Original Article

Comparison of efficacy and safety between endoscopic submucosal dissection and transanal endoscopic microsurgery for the treatment of rectal tumor

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Abstract

Background/Aim: To compare the treatment efficacy and safety between endoscopic submucosal dissection (ESD) and transanal endoscopic microsurgery (TEM) for the treatment of rectal epithelial tumors, including large adenoma, cancer, and subepithelial tumors (SET).

Patients and Methods: We conducted a retrospective analysis of the medical records of 71 patients with rectal tumors who were treated with ESD (48 patients) or TEM (23 patients) from January 2013 to December 2015. The patient group comprised 56 patients with epithelial tumors and 15 patients with SET. Treatment efficacy such as en bloc resection, procedure time, local recurrence, hospital stay, additional procedure rate, and safety between the treatment groups were evaluated and analyzed.

Results: There were no significant differences in tumor size, location, macroscopic appearance, and histological depth between ESD and TEM groups. For ESD compared to TEM in rectal epithelial tumors, en bloc resection rates were 95% vs. 93.7% and R0 resection rates were 92.5% vs. 87.5% ($P = 0.617$); in rectal SET, en bloc resection rates were 100% vs. 100% and R0 resection rates were 87% vs. 85% ($P = 0.91$). The procedure time was 71.5 ± 51.3 min vs. 105.6 ± 28.2 min ($P = 0.016$) for epithelial tumors and 32.13 ± 13.4 min vs. 80.71 ± 18.35 min ($P = 0.00$) for SET, respectively. Hospital stay was 4.3 ± 1.2 days vs. 5.8 ± 1.8 days ($P = 0.001$) for epithelial tumors and 4.1 ± 4.1 days vs. 5.5 ± 2 days ($P = 0.42$) for rectal SET, respectively. There were no significant differences between recurrence rates, additional procedure rates, and complications in the two groups.

Conclusions: ESD and TEM are both effective and safe for the treatment of rectal epithelial tumors and SET because of favorable R0 resection rates and recurrence rates. However, the ESD group showed shorter procedure times and hospital stays than the TEM group. Therefore, ESD should be considered more preferentially than TEM in the treatment of large rectal epithelial tumors and SET.

Keywords: Endoscopic submucosal dissection, rectal tumor, transanal endoscopic microsurgery

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INTRODUCTION

Colorectal cancer is the third most common cancer and one of the major causes of cancer-related death.[1] In many countries, a national colorectal screening program is being conducted, which is leading to an increased diagnosis of large adenomas, early colorectal cancer, and subepithelial

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tumor (SET). In particular, the rectum is reported to be the most common site of these tumors.[2] Minimally invasive surgery is the main treatment option for rectal tumors such as large adenoma, early cancer, and SET because of lower complications and mortality rates and shorter hospital stays rather than conventional surgery.[3] Particularly, transanal endoscopic microsurgery (TEM) has been the main treatment for large rectal tumors for nearly 30 years.[4,5] However, TEM must be performed under either general or spinal anesthesia, and expensive surgical instruments are required. Colorectal endoscopic submucosal dissection (ESD) is a novel endoscopic procedure that enables en bloc resection of benign colorectal lesions and early colorectal cancer.[2] ESD can be performed under conscious sedation without anesthesia, and there are fewer hospital days than those for TEM. In addition, ESD has evolved over the past decade with advances in techniques and equipment.[6-9] There are few studies comparing ESD and TEM for the treatment of rectal tumors.[10,11] Currently, there are no studies comparing treatment results between TEM and ESD for rectal SET. In the present study, we compared the treatment efficacy and safety between ESD and TEM for the treatment of rectal epithelial tumors and SET.

PATIENTS AND METHODS

Study design

From January 2013 to December 2015, we retrospectively analyzed patients who were treated using ESD or TEM for rectal epithelial and nonepithelial tumors. The patient enrollment process is depicted in Figure 1. A total of 175 patients underwent ESD for colorectal tumors, of which 62 were rectal tumor patients. Patients lost to follow-up (11 cases) and those with no tumor on pathologic examination (3 patients) were excluded from the study. A total of 48 patients treated using ESD were included in the study: 24 adenomas, 16 adenocarcinomas, and 8 SET. A total of 31 patients underwent TEM for rectal tumors. Patients lost to follow-up (6 patients) and those with no tumor on pathologic exam (2 patients) were excluded from the study. A total of 23 patients treated using TEM were included in the study: 5 with adenomas, 11 with adenocarcinomas, and 7 with SET.

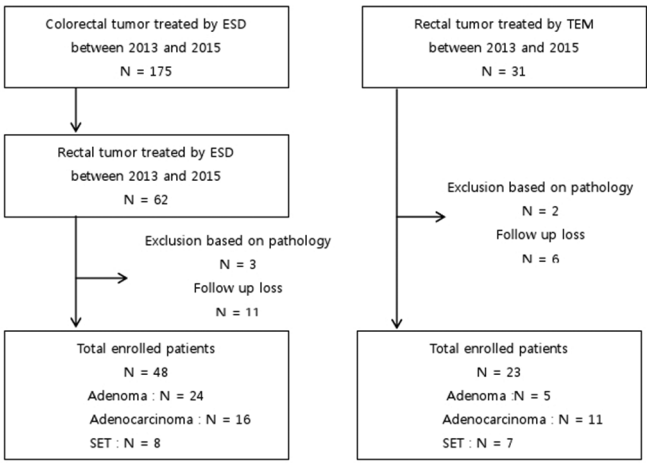

Figure 1: Flowchart of patient enrollment

Endoscopic submucosal dissection procedure

One experienced endoscopist (J.L.) performed all the ESD procedures. ESD was carried out with a high-definition endoscope (CF-H290I, Olympus Corporation, Tokyo, Japan) with CO_2 insufflation. Procedures were performed under conscious sedation by administration of midazolam. The ESD procedure is shown in Figure 2. A mixture of hypertonic saline (5% glycerin, 2.5% fructose, and 0.9% saline), 0.008% indigocarmine,

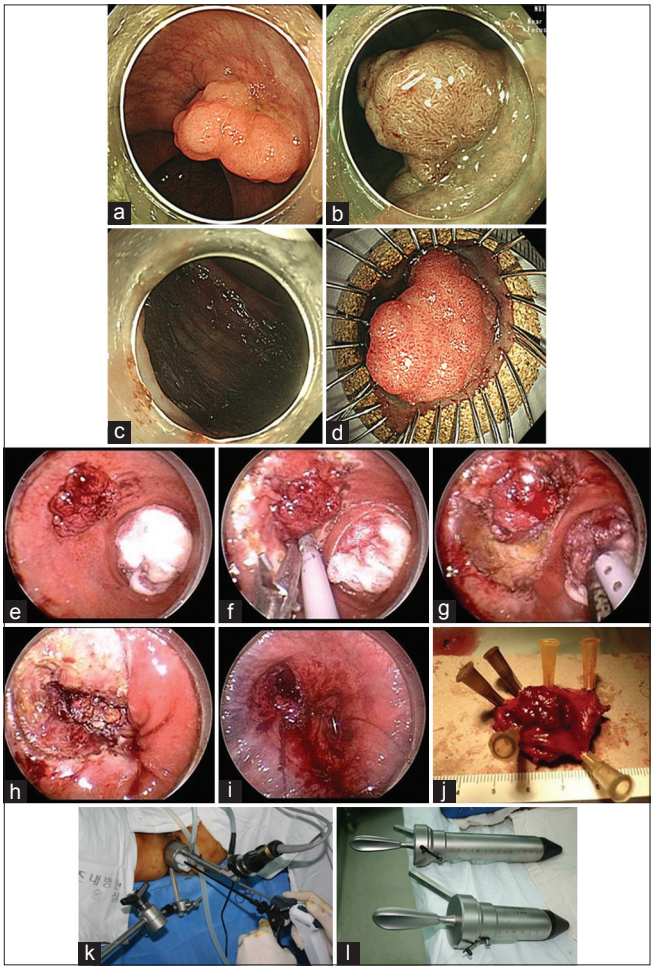

Figure 2: ESD (a-d) and TEM (e-l) procedure. (a) Subpedunculated polyp at rectum. (b) Narrow band image (type IV pit pattern). (c) Ulceration after ESD. (d) Resected specimen by ESD (intramucosal adenocarcinoma). (e) LST at rectum. (f) Operation site marking. (g) Full-thickness dissection by TEM procedure. (h) Resected area. (i) Closed by suture. (j) Resected specimen. (k) TEM port at the operating table with the anaesthetized patient. (l) Steroscope used in TEM

and 0.001% epinephrine was used as the submucosal injection solution. Injection was repeated several times until the mucosal lesion was sufficiently elevated. The circumferential incision and submucosal dissection was made with a dual knife (KD-650U, Olympus Corporation, Tokyo, Japan). The procedure time was considered to be from the start of submucosal injection to the complete removal of the specimen.

Transanal endoscopic microsurgery procedure

One experienced surgeon (K.J.K.) performed all the TEM procedures. The operation was carried out under general anesthesia with lithotomy or in a supine position according to the tumor's location. We used a transanal endoscopic operation (TEO) device by Karl Storz GmbH (Tuttlingen, Germany). The TEM procedure is shown in Figure 2. A rectoscope 7 or 15 cm in length and 4 cm in diameter is inserted through the anus and positioned for optimal visualization of the lesion. It has three working channels allowing the entrance of laparoscopic instruments. Insufflation is obtained using a conventional CO_2 insufflator, and an optical endoscope is introduced to provide the operation field. Using electrocautery, the operator marks the resection margin around the tumor. Full thickness excision with a 1-cm circumferential margin is intended. After the specimen is removed from the TEO device, the defect is closed using absorbable continuous sutures. The procedure time was considered to be from the incision of the lesion to the complete closure of the resection site.

Assessment

We defined en bloc resection as when the tumor was resected in one piece without fragmentation. R0 resection was defined as a negative margin in pathology. Histologic curability was defined as en bloc resection without unfavorable histopathologic features such as positive margins, lymphovascular invasion, or poor differentiation. In cases of TEM, invasion into the lower third of the submucosa (sm3) was added as an unfavorable feature. Additional surgery was recommended for unfavorable histology.[12] The first follow-up colonoscopy was done after 6–12 months. In patients with invasive cancer, abdominal computed tomography (CT) was performed with colonoscopy. After the first study, surveillance colonoscopy was performed according to guidelines.[13,14]

Statistical analysis

The statistical evaluation was performed using SPSS software version 18.0 (SPSS Inc., Chicago, IL, USA). Statistical differences were analyzed using the Chi-square test or Fisher's exact test for categorical data and using the independent sample *t*-test for continuous data. A *P* value of <0.05 was considered to be statistically significant.

RESULTS

Characteristics of patients and tumors

Demographic data and tumor characteristics (tumor size and location, endoscopic feature, grade of adenoma, histological depth of cancer, and diagnosis of SET) are presented in Table 1. There were no significant differences in demographic features and tumor characteristics between the two groups.

Epithelial tumors

The mean age of patients with epithelial tumors was 67.4 ± 9.3 in the ESD-treated group and 68.4 ± 8.9 in the TEM-treated group ($P = 0.72$). There was no difference in sex ratios between the two groups. Mean tumor size was 3.3 ± 1.3 cm in the ESD group and 2.7 ± 1.5 cm ($P = 0.22$) in the TEM group. Most tumors were in the mid-lower rectum, and sessile lesions were predominant in both groups. The proportion of cancer was higher in the TEM group. In the ESD group, 24 lesions (60%) were adenomas and 16 lesions (40%) were adenocarcinomas. In the TEM group, 5 lesions (31.3%) were adenomas and 11 lesions (68.7%) were adenocarcinomas. The depth of invasion varied from the mucosa to the sm2 in the ESD group and to the muscle layer in the TEM group.

Subepithelial tumors

The mean age of patients was 53.1 ± 16.8 years in the ESD-treated group and 52.2 ± 8.2 years in the TEM-treated group ($P = 0.9$). There were only male patients in the TEM group, but there was no statistical difference in sex ratios between the two groups. The mean tumor size was 1.37 ± 0.51 cm in the ESD group and 1.85 ± 1.76 cm in the TEM group ($P = 0.5$). The mid-lower rectum was the predominate location. In the ESD group, 8 patients (100%) had neuroendocrine tumors. In the TEM group, SET included neuroendocrine tumor (3 cases), gastrointestinal stromal tumors (GIST) (2 cases), leiomyoma (1 case), and mucinous cystadenoma (1 case).

Treatment outcomes

Treatment results were analyzed with respect to en bloc (R0) resection rate, procedure time, hospital stay, local recurrence, additional procedure rate and complications. Both methods showed good efficacy [Table 2].

Epithelial tumors

In a comparison of ESD with TEM, en bloc resection rates were 95% vs. 93.7% ($P = 1$) and R0 resection rates were 92.5% vs. 87.5% ($P = 0.617$), respectively. The

Table 1: Patients and tumor characteristics

Characteristics	Epithelial tumor		*P*	Characteristics	Subepithelial tumor		*P*
	ESD	TEM			ESD	TEM	
Patient characteristics				Patient characteristics			
No. of lesions	40	16		No. of lesions	8	7	
Age	67.4±9.3	68.4±8.9	0.72	Age	53.1±16.8	52.2±8.2	0.9
Sex			0.93	Sex			0.2
Male	22	9		Male	5	7	
Female	18	7		Female	3	0	
BMI	23.5±3.1	23.5±3.3	0.93	BMI	25.3±4.6	26.2±3.1	0.66
Tumor characteristics				Tumor characteristics			
Tumor size (cm)	3.3±1.3	2.7±1.5	0.22	Tumor size (cm)	1.37±0.51	1.85±1.76	0.5
Tumor location			0.33	Tumor location			0.26
Mid-lower rectum	37	13		Mid-lower rectum	8	6	
Upper rectum	3	3		Upper rectum	0	1	
Endoscopic appearance			N/A*				
Subpedunculated	12	1					
Sessile	19	14					
Flat	9	1					
NICE classification			0.735				
Type 1	0	0					
Type 2	22	8					
Type 3	18	8					
Final diagnosis			0.052	Final diagnosis			N/A*
Adenoma	24	5		Neuroendocrine tumor	8	3	
Low grade	16	2		GIST	0	2	
High grade	8	3		Leiomyoma	0	1	
Cancer	16	11		Mucinous cystadenoma	0	1	
Histological depth							
Mucosa/Sm1/Sm2/Sm3	10/5/1/0	4/3/0/2					
Muscularis propria	0	2					

*N/A: Not applicable

Table 2: Comparison of clinical results

Clinical results	Epithelial tumor		*P*	SET	TEM	*P*
	ESD	TEM		ESD		
No. of lesions	40	16		8	7	
En bloc resection rate	95% (38/40)	93.7% (15/16)	1	100% (8/8)	100% (7/7)	N/A*
En bloc (R0) resection rate	92.5% (37/40)	87.5% (14/16)	0.617	87% (7/8)	85% (6/7)	0.91
Procedure time (min)	71.5±51.3	105.6±28.2	0.016	32.13±13.4	80.71±18.35	0
Hospital stay (days)	4.3±1.2	5.8±1.8	0.001	4.1±4.1	5.5±2	0.42
Recurrence	2.5% (1/40)	6.2% (1/16)	0.49	0%(0/8)	0%(0/7)	N/A*
Additional procedure rate	7.5% (3/40)	25% (4/16)	0.094	0%(0/8)	0%(0/7)	N/A*

*N/A: Not applicable

procedure time was significantly shorter in the ESD group (71.5 ± 51.3 min vs. 105.6 ± 28.2 min, $P = 0.016$). Hospital stays were also significantly shorter in the ESD group (4.3 ± 1.2 days vs. 5.8 ± 1.8 days, $P = 0.001$). The recurrence rate was 2.5% vs. 6.2% ($P = 0.49$). There was one local recurrence in each group. In the ESD group, a local recurrence was found during a 6-month follow-up colonoscopy in a low-grade adenoma patient; this lesion was removed by endoscopic mucosal resection. In the TEM group, a recurrence was found in a rectal cancer patient. Even though there was an sm3 invasion at the original resected specimen, this patient did not undergo radical surgery because of the underlying disease and old age. The additional procedure rate was 7.5% vs. 25% ($P = 0.094$). Additional operations were needed in 3 patients in the ESD group and 4 patients in the TEM group because of unfavorable histology. In the ESD group, 1 patient underwent surgery because of an sm2 invasion and the other 2 patients because of lymphovascular invasions. In the TEM group, 1 patient underwent radical surgery because of positive margin and the other 3 patients because of deep tumor invasion (sm3 or muscularis propria). There was no recurrence in all patients who received additional surgery.

Subepithelial tumors

For ESD compared to TEM, en bloc resection rates were 100% vs. 100% and R0 resection rates were 87% vs. 85% ($P = 0.91$). The procedure time was significantly shorter in the ESD group (32.13 ± 13.4 min vs. 80.71 ± 18.35 min, $P = 0.00$). Hospital stays tended to be shorter in the ESD group (4.1 ± 4.1 days vs. 5.5 ± 2 days,

$P = 0.42$). No additional treatment was performed in both groups and there was no recurrence.

Complications

Complications of procedures are presented in Table 3.

Epithelial tumors

There were 3 perforation events in the ESD group and 2 perforation events in the TEM group. In the ESD group, 2 early perforations and 1 delayed perforation occurred. All these patients recovered with conservative treatment. In the TEM group, there were 2 intraoperative perforations. They were managed by laparoscopic-assisted rectum suture. There was no peritonitis or other complications.

Bleeding developed without unstable vital signs and severe changes of hemoglobin in 3 patients in the ESD group and 2 patients in the TEM group. In the ESD group, early bleeding spontaneously stopped (1 case) and endoscopic hemostasis was done successfully for delayed bleeding (2 cases). In the TEM group, early bleeding (1 case) and delayed bleeding (1 case) spontaneously stopped without an endoscopic procedure. Postpolypectomy syndrome occurred in 5 patients in the ESD group, and all patients improved within 3 days with conservative treatment.

Subepithelial tumors

Delayed bleeding events without changes in hemoglobin or vital signs occurred in the ESD group and were successfully managed with endoscopic hemostasis (2 cases). Delayed bleeding occurred in the TEM group and stopped spontaneously without special treatment (1 case). There was no perforation.

DISCUSSION

In our study, both ESD and TEM showed favorable treatment results for epithelial tumors (large adenoma and carcinoma). In addition, it was the first data comparing ESD and TEM for the treatment of SET.

Although TEM has long proven its effectiveness in the treatment of rectal tumors, it requires anesthesia associated with various morbidity and requires long recovery times and hospital stays.[15] In addition, high cost is incurred because of the use of anesthesia and expensive equipment, which is costly to the patient. Because TEM uses a rigid rectoscope, it cannot be performed within 5 cm of the anal verge.[16] ESD has recently become the most important option in the treatment of noninvasive colorectal neoplastic lesions and overcomes the disadvantages of TEM. ESD can be performed under conscious sedation without anesthesia, and there are fewer hospital days and lower costs than those for TEM.[17] In addition, ESD is easy to perform in the upper rectum and retroflexion is possible; hence, it is easy to treat lesions near the anus or on the anus.[18]

In a systematic review of the 11 ESD and 10 TEM series between 1984 and 2010 for large (>2 cm) noninvasive rectal neoplasms, TEM was associated with higher rates of en bloc resection (99% vs. 88%, $P < 0.001$) and R0 resection (89% vs. 75%, $P < 0.001$) than ESD. ESD was associated with lower recurrence (2.6% vs. 5.2%, $P < 0.001$).[5] The difference in our study from this systematic review was that ESD tended to achieve higher en bloc and R0 resection rates than TEM. The ESD studies included in the systematic review are pre-2010 and do not reflect the results of recent ESD developments, which can be regarded as the cause of the difference in this study.

In our study, both epithelial tumors and SET showed a significantly superior procedure time. (epithelial tumors: 71.5 ± 51.3 min vs. 105.6 ± 28.2 min, $P = 0.016$; SET: 32.13 ± 13.4 min vs. 80.71 ± 18.35 min, $P = 0.000$) and shorter hospital days (epithelial tumors: 4.3 ± 1.2 days vs. 5.8 ± 1.8 days, $P = 0.001$; SET: 4.1 ± 4.1 days vs. 5.5 ± 2.0 days, $P = 0.42$). In recent years, the proficiency of ESD practitioners has improved greatly, and the development of the knife and the use of a high-definition endoscope with a water jet function have facilitated lesion incision and bleeding control, improving the time and accuracy of ESD procedures.[6-9] For these reasons, we think that the duration of the ESD procedure is significantly shorter than the TEM in this study, which was based on relatively recent data from 2013–2015. However, because the time of the TEM procedure has been reported to vary, it is necessary to conduct a study with various practitioners.[19-21] ESD was also associated with shorter hospital days than TEM, probably because of preoperative laboratory tests, risk assessment, and

Table 3: Comparison of complications

Complications	Epithelial tumor		*P*	SET	TEM	*P*
	ESD	TEM		ESD		
Perforation	12.5% (3/40)	12.5% (2/16)	0.617	0% (0/8)	0% (0/7)	N/A*
Bleeding	12.5% (3/40)	12.5% (2/16)	1	25% (2/8)	14.3% (1/7)	0.6
Postpolypectomy syndrome	12.5% (5/40)	0% (0/16)	0.307	0% (0/8)	0% (0/7)	N/A*

*N/A: Not applicable

postoperative complications associated with general anesthesia.[17] In addition to these advantages, ESD's efficiency can be considered to be superior to TEM considering the induction time and recovery time caused by general anesthesia in TEM.

Complications such as perforation, bleeding, and postpolypectomy syndrome occurred, but there were no critical complications such as refractory peritonitis or unstable bleeding in both groups. All these complications were overcome easily with conservative medical treatment or endoscopic hemostasis.

Two retrospective studies directly compared ESD to TEM in the treatment of rectal neoplasm. Park *et al.* retrospectively analyzed 63 patients with nonpolypoid rectal high-grade dysplasia or submucosal invading cancer.[11] Patients treated with ESD (n = 30) and TEM (n = 33) had similar rates of en bloc resection (96.7% vs. 100%, P = 0.476) and R0 resections (96.7% vs. 97%, P = 1.000). ESD was associated with a shorter procedure time (84 ± 51.2 min vs. 116.4 ± 58.5 min, P = 0.0023) and hospital stay (3.6 ± 1.2 days vs. 6.6 ± 3.5 days, P < 0.001) than TEM. In another study, Kawaguti *et al.* retrospectively analyzed 24 patients with early rectal cancers treated with ESD (n = 11) or TEM (n = 13).[10] Both procedures showed favorable en bloc resection rates (81.8% and 84.6% respectively, P = 0.42) and R0 resection rates (81.8% vs. 84.6%, P = 0.40). ESD was associated with a shorter procedure time (133 ± 94.8 min vs. 150 ± 66.3 min, P = 0.69) and hospital stay (3.8 ± 3.3 days vs. 4.08 ± 1.7 days, P = 0.81) than TEM without statistical significance. Both these studies analyzed the procedures performed until 2011 and did not reflect the latest ESD technology and equipment development, and the sample size is small. On the other hand, our study is the most recent report comparing ESD and TEM based on data within the last 4 years.

We analyzed the treatment of rectal SET in our study. In a retrospective study conducted in 2012, the en bloc, R0 resection rate, and recurrence rate of rectal neuroendocrine tumor treated with ESD was reported to be 97.7%, 97.7%, and 0%, respectively.[22] TEM has also been recognized as an effective and safe treatment option for SET such as neuroendocrine tumor, GIST, neuroma/schwannoma, granular cell tumor, and lipoma.[4,23,24] In our study, in the SET group, both procedures showed favorable en bloc resection rates (100% vs. 100%) and R0 resection rates (87% vs. 85%, P = 0.91) in ESD and TEM. No recurrence was reported in both procedures. These results suggest that both ESD and TEM can be safely performed in rectal tumors, not only epithelial tumors, but also SET.

This study has some limitations. First, it was a single-center, nonrandomized clinical trial with selection bias in the treatment options. However, the indications of the procedure and the tumor characteristics were not different between both groups. Second, because both ESD and TEM were performed by a single practitioner, the experience, time, and complications of the procedures may depend on individual experience. Previous studies have reported varying amounts of time for TEM procedures.[19-21] Multicenter randomized controlled trials with a large sample size and endoscopists or surgeons of various levels of experience are needed. Third, only few cases of subpedunculated and flat polyp in the TEM group were registered in our study. Therefore, there is a limit to the comparison of the therapeutic effect of ESD and TEM according to the endoscopic shape of the tumor. Fourth, the number of SET included in the study in both the ESD and TEM groups was insufficient, which may not have resulted in statistically significant results. In addition, the SET of the ESD group were all neuroendocrine tumors. Therefore, it is necessary to analyze treatment results for various and sufficient numbers of SET.

CONCLUSION

In summary, we confirmed the similar efficacy and safety of ESD and TEM for rectal epithelial tumor and SET. However, the ESD group showed shorter procedure times and hospital stays than TEM group. Therefore, ESD should be considered more preferentially than TEM in the treatment of large rectal epithelial tumors and SET.

Our study is a relatively large study comparing ESD and TEM in the treatment of rectal tumors based on current (up to date) data and also the first study to compare the two procedures in the treatment of SET.

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Conflicts of interest

There are no conflicts of interest.

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