

The efficacy of the application of the curative criteria of the 5th edition Japanese gastric cancer treatment guidelines for early adenocarcinoma of the esophagogastric junction treated by endoscopic submucosal dissection

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Abstract

Background: The curative criteria after endoscopic submucosal dissection for early gastric carcinoma were updated by the Japanese Gastric Cancer Association. No study has shown promising results with endoscopic submucosal dissection for early adenocarcinoma of esophagogastric junction based on the new curative criteria. The purpose of this study was to validate clinical efficacy of the application of the curative criteria of the 5th edition Japanese gastric cancer treatment guidelines for early adenocarcinoma of esophagogastric junction after endoscopic submucosal dissection.

Methods: Patients who underwent endoscopic submucosal dissection for Siewert type II adenocarcinoma between January 2013 and June 2018 were eligible for this study. Clinical and pathological features and treatment outcomes were retrospectively reviewed using medical records.

Results: The success rate for en-bloc resection was 97.2% (172/177) and the curative resection rate was 71.2% (126/177). Additional endoscopic submucosal dissection or radical surgery was conducted in 10 patients (5.6%) who did not fulfil the curative resection criteria, while one patient with curative resection remedied with endoscopic submucosal dissection because of recurrence. According to eCura scoring system, 94 patients (53.1%) were categorized into eCura A, 34 patients (19.2%) into eCura B, 11 patients (6.2%) into eCura C-1, and 38 patients (21.5%) into eCura C-2. Five patients categorized as eCura C-2 underwent radical surgery, two of whom have lymph node metastasis.

Conclusions: Endoscopic submucosal dissection for early adenocarcinoma of esophagogastric junction that met the expanded criteria of the 5th edition Japanese gastric cancer treatment guidelines were acceptable and should be the standard treatment instead of surgical resection.

Keywords: Curative resection, eCura system, endoscopic submucosal dissection, esophagogastric junction, lymph node metastasis

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INTRODUCTION

The incidence of adenocarcinoma of the esophagogastric junction (AEGJ) as a consequence of gastroesophageal reflux disease and Barrett's esophagus showed an increasing trend over the last decades in Western countries.^[1,2] Although AEGJ accounted for only 1%-4% of the esophageal carcinoma in Eastern countries, including China and Japan, it is believed that the incidence of AEGJ will increase in Eastern countries in the future due to the decreasing incidence of *Helicobacter pylori* infection.^[3,4] Esophagectomy has long been regarded as the gold standard treatment for early AEGJ. However, esophagectomy is a complex surgical procedure, which entails the risk of overtreatment and reduces postoperative patient quality of life, with a reported mortality rate ranging between 3.0% and 12.2%.^[5,6] Endoscopic submucosal dissection (ESD) has been accepted as a minimally invasive and curative treatment for superficial gastrointestinal cancers, including esophageal, gastric, and colonic cancers.

In Japan, curative criteria after ESD for early gastric carcinoma (EGC) were updated by the Japanese Gastric Cancer Association in January 2018.^[7,8] These new criteria after ESD expanded the absolute indication as follows: intestinal-type gastric cancer (cT1a) including ulcer (UL)-negative tumor >2cm in size or UL-positive tumor <3 cm in size.^[7] Besides, the eCura system, which is a lymph node metastasis (LNM) risk scoring system, was also applied to assess the cancer residue status.^[9] These new criteria and new assessment systems were acceptable for ESD for EGC not involving the early AEGJ. However, AEGJ includes primarily cardiac adenocarcinoma in Japan and China. Hence, we hypothesized that these criteria of the 5th edition Japanese gastric cancer treatment guidelines are applicable to early AEGJ.

METHODS

Patient and lesion characteristics

Between January 2013 and June 2018, patients who met the absolute and expanded criteria for endoscopic resection and underwent ESD for Siewert type II adenocarcinoma at Cancer Institute and Hospital Chinese Academy of Medical Sciences (CICAMS), Beijing, China, were prospectively included in our database and analyzed. The diagnosis of AEGJ was made mainly by endoscopic findings, with the distal limit of palisading vessels or the proximal limit of the gastric rugal folds as landmarks for the esophagogastric junction (EGJ). Siewert type II adenocarcinoma is defined as a tumor with an epicenter located within 1 cm proximal and 2 cm distal to the EGJ.^[10-12]

Indications for ESD

We collected data from patients with early AEGJ who met the following indication criteria after obtaining approval from the institutional review board. The inclusion criteria for entry into this study were as follows: (1) biopsy-proven differentiated-type adenocarcinoma with clinical intramucosal cancer, any tumor size, without endoscopic findings of UL; (2) biopsy-proven differentiated-type adenocarcinoma with clinical intramucosal cancer, tumor less than 3 cm in size, with endoscopic findings of UL; and (3) biopsy-proven undifferentiated-type adenocarcinoma with clinical intramucosal cancer, tumor less than 2 cm in size, without endoscopic findings of UL.^[13]

Endoscopic submucosal dissection procedures

Surgical procedure was approved by the Department of Endoscopy at CICAMS, and the Ethics Committee of National Cancer Center/Cancer Hospital, Chinese Academy of Medical Science and Peking Union Medical College (Approval Number: 17-124/1380, Approval date: 20-07-2017). Written informed consent was obtained from the patient for the surgery and for publication of this cohort study and any accompanying images. Experienced endoscopists in CICAMS conducted all endoscopic procedures. The procedures were performed using a dual knife (KD-650Q; Olympus Optical, Tokyo, Japan) and a single-channel upper gastrointestinal endoscope (GIF-Q260J, GIF-H260 or GIF-H290; Olympus) with a transparent hood (D-201-11804; Olympus) attached to the tip of the endoscope. In brief, we marked the normal mucosa that surrounded the lesion at least 5 mm away from the tumor by using a dual knife. After injection of a saline solution with epinephrine (0.025 mg/mL) into the submucosa, an initial cut, also called a pre-cut, was made with a standard needle-knife on the oral side of the tumor, followed by a circumferential mucosa incision around the tumor. If necessary, during the procedure, the submucosal injection was repeated and endoscopic hemostasis was achieved. The tumor was then completely removed by submucosal dissection. After removal of lesions, preventive coagulation was performed for all visibly exposed vessels with hot biopsy forceps. A high-frequency electrosurgical current generator (Erbotom VIO 300D; ERBE, Tübingen, Germany) was used during marking, mucosal incision, submucosal dissection, and hemostasis.

Pathological assessment of resected specimens

The endoscopically resected specimens were sectioned serially at millimeter intervals. The histological classification of adenocarcinoma was done according to the Japanese classification of gastric carcinoma. The depth of invasion, the presence of lymphatic and/or vascular

invasion, the margins, and tumor differentiation were evaluated. An en-bloc resection refers to resection in one piece by endoscopy, whereas complete resection (CR) was histologically defined as ER of the tumor with horizontal margins (HM) and vertical margins (VM) free of tumor.^[7] Besides, we also defined histological curative resection (CuR) based on the following conditions: en-bloc resection, HM0, VM0, ly(-), v(-), and (1) Tumor size ≥ 2 cm, histologically of differentiated type, pT1a, UL(-); (2) Tumor size ≤ 3 cm, histologically of differentiated type, pT1a, UL(+); (3) Tumor size ≤ 2 cm, histologically of undifferentiated type, pT1a, UL(-); (4) Tumor size ≤ 3 cm, histologically of differentiated type, pT1b (SM1, $< 500 \mu\text{m}$ from the muscularis mucosae).^[8,13]

Definitions

We reclassified our pathologic findings specifically into 3 groups absolute indication group (group 1, G1), expanded indication group (group 2, G2), and relative indication group (group 3, G3). An absolute indication (G1) is defined as intestinal-type gastric cancer (cT1a) with UL-negative tumor ≤ 2 cm in size. An expanded indication (G2) is referred to intestinal-type gastric cancer (cT1a) including UL-negative tumor > 2 cm in size or UL-positive tumor ≤ 3 cm in size. And relative indication (G3) is redefined as undifferentiated-type gastric cancer with UL-negative tumor ≤ 2 cm in size.

Adverse events were classified according to the Clavien–Dindo classification.^[14] Adverse events occurring within 30 days of treatment were defined as early adverse events and those occurring thereafter as late adverse events. Stricture was defined as gross narrowing of the EGJ or anastomosis site and diameter reduction with dysphagia such that a standard 9.2-mm-diameter endoscope (GIF-Q260; Olympus) failed to pass through.^[15,16]

Follow-up

After ESD, the patients who had a curative resection underwent upper gastrointestinal endoscopy 3 and 12 months after ESD, and annual surveillance was performed thereafter. For the patients who had a noncurative resection, surgical resection was carried out in the normal fashion. The patients with noncurative resection who refused surgical resection were followed-up with endoscopy and/or ultrasonography (EUS), in addition to computed tomography (CT) every 3 to 6 months.

Statistical analysis

The baseline characteristics of the patients were expressed as mean \pm standard or median deviation. The differences in the distribution between the groups were analyzed

by using the X^2 test. The mean quantitative values were compared by using the Student t test, Chi-square test, Fisher's exact test, or the Mann–Whitney U test, as appropriate. All statistical analyses were performed using SPSS 24.0 (SPSS, Chicago, IL, USA), and a P value < 0.05 was considered statistically significant.

RESULTS

Baseline and clinicopathological characteristics

A total of 177 early AEGJ patients with a mean age of 63.5 years (range, 45–88) and a male/female ratio of 143/34 (80.8%:19.2%) were treated by ESD between January 2013 and July 2018 at the CICAMS in Beijing, China. Patient characteristics and operation details for the entire cohort are provided in Table 1. The mean diameter of the resected specimens was 58.7 (range 22–127) mm, and the mean diameter of the lesions was 21.8 (range 5–60) mm. The median operation time was 96.0 (range 31–360) min, and the average hospital stay was 6.6 (range 3–19) days.

Comparison between lesions with “absolute indication” versus “expanded indication” versus “relative” indication.

According to the final pathological diagnosis, 84 patients (47.5%) were included in the G1, 69 patients (39.0%) in the G2, and 24 (13.5%) in the G3. Results of comparison of patient characteristics and operation details between

Table 1: Patient characteristic and operation details of endoscopic submucosal dissection

Characteristic	Data
Mean age (years)	
Min-max	45-88
Mean \pm SD	63.5 \pm 8.0
Sex ratio (M/F)	143/34 (80.8%:19.2%)
Comorbid disease	
Hypertension	51 (28.8%)
Cardiovascular disease	5 (2.82%)
Diabetes	21 (11.7%)
Previous cerebrovascular event	4 (2.3%)
Respiratory disease	3 (1.7%)
Other previously treated malignancies	19 (10.7%)
Having ≥ 1 comorbidity	99 (55.9%)
Having ≥ 2 comorbidity	17 (9.6%)
Operation duration (minutes)	
Median (Min-max)	96 (31-360)
Size of resected specimen (mm)	
Min-max	22-127
Mean \pm SD	58.7 \pm 16.4
Hospital time (d)	
Min-max	3-19
Mean \pm SD	6.6 \pm 1.7
Complications, No. (%)	
Postoperative bleeding	11 (6.2%)
Perforation	3 (1.7%)
Stricture	14 (7.9%)

Min=Minimum; Max=Maximum; SD=Standard Deviation; M=Male; F=Female; No.=Number

these three groups are shown in Table 2. There were no significant differences in age, hospital time and complications, whereas patients in G2 had significantly larger size of resected specimen and longer operation duration than those in G1 and G3 (65.9 ± 17.6 vs 54.5 ± 13.8 vs 52.7 ± 13.6 , $P < 0.001$, and 92.5 vs 109.3 vs 90.6).

The pathological characteristics of ESD for early AEGJ are shown in Tables 3 and 4. ER was achieved in 172 lesions (97.2%), CR in 151 lesions (85.3%) and CuR in 128 lesions (72.3%). In contrast, 21 of the 172 en-bloc resected specimens showed resection margin positivity. When assessing the resection outcome according to ESD criteria, the CR and CuR rates were 89.3% (75/84) and 84.5% (71/84), respectively, for the G1; 84.1% (58/69) and 71.0% (49/69), respectively, for the G2; and 75.0% (18/24) and 33.3% (8/24), respectively, for the G3. CuR was significantly different between these three groups, with P value < 0.001 . Although CuR in G1 was higher than that in G2, there existed no statistical difference between these two groups.

eCura system

According to the pathological characteristics and eCure scoring system, 94 patients (53.1%) were categorized into eCura A, 34 patients (19.2%) into eCura B, 11 patients (6.2%) into eCura C-1, and the remaining 38 patients (21.5%) into eCura C-2. In the validation stage, eCura C-2 differed significantly among these groups (8.3%, 23.2% and 62.5%, respectively). But eCura A, eCura B and eCura C-1 were not significantly different between G1 and G2.

Local recurrence and distant metastasis

During a median follow-up period of 47 months (range 24-93 months), local tumor recurrence was detected in 3.4% of cases (6/177). Five patients were successfully managed with endoscopic treatment while another was treated with subsequent surgery. Of the 49 cases with

noncurative resection, 6 patients underwent subsequent surgery and two of them had LNM, while 4 cases with noncurative resection remedied with ESD. The remaining patients were followed-up with endoscopy and CT, either because of their advanced age or a refusal to undergo surgery. One patient died during the follow-up period, of causes unrelated to AEGJ, namely undifferentiated-type gastric antrum cancer. The 5-year overall survival and 5-year disease-free survival is 99.4% and 100%, respectively.

Complications

Adverse events occurred in 25 patients (14.1%), namely bleeding ($n = 11$, 6.2%), suspicious microperforation ($n = 3$, 1.7%) and stricture ($n = 14$, 7.9%). The incidence of overall treatment-related adverse events was similar in the three groups (15.5% vs 14.4% vs 20.8%, $P = 0.81$). Both delayed bleeding and postoperative esophageal stenosis occurred in two patients and another one patient suffered from both delayed bleeding and perforation. All adverse events were handled endoscopically, without any serious consequence.

DISCUSSION

Recent years have witnessed the clinical efficacy of the application of the Japanese curative criteria of gastric cancer for early AEGJ treated by ESD.^[6,15-21] In January 2018, the Japanese Gastric Cancer Association updated the Japanese gastric cancer treatment guidelines,^[8] including the curative criteria after ESD for EGC. Since AEGJ includes mainly cardiac adenocarcinoma in Japan and China, we hypothesized that these latest Japanese curative criteria are applicable to early AEGJ.

Removal of AEGJ is difficult using ESD because of its anatomic characteristics, including narrow lumen, sharp angle, poor accessibility, and movability of the lesion during esophageal peristalsis. These difficulties can affect the outcomes of ESD, such as ER or CR rates, operation

Table 2: Comparison of patient characteristic and operation details between lesions with “absolute” versus “expand” versus “relative” indication group

Items	Absolute (n=84)	Expanded (n=69)	Relative (n=24)	P
Mean age (years)				
Mean±SD	64.3±8.1	62.5±7.6	64.0±8.6	0.372
Operation duration (minutes)				
Median (Min-max)	92.5 (31-210)	109.3 (31-360)	90.6 (55-280)	0.009
Size of resected specimen (mm)				
Mean±SD	54.5±13.9	65.9±17.6	52.7±13.6	<0.001
Hospital time (d)				
Mean±SD	6.5±1.6	6.7±1.5	6.7±2.7	0.817
Complications, No. (%)	13 (15.5%)	10 (14.4%)	5 (20.8%)	
Postoperative bleeding	5 (6.0%)	4 (5.8%)	2 (8.3%)	0.898
Perforation	1 (1.2%)	1 (1.4%)	1 (4.2%)	0.597
Stricture	7 (8.3%)	5 (7.2%)	2 (8.3%)	0.966

Min=Minimum; Max=Maximum; SD=Standard Deviation, No=Number

Table 3: Tumor characteristics and pathological results of endoscopic submucosal dissection

Characteristic	Data
Ulcerative findings	
UL-negative	175 (98.9%)
UL-positive	2 (1.1%)
Tumor size (mm)	
Min-max	5-60
Mean±SD	21.8±12.21
Macroscopic type	
0-I	4 (2.3%)
0-IIa	28 (15.8%)
0-IIb	19 (10.7%)
0-IIc	34 (10.7%)
0-IIa + IIc	89 (50.3%)
0-IIb + IIc	2 (1.1%)
III	1 (0.6%)
Depth of invasion	
M	111 (62.7%)
SM ₁ (≤500 μm)	45 (25.4%)
SM ₂ (>500 μm)	21 (11.9%)
Lymphatic involvement	
Negative	177 (100%)
Positive	0
Vessel involvement	
Negative	174 (98.3%)
Positive	3 (1.7%)
Horizontal margin	
Negative	162 (91.5%)
Positive	15 (8.5%)
Vertical margin	
Negative	164 (92.7%)
Positive	13 (7.3%)
Predominant type	
Well-differentiated adenocarcinoma	45 (25.4%)
Moderately differentiated adenocarcinoma	108 (61.0%)
Poorly differentiated adenocarcinoma	21 (11.9%)
Signet-ring cell carcinoma	3 (1.7%)
Results of resection, No. (%)	
En-bloc resection	172 (97.2%)
Completed resection	151 (85.3%)
Curative resection	128 (72.3%)
eCura system	
eCura A	94 (53.1%)
eCura B	34 (19.2%)
eCura C-1	11 (6.2%)
eCura C-2	38 (21.5%)

UL=Ulcer, Min=Minimum; Max=Maximum; SD=Standard Deviation; M=Mucosa, SM=Submucosa, No.=Number

time and procedure-related bleeding or perforation.^[19] The procedure speed of ESD for early AEGJ in our study is slower than that for EGC,^[22] with two main reasons as follows: AEGJ may extend beyond the cardia, including the angle of His,^[15] or, the larger lesion area of the cases included in our study.

In this study, among the 177 AEGJ patients in our series who underwent ESD, the ER, CR, and CuR were 97.2%, 85.3%, and 72.3%, respectively, which are consistent with data from previous studies.^[6,19-21] Kim *et al.* have testified that CR rate was only related to ulcer and not to the size of lesion.^[19] Furthermore, it was proved by Gong *et al.*^[16] that there existed statistical differences between the CuR

and the degree of differentiation of lesions, endoscopic classification and indication criteria. Multivariate analysis also confirmed that the low CuR was related to the undifferentiated and elevated lesion.^[16] In our study, the relative indication group had a significant difference in CuR compared with absolute indication group and expanded indication group. However, there existed no statistical difference between absolute indication group and expanded indication group. Even CuR in absolute indication group was higher than that in expanded indication group. Therefore, more large-scale multi-center clinical trials will be needed to verify whether the criteria for expanded indications group can be incorporated into the absolute indication group, which is similar to the Japanese curative criteria of EGC.

eCura system, established by Hatta *et al.*, is a scoring system to stratify curability after ESD for EGC, which accurately predicts cancer-specific mortality and cancer recurrence of patients who did not receive additional treatment after ESD of EGC.^[23] Our study is the first research using eCura system to evaluate the risk of LNM and prognosis of ESD in early AEGJ. Among the 49 cases with noncurative resection, 38 cases were categorized as eCura C-2, in which only 5 patients underwent radical surgery and two of them were confirmed to have LNM according to postoperative pathology. These two cases showed at least three risk factors at the same time: vessel involvement, poorly differentiated adenocarcinoma, VM (+) or SM2 (>500 μm). According to the latest edition Japanese gastric cancer treatment guidelines,^[8] neither follow-up observation or ESD/radical surgery can be conducted for the patients with eCura C-1 under the guidance of doctors. In our study, only 1 case underwent surgical treatment, and 3 cases underwent endoscopic submucosal dissection. Seiichiro *et al.*^[24] reported that 6 (13%) of 46 patients in high risk group receiving radical surgery were found to have metastasis, while no patient in the noncurative group (15 patients, 29.4%) showed lymph node metastasis after additional surgery in the research of Liu *et al.*^[25] Hatta *et al.*^[26] demonstrated in their studies of noncurative ESD for EGC that cancer-specific survival and cancer recurrence in patients with no additional treatment was significantly lower than those in patients with radical surgery in the intermediate-risk and high-risk categories. The proportion of LNM in patients with additional surgery was relatively higher in our study, but no patient died of AEGJ during long-term follow-up. Besides, no recurrence, LNM, distant metastatic carcinomas or disease-related death was detected in the other 39 patients with noncurative resection during regular follow-up of endoscopy and CT. Similarly, Seiichiro *et al.*^[24] found that the 5-year disease-specific survival rates of ESD for early AEGJ

Table 4: Comparison of tumor characteristics and pathological results between lesions with “absolute” versus “expand” versus “relative” indication group

Items	Absolute (n=84)	Expanded (n=69)	Relative (n=24)	P
Tumor size (mm)				
Mean±SD	14.8±4.7	33.5±11.1	12.7±4.7	<0.001
Macroscopic type				
0-I	2	1	1	
0-IIa	14	10	4	
0-IIb	12	5	2	
0-IIc	16	14	4	
0-IIa + IIc	40	35	13	
0-IIb + IIc	0	2	0	
III	0	2	0	
Lymphatic involvement				1
Negative	84 (100%)	69 (100%)	24 (100%)	
Positive	0	0	0	
Vessel involvement				0.231
Negative	84 (100%)	67 (97.1%)	23 (95.8%)	
Positive	0	2 (2.9%)	1 (4.2%)	
Horizontal margin				0.705
Negative	78 (92.9%)	63 (91.3%)	21 (87.5%)	
Positive	6 (7.1%)	6 (8.7%)	3 (12.5%)	
Vertical margin				0.082
Negative	81 (96.4%)	63 (91.3%)	20 (83.3%)	
Positive	3 (3.6%)	6 (8.7%)	4 (16.7%)	
Predominant type				
Well-differentiated adenocarcinoma	25 (29.8%)	20 (29.0%)	0	
Moderately differentiated adenocarcinoma	59 (70.2%)	49 (71.0%)	0	
Poorly differentiated adenocarcinoma	0	0	21 (87.5%)	
Signet-ring cell carcinoma	0	0	3 (12.5%)	
Depth of invasion				
M	57 (67.9%)	46 (66.7%)	8 (33.3%)	
SM ₁ (≤500 μm)	23 (27.4%)	17 (24.6%)	5 (20.8%)	
SM ₂ (>500 μm)	4 (4.8%)	6 (8.7%)	11 (45.8%)	
Results of resection				
ER	83 (98.8%)	68 (98.6%)	22 (87.5%)	0.009
CR	75 (89.3%)	58 (84.1%)	18 (75.0%)	0.204
CuR	71 (84.5%)	49 (71.0%)	8 (33.3%)	<0.001
eCura system				
eCura A	52 (61.9%)	42 (60.9%)	0	
eCura B	19 (22.6%)	7 (10.1%)	8 (33.3%)	
eCura C-1	6 (7.1%)	4 (5.8%)	1 (4.2%)	
eCura C-2	7 (8.3%)	16 (23.2%)	15 (62.5%)	

SD=Standard Deviation; M=Mucosa, SM=Submucosa, ER=En-bloc resection; CR=Complete resection, CuR=Curative resection

were not significantly different between the high-risk group with additional surgery and those without additional surgery (94.4% vs 92.8%, respectively). Therefore, we proposed whether conservative follow-up, rather than additional surgery, could be used in patients with high-risk factors if they have indications of advanced age or intolerance of major surgery. Compared to the previous research,^[9,26,27] only a small number of patients categorized as eCura C-1 or eCura C-2 chose additional radical surgery in our study. Consequently, it is difficult to accurately assess the risk of LNM in these two high-risk groups in our study. Further studies with a larger sample size should be included to validate the risk of LNM in noncurative ESD for early AEGJ.

Treatment-related adverse events may affect patient quality of life and prolong hospital stay. In the present study, the bleeding rates, suspicious microperforation rates and

stricture rates were 6.2%, 1.7% and 7.9%, respectively, which conformed to data from previous studies.^[17,19,21] There existed no difference of complications among absolute indication group, expanded indication group and relative indication group. Even where complications occurred, endoscopic measures were executed promptly, which avoided serious consequences for the patients in our center. All bleeding events occurred within 7 days of the procedure and were successfully treated with endoscopic hemostasis. Three cases with perforation during the ESD were managed by endoclippping and maintained with restriction of oral intake and supportive care. Besides, postoperative stenosis occurred in 14 patients (7.9%) and was easily managed by endoscopic balloon dilation on a median of 3.7 occasions (range 0–7).

Our study had several limitations of note. Firstly, our analysis was retrospective, nonrandomized, and conducted at a single center, and hence potential selection bias

and referral bias cannot be excluded. Secondly, lesion characteristics were retrospectively assessed by review of the endoscopic images, however, unclear endoscopic images before 2015 influenced the judgment outcomes, such as classification of AEGJ, tumor size and macroscopic type. In addition, nearly 10% of ESD procedures were done before 2014, when the technology of ESD for early AEGJ and pathological assessment may not have been mature enough in our center. Finally, the follow-up time (median 47 months, range 24-93 months) was shorter than that in other studies and some outcomes could not be presented during this period.^[17,18,20] For instance, the proportion of patients with eCura C-2 who refused additional surgery was very high, and it was difficult to assess the risk of LNM of these patients in short-term follow-up of endoscopy and CT. However, our study is the first to explore the clinical efficacy of ESD for early AEGJ using the curative criteria of the 5th edition Japanese gastric cancer treatment guidelines. The eCura system is useful for selecting patients who require radical surgery after noncurative ESD for early AEGJ more precisely in clinical practices. Compared with previous studies,^[6,15-21] the sample size of this study was larger and all samples included in this research were strictly in accordance with the requirements of the latest edition of the guidelines.

In conclusion, ESD using the curative criteria of the 5th edition Japanese gastric cancer treatment guidelines may be a feasible and effective treatment for curative intent in patients with early AEGJ. Although additional prospective multi-center studies with a larger number of cases will be needed to confirm these results, the curative criteria and assessment system of the 5th edition Japanese gastric cancer treatment guidelines are likely to be useful for disease stratification and making decisions for early AEGJ after ESD.

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Conflicts of interest

There are no conflicts of interest.

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