



Digestive Endoscopy

Clinical outcomes of endoscopic submucosal dissection (ESD) for treating early gastric cancer: Comparison with endoscopic mucosal resection after circumferential precutting (EMR-P)

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Abstract

Background. To achieve en bloc resection for large lesions, endoscopic mucosal resection after circumferential precutting and endoscopic submucosal dissection techniques have been developed.

Aim. To compare endoscopic submucosal dissection with endoscopic mucosal resection after circumferential precutting in terms of the clinical efficacy and safety.

Patients and methods. 346 consecutive patients underwent their first endoscopic mucosal resection after circumferential precutting (103 patients) or endoscopic submucosal dissection (243 patients) for early gastric cancer and their clinical outcomes were compared.

Results. For early gastric cancer ≥ 20 mm endoscopic submucosal dissection group demonstrated significantly higher en bloc resection and en bloc plus R0 resection rate compared with endoscopic mucosal resection after circumferential precutting group. For early gastric cancer with size of 10–19 mm, endoscopic submucosal dissection group also showed significantly higher en bloc resection rate. For early gastric cancer < 20 mm, however, en bloc plus R0 resection rate for endoscopic mucosal resection after circumferential precutting group was comparable to that for endoscopic submucosal dissection group. In case of R0 resection of intramucosal differentiated cancer, neither group showed local recurrence during the median 29 and 17 months of follow-up. Two groups did not show significant difference in the bleeding or perforation rates.

Conclusion. For early gastric cancer < 20 mm endoscopic mucosal resection after circumferential precutting may be considered as an alternative choice to endoscopic submucosal dissection. However, for early gastric cancer ≥ 20 mm endoscopic submucosal dissection should be considered as the first choice for treating early gastric cancer.

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Keywords: En bloc plus R0 resection; En bloc resection; Endoscopic mucosal resection after circumferential precutting; Endoscopic submucosal dissection

1. Introduction

Endoscopic mucosal resection (EMR) has become a standard treatment for selected cases of early gastric cancer (EGC) because of its minimal invasiveness and excellent long-term survival comparable to surgical resection [1–5].

When performing EMR, en bloc resection is desirable for a successful treatment outcome, as an accurate and reliable histopathological evaluation is occasionally difficult to achieve for a piecemeal resection. An inaccurate histopathological assessment for the completeness of resection can result in an inaccurate decision for further treatment and, ultimately, local tumour recurrence [6,7].

When using a conventional technique such as a strip biopsy, EMR has been limited to small (typically < 2.0 cm) lesions because a trial of the resection for larger lesions

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may result in piecemeal resections [8,9]. To achieve en bloc resection for larger lesions, EMR after circumferential precutting (EMR-P) [10–15], and more recently, endoscopic submucosal dissection (ESD) method have been developed [16–25]. EMR-P method, in which lesions are resected using a snare after circumferential precutting, allows en bloc resection of the lesion with a maximal diameter of 2–3 cm [10,26]. This limitation is mainly due to the difficulty in ensnaring a large lesion even after successful circumferential precutting [12,14]. In contrast to conventional EMR and EMR-P, ESD method is considered to allow en bloc resection regardless of tumour size, because the submucosa beneath the lesion is dissected directly by an electrosurgical knife without using a snare [7,17,18]. However, ESD method usually requires long procedure time and learning curve [19]. In addition, it is also thought that the ESD method may cause complications such as bleeding and perforation more frequently than conventional EMR or EMR-P [7,17,18,21]. There have been several studies comparing the treatment outcomes of ESD and conventional EMR for treating EGC [20,21,27]. To date, however, advantages and disadvantages of ESD compared with EMR-P are unknown.

The aim of this study was to compare ESD with EMR-P in terms of the clinical efficacy and safety on treating EGC.

2. Patients and methods

2.1. Patients

All the patients who underwent their first EMR-P (103 lesions, 103 patients) or ESD (243 lesions, 243 patients) for EGC in our institution from July 2003 to June 2006 were enrolled consecutively. From July 2003 to December 2004, the first half period of the present study, 32 cases (29.6%) of ESD and 76 cases (70.4%) of EMR-P were performed. During this period ESD technique was introduced into our institution and ESD was mainly performed for the lesion located at the antrum or the angle where the procedure is relatively easy to perform (28 cases (87.5%) for the antrum or angle, 4 cases (12.5%) for the lower body) [15,19,28]. All lesions located at the mid or high body were resected using EMR-P (57 cases (75.0%) for the antrum or angle, 12 cases (15.8%) for the lower body, 7 cases (9.2%) for the mid or high body) in this period. From January 2005 to June 2006, the second half period of the present study, 211 cases (88.7%) were resected using ESD and only 27 cases (11.3%) were resected using EMR-P. During this period most cases of EMR-P were performed for the cases initially diagnosed as adenoma, not EGC, by forceps biopsy prior to the procedure (6/27, 22.2%) or for the small lesions (lesion size ≤ 10 mm on endoscopic findings; 17/27, 63.0%). All the patients enrolled provided written informed consent for the procedures. Two experienced endoscopists (JJ Kim and JH Lee) performed all the procedures.

The indications for EMR were as follows: (1) tumour regarded as an intramucosal lesion on endoscopic finding [29]; (2) well or moderately differentiated histology on biopsy performed before ESD or EMR-P; (3) <2 cm in diameter for an elevated lesion and <1 cm for a flat or depressed lesion on endoscopic finding; (4) no evidence of ulcer or ulcer scar on endoscopic finding; and (5) no lymph node involvement or distant metastasis on abdominal computed tomography (CT). However, EMR-P or ESD were performed for 28 patients who did not meet these indications. These cases included patients that were diagnosed to have adenoma, not EGC, by forceps biopsy prior to the procedure and patients who refused to undergo surgery or had severe comorbidity that made them unsuitable as candidates for surgery. Endoscopic ultrasonography was not performed before the procedures, because of its limited accuracy on predicting the depth of tumour invasion [1,7,17,30–32].

2.2. Techniques of endoscopic resections

2.2.1. EMR-P (Fig. 1)

There have been several reports describing EMR-P [10–15]. Among them, the technique we used here was almost the same as Choi et al. have previously described [15]. After identifying the target lesion, marking dots were made circumferentially at approximately 5 mm lateral to the margin of the lesion using a needle knife (KD-1L-1; Olympus Optical Co., Tokyo, Japan, or Needle papillotome; MTW Endoscopy, Wesel, Germany). After marking, a submucosal injection of saline with epinephrine mixed with indigocarmine was performed around the lesion to lift it off the muscle layer. Then, an initial incision of mucosa was made with the needle knife to allow insertion of the tip of the knife into the submucosa. After the initial incision, a circumferential mucosal incision was performed outside the marking dots to separate the lesion from the surrounding non-neoplastic mucosa. This step was done using the electrosurgical knife such as needle, Flex (KD-630L; Olympus) or insulated-tipped (IT) knife (KD-610L; Olympus) with a high-frequency generator (Erbotom ICC 200; ERBE Elektromedizin Ltd., Tübingen, Germany). After the circumferential incision, an additional submucosal injection of saline with epinephrine mixed with indigocarmine was performed beneath the lesion. Finally, the adequately raised lesion was ensnared using snare (SD-9U-1 or SD-12U-1; Olympus) and removed in the same fashion as with the standard snare polypectomy technique.

2.2.2. ESD (Fig. 2)

ESD procedure was the same as EMR-P method until the step of circumferential mucosal incision and additional submucosal injection. After these steps were completed, the submucosal connective tissue just beneath the lesion was directly dissected using an electrosurgical knife such as needle, Flex or IT knife [17,18].

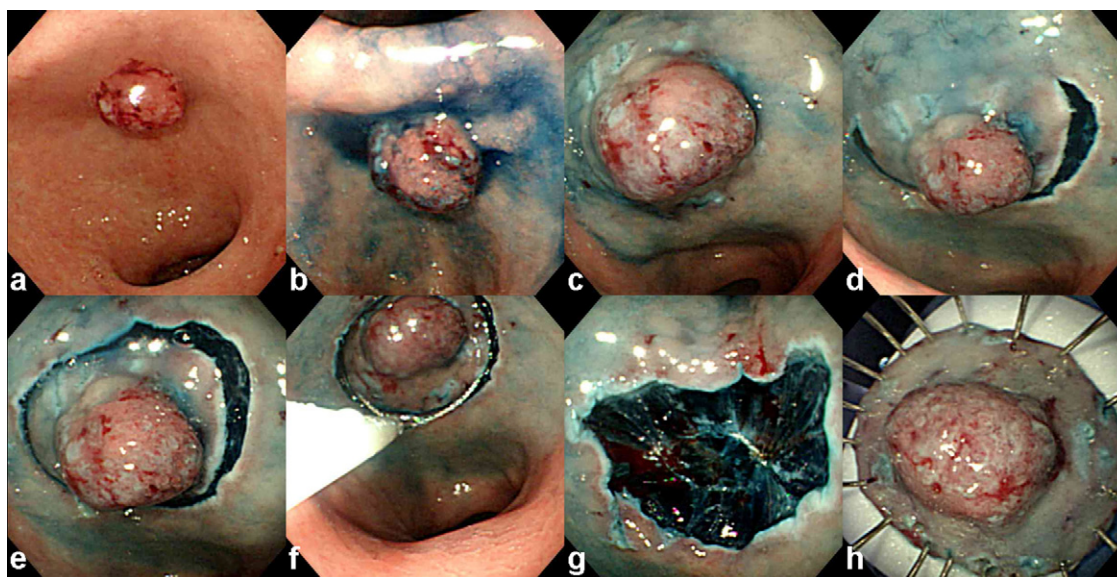


Fig. 1. Procedure of endoscopic mucosal resection after circumferential precutting (EMR-P). (a) A type I early gastric cancer was located at the lesser curvature side of the antrum. (b) Indigo carmine dye was sprayed around the lesion to define the margin accurately. (c) Marking dots were made circumferentially at approximately 5 mm lateral to the margin of the lesion. (d)–(e) After a submucosal injection of saline with epinephrine mixed with indigocarmine, a circumferential mucosal incision was performed outside the marking dots to separate the lesion from the surrounding non-neoplastic mucosa. (f) After an additional submucosal injection, the lesion was ensnared and removed in the same fashion as with the standard snare polypectomy technique. (g) The lesion was completely resected using the snare and the consequent artificial ulcer was seen. (h) The resected specimen with a central early gastric cancer.

2.3. Assessment of the therapeutic efficacy and procedure time

We defined the resection as “en bloc” when the tumour was resected in one piece without fragmentation. The complete-

ness of resection was classified according to the extension of tumour cells into the resection margin [24]: (1) complete (R0) resection: when the lateral and vertical resection margins are free of tumour; (2) incomplete (R1) resection: when the tumour extends into the lateral or vertical

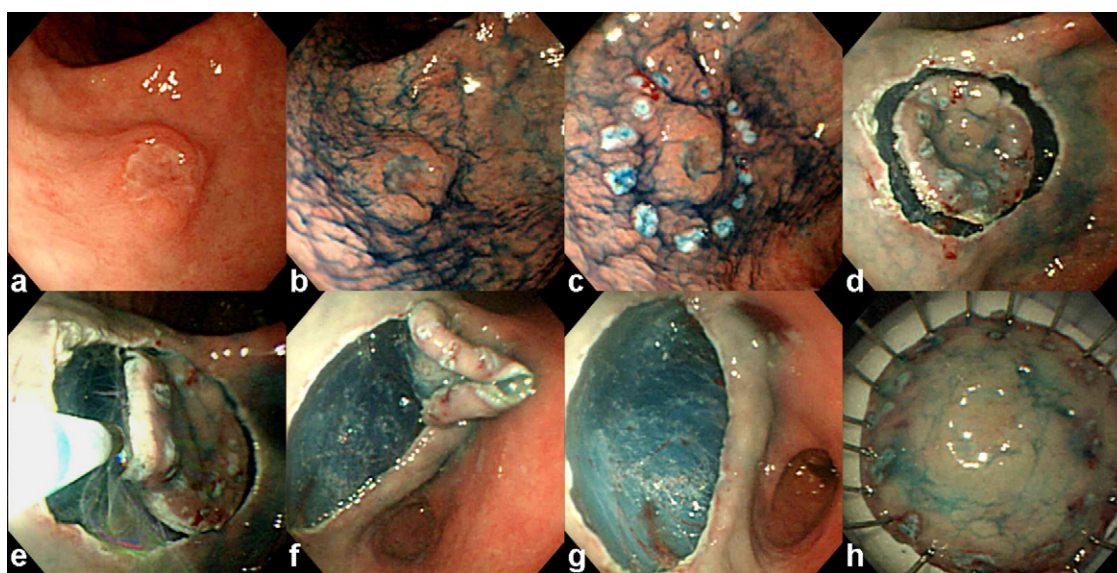


Fig. 2. Procedure of endoscopic submucosal dissection (ESD). (a) A type IIa + IIc early gastric cancer was located at the lesser curvature side of the antrum. (b) Indigo carmine dye was sprayed around the lesion to define the margin accurately. (c) Marking dots were made circumferentially at approximately 5 mm lateral to the margin of the lesion. (d) After a submucosal injection of saline with epinephrine mixed with indigocarmine, a circumferential mucosal incision was performed outside the marking dots to separate the lesion from the surrounding non-neoplastic mucosa. (e)–(f) After an additional submucosal injection, the submucosal connective tissue just beneath the lesion was directly dissected using an electrosurgical knife instead of using a snare. (g) The lesion was completely resected and the consequent artificial ulcer was seen. (h) The resected specimen with a central early gastric cancer.

resection margin; (3) resection not evaluable (Rx): when the margins are not evaluable due to artificial effects of coagulation or piecemeal resection. In case of submucosal invasion, lymphovascular invasion, poorly differentiated histology or signet ring cell carcinoma, additional gastrectomy was strongly recommended for the fear of lymph node involvement. In case of R1/Rx resection or tumour-free lateral resection margin <2 mm, additional EMR or gastrectomy was recommended.

The procedure time was defined as the required time from marking to resection of the lesion. The required time for haemostasis after resection was not included in the procedure time.

2.4. Complications

Perforation was diagnosed when mesenteric fat or intra-abdominal space was directly observed during the procedure (frank perforation) or free air was found on a plain chest X-ray after the procedure without a visible gastric wall defect during the procedure (microperforation) [33]. Bleeding was defined as (1) intraoperative massive bleeding that required blood transfusion, (2) postoperative bleeding that required blood transfusion or endoscopic or surgical intervention because of hematemesis or melena or (3) a decrease of the hemoglobin level more than 2 g/dL after the procedure.

2.5. Follow-up after EMR-P and ESD

The patients were followed up with an esophagogastroduodenoscopy (EGD) with a biopsy 1 month after EMR-P or ESD to confirm healing of the artificial ulcer and to exclude the presence of any residual tumour. Then, EGD was performed every 3 months for the first year and every 6 months for the second and the third year to check for local or metachronous recurrence. From the fourth year, EGD was performed annually. In addition, an abdominal CT was performed every 6 months for the first year and then performed annually to detect extragastric recurrence.

When the cancer was detected at the resection site in the first or second follow-up EGD within the 12 months after the procedure, the detected cancer was regarded as “residual disease”. When the cancer was detected at the resection site during the EGD after two negative follow-up EGD, the detected cancer was regarded as “local recurrence”. Patients who did not undergo at least two follow-up EGD within 12 months after the procedure were excluded in estimating the local recurrence rate due to the difficulty in distinguishing local recurrence from residual disease. When the cancer was detected at the site other than resection area during the follow-up EGD, the detected cancer was regarded as “metachronous recurrence”. EGD and CT results until June 2007 were reviewed using medical records. The median duration of follow-up in R0 resection cases of intramucosal differentiated cancer was 29 months (range, 4–44 months) for

EMR-P and 17 months (range, 4–37 months) for ESD cases, respectively.

2.6. Statistical analysis

Categorical data analysis was conducted using the χ^2 test or Fisher's exact test. Continuous data were analyzed using the Student *t* test. All *P*-values were 2-tailed and *P*-values less than 0.05 were considered statistically significant.

3. Results

3.1. Characteristics of the patients and the tumours

Table 1 summarized the characteristics of the patients and the tumours. No significant difference was found between EMR-P and ESD group in terms of age, gender, or tumour location. However, flat or depressed lesions and tumours with size ≥ 20 mm were significantly more frequent in the ESD group than in the EMR-P group.

3.2. Rates of en bloc resection, R0 resection and en bloc plus R0 resection

For all study subjects, ESD group showed significantly higher en bloc resection and en bloc plus R0 resection rates

Table 1
Characteristics of the patients and the tumours

Characteristics	EMR-P (n = 103)	ESD (n = 243)	P-value
Age (years)			0.689
Mean $\pm$ S.D.	61.3 $\pm$ 10.0	61.8 $\pm$ 10.0	
Median (range)	62 (26–84)	62 (34–84)	
Gender (%)			0.329
Male	76 (73.8)	191 (78.6)	
Female	27 (26.2)	52 (21.4)	
Macroscopic appearance (%)			0.034
Elevated	75 (72.8)	148 (60.9)	
Flat or depressed	28 (27.2)	95 (39.1)	
Tumour location (%)			0.394 ^a
Antrum	66 (64.1)	157 (64.6)	
Angle	12 (11.7)	37 (15.2)	
Body	24 (23.3)	49 (20.2)	
Fundus	1 (1.0)	0 (0.0)	
Tumour size (%) ^b			0.013 ^c
<10 mm	38 (36.9)	58 (23.9)	
10–19 mm	48 (46.6)	114 (46.9)	
20–29 mm	12 (11.7)	45 (18.5)	
≥ 30 mm	5 (4.9)	26 (10.7)	

EMR-P, endoscopic mucosal resection after circumferential precutting; ESD, endoscopic submucosal dissection; S.D., standard deviation.

^a The result from the comparison of the cases located at the antrum or angle and the cases located at the body or fundus.

^b Tumour size was determined according to pathologic findings.

^c The result from the comparison of the cases with size <20 mm and the cases with size ≥ 20 mm.

Table 2
Clinical outcomes of EMR-P and ESD for all study subjects

Characteristics	EMR-P (n = 103)	ESD (n = 243)	P-value
En bloc resection (%)	80 (77.7)	233 (95.9)	<0.001
R0 resection (%)	92 (89.3)	226 (93.0)	0.251
En bloc plus R0 resection (%)	78 (75.7)	216 (88.9)	0.002
Procedure time (min) ^a	24.3 ± 16.2	33.4 ± 16.6	<0.001
Bleeding (%)	4 (3.9)	13 (5.3)	0.564
Perforation (%)	2 (1.9)	11 (4.5)	0.359

EMR-P, endoscopic mucosal resection after circumferential precutting;
ESD, endoscopic submucosal dissection.

^a The value was expressed as mean ± standard deviation.

compared with EMR-P group. However, no significant difference was found between two groups in R0 resection rate (Table 2).

We sub-analyzed the rates of en bloc resection, R0 resection, and en bloc plus R0 resection for two groups according to tumour size (Table 3A). In case of tumour size <10 mm,

no significant difference was observed between two groups in the rates of en bloc resection, R0 resection, or en bloc plus R0 resection. In case of tumour size between 10 mm and 19 mm, ESD group showed significantly higher en bloc resection rate compared with EMR-P group. However, no significant difference was found between two groups in R0 resection or en bloc plus R0 resection rate. In case of tumour size ≥20 mm, the rates of en bloc resection, R0 resection, and en bloc plus R0 resection for ESD group were all significantly higher than those of EMR-P group. In EMR-P group, en bloc resection rate decreased from 86.8% to 41.2% as tumour size increased. In ESD group, however, en bloc resection rate was over 90% irrespective of tumour size. Same results were obtained when data were sub-analyzed according to the macroscopic appearance of tumours (Table 3B for elevated lesions and Table 3C for flat or depressed lesions). The rates of en bloc resection, R0 resection, and en bloc plus R0 resection did not show any significance differences between the two operators for either EMR-P or ESD.

Table 3
Clinical outcomes of EMR-P and ESD according to tumour size for all enrolled patients (A), patients with elevated lesions (B) and patients with flat or depressed lesions (C)

	Tumour size					
	<10 mm		10–19 mm		≥20 mm	
	EMR-P (n = 38)	ESD (n = 58)	EMR-P (n = 48)	ESD (n = 114)	EMR-P (n = 17)	ESD (n = 71)
(A)						
En bloc resection (%)	33 (86.8)	54 (93.1)	40 (83.3)	112 (98.2)	7 (41.2)	67 (94.4)
P value		0.476		0.001		<0.001
R0 resection (%)	37 (97.4)	58 (100.0)	45 (93.8)	105 (92.1)	10 (58.8)	63 (88.7)
P value		0.396		1.000		0.008
En bloc plus R0 resection (%)	33 (86.8)	54 (93.1)	39 (81.3)	103 (90.4)	6 (35.3)	59 (83.1)
P value		0.476		0.108		<0.001
	Tumour size					
	<10 mm		10–19 mm		≥20 mm	
	EMR-P (n = 26)	ESD (n = 26)	EMR-P (n = 36)	ESD (n = 69)	EMR-P (n = 13)	ESD (n = 53)
(B)						
En bloc resection (%)	23 (88.5)	24 (92.3)	30 (83.3)	67 (97.1)	6 (46.2)	49 (92.5)
P value		1.000		0.019		<0.001
R0 resection (%)	25 (96.2)	26 (100.0)	33 (91.7)	62 (89.9)	8 (61.5)	47 (88.7)
P value		1.000		1.000		0.033
En bloc plus R0 resection (%)	23 (88.5)	24 (92.3)	29 (80.6)	60 (87.0)	5 (38.5)	43 (81.1)
P value		1.000		0.386		0.004
	Tumour size					
	<10 mm		10–19 mm		≥20 mm	
	EMR-P (n = 12)	ESD (n = 32)	EMR-P (n = 12)	ESD (n = 45)	EMR-P (n = 4)	ESD (n = 18)
(C)						
En bloc resection (%)	10 (83.3)	30 (93.8)	10 (83.3)	45 (100.0)	1 (25.0)	18 (100.0)
P value		0.297		0.041		0.003
R0 resection (%)	12 (100.0)	32 (100.0)	12 (100.0)	43 (95.6)	2 (50.0)	16 (88.9)
P value		1.000		1.000		0.135
En bloc plus R0 resection (%)	10 (83.3)	30 (93.8)	10 (83.3)	43 (95.6)	1 (25.0)	16 (88.9)
P value		0.297		0.192		0.024

EMR-P, endoscopic mucosal resection after circumferential precutting; ESD, endoscopic submucosal dissection.

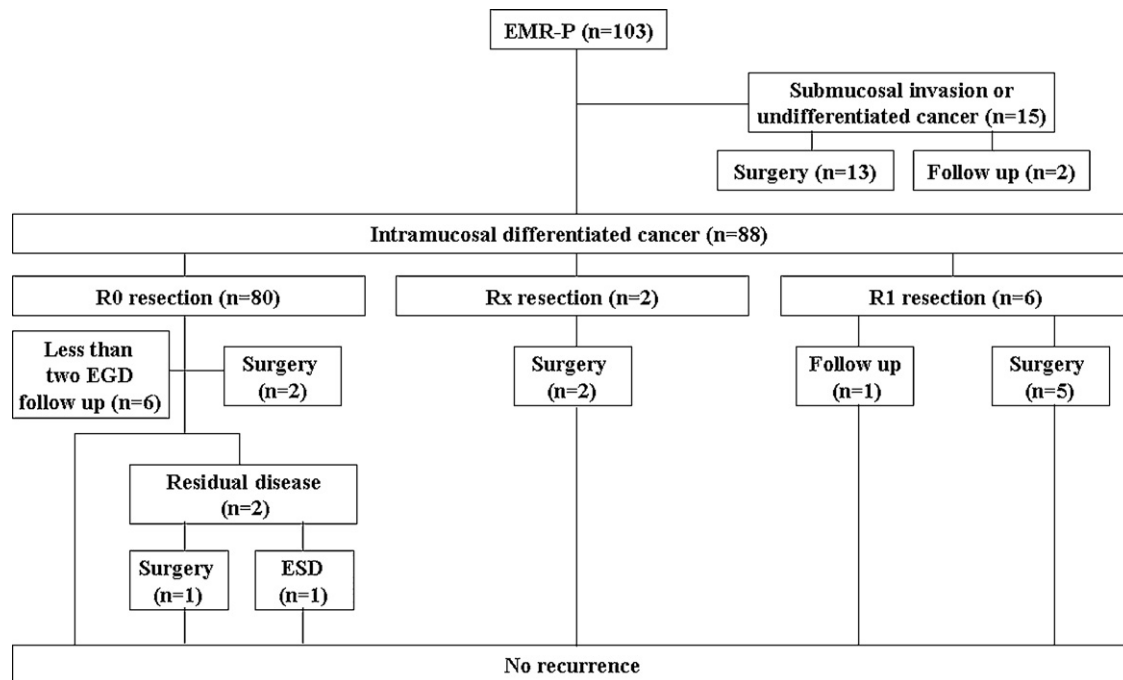


Fig. 3. Clinical courses after endoscopic mucosal resection after circumferential precutting (EMR-P). EGD, esophagogastroduodenoscopy; ESD, endoscopic submucosal dissection.

3.3. Time required for resection

The procedure time of EMR-P group was significantly shorter than that of ESD group for all study subjects (Table 2) and regardless of tumour size (data not shown).

3.4. Complications

The rate of bleeding for all study subjects was 3.9% and 5.3% for EMR-P and ESD group, respectively, and no significant difference was found between the two groups (Table 2). Bleeding could be successfully treated by placement of metallic clips or coagulation of the bleeding vessels except for one patient that underwent emergency surgery for uncontrolled bleeding during the EMR-P procedure. No significant difference was found between the two groups in the rate of bleeding, regardless of tumour size (data not shown).

The rate of perforation for all study subjects was 1.9% and 4.5% for EMR-P and ESD group, respectively, and no significant difference was observed between the two groups (Table 2). There were 1 frank perforation and 1 microperforation for EMR-P group and 3 frank perforations and 8 microperforations for ESD group. A perforation could be successfully treated non-surgically with a combination of endoscopic clipping, fasting, nasogastric tube drainage, and broad-spectrum antibiotics except for one patient that underwent emergency surgery due to frank perforation during the EMR-P procedure. No significant difference was found between the two groups in the rate of perforation, regardless of tumour size (data not shown).

3.5. Clinical courses after EMR-P and ESD

The clinical outcomes of the patients after undergoing EMR-P and ESD were shown in a schematic diagram in Figs. 3 and 4, respectively. As EMR-P and ESD groups demonstrated the difference in the frequency of the factors associated with poor prognosis after endoscopic resection (Table 4), analysis was confined to R0 resection cases of intramucosal differentiated cancer. Among the 80 R0 resection cases of intramucosal differentiated cancer in EMR-P group, no case of local recurrence was found during the median 29 months (range, 4–44 months) of follow-up. Two patients underwent surgeries after EMR-P without follow-up EGD because of the frank perforation and the tumour-free lateral resection margin <2 mm. Two patients (2.8%, 2/72) showed residual diseases 1 month after EMR-P in their first follow-up EGD. These two cases were resected in a piecemeal fashion (2 pieces and 3 pieces) and the nearest lateral resection margins were 5 mm and 2 mm apart from the cancers, respectively. These two patients underwent surgery and an additional ESD for the residual tumour, respectively, and did not show recurrence after the second treatment during the 25 and 30 months of follow-up, respectively. Among the 191 R0 resection cases of intramucosal differentiated cancer in ESD group, no case of local recurrence was observed during the median 17 months (range, 4–37 months) of follow-up. Four patients underwent surgeries or additional ESDs after ESD without follow-up EGD because of the tumour-free lateral resection margin <2 mm. One patient (0.56%, 1/180) showed residual disease 1 month after ESD in their first follow-up

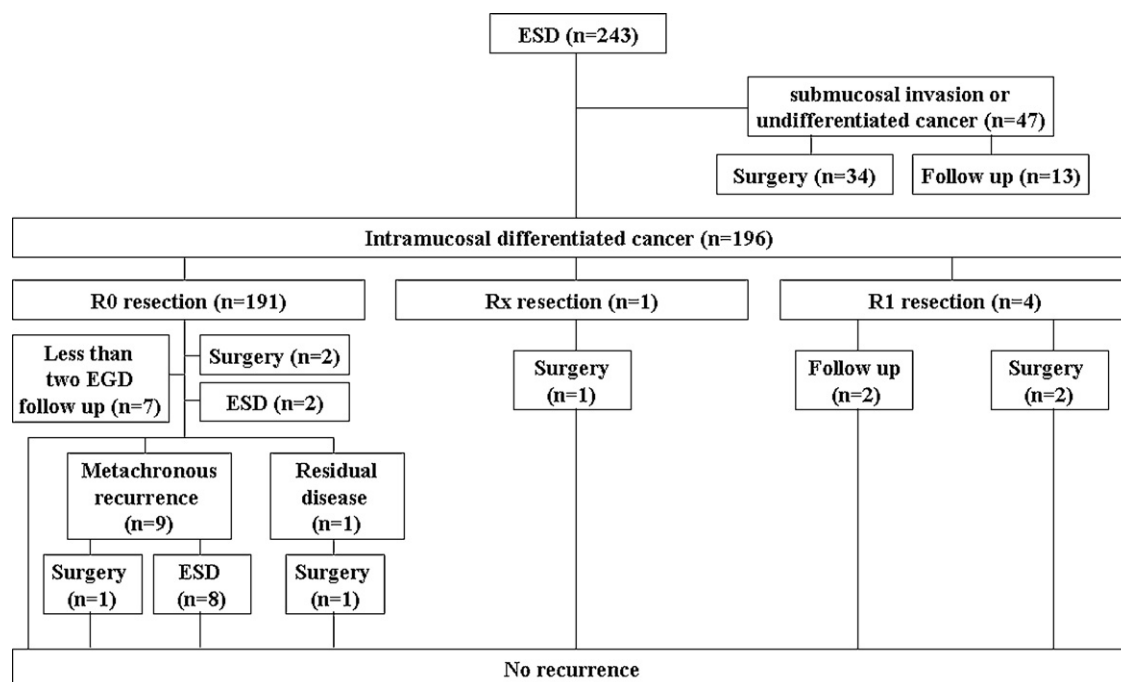


Fig. 4. Clinical courses after endoscopic submucosal dissection (ESD). EGD, esophagogastroduodenoscopy.

EGD. This case arose from a background flat adenoma and was resected in en bloc. The nearest lateral resection margin was 2 mm apart from the cancer. However, the margin was involved by the background adenoma. This patient underwent surgery for the residual tumour and did not show recurrence after the second treatment during the 35 months of follow-up. Nine patients showed metachronous recurrence and the median duration between ESD and metachronous recurrence was 7 months (range, 1–27 months).

4. Discussion

There have been several large retrospective studies showing the superiority of EMR-P and ESD over conventional EMR for treating EGC [11,20,21,27]. In the three studies

comparing ESD with conventional EMR, en bloc and complete resection rates for ESD group were reported to be over 85% regardless of tumour size [20,21,27]. However, en bloc and complete resection rates for the conventional EMR group in these studies were much lower and very disappointing. In the study by Oka et al. [21], en bloc resection rate for the conventional EMR group was reported to be 61.9%, 27.0% and 13.7% for the tumour with size ≤ 10 mm, 11–20 mm and ≥ 21 mm, respectively. In the same study, complete resection rate for the conventional EMR group was reported to be only 34.6%, 15.5% and 8.8% for the tumour with size ≤ 10 mm, 11–20 mm and ≥ 21 mm, respectively. A study by Ohkuwa et al. [11], that compared EMR-P with conventional EMR, has revealed the similar results. In that study, the rate of en bloc resection (defined as an intramucosal cancer resected in en bloc with negative resection margin) for the tumour

Table 4
Frequency of factors associated with poor prognosis after endoscopic resection

	Tumour size					
	<10 mm		10–19 mm		≥ 20 mm	
	EMR-P (n = 38)	ESD (n = 58)	EMR-P (n = 48)	ESD (n = 114)	EMR-P (n = 17)	ESD (n = 71)
Undifferentiated histology (%) ^a	0(0.0)	0(0.0)	3(6.3)	4(3.5)	2(11.8)	4(5.6)
Submucosal invasion (%)	4(10.5)	4(6.9)	5(10.4)	17(14.9)	2(11.8)	21(29.6)
Vascular or lymphatic invasion (%) ^b	0(0.0)	1(1.7)	1(2.1)	1(1.0)	1(5.9)	5(7.0)
Lateral resection margin invasion (%)	0(0.0)	0(0.0)	1(2.1)	2(1.8)	6(35.3)	6(8.5)
Vertical resection margin invasion (%)	1(2.6)	0(0.0)	1(2.1)	6(5.3)	0(0.0)	2(2.8)
Impossible complete reconstruction (%)	0(0.0)	0(0.0)	1(2.1)	0(0.0)	2(11.8)	0(0.0)

EMR-P, endoscopic mucosal resection after circumferential precutting; ESD, endoscopic submucosal dissection.

^a Undifferentiated histology included the cases with poorly differentiated or signet ring cell carcinoma.

^b All the cases with vascular or lymphatic invasion had submucosal invasion.

with size between 11 mm and 20 mm was only 29% for the conventional EMR group while the rate for EMR-P group was 75% for the tumour with same size. To date, however, advantages and disadvantages of ESD compared with EMR-P are unknown in terms of the clinical efficacy and safety on treating EGC.

The results of the present study demonstrated that the both en bloc resection and en bloc plus R0 resection rates for ESD group were significantly higher than those for EMR-P group in case of tumour size ≥ 20 mm. In case of tumour size between 10 mm and 19 mm, ESD group also showed significantly higher en bloc resection rate compared with EMR-P group. In case of tumour size < 20 mm, however, en bloc plus R0 resection rate for EMR-P group was comparable to that for ESD group. Residual tumours after the R0 resection of intramucosal differentiated cancer were found in 2.8% of the EMR-P cases and 0.56% of ESD cases. However, neither group showed local recurrence after resection.

The rates of bleeding and perforation were reported to be 0–4.0% and 0–0.9% for EMR-P group, respectively [11–14], and 6.0–9.9% and 3.5–9.7% for ESD group, respectively [16,20–23]. Based on data from previous studies, the complication rate of ESD seemed to be higher than that of EMR-P. However, the present study did not reveal a significant difference in the complication rate between the two groups. Most cases of bleeding and perforation in this study could be successfully treated non-surgically, as reported in the previous studies [33,34].

In the present study, no local recurrence occurred in the R0 resection cases of intramucosal differentiated cancer during the median 29 and 17 months of follow-up after either EMR-P or ESD. However, three cases (two cases from EMR-P group and one case from ESD group) of residual diseases were found in their first follow-up EGD 1 month after the procedure. All the cases of residual disease from EMR-P group were resected in a piecemeal fashion. The case from ESD group was resected in en bloc. However, the resection margin of this case was involved by the background adenoma. Initially, all these cases were reported to have cancer-free resection margins. However, the possibility of pathological misdiagnosis could not be excluded in these cases. Piecemeal resection does not permit an accurate and reliable histological assessment on the completeness of resection in some cases, with an implied risk of residual disease [6,7,19]. For ESD case, a cancer focus might be present in the unresected background adenoma involving the resection margin.

In the present study, required procedure time of EMR-P group was significantly shorter than that of ESD group regardless of tumour size. In addition, for EGC < 20 mm, the rates of en bloc resection, R0 resection and en bloc plus R0 resection for EMR-P group were all over 80% and EMR-P group demonstrated the comparable result to the ESD group in en bloc plus R0 resection rate, the main endpoint of endoscopic resection. It is well known that ESD is technically difficult procedure and it can frequently cause serious complication such as perforation if the operator is

not very skillful [35]. Therefore, considering technical feasibility and the considerable results for EGC < 20 mm in this study, EMR-P may be considered as an alternative choice to ESD for EGC < 20 mm, especially for Western centers where advanced endoscopic resection procedure is not prevalent. As mentioned above, the results of conventional EMR were very disappointing even if the tumour size was less than 20 mm [11,20,21,27]. Therefore, although conventional EMR is easy to perform, it may hardly be regarded as an appropriate substitute for ESD even if the tumour size is small.

This study was limited by its non-randomized design and probable selection bias. However, although ESD was mainly performed for the lesions of limited location at the first half period, there was no significant difference in tumour location between two groups as shown in Table 1. In the second half period of the present study, EMR-P was mainly performed for the small lesions. However, in this study, we analyzed the main measurement outcomes such as en bloc resection and en bloc plus R0 resection rates with the stratification according to the tumour size. Considering these points, the influence of these biases on the conclusions of this study might be insignificant.

In conclusion, the results of the present study indicated that ESD for EGC provided higher en bloc resection and en bloc plus R0 resection rate in case of tumour size ≥ 20 mm compared with EMR-P. In case of tumour size between 10 mm and 19 mm, ESD group also showed significantly higher en bloc resection rate compared with EMR-P group. In addition, two groups did not show significant difference in the bleeding or perforation rates. However, in case of tumour size < 20 mm EMR-P group demonstrated the comparable results to the ESD group in en bloc plus R0 resection rate, the main endpoint of endoscopic resection. In addition, neither group showed local recurrence after R0 resection of intramucosal differentiated cancer. Therefore, for the cases with tumour size < 20 mm EMR-P may be considered as an alternative choice to ESD. However, for the cases with tumour size ≥ 20 mm ESD should be considered as the first choice of the treatment for EGC.

Practice points

- In the large retrospective, single center study including 346 consecutive patients, ESD group demonstrated significantly higher en bloc resection and en bloc plus R0 resection rate in case of tumour size ≥ 20 mm compared with EMR-P group.
- However, in case of tumour size < 20 mm EMR-P group demonstrated the comparable results to the ESD group in en bloc plus R0 resection rate, the main endpoint of endoscopic resection.

Research agenda

- To confirm the results of this study, prospective and multi-center study may be necessary.
- All the procedures in this study were performed by only two endoscopists, the experts for advanced endoscopic resection procedures, as these techniques, especially ESD, require special skill and long learning curve. Advancement and standardization of the techniques are required for ESD to become a prevalent procedure.

Conflict of interest statement

None declared.

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