Endoscopic submucosal dissection for rectal-sigmoid laterally spreading tumors ≥10 cm: an analysis of 10 cases

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Background: Endoscopic submucosal dissection (ESD) is a standard method for treating selected colorectal laterally spreading tumors (LSTs). However, technical difficulty occurs with the increase in tumor size, and little is known about the efficacy of ESD treatment in colorectal LSTs ≥10 cm. The present study aimed to report the feasibility, safety, and efficacy of ESD for rectal-sigmoid LSTs ≥10 cm.

Methods: From May 2012 to December 2019, patients with rectal-sigmoid LSTs ≥10 cm and underwent colorectal ESD were enrolled retrospectively. Demographic features, procedure-related parameters (procedure time, adverse events, rate of en bloc resection and complete resection), and follow-up results were recorded and analyzed.

Results: A total of 10 patients successfully underwent ESD: nine patients received conventional ESD, while the other one underwent tunneling ESD. The median diameter of the LSTs was 11.5 cm, and the median procedure time was 210 minutes. The rates of en bloc and curative resection rates were 100% and 90%, respectively. Of the ten patients, four had developed adverse events, one had intraoperative bleeding, two patients had delayed bleeding, and the other one had postoperative fever and rectum stricture postoperatively. None of the patients experienced recurrence during a median follow-up of 62 months.

Conclusions: ESD can be used as a feasible, safe and effective treatment modality for the management of rectal-sigmoid LSTs ≥10 cm.

Keywords: Laterally spreading tumor (LST); endoscopic submucosal dissection (ESD); en bloc resection; adverse events; colorectal neoplasm

Introduction

Laterally spreading tumors (LSTs) are defined as superficial lesions with diameter of ≥10 mm, which typically extend laterally rather than vertically along the gastrointestinal wall (1). Based on their endoscopic appearance, LSTs were classified into two subtypes, a granular and a non-granular pattern. The former is further subdivided into homogeneous and nodular mixed, while the latter into flat elevated and pseudo-depressed (2).

Endoscopic resection is recommended as the initial treatment for selected colorectal LSTs, and reported methods include endoscopic mucosal resection (EMR), endoscopic piecemeal mucosal resection (EPMR), and endoscopic submucosal dissection (ESD) (3). EMR is a well-established method and more cost-effective treatment for colorectal LSTs compared with surgery (4,5). However, for lesions >20 mm, EMR is associated with the risk

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of piecemeal resection and relatively high rate of local recurrence (6). Moreover, extended EMR does not the reduce recurrence rate (7). Although EPMR can remove LSTs larger than 20 mm, it is associated with a higher local recurrence rate than when performed after en bloc resection (8,9). ESD is preferred as it allows en bloc resection, and has been adopted for the treatment of large colorectal neoplasms, which cannot be completely resected by EMR (9-12). ESD is associated with higher rate of en bloc resection and complete resection compared with EMR, thus allowing complete histologic evaluation of the resected lesions (12-14). However, resection of extensive lesions, especially LSTs measuring ≥10 cm in diameter, remains challenging, and only a few cases have been reported (15-17). Hence, the present study, aimed to examine the feasibility, safety, and efficacy of ESD in the treatment of colorectal LSTs ≥10 cm.

We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/tcr-20-2659).

Methods

Patients

All the participants signed an informed consent before undergoing endoscopic treatment. The inclusion criteria of the study were as follows: (I) presence of colorectal LSTs ≥10 cm found during colonoscopy; (II) with no evidence of submucosal invasion deeper than SM1 by a comprehensive preoperative assessment of biopsy, narrow band image and magnifying endoscopy (NBI-ME), endoscopic ultrasonography (EUS) and/or computerized tomography (CT) performed preoperatively; (III) patient consent to undergo an ESD procedure. Those patients with severe cardiopulmonary disease or blood coagulation disorders were excluded. Between May 2012 and December 2019, 10 consecutive patients were enrolled. Their demographic data, tumor- and procedure-related parameters, adverse events, length of hospital stay, and follow-up data were retrospectively collected.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional ethics committee of the Second Xiangya Hospital (No.: LYF2020129).

Equipment of ESD

ESD was performed under conscious sedation (6 patients) or general anesthesia (4 patients) using a colonoscope (CF-Q260 or CF-HQ290, Olympus) with an attached transparent cap. Carbon dioxide was used for insufflation. Other equipment and accessories used during the procedure included a high-frequency generator (VIO 200D; ERBE), an argon plasma coagulation unit (APC300; ERBE), various dissecting knives (hybrid knife, dual knife, and insulation-tip knife), an injection needle (NM-4L-1; Olympus), and hemostatic clips (HX-600-90; Olympus).

ESD procedure

All the ESD procedure was carried out by an experienced operator, who had performed more than 100 colorectal ESDs before treating the first patient in the present study. Nine patients underwent conventional ESD, and the procedure was performed as follows: (I) determine the boundary using white light endoscopy, NBI, ME and/or chromoendoscopy. (II) Submucosal injection was applied around the lesion with a mixed solution of 100 mL saline, 1 mL 1:2,000 adrenaline, 5 mL indigo carmine. For lesions involving the dentate line, 1% lidocaine was added into the submucosal injection solution and injected into the submucosal layer of the anal side (with a maximum volume of 10 mL). (III) Then, semi-circular dissection was then performed 0.5 cm outside along the longitudinal axis of the bowel lesions. The patient's position was changed occasionally to permit gravity to pull the bulk of the dissected tumor away from the base in order to facilitate dissection. Repeated submucosal injections were performed during dissection. (IV) The bleeding wound was appropriately coagulated and the visible blood vessels were clamped with hemostatic forceps. The wound was carefully assessed for presence of any bleeding, perforation, or local residual after dissection. One patient underwent tunneling ESD, which involved the creation of a submucosal tunnel created to facilitate the dissection. *Figure 1* provides a case illustration of conventional ESD.

Postoperative management and follow-up strategy

The specimen was fixed and embedded in paraffin before sectioning. Hematoxylin and eosin staining was performed to determine the features of the resected tumors. The patients were asked to keep nil per os for one day and liquid diet for 6 days, and then returned gradually to a normal diet within two weeks. Patients were asked to stay in bed for at least 3 days. They were followed up at 1, 3, 6 and 12 months
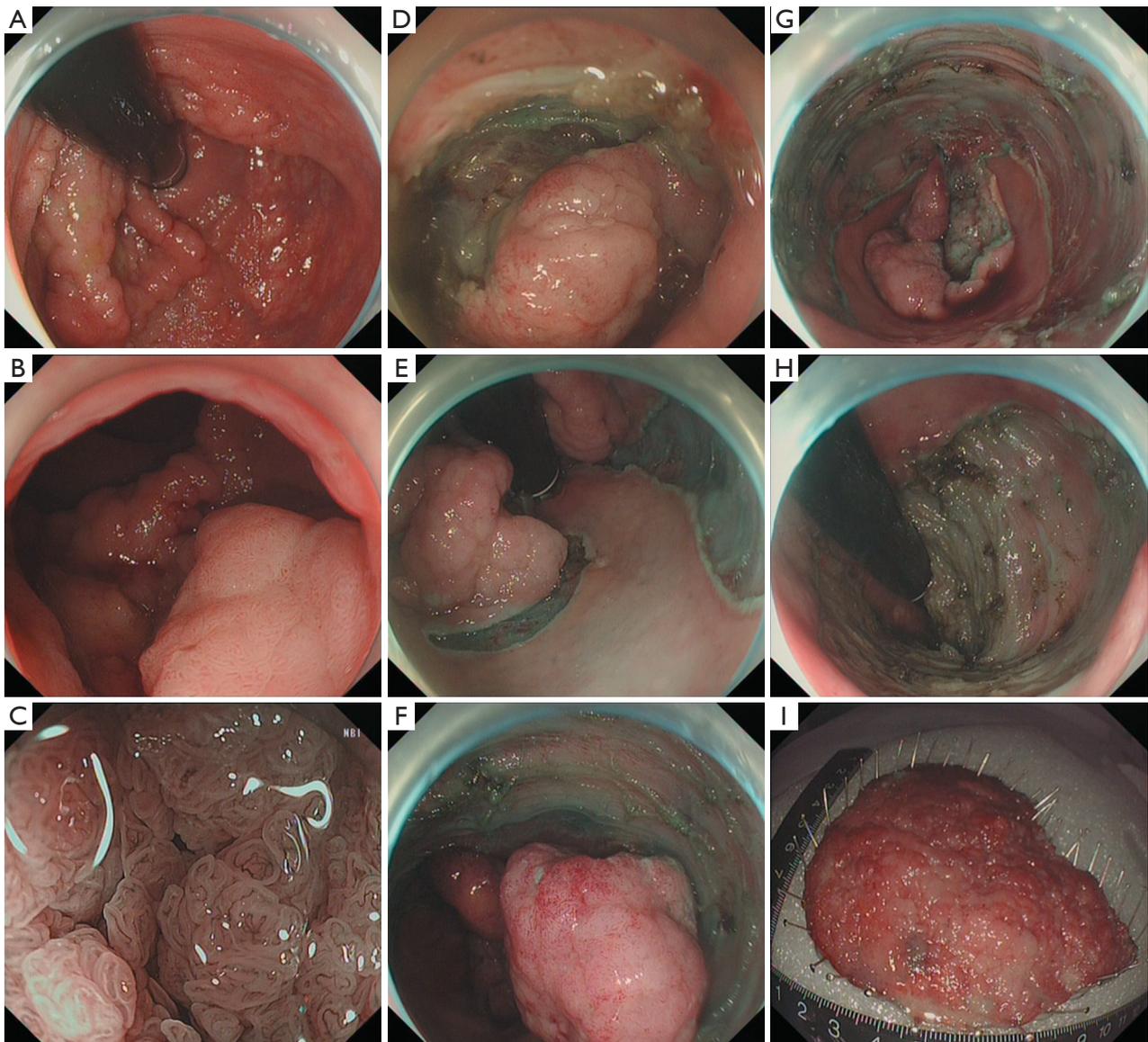
Figure 1 Case illustration of colorectal endoscopic submucosal dissection (ESD). (A) We could see a large laterally spreading tumor (LST) in the rectum (view from the oral side); (B) we could see a large LST in the rectum (view from the anal side); (C) magnifying endoscopy revealed type IV pit pattern; (D) incision from the anal side; (E) incision from the anal side; (F,G) dissecting the LST; (H) wound surface after removal of the LST; (I) the resected specimen.

for the first year and then once a year. White light endoscopy with NBI was initially performed, and biopsy, ME, EUS or CT was used for further evaluation in patients with suspected recurrence or residue.

Definitions

The duration of ESD was defined as the duration from the time of submucosal injection of solution to the management of the wound surface after removal of the lesion. Perforation was characterized by presence of endoscopically visible pericolic fat or exposure of other intra-abdominal structures through a tear in the muscularis propria or when visible of free or retroperitoneal air shadows on postoperative radiographs. Delayed bleeding was defined as the presence of melena or hematochezia 6 hours after completion of

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ESD, which required blood transfusion or endoscopic hemostasis.

En bloc resection was defined as the removal of an LST in a single piece. Curative resection was defined as an R0 resection with submucosal invasion of <1,000 mm, without lymphovascular invasion or poorly differentiated components.

Statistical analysis

SPSS 21.0 software was used for data analysis. Due to the relatively small sample size, the results were presented as median and range.

Results

A total of 748 patients underwent colorectal ESD between May 2012 and December 2019, and 259 had LSTs. Among the 259 patients, 10 had a lesion diameter of ≥10 cm, and all the lesions were located at rectal-sigmoid. *Table 1* shows the characteristics of the 10 patients, of whom 6 were male and 4 were female. The median age of the patients was 65 years. Three patients had hypertension as comorbidities, but none of the 10 patients had a history of receiving antithrombotic or antiplatelet therapy. Eight of the ten lesions were located in the distal rectum, 1 in the recto-sigmoid junction, and 1 in the sigmoid colon. Two of the lesions were classified as granular homogeneous type, while the other eight were of granular nodular mixed type.

The lesions in all 10 patients were removed successfully by ESD, of them, nine underwent conventional ESD, while the other one had tunneling ESD. The en bloc resection rate was 100%. The median size of the resected lesions was 11.5 cm (range, 10–17 cm), and the median procedure time was 210 min (range, 120–480 min). Clips were used in two patients to prevent postoperative bleeding. Histologically, five patients were diagnosed with low-grade intraepithelial neoplasm, one with high-grade intraepithelial neoplasm, and the other four with intramucosal cancers. The curative resection rate was 90%: nine patients underwent curative resection, while the other one patient had a low-grade dysplasia residue at the horizontal margin. The patient refused further endoscopic treatment and no local recurrences occurred during a follow-up period of 93 months.

Four patients developed adverse events. One patient had profound intraoperative bleeding, who underwent endoscopic hemostasis and required blood transfusion during ESD. Two patients experienced delayed bleeding

and they underwent endoscopic hemostasis without blood transfusion. None of the patients had perforation. All the three patients with bleeding had LST lesions at rectum, which is a well-known risk factor for post-ESD bleeding. One patient developed a fever up to 38.5 centigrade and had an elevated white blood cell count after ESD, and the temperature and white blood cells returned to normal after receiving intravenous antibiotics for 3 days. The patient also suffered from rectum stricture 40 days after ESD and the stricture was released after 4 sessions of endoscopic balloon dilations.

The median length of hospital stay was 4.5 days (range, 3–6 days). None of the patients experienced local recurrence, or distant metastases was noticed within a median follow-up period of 62 months (range, 1.0–104 months).

Discussion

In the present study, we reported 10 cases of rectal-sigmoid LSTs, which were successfully removed by ESD, suggesting that ESD is feasible, safe and effective for treatment for rectal-sigmoid LSTs ≥10 cm. To our knowledge, this is the largest case series on ESD for treatment of rectal-sigmoid LSTs ≥10 cm.

With the development of endoscopic technology and other medical devices, an increasing number of colorectal cancers are detected at an early stage, which can be managed using minimally invasive endoscopic methods. ESD is a widely accepted method for treating precancerous lesions and early stage colorectal cancers, moreover, it is superior to surgical resection in terms of morbidity, life quality, recovery speed, and health care costs (18-20). ESD has advantages over EMR and EPMR, including higher rate of complete resection and en bloc resection, which allows for complete histologic assessment and results in a lower incidence of recurrence (12-14).

However, colorectal ESD is technically difficult because of the tortuous or angulated lumens and the relatively thin intestinal wall. The technical difficulty increases with the increase in tumor size, especially for lesions larger than 5 cm (16,21,22). This is because of the inability to provide a clear visualization of the submucosal layer due to the contraction or curling of the resected mucosa. Several traction methods have been reported to facilitate the ESD procedure, such as clip and snare, internal traction, clip with line, external forceps, and magnetic anchor (23-25). Another important modification of ESD is the pocket-creation method (PCM), which was first reported by Hayashi *et al.* (26) for en

Table 1 Clinical features of the ten patients with rectal-sigmoid LSTs ≥10 cm

Case No.	Age	Gender	Location	Symptoms	Involving the dentate line	CE	Morphology type	Pit pattern type	Procedure time (mins)	Size of resected lesion (cm)	Resection method	HS	HD	Perforation	Bleeding	Stricture	Duration of follow-up (months)
1	64	Female	Rectum	Loose stool	Yes	3/5	LST-G (H)	IIIL + IV	260	10×7	Conventional ESD	6	LGIN	No	Yes	No	104
2	38	Male	Recto-sigmoid junction	Bloody stool	No	4/5	LST-G (H)	IIIL + IV + V1	480	17×7	Conventional ESD	5	LGIN	No	No	Yes	93
3	67	Male	Rectum	Increased stool frequency	No	Whole	LST-G (M)	IV	170	10×4.5	Conventional ESD	3	LGIN	No	No	No	87
4	68	Male	Rectum	Bloody stool	No	1/2	LST-G (M)	IV + VA	120	10×7	Conventional ESD	4	IMC	No	No	No	78
5	65	Female	Rectum	Mucous stool	Yes	5/7	LST-G (M)	IIIL + IV	360	13×13	Conventional ESD	5	LGIN	No	No	No	64
6	57	Male	Rectum	Rectal bleeding	Yes	Whole	LST-G (M)	IIIL + IV	175	12×9.5	Conventional ESD	4	IMC	No	No	No	60
7	65	Female	Rectum	Bloody stool	Yes	4/5	LST-G (M)	IIIL + IV	220	10.5×7.5	Conventional ESD	4	LGIN	No	No	No	46
8	60	Male	Sigmoid colon + proximal rectum	Increased stool frequency	No	3/5	LST-G (M)	IIIL + IV	200	13×6.5	Tunneling ESD	4	HGIN	No	No	No	16
9	70	Male	Rectum	Increased stool frequency	Yes	whole	LST-G (M)	IV	420	14×9.6	Conventional ESD	4	IMC	No	Yes	No	2
10	70	Female	Rectum	Increased stool frequency	No	2/3	LST-G (H)	IIIL + IV + V1	120	11×10	Conventional ESD	5	IMC	No	Yes	No	1

CE, circumferential extent; ESD, endoscopic submucosal dissection; HS, hospital stay (days); HD, histopathology diagnosis; HGIN, high-grade intraepithelial neoplasia; IMC, intramucosal cancer; LGIN, low-grade intraepithelial neoplasia; LST-G(H), laterally spreading tumor granular homogeneous type; LST-G(M), laterally spreading tumor granular mixed type.

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bloc resection of a giant colorectal subpedunculated neoplastic lesion with fibrosis. During PCM, the submucosal layer is dissected to create a wide pocket under a lesion after performing a minimal mucosal incision, PCM has been demonstrated to facilitate the ESD procedure in term of dissection speed and en bloc resection (27-29). Tunneling ESD, which involves the creation of a submucosal tunnel from the oral to the anal side of the lesion, was initially adopted as a treatment for superficial esophageal lesions (30), and it could accelerate the dissection speed (31,32). Several researchers have reported the application of tunneling ESD for colorectal lesions (33-39). Although no comparative study has been conducted to examine the superiority of this method, tunneling ESD may provide a clearer visualization and decrease the frequency of submucosal injection, thus potentially reducing the risk of adverse events and accelerating the operation speed. In the present study, nine patients underwent conventional ESD without additional traction method, while one patient underwent tunneling ESD.

Jung *et al.* (16) found that ESD was associated with a higher complication rate, higher technical difficulty degree, and longer procedure time, when it was performed in patients with giant colorectal LSTs ≥10 cm. In the present study, 40% of the 10 patients developed adverse events, and the median procedure time was 210 min, suggesting a relatively high rate of adverse events and long procedure time. This finding may be due to the large size of the 10 lesions. Therefore, we suggest that ESD for removal of large lesions should be performed by highly experienced operators. In our opinion, the following tips may facilitate ESD procedure: (I) the blood vessels should be appropriately clamped with hemostatic forceps, the bleeding surface should be electrocoagulated and prophylactic clips should be applied for 3 days to prevent bleeding. (II) Mucosal incision and submucosal dissection should begin from the anal side, the patient's position should be changed when needed in order to have a clear visualization and a certain order should be followed when the lesion is dissected. (III) Tunneling ESD or PCM-ESD may be attempted to facilitate dissection. We suggest tunneling ESD as an attempt for LSTs located at rectum with a diameter of ≥5 cm. (IV) CO_2 insufflation is recommended in order to reduce the occurrence of abdominal distension, abdominal pain and micro-perforation during ESD procedure (40), as giant lesions are associated with long procedure time. (V) A circumferential mucosal defect of more than 80% is a risk factor for post-ESD colorectal stricture (41); thus, periodical endoscopic surveillance is necessary to assess the presence of post-ESD stricture, or preventive balloon dilatation after ESD may be performed. In the present study, a patient with 80% circumferential involvement developed a stricture postoperatively and it was managed consecutively with balloon dilation. (VI) As most of the patients experienced delayed bleeding occurs within the first week after ESD, adequate rest and liquid diet were suggested for at least one week to lessen bowel movement and maintain the passage of loose stools, which can reduce friction between the feces and surface of the wound. (VII) For lesions involving the dentate line, the local injection of 2% lidocaine on the anal side of the lesion before submucosal injection is recommended to prevent pain (42,43).

The present study has several limitations. First, this was a retrospective study conducted in a tertiary hospital with only 10 patients enrolled due to the rarity of lesions with such a large size, and all the procedures were performed by experienced operators. Thus, the conclusion may not be applicable in other non-tertiary hospitals. Second, no comparison was made between surgical and ESD procedures for this type of LSTs, and between LSTs ≥10 cm and or LSTs <10 cm. Third, all the 10 LSTs were located in the rectal-sigmoid, possibly because of the tendentious location of LST, and the abovementioned technical skills may not be suitable for patients with LSTs located in the right colon. Fourth, three of the 10 patients had a follow-up time of less than 24 months, which is relatively short to evaluate the long-term efficacy, as some mucosal or ganglionar recurrence can occur after 24 months. In conclusion, ESD can serve as a feasible, safe and effective treatment for rectal-sigmoid LSTs ≥10 cm.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/tcr-20-2659

Data Sharing Statement: Available at http://dx.doi.

org/10.21037/tcr-20-2659

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/tcr-20-2659). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). ESD database performed for rectal-sigmoid LSTs ≥10 cm from May 2012 to December 2019 were investigated retrospectively under IRB approval of the Second Xiangya Hospital (No.: LYF2020129) and written informed consent was obtained from all patients.

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