

Retrospective Study

Management and associated factors of delayed perforation after gastric endoscopic submucosal dissection

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Author contributions: Suzuki H and Oda I designed the study, analyzed and interpreted the data, and wrote the draft; Sekiguchi M, Abe S, Nonaka S, Yoshinaga S, Nakajima T, and Saito Y contributed to the critical revisions of the article for important intellectual content; all authors had final approval of this article.

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Conflict-of-interest statement: No conflict of interest was declared by the authors.

Data sharing statement: No additional data are available.

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Received: May 25, 2015

Peer-review started: May 27, 2015

First decision: June 19, 2015

Revised: July 15, 2015

Accepted: September 30, 2015

Article in press: September 30, 2015

Published online: November 28, 2015

Abstract

AIM: To identify the actual clinical management and associated factors of delayed perforation after gastric endoscopic submucosal dissection (ESD).

METHODS: A total of 4943 early gastric cancer (EGC) patients underwent ESD at our hospital between January 1999 and June 2012. We retrospectively assessed the actual management of delayed perforation. In addition, to determine the factors associated with delayed perforation, after excluding 123 EGC patients with perforations that occurred during the ESD procedure, we analyzed the following clinicopathological factors among the remaining 4820 EGC patients by comparing the ESD cases with delayed perforation and the ESD cases without perforation: age, sex, chronological periods, clinical indications for ESD, status of the stomach, location, gastric circumference, tumor size, invasion depth, presence/absence of ulceration, histological type, type of resection, and procedure time.

RESULTS: Delayed perforation occurred in 7 (0.1%) cases. The median time until the occurrence of delayed perforation was 11 h (range, 6-172 h). Three (43%) of the 7 cases required emergency surgery, while four were conservatively managed without surgical intervention. Among the 4 cases with conservative management, 2 were successfully managed endoscopically using the endoloop-endoclip technique. The median hospital stay was 18 d (range, 15-45 d). There were no delayed perforation-related deaths. Based on a multivariate analysis, gastric tube cases (OR = 11.0; 95%CI: 1.7-73.3; $P = 0.013$) were significantly associated with delayed perforation.

CONCLUSION: Endoscopists must be aware of not only the identified factors associated with delayed perforation, but also how to treat this complication

effectively and promptly.

Key words: Early gastric cancer; Endoscopic submucosal dissection; Delayed perforation; Emergency surgery; Conservative management

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Core tip: In this study, delayed perforation occurred in 0.1% (7 cases) of 4943 early gastric cancer patients undergoing endoscopic submucosal dissection (ESD); 43% (3 cases) of these cases required emergency surgery. This study also showed that the gastric tube was an independent risk factor associated with delayed perforation. This study is significant because it clarified both the clinical management and risk factors of delayed perforation based on data from a large series of consecutive patients undergoing ESD. Endoscopists must be aware of not only the identified factors associated with delayed perforation, but also how to treat this complication effectively and promptly.

Suzuki H, Oda I, Sekiguchi M, Abe S, Nonaka S, Yoshinaga S, Nakajima T, Saito Y. Management and associated factors of delayed perforation after gastric endoscopic submucosal dissection. *World J Gastroenterol* 2015; 21(44): 12635-12643 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v21/i44/12635.htm> DOI: <http://dx.doi.org/10.3748/wjg.v21.i44.12635>

INTRODUCTION

Endoscopic submucosal dissection (ESD) is widely used in East Asia (e.g., Japan and Korea) as an initial treatment for early gastric cancer (EGC) with a negligible risk of lymph node (LN) metastasis, even for cases that involve large and ulcerative lesions^[1-4]. The therapeutic outcomes of gastric ESD are excellent; however, there are still cases of various complications, such as bleeding and perforation^[5,6]. ESD procedure-related perforations can be subdivided into perforations that occur during gastric ESD and delayed perforations occurring after the completion of gastric ESD. Most perforations occur during gastric ESD, and the risk of perforation reportedly ranges from 1.2% to 9.6% for gastric ESD^[5-12]. The majority of perforation cases can be treated conservatively using complete endoscopic closure with endoclips^[5,6,13]. In contrast, delayed perforation is a rare (with an incidence of 0.43% to 0.45%) but serious complication that sometimes requires emergent surgery^[6,14-20]. Under these circumstances, the actual clinical management and the associated factors of delayed perforation induced by gastric ESD should be clarified to minimize its incidence and to treat this complication effectively and promptly. Although several reports have described

delayed perforation after gastric ESD, no published report has thoroughly evaluated the various factors associated with delayed perforation based on data from a large series of consecutive EGC patients undergoing ESD^[14-20]. Therefore, we attempted to identify the actual clinical management and the associated factors of delayed perforation induced by ESD for EGC based on our extensive clinical experience.

MATERIALS AND METHODS

Patients

A total of 4943 EGC patients (male:female ratio, 3.9:1; median age, 69 years; range, 27-96 years) underwent ESD at our hospital between January 1999 and June 2012. The clinicopathological findings of these 4943 EGC patients are shown in Table 1. In our hospital, according to the Japanese gastric cancer treatment guideline, ESD is generally performed based on two independent sets of clinical indications: absolute indications for standard treatment, and expanded indications for investigational treatment^[3]. Furthermore, ESD is also performed for a small number of patients with locally recurrent EGC or EGC lesions outside the clinical indications for ESD, particularly gastric tube cases, because the mortality rate for surgical resection is remarkably high^[21-24]. The definitions for the characteristics of EGC lesions, such as status of the stomach (normal stomach/remnant stomach after a gastrectomy/gastric tube after an esophagectomy), lesion location (upper/middle/lower third of the stomach), gastric circumference (greater curvature/lesser curvature/anterior wall/posterior wall), tumor size, depth of invasion [mucosa (M)/submucosa (SM)], presence of ulcerations, and histological type (differentiated-type/undifferentiated-type), were based on the Japanese classification of gastric carcinoma and the Japanese gastric cancer treatment guidelines^[3,25]. The term "gastric tube" refers to a stomach conduit that has been pulled up into the thorax for use as an esophageal substitute after an esophagectomy^[23,24]. The histological type was defined according to the major histological features of the lesion. Differentiated-type adenocarcinoma included tubular adenocarcinoma and papillary adenocarcinoma, while undifferentiated-type adenocarcinoma included poorly differentiated adenocarcinoma, signet-ring cell adenocarcinoma and mucinous adenocarcinoma.

ESD procedure

The ESD procedure began with the identification of the lesion and the marking of dots at a distance of about 5 mm outside of the lesion. After submucosal injection using a saline solution or sodium hyaluronate (MucoUp; Johnson & Johnson Corp., Tokyo, Japan) with epinephrine, a 1- to 2-mm precut was made with an electrosurgical needle knife (KD-1L-1; Olympus Optical, Tokyo, Japan) or the Dual knife (KD-650Q; Olympus

Table 1 Clinicopathological findings of 4943 early gastric cancer patients undergoing endoscopic submucosal dissection

Clinicopathological finding	n (%)
Age (yr)	
median (range)	69 (27-96)
< 70	2608 (52.8)
≥ 70	2335 (47.2)
Sex	
Male	3930 (80.0)
Female	1013 (20.0)
Chronological periods	
1 st period: 1999-2005	2285 (46.2)
2 nd period: 2006-2012	2658 (53.8)
Clinical indications	
Absolute indications	2884 (58.3)
Expanded indications	1737 (35.1)
Locally recurrent EGC	141 (2.9)
Outside indications	181 (3.7)
Stomach status	
Normal stomach	4704 (95.2)
Remnant stomach	152 (3.1)
Gastric tube	87 (1.7)
Location	
Upper	904 (18.3)
Middle	2100 (42.5)
Lower	1939 (39.2)
Circumference	
Greater curvature	807 (16.3)
Lesser curvature	2005 (40.6)
Anterior wall	963 (19.5)
Posterior wall	1168 (23.6)
Size (mm)	
median (range)	15 (0.4-120)
≤ 20	3457 (69.9)
> 20	1486 (30.1)
Depth of invasion	
M	4075 (82.4)
SM	868 (17.6)
Ulceration	
Absent	4073 (82.4)
Present	870 (17.6)
Histological type	
Differentiated	4581 (92.7)
Undifferentiated	362 (7.3)
Type of resection	
<i>En bloc</i> resection	4859 (98.3)
Piecemeal resection	84 (1.7)
Procedure time (h)	
mean ± SD	1.4 ± 1.1
< 2	3811 (77.1)
≥ 2	1132 (22.9)

EGC: Early gastric cancer; M: Mucosa; SM: Submucosa.

Optical, Tokyo, Japan), followed by a circumferential mucosal incision outside the marking dots with an insulation-tipped (IT) diathermy knife (KD-610L; Olympus Optical, Tokyo, Japan) or IT knife 2 (KD-611L; Olympus Optical, Tokyo, Japan). The submucosal layer was then dissected using an IT knife or an IT knife 2 after an additional submucosal injection. Cases with bleeding during or after the ESD procedure were controlled by coagulating the bleeding vessels with the IT knife itself and/or hemostatic forceps [Coagrasper (FD-410LR; Olympus Optical, Tokyo, Japan) and Radial

Jaw hot biopsy forceps (Boston Scientific Japan, Tokyo, Japan)], or by grasping them with endoclips. The set-up for the high-frequency generators for ESD along with the IT knife for early gastric cancer (ICC200 Erbe Elektromedizin, Tübingen, Germany, ESG100 Olympus Medical and VIO300D Erbe Elektromedizin, Tübingen, Germany) is shown in Table 2. The risks and benefits of ESD were thoroughly explained to each patient, and written informed consent was obtained from them in accordance with our institutional protocols prior to treatment.

The procedure time was defined as the time from circumferential marking around the lesion to the completion of the ESD procedure. An *en bloc* resection was defined as a one-piece resection, and a piecemeal resection was defined as the removal of a lesion in more than one piece^[3,25].

Assessments of actual clinical management and associated factors of delayed perforation

We retrospectively assessed the incidence of delayed perforation and the actual clinical management of this complication, including the need for emergency surgery, the methods of conservative management, and the median hospital stay. For the cases with delayed perforation requiring emergency surgery, the reason for the emergency surgery was also clarified. Finally, to determine the factors associated with delayed perforation induced by gastric ESD, after excluding 123 (2.5%) EGC patients with perforations that occurred during the ESD procedure, we retrospectively analyzed the following clinicopathological factors among the remaining 4820 EGC patients by comparing the ESD cases with delayed perforation with the ESD cases without perforation: age (< 70 years vs ≥ 70 years), sex (male vs female), chronological periods (1st period: 1999-2005 vs 2nd period: 2006-2012), clinical indications for ESD (absolute indications vs expanded indications vs locally recurrent EGC vs outside indications), status of the stomach (normal stomach vs remnant stomach after gastrectomy vs gastric tube after esophagectomy), lesion location (upper/middle vs lower), gastric circumference (greater curvature vs lesser curvature vs anterior wall vs posterior wall), tumor size (≤ 20 mm vs > 20 mm), depth of invasion (M vs SM), presence/absence of ulceration, histological type (differentiated-type vs undifferentiated-type), type of resection (*en bloc* resection vs piecemeal resection), and procedure time (< 2 h vs ≥ 2 h).

Definition of delayed perforation induced by gastric ESD

Delayed perforation was identified by the sudden appearance of symptoms of peritoneal or mediastinal pleura irritation (gastric tube case) after the completion of gastric ESD, with free air visible on X-ray or computed tomography (CT) images and/or with a gross defect observed endoscopically, although endoscopically visible perforations did not occur

Table 2 Set-up for the high-frequency generators for endoscopic submucosal dissection along with the IT knife for early gastric cancer

Procedure	Device	Mode	Output
ICC200			
Marking	Needle knife	Forced coag	20W
Precutting	Needle knife	ENDO CUT	Effect 3, 80W
Mucosal incision	IT knife	ENDO CUT	Effect 3, 80W
Submucosal dissection	Needle knife	ENDO CUT	Effect 3, 80W
		Forced coag	50W
	Needle knife	ENDO CUT	Effect 3, 80W
		Forced coag	50W
Endoscopic hemostasis	IT knife	Forced coag	50W
	Needle knife		
	Hot biopsy Coagrasper	Soft coag	80W
ESG100			
Marking	Needle knife	Forced coag 1	20W
Precutting	Needle knife	Pulse cut slow	40W
Mucosal incision	IT knife	Pulse cut slow	40W
Submucosal dissection	Needle knife	Pulse cut slow	40W
		Forced coag 2	50W
	Needle knife	Pulse cut slow	40W
		Forced coag 2	50W
Endoscopic hemostasis	IT knife	Forced coag 2	50W
	Needle knife		
	Hot biopsy Coagrasper	Soft coag	80W
VIO300D			
Marking	Needle knife	Swift coag	Effect 2, 50W
Precutting	Needle knife	ENDO CUT I	Effect 2, CUT duration 2, CUT interval 3
Mucosal incision	IT knife	ENDO CUT I or Q	Effect 2, CUT duration 2, CUT interval 3
		ENDO CUT I	Effect 2, CUT duration 2, CUT interval 3
	Needle knife	ENDO CUT I	Effect 4, 50W
		ENDO CUT I	Effect 2, CUT duration 2, CUT interval 3
Submucosal dissection	IT knife	ENDO CUT I or Q	Effect 4, 50W
		ENDO CUT I	Effect 2, CUT duration 2, CUT interval 3
	Needle knife	ENDO CUT I	Effect 4, 50W
		ENDO CUT I	Effect 5, 50W
Endoscopic hemostasis	IT knife	Swift coag	Effect 2, CUT duration 2, CUT interval 3
	Needle knife	Swift coag	Effect 4, 50W
	Hot biopsy Coagrasper	Swift coag	Effect 5, 50W
	Hot biopsy Coagrasper	Soft coag	Effect 5, 80W

during the ESD procedure and no remarkable clinical symptoms were observed, suggesting perforation, just after the ESD procedures.

Statistical analysis

The Fisher exact test or the χ^2 test was used for the univariate analyses to assess the above-mentioned clinicopathological factors by comparing the ESD cases with delayed perforation with the ESD cases without

perforation. We performed a multivariate analysis for clinicopathological factors that were significant in univariate analyses. A logistic regression analysis was used for the multivariate analysis. All the statistical analyses were performed using the statistical analysis software SPSS, version 20 (SPSS Japan Inc., Tokyo, Japan). A *P*-value < 0.05 was considered statistically significant.

RESULTS

Incidence and actual management of delayed perforation

Delayed perforation occurred in 7 (0.1%) ESD cases (Table 3). The median time until the occurrence of delayed perforation was 11 h (range, 6-172 h). As for the management of the delayed perforations, 3 (43%) of the 7 delayed perforation cases underwent emergency surgery, while 4 were conservatively managed with nasogastric tube placement, fasting, and the use of intravenous antibiotics and proton pump inhibitors. Two of the 3 patients who required emergency surgery received an omentoplasty or simple closure of the perforation hole; however, one patient underwent a distal gastrectomy because the ESD was evaluated as a non-curative resection. The reason for the emergency surgery in these three cases was panperitonitis with remarkable clinical symptoms, such as diffuse and severe tenderness and/or defense musculaire. Among the 4 cases treated with conservative management, 2 were successfully managed endoscopically using an endoloop-endoclip technique^[23,26]. In this technique, the endoloop snare was anchored with some clips to the normal mucosa around the delayed perforation defect^[26]. The endoloop snare was tightened slightly, approximating the borders of the defect. Finally, additional clips were placed to achieve complete closure. The median hospital stay in the delayed perforation cases was 18 d (range, 15-45 d). No delayed perforation-related deaths occurred in this series.

Factors associated with delayed perforation

Based on univariate analyses, outside clinical indications, gastric tube cases, location in the upper/middle third of the stomach, and procedure time ≥ 2 h were significantly associated with a delayed perforation (Table 4). No significant difference between the rates of delayed perforation was observed when the absolute indications (0.1%) and expanded indications (0.1%) were applied. Using a multivariate analysis for these cases, gastric tube cases (OR = 11.0; 95%CI: 1.7-73.3; *P* = 0.013) were found to be significantly associated with delayed perforation (Table 4).

A representative case (Case 4 in Table 3) with delayed perforation is shown in Figures 1-5. A 64-year-old woman underwent surveillance endoscopy after an esophagectomy for esophageal cancer. The endoscopy showed a superficial depressed EGC lesion, 33 mm

Table 3 Clinical management of delayed perforation induced by gastric endoscopic submucosal dissection

Case	Age (yr)	Sex	Stomach status	Time until the occurrence of delayed perforation (h)	Panperitonitis or severe mediastinitis	Management of delayed perforation	Hospital stay (d)
1	68	Male	Gastric tube	11	Absent	Conservative management	45
2	75	Male	Normal stomach	35	Absent	Conservative management	18
3	80	Male	Normal stomach	6	Absent	Conservative management with endoloop-endoclip technique	18
4	64	Female	Gastric tube	7	Absent	Conservative management with endoloop-endoclip technique	25
5	73	Male	Normal stomach	9	Present (Panperitonitis)	Emergency surgery	15
6	62	Female	Normal stomach	27	Present (Panperitonitis)	Emergency surgery	18
7	56	Female	Normal stomach	172	Present (Panperitonitis)	Emergency surgery	15

Table 4 Factors associated with delayed perforation induced by gastric endoscopic submucosal dissection *n* (%)

Clinicopathological finding	Univariate analysis			Multivariate analysis, OR (95%CI), <i>P</i> value
	ESD cases without perforation (<i>n</i> = 4813)	ESD cases with delayed perforation (<i>n</i> = 7)	<i>P</i> value	
Age (yr)			1.00	-
< 70	2538 (99.8)	4 (0.2)		
≥ 70	2275 (99.9)	3 (0.1)		
Sex			0.16	-
Male	3828 (99.9)	4 (0.1)		
Female	985 (99.7)	3 (0.3)		
Chronological periods			1.00	-
1 st period: 1999-2005	2194 (99.9)	3 (0.1)		
2 nd period: 2006-2012	2619 (99.8)	4 (0.2)		
Clinical indications			0.02	NS
Outside indications	169 (98.8)	2 (1.2)		
Other indications ¹	4644 (99.9)	5 (0.1)		
Stomach status			0.006	11.0 (1.7-73.3), 0.013
Normal stomach/Remnant stomach	4732 (99.9)	5 (0.1)		
Gastric tube	81 (97.6)	2 (2.4)		
Location			0.047	NS
Upper/Middle	2894 (99.8)	7 (0.2)		
Lower	1919 (100)	0 (0.0)		
Circumference			0.09	-
Greater curvature	774 (99.6)	3 (0.4)		
Others ²	4039 (99.9)	4 (0.1)		
Size (mm)			0.43	-
≤ 20	3395 (99.9)	4 (0.1)		
> 20	1418 (99.8)	3 (0.2)		
Depth of invasion			0.34	-
M	3988 (99.9)	5 (0.1)		
SM	825 (99.8)	2 (0.2)		
Ulceration			0.34	-
Absent	3982 (99.9)	5 (0.1)		
Present	831 (99.8)	2 (0.2)		
Histological type			0.09	-
Differentiated	4466 (99.9)	5 (0.1)		
Undifferentiated	347 (99.4)	2 (0.6)		
Type of resection			1.00	-
<i>En bloc</i> resection	4743 (99.9)	7 (0.1)		
Piecemeal resection	70 (100)	0 (0.0)		
Procedure time (h)			0.046	NS
< 2	3758 (99.9)	3 (0.1)		
≥ 2	1055 (99.6)	4 (0.4)		

¹Other indications, absolute indications, expanded indications and locally recurrent early gastric cancer; ²Others, lesser curvature, anterior wall and posterior wall. ESD: Endoscopic submucosal dissection; M: Mucosa; SM: Submucosa; NS: Not significant.

in size, at the greater curvature of the upper gastric body of the gastric tube (Figure 1). The estimated tumor depth was the submucosa, and a biopsy revealed a poorly differentiated adenocarcinoma.

ESD was performed for this lesion as a diagnostic procedure, and an *en bloc* resection with negative margins was achieved without any complications. As for the mucosal defect just after the completion

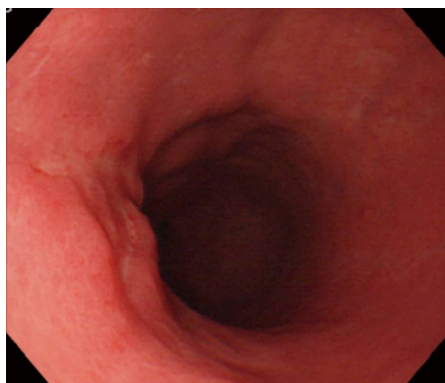


Figure 1 A superficial depressed early gastric cancer lesion located at the greater curvature of the upper gastric body of the gastric tube.

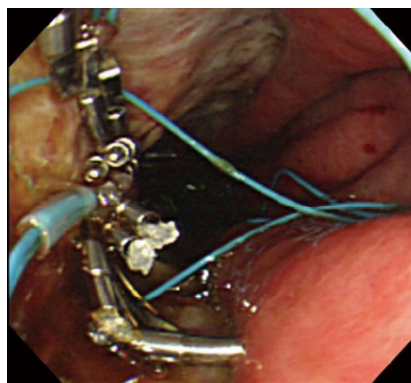


Figure 4 The delayed perforation was successfully closed using the endoloop-endoclip technique.

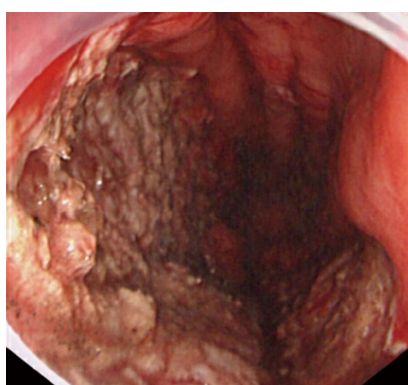


Figure 2 Mucosal defect just after the completion of endoscopic submucosal dissection (60 mm in size and half circumference).

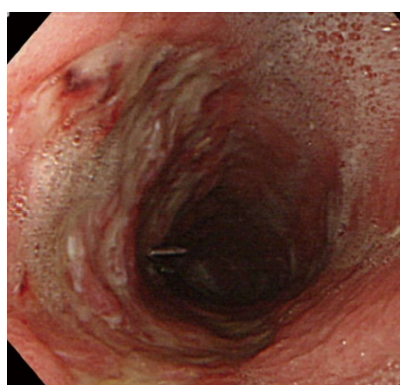


Figure 5 The delayed perforation had almost completely healed 15 d after endoscopic submucosal dissection.

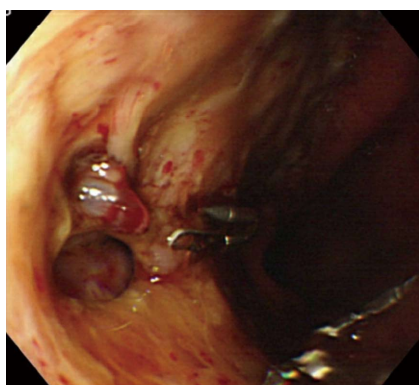


Figure 3 A delayed perforation occurred 7 h after endoscopic submucosal dissection.

of ESD, the size of the defect was 60 mm, and the circumferential extent of the defect was one half of the lumen of the gastric tube. At the proximal edge of the ulceration, severe damage to the surface of the muscularis propria as a result of electrical cautery was seen, but no remarkable clinical symptoms, suggesting perforation, were observed (Figure 2). Seven hours after the ESD, a delayed perforation occurred with chest pain (Figure 3). However, this patient did not develop severe mediastinitis, so endoscopic closure

using the endoloop-endoclip technique was attempted and successfully performed (Figure 4). In detail, the endoloop snare was anchored with some clips to the normal mucosa around the delayed perforation defect^[23,26]. The endoloop snare was tightened slightly, which approximated the borders of the defect. To achieve complete closure, two endoloop snares with additional clips were needed. The delayed perforation had almost completely healed 15 d after ESD (Figure 5) and finally, the patient was conservatively managed and was discharged 25 d after ESD.

DISCUSSION

Delayed perforation is reported to be a rare (incidence of 0.43% to 0.45%) but serious complication induced by gastric ESD that can sometimes require emergent surgery^[6,14-20]. Although several reports have described delayed perforation after gastric ESD, no published report has thoroughly evaluated the various factors that are associated with delayed perforation based on data from a large series of consecutive EGC patients undergoing ESD^[6,14-20]. Therefore, the present study is significant because it clarified both the actual clinical management and the associated factors of delayed perforation induced by ESD for EGC based on data

from a large series of consecutive patients undergoing gastric ESD.

In the present study, delayed perforation after gastric ESD occurred in 7 (0.1%) ESD cases, and 3 (43%) of these 7 cases required emergency surgery. Another report from Hanaoka *et al.*^[14] described 6 (0.45%) cases with delayed perforation among 1329 EGC lesions, and 5 (83%) of these 6 cases underwent emergency surgery. In addition, Kato *et al.*^[16] reported 2 (0.43%) cases of delayed perforation occurring after the completion of ESD among 468 cases of gastric non-invasive neoplasia, both of which required emergency surgery. Several case reports of delayed perforation after gastric ESD that were successfully managed conservatively have also been reported^[15,17,18,20]. Thus, although a small number of cases of delayed perforation might be successfully managed conservatively (9 among 21 delayed perforation patients, including 14 patients in previous reports^[14-20] and our 7 patients, were successfully managed conservatively), we need to remember that in delayed perforation cases, emergency surgery may be required with a high probability and conservative management might not always be feasible. In the near future, the establishment of effective conservative treatments may reduce the rate of delayed perforation cases requiring emergency surgery^[20]. The early recognition of the onset of delayed perforation after the sudden appearance of symptoms of peritoneal or mediastinal pleura irritation (gastric tube cases) within 24 h after gastric ESD followed by prompt conservative treatment may be useful for avoiding emergency surgery. In the case of delayed perforation without any findings of panperitonitis or severe mediastinitis (gastric tube cases), the endoloop-endoclip technique under CO₂ insufflation might make it possible to close defects of the gastric wall caused by delayed perforation in a conservative manner, as in our representative case^[23,26,27]. CO₂ insufflation has increasingly been used instead of air insufflation to minimize pneumoperitoneum caused by perforation^[27].

The results of the present study also showed that gastric tube cases were an independent risk factor associated with delayed perforation after ESD, based on a large consecutive series of EGC patients. Hanaoka *et al.*^[14] reported that 5 out of 6 delayed perforations occurred in the upper third of the stomach; however, this report represented a case series of delayed perforations without any assessment of the risk factors associated with delayed perforation by comparing the ESD cases with delayed perforation with ESD cases without perforation. The reason for the high frequency of delayed perforations in the gastric tube was uncertain, but reduced vascular circulation of the reconstructed gastric tube may have resulted in slower ESD ulcer healing^[23]. In addition, Hanaoka *et al.*^[14] reported that the mechanism of delayed perforation was thought to be due to electrical cautery during the submucosal dissection or repeated coagulation

causing ischemic changes to the gastric wall, resulting in necrosis. Furthermore, Onogi *et al.*^[28] reported the existence of a "transmural air leak" after gastric ESD, as detected by a CT examination. In the present study, we cannot rule out the possible existence of severe damage to the surface of the muscularis propria with a transmural air leak, since we did not perform a CT examination in most of the cases undergoing gastric ESD. Thus, there might be a possibility of developing delayed perforation from severe damage to the surface of the muscularis propria with transmural air leaks after the ESD procedure. More recently, the feasibility and effectiveness of ESD for gastric tube cancer after esophagectomy have been reported^[23,24]. Thus, awareness of this finding is important before the widespread use of this treatment, and in cases of ESD for gastric tube cancer, it might be better to avoid excessive electrical cautery during submucosal dissection or repeated coagulation so as to prevent delayed perforation.

Our study had several limitations. First, the results of the present study were based on retrospective assessments of the medical records of patients with gastric ESD, although these data were based on a large consecutive series of gastric ESDs. Second, the present study was conducted at a single major referral cancer center in a large metropolitan area of Japan with many highly experienced endoscopists with specific expertise in ESD. Thus, a prospective multicenter study is required for a more precise evaluation of the actual clinical management and the associated factors of delayed perforation induced by gastric ESD. Several multicenter prospective cohort studies on gastric ESD are currently underway^[29-31].

In conclusion, endoscopists must be aware of not only the identified factors associated with delayed perforation induced by gastric ESD, but also how to treat this complication effectively and promptly.

ACKNOWLEDGMENTS

We thank Dr. Hiroyuki Ono and Dr. Takuji Gotoda (our mentors of National Cancer Center Hospital in Tokyo) for their efforts in developing ESD.

COMMENTS

Background

Delayed perforation after gastric endoscopic submucosal dissection (ESD) is a rare but serious complication that sometimes requires emergent surgery. Therefore, the actual clinical management and the associated factors of delayed perforation after gastric ESD should be clarified to minimize its incidence and to treat this complication effectively and promptly.

Research frontiers

Although several reports have described delayed perforation after gastric ESD, no published report has thoroughly evaluated the various factors associated with delayed perforation in addition to the actual clinical management of this complication based on data from a large series of consecutive patients undergoing gastric ESD.

Innovations and breakthroughs

The early recognition of the onset of delayed perforation after the sudden appearance of symptoms of peritoneal or mediastinal pleura irritation (gastric tube cases) within 24 h after gastric ESD followed by prompt conservative treatment may be useful for avoiding emergency surgery. In addition, in cases of ESD for gastric tube cancer, it might be better to avoid excessive electrical cautery during submucosal dissection or repeated coagulation so as to prevent delayed perforation.

Applications

The results of the present study suggest that endoscopists should be aware of not only the identified factors associated with delayed perforation, but also how to treat this complication effectively and promptly.

Terminology

Bleeding and perforation are major complications of gastric ESD. ESD-related perforations can be subdivided into perforations that occur during gastric ESD and delayed perforations occurring after the completion of gastric ESD. Most perforations occur during gastric ESD, and the majority of perforation cases can be treated conservatively using complete endoscopic closure with endoclips. In contrast, delayed perforation is a rare but serious complication that sometimes requires emergent surgery.

Peer-review

This study is significant because it clarified both the actual clinical management and the associated factors of delayed perforation based on data from a large consecutive series of patients undergoing gastric ESD.

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P- Reviewer: Chung JW, Gonzalez N, Kim GH, Man-I M, Matsumoto

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ISSN 1007-9327



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