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Research Article

Efficacy of Endoscopic Submucosal Dissection in Gastric Neoplastic Lesions: A Single-Center Experience

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Abstract

Objective: Endoscopic submucosal dissection (ESD) is an endoscopic treatment method that has been indicated as the preferred method for the treatment of early gastric cancer (EGC) and finds increased use in Western countries. This study analyzed the experience of a tertiary center in Türkiye using the ESD method for the treatment of gastric neoplastic lesions.

Methods: Patients with gastric neoplastic lesions who underwent ESD between March 2019 and March 2023 were included in the study. The rates of en bloc and R0 resection were investigated. The curability of EGC was evaluated according to the current guidelines of the Japan Gastroenterological Endoscopy Society. Patients with a follow-up period of <1 year were excluded from the study.

Results: In total, 42 gastric neoplastic lesions from 38 patients were included in the study. The mean tumor diameter was 26.39 mm (range: 10-75 mm). The success rates of en bloc and R0 resection were 97.6% and 90.4%, respectively. Curative resection was achieved in 8/13 (61.5%) patients diagnosed with EGC. The median length of hospital stay was 1 day (range: 1-3 days). Complications occurred postoperatively in 13.1% of the patients. Recurrence was observed in 1 patient (2%) at a median follow-up of 18 months (range: 12-57 months).

Conclusion: Endoscopic submucosal dissection is an effective and safe method for treating gastric neoplastic lesions. The rate of curative treatment with the ESD method in EGC should be improved.

Keywords: Endoscopic submucosal dissection, endoscopy, gastric neoplasm

INTRODUCTION

Gastric cancer is the third leading cause of mortality following lung and colon cancers.[1] Considering the historically low survival rates, early detection and resection are considered the most effective strategies for improving prognosis. The incidence of early diagnosed gastric cancer (EGC) has increased because of advances in endoscopic imaging methods.[2]

Endoscopic submucosal dissection (ESD) has been indicated as the preferred method by relevant guidelines for the treatment of EGC.[2-4] Recently, this technique has been increasingly used in Türkiye, consistent with that of other Western countries. The primary advantage of ESD is that it facilitates accurate histopathologic evaluation via en bloc resection. The major disadvantages include the need for additional technical skills and the risk of complications.[3,4]

There are significant differences between the first (2016) and second (2021) guidelines of the Japan Gastroenterological Endoscopy Society (JGES).[2,3] Conditions previously included in the expanded criteria are now included in the definitive indication criteria based on the results from multicenter studies.[5-9] Accordingly, the exact indications for ESD in the current JGES guideline include the following: (i) nonulcerated intramucosal (cT1a) differentiated tumors (no size limit), (ii) nonulcerated intramucosal (cT1a) undifferentiated tumors smaller than 2 cm, and (iii) ulcerated intramucosal (cT1a) differentiated tumours smaller than 3 cm[3].

Certain Western centers have published promising results regarding tumors that met the strict indication for ESD for EGC treatment;[10-17] however, there is limited data on applying the expanded indication to Western cohorts.[18,19] The applicability of the expanded criteria is uncertain in Türkiye. Our study presents the short-term follow-up results of patients who underwent ESD for gastric neoplastic lesions.

METHODS

This study included retrospective data collected from a single center. Ege University The Ethics Committee of Medical Research approved the study protocol (Approval date: April 25, 2024, Approval number: 24-4.1T/67). Demographic data of the patients, endoscopic findings, and procedural details were retrieved from hospital information and endoscopic reporting systems, respectively. Written informed consent was obtained from patients who participated in this study. Patients with benign lesions, subepithelial lesions, carcinoid tumors, and a follow-up period <1 year were excluded from the study. The comorbid conditions of the patients were assessed using the Charlson Comorbidity Index (CCI).[20]

Primary Endpoints of the Study

What are the rates of en bloc and R0 resection with the ESD procedure in gastric neoplasm?

What is the curative resection rate with the ESD procedure in EGC?

Secondary Endpoints

What are the complication rates associated with gastric ESD?

What is the recurrence rate of EGC after ESD?

Lesion Morphology

Three factors, i.e., size, ulcer occurrence, and invasion depth, were evaluated in all lesions before endoscopic treatment. All lesions evaluated for endoscopic resection were defined based on the Paris endoscopic classification of superficial neoplastic lesions.[21] Lesions were grouped as cardia, fundus, corpus, and antrum based on localization.

Endoscopic Submucosal Dissection Procedure

All procedures within the scope of the study were performed by a single endoscopist. The procedures were performed following light sedation or general anesthesia. A 3-mm FlushKnife (Fujifilm, Tokyo, Japan) was used during the ESD procedure. An ESG 400 (Olympus, Japan) electrosurgical cautery device was used for the aforementioned purposes. Forced coagulation (effect 2, 40 W) and pulse-cut slow (effect 2, 40 W) modes were used for marking and mucosal incision, respectively. Forced coagulation and pulse-cut slow modes were used in combination for submucosal dissection. Hemostatic forceps (soft coagulation effect 4, 60 W) were used in cases of massive bleeding. The conventional, pocket creation method, and tunneling method were used in the scope of the ESD procedures. Traction was applied using the clip-with-loops method because of severe submucosal fibrosis in certain procedures. As submucosal injection fluid, Gelofusine (B. Braun, Melsungen, Germany) with indigo carmine dye was used, and normal saline with indigo carmine dye (40 mg per 500 mL solution) was used for injection with a sclerotherapy needle and when injecting with a knife. Adrenaline was not added to the solutions.

MAIN POINTS

- The RO and en bloc resection rates with ESD for gastric neoplasia treatment in this study were similar to those of previous studies.
- The curative resection rate with ESD was low for EGC treatment in this study.
- Delayed bleeding after ESD was the most common complication observed among the patients included in this study.
- There were no complications requiring surgical intervention after ESD.

All lesions were resected en bloc. The procedure duration was calculated as the difference between the first submucosal injection time and the end of the resection.

Early bleeding was defined as postprocedural bleeding in the first 24 hours. Delayed bleeding was defined as bleeding resulting in a severe drop in hemoglobin (≥2 points), hemodynamic deterioration, and/or the need for endoscopic, radiologic, or surgical intervention, or blood transfusion 24 hours after the procedure. Perforation was defined as mesenteric fat or intra-abdominal space, which is visible through the stomach wall during the procedure.

Patients were followed up with hydration therapy with enteral nutrition turned off in the first 24 hours postprocedurally. Prophylactic antibiotics were not routinely administered for this procedure. The treatment continued with pantoprazole 40 mg/day for 8 weeks after the ESD procedure.

Histopathologic Examination

The resected specimen was fixed to a board using pins following the ESD procedure (Figure 1). It was then referred to pathology in formalin solution. The gastrointestinal tract was examined by specialist pathologists. Early-diagnosed gastric cancer was defined as histologically confirmed gastric adenocarcinoma. Precancerous lesions were classified as low-grade dysplasia (LGD) or high-grade dysplasia (HGD). The grade of adenomatous dysplasia was based on the Vienna classification.[22] The cutoff value for deep submucosal invasion was considered 500 µm. The lesions were divided into 2 groups as follows: well-differentiated (papillary adenocarcinoma and well-differentiated or moderately differentiated tubular adenocarcinoma) and poorly differentiated (poorly differentiated adenocarcinoma and signet ring cell carcinoma). Early-diagnosed gastric cancer curability was assessed according to the latest JGES guidelines.[3] Accordingly, tumors resected as en bloc and R0 were divided into 4 groups.

eCuraA

- Differentiated type, pT1a (presence of submucosal invasion <500 µm relative to the muscularis mucosa), nonulcerated (UL0), no tumor at the horizontal border (HM0), no tumor at the vertical border (VM0), no lymphatic invasion (Ly0), and no venous invasion (V0) tumors or;
- Tumors <2 cm, undifferentiated type, pT1a, UL0, HM0, VM0, Ly0, and V0 tumors, or;
- Tumors <3 cm, markedly differentiated type, pT1a, ulcerated (UL1), HM0, VM0, Ly0, and V0 tumors.

eCuraB

- Tumors <3 cm, differentiated type, and pT1b1(SM1) (presence of >500 µm of submucosal invasion compared with the muscularis mucosa), HM0, VM0, Ly0, and V0 tumors.

eCuraC1

- This group included tumors that met the eCuraA or eCuraB criteria but were not resectable via en bloc resection or HM1-differentiated tumors.

eCuraC-2

- Early-diagnosed gastric cancers that do not fall into the eCuraA, eCuraB, and eCuraC1 groups.

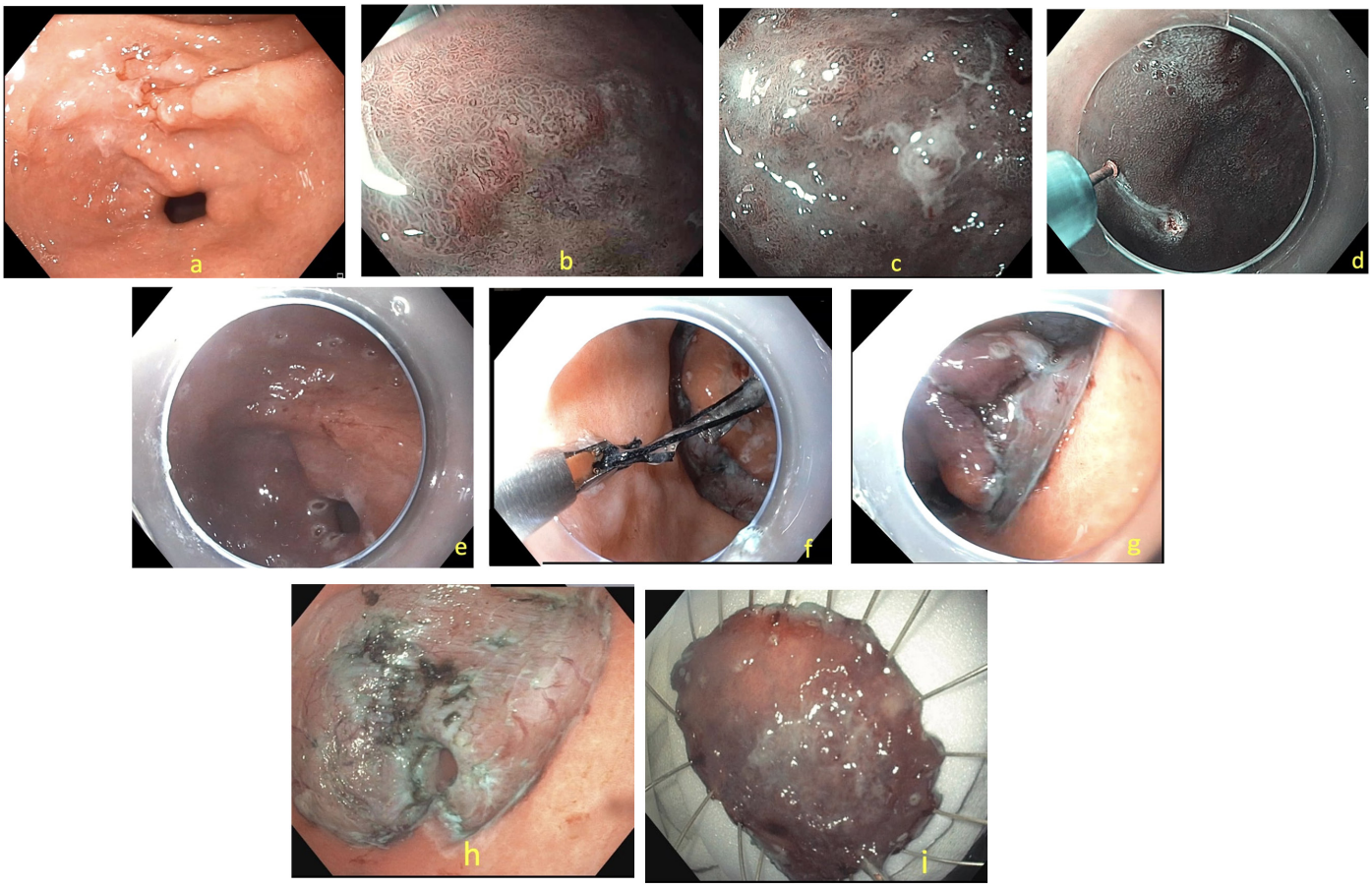

Figure 1. A–J (A) Early gastric cancer on the gastric antrum; (B) irregular surface and vascular pattern; (C) absent surface pattern and vascular pattern; (D) a clear demarcation line; (E) dots were marked around the lesion; (F, G) internal traction method using double clips-with-loop; (H) the post-ESD ulcer; (I) fixation of the lesion; and (J) post-ESD stricture.

Surveillance

Recurrence was defined as the presence of atypical vascular formation or atypical surface pattern on ESD scars, identified through both high-resolution white light and narrow-band imaging (Olympus) during survey endoscopy, and confirmed by histopathological examination. The follow-up period was scheduled as 3-month intervals during the first year, 6-month intervals in the second year, and annual endoscopic control in the following years.

Statistical Analyses

The data were processed using Statistical Package for Social Sciences (IBM SPSS Corp.; Armonk, NY, USA) statistical software (version 28). The data are presented as mean, median, or frequency with range or percentage in parentheses. A univariate analysis was performed using Fisher's exact test for categorical variables; a *P*-value of <.05 was considered statistically significant.

RESULTS

Endoscopic submucosal dissection was performed on 56 gastric lesions from 50 patients during the timeframe decided for the study group. Two patients who underwent ESD for subepithelial lesions, 3 patients who underwent ESD for carcinoid tumors, and 7 patients with a follow-up period <1 year were excluded from the study. Accordingly, 42 gastric neoplasms from 38 patients were included in the study. The mean patient age was 65.92 years (range: 32-88 years). The median CCI score was 2.5 (range: 1-5). Synchronous lesions were observed in 4 patients (10.5%). The mean tumor diameter was 26.39 mm (range: 10-75 mm). Five lesions were localized in the cardia, 1 in the fundus, 16 in the corpus, and 20 in the antrum. Six lesions had a polypoid (Paris Ip/Is) appearance in morphological terms (Table 1). Ulcers were detected in 5 lesions (11.9%). Most procedures (86.8%, 33/38 patients) were performed under general anesthesia. Conventional ESD, pocket creation method, and tunnel method were applied in 27, 6, and 9 lesions, respectively. The traction method was applied in 11 ESD procedures. The median duration of the procedure was 47 minutes (range: 12-190 min). The number (rate) of successful en bloc resection and R0 resection was 41 lesions (97.6%) and 38 lesions (90.4%), respectively. Six patients were discharged on the day of the procedure, and the median length of hospital stay following the ESD procedure was 1 day (range: 1-3 days). Postoperative complications occurred in 5 patients (13.1%). Four patients (10.5%) experienced delayed bleeding, among whom 1 had stenosis. Bleeding and cardiac ESD scar-related stenosis were treated with endoscopic clip application and balloon dilatation, respectively. There were no complications that required surgical treatment. Upon histopathologic examination, 7 lesions were evaluated as LGD, 13 as high HGD, 4 as carcinoma in situ (Tis), 6 as intramucosal cancer, and 7 as submucosal invasive cancer. There was deep submucosal involvement in 4submucosal invasive lesions. The successful number (rate) of curative resection was 8 (61.5%) out of 13 patients with EGC (Table 1). Of the 5 patients without successful curative resection, 1 was

Table 1. Demographic, Endoscopic and Histopathological Data of Early Gastric Cancer Cases

No	Age	Gender	Size	Location	Ulcer	Paris	Patology+	Lm	Vm	D	Lvi	SMI	eCura**	Surgery
1	64	M	20 × 20	Antrum	−	2a	5	−	−	Well	−	+*	C2	−
2	69	M	30 × 25	Corpus	−	2a	5	−	−	Well	−	+	B	−
3	72	M	10 × 8	Antrum	−	2a+2c	5	−	−	Well	−	+	B	−
4	68	F	12 × 10	Corpus	+	2a	5	−	+	Well	+	+*	C2	+
5	54	F	30 × 30	Corpus	−	Ip	4.4	−	−	Well	−	−	A	−
6	67	F	45 × 30	Coprus	−	2a	4.4	+	−	Well	−	−	C1	+
7	76	M	38 × 34	Corpus	−	2a	5	−	−	Well	−	+	B	−
8	77	M	10 × 8	Corpus	+	2a+2c	4.4	−	−	Well	−	−	A	−
9	62	F	10 × 10	Antrum	−	2a	4.4	−	−	Well	−	−	A	−
10	88	M	75 × 40	Antrum	−	1s+2a	4.4	−	−	Well	−	−	A	−
11	63	M	15 × 15	Antrum	−	2a	5	−	−	Well	+	+*	C2	+
12	75	M	25 × 20	Corpus	−	1s	4.4	−	−	Well	−	−	A	−
13	32	F	35 × 30	Cardia	−	1s+2a	5	−	−	Well	+	+*	C2	+

+=The grade of adenomatous dysplasia was based on the Vienna classification. 4.4=Intramucosal carcinoma, 5=Submucosal invasion (SMI) by carcinoma.
*500 micron.
**EGC curability was assessed according to the latest JGES guidelines.[3]
M, male; F, female; SMI, submucosal invasion; Lm, lateral margin; Vm, vertical margin; D, differentiation; Lvi, lymphovascular invasion.

included in the eCura C1 group, and the remaining were included in the eCura C2 group. Complementary surgery was performed in 4 out of 5 patients without successful curative resection. Upon histopathologic examination of the resected specimens, no residue was found in the ESD resection areas. Low-grade dysplasia was observed in synchronous foci in 3 patients and indeterminate dysplasia in 1 patient. Lymph node metastasis was not observed in any patient. The histopathologic correlation between biopsy and diagnosis of ESD was 41.6% (10/24). Compared with the biopsy results, 13 lesions were in more advanced histopathological stages following the ESD procedure and 1 lesion was in an earlier histopathological stage. There was no difference between the prevalence of *Helicobacter pylori* in the 2 groups ($P=.487$). The prevalence in participants was 26.31% (10/38), and it was 38.4% (5/13) in patients with EGC.

Recurrence was observed in 1 patient (2%) and metachronous lesions in 5 patients (13.1%) with a median follow-up of 18 months (range: 12-57 months). There were no ESD-related deaths.

DISCUSSION

This is the first study in Türkiye to investigate the follow-up results of ESD treatment for gastric neoplastic lesions. In the present study, en bloc and R0 resection rates using the ESD method were 97.6% and 90.4%, respectively. The perforation rate was 0%, whereas delayed bleeding was 10.5%.

In a multicenter European cohort study by Bandari et al on gastric ESD with long-term follow-up (median follow-up: 52 months), the en bloc and R0 resection rates were 94.7% and 83.4%, respectively.[15] Based on a meta-analysis by Zullo et al[17], which investigated the efficacy of ESD in the treatment of gastric neoplastic lesions in 22 European centers, the en bloc and R0 resection rates were 96% (95% CI: 93%-98%) and 84% (95% CI: 79%-89%; $I^2=79.9\%$; $P < .001$), respectively. In conclusion, the results of our study are consistent with those of other large Western studies.[14] The results of this study demonstrate that Western endoscopists achieve success rates similar to those in the East.

The complete resection rate is higher with the ESD method than with endoscopic mucosal resection (EMR) in EGC. Because it allows the resection of larger and ulcerated tumors, the ESD method has also contributed to the expansion of the criteria for EMR. Endoscopic mucosal resection has poorer outcomes than ESD for the treatment of early gastric cancers, particularly in patients with broad indications, indicating that ESD should be the method of choice for the treatment of such cancers. The ESD method is associated with a higher risk of complications compared with EMR.[2] The frequency of complications in the patients included in this study was consistent with that of other studies.[12-17] The lack of perforation among the patients included in the present study might be associated with the fact that all the procedures were performed by an endoscopist specializing in ESD.

In the East, preprocedural staging is largely based on endoscopic observation of the lesion, whereas tissue biopsy before ESD is commonly used in the West. Pre-ESD biopsy has limited applicability to Barrett's esophagus, stomach, and duodenum.[23] Moreover, the histopathologic correlation between biopsy and ESD diagnoses was approximately 40% in the present study. This result raises the question of whether diagnostic ESD plays a role in gastric cancer to obtain the most accurate histopathological examination.

The 5-year long-term follow-up results reported by Suzuki et al[8] were indicative of the fact that the ESD method was a reliable treatment for expanding indications in EGC. Nevertheless, data about the efficacy of ESD for extended indications in Western countries are limited. In this study, all but one of the patients with EGC in a limited number of patients were on extended indication. The low rate of curative resection in the present study, with a limited number of patients with EGC, was consistent with that of other Western studies and may be related to expanded indications. However, although the short-term recurrence rate in these patients was low in the present study, the lack of long-term follow-up results is a major limitation. Therefore, whether the extended criteria can be transferred to patients in Türkiye should not be decided based only on the results of the present study.

The fact that the present study was a single-center retrospective study with a limited number of patients is an important limitation. Nevertheless, this study is important, as it is the first study on gastric ESD in Türkiye. In clinical practice, 2 conditions (size and ulceration) are evaluated via macroscopy before ESD in EGC. Nevertheless, ulceration is determined based on endoscopic findings.[24] Occasionally, misinterpretation of endoscopic ulcerations may lead to more aggressive treatment; therefore, precise identification of the ulceration is important

when choosing endoscopic resection or surgery. Accordingly, ulcers were evaluated only endoscopically in this study. This is another limitation of the present study. However, endoscopic resection for confirmatory diagnosis before gastrectomy may be an option to consider given the higher rate of discordance between endoscopic and pathologic findings vis-a-vis ulceration.

Endoscopic submucosal dissection is an efficient and safe treatment for gastric neoplastic lesions. Care should be taken in such patients regarding bleeding in the delayed period. The curative resection rate for EGC has been found to be low in our study. This may be due to the difficulty in recognizing lesions at an early stage. In this context, it has been suggested that the more frequent use of chromoendoscopy, which aids in the recognition of lesions, should be promoted in our country.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Ege University (Date: April 25, 2024, Number: 24-4.1T/67).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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