

The feasibility of colorectal endoscopic submucosal dissection for the treatment of residual or recurrent tumor localized in therapeutic scar tissue



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Bibliography

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ABSTRACT

Background and study aims Endoscopic submucosal dissection (ESD) is used to treat superficial colorectal tumors. Previous studies have reported the efficacy of ESD for treat-

ing residual or local recurrent colorectal tumors. This study sought to evaluate the efficacy of ESD in treating these lesions and to assess factors that prevent successful ESD.

Methods This retrospective study assessed 25 cases of residual or local recurrent lesions that were previously treated using EMR (18 lesions), TEM (5 lesions), ESD (1 lesion) or surgery (1 lesion), and 459 primary lesions treated using ESD between April 2008 and September 2015. Clinicopathological characteristics, treatment outcome and adverse events were compared between groups with or without scar tissue. Factors related to perforation and a prolonged treatment time, which indicate the likelihood of technical difficulties, were identified using multiple logistic regression analysis.

Results In residual or local recurrent lesions groups, patients experienced more perforations (32% vs 4%, $P < 0.001$) and required a longer treatment time (117 min vs 61 min, $P < 0.001$) compared with the primary lesions group. Both groups showed a similar curative resection rate. Emergency surgery was not needed in any case. Multiple logistic regression analysis indicated that tumor location and therapeutic scar tissue were high risk factors for perforation, and that large tumor size and therapeutic scar tissue were high risk factors for prolonged treatment time.

Conclusions ESD for residual or local recurrent colorectal tumors is a technically challenging, but effective and minimally invasive treatment. When performed carefully with sufficient proficiency, it is a useful treatment option.

Introduction

Superficial colorectal neoplasms are treated by endoscopic mucosal resection (EMR), which is an internationally accepted method because of its safety and success. Nevertheless, there are several technical limitations when treating large lesions, lesions that span a haustral fold in the colon, or lesions that exhibit a non-lifting sign, since this technique employs snare. [1–3] Instead, endoscopic piecemeal mucosal resection (EPMR) has been used for the treatment of larger lesions; however, EPMR

is associated with a residual or local recurrence rate of approximately 6–27%. [4–6] These residual or local recurrent tumors are treated by repeated EMR; [4–7] however, curative resection by repeated EMR is made difficult by the formation of submucosal fibrosis. [6] Such lesions often require repeated therapy, with some cases requiring surgical resection. While transanal endoscopic microsurgery (TEM) was introduced as a treatment for large rectal adenomas and early cancers, [8] some studies have reported a recurrence rate of 3–19% for patients treated with TEM. [9, 10]

Endoscopic submucosal dissection (ESD) is widely performed for treatment of superficial gastric neoplasms. ESD improves a clinician's ability to resect tissue, regardless of lesion size or presence of peptic ulcer scar tissue. [11, 12] In recent years, this novel technique has been used to treat colorectal cancer, for which it has been reported to be safe and effective. [13–15] Moreover, en bloc resection by colorectal ESD offers an advantage over conventional treatment due to its precise histological evaluation and the low rate of recurrence after ESD, which is reported to be 0–2%. [6, 15, 16] However, clinicians believe that it is more difficult to perform colorectal ESD than gastric ESD because of the thin walls of the colon and rectum, which easily results in perforation [17] and increases the risk of peritonitis. [18]

Some reports on gastric ESD for peptic ulcer scars have suggested the possibility of residual or local recurrent lesions. [11, 19, 20] Performing colorectal ESD for residual or local recurrent tumors remains controversial because of the technical difficulty in dissecting submucosal severe fibrosis. Some studies have reported that severe fibrosis is the most significant risk factor for adverse events and can interfere with en bloc resections. [21, 22] However, if ESD is performed successfully, it can reduce the need for future surgery and frequent follow-up examinations. Therefore, we assessed whether colorectal ESD can be used successfully to treat residual or local recurrent tumors after previous treatment methods, such as EMR and TEM, have been attempted.

In the current study, we sought to assess clinical outcomes with colorectal ESD for residual or local recurrent tumors localized in therapeutic scar tissue using endoscopic treatment (EMR, ESD, TEM) or surgery. The secondary objective was to analyze the risk of ESD and its feasibility for use in treating residual or local recurrent colorectal lesions.

Patients and methods

Enrolled patients

From April 2008 to September 2015, 532 consecutive superficial colorectal neoplasms in 498 patients were treated with ESD at the Yokohama City University Medical Center.

We excluded neuroendocrine tumor (NET) cases ($n=31$), cases in which ESD was interrupted due to signs of muscle retraction [23] caused by tumor submucosal or deep invasion ($n=9$), and cases of ulcerative colitis ($n=7$) or condyloma acuminatum ($n=1$). As a result, we retrospectively analyzed 484 consecutive lesions from 452 cases (395 early colorectal carcinomas, 74 adenomas, and 15 serrated lesions). There were 25 residual or local recurrent tumors localized in therapeutic scars, of which 18 were treated by EMR, 5 were treated by TEM, 1 was treated by ESD, and 1 was treated surgically. Patients were divided into either a “scar group” or a “non-scar group,” and treatment outcomes and adverse events were evaluated between the two groups. All patients provided written informed consent before enrolling and this study was approved by the Institutional Review Board.

Indications for ESD in colorectal tumors

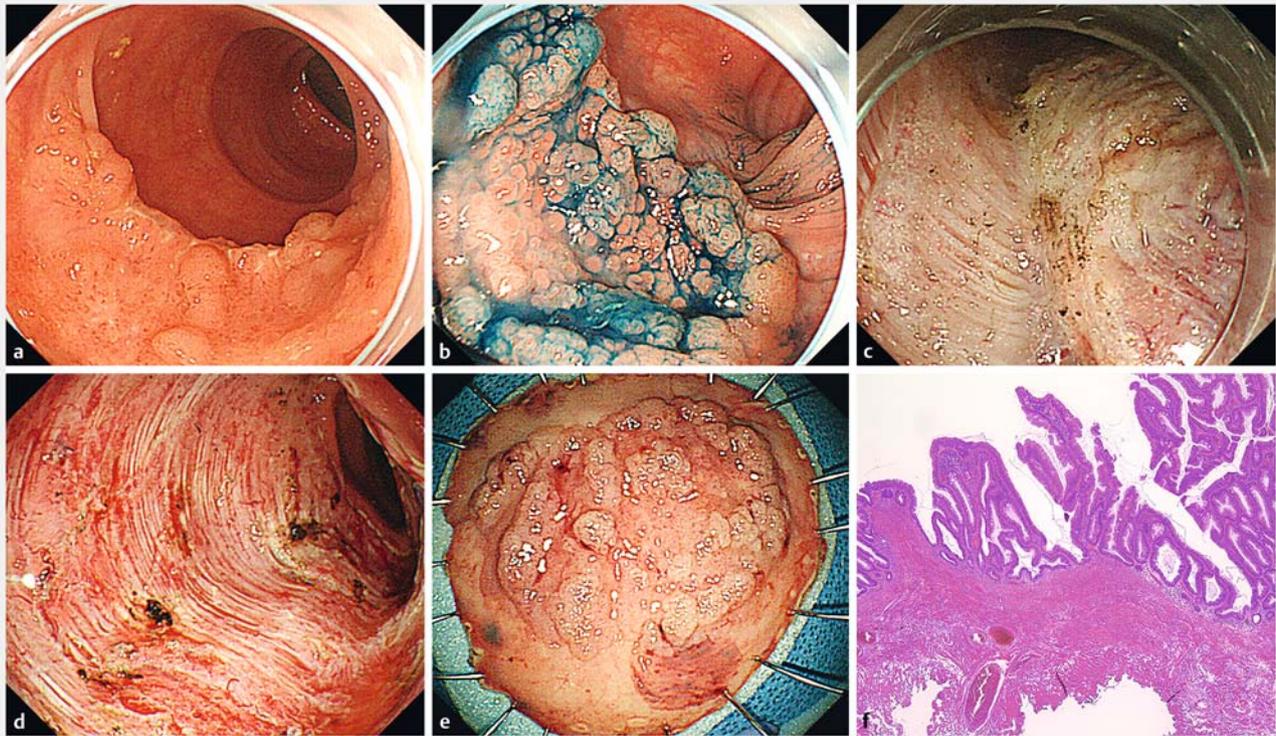
ESD for colorectal lesions was performed in accordance with Japan Gastroenterological Endoscopy Society (JGES) guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection. [24] Briefly, we treated lesions that were difficult to treat using endoscopic en bloc resection with snare EMR, such as non-granular lateral spreading tumor (LST-NG); lesions showing a Vi-type pit pattern; large, depressed-type tumors; and large protruded-type lesions suspected to be carcinoma.

ESD procedure and technique

Colorectal ESD was performed by 5 experienced gastrointestinal endoscopists who have performed more than 100 gastric ESDs, 30 esophageal ESDs, and 2000 colonoscopies. We mainly used a water-jet system-furnished colonic endoscope (PCF-Q260AZI; Olympus, Tokyo, Japan) for all lesions other than rectal lesions, which were treated using an upper gastrointestinal endoscope with a water-jet system (GIF-Q260J; Olympus). We introduced a carbon dioxide insufflation system in March 2008 to relieve abdominal discomfort of patients and to avoid abdominal compartment syndrome in the event of perforation. [25] In all procedures, a 1.5-mm Dual knife (KD650Q; Olympus) was used. A Hook knife (KD-260R; Olympus) was also used in the scar group. The electrosurgical unit ICC200 (ERBE, Tübingen, Germany) was used in two modes: ‘endocut’ mode (60 W, effect 3) and ‘forced coagulation’ mode (40 W). We used a 0.4% sodium hyaluronate solution [26] for submucosal injections in all cases. During the procedure, a 4-mm-long transparent hood was systematically attached to the tip of the endoscope (D-201–11804; Olympus) to facilitate optimal field visualization and stable dissection. A small caliber-tip transparent hood (ST hood short type) (DH-29CR; Fujifilm, Tokyo, Japan) was used for all participants in the scar group to facilitate the entry of endoscopic devices into the submucosal layer. Colorectal tumors were usually not marked since the border between the lesion and normal mucosa was clear upon visualization with indigo carmine or narrow band imaging (NBI). However, all tumors in the scar group were marked so as to initiate dissection in tissue without scar-induced submucosal fibrosis. Therefore, in the scar group, markings were often made less than 10 mm away from the tumor margin. During the submucosal dissection, we carefully dissected the fibrotic part. We used the Hook knife to prevent perforation in cases in which fibrosis was prevalent (► **Fig. 1**). Meticulous hemostasis was performed when intraoperative bleeding occurred. Endoscopic clipping was used to treat intraoperative perforations.

Terminology and definition related to treatment

En bloc resection indicates tumor resection in 1 piece. R0 resection indicates en bloc resection wherein the lateral and vertical margins of the specimens are free of tumor cells. Curative resection indicates that: (i) a R0 resection was completed; (ii) the lesion was an adenoma, papillary adenocarcinoma, or tubular adenocarcinoma; (iii) intramucosal colorectal neoplasm or submucosal invasion was less than 1000 μm deep; (iv) the lym-



► **Fig. 1** The images are of a patient who received a rectal EPMP 5 years ago. **a, b** Conventional imaging of the recurrent tumor in Rb revealed a flat, elevated lesion with scar tissue. **c** During ESD, severe fibrosis was observed in the submucosa at the site of the scar that formed following the previous EPMP. **d, e** ESD was achieved by en bloc resection without perforation. The procedure time was 155 minutes. **f** Histological findings showed well-differentiated adenocarcinoma tissue confined within the mucosa and measuring 48 mm in diameter, with severe fibrosis beneath the tumor.

phatic or vascular systems were not involved; and (v) the budding was grade 1 if the tumor invaded into the submucosa. [27] Perforation was indicated by extra-intestinal tissue projecting through a hole during treatment and/or the presence of empty space upon postoperative abdominal XP or CT. Post ESD bleeding was identified by the presence of bloody stool at any time point after ESD and by the need for endoscopic hemostasis, regardless of the outcome of hemostasis.

The right colon included the cecum, ascending colon, and transverse colon; the left colon included the descending colon, sigmoid colon, and rectosigmoid colon; and the rectum included the Ra and Rb. Tumor morphology included granular lateral spreading tumor (LST-G) and LST-NG, as indicated by the Kudo classification, or protruding tumor (0-Is/Ip), as indicated by the Paris classification. [28, 29] Histology included either tubular adenoma, tubular adenocarcinoma, or serrated lesion. The depth of the tumor was categorized as either a mucosal lesion (Tis), a submucosal invasion lesion <1000 μ m from the muscularis mucosae (T1a), or a submucosal invasion lesion \geq 1000 μ m from the muscularis mucosae (T1b). The non-tumor size was defined as the maximum diameter of the non-tumor mucosa, which indicated the sum of the major axes of the non-tumor mucosa in the sections in which the tumor was at its maximum diameter.

Indications for using ESD to treat residual or local recurrent lesions

Residual or local recurrent lesions were defined as lesions at the same site after previous endoscopic treatment (i. e., EMR, ESD), TEM, or surgery; previous pathological examination indicating the presence of superficial colorectal tumor tissue, including adenoma, intramucosal carcinoma, or carcinoma, with submucosal invasion of less than 1000 μ m in depth, and without lymphovascular invasion, namely, the absence of non-curative factors in previous pathological examinations only except lateral margin; a lesion without invasion, as indicated by macroscopic endoscopic evaluation according to the Paris morphological and Kudo classifications, [28,29] regardless of tumor morphology; a lesion that was difficult to resect using conventional EMR in en bloc fashion; and confirmed absence of evidence of metastasis or recurrence in a whole body CT and no increase of tumor markers, if pathological results from previous treatments from more than five years ago could not be obtained.

Histopathological evaluation

All specimens were “pinned out” onto polystyrene receivers to facilitate subsequent histopathological sectioning prior to immediate fixation in 10% buffered formalin solution and were also cut into 2-mm-wide slices the following day. The frag-

► **Table 1** Clinicopathological characteristics of all patients (n = lesions).

	Scar group (n = 25)	Non-scar group (n = 459)	P value
Sex			0.238
▪ Male (n = 274)	17	257	
▪ Female (n = 210)	8	202	
Age (average)	47 – 84 (72)	30 – 95 (69)	0.26
Tumor location			0.773
▪ Right colon region (n = 268)	14	254	
▪ Left colon region (n = 81)	3	78	
▪ Rectum (n = 135)	8	127	
Tumor morphology			0.732
▪ 0-Is/Ip (n = 54)	4	50	
▪ LST-G (n = 224)	11	213	
▪ LST-NG (n = 206)	10	196	
Histology			0.328
▪ Tubular adenoma (n = 74)	6	68	
▪ Tubular adenocarcinoma (n = 395)	19	376	
▪ Serrated lesion (n = 15)	0	15	
Tumor depth			0.109
▪ Tis/T1a (n = 444)	25	419	
▪ T1b (n = 40)	0	40	
Tumor size (average) mm	6 – 75 (24)	5 – 130 (33)	0.011
Specimen size (average) mm	30 – 75 (48)	15 – 150 (43)	0.101
Non-tumor size (average) mm	0 – 63 (24)	0 – 35 (9)	<0.001

ments or slices were embedded in paraffin, cut into 3- μ m sections, stained with hematoxylin – eosin, and microscopically examined for histologic type.

Post ESD follow-up protocol

All resected cases were followed up with endoscopic examinations within six months after ESD. Patients then received endoscopic examinations annually, which allowed for the assessment of the presence of local recurrence. Recurrence was defined as new visible tumor on a therapeutic scar more than 6 months after treatment.

Statistical analysis

Statistical analyses were performed using SPSS 22.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as the mean \pm standard deviation (SD) or medians and ranges. Categorical parameters were expressed as numbers and frequencies. The rate of en bloc resection, the rate of R0 resection, the rate of curative resection, the rate of perforation, the rate of post-operative bleeding, and mean treatment time, were com-

pared between the two groups. Categorical parameters were statistically compared using the chi-square test and the Fisher exact test, and continuous parameters were compared using Student's t-test. To identify factors associated with perforation and prolonged treatment time, clinicopathological factors were compared. Those variables with a *P* value < .05 in the univariate analysis were examined in multivariate logistic regression models. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using a logistic regression analysis. *P* values < .05 were considered statistically significant.

Results

Clinicopathological characteristics of patients are shown in ► **Table 1**. We compared sex, average age, location of tumor, morphology, histology, depth of tumor invasion, average tumor size, average specimen size, and average non-tumor size between the scar and non-scar groups. The 2 groups did not differ by sex, age, tumor location, tumor morphology, histology, tumor depth, and specimen size. Tumor size was significant-

► **Table 2** Treatment outcomes between the scar and non-scar groups.

	Scar group (n = 25)	Non-scar group (n = 459)	P value
En bloc resection, n (%)	24 (96.0)	457 (99.6)	0.147
R0 resection, n (%)	21 (84.0)	421 (91.7)	0.259
Curative resection, n (%)	21 (84)	387 (84.3)	1.000
Perforation, n (%)	8 (32)	19 (4.1)	<0.001
Post-operative bleeding, n (%)	0 (0.0)	16 (3.5)	1.000
Treatment time (average) min.	24–210 (117)	10–273 (61)	<0.001

► **Table 3** Clinicopathological characteristics and treatment outcomes of previous treatments of patients in the scar group

	post-EMR (n = 18)	post-TEM (n = 5)	Others (n = 2)
Tumor morphology (0-IIa / 0-I)	16/2	4/1	2/0
Histology (adenoma/adenocarcinoma)	4/14	2/3	0/2
Tumor size mm (average)	6–48 (19)	7–75 (45)	16–30 (23)
Specimen size mm (average)	30–74 (44)	45–75 (65)	36–65 (51)
Tumor depth (Tis·T1a / T1b)	18/0	5/0	2/0
R0 resection, n (%)	16 (89)	4 (80)	1(50)
Curative resection, n (%)	16 (89)	4 (80)	1(50)
Perforation, n (%)	6 (33)	1 (20)	1 (50)
Treatment time min. (average)	24–210 (107)	115–175 (145)	105–195 (150)

ly larger and non-tumor size was significantly smaller in the non-scar group. Evaluation of previous histological reports in the scar group identified eight cases of tubular adenoma, 11 cases of tubular adenocarcinoma confined to mucosa without lymphovascular invasion, and 6 cases of unknown histological information since previous treatment was performed more than 5 years ago and there was no evidence of metastasis at the time of treatment in our hospital.

► **Table 2** indicates treatment outcomes between the scar and non-scar groups. En bloc resection rate (96% and 99.6%), R0 resection rate (84.0% and 91.7%), and curative resection rate (84.0% and 84.3%) did not differ between both groups. Intraoperative perforation rate was significantly higher in the scar group (32% in the scar group and 4.1% in the non-scar group). Conversely, postoperative bleeding did not differ (0% and 3.5%). Moreover, treatment time in the scar group was approximately twice as long compared to the non-scar group. All cases of intraoperative perforation were conservatively managed after endoscopic closure using endoclips, and no cases required emergent surgery nor were there any cases of uncontrolled intraoperative or postoperative bleeding. There were no deaths related to ESD. The median length of hospital stay was four days (range 4–8 days).

We compared the results of previous treatments, including EMR (n = 18), TEM (n = 5), ESD (n = 1), and surgery (n = 1) in the scar group (► **Table 3**). The average tumor size of participants in the post-TEM group was larger than that of the post-EMR group. Therefore, treatment time was longer in the post-TEM group compared with the post-EMR group. However, the perforation rate in the post-TEM group was lower than in the post-EMR group. Additionally, the rate of curative and R0 resection in the post-EMR group and post-TEM group was similar.

Factors indicating treatment difficulty

The above-described results indicate the efficacy of ESD, as indicated by the favorable en bloc, R0, and curative resection rates, as well as the increased perforation rate and longer treatment time compared to the scar group. Thus, we hypothesized that therapeutic failure caused by technical difficulties could be indicated by perforation rate and treatment time. Therefore, we evaluated factors potentially affecting perforation and treatment time (≥ 90 min) and, thus, reflecting the difficulty of performing ESD. The factors of sex, age, tumor location, tumor morphology, tumor depth, tumor size, and scar presence following previous treatment were examined by univariate and multivariate analysis (► **Table 4** and ► **Table 5**). In doing so, we

► **Table 4** Comparison of clinicopathological characteristics of resections involving perforation.

	non-perforation	perforation	Univariate	Multivariate	
			P value	P value	OR (95% CI)
Sex			0.775		
▪ Male (n = 274)	258	16			
▪ Female (n = 210)	199	11			
Age, years			0.969		
▪ <75 (n = 321)	303	18			
▪ ≥75 (n = 163)	154	9			
Tumor location			0.041	0.019	
▪ Right colon region (n = 268)	258	18		1 (reference)	
▪ Left colon region (n = 81)	68	7		0.42	1.485 (0.569–3.867)
▪ Rectum (n = 135)	131	2		0.026	0.178 (0.039–0.812)
Tumor morphology			0.583		
▪ 0–Is/Ip (n = 54)	50	4			
▪ LST-G (n = 224)	214	10			
▪ LST-NG (n = 206)	193	13			
Tumor depth			0.868		
▪ Tis/T1a (n = 444)	419	25			
▪ T1b (n = 40)	38	2			
Tumor size			0.764		
▪ ≤20 mm (n = 123)	115	8			
▪ >20 mm, ≤40 mm (n = 248)	236	12			
▪ >40 mm (n = 113)	106	7			
Scar			<0.001		
▪ Absent (n = 459)	440	19		1 (reference)	
▪ Present (n = 25)	17	8		<0.001	18.052 (5.889–55.341)

identified which factors predict treatment difficulty. Tumors located in regions other than the rectum and the presence of post-therapeutic scar tissue was an independent risk factor of perforation. The odds ratio for presence of post-therapeutic scar tissue was elevated (18.052; 95% CI: 5.889–55.341). Tumor size and the presence of post-therapeutic scar tissue were independent risk factors that indicate prolonged treatment time. The odds ratio for presence of post-therapeutic scar tissue was 43.283 (95% CI: 14.19–132.58).

Long-term clinical result

In the non-scar group, 89% of patients (383/430) underwent scheduled examinations, while the remaining patients were lost by the time of endoscopic follow up. The median follow-up time was 20 months (range: 9–87 months). No patients in the scar group were lost by the time of follow-up after ESD. The median follow-up time was 24 months (range: 9–59 months).

No cases of recurrent tumor formation were observed in the non-scar group, while one case was observed in the scar group. The patient with recurrence in the scar group was treated by performing two-piece resection after TEM.

Discussion

The first aim of the current study was to compare the scar and non-scar groups in order to evaluate the technical feasibility, safety, and efficacy of ESD. This study indicated that en bloc and R0 resections were successfully performed in the scar group in comparison with the non-scar group. This result is similar to previous reports that indicated that the R0 resection rate for residual or local recurrent tumor was 83–96.4%. [30, 31, 32] In addition, because all the tumors in the scar group were intramucosal, the curative resection rate was equal to the R0 resection rate, which was also increased. Because previous his-

► **Table 5** Comparison of clinicopathological characteristics of resections with a prolonged treatment time (≥ 90 min).

	Time ≤ 90 min	Time > 90 min	Univariate	Multivariate	
			P value	P value	OR (95% CI)
Sex			0.429		
▪ Male (n = 274)	211	63			
▪ Female (n = 210)	168	42			
Age, years			0.309		
▪ < 75 (n = 321)	247	74			
▪ ≥ 75 (n = 163)	132	31			
Tumor location			0.154		
▪ Right colon region (n = 268)	217	51			
▪ Left colon region (n = 81)	64	17			
▪ Rectum (n = 135)	98	37			
Tumor morphology			0.006		
▪ 0-Is/Ip (n = 54)	46	8		1 (reference)	
▪ LST-G (n = 224)	161	63		0.201	1.744 (0.737 – 4.274)
▪ LST-NG (n = 206)	172	34		0.431	1.441 (0.581 – 3.574)
Tumor depth			0.596		
▪ Tis/T1a (n = 444)	349	95			
▪ T1b (n = 40)	30	10			
Tumor size			< 0.001		
▪ ≤ 20 mm (n = 123)	105	18		1 (reference)	
▪ > 20 mm, ≤ 40 mm (n = 248)	207	41		0.055	4.076 (0.984 – 4.378)
▪ > 40 mm (n = 113)	67	46		< 0.001	7.059 (3.072 – 16.225)
Scar			< 0.001		
▪ Absent (n = 459)	374	85		1 (reference)	
▪ Present (n = 25)	5	20		< 0.001	43.283 (14.19 – 132.58)

tological evaluation is important for treating residual or local recurrent lesions, we confirmed that most histopathological findings indicated intramucosal cancer or tubular adenoma in the scar group, which accounted for our positive findings. Despite the significantly smaller size of the tumors in participants in the scar group, similarly sized tissue was resected in both groups, thereby indicating that the size of non-tumor tissue was significantly larger in the scar group. This was due to our dissection into healthy submucosal tissue that does not exhibit fibrotic tissue in order to ensure a sufficient margin for dissecting submucosal tissue. If we were to encounter submucosal fibrosis after performing the circumference incision, we would have become disoriented, which can result in tumor incision directly or perforation. This is central to the safe and effective completion of ESD with a high en bloc and R0 resection rate in the scar group. We also use the tapered attachment hood (ST hood) and Hook knife to perform ESD for all patients in the scar group. This combination allows for a reliable view and

avoids perforation. However, because the field of view becomes narrower, this equipment is usually not required in the non-scar group. Despite the high en bloc and R0 resection rate, we could not avoid a high perforation rate and a longer procedure time in the scar group. The high perforation rate of 32% in the present study was higher than previous reports. This is likely due to the small sample size, which could have greatly affected the rate of perforation. Additionally, the rate of 0% reported by Hurlstone DP et al. [31] and 3.6% by Gabriel RAHMI et al. were too low because even the perforation rate of ordinary colorectal ESD has been reported to be approximately 5% [13 – 15, 17]. Due to severe fibrosis and insufficient submucosal injection, it was difficult to visualize the laminar structure of the colorectal wall. Several breakthroughs are needed for this procedure to be safer and more effective.

We next analyzed incidence of perforation and prolonged procedure time in all subjects to clarify the technical difficulty of ESD for the scar group. Multivariate analysis indicated that

tumors located in the colon, but not the rectum, and those with scars formed by previous interventions are both risk factors for perforation. Sub-analysis indicated that perforation occurs easily in the descending colon near its junction with the sigmoid colon (15%, data were not shown). ESD of lesions located at the sigmoid-descending junction is more difficult to treat than are those in other colorectal regions due to the mobility of the endoscope. In an analysis of prolonged treatment time, larger lesions and therapeutic scars were also found to be independent risk factors. This suggests that ESD for large lesions requires a longer treatment time, but is safe due to the low risk of perforation. In conclusion, because the therapeutic scar is an independent risk factor of a prolonged procedure time and perforation, a unique technique was required.

In comparing post-EMR groups and post-TEM groups, the perforation rate was found to be lower in post-TEM groups despite the larger average size of resected tissue and longer treatment time in post-TEM groups. This was often due to the rectal-located residual or local recurrent tumors in patients in the post-TEM group, which made them easier to treat. Moreover, the rate of curative and R0 resection in the post-EMR group and post-TEM group was almost the same. Because previous reports of colorectal ESD for residual or local recurrent tumors were limited to reports of ESD after EMR, [30–32], the current study is the first report that ESD is an effective therapy for not only endoscopic therapy, but also for post-TEM. Furthermore, clinicians can avoid performing a second TEM, which requires general anesthesia. However, given the small number of patients in the post-TEM group, further investigation is necessary to evaluate the effectiveness of ESD for post-TEM.

We next assessed long-term outcomes. In doing so, we did not observe local recurrence confined to the R0 resected cases both in the scar and non-scar groups. However, we observed 1 case of a local recurrent lesion, which was previously treated using ESD. This case was initially treated in a previous hospital using TEM 19 years prior to admission. Then a local recurrent tumor developed on the treatment scar, which appeared as a type 0-IIa that was 65 mm diameter and was treated using ESD in our hospital. The lesion was resected with two specimens due to severe fibrosis. The pathological diagnosis showed tubular adenocarcinoma confined to the mucosa with unknown horizontal margin caused by piecemeal resection. It was possible that undetected tumor cells remained in the ulcer bed. After 1 year, the tumor re-occurred as a type 0-IIa that was 15 mm diameter on the ESD scar and was treated using ESD. Repeated ESD was performed for this lesion by en-bloc resection. Final pathological diagnosis showed tubular adenocarcinoma confined to the mucosa that was negative for the horizontal margin.

Other treatments for residual or local recurrent colorectal tumors include Laparoscopic Endoscopic Cooperative Surgery (LECS) or laparoscopic colorectal surgery (LAC). [33] The advantage of LECS is that it involves a local excision with adequate minimal surgical margins; however, the disadvantage of LECS is that it requires general anesthesia and the necessity of additional treatment when the tumor showed submucosal invasion. LAC can be used for tumor and regional lymph node removal;

however, it could be overly aggressive for tumors confined to the mucosa. In both, surgical adverse events, such as anastomotic leakage or appearance of a rectal tumor near the anus, require Miles operation and colostomy. [34, 35] Colorectal ESD is always performed under conscious sedation, therefore, there was no fear of perioperative adverse events, such as pneumonia or barotrauma.

In the current study, ESD for residual or local recurrent lesions allows for en bloc, R0 and curative resection. This result contributes the most beneficially to ESD, which allows for pathological evaluation and is free from neoplastic cells. However, perforation rate is significantly higher and requires a prolonged treatment time than in comparable groups. In addition, presence of a therapeutic scar is an independent risk factor for perforation and prolonged procedure time. Fortunately, all perforations were treated with endoscopic closure by clipping and with prescribed antibiotics. Therefore, no patient experiencing perforation required emergent surgery. Furthermore, the subsequent hospitalization was less than 1 week. This indicated that ESD for residual or local recurrent tumors may be a treatment choice that requires meticulous attention.

Limitations of the current study were as follows:

1. This was a retrospective study conducted at a single institution.
2. The sample size of the scar group was small.
3. This study investigated patients over the course of 7 years.

Therefore, the endoscopist's skill had been improved during this period. This might affect treatment outcome.

Conclusion

In conclusion, this study suggests that colorectal ESD can be used as a treatment choice for residual or local recurrent tumors; however, it can only be performed in specialized hospitals. Furthermore, ESD can be performed depending upon the risk for perforation and requires cooperation with other surgical departments when treating colorectal residual or recurrent tumors.

Competing interests

None

References

- [1] Tanaka S, Haruma K, Oka S et al. Clinicopathologic features and endoscopic treatment of superficially spreading colorectal neoplasms larger than 20 mm. *Gastrointest Endosc* 2001; 54: 62–66
- [2] Yokota T, Sugihara K, Yoshida S. Endoscopic mucosal resection for colorectal neoplastic lesions. *Dis Colon Rectum* 1994; 37: 1108–1111
- [3] Repici A, Pellicano R, Strangio G et al. pathologic basis, procedures, and outcomes. *Dis Colon Rectum* 2009; 52: 1502–1515
- [4] Buchner AM, Guarner-Argente C, Ginsberg GG. Outcomes of EMR of defiant colorectal lesions directed to an endoscopy referral center. *Gastrointest Endosc* 2012; 76: 255–263

- [5] Hotta K, Fujii T, Saito Y et al. Local recurrence after endoscopic resection of colorectal tumors. *Int J Colorectal Dis* 2009; 24: 225–230
- [6] Saito Y, Fukuzawa M, Matsuda T et al. Clinical outcome of endoscopic submucosal dissection versus endoscopic mucosal resection of large colorectal tumors as determined by curative resection. *Surg Endosc* 2010; 24: 343–352
- [7] Uraoka T, Fujii T, Saito Y et al. Effectiveness of glycerol as a submucosal injection for EMR. *Gastrointest Endosc* 2005; 61: 736–740
- [8] Buess G, Hutterer F, Theiss J et al. A system for a transanal endoscopic rectum operation. *Chirurg* 1984; 55: 677–680
- [9] Barendse RM, van den Brock FJ, Dekker E et al. Endoscopic mucosal resection vs transanal endoscopic microsurgery for the treatment of large rectal adenomas. *Colorectal Dis* 2011; 14: e191–196
- [10] Lev-Chelouche D, Margel D, Goldman G et al. Transanal endoscopic microsurgery: experience with 75 rectal neoplasms. *Dis Colon Rectum* 2000; 43: 662–667
- [11] Hoteya S, Iizuka T, Kikuchi D et al. Benefits of endoscopic submucosal dissection according to size and location of gastric neoplasm, compared with conventional mucosal resection. *J Gastroenterol Hepatol* 2009; 24: 1102–1106
- [12] Hirasawa K, Kokawa A, Oka H et al. Risk assessment chart for curability of early gastric cancer with endoscopic submucosal dissection. *Gastrointest endosc* 2011; 75: 1268–1275
- [13] Saito Y, Uraoka T, Yamaguchi Y et al. A prospective, multicenter study of 1111 colorectal endoscopic submucosal dissections (with video). *Gastrointest Endosc* 2010; 72: 1217–1225
- [14] Repici A, Hassan C, De Paula Pessoa et al. Efficacy and safety of endoscopic submucosal dissection for colorectal neoplasia: a systematic review. *Endoscopy* 2012; 44: 137–150
- [15] Lee EJ, Lee JB, Lee SH et al. Endoscopic submucosal dissection for colorectal tumors -1,000 colorectal ESD cases: one specialized institute's experiences. *Surg Endosc* 2013; 27: 31–39
- [16] Tanaka S, Oka S, Kaneko I et al. Endoscopic submucosal dissection for colorectal neoplasia: possibility of standardization. *Gastrointest Endosc* 2007; 66: 100–107
- [17] Hirakawa T, Asano K, Katou Y. Learning experiences of colorectal ESD in a community general hospital. *Gan To Kagaku Ryoho* 2014; 12: 1651–1653
- [18] Taku K, Sano Y, Fu KI et al. Iatrogenic perforation associated with therapeutic colonoscopy: a multicenter study in Japan. *J Gastroenterol Hepatol* 2007; 22: 1409–1414
- [19] Higashi S, Tanaka S, Kaneko I et al. Endoscopic submucosal dissection for residual/local recurrence of early gastric cancer after endoscopic mucosal resection. *Endoscopy* 2006; 38: 996–1000
- [20] Higashimaya M, Oka S, Tanaka S et al. Endoscopic submucosal dissection for residual early gastric cancer after endoscopic submucosal dissection. *Gastrointest Endosc* 2013; 77: 298–302
- [21] Lee SP, Kim JH, Sung IK et al. Effect of submucosal fibrosis on endoscopic submucosal dissection of colorectal tumors. *J Gastroenterol Hepatol* 2015; 30: 872–878
- [22] Sato K, Ito S, Kitagawa T et al. Factors affecting the technical difficulty and clinical outcome of endoscopic submucosal dissection for colorectal tumors. *Surg Endosc* 2014; 28: 2959–2965
- [23] Toyonaga T, Tanaka S, Man-I M et al. Clinical significance of the muscle-retracting sign during colorectal endoscopic submucosal dissection. *Endosc Int Open* 2015; 3: E246–251
- [24] Tanaka S, Kashida H, Saito Y et al. JGES guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection. *Dig Endosc* 2015; 4: 417–434
- [25] Saito Y, Uraoka T, Matsuda T et al. A pilot study to assess the safety and efficacy of carbon dioxide insufflation during colorectal endoscopic submucosal dissection with the patient under conscious sedation. *Gastrointest Endosc* 2007; 65: 537–542
- [26] Yamamoto H, Yahagi N, Oyama T et al. Usefulness and safety of 0.4% sodium hyaluronate solution as a submucosal fluid 'cushion' in endoscopic resection for gastric neoplasms: a prospective multicenter trial. *Gastrointest Endosc* 2008; 67: 830–839
- [27] Japanese Society for Cancer of the Colon and Rectum. JSCCR Guidelines 2014 for the Treatment of Colorectal Cancer.
- [28] The Paris endoscopic classification of superficial neoplastic lesions. esophagus, stomach, and colon: November 30 to December 1, 2002. *Gastrointest Endosc* 2003; 58: S3–43
- [29] Kudo S, Tamura S, Nakajima T et al. Diagnosis of colorectal tumorous lesions by magnifying endoscopy. *Gastrointest Endosc* 1996; 44: 8–14
- [30] Kuroki Y, Hoteya S, Mitani T et al. Endoscopic submucosal dissection for residual/locally recurrent lesions after endoscopic therapy for colorectal tumors. *J Gastroenterol Hepatol* 2010; 25: 1747–1753
- [31] Hurlstone DP, Shorthouse AJ, Brown SR et al. Salvage endoscopic submucosal dissection for residual or local recurrent intraepithelial neoplasia in the colorectum: a prospective analysis. *Colorectal Dis* 2008; 10: 891–897
- [32] Gabriel RAHMI, Tanaka S, Ohara Y et al. Efficacy of endoscopic submucosal dissection for residual or recurrent superficial colorectal tumors after endoscopic mucosal resection. *J Dig Dis* 2015; 16: 14–21
- [33] Hiki N, Nunobe S, Matsuda T et al. Laparoscopic and endoscopic cooperative surgery. *Dig Endosc* 2015; 2: 197–204
- [34] Kitano S, Kitajima M, Konishi F et al. A multicenter study on laparoscopic surgery for colorectal cancer in Japan. *Surg Endosc* 2006; 20: 1348–1352
- [35] Miyajima N, Fukunaga M, Hasegawa H et al. Results of a multicenter study of 1057 cases of rectal cancer treated by laparoscopic surgery. *Surg Endosc* 2009; 23: 113–118