

Open Access

Endoscopic Submucosal Dissection for Early Gastric Neoplasia Occurring in the Remnant Stomach after Distal Gastrectomy

Ji Young Lee, Byung-Hoon Min, Jung Gyu Lee, Donghyo Noh, Jun Haeng Lee, Poong-Lyul Rhee and Jae J. Kim

Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Background/Aims: Endoscopic submucosal dissection (ESD) for tumors occurring in the remnant stomach is technically difficult to perform because of limited working space and severe fibrosis and staples present around the suture line. We aimed to elucidate the feasibility and clinical outcomes of performing ESD for tumors in the remnant stomach.

Methods: Between December 2007 and January 2013, 18 patients underwent ESD for tumors (six adenomas and 12 differentiated-type early gastric cancers [EGCs]) occurring in the remnant stomach after distal gastrectomy. Clinicopathologic features and clinical outcomes after ESD were retrospectively analyzed.

Results: Two-thirds of the lesions were located on the body, and half were located on the suture line. *En bloc* resection, R0 resection, and *en bloc* with R0 resection rates were 88.9%, 100%, and 88.9%, respectively. Curative resection rate for EGC was 91.7%. Perforation occurred in one patient (5.6%) and was successfully managed by endoscopic closure with metallic clips and conservative management. There was no significant bleeding after ESD. During a median follow-up of 47.5 months, no local, metachronous, or extragastric recurrence was seen for either EGC or adenoma lesions.

Conclusions: ESD is a feasible and effective treatment modality and can be considered a primary intervention for early gastric neoplasia occurring in the remnant stomach. **Clin Endosc 2016;49:182-186**

Key Words: Endoscopic submucosal dissection; Gastric stump; Gastric tumor

INTRODUCTION

After subtotal gastrectomy for gastric cancer, patients are at risk for occurrence of metachronous tumors in the remnant stomach. Patients who underwent distal gastrectomy more than 20 years ago for benign diseases such as peptic ulcer are also at risk for cancer occurrence in the remnant stomach. Therefore, periodic surveillance endoscopy is currently recommended for these patients.¹ Because of this surveillance program, the detection of early gastric cancer (EGC) or early

gastric neoplasia such as high-grade dysplasia (HGD) in the remnant stomach is increasing. Given the morbidity and mortality associated with total gastrectomy,² endoscopic submucosal dissection (ESD) can be an attractive alternative to radical surgery for these lesions. However, performing endoscopic treatment in the remnant stomach is technically difficult because of limited working space and severe fibrosis and staples being present around the suture line.³ Therefore, ESD for tumors in the remnant stomach is not yet common, and data are still limited.⁴ In this study, we elucidated the feasibility and clinical outcomes of ESD for tumors occurring in the remnant stomach after distal gastrectomy.

MATERIALS AND METHODS

Patients

Between December 2007 and January 2013, 18 patients underwent ESD for tumors (six adenomas with HGD and 12

Received: March 19, 2015 Revised: October 27, 2015

Accepted: November 14, 2015

Correspondence: Byung-Hoon Min

Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 06351, Korea
Tel: +82-2-3410-3409, Fax: +82-2-3410-6983, E-mail: bhmin@skku.edu

© This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

differentiated-type EGCs) occurring in the remnant stomach after distal gastrectomy at the Samsung Medical Center. ESD for EGC was performed based on the Japanese Gastric Cancer Treatment Guidelines.⁵ All ESDs were performed by three experienced endoscopists (B.H.M., J.H.L., and J.J.K.). We retrospectively reviewed the outcomes after ESD in 18 consecutive patients who were identified from a prospectively collected database. ESD procedures of our institution are described in detail elsewhere.⁶ In brief, ESD consisted of three steps: (1) injecting fluid into the submucosal layer to separate it from the proper muscle layer, (2) circumferential cutting of the mucosa surrounding the lesion, and (3) submucosal dissection of the connective tissue under the lesion with an electrosurgical knife. During the procedure, surgical staples were removed by using coagrasper or alligator. We mainly used IT knife (KD-610L; Olympus, Tokyo, Japan) or IT knife-2 (KD-611L; Olympus) for submucosal dissection. However, in cases of submucosal fibrosis around the suture line, submucosal dissection was performed with needle knife (MTW Endoscopy, Wesel, Germany) or dual knife (KD-650L; Olympus) after sufficient submucosal injection around the fibrotic area. The study protocol was approved by the Institutional Review Board at Samsung Medical Center.

Follow-up after EMR or ESD

Esophagogastroduodenoscopy (EGD) with a biopsy was performed 2 months after ESD to confirm healing of the ESD-induced artificial ulcer and to exclude the presence of any residual tumor. In EGC cases, EGD with a biopsy and abdominal computed tomography (CT) were performed every 6 months thereafter for 3 years to detect local, metachronous, or extragastric recurrence. After 4 to 5 years of performing ESD for EGC, EGD with a biopsy and abdominal CT were performed annually. In cases of adenoma with HGD, EGD with a biopsy was performed annually.

Definition

En bloc resection was defined as resection of the tumor in one piece with no endoscopically residual tumor. R0 resection was defined as tumor resection with no histological evidence of cancer cells on the lateral or vertical margins. In EGC cases, resection was judged as curative when all of the following conditions were fulfilled: well-differentiated or moderately differentiated EGC or papillary EGC, *en bloc* resection or piecemeal resection with successful reconstruction, negative lateral resection margins, negative vertical resection margin, no lymphovascular invasion and: (1) tumor size ≤ 2 cm, mucosal cancer, no ulcer in tumor (EGC meeting absolute indication); (2) tumor size > 2 cm, mucosal cancer, no

ulcer in tumor; (3) tumor size ≤ 3 cm, mucosal cancer, ulcer in tumor, or (4) tumor size ≤ 3 cm, SM1 cancer (submucosal invasion depth < 500 μm from muscularis mucosa layer). *En bloc* resection and R0 resection rates were assessed in both the adenoma with HGD and differentiated-type EGC cases. Curative resection rate was assessed only in EGC cases. Bleeding was defined as (1) intraoperative massive bleeding that required blood transfusion, (2) postoperative bleeding that required blood transfusion or endoscopic or surgical intervention because of hematemesis or melena, or (3) a greater than 2 g/dL decrease in the hemoglobin level after the procedure. Perforation was diagnosed when the mesenteric

Table 1. Clinicopathologic Features of the Patients Undergoing Endoscopic Dissection for Tumors Occurring in the Remnant Stomach after Distal Gastrectomy

Variable	Value
Patients/tumors	18/18
Age, yr	72 (52–81)
Sex	
Male	17 (94.4)
Female	1 (5.6)
Type of previous gastrectomy	
Billroth I	17 (94.4)
Billroth II	1 (5.6)
Tumor location	
Cardia	4 (22.2)
Fundus	2 (11.1)
Body	12 (66.7)
Tumor located on the suture line	9 (50.0)
Tumor located on the anastomosis site	0
Macroscopic type	
Elevated	6 (33.3)
Flat or depressed	12 (66.7)
Tumor size, mm	13 (4–22)
Histologic type	
High-grade dysplasia	6 (33.3)
Differentiated-type early gastric cancer	12 (66.7)
Tumor depth	
High-grade dysplasia	6 (33.3)
Mucosal cancer	9 (50.0)
Submucosal cancer	3 (16.7)
Lymphovascular invasion among 12 cancers	
Negative	11 (91.7)
Positive	1 (8.3)

Values are presented as median (range) or number (%).

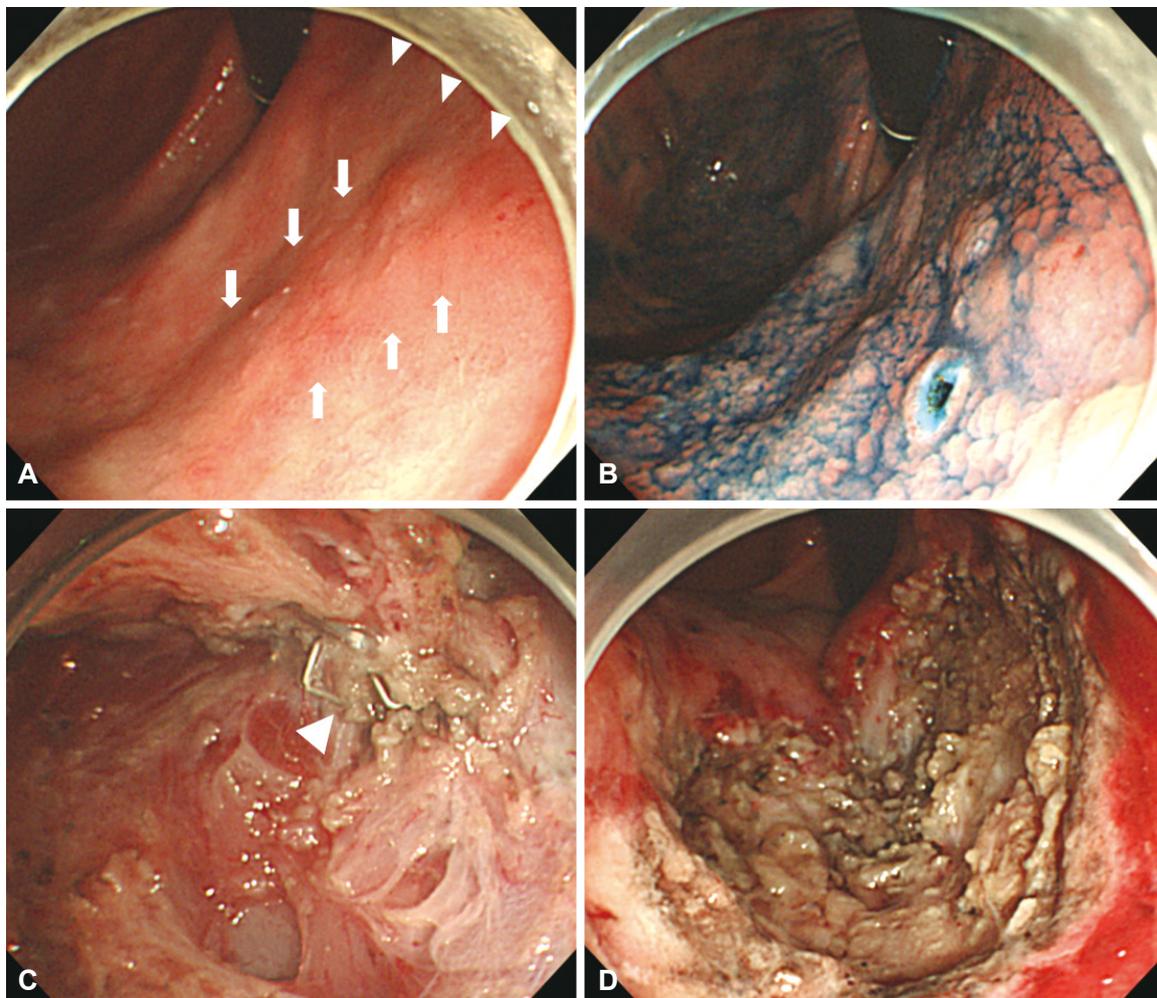


Fig. 1. (A) A 1.5-cm, flat, elevated-type early gastric cancer (arrows) is noted on the suture line (arrowheads) of the lesser curvature of high body in the remnant stomach. (B) Chromoendoscopy with indigo carmine dye. (C) Dissection of the submucosal layer after circumferential incision of the mucosa. Staples (arrowhead) and severe fibrosis are observed around the suture line. (D) The tumor is completely removed by *en bloc* resection.

fat or intra-abdominal space was observed directly during the procedure (frank perforation), or if free air was found on performing plain chest radiography after the procedure without a visible gastric wall defect noted during the procedure (microperforation).

RESULTS

Patients and tumor characteristics

Table 1 summarizes the clinicopathologic characteristics of the enrolled patients and tumors. Median tumor size was 13 mm. Two-thirds of the lesions were located on the body, and half were located on the suture line due to the previous gastrectomy (17 Billroth I and 1 Billroth II gastrectomy) (Fig. 1). No lesions involved the anastomosis site. The median period between previous gastrectomy and ESD was 80 months (range, 14 to 207) in cases of Billroth I and was 13 months in case of

Billroth II.

Outcomes and complications of ESD

Table 2 summarizes the clinical outcomes of ESD for tumors occurring in the remnant stomach after distal gastrectomy. *En bloc* resection, R0 resection, and *en bloc* with R0 resection rates were 88.9%, 100%, and 88.9%, respectively. Two EGCs were resected in piecemeal fashion with one lesion located on the suture line. Among 12 enrolled patients with EGC, curative resection was achieved for 11 cases (91.7%). Eight EGCs met the absolute indication criteria, and three met expanded indication criteria. One patient had EGC with a lymphatic invasion and a submucosal invasion up to 900 μ m and underwent completion total gastrectomy after ESD. Perforation occurred in one patient and was successfully managed by endoscopic closure with metallic clips and conservative management. In this patient, the lesion was not located on the suture line. Tumors located on the suture line

Table 2. Outcomes of Endoscopic Submucosal Dissection

Variable	Value
<i>En bloc</i> resection	16 (88.9)
R0 resection	18 (100.0)
<i>En bloc</i> with R0 resection	16 (88.9)
Curation resection among 12 cancers	11 (91.7)
Complication	
Perforation	1 (5.6)
Bleeding	0
Procedure time, min	
Tumor located on the suture line	102.6±58.2
Tumor not involving the suture line	69.1±52.3

Values are presented as number (%) or mean±SD.

showed longer procedure time than tumors not involving the suture line, although the difference between the two groups did not reach statistical significance ($p=0.218$). During the median 47.5 months of follow-up, no local, metachronous, or extragastric recurrence was seen for either EGC or adenoma with HGD lesions.

DISCUSSION

ESD for EGC in the remnant stomach after distal gastrectomy is technically demanding because of the limited working space in which the surgery is performed and because of severe fibrosis and staples present around the suture line. Despite these limitations and the high frequency of lesions on the suture line where submucosal dissection was difficult, *en bloc* resection rate and R0 resection rate in the present study were 88.9% and 100%, respectively. In addition, perforation occurred in only one patient during the procedure (5.6%). These favorable results showed the efficacy and safety of ESD for tumors occurring in the remnant stomach after distal gastrectomy. Previous studies showed that surgical resection for remnant gastric cancers involved high post-operative morbidity ranging from 19% to 41%.^{2,7} Given this high morbidity associated with surgery and the favorable results of endoscopic treatment shown in this study, ESD can be considered an effective alternative treatment modality to completion total gastrectomy.

In addition to high *en bloc* resection and R0 resection rates, this study showed favorable long-term outcomes. During a median follow-up of 47.5 months, no local, metachronous, or extragastric recurrence was seen in either EGC or adenoma with HGD lesions. Additionally, previous studies showed favorable long-term outcomes after ESD for EGC in the rem-

nant stomach. Lee et al.⁸ reported that no local recurrence was seen after ESD for EGC or dysplasia occurring in the remnant stomach. Nonaka et al.³ reported that the 5-year overall and cause-specific survival rates after ESD for EGC in the remnant stomach were 87.3% and 100%, respectively. During the median follow-up of 54 months, the local recurrence rate was 1.6%, and the metachronous recurrence rate was 6.3%.

Previous studies showed that the perforation rate of ESD for tumors in the remnant stomach ranged from 0% to 13%.^{9,10} Several studies including both tumors occurring in the remnant stomach and tumors in gastric conduit after esophagectomy argued that tumors on the suture line are at higher risk of perforation compared to tumors not involving the suture line.¹¹ However, studies only including tumors occurring in the remnant stomach showed comparable perforation rate between the two groups.¹⁰ In the present study, we experienced only one case of perforation, which did not involve the suture line. As previous studies show inconsistent results, further large studies are required to identify whether tumor location on the suture line is associated with a higher risk of perforation during ESD.

Recently, stapled anastomosis method is more commonly used than hand-suture in distal gastrectomy. In surgical procedure of subtotal gastrectomy, surgeons transect the distal stomach that is to be resected and complete the gastrojejunostomy with the linear stapler. After performing anastomosis by using stapler, suture line with stapling material is usually located in the lesser curvature side of the remnant stomach and around gastrojejunostomy site.^{12,13} Therefore, performing ESD for the remnant stomach lesion around these sites is frequently technically demanding. As submucosal dissection is usually very difficult with the stapling material present, it would be better to remove the surgical staples with a device such as alligator when they are found during the procedure.

In this study, tumors located on the suture line showed longer procedure time than tumors not involving the suture line (mean, 102.6 minutes vs. 69.1 minutes). This result indicated the difficulty of submucosal dissection for tumors on the suture line likely because of the massive fibrosis and staples around the suture line.

The present study demonstrated that ESD is a feasible and effective treatment modality for early gastric neoplasia occurring in the remnant stomach after distal gastrectomy for the following reasons: (1) high *en bloc* resection rate and R0 resection rates, (2) low complication rate, and (3) no local, metachronous, or extragastric recurrence during the follow-up period. Owing to the high morbidity associated with completion total gastrectomy, ESD can be considered a primary intervention for early gastric neoplasia occurring in the remnant stomach. Given the small number of enrolled patients and the

relatively short follow-up period in this study, further large studies with long-term follow-ups are required to confirm our results.

Conflicts of Interest

The authors have no financial conflicts of interest.

REFERENCES

1. Nozaki I, Nasu J, Kubo Y, Tanada M, Nishimura R, Kurita A. Risk factors for metachronous gastric cancer in the remnant stomach after early cancer surgery. *World J Surg* 2010;34:1548-1554.
2. Sasako M, Maruyama K, Kinoshita T, Okabayashi K. Surgical treatment of carcinoma of the gastric stump. *Br J Surg* 1991;78:822-824.
3. Nonaka S, Oda I, Makazu M, et al. Endoscopic submucosal dissection for early gastric cancer in the remnant stomach after gastrectomy. *Gastrointest Endosc* 2013;78:63-72.
4. Ojima T, Takifuji K, Nakamura M, et al. Endoscopic submucosal dissection for gastric tumors in various types of remnant stomach. *Endoscopy* 2014;46:645-649.
5. Oh SJ, Hong JJ, Oh CA, et al. Stapling technique for performing Billroth II anastomosis after distal gastrectomy. *J Gastrointest Surg* 2011;15:1244-1246.
6. Min BH, Lee JH, Kim JJ, et al. Clinical outcomes of endoscopic submucosal dissection (ESD) for treating early gastric cancer: comparison with endoscopic mucosal resection after circumferential precutting (EMR-P). *Dig Liver Dis* 2009;41:201-209.
7. Piso P, Meyer HJ, Edris C, Jähne J. Surgical therapy of gastric stump carcinoma: a retrospective analysis of 109 patients. *Hepatogastroenterology* 1999;46:2643-2647.
8. Lee JY, Choi IJ, Cho SJ, et al. Endoscopic submucosal dissection for metachronous tumor in the remnant stomach after distal gastrectomy. *Surg Endosc* 2010;24:1360-1366.
9. Hirasaki S, Kanzaki H, Matsubara M, Fujita K, Matsumura S, Suzuki S. Treatment of gastric remnant cancer post distal gastrectomy by endoscopic submucosal dissection using an insulation-tipped diathermic knife. *World J Gastroenterol* 2008;14:2550-2555.
10. Takenaka R, Kawahara Y, Okada H, et al. Endoscopic submucosal dissection for cancers of the remnant stomach after distal gastrectomy. *Gastrointest Endosc* 2008;67:359-363.
11. Nishide N, Ono H, Kakushima N, et al. Clinical outcomes of endoscopic submucosal dissection for early gastric cancer in remnant stomach or gastric tube. *Endoscopy* 2012;44:577-583.
12. An JY, Yoon SH, Pak KH, et al. A novel modification of double stapling technique in Billroth I anastomosis. *J Surg Oncol* 2009;100:518-519.
13. Seo SH, Kim KH, Kim MC, Choi HJ, Jung GJ. Comparative study of hand-sutured versus circular stapled anastomosis for gastrojejunostomy in laparoscopy assisted distal gastrectomy. *J Gastric Cancer* 2012;12:120-125.