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SHORT COMMUNICATION

Endoscopic submucosal dissection for early gastric cancer in anastomosis site after distal gastrectomy

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Abstract
Background Detection of early gastric cancer (EGC) in the remnant stomach is increasing because of follow-up endoscopic surveillance programs. Endoscopic treatment appears to be desirable for EGC in the remnant stomach because it is less invasive than surgical resection.
Methods In this retrospective study, to evaluate the feasibility of endoscopic submucosal dissection (ESD) for EGC in an anastomotic site, treatment results of ESD for EGC in an anastomotic site and in remnant stomach not involving an anastomotic site were compared. In total, 11 EGC lesions of anastomotic sites in 11 patients and 22 EGC lesions of remnant stomach not involving an anastomotic site in 21 patients were treated by ESD.
Results All lesions were successfully treated by en bloc resection. There were three patients with perforations in the anastomotic site group. Although resected specimen size and tumor size were larger in the anastomotic site group than in the non-anastomotic site group ($P < 0.01$), the procedure duration was far longer in the anastomotic site group than in the non-anastomotic site group ($P < 0.01$). The speed of the procedure was faster in the non-anastomotic site group than in the anastomotic site group ($P < 0.05$).
Conclusions Although ESD for EGC in an anastomotic site is a time-consuming procedure and requires advanced techniques compared with ESD for EGC not involving an anastomotic site, a high en bloc resection rate was achieved. ESD by endoscopists with sufficient experience appears to be a feasible treatment for EGC in an anastomotic site.

Keywords ESD · Gastric cancer · Anastomosis site · Distal gastrectomy · Remnant stomach

Introduction

Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) have been widely accepted as standard treatments for early gastric cancer (EGC) in Japan [1]. ESD offers advantages in terms of the shape and size of the resectable lesions compared with conventional EMR and has enabled successful en bloc resection of various cancers [2–4]. Several reports have indicated that a high en bloc resection rate was achieved by ESD in the remnant stomach, despite some technical difficulties [5–9]. Lesions located at anastomotic sites are expected to be much more difficult because there are severe fibrosis and staples from the previous surgery, and because there is the need for resection of duodenal or small intestinal mucosa.

To our knowledge, the feasibility of ESD for EGC in an anastomotic site has not been fully studied. In this retrospective study, we evaluated the treatment results of ESD for EGC in an anastomotic site compared with ESD for EGC in remnant stomach not involving an anastomotic site.

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Materials and methods

Patients

From April 2008 through April 2012, 11 EGC lesions of anastomotic sites in 11 patients and 22 EGC lesions of remnant stomach not involving an anastomotic site in 21 patients were treated by ESD at Kobe University Hospital. EGC in an anastomotic site was defined as a lesion expanding to an anastomotic site or a lesion requiring resection including an anastomotic site.

The indications for ESD were EGC lesions that meet the criteria for EMR proposed by the Japanese Gastric Cancer Society [10]. The clinicopathological features and procedural details of ESD were obtained from a prospectively collected database. Before endoscopic treatment, written informed consent was obtained from all patients, after explanation of the possible risks and complications of the procedures, anticipated results, and alternative approaches including surgery.

ESD procedure

ESD was carried out with a Flush Knife-BT (DK-2618JN; FTS, Tokyo, Japan), through a conventional single-channel endoscope (GIFQ240, Q260; Olympus) (Fig. 1). In all cases of ESD, the length of the Flush Knife-BT was 2.5 mm. A transparent hood (D-201-10704; Olympus) was mounted on the tip of the endoscope to maintain a clear operative field. In cases of severe fibrosis in particular, a small-caliber-tip transparent hood (ST hood) (DH-16CR; Fujinon Optical) and a Flush Knife 1.0 mm in length (DK2618JN10; FTS) were used at the endoscopist's discretion. VIO 300D (ERBE Elektromedizin, Tübingen, Germany) was used as the power source for electrical cutting and coagulation.

The procedure time was defined as the time from the beginning of marking to the completion of resection.

Complications

Bleeding after ESD was defined as requiring endoscopic hemostasis or other measures to affect hemostasis. When Hb fell by 2 g/dl or more compared with the last preoperative level, or when there was any other apparent source of bleeding or massive melena, this was also defined as bleeding after ESD [11]. Perforation was diagnosed endoscopically during endoscopic treatment or was diagnosed by the presence of free air on abdominal plain radiography or computed tomography (CT).

Statistical analysis

Statistical analyses were conducted using SPSS Statistics 18.0 (SPSS, Chicago, IL, USA). Proportions of categorical variables were compared using two-sided Fisher's exact test and chi-square test. Continuously distributed variables were compared using Student's t test, and noncontinuous variables were assessed using Wilcoxon's rank-sum test. Values of $P < 0.05$ were considered significant.

Results

Clinicopathological features and clinical outcomes

The clinicopathological features and clinical outcomes of 11 patients with EGC in an anastomotic site treated by ESD are shown in Table 1. All lesions were successfully treated by en bloc resection. There were 3 patients with perforations. Two patients did not require emergency surgery because the peritonitis was controlled in the localized area and was improved by antibiotics. However, 1 patient underwent emergency surgery because of panperitonitis. Tumor size in patients with perforation was larger than that in patients without perforation ($P < 0.05$).

Comparison of the patients between anastomosis site and non-anastomosis site

A comparison of the clinical features and endoscopic findings of the patients between the anastomotic site and non-anastomotic site groups is shown in Table 2. There were no significant differences in age, sex, and the grade of American Society of Anesthesiologists (ASA) Physical Status Classification between the two groups. Although the proportion of patients who underwent Billroth II reconstruction in the anastomotic site group was greater than that in the non-anastomotic site group, no significant difference was found. There were no cases of Roux-en-Y (R-Y) reconstruction in either group. The interval from previous surgery was longer in the anastomotic site group than in the non-anastomotic site group ($P < 0.01$). In terms of the reason for previous surgery, the proportion with malignancy was higher in the non-anastomotic group than in the anastomotic group ($P < 0.05$). Morphological types of EGC were mainly 0-IIa in both groups.

A comparison of the pathological features and clinical outcomes of the patients between the anastomotic site and non-anastomotic site groups is shown in Table 3. Although resected specimen size and tumor size were larger in the anastomotic site group than in the non-anastomotic site group ($P < 0.01$), the procedure duration was far longer in the anastomotic site group ($P < 0.01$). The procedure speed was faster in the non-anastomotic site group than in the anastomotic site group ($P < 0.05$). All lesions in both groups were successfully treated by en bloc resection. There were three patients with perforations only in the

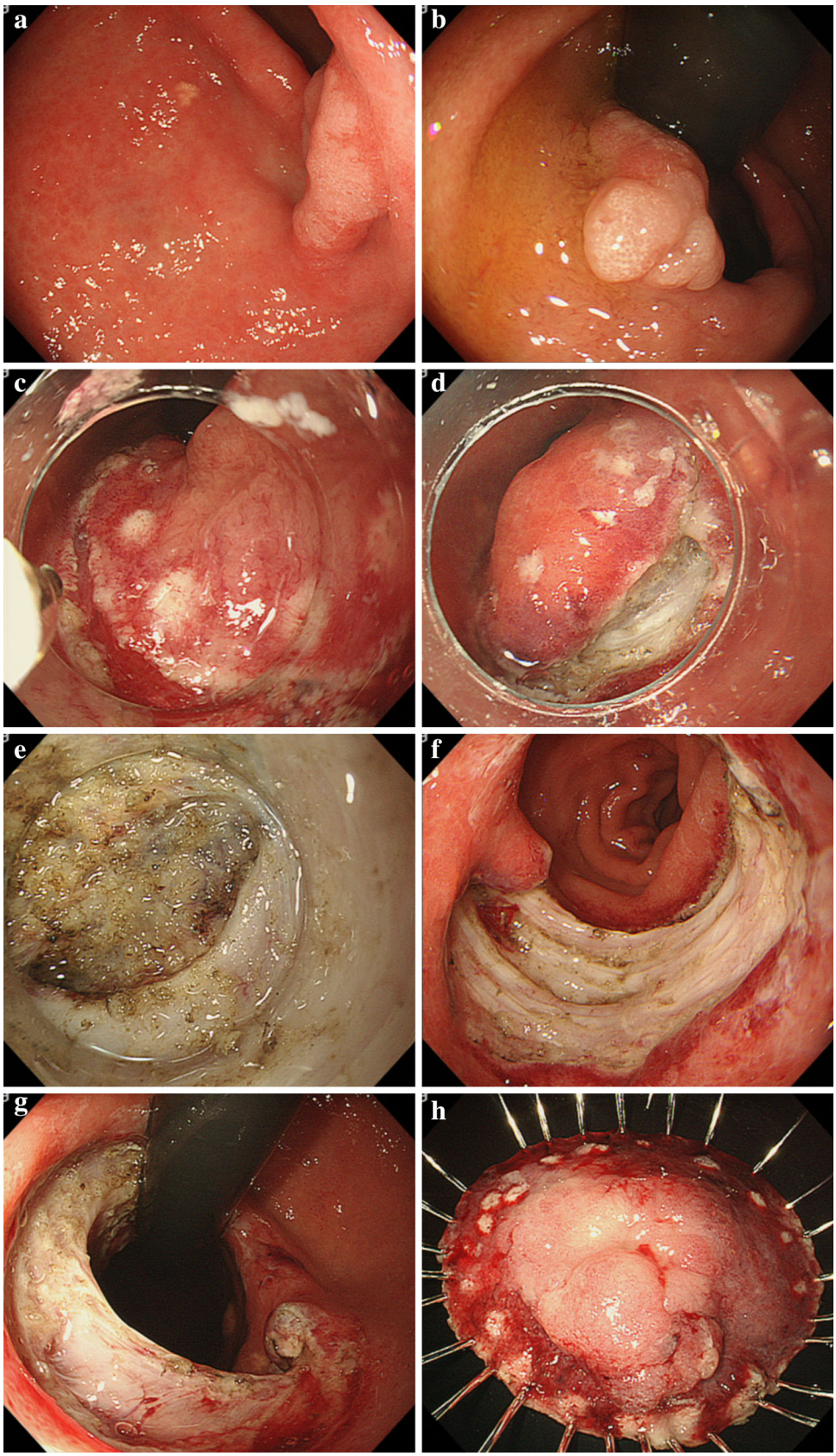

Fig. 1 Endoscopic submucosal dissection (ESD) procedure for lesion located at an anastomotic site. **a** The whitish protruding lesion located at anastomosis. **b** The lesion expanded to the duodenal side. **c** Incision at the oral side by forward manipulation. **d** Incision at the anal side by inverted manipulation. **e** Submucosal layer at anastomosis had severe fibrosis. **f**, **g** Ulceration after ESD. **h** Complete removal was achieved

Table 1 Clinicopathological features and clinical outcomes of 11 patients with early gastric cancer (EGC) in anastomotic site treated by endoscopic submucosal dissection (ESD)

Case	Age (years)	Sex	ASA physical status classification	Reconstruction	Interval from previous surgery (years)	Reason for previous surgery	Morphological type	Resected specimen size (mm)	Tumor size (mm)	Procedure duration (min)	Procedure speed (mm^2/min)	Histological type	Depth of invasion	Presence of ulceration	Resection	Complication
1	79	Male	3	B-II	35	Gastric cancer	0-IIa + IIc	60	18	209	9	Differentiated	SM2	Absent	En bloc	None
2	68	Male	1	B-I	4	Gastric cancer	0-IIa	39	13	91	10.1	Differentiated	M	Absent	En bloc	None
3	77	Male	2	B-II	2	Bile duct cancer	0-IIc	60	15	203	9.4	Differentiated	M	Absent	En bloc	None
4	68	Female	2	B-II	35	Gastric ulcer	0-IIc	53	11	145	16.4	Differentiated	M	Present	En bloc	None
5	60	Male	2	B-II	40	Duodenal ulcer	0-IIa	40	15	102	9.2	Differentiated	M	Present	En bloc	None
6	77	Male	1	B-I	38	Gastric cancer	0-IIa	79	48	369	12.1	Differentiated	M	Absent	En bloc	None
7	70	Male	1	B-I	44	Duodenal ulcer	0-IIa + IIc	58	39	396	4.1	Differentiated	SM2	Absent	En bloc	None
8	84	Male	2	B-II	36	Gastric ulcer	0-IIa	64	18	120	19.2	Differentiated	M	Absent	En bloc	None
9	72	Male	2	B-II	23	Gastric cancer	0-IIa	97	65	165	25.4	Differentiated	M	Present	En bloc	Perforation
10	65	Male	1	B-II	16	Gastric cancer	0-IIa	58	48	345	7.5	Differentiated	SM2	Absent	En bloc	Perforation
11	72	Male	3	B-II	30	Gastric cancer	0-IIa	80	67	399	6.5	Differentiated	M	Absent	En bloc	Perforation

Table 2 Clinical features and endoscopic findings of patients with EGC in anastomotic site and non-anastomotic site

	Anastomosis site ($n = 11$)	Non-anastomosis site ($n = 22$)	P value
Age (years)	72 ± 6.9 (60–84)	70.4 ± 7.0 (56–82)	NP*
Sex (male/female)	10/1	2/19	NP**
ASA physical status classification	2 (1–3)	2 (1–4)	NP***
Reconstruction (Bil-I/Bil-II)	3/8	11/10	NP**
Interval from previous surgery (years)	27.5 ± 14.4 (2–44)	11.8 ± 11.4 (1–44)	<0.01*
Reason for previous surgery	7/4	17/4	<0.05**
Morphological type			
0-IIa	7	17	
0-IIc	2	4	
0-IIb	0	1	
0-IIa + IIc	2	0	

Data represent n, mean ± SD (range), or median (range)

B–I Billroth I, *B-II* Billroth II

Data were evaluated with the * two-sample t test, ** Fisher's exact test, or *** Wilcoxon rank-sum test as appropriate

anastomotic site group. Bleeding occurred in one patient in the non-anastomotic site group. Although this patient needed a blood transfusion, neither emergency surgery nor transcatheter arterial embolization was carried out.

Discussion

In this study, we needed much time to complete ESD of EGC in anastomotic sites and frequently experienced perforation. These results indicate the greater difficulty of ESD in anastomotic sites than for ESD in non-anastomotic sites. Nevertheless, en bloc resection was achieved in all cases in the anastomotic group in this study, although the number of cases was small. There are two possible reasons to explain this high en bloc resection rate. One is that all procedures were performed by two expert endoscopists with substantial experience of ESD (more than 1,000 cases). We consider that it is necessary for the operator to have at least sufficient technical ability to treat severe fibrosis safely and to control the scope precisely in a limited working space. The other reason is that appropriate devices were selected according to the situation. To overcome limited space, we use mainly the Flush Knife-BT to enable more precise manipulation. Although many endoscopists use the IT knife (Olympus Medical Systems) when performing gastric ESD, we consider that an electroknife

Table 3 Pathological features and clinical outcomes of patients with EGC in the anastomosis site or non-anastomosis site

	Anastomosis site ($n = 11$)	Non-anastomosis site ($n = 22$)	P value
Resected specimen size (mm)	60 (39–97)	42 (18–58)	<0.01*
Tumor size (mm)	21.5 (11–67)	15 (4–38)	<0.05*
Procedure duration (min)	203 (91–399)	62.5 (23–185)	<0.01*
Procedure speed (mm^2/min)	9.4 (4.1–25.4)	16.2 (6.7–30.4)	<0.05*
Histological type			
Differentiated	11	22	NP
Depth of invasion			
M	8	17	
SM1	0	3	
SM2	3	2	
Presence of ulceration	3	2	NP**
En bloc resection	11	22	NP**
En bloc with R0 resection	9	22	<0.01**
Complication			
Perforation	3	0	<0.01**
Bleeding	0	1	NP**
Emergency surgery	1	0	NP**

Data represent n, mean ± SD (range), or median (range)

SM submucosa, *M* mucosa

Data were evaluated with the * Wilcoxon rank sum test, or ** Fisher's exact test as appropriate

with a blade on its tip such as the Flush Knife-BT is suitable to adjust to the narrow lumen in a remnant stomach, especially at an anastomotic site, as is the case in the esophagus or the colorectum. In addition, in cases of severe fibrosis, we used the ST hood and a 1.0-mm-long Flush Knife. Previous studies reported that the ST hood and Flush Knife were effective for safe dissection in cases of severe fibrosis [12, 13]. In this study, we used the ST hood in three patients and a Flush Knife 1.0 mm in length in four patients.

Three perforations occurred at the small intestine in the anastomotic site group. Two perforations occurred in the procedure of dissecting and one perforation occurred by pressing of an endoscope upon inverted manipulation. Forward manipulation of the endoscope should be performed as much as possible in the duodenum or small intestine to avoid perforation because inverted manipulation conveys the risk of exerting strong pressure on the thin duodenal or small intestinal wall. Additionally, all perforation cases occurred in Billroth II reconstruction. Severe fibrosis by reflex bile acids and the narrower lumen in Billroth II reconstruction might make the procedure more complicated than in Billroth I construction. Therefore, Billroth II cases should be more carefully treated.

Perforation in remnant stomach is likely to cause peritonitis. Therefore, rapid endoscopic treatment for perforation is essential for minimizing complications. In our study, although all three patients who experienced perforation were immediately treated by endoscopic closure with a clip, one case required emergency surgery because the endoscopic closure was incomplete because of locational difficulty.

Among three patients diagnosed with SM2 invasion after ESD, two underwent an operation and one was followed closely without undergoing an operation. All three patients have been free of recurrence. In addition, the other patients could achieve relapse-free survival.

In conclusion, although ESD for EGC in an anastomotic site is a time-consuming procedure and requires advanced techniques compared with ESD for EGC not involving an anastomotic site, a high en bloc resection rate was achieved. ESD by endoscopists with sufficient experience appears to be a feasible treatment for EGC in an anastomotic site.

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