Risk factors and management for gastric stenosis after endoscopic submucosal dissection for gastric epithelial neoplasm

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Abstract

Background Only a few studies have reported treatment options for stenosis after endoscopic submucosal dissection (ESD) for gastric neoplasms. This study aimed to identify the risk factors for and evaluate the management of stenosis after ESD for gastric epithelial neoplasms in the cardia and antrum.

Methods We retrospectively reviewed 1218 patients (1447 gastric epithelial neoplasms) who underwent ESD at Tonan Hospital from June 2004 to November 2015. Post-ESD stenosis was defined when a standard endoscope could not be passed through the site.

Results Post-ESD stenosis occurred in 10 (21.3%) of the 47 cardia cases and 14 (3.2%) of the 432 antrum cases. A wide resection of more than three fourths of the circumferential extent was the sole significant risk factor related to post-ESD stenosis in both cardia and antrum. Prophylactic endoscopic balloon dilation (EBD) was performed in 3 of 10 patients with cardiac stenosis and 4 of 14 with antral stenosis. Post-EBD bleeding occurred in one cardia (10%) and one antrum (7.1%) case each and was endoscopically treated. Perforation during EBD occurred in two (14.3%) antrum cases, both of which required emergency open surgery. All complications were observed in patients with

conventional EBD, and no complications were associated with prophylactic EBD.

Conclusions A wide resection of more than three fourths of the circumferential extent was the significant risk factor for post-ESD stenosis in both cardia and antrum, and prophylactic EBD could be a promising procedure for the management of post-ESD stenosis.

Keywords Early gastric cancer · Endoscopic submucosal dissection (ESD) · Endoscopic balloon dilation (EBD) · Gastric stenosis · Prophylactic endoscopic balloon dilation

Introduction

Although endoscopic resection is a useful treatment option for gastric epithelial neoplasms with a negligible risk of lymph node metastasis, its indication was previously limited to small (<2 cm) intramucosal lesions without ulceration owing to the technical limitations of conventional endoscopic mucosal resection [1–3]. To overcome this limitation, endoscopic submucosal dissection (ESD) was developed to enable en bloc resection of gastric neoplasms irrespective of size or ulceration within the lesion, resulting in a precise histological assessment of the resected specimen and reducing the risk of local recurrence [4–6]. Moreover, based on the findings of a retrospective analysis of lymph node metastasis in a large number of surgical cases with early gastric cancer (EGC) [7], indications for ESD have been expanded to larger and ulcerative lesions [8]. However, the use of ESD for extensive resection of large lesions, particularly those in the cardia or antrum, often leads to gastric stenosis, thereby decreasing the patient's quality of life [9–12]. Although a few studies have reported that post-ESD stenosis can be well managed by

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endoscopic balloon dilation (EBD), local steroid injection into the post-ESD ulcer, mucosal incision with steroid injection, or oral administration of steroids [9–15], the optimal management for post-ESD stenosis remains controversial because of the high risk of complications associated with EBD, such as bleeding and perforation; also, the number of studies (all single center) investigating the efficacy of local injection and oral administration of steroids is limited, although several publications report good results with esophageal stenosis. Consequently, the present study aimed to identify risk factors and evaluate management options for stenosis after ESD for gastric epithelial neoplasms in the cardia and antrum, which are particularly susceptible to stenosis after gastric ESD.

Patients and methods

Patients

A total of 1218 consecutive patients with 1447 gastric epithelial neoplasms, including EGCs and adenomas, underwent ESD at Tonan Hospital from June 2004 to November 2015. The locations of the lesions in the stomach were 288 in the upper third, 507 in the middle third, and 652 in the lower third. Cardiac resection was defined as extending to esophagogastric junction, and antral resection was defined as localized to the lower third of the stomach, including the gastric angulus and pyloric ring, except for resections that extended to the gastric body. Ninety-one patients with 99 lesions underwent cardiac resection, and 570 patients with 636 lesions underwent antral resection. Among these patients, those with lesions in the gastric tube ($n = 5$), who underwent additional surgery owing to noncurative ESD ($n = 67$), with a lesion that could not be resected ($n = 1$), and who did not undergo initial follow-up esophagogastroduodenoscopy (EGD) after ESD at our hospital ($n = 54$) were excluded. In addition, patients with multiple lesions in the same region ($n = 55$) were excluded. Finally, 47 patients with 47 lesions were enrolled in the cardiac resection group and 432 patients with 432 lesions were involved in the antral resection group (Fig. 1). All patients were ESD naïve.

The medical records of patients in both groups were retrospectively reviewed, and data pertaining to clinico-pathological features, endoscopic images, and endoscopic and histopathological reports were extracted. Written informed consent was obtained from either the patients or their families before ESD. The study protocol was approved by the Institutional Review Board of Tonan Hospital and conducted in accordance with the Declaration of Helsinki.

Indications for ESD

Lesions that clinically fulfilled the absolute or expanded indication criteria according to the Japanese gastric cancer treatment guidelines of 2010 [8] were targeted for ESD. The curability of the resected specimens was also pathologically assessed based on the Japanese gastric cancer treatment guidelines of 2010 [8]. The ESD procedure was performed using an insulated-tipped knife (IT knife, KD-610L; Olympus, Tokyo, Japan) or an IT knife-2 (KD-611L; Olympus), as previously reported [16–18].

Post-ESD stenosis

Post-ESD stenosis was defined as a narrowing of the stomach lumen to the extent that a standard 10-mm-diameter endoscope could not be smoothly passed through without endoscopic dilation. Risk factors for post-ESD stenosis in both the cardiac and antral resection groups were analyzed with regard to age, sex, macroscopic type of the lesion, findings of ulceration within the lesion, maximum diameter of the resected specimen, circumferential extent of the mucosal defect, longitudinal extent of the mucosal defect, location of the mucosal defect center, occurrence of post-ESD bleeding, and perforation during ESD. In addition, the incidence of resection extending to the pyloric ring was examined in the antral resection group.

All post-ESD bleeding episodes were successfully treated by endoscopic coagulation, and all perforations could be managed by conservative therapy.

Management for post-ESD stenosis

EBD was performed for the management of post-ESD stenosis, and a 12- to 15-mm, 15- to 18-mm, or 18- to 20-mm controlled radial expansion balloon dilator (CRE Wire-Guided Balloon Dilation Catheter; Boston Scientific, Tokyo, Japan) with an adjustable diameter was used for dilation. EBD was then classified as either “conventional EBD” or “prophylactic EBD”. Conventional EBD was carried out for patients who suffered from any clinical symptoms after development of post-ESD stenosis, and prophylactic EBD was generally performed for patients at a high risk of development of post-ESD stenosis resulting from wide resection extending to the entire circumference or sub-circumference of the gastric lumen. Conventional EBD was routinely performed once a week, but also as needed for relief of symptoms related to stenosis, such as dysphagia, nausea, and vomiting, until a standard endoscope could be passed through the stenotic lumen without any resistance. In general, prophylactic EBD was commenced within approximately 2–3 weeks after the ESD and repeated once a week or per 2 weeks until the mucosal

Fig. 1 Patient selection flow diagram for the study

defect was completely healed without gastric stenosis. If the patients experienced any symptoms related to stenosis despite prophylactic EBD, EBD was also performed as necessary for the management of post-ESD stenosis.

The clinical course of patients following EBD was compared relative to the number of EBD sessions, the period EBD was required, and complications associated with EBD between patients with conventional EBD and those with prophylactic EBD. Cases of perforation during EBD were excluded from the analysis of the median number of EBD sessions and period of EBD. Post-EBD bleeding was defined as bleeding from the dilated site with occurrence of hematemesis and/or melena after a procedure requiring hemostatic treatment such as endoscopic clipping or coagulation by hemostatic forceps. Perforation was diagnosed endoscopically during the procedure or detected as pneumoperitoneum either by abdominal computed tomography or by roentgenography after the procedure.

Statistical analysis

Data were analyzed using the Fisher's exact test, chi-square test, or Student's *t* test as appropriate for univariate analysis. The categorical variables with $p < 0.05$ in the univariate analysis, except for age and sex, were examined in multivariate analysis using logistic regression models. Odds ratios (OR) and 95% confidence intervals (CI) were calculated by logistic regression analysis to identify risk factors associated with post-ESD stenosis. A

value of $p < 0.05$ was considered to indicate statistical significance.

Results

Patient characteristics (Table 1)

The mean patient age was 72.8 years (range, 35–88 years) in the cardiac resection group and 71.5 years (range, 34–91 years) in the antral resection group. The male/female ratio was 2.4:1 (33:14) and 2.5:1 (309:123) in the cardiac and antral resection groups, respectively. The mean tumor size was 21.9 mm (range, 4–68 mm) in the cardiac resection group and 16.6 mm (range, 1–80 mm) in the antral resection group.

Risk factors for post-ESD stenosis (Tables 2, 3)

Post-ESD stenosis occurred in 10 (21.3%) of the 47 cardiac resection cases and 14 (3.2%) of the 432 antral resection cases. All cases with post-ESD stenosis in the antrum and 7 of 10 in the cardia were diagnosed with adenocarcinoma.

For univariate analysis, the risk factors associated with post-ESD stenosis were maximum diameter of the resected specimen more than 50 mm, circumferential extent of the mucosal defect more than three fourths, and longitudinal extent of the mucosal defect more than 50 mm in both the

Table 1 Clinicopathological characteristics of patients with cardiac and antral resection

	Cardiac resection group <i>n</i> = 47	Antral resection group <i>n</i> = 432
Mean age, range (years)	72.8 (35–88)	71.5 (34–91)
Sex ratio (M:F)	33:14	309:123
Lesion macroscopic type		
Elevated type	27	210
Flat or depressed type	18	195
Elevated and depressed type	2	27
Mean tumor size, range (mm)	21.9 (4–68)	16.6 (1–80)
Ulcer findings		
Present	1	42
Absent	46	390
Histology		
Adenoma	11	117
Carcinoma	36	315
Maximum diameter of resected specimen (mm)		
≤50	37	380
>50	10	52
Circumferential extent of mucosal defect		
<1/2	23	359
1/2–3/4	14	53
>3/4	10	20
Longitudinal extent of mucosal defect (mm)		
≤50	38	400
>50	9	32
Location of mucosal defect		
Anterior wall	4	106
Posterior wall	8	71
Greater curvature	6	113
Lesser curvature	29	142
Resection over pylorus ring		
Present	–	42
Absent	–	390
Perforation during ESD		
Present	0	3
Absent	47	429
Bleeding post ESD		
Present	2	18
Absent	45	414

ESD endoscopic submucosal dissection

cardiac and antral resection groups. Moreover, resection extending to the pyloric ring and post-ESD bleeding were also significant risk factors in the antral resection group. However, for multivariate analysis, only the circumferential extent of the mucosal defect of more than three fourths was a significant risk factor associated with post-ESD stenosis in both the cardiac and antral resection groups (OR

20.07, 95% CI 2.78–144.7 and OR 16.67, 95% CI 5.20–53.49, respectively).

Treatment outcomes for post-ESD stenosis (Tables 4, 5, 6)

Prophylactic EBD was performed in 3 of 10 patients with post-ESD stenosis in the cardiac resection group and 4 of 14 with post-ESD stenosis in the antral resection group. There were no significant differences with respect to the patient's background between patients with conventional EBD and those with prophylactic EBD in the cardiac and antral stenosis cases, respectively.

In the cardiac stenosis cases, the number of total EBD sessions and the period required for EBD tended to be greater and longer, respectively, in patients with prophylactic EBD compared with those with conventional EBD. In the antral stenosis cases, however, the period of EBD tended to be shorter in patients with prophylactic EBD compared with those with conventional EBD, although the cases of perforation during EBD were excluded from analysis.

With regard to complications, post-EBD bleeding occurred in one (10%) of the cardiac stenosis cases and one (7.1%) of the antral stenosis cases, which were successfully treated by endoscopic coagulation. Although one of the post-EBD bleeding cases was an extremely aged patient who took daily low-dose aspirin for cardiovascular disease, EBD was performed without discontinuation of the use of antithrombotic agent during and after the procedure because of the high risk of thromboembolism. Perforation during EBD occurred in two (14.3%) of the antral stenosis cases and none of the cardiac stenosis cases. All perforations occurred during the first EBD, and a 15- to 18-mm balloon dilator was used in one patient and an 18- to 20-mm dilator in another. These patients underwent emergency open surgery because of the large amount of food retained in their stomachs. In addition, all complications were observed in the patients with conventional EBD and none in patients with prophylactic EBD.

Although most of the patients with post-ESD stenosis experienced symptoms related to the stenosis, such as dysphagia, abdominal fullness, nausea, and/or vomiting, EBD contributed to symptomatic relief as well as improvement of stenosis in every patient, except for the cases of perforation.

Discussion

The incidence of post-ESD stenosis has been reported to be 1.9–2.5% of all gastric ESD cases, including 0–17% in the cardia and 3.7–18.8% in the antrum or prepylorus [9–12];

Table 2 Risk factors for post-ESD stenosis in the cardia

	Non-stenosis <i>n</i> = 37	Stenosis <i>n</i> = 10	Univariate <i>p</i> value	Multivariate	
				OR (95% CI)	<i>p</i> value
Mean age, range (years)	72.0 (35–88)	77.0 (60–87)	0.22		
Sex ratio (M:F)	29:8	4:6	0.03		
Lesion macroscopic type			0.75		
Elevated type	21	6			
Flat or depressed type	14	4			
Elevated and depressed type	2	0			
Ulcer findings			0.79		
Present	1	0			
Absent	36	10			
Maximum diameter of resected specimen (mm)			0.003	2.13 (0.05–91.20)	0.69
≤50	33	4			
>50	4	6			
Circumferential extent of mucosal defect			<0.0001	20.07 (2.78–144.70)	0.001
<1/2	23	0			
1/2–3/4	12	2			
>3/4	2	8			
Longitudinal extent of mucosal defect (mm)			0.001	2.29 (0.05–99.08)	0.67
≤50	34	4			
>50	3	6			
Location of mucosal defect			0.82		
Anterior wall	3	1			
Posterior wall	6	2			
Greater curvature	4	2			
Lesser curvature	24	5			
Bleeding post ESD			0.38		
Present	1	1			
Absent	36	9			

ESD endoscopic submucosal dissection

these findings were similar to the results of our study. Although the risk factors related to the development of post-ESD stenosis are reported to be a circumferential mucosal defect of extent more than three fourths and a longitudinal mucosal defect of extent greater than 50 mm in length in both cardiac and pyloric resections [10], these factors were shown as the result of univariate analysis, and confounding factors were not adjusted by the multivariate analysis. In the present study, the results of multivariate analysis showed that a wide resection of more than three fourths of the circumferential extent was the sole significant risk factor for the development of post-ESD stenosis in both cardiac and antral resection groups (although a longitudinal mucosal defect of extent of greater than 50 mm in length was also significant in the univariate analysis). Furthermore, “pyloric resection” was defined as located less than 10 mm from the pyloric ring and “cardiac resection” as located in the squamocolumnar junction in

the previous study [10]; these definitions were somewhat different from those of the present study. These differences in methods of analysis (univariate or multivariate analysis) and definitions might result in the different risk factors related to the development of post-ESD stenosis.

As described in previous reports, although EBD is often performed for post-ESD stenosis, it carries some risk of complications, such as post-EBD bleeding and perforation. Post-EBD bleeding does not occur very frequently and can be well managed endoscopically [19]. By contrast, the incidence of perforation is relatively high, at 7.8–50% [9, 11, 12], and often requires emergency surgery (although one case study [10] reported no complications). In the present study, post-EBD bleeding occurred in one cardiac stenosis case (10%) and in one antral stenosis case (7.1%), both of which were successfully treated by endoscopic coagulation. However, EBD should be carefully performed for patients with regular use of antithrombotic agents

Table 3 Risk factors for post-ESD stenosis in the antrum

	Non-stenosis <i>n</i> = 418	Stenosis <i>n</i> = 14	Univariate <i>p</i> value	Multivariate	
				OR (95% CI)	<i>p</i> value
Mean age, range (years)	71.0 (34–91)	75.0 (63–84)	0.93		
Sex ratio (M:F)	298:120	11:3	0.77		
Lesion macroscopic type			0.36		
Elevated type	205	5			
Flat or depressed type	188	7			
Elevated and depressed type	25	2			
Ulcer findings			0.38		
Present	42	0			
Absent	376	14			
Maximum diameter of resected specimen (mm)			0.0003	3.87 (0.31–48.64)	0.29
≤50	372	8			
>50	46	6			
Circumferential extent of mucosal defect			<0.0001	16.67 (5.20–53.49)	<0.01
<1/2	358	1			
1/2–3/4	50	3			
>3/4	10	10			
Longitudinal extent of mucosal defect (mm)			0.002	8.70 (0.65–115.69)	0.10
≤50	391	9			
>50	27	5			
Location of mucosal defect			0.88		
Anterior wall	103	3			
Posterior wall	69	2			
Greater curvature	108	5			
Lesser curvature	138	4			
Resection over pylorus ring			<0.0001	2.01 (0.30–13.41)	0.47
Present	35	7			
Absent	383	7			
Perforation during ESD			0.90		
Present	3	0			
Absent	415	14			
Bleeding post ESD			0.02	3.49 (0.38–32.28)	0.27
Present	15	3			
Absent	403	11			

ESD endoscopic submucosal dissection

because EBD is proposed as a high-risk procedure for bleeding according to the Japan Gastroenterological Endoscopy Society guidelines [20].

Conversely, perforation during EBD occurred in two patients (14.3%) in the antrum, and all were repaired by emergency surgery. Notably, all complications occurred in the patients undergoing conventional EBD, and no complications were associated with prophylactic EBD in this study; this finding suggests that prophylactic EBD could be a feasible procedure for the management of post-ESD stenosis, although repetitive EBD may be required, particularly in cardiac stenosis cases. It was reported that the

narrowest ulcerative area, which was thought to be fragile because of the lack of the mucosal and submucosal layer, would receive the strongest pressure irrespective of balloon diameter [19], and therefore prophylactic EBD could avoid overpressure to the stenotic area, resulting in fewer complications.

The curability of ESD is based on pathological evaluation of the resected specimen because it is sometimes difficult to precisely assess the depth of tumor invasion before ESD, although lesions greater than 30 mm were significantly associated with an increased risk of submucosal invasion [21]. If the lesion is pathologically diagnosed as

Table 4 Characteristics of the patients undergoing conventional EBD and those with prophylactic EBD

	Cardiac stenosis (<i>n</i> = 10)			Antral stenosis (<i>n</i> = 14)		
	Prophylactic EBD			Prophylactic EBD		
	(+) <i>n</i> = 3	(-) <i>n</i> = 7	<i>p</i> value	(+) <i>n</i> = 4	(-) <i>n</i> = 10	<i>p</i> value
Mean age, range (years)	76.0 (73–80)	77.0 (60–87)	0.88	75.8 (71–79)	74.5 (63–84)	0.74
Sex ratio (M:F)	2:1	2:5	0.33	4:0	7:3	0.33
Maximum diameter of resected specimen (mm)			0.17			0.41
≤50	0	4		3	5	
>50	3	3		1	5	
Circumferential extent of mucosal defect			0.47			0.69
≤3/4	0	2		1	3	
>3/4	3	5		3	7	
Longitudinal extent of mucosal defect (mm)			0.17			0.13
≤50	0	4		4	5	
>50	3	3		0	5	
Resection over pylorus ring						0.28
Present	–	–	3	4		
Absent	–	–	1	6		

EBD endoscopic balloon dilation

Table 5 Treatment outcomes for stenosis after gastric ESD

	Cardiac stenosis (<i>n</i> = 10)		Antral stenosis (<i>n</i> = 14)	
	Prophylactic EBD		Prophylactic EBD	
	(+) <i>n</i> = 3	(-) <i>n</i> = 7	(+) <i>n</i> = 4	(-) <i>n</i> = 10
Number of EBD sessions, median (range)	5 (5–8)	2 (1–7)	4.5 (3–11)	4.5 (2–10) ^a
Period of EBD, median days (range)	40 (29–98)	15 (1–85)	30.5 (29–57)	47 (15–71) ^a
Commencing time of EBD, median days (range)	15 (8–21)	28 (23–63)	21 (8–23)	39.5 (22–78) ^a
Complication of EBD				
Post-EBD bleeding	0	1	0	1
Perforation	0	0	0	2

EBD endoscopic balloon dilation

^a These were calculated except for the cases of perforation during EBD

having a risk of lymph node metastasis, additional gastrectomy with lymph node dissection is principally required. Therefore, the indication for ESD of large EGC, which requires a wide resection with the risk of the development of post-ESD stenosis, should be carefully decided in terms of invasiveness and cost-effectiveness because of the possibility of frequent EBD, complications of EBD, and additional surgery.

In recent years, laparoscopic distal gastrectomy (LDG) for EGC has been widely accepted as a less invasive surgery than open distal gastrectomy [22–24], and there are no significant differences in long-term clinical outcomes between the two surgical procedures [25–27]. EBD in the lower stomach has been reported to be associated with a

substantial risk of perforation if post-ESD stenosis developed [19]. Similarly, in the present study, all perforations during EBD occurred in antral cases and required emergency open surgery, although LDG could have been performed if surgical treatment had been initially selected. Therefore, LDG may be also considered a treatment option for gastric antral neoplasms, particularly EGCs, which require a wide resection, leading to the development of post-ESD stenosis.

With regard to the limitations of this study, the results were retrospectively obtained at a single center and the number of cases with post-ESD stenosis was relatively small (specifically, patients with prophylactic EBD). Moreover, this study was not randomized or controlled, as

Table 6 Details of complication cases related to endoscopic balloon dilation after ESD

Sex	Age (years)	Complication	Antithrombotic agents use	Location	Circumferential extent	Prophylactic EBD	Number of EBD at complication	Balloon diameter at complication (mm)	Day of complication after ESD (day)	Emergency surgery or conservative therapy
M	87	Post-EBD bleeding	Present	Cardia	1/2–3/4	Absent	1	15 → 16.5	63	Conservative
M	63	Post-EBD bleeding	Absent	Antrum	>3/4	Absent	4	15 → 18	52	Conservative
M	65	Perforation	Absent	Antrum	>3/4	Absent	1	15 → 16.5	78	Surgery
F	84	Perforation	Absent	Antrum	>3/4	Absent	1	18	41	Surgery

ESD endoscopic submucosal dissection, *EBD* endoscopic balloon dilation

the aim was to compare prophylactic EBD with conventional EBD for the management of post-ESD stenosis. Despite these limitations, because there have been no previously published reports of the effectiveness of prophylactic EBD for the management of stenosis after gastric ESD, we therefore believe that this study is meaningful. We hope that a multicenter study incorporating a large number of cases is conducted in the near future to establish an optimal management strategy for post-ESD stenosis.

In conclusion, a wide resection of more than three fourths of the circumferential extent was the sole significant risk factor for the development of post-ESD stenosis in both cardiac and antral resections. Prophylactic EBD may be a promising procedure for the management of post-ESD stenosis.

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Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to disclose.

Ethical standards All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent or a substitute for it was obtained from all patients for being included in the study.

References

- Rembacken BJ, Gotoda T, Fujii T, Axon AT. Endoscopic mucosal resection. *Endoscopy*. 2001;33:709–18.
- Soetikno RM, Gotoda T, Nakanishi Y, Soehendra N. Endoscopic mucosal resection. *Gastrointest Endosc*. 2003;57:567–79.
- Gotoda T, Yamamoto H, Soetikno RM. Endoscopic submucosal dissection of early gastric cancer. *J Gastroenterol*. 2006;41:929–42.
- Oda I, Saito D, Tada M, Iishi H, Tanabe S, Oyama T, et al. A multicenter retrospective study of endoscopic resection for early gastric cancer. *Gastric Cancer*. 2006;9:262–70.
- Ono H, Kondo H, Gotoda T, Shirao K, Yamaguchi H, Saito D, et al. Endoscopic mucosal resection for treatment of early gastric cancer. *Gut*. 2001;48:225–9.
- Yamamoto H, Sekine Y, Higashizawa T, Kihira K, Kaneko Y, Hosoya Y, et al. Successful en bloc resection of a large superficial gastric cancer by using sodium hyaluronate and electrocautery incision forceps. *Gastrointest Endosc*. 2001;54:629–32.
- Gotoda T, Yanagisawa A, Sasako M, Ono H, Nakanishi Y, Shimoda T, et al. Incidence of lymph node metastasis from early gastric cancer: estimation with a large number of cases at two large centers. *Gastric Cancer*. 2000;3:219–25.
- Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2010 (ver. 3). *Gastric Cancer*. 2011;14:113–23.
- Tsunada S, Ogata S, Mannen K, Arima S, Sakata Y, Shiraishi R, et al. Case series of endoscopic balloon dilation to treat a stricture caused by circumferential resection of the gastric antrum by endoscopic submucosal dissection. *Gastrointest Endosc*. 2008;67:979–83.

10. Coda S, Oda I, Gotoda T, Yokoi C, Kikuchi T, Ono H, et al. Risk factors for cardiac and pyloric stenosis after endoscopic submucosal dissection, and efficacy of endoscopic balloon dilation treatment. *Endoscopy*. 2009;41:421–6.
11. Iizuka H, Kakizaki S, Sohara N, Onozato Y, Ishihara H, Okamura S, et al. Stricture after endoscopic submucosal dissection for early gastric cancers and adenomas. *Dig Endosc*. 2010;22:282–8.
12. Kakushima N, Tanaka M, Sawai H, Imai K, Kawata N, Hagiwara T, et al. Gastric obstruction after endoscopic submucosal dissection. *U Eur Gastroenterol J*. 2013;1:184–90.
13. Mori H, Rafiq K, Kobara H, Fujihara S, Nishiyama N, Kobayashi M, et al. Local steroid injection into the artificial ulcer created by endoscopic submucosal dissection for gastric cancer: prevention of gastric deformity. *Endoscopy*. 2012;44:641–8.
14. Mori H, Kobara H, Rafiq K, Fujihara S, Nishiyama N, Kobayashi M, et al. Novel method for the management of stenosis after gastric endoscopic submucosal dissection: mucosal incision with steroid injection contralateral to the severely contracted scar. *Dig Endosc*. 2015;27:622–6.
15. Shoji H, Yamaguchi N, Isomoto H, Minami H, Matsushima K, Akazawa Y, et al. Oral prednisolone and triamcinolone injection for gastric stricture after endoscopic submucosal dissection. *Ann Transl Med*. 2014;2:22.
16. Takeuchi Y, Uedo N, Iishi H, Yamamoto S, Yamamoto S, Yamada T, et al. Endoscopic submucosal dissection with insulated-tip knife for large mucosal early gastric cancer: a feasibility study (with videos). *Gastrointest Endosc*. 2007;66:186–93.
17. Ono H, Hasuike N, Inui T, Takizawa K, Ikehara H, Yamaguchi Y, et al. Usefulness of a novel electrosurgical knife, the insulation-tipped diathermic knife-2, for endoscopic submucosal dissection of early gastric cancer. *Gastric Cancer*. 2008;11:47–52.
18. Tanaka M, Ono H, Hasuike N, Takizawa K. Endoscopic submucosal dissection of early gastric cancer. *Digestion*. 2008;77:23–8.
19. Kishida Y, Kakushima N, Kawata N, Tanaka M, Takizawa K, Imai K, et al. Adverse events associated with endoscopic dilation for gastric stenosis after endoscopic submucosal dissection for early gastric cancer. *Surg Endosc*. 2015;29:3776–82.
20. Fujimoto K, Fujishiro M, Kato M, Higuchi K, Iwakiri R, Sakamoto C, et al. Guidelines for gastroenterological endoscopy in patients undergoing antithrombotic treatment. *Dig Endosc*. 2014;26:1–14.
21. Abe S, Oda I, Shimazu T, Kinjo T, Tada K, Sakamoto T, et al. Depth-predicting score for differentiated early gastric cancer. *Gastric Cancer*. 2011;14:35–40.
22. Kim YW, Baik YH, Yun YH, Nam BH, Kim DH, Choi IJ, et al. Improved quality of life outcomes after laparoscopy-assisted distal gastrectomy for early gastric cancer: results of a prospective randomized clinical trial. *Ann Surg*. 2008;248:721–7.
23. Ohtani H, Tamamori Y, Noguchi K, Azuma T, Fujimoto S, Oba H, et al. A meta-analysis of randomized controlled trials that compared laparoscopy-assisted and open distal gastrectomy for early gastric cancer. *J Gastrointest Surg*. 2010;14:958–64.
24. Deng Y, Zhang Y, Guo TK. Laparoscopy-assisted versus open distal gastrectomy for early gastric cancer: a meta-analysis based on seven randomized controlled trials. *Surg Oncol*. 2015;24:71–7.
25. Kitano S, Shiraishi N, Uyama I, Sugihara K, Tanigawa N, Japanese Laparoscopic Surgery Study Group. A multicenter study on oncologic outcomes of laparoscopic gastrectomy for early gastric cancer in Japan. *Ann Surg*. 2007;245:68–72.
26. Kim YW, Yoon HM, Yun YH, Nam BH, Eom BW, Baik YH, et al. Long-term outcomes of laparoscopy-assisted distal gastrectomy for early gastric cancer: result of a randomized controlled trial (COACT 0301). *Surg Endosc*. 2013;27:4267–76.
27. Kim HH, Han SU, Kim MC, Hyung WJ, Kim W, Lee HJ, et al. Long-term results of laparoscopic gastrectomy for gastric cancer: a large-scale case-control and case-matched Korean multicenter study. *J Clin Oncol*. 2014;32:627–33.