The retrospective comparison between submucosal tunneling endoscopic resection and endoscopic submucosal excavation for managing esophageal submucosal tumors originating from the muscularis propria layer

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Abstract

Background Submucosal tunneling endoscopic resection (STER) and endoscopic submucosal excavation (ESE) were recently introduced to cure submucosal tumors (SMTs) originating from the muscularis propria (MP) layer. This study aimed to compare clinical performance and safety of STER and ESE in treating esophageal SMTs originating from the MP layer.

Methods From January 2011 to December 2017, retrospective data collection and follow-up were applied for all STER or ESE cases with esophageal SMTs originating from the MP layer in our endoscopy center, including clinical characteristics, procedure success, efficacy, and adverse events. Subgroup analysis was further done based on tumor size and origin.

Results 90 STER and 77 ESE were enrolled in this study. There were no significant difference for patient characteristics, procedure performance, and complications for ESE and STER intervention ($P > 0.05$). STER was faster than ESE (3.90 mm^2/min vs 2.82 mm^2/min, $P < 0.05$). For large tumors (≥ 20 mm), both techniques had the similar performance ($P > 0.05$), while STER led to the shorter hospitalization (4.0d vs 7.0d, $P < 0.05$) and lower postoperative complication (16.3% vs 45.5%, $P < 0.05$). For small tumors (< 20 mm), STER achieved faster operation (STER vs ESE, 2.57 mm^2/min vs 1.83 mm^2/min, $P < 0.05$). Regardless of tumor origin, there were no significant difference for both techniques, but STER resulted in short hospitalization for SMTs from the deep MP layer (STER vs ESE, 5.0d vs 7.0d, $P < 0.05$). During the follow-up, 2 residual and 4 recurrence occurred in the STER group, as well as 1 residual and 2 recurrence in the ESE group.

Conclusions Both STER and ESE were effective for treating esophageal SMTs originating from the MP layer. STER might be better due to its faster operation, less complications, and shorter hospitalization.

Keywords Submucosal tunneling endoscopic resection (STER) · Endoscopic submucosal excavation (ESE) · Esophageal submucosal tumors (SMTs) · The muscularis propria (MP) layer · Comparison

Esophageal submucosal tumors (SMTs) are tissue protuberances covered with normal mucosa, usually without clinical

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symptoms [1–3]. In esophagus, leiomyomas and gastrointestinal stromal tumors (GISTs) are two common SMTs and originate from the muscularis propria (MP) layer. The most are benign, but 10.8% leiomyomas might turn into leiomyosarcomas [4]. GISTs are reported to be potentially malignant, especially with the large size or irregular boundary [5, 6]. Conventional thoracotomy, thoracoscopic enucleation, and endoscopic resection are commonly applied to remove esophageal SMTs, while endoscopic resection was recently developed as the first strategy due to its micro-invasiveness, high efficacy, and low complication [7–9]. The National Comprehensive Cancer Network (NCCN) guidelines recommend that GISTs ≥ 2 cm should be dissected, while endoscopic surveillance could be considered for GISTs < 2 cm

without high-risk EUS features [6]. Ramos *et al* recommended that asymptomatic esophageal leiomyomas (< 1 cm) could be supervised without therapeutic intervention; SMTs between 1 cm and 3 cm should be managed via endoscopic submucosal dissection (ESD), endoscopic submucosal tunnel dissection (ESTD), or thoracoscopic enucleation; Thoracoscopic enucleation might be applied for > 3 cm tumors [10].

Submucosal tunneling endoscopic resection (STER) and endoscopic submucosal excavation (ESE) were recently developed for treating SMTs. ESE is the modified ESD approach for SMTs. ESE was successfully applied for SMTs at esophagogastric junction, cardia, and stomach [2, 11, 12]. Inspired by peroral endoscopic myotomy (POEM), STER was introduced in 2011 [13]. It could preserve the mucosa integrity and prevent the undesired perforation during the procedure. Several studies confirmed STER was safe and efficient for esophageal SMTs treatment [14–16]. Nevertheless, few studies were presented for comparing both techniques on esophageal SMTs. Our study aimed to retrospectively analyze their difference and superiority in treating esophageal SMTs originating from the MP layer.

Methods

Patients

Patients with esophageal SMTs, who underwent endoscopic intervention between January 2011 and December 2017 at our institution, were collected from clinical database. The enrolled cases in this study should satisfy the following criteria (1) esophageal SMTs originating from the MP layer determined by endoscopic ultrasonography (EUS) or computed tomography (CT); (2) no malignant manifestation; (3) either STER or ESE treatment; and (4) Operation informed consent. Exclusion criteria included (1) disagreement for study inclusion and follow-up; (2) multiple esophageal SMTs; and (3) operation conversion for general surgery. A total of 167 cases with single lesion were included, 90 for STER and the others for ESE (Fig. 1). Two experienced endoscopists performed STER or ESE procedure. The demographic characteristics, tumor features, and procedure performance were recorded. This study was approved by the Institutional Review Board of the First Affiliated Hospital with Nanjing Medical University and conformed to the provisions of the Declaration of Helsinki.

Fig. 1 Flow chart of the patient enrollment
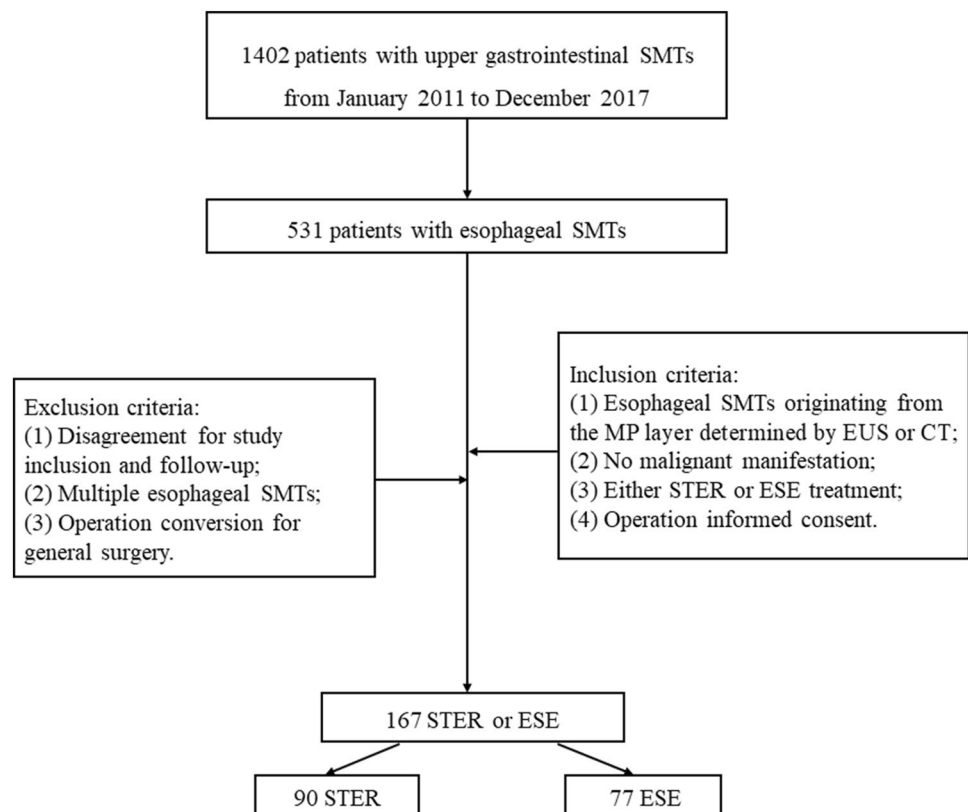
STER and ESE techniques

A single-channel gastroscope (GIF-HQ290 or GIF-Q260 J, Olympus) and a carbon dioxide (CO_2) insufflator (UCR, Olympus) were used for STER and ESE. Other relative equipment included a transparent cap (D-201-11804, Olympus), an injection needle (NM-200L-0423, Olympus), a hook knife (KD-620LR, Olympus), an insulation-tip knife (KD-611L, Olympus), a dual knife (KD-650Q/KD-650L, Olympus), a snare (SD-5L/6L-1, Olympus), hemostatic forceps (FD-410LR, Olympus), hemostatic clips (HX-610-135, Olympus), a high-frequency generator (VIO 300D, ERBE, Germany), and an argon plasma coagulation unit (APC300, ERBE).

The STER procedure was performed via the single-channel gastroscope with a transparent cap. The tumor was firstly detected and located under endoscopy. Then mucosa was lifted at 3–5 cm proximal to the tumor by submucosal cushion solution (saline + 2% indigo carmine + 1% epinephrine). For the tunnel entry, the 2-cm longitudinal/transverse incision was made on mucosa by a hook knife or a dual knife. Endoscope was then advanced into submucosal space and created a tunnel between the mucosal and MP layer. The tunnel ended at 1–2 cm distal to SMT. The submucosal tunnel should be allowed for adequate operating space and clear view for tumors. Subsequently, tumor dissection using an insulation-tip knife should be careful to avoid the intact capsule damage and esophageal mucosa injury. If required, a snare might be applied for piecemeal resection. After tumor retrieval from the tunnel, the tunnel entry was closed with several clips. If necessary, hot biopsy forceps or argon plasma coagulation (APC) was applied for hemostasis during the procedure (Fig. 2).

The ESE procedure was similar as ESD. The procedure began with argon electrocoagulation marking around the lesion. Afterwards, the saline solution mixed with 2% indigo carmine and 1% epinephrine was injected at multiple points to fully lift the mucosa and create submucosal cushion. A longitudinal incision was then made along the two proximal and distal mucosal markers with a hook knife, in order to open the overlying mucosa and expose the tumor. Tumor separation from submucosal tissues and muscle fibers was performed carefully using an insulation-tip knife without the capsule damage. Piecemeal resection by a snare was applied if required. After complete tumor removal, the defect was closed with endoscopic clips. Hot biopsy forceps or argon plasma coagulation (APC) was used for intraoperative bleeding (Fig. 3).

Postoperative management and follow-up

All patients were usually fast for 24 h and managed with routine medicines such as hemostatic drugs, proton pump inhibitors (PPIs), and antibiotics. The adverse events were recorded, including fever, chest pain, abdominal pain or distention, aerodermectasia, and haematemesis. For cases with large defect or perforation, gastrointestinal decompression was used and fast for more days.

Pathological evaluation was applied to discriminate the tumor type and malignancy. Accordingly, the endoscopy follow-up was applied at 3, 6, 12 months and then annually, to evaluate wound recovery, residual, and recurrent tumor. For GISTs, abdominal–pelvic CT was recommended every 3 to 6 months to determine the potential metastasis or recurrence [6].

Outcome measurements

The intraoperative and postoperative performances were compared for STER and ESE, including operation time, procedure speed, clip number, clip-size parameter, complete resection, complications, postoperative hospital stay, and follow-up (recurrence and residual rate). Operation period was counted from submucosal injection to complete tumor removal. Operation speed was defined as the ratio of tumor area to operation period (tumor area $= \pi \times T/2 \times L/2$, $T =$ maximum transverse diameter, $L =$ maximum longitudinal diameter) [17]. In addition to clip number, clip-size was invented to eliminate the tumor size variance, which meant clips used for unit size. Complete resection was regarded as *en bloc* resection with negative margins laterally and basically via pathological evaluation [1, 11, 18]. Intraoperative complications included bleeding, mucosal injury, and subcutaneous emphysema, while fever (> 38 °C), retrosternal pain, pneumothorax, and delayed hemorrhage might appear after operation. Recurrent SMTs were defined for lesions arising 1 cm around the original site and more than 6 months after the procedure. Residual SMTs were defined as lesion reappearance around the original focus within 1 cm and less than 6 months after the procedure [19].

Statistical analysis

All data analyses were completed by IBM SPSS 19.0 software (IBM SPSS Inc., Chicago, IL, USA). Quantitative data of normal distribution were shown as mean ± standard deviation (SD) and assessed by independent t test. Quantitative data of skewed distribution were presented as median, interquartile range (IQR), and range compared by Mann–Whitney U test. Categorical data were expressed as number (n) and percentage (%) and analyzed by Chi-square test or Fisher's exact test. Statistical significance was defined as P value < 0.05.

Fig. 2 Submucosal tunneling endoscopic resection (STER) to remove an esophageal submucosal tumor (SMT) originating from the muscularis propria (MP) layer. **A** An esophageal SMT was detected by endoscopy. **B** Submucosal injection at 5 cm proximal to the tumor and a 2-cm longitudinal mucosal incision was made as the tunnel entry. **C** Tumor dissection and exposure. **D** Submucosal tunnel after tumor removal. **E** Closure of the tunnel entry with several clips. **F** Complete resection of the esophageal SMT
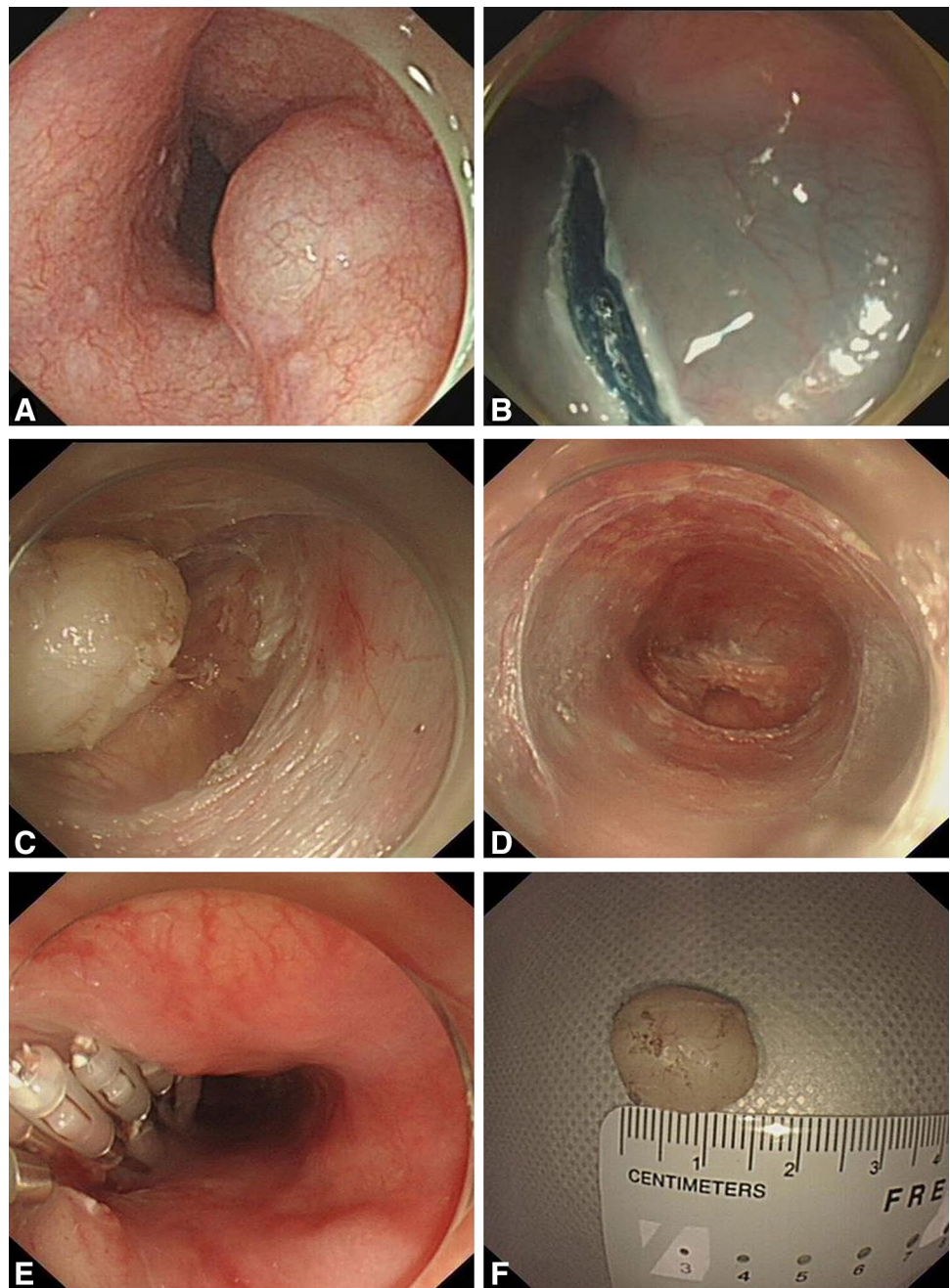

Results

Clinical characteristics

A total of 167 patients from January 2011 to December 2017 received STER and ESE, including 90 STER and 77 ESE. Their mean age was 52.2 years (20–78 years), with a male/female ratio of 102/65. The average tumor size was 19.1 mm (5–80 mm). For all tumors, none was detected at the upper esophagus, while 76 at the middle esophagus and 91 at the lower esophagus. Among them, 49 patients suffered from dysphagia, 59 complained about retrosternal pain, and 42 with upper abdominal pain when admitted. Other 17 cases were with no discomfort while esophageal SMTs were found accidentally by endoscopy. The postoperative histology confirmed 160 leiomyomas, 5 GISTs, 1 granular cell tumor, and 1 fibroma. 5 GISTs were classified to be very low risk and their sizes were 5, 10, 10, 15, and 20 mm, respectively.

There was no significant difference between the STER and ESE group for age, gender, tumor location, and pathological types ($P > 0.05$, Table 1). Tumors were larger in the STER group (STER vs ESE, 21.1 ± 12.7 mm vs 16.8 ± 15.4 mm, $P < 0.05$, Table 1).

Fig. 3 Endoscopic submucosal excavation (ESE) to remove an esophageal submucosal tumor (SMT) originating from the muscularis propria (MP) layer. **A** An esophageal SMT was detected by endoscopy. **B** Submucosal injection and a longitudinal incision was made. **C** Tumor dissection and exposure. **D** The defect after tumor removal. **E** Closure of the defect with several clips. **F** Complete resection of the esophageal SMT
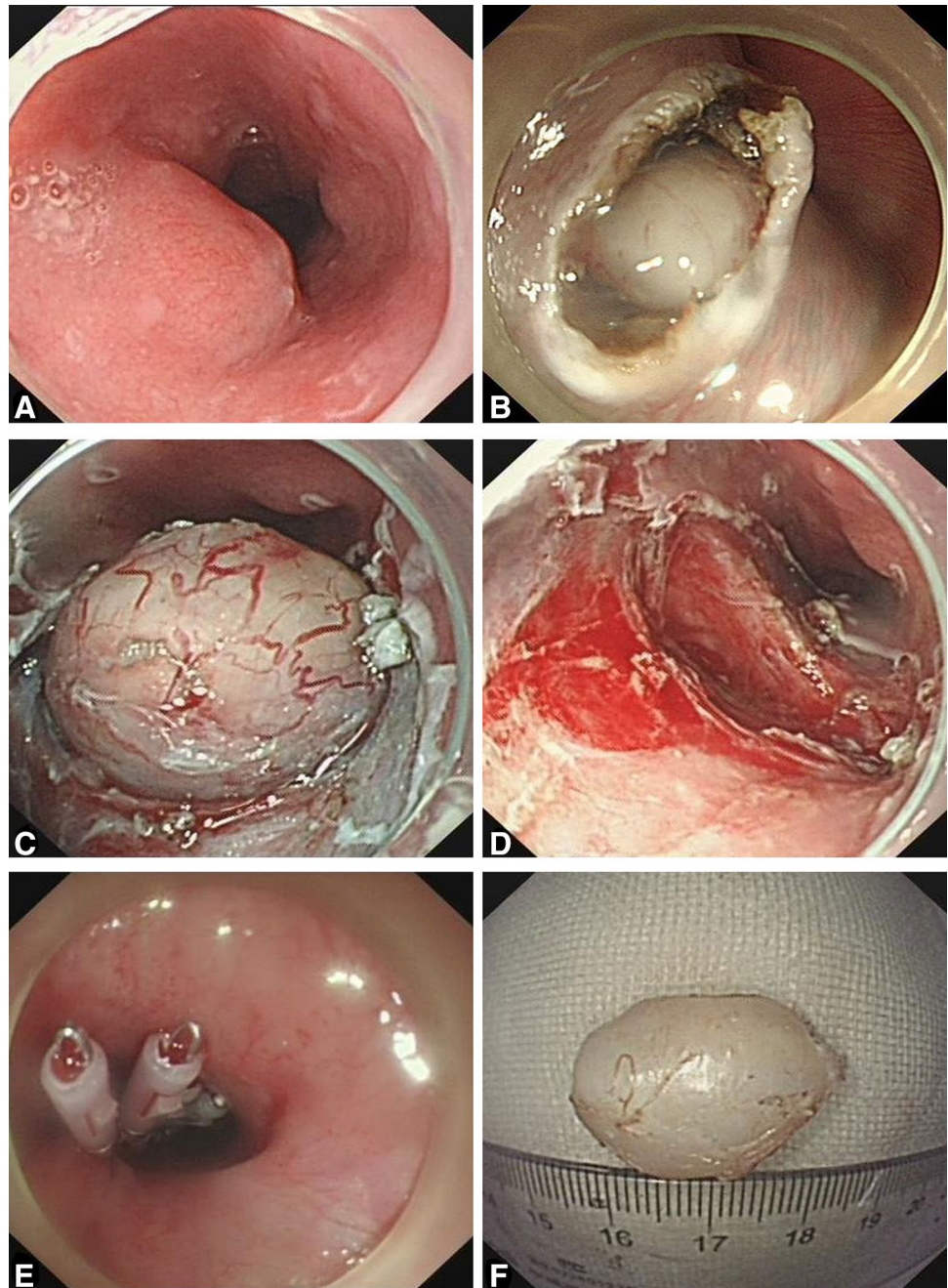
Therapeutic outcomes

STER and ESE were compared based on intraoperative and postoperative performance, including procedure time, operation speed, clip number, clip-size, complete resection rate, postoperative hospitalization, and complications (Table 2). Both STER and ESE achieved successful complete resection, with 90.0% (81/90) and 89.6% (69/77), respectively. Except for 17 lesions with piecemeal resection (Table 3), lateral and basal histology margins were histologically negative for other 150 specimens.

STER need longer operation time and more closure clips (STER vs ESE, 43 min vs 30 min and 7.0 vs 5.0, respectively, $P < 0.05$, Table 2) due to larger tumor size in this group. Readjusted by tumor size, STER performance was superior to ESE on operation speed (STER vs ESE, 3.90 mm^2/min vs 2.82 mm^2/min, $P < 0.05$, Table 2).

Intraoperative complications happened in 6 STER cases (6.7%), including 3 hemorrhage and 3 subcutaneous emphysema. Another 3 subcutaneous emphysema (3.9%) occurred during ESE operation. Hot biopsy forceps and APC were used for hemostasis. No patients needed blood transfusion.

Table 1 Clinical characteristics and follow-up results of STER and ESE

	STER (n = 90)	ESE (n = 77)	P value
Age, mean ± SD, year	52.0 ± 10.0	52.3 ± 10.0	0.823
Sex, male/female	59/31	43/34	0.199
Tumor location, n (%)			0.524
Middle	43 (47.8)	33 (42.9)	
Lower	47 (52.2)	44 (57.1)	
Tumor size, mean ± SD, mm	21.1 ± 12.7	16.8 ± 15.4	0.000
< 20, n (%)	47 (52.2)	55 (71.4)	
≥ 20, n (%)	43 (47.8)	22 (28.6)	
Pathological types, n			0.257
Leiomyoma	87	73	
GIST	1	4	
Granular cell tumor	1	0	
Fibroma	1	0	
Follow-up results			
Follow-up time, median (range), month	11.5 (1–77)	18 (1–80)	0.005
Residual, n (%)	2 (2.22)	1 (1.30)	1.000
Recurrence, n (%)	4 (4.44)	2 (2.60)	0.688

Table 2 Comparison of therapeutic outcomes between STER and ESE

	STER (n = 90)	ESE (n = 77)	P value
Operation time, median (IQR), min	43 (31.75–63.00)	30 (21.5–59.5)	0.005
Operation speed, median (IQR), mm^2/min	3.90 (2.04–5.89)	2.82 (1.26–4.49)	0.018
Number of clips, median (IQR), n	7 (6–9)	5 (3–7)	0.000
Clips-size, median (IQR), /mm	4.56 (3.00–5.75)	4.00 (2.80–6.00)	0.439
Complete resection, n (%)	81(90)	69 (89.6)	0.934
Postoperative hospital stay, median (IQR), day	5(4–6)	5 (4–7)	0.308
Intraoperative complications, n (%)	6 (6.7)	3 (3.9)	0.508
Subcutaneous emphysema, n	3	3	
Massive small blood vessel hemorrhage, n	3	0	
Postoperative complications, n (%)	12 (13.3)	12 (15.6)	0.679
Fever, n	1	3	
Retrosternal pain/discomfort, n	7	8	
Upper abdominal pain/discomfort, n	4	1	

For subcutaneous emphysema, nasogastric tube was applied and patients recovered 1–2 days afterwards. Both groups had 12 cases of postoperative complications (13.3% and 15.6% respectively), including fever, retrosternal pain/discomfort, and upper abdominal pain/discomfort (Table 2). No pneumothorax or pneumoperitoneum was detected via CT or X-ray. Their symptoms were relieved after intravenous PPIs and antibiotics.

Subgroup analysis

Tumor size and origin would affect operation difficulty and efficacy. Referred to NCCN guidelines, our cohorts were further classified by tumor size (< 20 mm and ≥ 20 mm) and the MP origin (upper and lower 1/2 of the MP layer determined by EUS) [6]. For larger tumors (≥ 20 mm), operation performance was similar for STER and ESE (P > 0.05, Table 4). STER led to the shorter hospitalization (STER vs ESE, 4.0d vs 7.0d, P < 0.05, Table 4) and less postoperative complications (STER vs ESE, 16.3% vs 45.5%, P < 0.05, Table 4). For smaller tumors (< 20 mm), STER achieved faster operation (STER vs ESE, 2.57 mm^2/min vs 1.83 mm^2/min, P < 0.05, Table 5). Regardless of tumors origin, STER and ESE had similar clinical performance (P > 0.05, Tables 6, 7), but STER resulted in rapid recovery and the shorter hospital stay for cases from the deep MP layer (STER vs ESE, 5.0d vs 7.0d, P < 0.05, Table 7).

Table 3 Patients' characteristics and operation evaluation with piecemeal resection

	Total	STER	ESE
Number of patients, n	17	9	8
Age, mean ± SD, year	52.8 ± 11.5	50.6 ± 9.9	55.3 ± 13.3
Sex, male/female	13/4	5/4	8/0
Tumor location, n			
Middle	5	2	3
Lower	12	7	5
Tumor size, mean ± SD, mm	34.6 ± 20.8	39.2 ± 20.5	29.4 ± 21.3
Pathological types, n			
Leiomyoma	15	9	6
GIST	2	0	2
Follow-up results			
Follow-up time, median (range), month	14 (3–53)	9 (3–36)	35 (11–53)
Residual, n	0	0	0
Recurrence, n	1	1	0
Operation time, median (IQR), min	85 (51.5–127.0)	91 (61.5–210.0)	64.5 (44.5–103.0)
Operation speed, median (IQR), mm^2/min	3.41 (1.80–9.04)	3.51 (1.80–11.09)	3.30 (1.63–1.88)
Number of clips, median (IQR), n	9.69 (6.50–12.50)	10.00 (7.00–14.00)	9.69 (4.25–9.69)
Clips-size, median (IQR), /mm	3.85 (1.88–4.67)	3.33 (1.71–4.67)	3.85 (2.46–4.71)
Postoperative hospital stay, median (IQR), day	6 (4.25–7.75)	7 (6–7.75)	5 (4–9)
Intraoperative complications, n, n	1	1	0
Subcutaneous emphysema, n	1	1	0
Massive small blood vessel hemorrhage, n	0	0	0
Postoperative complications, n	7	6	1
Fever, n	4	3	1
Retrosternal pain/discomfort, n	1	1	0
Upper abdominal pain/discomfort, n	2	2	0

Table 4 Subgroup comparison of tumor size ≥ 20 mm between STER and ESE

	STER	ESE	P value
Number of patients, n	43	22	
Age, mean ± SD, year	50.0 ± 9.8	51.2 ± 11.6	0.642
Sex, male/female	26/17	12/10	0.647
Tumor location, n (%)			0.929
Middle	21 (48.8)	11 (50.0)	
Lower	22 (51.2)	11 (50.0)	
Tumor size, mean ± SD, mm	30.1 ± 12.9	34.1 ± 19.5	0.568
Operation time, median (IQR), min	55 (40–91)	54 (39.5–82.8)	0.437
Operation speed, median (IQR), mm^2/min	5.81 (3.51–7.76)	6.20 (3.95–11.86)	0.292
Number of clips, median (IQR), n	8 (7–11)	7 (4–8)	0.089
Clips size, median (IQR), /mm	3.30 (2.49–4.00)	2.80 (1.20–3.64)	0.350
Complete resection, n (%)	36 (83.7)	17 (77.3)	0.521
Postoperative hospital stay, median (IQR), day	4 (4–6)	7 (5–9)	0.001
Intraoperative complications, n (%)	4 (9.3)	2 (9.1)	1.000
Postoperative complications, n (%)	7 (16.3)	10 (45.5)	0.011

Follow-up results

The median follow-up time was 11.5 months (range 1–77 months) and 18.0 months (range 1–80 months) for STER and ESE patients, respectively. Their follow-up results were presented in Figs. 4 and 5. No metastasis and mortality were reported. There were 2 cases of residual tumors and 4 recurrences after STER treatment, while 1 residual

Table 5 Subgroup comparison of tumor size < 20 mm between STER and ESE

	STER	ESE	*P* value
Number of patients, *n*	47	55	
Age, mean ± SD, year	53.9 ± 9.9	52.8 ± 9.0	0.567
Sex, male/female	33/14	31/24	0.149
Tumor location, *n* (%)			0.489
Middle	22 (46.8)	22 (40.0)	
Lower	25 (53.2)	33 (60.0)	
Tumor size, mean ± SD, mm	12.9 ± 3.6	9.9 ± 3.6	0.000
Operation time, median (IQR), min	33 (29–45)	27 (20–40)	0.046
Operation speed, median (IQR), mm^2/min	2.57 (1.47–3.93)	1.83 (1.18–3.14)	0.038
Number of clips, median (IQR), *n*	6 (5–8)	5 (3–6)	0.000
Clips size, median (IQR), /mm	5.00 (4.00–6.25)	5.00 (3.33–6.06)	0.767
Complete resection, *n* (%)	45 (95.7)	52 (94.5)	1.000
Postoperative hospital stay, median (IQR), day	5 (3–5)	5 (4–6.25)	0.042
Intraoperative complications, *n* (%)	2 (4.3)	1 (1.8)	0.594
Postoperative complications, *n* (%)	5 (10.6)	2 (3.6)	0.244

Table 6 Subgroup comparison of superficial MP origin between STER and ESE

	STER	ESE	*P* value
Number of patients, *n*	64	61	
Age, mean ± SD, year	53.0 ± 10.0	53.0 ± 10.9	0.722
Sex, male/female	43/21	32/29	0.103
Tumor location, *n* (%)			0.715
Middle	27 (42.2)	23 (39.2)	
Lower	37 (57.8)	38 (60.8)	
Tumor size, mean ± SD, mm	17.1 ± 9.6	12.9 ± 6.7	0.019
Operation Time, median (IQR), min	37 (29–51)	29 (22–53)	0.170
Operation speed, median (IQR), mm^2/min	3.14 (1.85–4.87)	1.87 (1.15–3.85)	0.059
Number of clips, median (IQR), *n*	6.50 (5.00–8.25)	5.00 (3.25–6.00)	0.002
Clips size, median (IQR), /mm	4.80 (3.33–6.00)	4.50 (2.83–5.50)	0.393
Complete resection, *n* (%)	60 (93.8)	55 (90.2)	0.524
Postoperative hospital stay, median (IQR), day	5 (4–6)	5 (4–5.75)	0.812
Intraoperative complications, *n* (%)	3 (4.7)	1 (1.6)	0.619
Postoperative complications, *n* (%)	8 (12.5)	6 (9.8)	0.779

and 2 recurrence in the ESE group during the follow-up (Table 1). Only one recurrence occurred at 14 months after STER among the 17 cases undergoing piecemeal resection. All residual and recurrent tumors were solitary around the original tumor location within 1 cm. Endoscopic surveillance was applied for these cases due to their previous benign histology.

Discussion

Esophageal submucosal tumors (SMTs) are commonly discovered during endoscopic surveillance. Esophageal leiomyomas are the most common benign SMTs (over 80%), usually originating from the smooth muscle layers in the lower two-thirds of the esophagus [3, 10, 20]. GISTs are the mesenchymal tumors with potential malignancy in the gastrointestinal tract, more often in the stomach [6, 21]. Most small esophageal SMTs (< 3 cm) are asymptomatic, while medical intervention should be considered for large cases with dysphagia or chest pain [3, 22]. The clinical guidelines about SMTs resection are still inconsistent nowadays. NCCN guidelines recommend that GISTs ≥ 2 cm in diameter should be resected, while all GISTs should be removed regardless of size from the European Society for Medical Oncology (ESMO) consensus [6, 23]. It is hard to discriminate SMTs cytology and malignancy via CT [7, 24–26]. Simple mucosal biopsy histology is also not recommended, which presents limited information for SMTs histologic diagnosis. Multiple biopsy might cause

Table 7 Subgroup comparison of deep MP origin between STER and ESE

	STER	ESE	P value
Number of patients, n	26	16	
Age, mean ± SD, year	48.3 ± 9.6	52.4 ± 10.9	0.154
Sex, male/female	16/10	11/5	0.199
Tumor location, n (%)			0.950
Middle	16 (61.5)	10 (62.5)	
Lower	10 (38.5)	6 (37.5)	
Tumor size, mean ± SD, mm	26.9 ± 12.2	25.3 ± 24.1	0.142
Operation time, median (IQR), min	60 (39–90.25)	62.5 (56.75–88)	0.517
Operation speed, median (IQR), mm^2/min	4.93 (2.67–7.74)	3.10 (1.40–4.63)	0.097
Number of clips, median (IQR), n	8 (6.00–10.00)	7 (5.50–12.50)	0.699
Clips size, median (IQR), /mm	3.41 (2.49–4.63)	6.00 (2.60–10.00)	0.166
Complete resection, n (%)	21 (80.8)	14 (87.5)	0.934
Postoperative hospital stay, median (IQR), day	5 (3–7)	7 (5–9)	0.019
Intraoperative complications, n (%)	3 (6.7)	2 (3.9)	1.000
Postoperative complications, n (%)	4 (15.4)	6 (37.5)	0.142

mucosal fibrosis and hamper further endoscopic resection [6, 27]. EUS-guided fine needle aspiration (EUS-FNA) is an available approach for SMTs cytologic and histologic diagnosis, about 70% to 90% accuracy [5]. EUS-guided Trucut biopsy (EUS-TCB) and EUS-guided fine needle biopsy (EUS-FNB) could acquire core tissues and provide more histologic information other than EUS-FNA. Tumors smaller than 2 cm or benign SMTs do not need operative treatment according to current studies [28]. During the follow-up practice, patients always complained about anxiety for tumor potential malignancy and medical cost of repeated endoscopic examination [10, 18, 29, 30]. In our study, clinical intervention was advised at the early stage according to patients' active aspiration for surgical therapy.

Open and thoracoscopic surgery are the traditional strategies for managing esophageal SMTs. With complete tumor enucleation, open surgery might bring some undesired problems, such as large trauma, slow recovery, complications, and poor life quality. Thoracoscopic surgery is further developed as the mini-invasive approach. With similar efficacy, thoracoscopic intervention results in shorter hospital stay, better lung recruitment, and reduced complications, but is incapable to locate intraluminal-growth tumors [10, 18, 31]. ESD has been successfully introduced to treat various gastrointestinal lesions, either in the mucosal or the submucosal layer. For SMTs from the deep MP layer, general ESD was less efficient with lower complete resection (64–75%) and higher perforation incidence(up to 20%) [1, 9]. More improved technologies are invented to treat these SMTs, such as endoscopic full-thickness resection (EFR), endoscopic submucosal excavation (ESE), and submucosal tunneling endoscopic resection (STER) [9, 32, 33]. EFR is rarely applicable for

esophageal SMTs probably owing to tight connection with surrounded organs.

ESE was created in 2008 for gastrointestinal SMTs with a high resection rate of 91.9%. The ESE procedure is similar to ESD. Instead of mucosal circumferential incision, the mucosa was separated longitudinally to reduce the mucosal defect and simplify ESE procedure [11, 34]. Liu et al. conducted ESE for 31 upper gastrointestinal SMTs originating from the MP layer in 2012, with the mean 76.8 min operation and 12.9% perforation. Complete resection was achieved for 30/31 cases while one was removed partially because of tight tissue adhesion with surrounding organs [34]. The succedent reports confirmed the ESE safety and efficacy for managing SMTs originating from the MP at the esophagogastric junction, cardia, and stomach, with 95.6–100% complete resection. Perforation and massive bleeding are still the main concerns during ESE procedure [2, 11, 12, 16]. Few ESE studies have reported about the management of esophageal SMTs from the MP layer possibly due to limited operation space and thinner esophageal wall.

Inspired by POEM, STER has served as a novel technique to treat upper gastrointestinal SMTs originating from the MP layer. The technique creates the operation space between the mucosal and MP layer via artificial tunnel, which could keep the mucosa intact and prevent perforations [13]. Its safety and feasibility were verified for cases in the esophagus, esophagogastric junction, cardia, and stomach [13–15, 18, 19, 30, 35, 36]. STER also achieved rapid recovery, reduced operation time, and shorten hospital stay [1, 7, 16, 25, 29, 37]. For gastric stromal tumors originating from the MP layer, STER needed less time and fewer clips for defect closure than EFR [29]. For tumors with different sizes, STER was reported to be better than ESE for ≥ 10 mm ones [37]. Compared with thoracoscopic enucleation, STER was
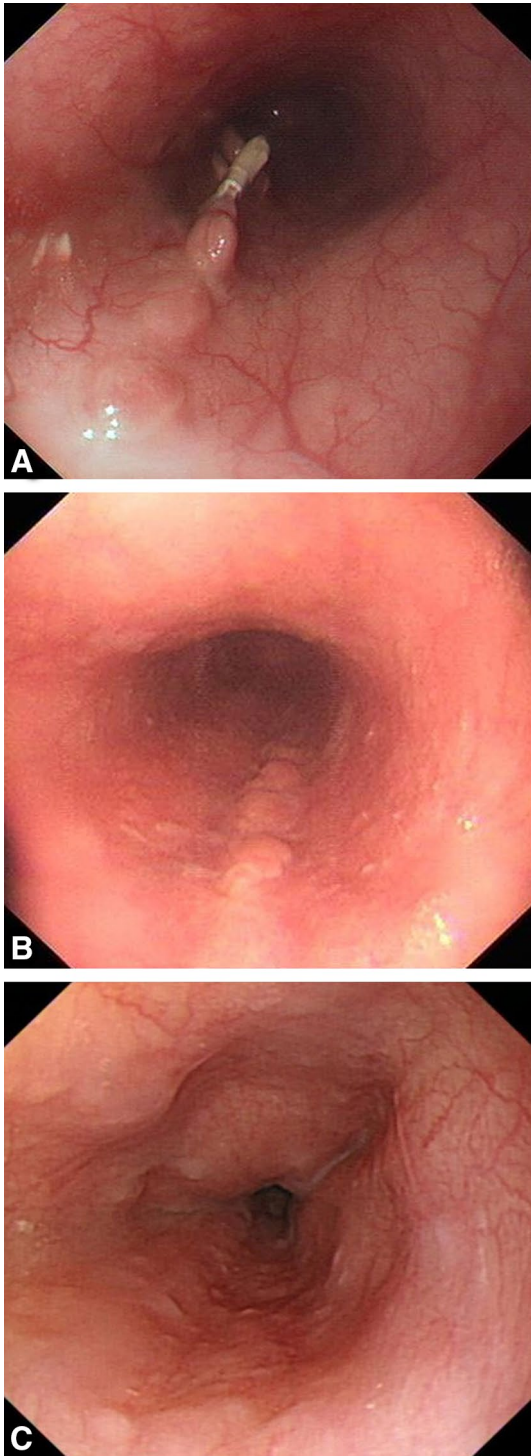
Fig. 4 Follow-up results of STER. **A** Endoscopic view of the esophagus 3 months after STER. Mucosal hyperplasia was seen at the operation site and a titanium clip was remained. **B** Endoscopic view of the esophagus 6 months after STER. Slight mucosal hyperplasia was visualized at the operation site. **C** Endoscopic view of the esophagus 12 months after STER. No obvious abnormalities were observed in the esophageal mucosa
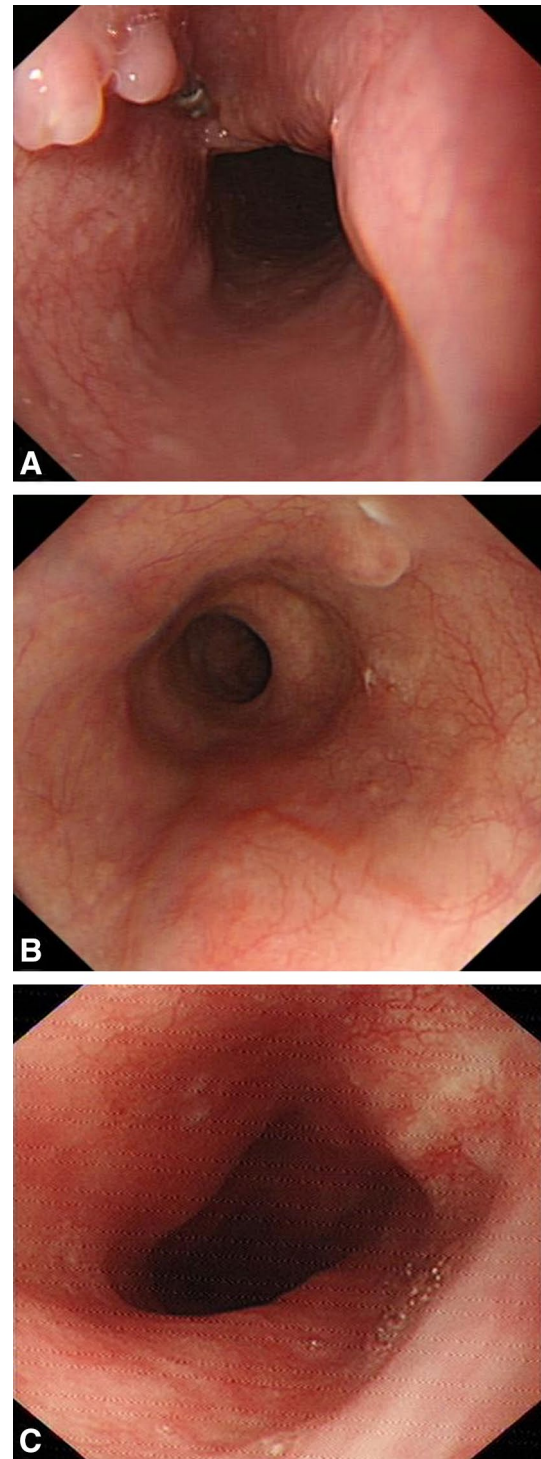

Fig. 5 Follow-up results of ESE. **A** Endoscopic view of the esophagus 3 months after ESE. Mucosal hyperplasia was seen at the operation site and a titanium clip was remained. **B** Endoscopic view of the esophagus 6 months after ESE. Slight mucosal hyperplasia and a white scar were discovered at the operation site. **C** Endoscopic view of the esophagus 12 months after ESE. A white scar was left over at the operation site

superior in the aspects of operation time, estimated blood loss during the procedure, and postoperative hospital stay [25]. Air leakage symptoms should be carefully adverted during STER management [38].

Our study also confirmed these findings for managing esophageal SMTs via STER or ESE. Seventeen asymptomatic patients chose tumor resection instead of regular observation after close conversation with doctors, with tumor size ranging from 5 mm to 20 mm. Complete resection rate was 90.0% and 89.6% for STER and ESE, respectively, which was lower than the previous reports due to some larger tumors. Owing to limited space in submucosal tunnel, ≥ 35 mm SMTs was regarded to be hard for STER removal [7, 39]. There were 17 patients undergoing piecemeal resection with the mean tumor size of (34.6 ± 20.8) mm. Their histopathology revealed 15 leiomyomas and 2 GISTs with very low risk. One patient suffered from subcutaneous emphysema during STER procedure, while postoperative complications occurred in another seven patients. Piecemeal resection attributed to larger tumor size and operational difficulties for endoscopy. In our study, there were 12 tumors larger than 35 mm in the STER group and the largest one was 80 mm × 25 mm. All these 12 tumors were successfully removed, with 5 of them undergoing piecemeal resection. After removal, no residual tumors were confirmed under the direct endoscopic view. Histopathology revealed tumor-free margins in each *en bloc* resected specimens and follow-up results showed no recurrence of the 5 patients undergoing piecemeal resection. With size bias adjustment, STER resection speed was actually faster. Via subgroup analysis for SMTs larger than 20 mm, STER intervention brought shorter hospital stay and less postoperative complications than ESE. Also, STER was also superior due to faster resection on SMTs smaller than 20 mm. Regardless of SMTs origin, STER and ESE had comparative therapeutic effects, while STER slightly helped patients' rapid recovery and shorter hospital stay. The main intraoperative complications were subcutaneous emphysema and massive small vessels bleeding in this study, with the low incidence of 6.7% (6/90) and 3.9% (3/77) in the STER and ESE group. No serious postoperative complication happened.

Both STER and ESE are available to manage esophageal SMTs originating from the MP layer. Few studies were reported to compare STER and ESE applicability. Our analysis on tumor size and origin provided further guidelines on clinical practice. Operation speed and clip size were innovatively proposed and compared in this study, which neglected the size bias and indicated STER's superiority. STER might be a primary approach as it could preserve the intact mucosa and reduce undesired complications. Our findings were limited due to the retrospective and single-center design. Also, two experienced endoscopists performing STER and ESE might cause some bias. The large cohort and randomized trials should be considered to verify our conclusion.

Compliance with ethical standards

Disclosures Drs. Yingtong Chen, Min Wang, Lili Zhao, He Chen, Li Liu, Xiang Wang, and Zhining Fan have no conflicts of interest or financial ties to disclose.

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