Surgical Endoscopy (2019) 33:4008–4015
https://doi.org/10.1007/s00464-019-06690-5

Exploring the possibility of endoscopic submucosal dissection for clinical submucosal invasive early gastric cancers

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Received: 7 November 2018 / Accepted: 25 January 2019 / Published online: 6 February 2019
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Abstract

Background The current standard treatment modality for clinical submucosal invasive (cT1b) early gastric cancer (EGC) is surgery. However, there are discrepancies in T staging between pre- and post-operative findings, and in cases of overestimation, patients may lose the opportunity to preserve the stomach. The aim of this study was to analyze surgical outcomes of cT1b EGC and determine the pre-treatment factors favoring ESD.

Methods Patients who underwent gastrectomy for cT1b EGC with a tumor size of 30 mm or less in diameter and differentiated-type histology were retrospectively reviewed from January 2010 to December 2014. According to the final surgical pathologic results, two groups were classified: patients whose pathologic results qualified for current ESD indication (ESD-qualified group, $n = 203$) and patients whose pathologic results made them ineligible for ESD (ESD-disqualified group, $n = 261$). The preoperative clinical characteristics were compared.

Results Forty-three percent of the patients (203/464) who underwent gastrectomy for cT1b EGC qualified for ESD; their endoscopic lesion tended to be smaller than 20 mm in size and located in the distal part of stomach. In addition, the ESD-qualified group showed a significantly higher proportion of well-differentiated tubular adenocarcinoma on endoscopic biopsy and of the flat/depressed type in the endoscopic evaluation.

Conclusion Forty-three percent of the patients with cT1b EGC who underwent gastrectomy had a chance to preserve their stomach by ESD. Therefore, pre-treatment factors such as endoscopic lesion size, location, histology, and gross type should be considered for treatment modality selection for cT1b EGC.

Keywords Clinical submucosal invasive early gastric cancer · Endoscopic submucosal dissection · Pre-treatment factors

According to the Japanese Gastric Cancer Association (JGCA) guideline, gastrectomy is indicated as the standard treatment for clinical submucosal invasive (cT1b) early gastric cancer (EGC). Endoscopic submucosal dissection (ESD) for cT1b EGC is neither a standard treatment nor an investigational treatment [1].

Identifying patients with cT1b EGC has relied largely on endoscopy, endoscopic ultrasonography (EUS), and multidetector computed tomography (MDCT). Unfortunately, these evaluations show unsatisfactory accuracy for distinguishing between stages T1a and T1b EGC [2–4]. Moreover, curative resection by ESD can be achieved in minimally submucosal invasive gastric cancer with tumor size 30 mm or less with differentiated-type histology [5]. Therefore, patients with T1a gastric cancer who were overestimated as T1b and patients with ESD-treatable T1b gastric cancer may lose the opportunity to preserve their stomach in current clinical practice.

Fujiya et al. reported that 28.8% of cT1b EGC patients with lesions 30 mm or less in diameter and a differentiated-type histology were treatable by ESD, leading to preservation of the stomach [6]. We were interested in the clinicopathologic characteristics of patients who were eligible for ESD among patients with cT1b EGC. The aim of this study was to determine the pre-treatment factors indicating treatment by ESD in cT1b EGC.

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Methods

Patients

We retrospectively reviewed 3821 patients who visited and worked up for EGC at the Seoul National University Hospital (SNUH) from January 2010 to December 2014. Endoscopy, EUS, and MDCT were used for preoperative evaluation. We identified 1061 patients who diagnosed as cT1b EGC with clinically no evidence of lymph node metastasis (LNM) and distant metastasis (cN0, cM0) and underwent gastrectomy. Among them, 482 patients who met the following inclusion criteria were selected: lesions 30 mm or less in diameter in endoscopic evaluation, and differentiated-type histology diagnosed by endoscopic biopsy. Differentiated-type histopathology includes well- or moderately differentiated tubular adenocarcinoma or papillary adenocarcinoma.

Patients were excluded if they had previous history of stomach surgery due to gastric ulcer ($n=2$), endoscopic treatment for EGC ($n=3$), were recommended additional surgery after ESD failure ($n=1$), or had other malignancies ($n=10$). Two patients who were diagnosed with papillary adenocarcinoma by endoscopic biopsy were excluded, for the convenience of analysis. The clinicopathologic characteristics of the remaining 464 patients were analyzed (Fig. 1). The Institutional Review Board (IRB) of the SNUH approved this study (IRB No. H-1710-029-891).

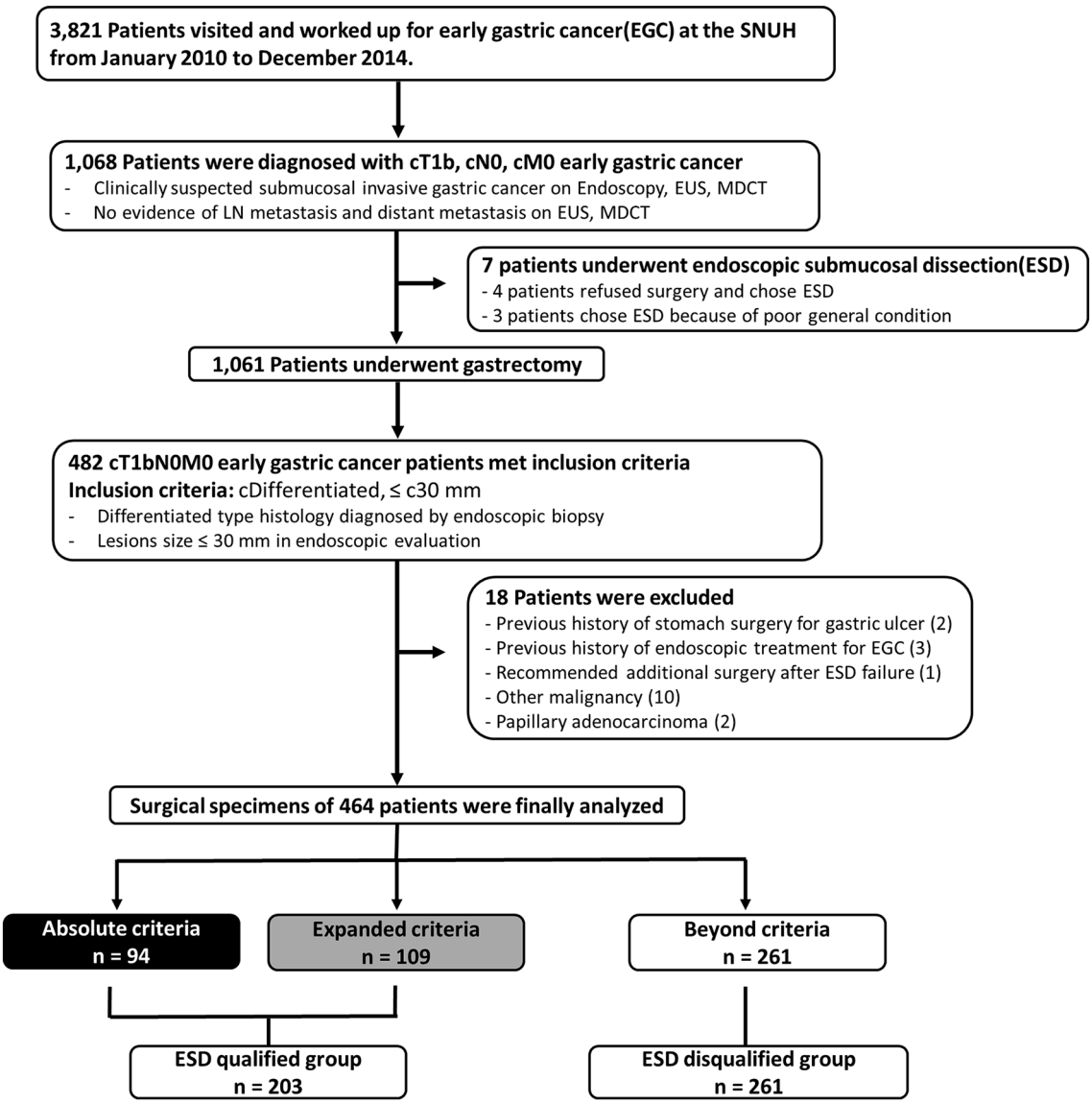

Fig. 1 Flow diagram of the study. *EGC* early gastric cancer, *ESD* endoscopic submucosal dissection, *EUS* endoscopic ultrasonography, *LN* lymph node, *MDCT* multidetector computed tomography, *SNUH* Seoul National University Hospital

Determination of perioperative staging

Staging was determined according to the American Joint Committee on Cancer (AJCC) 8th edition TNM staging system. All patients underwent endoscopic biopsy to diagnose gastric cancer. Endoscopy, MDCT, and EUS were used for preoperative staging.

Endoscopic evaluation

Endoscopic evaluation was performed on GIFH260 (Olympus, Tokyo, Japan). The gross type of EGC was as follows: type I (protruded), type IIa (superficial elevated), type IIb (superficial flat), type IIc (superficial depressed), and type III (excavated). In this study, types I and IIa were classified as the elevated type; type IIb, as the flat type; and types IIc and III as the depressed type. Endoscopic criteria for submucosal invasion were as follows: abnormal converging folds (clubbing/abrupt cutting/fusion), irregular surface, irregular protrusion with a rigid base; and deep ulceration with elevated margin [3].

MDCT evaluation

The MDCT models used this study were Somatom definition (Simens, Munich, Germany), Somatom sensation 16 (Simens, Munich, Germany), Brilliance 64 (Philips, Amsterdam, Netherlands), and Ingenuity CT (Philips, Amsterdam, Netherlands). Normal gastric walls show multilayered patterns on MDCT. The innermost enhancing layer and intermediate hypoattenuating layer correspond histologically to the gastric mucosa and submucosa. Criteria for T1 tumors were as follows: strong enhanced focal lesion with thickening of the inner and/or middle layer; unenhanced outer layer; and absence of abrupt obliteration of the middle and outer layers. Negative LNM was defined by the absence of the following features: ≥8 mm diameter on the short-axis, round shape, enhancement by contrast, and necrotic change. Metastasis was considered absent if there was no evidence of intra-abdominal solid organ and peritoneal involvement [2].

EUS evaluation

The radial echoendoscopes used in this study were the GF-UM 2000 (Olympus, Tokyo, Japan). T stage and N stage were evaluated at 12 MHz and 5 MHz, respectively. EUS evaluates the gastric wall on the basis of the standard five-layered structure. Submucosal invasion was defined as disruption of the third layer. Negative perigastric LNM was defined when the following features were absent: lesion > 5 mm in size, well-demarcated round shape, homogenous, and hypoechoic pattern [7, 8].

Determination of final pathology and pathologic staging

Surgical specimens were fixed in 10% formalin and stained with hematoxylin and eosin. Histopathological evaluation was performed on 4-mm-thick sections. The World Health Organization (WHO) classification of gastric cancer was used to classify histological subtypes of the tumor. When the tumor had a mixed histological type, the tumor was classified according to the predominant component of the tumor (50% or more) [9]. In present study, the histology of gastric cancer was classified into two groups: differentiated-type histology (well- or moderately differentiated tubular adenocarcinoma, or papillary adenocarcinoma) and undifferentiated-type histology (poorly cohesive carcinoma, poorly differentiated tubular adenocarcinoma, or mucinous adenocarcinoma). A deformity of the muscularis propria or fibrosis in the submucosal layer was regarded as pathologic ulceration. The depth of submucosal invasion was classified into three groups: sm1 (invasion into the submucosal layer < 500 μm from the muscularis mucosae), sm2 (500–1000 μm from the muscularis mucosae), and sm3 (≥ 1000 μm from the muscularis mucosae).

Investigated variables

The following clinical variables were investigated: patient age, sex, endoscopic information (tumor location, gross type, size, ulceration, histopathological diagnosis derived from endoscopic biopsy specimen), pathologic information (tumor location, gross type, size, ulceration, histologic type, lymphovascular involvement), operation adverse events, and length of hospital stay.

Statistical analysis

Student's *t* test or the Mann–Whitney *U* test was used to compare categorical variables. The χ^2 test was used to compare continuous variables. Factors associated with ESD as a treatment option were analyzed using logistic regression analysis. To estimate the effect of factors, odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. In all tests, a two-tailed p value < 0.05 was considered statistically significant. All statistical analyses were performed on SPSS version 23.0 (SPSS, Chicago, USA).

Results

Surgical outcomes and pathologic characteristics

Among 464 patients, the most common surgical approach was the laparoscopic approach (394/464, 84.9%) followed by open (55/464, 11.9%) and then robot assisted (15/464,

3.2%). Distal gastrectomy (277/464, 59.7%) was the most common followed by pylorus-preserving subtotal gastrectomy (111/464, 23.9%). D1+ lymphadenectomy (313/464, 67.4%) and D2 lymphadenectomy (146/464, 31.5%) were performed frequently. Postoperative adverse events occurred in 87 (18.8%) patients and the most common adverse event was stenosis/narrowing (28/464, 6.1%). The mean length of hospital stay was 13.0 ± 7.0 days (± standard deviation, SD) (Table 1).

Surgical specimens of 464 patients were analyzed. Table 2 describes the postoperative pathological characteristics of all patients. The mean tumor size was 24.3 ± 12.5 mm (± SD). According to the final pathologic results, 382 (82.3%) patients had differentiated-type histology and 82 (17.7%) patients had undifferentiated-type histology. Pathological analysis revealed T1a in 198 (42.7%), T1b in 226 (48.7%), and T2–T4 in 40 (8.6%) patients. The diagnostic accuracy of submucosal invasion by preoperative evaluation was 48.7%. The proportions of overestimation and underestimation were 42.7% and 8.6%, respectively. LNM was found in 39 (8.4%) patients and lymphovascular invasion was found in 80 (17.2%) patients.

Table 1 Surgical characteristics and postoperative adverse events

	No. of patients (%)
Surgical approach, *n* (%)	
Open	55 (11.9)
Laparoscopic assisted	394 (84.9)
Robot assisted	15 (3.2)
Surgical procedure, *n* (%)	
Total gastrectomy	45 (9.7)
Distal gastrectomy	277 (59.7)
Proximal gastrectomy	31 (6.7)
Pylorus-preserving subtotal gastrectomy	111 (23.9)
Lymphadenectomy, *n* (%)	
D1 dissection	5 (1.1)
D1+ dissection	313 (67.4)
D2 dissection	146 (31.5)
Adverse events, *n* (%)	
Yes	87 (18.8)
Bleeding	8 (1.7)
Stenosis/narrowing	28 (6.1)
Leakage	11 (2.4)
Incisional hernia	3 (0.6)
Atelectasis/pneumonia	14 (3.0)
Ileus	5 (1.1)
Wound problem	15 (3.2)
Other	17 (3.7)
No	377 (81.2)
Length of hospital stay, days, mean (SD)	13.0 (7.0)

SD standard deviation

Table 2 Postoperative pathological characteristics of all patients

	Total (*n* = 464)
Tumor size, mm, mean (SD)	24.3 (12.5)
Histology, *n* (%)	
Well-differentiated adenocarcinoma	137 (29.5)
Moderately differentiated adenocarcinoma	244 (52.6)
Poorly differentiated adenocarcinoma	43 (9.3)
Poorly cohesive carcinoma	39 (8.4)
Papillary carcinoma	1 (0.2)
Ulcer, *n* (%)	
Yes	50 (10.8)
No	414 (89.2)
Depth of invasion, *n* (%)	
T1a	198 (42.7)
T1b	
SM1	59 (12.7)
SM2	151 (32.5)
SM3	16 (3.5)
T2	28 (6.0)
T3	9 (2.0)
T4a	3 (0.6)
Status of LN metastasis, *n* (%)	
N0	425 (91.6)
N1 (1–2)	30 (6.5)
N2 (3–6)	6 (1.3)
N3a (7–)	3 (0.6)
Lymphovascular invasion, *n* (%)	
Yes	80 (17.2)
No	384 (82.8)

SD standard deviation, *LN* lymph node, *SM1* submucosal invasion, < 500 μm from the muscularis mucosae, *SM2* submucosal invasion, 500–1000 μm from the muscularis mucosae, and *SM3* submucosal invasion, ≥ 1000 μm from the muscularis mucosae

The pathological results obtained through surgery were classified according to JGCA's curative resection criteria (Table 3). All surgical specimens were assumed to be capable of en bloc resection if ESD was performed. The numbers of patients who satisfied with the JGCA's absolute criteria and expanded criteria were 94 and 109, respectively. There were 261 patients who did not meet absolute and expanded criteria. We classified the entire patient set into two groups: the group of patients whose pathologic results qualified for ESD (ESD-qualified group, *n* = 203) and the group of patients whose pathologic results were not suitable for ESD (ESD-disqualified group, *n* = 261). According to the above results, 43.7% (203/464) of patients were eligible for ESD.

Preoperative clinicopathological characteristics

Table 4 describes the preoperative clinicopathological characteristics. The mean age of the patients was 62.9 years

Table 3 Pathologic results according to the curative resection criteria of Japanese Gastric Cancer Association guideline

	T1a (mucosa)				T1b (submucosa)			T2–T4	Total
	No ulceration		Ulcerated		sm1		sm2/sm3		
	≤ 20 mm	> 20 mm	≤ 30 mm	> 30 mm	≤ 30 mm	> 30 mm	Any size		
Diff.[a]	**94(20.2%)** **3**[b]	*63 (13.5%)* *3*[b]	*5 (1.1%)*	1 (0.2%)	*30 (6.4%)* *5*[b] *3*[c]	12 (2.6%)	135 (29.1%)	28 (6.0%)	382 (82.3%)
Undiff	*11 (2.4%)* *2*[c]	16 (3.4%)	0 (0.0%)	0 (0.0%)	8 (1.7%)	1 (0.2%)	32 (6.9%)	12 (2.6%)	82 (17.7%)
Total	192 (41.4%)		6 (1.3%)		59 (12.7%)		167 (36.0%)	40 (8.6%)	464 (100%)

Bold: absolute curative resection criteria; italics: expanded curative resection criteria

Diff. differentiated. *Undiff*. undifferentiated, *T1a* tumor confined to the mucosa, *T1b* submucosal invasive tumor, *sm1* tumor invasion into the upper third of submucosal layer, *sm2* middle third, and *sm3* lower third

[a]Well- or moderately differentiated tubular adenocarcinoma or papillary adenocarcinoma was categorized as undifferentiated type; poorly differentiated tubular adenocarcinoma or signet-ring cell carcinoma or mucinous adenocarcinoma was classified as undifferentiated type

[b]Eleven patients were classified as ESD-disqualified group because lymphatic invasion was identified in the surgical specimen

[c]Five patients were classified as ESD-disqualified group because positive lymph node metastasis was identified in surgical specimen

(range 31–81 years). The patients included 365 (78.7%) men and 99 (21.3%) women. On endoscopic evaluation, the mean tumor diameter was 19.4 ± 7.0 mm (± SD). The proportions of tumor located in the upper third, middle third, and lower third regions were 16.8%, 22.4%, and 60.8%, respectively. On endoscopic biopsy, well-differentiated

Table 4 Preoperative clinicopathological characteristics of all patients in the ESD-qualified group and ESD-disqualified group

	All (n = 464)	ESD-qualified group (n = 203)	ESD-disqualified group (n = 261)	p value
Age, years, mean (SD)	62.9 (10.4)	63.0 (9.5)	62.8 (11.1)	0.856
BMI, kg/m^2, mean (SD)	24.4 (2.8)	24.4 (2.7)	24.3 (2.9)	0.526
Sex, *n* (%)				
Male	365 (78.7)	159 (78.3)	206 (78.9)	0.875
Female	99 (21.3)	44 (21.7)	55 (21.1)	
Tumor size, *n* (%)				
20 mm < size ≤ 30 mm	125 (26.9)	38 (18.7)	87 (33.3)	< 0.001*
10 mm < size ≤ 20 mm	261 (56.2)	120 (59.1)	141 (54.0)	
Size ≤ 10 mm	78 (16.8)	45 (22.2)	33 (12.6)	
Location, *n* (%)				
Upper third	78 (16.8)	23 (11.3)	55 (21.0)	0.009*
Middle third	104 (22.4)	43 (21.2)	61 (23.4)	
Lower third	282 (60.8)	137 (67.5)	145 (55.6)	
Histology, *n* (%)				
Moderately differentiated	300 (64.7)	115 (56.7)	185 (70.9)	0.001*
Well differentiated	164 (35.3)	88 (43.3)	76 (29.1)	
Gross type[a], *n* (%)				
Elevated	86 (18.5)	29 (14.3)	57 (21.8)	0.038*
Flat/depressed	378 (81.5)	174 (85.7)	204 (78.2)	
Ulcer, *n* (%)				
Yes	17 (3.7)	6 (3.0)	11 (4.2)	0.474
No	447 (96.3)	197 (97.0)	250 (95.8)	

ESD endoscopic submucosal dissection, *SD* standard deviation

[a]Types I and IIa were categorized as elevated type; types IIb, IIc, and III as flat/depressed type

tubular adenocarcinoma was found in 164 (35.3%) patients and moderately differentiated tubular adenocarcinoma, in 300 (64.7%) patients. The majority of tumors were found to be flat/depressed (378, 81.5%). An ulcer was exhibited in 17 (3.7%) patients.

There were no significant differences in age, sex, BMI, and ulceration between the two groups. In the ESD-qualified group, the endoscopic lesion tended to be smaller ($p < 0.001$) and was located to the distal part of stomach ($p = 0.009$), and this group showed a significantly higher proportion of well-differentiated tubular adenocarcinomas on endoscopic biopsy ($p = 0.001$) that were of the flat/depressed type ($p = 0.038$).

Univariate and multivariate analyses of factors favoring ESD

Univariate logistic regression analysis showed that small-sized tumors, tumors located in the distal part of stomach, well-differentiated tubular adenocarcinomas, and flat/depressed-type tumors were significantly associated with favoring ESD as a treatment (Table 5). On multivariate logistic regression analysis, the following factors were found to be significantly associated with qualification of ESD: lesion size 20 mm or less (10 mm < size ≤ 20 mm, OR = 0.502, 95% CI 0.314–0.802, $p = 0.004$; size ≤ 10 mm, OR = 0.281, 95% CI 0.151–0.523, $p < 0.001$), tumor located in the distal part of the stomach (middle third, OR = 0.505, 95% CI 0.264–0.965, $p = 0.039$; lower third, OR = 0.354, 95% CI 0.200–0.626, $p < 0.001$), well-differentiated tubular adenocarcinoma (OR = 0.535, 95% CI 0.356–0.803, $p = 0.003$) on endoscopic biopsy, and a flat/depressed-type tumor (OR = 0.561, 95% CI 0.334–0.942, $p = 0.029$) (Table 5).

Discussion

Clinical T1b EGC usually shows heterogeneous characteristics with various pathologic histologies and stages. Some of them may be subject to absolute or expanded indication for ESD and, as such, could have a chance to preserve the stomach. Considering the inaccurate diagnosis, it is valuable to inspect the ESD-treatable ones among cT1b EGC patients. Current preoperative evaluations using endoscopy, EUS, and MDCT have differing accuracies when staging depth of invasion. Diagnostic accuracy of overall T staging for endoscopy, EUS, and MDCT varied between

Table 5 Logistic regression analysis for factors favoring endoscopic submucosal dissection

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age	0.999 (0.981–1.016)	0.870		
BMI	0.986 (0.925–1.051)	0.662		
Sex				
Male	1 (reference)			
Female	0.965 (0.617–1.509)	0.875		
Tumor size				
20 mm < size ≤ 30 mm	1 (reference)		1 (reference)	
10 mm < size ≤ 20 mm	0.513 (0.327–0.807)	0.004*	0.502 (0.314–0.802)	0.004*
Size ≤ 10 mm	0.320 (0.178–0.577)	< 0.001*	0.281 (0.151–0.523)	< 0.001*
Location				
Upper third	1 (reference)		1 (reference)	
Middle third	0.593 (0.318–1.107)	0.101	0.505 (0.264–0.965)	0.039*
Lower third	0.443 (0.258–0.759)	0.003*	0.354 (0.200-0.626)	< 0.001*
Histology				
Moderately differentiated	1 (reference)		1 (reference)	
Well differentiated	0.537 (0.365–0.789)	0.002*	0.535 (0.356–0.803)	0.003*
Gross type[a]				
Elevated	1 (reference)		1 (reference)	
Flat/depressed	0.596 (0.365–0.974)	0.039*	0.561 (0.334–0.942)	0.029*
Ulcer				
Yes	1 (reference)			
No	0.692 (0.252–1.904)	0.476		

OR Odd ratio, *CI* confidence interval

[a]Types I and IIa were categorized as elevated type; types IIb, IIc, and III as flat/depressed type

63–78.0%, 65–92%, and 80–89%, respectively [2, 3, 10]. Moreover, distinguishing between stages T1a and T1b was more difficult. Recently, two studies reported the diagnostic accuracy of T1b by endoscopy and EUS as 78.2% and 57.3%, respectively. The overestimation rate (T1a overestimated as T1b) of endoscopy and EUS was 21.4% and 33.3%, respectively [3, 4]. In our study, the overall diagnostic accuracy of the preoperative evaluation was 48.7% and overestimation rate was 42.7%. These results suggest that it is important to find appropriate patients for ESD rather than considering cT1b EGC as a contraindication for ESD.

Owing to the technological advances in ESD, the safety and efficacy of ESD is better than that of surgery. Previous retrospective studies have shown that ESD has a lower complication rate (5 vs. 15%), shorter average procedure time (90 vs. 260 min), shorter length of hospital stays (3–7 days vs. 9–14 days), and better quality of life than surgery [11–15]. Moreover, additional surgical resection following non-curative ESD does not affect the 5-year survival rate, and prior ESD has almost no effect on additional surgical procedures [16]. Diagnostic ESD for selected cT1b EGC will reduce the adverse event rate, shorten the length of hospital stay, and improve the quality of life of patients.

In this background, the necessity of diagnostic ESD for selected cT1b EGC has been suggested. Recently, Fujiya et al. reported that 28.8% of cT1b EGC with lesions 30 mm or less in diameter and a differentiated-type histology are eligible for ESD [6]. With the same criteria, our study found 43.7% of cT1b patients eligible for ESD. Furthermore, we also revealed the pre-treatment factors favoring ESD. Pre-treatment factors such as tumor size, histologic differentiation, location, and gross type were significant contributors in determining eligibility for ESD. Previous studies have reported that the above factors were associated with the accuracy of preoperative evaluation. On endoscopic evaluation, tumors located in the upper third, large tumors of size > 10 mm, and an undifferentiated-type histology were associated with a lower diagnostic accuracy [3]. On EUS evaluation, diagnostic accuracy decreased for lesions located in the upper third, large tumors (> 10 mm), and ulcerated tumors [17, 18]. In addition, submucosa-invasive EGCs were more frequent in the middle-to-upper third than in the lower third of the stomach [19]. Considering the factors affecting preoperative diagnosis accuracy, conservative selection of tumor size, location, histology, and gross type may help determine which patients qualify for ESD.

We found some discrepancies with previous reports. First, the rate of stomach preservation is about 15% higher than previous Japanese study (28.8% vs. 43.7%) [6]. The authors concluded that difference comes from evaluation policy of the hospital. In the previous study, EUS was performed in 35.8% (103/288) of patients. Unlike Japanese study, performing EUS in all EGC patients is the policy of our institution. Because of the general use of EUS, the proportion of overestimated cT1b patients increased. This would have increased the ESD-qualified group. Second, a significant percentage of tumors with expanded indication showed LNM in our study. Two cases (15.3%: 2/13) of LNM were identified in intramucosal tumor with undifferentiated-type histology, 20 mm or less in size, without ulcer, and without lymphovascular invasion. Three cases (7.9%: 3/38) of LNM were found in minimally submucosal invasive (sm1) tumor with differentiated-type histology, 30 mm or less in size, and without lymphovascular invasion. Recent studies showed the incidence of LNM in expanded indication ranges from 0 to 15.0% [8]. Direct comparison with previous studies is hard. We only targeted patients with selected cT1b EGC and size of subgroup is too small to compare LNM incidence.

This study has some limitations. First, this study is a retrospective single-center study, which has a potential for bias. Second, this study is based on the pathologic result of patients who underwent gastrectomy for cT1b EGC and we initially assumed all patients were technically eligible for en bloc resection if ESD was performed. However, this does not accurately reflect the clinical situation when ESD is performed. Finally, we did not use image-enhanced endoscopy (IEE), such as magnifying endoscopy with narrow-band imaging (ME-NBI), for assessing the depth of invasion; however, its usefulness in measuring the depth of invasion is yet to be verified. The non-structural pattern known to be observed in submucosal invasive EGC could also be observed in EGC confined to the mucosa with an undifferentiated-type histology [20, 21]. Moreover, in some countries, IEE is not easy to undertake because of the necessity of additional observation time and/or additional costs in the clinical setting. Despite these limitations, this study has several strengths. First, our study analyzed the largest number of cT1b EGC patients compared with previous studies. Second, selection bias was minimized because our study was based on a non-selected surgical cohort. In this study, almost patients of cT1b EGC who are capable of invasive operation experience surgeries according to current guideline and institutional policy. Finally, we focused on pre-treatment factors related to ESD eligibility. This approach is more useful for selecting appropriate target groups for ESD in a clinical setting.

In conclusion, diagnostic ESD may be useful in patients with selected cT1b EGC. The pre-treatment factors such as endoscopic lesion size, location, gross type, and histology should be considered for selecting the appropriate treatment modality for cT1b EGC.

Compliance with ethical standards

Disclosures Hyun Deok Lee, Hyunsoo Chung, Sang Gyun Kim, Jung Kim, Jue Lie Kim, Eunwoo Lee, and Hyun Chae Jung have no conflicts of interest or financial ties to disclose.

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