046]
16 **Lee IL**, Wu CS, Tung SY, Lin PY, Shen CH, Wei KL, Chang TS. Endoscopic submucosal dissection for early gastric cancers: experience from a new endoscopic center in Taiwan. *J Clin Gastroenterol* 2008; **42**: 42-47 [PMID: 18097288 DOI: 10.1097/01.mcg.0000225696.54498.ff]
17 **Yamamoto S**, Uedo N, Ishihara R, Kajimoto N, Ogiyama H, Fukushima Y, Yamamoto S, Takeuchi Y, Higashino K, Iishi H, Tatsuta M. Endoscopic submucosal dissection for early gastric cancer performed by supervised residents: assessment of feasibility and learning curve. *Endoscopy* 2009; **41**: 923-928 [PMID: 19802773 DOI: 10.1055/s-0029-1215129]
18 **Isomoto H**, Shikuwa S, Yamaguchi N, Fukuda E, Ikeda K, Nishiyama H, Ohnita K, Mizuta Y, Shiozawa J, Kohno S. Endoscopic submucosal dissection for early gastric cancer: a large-scale feasibility study. *Gut* 2009; **58**: 331-336 [PMID: 19001058 DOI: 10.1136/gut.2008.165381]
19 **Jang JS**, Choi SR, Qureshi W, Kim MC, Kim SJ, Jeung JS, Han SY, Noh MH, Lee JH, Lee SW, Baek YH, Kim SH, Choi PJ. Long-term outcomes of endoscopic submucosal dissection in gastric neoplastic lesions at a single institution in South Korea. *Scand J Gastroenterol* 2009; **44**: 1315-1322 [PMID: 19891582 DOI: 10.3109/00365520903254304]
20 **Yoo JH**, Shin SJ, Lee KM, Choi JM, Wi JO, Kim DH, Lim SG, Hwang JC, Cheong JY, Yoo BM, Lee KJ, Kim JH, Cho SW. Risk factors for perforations associated with endoscopic submucosal dissection in gastric lesions: emphasis on perforation type. *Surg Endosc* 2012; **26**: 2456-2464 [PMID: 22398962 DOI: 10.1007/s00464-012-2211-x]
21 **Shiba M**, Higuchi K, Kadouchi K, Montani A, Yamamori K, Okazaki H, Taguchi M, Wada T, Itani A, Watanabe T, Tominaga K, Fujiwara Y, Hayashi T, Tsumura K, Arakawa T. Risk factors for bleeding after endoscopic mucosal resection. *World J Gastroenterol* 2005; **11**: 7335-7339 [PMID: 16437638]
22 **Okada K**, Yamamoto Y, Kasuga A, Omae M, Kubota M, Hirasawa T, Ishiyama A, Chino A, Tsuchida T, Fujisaki J, Nakajima A, Hoshino E, Igarashi M. Risk factors for delayed bleeding after endoscopic submucosal dissection for gastric neoplasm. *Surg Endosc* 2011; **25**: 98-107 [PMID: 20549245 DOI: 10.1007/s00464-010-1137-4]
23 **Takizawa K**, Oda I, Gotoda T, Yokoi C, Matsuda T, Saito Y, Saito D, Ono H. Routine coagulation of visible vessels may prevent delayed bleeding after endoscopic submucosal dissection--an analysis of risk factors. *Endoscopy* 2008; **40**: 179-183 [PMID: 18322872 DOI: 10.1055/s-2007-995530]

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