# **Endoscopic Submucosal Dissection in 100 Lesions with Early Gastric Carcinoma**

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### **KEY WORDS:**

Endoscopic submucosal dissection, Flex knife, Early gastric carcinoma, Specified indications, Eexpanded indications

#### ARBREVIATIONS:

Japanease Gastric Cancer Association (JGCA); Endoscopic Mucosal Resection (EMR); Endoscopic Submucosal Dissection (ESD); Endoscopic Ultrasonography (EUS)

### ABSTRACT

Background/Aims: ESD is a new diagnostic and treatment technique for early gastric cancer. This study aimed to evaluate the therapeutic effects observed at our department.

Methodology: The subject group included 95 patients with 100 early-stage gastric cancers. According to the Gastric Cancer Treatment Guidelines published by the Japanease Gastric Cancer Association (JGCA) in 2001. Sixty-seven lesions presented a tumor measuring less than 20 mm and were concave (if not flat) without ulceration (specified indication of the guidelines of the Japanese Gastric Cancer Association), and 33 lesions were expanded indications. We then compared one-piece resection rates, en-bloc resection rates (one-piece resection that is lateral- and vertical-stump negative), curative en-bloc resection rates (en-bloc resection that fulfills the following

three criteria: 1. differentiated adenocarcinoma; 2. no lymphtic or venous invasion, 3a. intramucosal cancer regardless of tumor size without ulceration, 3b. intramucosal cancer 30 mm in size with ulceration, 3c. minute submucosal cancer 30 mm in size). RESULTS: Among the specified indications and expanded indications, one-piece resection rates accounted for 97.0% and 75.8%, en-bloc resection rates for 83.6% and 60.6%, and curative en-bloc resection rates for 83.6% and 57.6%. The numbers of accident cases were three (postoperative hemorrhage; n=1 perforation; n=2) and four (postoperative hemorrhage; n=1, perforation; n=3), respectively. Conclusions: These studies indicated higher onepiece resection rates, en-bloc resection rates and curative en-bloc resection rates for lesions based on the guidelines than those based on the expanded guidelines.

### INTRODUCTION

A number of endoscopic mucosal resection (EMR) techniques have been developed in Japan for the treatment of gastric tumorous lesions. Among these techniques, strip biopsy (1)and aspiration mucosectomy using an attached hood on the tip of endoscope (2,3) have become popular practice for their convenience and reliability. However, the specimens obtained by these techniques are limited in size (approximately 10-20 mm, according to the tumor location and operator's skills) and the technique often becomes piecemeal resection in larger tumors. One-piece resection is desirable in especially larger tumors, because histological evaluation is essential to estimate the risk for lymph node metastasis. Moreover, it is also very important for the prevention of local recurrence, as a high recurrence rate after piecemeal resection has been reported (4). Endoscopic submucosal dissection (ESD) techniques have been introduced to overcome this disadvantage. We have used ESD to treat patients with early-stage gastric cancer since January 2004. We have treated 100 patients with early gastric cancer by ESD. This report presents the treatment results evaluated for

lesions that were classified as indications for EMR specified in the Japanese Gastric Cancer Association guidelines (hereafter referred to as "specified indications") or as expanded indications for EMR (hereafter referred to as "expanded indications").

### METHODOLOGY

The subject group included 95 patients (73 males, 22 females; mean age 71.3 years) with 100 early-stage gastric cancer lesions who underwent ESD at our department from January 2004 to January 2007. Candidates for endoscopic treatment were determined from their endoscopic features with chromoendoscopy, endoscopic ultrasonography (EUS) and endoscopic biopsy. EUS findings of early gastric mucosal cancer (M) were defined as abnormal findings up to the second layer of the gastric wall without abnormal changes in the third layer, and EUS findings of minimal submucosal gastric cancer (SM1) were defined as abnormal changes, such as low echoic images, just beyond the second layer of the gastric wall. Moderate and severe invasions to the submucosal layer were defined as SM2 and SM3, respectively. Preoperative indications for

ESD in the treatment of early-stage gastric cancer were as follows: 1. differentiated adenocarcinoma; 2. no clear findings of submucosal deep invasion (invasion depth  $\leq$  SM1); 3. no size limitation in the absence of an ulcer and 30mm in the presence of an ulcer.

Before the operation, the lesions were classified as specified indications or expanded indications. The specified indications applied to the following: (i) differentiated adenocarcinoma; (ii) intramucosal cancer; (iii) a size of 20 mm or less; and (iv) absence of ulcer.(5) For the expanded indications, the following criteria were applied according to the report from Gotoda *et al.* (6): (i) differentiated adenocarcinoma; and (ii) intramucosal cancer with a size of  $\geq$ 20 mm without ulcer or intramucosal cancer with a size of  $\leq$  30 mm with ulcer or minute submucosal cancer (SM1) which is  $\leq$  30 mm in size.

### Procedure of endoscopic submucosal dissection

The tumors were treated by the standard ESD procedures by using the Flex knife (KD-630L; Olympus Optical Co, Tokyo, Japan) alone or in combination with the Hook knife (KD-620LR; Olympus). The equipment was a single-channel endoscope with a water-jet system (XGIF-Q240M, Olympus). The high-frequency electrosurgical unit used was the Erbotom ICC 200 (ERBE Elelektrom endizin GmbH, Tubingen, Germany). The practical ESD procedure was performed as already reported (7,8).

First, marks were made around the lesions using the tip of the Flex knife. Following lesion lifting with a submucosal injection, an incision was made in the surrounding mucosa with the Flex knife, with consecutive dissection of the submucosal tissue. In some cases, standard polypectomy using an electrosurgical snare loop was performed to finally remove the circumferentially incised area. A mixture of glycerin containing normal saline and 5% fructose (Glyceol; Chugai Pharmaceutical Co., Ltd., Tokyo, Japan) and high-molecular-weight hyaluronic acid (Suvenyl; Chugai Pharmaceutical Co., Ltd., Tokyo) was used for the submucosal injection (9,10).

Oral intake of liquid food was permitted from the day after treatment if there was no severe complication. Patients underwent follow-up endoscopy after 1 week to check the ulcer bed for any exposed vessels and were then discharged from the hospital. For postoperative treatment, a proton-pomp inhibitor (20 mg rabeprazole) was administered daily in the outpatient clinic until 8 weeks after ESD.

In all cases, endoscopic follow-up examination was performed routinely at 1 week, 3 months, 9 months and then every 6 months after ESD.

# Histological evaluation & assessment of therapeutic efficacy

The specimen resected in one-piece form by ESD fell under the one-piece resection category, regardless of whether the margin was positive or negative.

The resected specimen was fixed with formalin

and cut into 2-mm slices, then embedded in paraffin. A histological section was made from each block and stained with hematoxylin eosin. Histological assessment was microscopically performed in detail according to the Japanese Classification of Gastric Carcinoma (11). The depth of submucosal penetration was classified into two groups: SM1 ( $\leq 500\mu$ m penetration into submucosa) and SM2 ( $>500\mu$ m).

Evaluation of the extension of cancer cells to the lateral and/or vertical margin was classified into the following three groups.

- Complete resection: free of cancer glands on cut ends (lateral stump, and deep stump negative).
- Incomplete resection: exposure of cancer glands on cut ends.
- Not evaluable: impossibility of evaluation due to burn effect by diathermic treatment, mechanical damage or piecemeal resection.

En-bloc resection was defined as the resected tumor being confined to one-piece resection with complete resection as above.

Curative en-bloc resection was defined as en-bloc resection that fulfills the following three criteria (12).

1. differentiated adenocarcinoma; 2. no lymphatic or venous invasion 3a. intramucosal cancer regardless of tumor size without ulcer 3b. intramucosal cancer 30 mm in size with ulcer 3c. minute submucosal cancer (sm1) 30 mm in size.

The cases in whom the above criteria were not fulfilled were regarded as noncurative resection. Accordingly, all the cases in whom a piecemeal resection was carried out were regarded as noncurative resection.

### Complication: bleeding and perforation

Bleeding was defined as massive bleeding during the procedure requiring blood transfusion or when postoperative bleeding required hemostatic treatment, such as endoscopic clipping, thermocoagulation, argon plasma coagulation, and/or injection therapy. Perforation was diagnosed endoscopically when another abdominal organ, mesenteric fat, or intra-abdominal space was observed during the procedure and/or by the presence of free air in the peritoneal cavity, or air extending into the retroperitoneal or mediastinal space in the plain radiograph.

### Statistics

Values were expressed as mean $\pm$ SD. Statistical analysis was performed using the unpaired Student's t-test and chi-square test. A p value of less than 0.05 was considered to be significant.

### RESULTS

There were 67 specified indications, and 33 expanded indications.

Endoscopic resection was conducted with all lesions and a histological examination was performed on every resected specimen. **Table 1** summarizes the clinicopathological features of the lesions treated with ESD.

TABLE 1 Patient Characteristics							
	Specified indication	Expanded indication	Total				
Tumors	n=67	n=33	n=100				
Gender (male/female)	45/18	28/4	73/22				
Age (mean±SD)	$71.9 \pm 8.4$	$70.1 \pm 1.3$	$71.3 \pm 8.0$				
(range)	(43 - 94)	(53 - 84)	(43 - 94)				
Location							
U	14	7	21				
M	17	5	22				
L	36	21	57				
Macroscope							
0-IIa	33	16	49				
0-IIa+IIc	17	10	27				
0-IIc	17	6	23				
0-IIb	0	1	1				

U: upper third; M: middle third; L: lower third of the stomach

# TABLE 2 Summarizes the Treatment Outcomes According to Preoperative Indication

	One-piece resection	En bloc resection	Curative En bloc resection
Specified indication	65 (97.0%) ¬	56 (83.6%)	56 (83.6%)
(n=67)	***	*	**
Expanded indication	25 (75.8%)	20 (60.6%)	19 (57.6%)
(n=33)	90 (90.0%)	76 (76.0%)	75 (75.0%)

 Resected sample diameter, tumor diameter and procedure time according to preoperative indication

	Resected sample Diameter,mm	Tumor diameter mm	Procedure time min.
Specified indication	$26.7 \pm 9.2$	$11.6 \pm 4.4$	82.4 ± 33.7 ¬
(n=67)	(10-60)	(2-20)	(30-210) *
Expanded indication	$35.9 \pm 9.5$	$26.3 \pm 5.3$	$101.2 \pm 43.5$
(n=33)	(16-60)	(15-37)	(45-210)
Total	$29.8 \pm 10.2$	$16.5 \pm 8.4$	$88.6 \pm 38.1$
(n=100)	(10-60)	(2-37)	(30-210)

\*p<0.05; \*\*p<0.01; \*\*\*p<0.005

. One piece resection	65	
(i) En bloc resection	56	
<ul> <li>a. Curative-en bloc resection</li> </ul>		56
<ul> <li>b. Non curative-en bloc resection</li> </ul>		0
(ii) Non en bloc resection	6	
Lateral margin positive		1
Vertical margin positive		4
Lymphovascular involvement		3
Submucosal invasion (SM2)		3
(iii) Not evaluated	3	
Lateral margin not evaluated		3
2. Piecemeal resection	2	

**Table 2 (ab)** summarizes the treatment outcomes according to preoperative indications. The overall one-piece resection rates, en-bloc resection rates and curative en-bloc resection rates were 90.0%, 76.0% and 75.0%, respectively. For lesions with specified

indications and expanded indications, the one-piece resection rates were 97.0% and 75.8% (p=0.002), enbloc resection rates were 83.6% and 60.6% (p=0.022), and curative en-bloc resection rates were 83.6% and 57.6% (p=0.009), respectively (**Table 2-a**)

For lesions with specified indications and expanded indications, the time of the procedure was  $82.4\pm33.7$  and  $101.2\pm43.5$  minutes, respectively (p=0.02) (Table 2-a)

Table 3 (ab) summarizes the cure rate for one-piece resection. Of the 65 patients with specified indications who underwent one-piece resection, 56 had a curative en bloc resection, but the remaining 9 patients — 6 with non-en bloc resection and 3 whose lesions were not evaluated — did not have a curative en bloc resection. These 9 patients were classified according to the interfering factor in curative resection as follows: "lateral margin positive or not evaluated" in 4 patients; "vertical margin positive" in 4 patients; "lymphovascular involvement" in 3 patients; and "SM2 invasion" in 3 patients (there were overlapping cases).

For the expanded indications, 20 of 25 patients who underwent a one-piece resection had an en bloc resection. Of these 20 patients, 19 underwent a curative en bloc resection and the remaining one patient did not have a curative en bloc resection because of a positive lymphovascular involvement. Furthermore, 5 of 25 patients undergoing one-piece resection did not have an en bloc resection. These 5 patients were classified according to the interfering factor in curative resection as follows: a positive lateral margin in 4 patients; a positive vertical margin in 2 patients; a lymphovascular involvement in 2 patients; and SM2 invasion in 2 patients (there were overlapping cases).

The patients who underwent one-piece resection, but did not have curative resection, are summarized in **Tables 4-a** and **4-b**.

Laparotomy was performed in 6 of 9 patients. The remaining three patients were followed up at their own will. Of the 6 patients undergoing laparotomy, four had no residual cancer in the stomach or lymph node metastasis after resection, one (case 1) had lymph node metastasis in spite of there being no residual cancer in the stomach, and one (case 8) had residual cancer in the stomach.

Of the 6 patients, 5 underwent laparotomy and the remaining patient was followed up at his own will. Of the 5 laparotomized patients, 4 had no residual cancer in the stomach or lymph node metastasis after resection and the remaining patient did not have lymph node metastasis in spite of the presence of residual cancer in the stomach. **Table 5** shows the occurrence of complications.

Minor bleeding was encountered in all the lesions when the mucosa was incised or the submucosa dissected, but complete hemostasis was achieved within a few minutes with thermocoagulation using hemostatic forceps. Massive bleeding requiring blood transfusion was not observed. Bleeding as hemateme-

sis a day after the procedure was experienced in two cases (2%). In one (having expanded indications) of 2 patients with hemorrhage, emergency endoscopy revealed bleeding from the visible vessel of the ulcer bed and hemostasis was achieved with argon plasma coagulation. In the remaining one patient with hemorrhage (having specified indications), emergency endoscopy was performed, but blood clots did not allow satisfactory visual-field acquisition, making it impossible to follow an adequate endoscopic procedure. Emergency laparotomy was thus performed.

Perforation was observed in 5 cases (5%). In one case (having expanded indications), no perforated hole was noticed during the procedure, but the abdominal X ray on the next day revealed free air, probably due to microperforation. The patient had no symptom and recovered well with 3 days of fasting and the administration of antibiotics. In four cases, a small perforated hole was closed immediately with hemoclips, and the patient was discharged uneventfully at 7 days after the treatment.

The mean follow-up period was  $25.2\pm11.0$  months (range 9-46 months). There were no local recurrences after en-bloc curative resection.

### DISCUSSION

Eligibility of EMR for the treatment of early gastric cancer has been discussed for more than 10

TABLE 3-b Cure Rate for One Piece Resection 33 Candidates Evalu	ated
Expanded Indication	

One piece resection	25			
(i) En bloc resection		20		
a. Curative en bloc resection			19	
b. Non curative en bloc resection			1	
Lymphovascular involvement				1
(ii) Non en bloc resection		5		
Lateral margin positive				4
Vertical margin positive				2
Lymphovascular involvement				2
Submucosal invasion (SM2)				2
(iii) Not evaluated		0		
Piecemeal resection	8			

years, with consideration of lymph node metastasis and technical problems. According to the Gastric Cancer Treatment Guidelines (GL) published by the Japanese Gastric Cancer Association in 2001, the indications for early gastric cancer (EGC) are restricted to (i) differentiated adenocarcinoma; (ii) intramucosal cancer; (iii) a size of 20 mm or less; and (iv) absence of ulcer (5).

These conditions reflect the conventional technical limitations of EMR, however. Indeed, a number of lesions, even when more than 2 cm in size, have been

TABLE 4-a Patients' Characteristics in Non Curative Cases. Specified Indications													
Case	Age/sex	Macroscope	Location	Histology	Depth	lyv	UL	LM	VM	SD (mm)	TD (mm)	Additional treatment	Residual cancer in the R.S./LN meta
1	71/M	IIa	M	Tub 1	SM2	+	_	_	+	25	15	Surgery	-/+
2	72/M	IIa	L	Tub 1	SM2	+	-	-	+	35	20	Surgery	-/-
3	67/M	IIc	U	Tub 1	SM1	+	-	-	+	21	15	Surgery	-/-
4	69/F	IIa + IIc	U	Tub 1	M	_	-	+		20	15	Follow up	
5	82/M	IIa + IIc	U	Tub 1	SM1	-	-	_	+	40	10	Surgery	-/-
6	70/M	IIa + IIc	L	Tub 1	SM2	-	_	-		20	18	Surgery	-/-
7	43/M	IIc	M	Tub 1	M	_	_	N.E.	_	20	10	Follow up	70
8	79/M	IIc	L	Tub 1	M	-	_	N.E.	_	23	10	Surgery	+/-
9	70/F	IIc	L	Tub 1	M	-	_	N.E.	_	18	7	Follow up	

U: upper third; M: middle third; L: lower third of the stomach

Tub 1, Well-differentiated tubular adenocarcinoma Tub 2, Moderately-differentiated tubular adenocarcinoma

M: mucosa; SM: submucosa; Lyv: Lymphovascular involvement; LM: Lateral margin; VM: Vertical margin; SD: sample diameter; TD: tumor diameter N.E.: Not evaluated

TABLE 4-b Patients' Characteristics in Non Curative Cases. Expanded Indications													
Case	Age/sex	Macroscope	Location	Histology	Depth	lyv	UL	LM	VM	SD (mm)	TD (mm)	Additional treatment	Residual cancer in the R.S./LN meta
1	64/M	IIa + IIc	U	Tub 1	SM1	+	-	_	=	40	21	Surgery	-/-
2	59/M	IIa	M	Tub 1	M	_	+	+	_	35	35	Surgery	-/-
3	71/M	IIa	L	Tub 1	SM1	-	_	+	_	30	25	Surgery	-/-
4	66/M	IIa + IIc	U	Tub 2	SM1	-	_	+	_	40	30	Follow up	
5	67/M	IIc	L	Tub 1	SM2	+	-	_	+	32	28	Surgery	-/-
6	69/M	IIa	U	Tub 2	SM2	+	-	+	+	40	30	Surgery	+/-

U: upper third; M: middle third; L: lower third of the stomach

Tub 1, Well-differentiated tubular adenocarcinoma Tub 2, Moderately-differentiated tubular adenocarcinoma

M: mucosa; SM: submucosa; Lyv: Lymphovascular involvement; LM: Lateral margin; VM: Vertical margin; SD: sample diameter; TD: tumor diameter N.E.: Not evaluated

TABLE 5 Complications								
	Specified indication n=67	Expanded indication n=33	Total n=100					
Hemorrhage	1 (1.5%)	1 (3.0%)	2 (2.0%)					
Perforation	2 (3.0%)	3 (9.1%)	5 (5.0%)					

shown to have no lymph node metastasis. Gotoda et~al. studied the probability of lymph node metastasis in 5265 patients with early gastric cancer treated surgically (13). As a result, they found the probability of lymph node metastasis to be very low in the following (6), which, in turn, were regarded as expanded criteria for ESD: the differentiated type of intramucosal cancer >20 mm in size without ulcer; intramucosal cancer  $\le$ 30 mm in size with ulcer; or minute submucosal cancer (SM1)  $\le$  30 mm in size.

According to these criteria, our department established preoperative indications for ESD in the treatment of early-stage gastric cancer as follows: (1) differentiated adenocarcinoma; (2) with a submucosal invasion (invasion depth:  $\leq$ sm1) with no clear findings; and (3) with no size limitation in the absence of an ulcer or  $\leq$ 30 mm in the presence of an ulcer.

For evaluation, these indications were further classified into two categories: specified indications and expanded indications. The above-mentioned indications (i) to (iv), (5) provided by the Japanese Gastric Cancer Association, were defined as the specified indications and the above-mentioned criteria established by Gotoda *et al.* (6) were applied to the expanded indications.

Endoscopic resection techniques that have utilized direct dissection of the submucosa using a modified needle knife have recently been classified as ESD techniques (14). ESD using an insulationtipped disthermic knife, developed at the National Cancer Cancer Hospital, was the first of such techniques (15-17). ESD is superior to standard EMR, and provides a one-piece specimen with a standard single channel gastroscope. ESD has the advantage of achieving large one-piece resections, allows precise histological staging and may prevent disease recurrence compared with standard EMR methods. Other ESD techniques have been described using the hook knife (18), Flex knife (7), and the knife for the small cap technique (19). We used a Flex knife as the main device. The Flex knife designed by Yahagi, is rounded with a twisted wire like a snare. The sheath is soft and flexible. Compared to a needle knife, the flex knife is less likely to cause perforation when it reaches the muscular layer, since the tip is round, and the entire knife is soft and flexible. The length of the knife is

adjustable for different situations. Since the tip of the sheath is thick and functions as a stopper, operations can control the depth of incision easily.

The one-piece resection rate in total was 90.0% in the present study. The corresponding value was 98% (1008/1033) according to Oda et al., (12) 93% (183/196) according to Imagawa et al., (20) and 91% (63/71) according to Abe et al. (21) A multicenter retrospective study of endoscopic resections of early gastric cancer conducted in Japan (22) showed that the rate of one-piece resection by ESD was 92.7% (the rate of one-piece resection by EMR was 56.0% in this study). The larger the number of patients treated the greater improvement in technique proved to be. It therefore seems that one-piece resection rates increase. Indeed, Abe et al. (21) stated that the rate of one-piece resection by ESD was 97% in the latter half of the study in spite of a rate of 76% for the first half.

In the present study, a curative en bloc resection rate of 75.0% in total was obtained. The corresponding value was 84% (164/196) according to Imagawa *et al.*, (20) 81.5% (842/1033) according to Oda *et al.*, (12) 94.2% (161/171) according to Onozato *et al.*, (23) and 91% (396/434) according to Oyama *et al.* (24).

A multicenter retrospective study of endoscopic resection of early gastric cancer conducted in Japan (22) yielded a curative ESD resection rate of 73.6%. Of the patients at our institution who underwent one-piece resection, those without curative resection were examined for factors underlying an unsuccessful outcome.

In 4 (cases 4, 7, 8, and 9) of the 9 patients with specified indications, curative en bloc resection was not achieved because of being "lateral margin positive or not evaluated." In these cases, however, it would have been possible to achieve a curative en bloc resection if a correct diagnosis at the lateral margin had been made, thereby enabling the lesion to be resected more extensively. In 3 of the 9 patients, the depth of invasion was classified as SM2, hence the lesion was beyond the indications for ESD from the outset (Table 4-a).

Of the 6 patients with expanded indications, 4 (cases 2, 3, 4, and 6) did not undergo a curative en bloc resection because of having a positive lateral margin, but a curative en bloc resection could have been achieved if a correct diagnosis at the lateral margin had been made, thereby enabling the lesion to be resected more extensively. In 2 patients, the lesion was classified according to the depth of invasion as SM2 and was beyond the indications for ESD from the outset (Table 4-b).

Of the 15 combined patients with specified indications and expanded indications, 13 would have undergone a curative en bloc resection or a laparotomy without ESD if a correct preoperative diagnosis of lateral margin or invasion depth had been made. The main reason why a high curative en bloc resection rate was not obtained in the present study may lie in the low correct preoperative diagnosis rates for lateral margin and invasion depth.

The ability of EUS to evaluate the depth of early gastric cancer is not sufficiently high, for the diagnostic accuracy has been reported to be 70-80% at most (25,26).

Curative en bloc resection was not achieved in spite of one-piece resection in 4 of 65 patients with specified indications (6.2%) and 4 of 25 patients with expanded indications (16.0%), although the difference was not statistically significant (p=0.146).

In recent years, magnifying endoscopy combined with a narrow band imaging system has been used for the diagnosis of early gastric cancer (27,28). Sumiyama (27) et al. have stated that the use of magnifying endoscopy combined with a narrow band imaging system for the EMR of early gastric cancer permitted correct diagnosis of the boundary between the cancer and normal mucosa, thereby improving the results of treatment. Therefore, if the introduction of magnifying endoscopy combined with a narrow band imaging system permits a reliable diagnosis of the boundaries of a tumor, it can be expected that curative en bloc resection rates will rise.

Onozato et al. have reported that bleeding following ESD occurred in 9.9% (17/171) of patients. (23) The corresponding values reported by Oda et al. (12) and Abe et al. (21) were 6% (59/1033) and 7% (5/71), respectively. In the present study, bleeding was experienced 1 day after the procedure by two patients (2%). The incidence of bleeding was 1.5% (1/67) for the specified indications and 3.0% (1/33)

for the expanded indications, with no statistically significant difference being noted (p=0.55).

The incidence of perforation following ESD has been reported by Onozato *et al.* (23) to be 3.5% (6/171), by Oda *et al.* (12) to be 3.4% (35/1033), and by Abe *et al.* (21) to be 7% (5/71). In our study, perforation was observed in 5 patients (5%).

Furthermore, the incidence of perforation was 3.0% (2/67) for the specified indications and 9.1% (3/33) for the expanded indications, there being no statistically significant difference (p=0.20).

Although our experience of ESD is limited to 100 patients, the incidence of complications is considered to be low.

In recent years, much information has accumulated concerning the results of treatment of early gastric cancer with ESD. However, there has been only one reports on the results of treatment of lesions classified separately as specified indications or as expanded indications (22).

The results of the present study indicate that the one-piece resection, en bloc resection and curative en bloc resection rates are higher for lesions with specified indications than those with expanded indications. No lethal complication has been observed in either group of indications. In addition, the findings of the present study suggest that treatment results for expanded indications will be improved if improvement in preoperative diagnosis is achieved.

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