

Performance of endoscopic submucosal dissection and submucosal tunneling endoscopic resection for esophageal submucosal tumors: A multicenter retrospective cohort study

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Abstract

Background Esophageal submucosal tumors (ESTs) were typically managed through surveillance, but there is now a shift towards endoscopic resection. Endoscopic submucosal dissection (ESD) and submucosal tumor endoscopic resection (STER) appear to be safe and effective treatment options; however, evidence from non-East Asian centers is limited.

Methods This retrospective multicenter study included 97 patients from 15 centers across 9 countries who underwent endoscopic resection of ESTs via ESD or STER. Demographics, tumor characteristics, procedural details, adverse events and follow-up outcomes were recorded and analyzed.

Results Of the 97 patients, 48 underwent ESD and 49 STER. Most lesions were located in the lower esophagus and originated from the *muscularis propria*. *En bloc* resection was achieved in 95% of cases, with no significant difference between techniques (STER: 92% vs. ESD: 98%, $P=0.18$). The most common histologic diagnosis was leiomyoma (52%), followed by granular cell tumors (22%) and gastrointestinal stromal tumors (6%). Adverse events were infrequent: 9 cases of perforation were recorded, with only 4 being unintentional and all managed endoscopically. Follow-up data revealed only 1 case of local recurrence in a patient with a 50 mm lesion treated by STER. Hospital stay was longer after STER than ESD (3 vs. 2 days, $P<0.001$).

Conclusions ESD and STER are effective and safe for ESTs, with high *en bloc* resection rates, minimal adverse events and very low recurrence during short-term follow up. These findings support the broader adoption of advanced endoscopic resection, which is transforming the management of ESTs from surgical to endoscopic treatment.

Keywords Esophageal submucosal tumors, submucosal tunneling endoscopic resection, endoscopic submucosal dissection

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Introduction

Esophageal submucosal tumors (ESTs) are potentially malignant lesions that originate from the *muscularis mucosae*, submucosa, or *muscularis propria*. Most ESTs are detected incidentally during routine endoscopic examinations, although in some cases, they may be symptomatic [1]. ESTs appear to

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be relatively uncommon. A recent Korean retrospective study of approximately 65,000 screening gastroscopies reported an incidence of 0.37% [2]. Endoscopy provides useful information regarding the surface characteristics, color, mobility and firmness of ESTs. However, endoscopic ultrasound (EUS) offers superior diagnostic capability by delineating lesion size, layer of origin, vascularity, and relation to adjacent anatomic structures [3].

The management of ESTs depends on histopathology, malignancy risk, symptoms, size and location. Although most ESTs are benign and asymptomatic, resection may be needed in cases of diagnostic uncertainty, symptom burden or malignancy risk. Historically, thoracic surgical resection has been the standard treatment [4]. However, advances in therapeutic endoscopy have enabled minimally invasive endoscopic techniques, endoscopic submucosal dissection (ESD) and submucosal tunneling endoscopic resection (STER), to replace surgery in selected ESTs cases. While ESD was first developed for superficial premalignant or malignant lesions of the upper gastrointestinal tract, it is now also used for removing submucosal tumors [5,6]. Conversely, STER—introduced in 2012 in China—allows resection of submucosal or *muscularis propria* tumors while preserving mucosal integrity [7]. By

maintaining mucosal continuity, STER enables faster healing, with lower risks of perforation and postoperative bleeding than ESD [8].

Both ESD and STER offer important advantages over surgical approaches, including shorter hospital stays and lower complication rates [9]. Additionally, endoscopic resection enables definitive histological diagnosis, eases the psychological and financial burden of surveillance, and avoids the morbidity associated with invasive surgery. However, endoscopic resection of ESTs has its drawbacks, including challenges with larger lesions (>2 cm), limited availability of trained experts, and safety risks without adequate surgical backup or endoscopist proficiency. Successful outcomes require advanced training in ESD, peroral endoscopic myotomy (POEM), and reliable closure methods using various endoscopic tools.

Given the rarity of ESTs and the lack of universal endoscopic management guidelines, data from non-East Asian centers with ESD and POEM experience are needed. This study evaluated the efficacy and safety of ESD and STER for ESTs through a multicenter retrospective cohort analysis.

Patients and methods

Study design

This was a retrospective, multicenter study involving 15 centers across 9 countries (Egypt, France, Greece, India, Italy, the Netherlands, Portugal, Spain, and Ukraine). A prerequisite for participation was prior published experience in ESD and/or POEM. The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [10], and was approved by the Ethics Committee of Mediterraneo Hospital (Approval No.:2771). Patient anonymity was maintained, and all data were de-identified prior to analysis.

Patients

Inclusion criteria

Eligible patients were adults (≥ 18 years) with imaging-confirmed submucosal tumors of the esophagus who underwent endoscopic resection via ESD or STER. Tumor diagnosis was established by EUS, magnetic resonance imaging (MRI), or computed tomography (CT).

Exclusion criteria

Patients were excluded in cases of ulceration or suspected malignant transformation of the lesion, presence of perilesional lymph nodes, limited life expectancy, severe coagulation disorders or pregnancy.

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Conflict of Interest: None

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Data collection

Patients who met the inclusion criteria were identified retrospectively. Eligibility assessment was performed independently by 2 investigators (FF and GM). The following variables were extracted:

- (1) Demographics and clinical parameters: age, sex, American Society of Anesthesiologists (ASA) score [11], Charlson Comorbidity Index [12], procedural indication, and presenting symptoms.
- (2) Tumor characteristics: size, location, morphology (as observed on endoscopy, EUS, MRI and/or CT), and preoperative diagnostic impressions.
- (3) Procedure details: resection technique, duration, and procedural complexity.
- (4) Adverse events: including intraoperative and delayed bleeding, intentional or unintentional transmural defect, gas-related events (e.g., pneumoperitoneum, pneumomediastinum), and post-procedural strictures.
- (5) Histopathology: final diagnosis and specimen size.
- (6) Institutional data: hospital type (public vs. private, academic vs. non-academic), presence of on-site surgical services, and procedural location (endoscopy suite vs. operating room).
- (7) Follow up: recurrence status and duration of follow up. Postoperative follow up was not standardized across participating centers, and surveillance intervals varied according to local practice. Follow-up assessments were performed either endoscopically or by cross-sectional imaging. For the purposes of this study, recurrence was reported by investigators as occurring within the first 3 months or within 12 months after the index resection.

Data were collected using a standardized Excel spreadsheet with predefined variable fields, distributed to and completed by all participating centers.

Technique

All procedures were carried out under general anesthesia with the patient supine. A standard or therapeutic gastroscope

with transparent distal cap and CO₂ insufflation was used, along with tip-cutting, ceramic tip, and/or hook-type knives; coagulation forceps were applied for hemostasis. Procedures took place in endoscopy or operating rooms, depending on the center's infrastructure.

The choice between ESD and STER was based on preoperative imaging and lesion characteristics, particularly the relationship to the *muscularis propria* and the presence of an extraluminal component. STER was preferred for tumors with deep muscular involvement requiring intramucosal or full-thickness dissection. ESD was selected for submucosal lesions without significant muscular involvement. Mucosal entry sites and post-resection defects were closed with clips or suturing devices. Representative examples are shown in Fig. 1.

Definitions

- Muscle involvement during ESD was categorized as:
 1. Submucosal dissection: tumor removed without transecting muscular fibers (lesion confined to the submucosa).
 2. Intramucosal dissection: partial dissection of *muscularis propria* because of tumor attachment.
 3. Full-thickness dissection: intentional transmural dissection for complete resection of tumors extending beyond the *muscularis propria*.
- Gas-related complications: adverse events from gas escape into extraluminal spaces during or after the procedure, including subcutaneous emphysema, pneumomediastinum, pneumothorax and pneumoperitoneum.
- *En bloc* resection: removal of the entire lesion in a single, unfragmented piece.
- Intraoperative bleeding: defined as bleeding during the procedure that required endoscopic hemostasis.
- Perforation: defined as full-thickness dissection. Intentional perforation for oncologic completeness in *muscularis propria* tumors, followed by closure with a mucosal flap, clips or suturing, was not considered a complication.

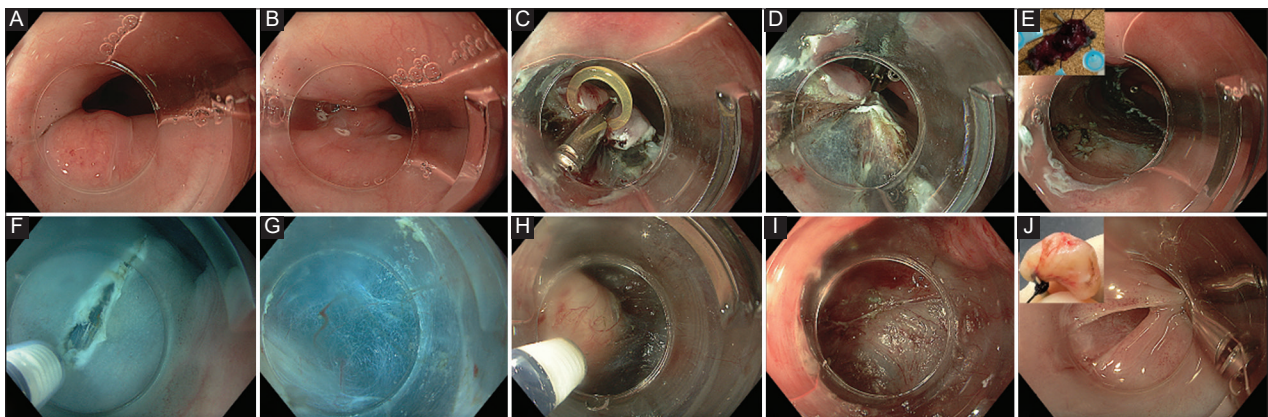


Figure 1 Steps of ESD: (A) Neuroendocrine tumor of the lower esophagus. (B) Demarcation. (C and D) Circumferential incision and clip and rubber countertraction. (E) *En bloc* resection. Steps of STER: (F) mucosal incision 4 cm proximally to a leiomyoma of the lower esophagus; (G) submucosal tunneling; (H) enucleation of the tumor; (I) inspection of the tunnel after resection; and (J) closure of the entrance with clips
ESD, endoscopic submucosal dissection; STER, submucosal tunneling endoscopic resection

- Postoperative bleeding: bleeding after the procedure, presenting as hematemesis, melena or hemoglobin drop, requiring intervention.
- Procedure time: the interval from the initial mucosal incision to the completion of defect closure.
- Stenosis: endoscopic luminal narrowing resulting in passage limitation.
- Recurrence: reappearance of submucosal or stromal tissue at the original resection site during follow-up evaluations.
- R0 resection: Not applied for leiomyomas and gastrointestinal tumors (GISTs), as enucleation precludes margin assessment; applicable only to purely submucosal tumors (e.g., neuroendocrine tumors [NETs], Abrikossoff), while for GISTs and leiomyomas only capsule integrity can be evaluated.

Outcomes

The primary outcome of the study was the feasibility, efficacy and safety of endoscopic resection of ESTs using ESD or STER, as reflected by *en bloc* resection rates and procedure-related adverse events. Secondary outcomes included evaluation and comparison of procedural parameters (procedure duration, location, closure techniques), tumor characteristics (size, layer of origin, histological subtype), hospital stay duration, recurrence rates during follow up; institutional characteristics (hospital type, surgical backup) were also examined. Additionally, the study examined factors associated with procedural choice, technical success and complication risk. All outcomes were predefined before data extraction and analysis.

Statistical analysis

Continuous variables were assessed for normality using visual inspection of histograms and the Shapiro-Wilk test. Normally distributed variables were expressed as mean $\pm$ standard deviation, whereas non-normally distributed variables were summarized as median and range. Categorical variables were reported as absolute numbers (n) and percentages. For group comparisons, Student's *t*-test or 1-way ANOVA was applied to continuous variables, depending on the number of groups. The chi-square (χ^2) test or Fisher's exact test (when expected frequencies were <5) was used for categorical variables. All statistical tests were 2-tailed, and a P-value <0.05 was considered statistically significant. Due to the very small number of non-*en bloc* resections and adverse events across subgroups, multivariate regression analysis was not feasible, and the statistical approach was therefore restricted to descriptive and univariate analyses. All analyses were performed using STATA software (version 17.0; StataCorp, College Station, TX, USA).

Results

A total of 97 patients (55% male) with a median age of 48 years were included in the study, recruited across 15 centers. The median ASA score was 1 (range: 1-4). The majority of patients were classified as ASA I (54.6%) or II (39.2%), together comprising 93.8% of the cohort. Charlson Comorbidity Index was available for 91 patients, with a median value of 2 (range: 0-6). Clinical and demographic characteristics are presented in Table 1. The median lesion size was 20 mm (range: 8-90 mm), and the tumors were located in the upper, middle and lower esophagus in 11%, 31% and 58% of cases, respectively. The median distance from the incisors was 31 cm. Mean tumor size differed significantly by esophageal segment, as illustrated in Fig. 2. Specifically, the mean lesion size was 24 mm in the upper, 22 mm in the middle, and 30 mm in the lower esophagus ($P=0.02$). Of the total 97 patients, 86 had undergone EUS prior to the procedure (88.6%). Based on EUS, most tumors originated from the *muscularis propria* (45%), followed by the submucosa (30%) and the *muscularis mucosa* (20%). Of the patients who underwent EUS, 40 (41.2%) patients additionally underwent preoperative EUS fine-needle aspiration (FNA) or fine-needle biopsy (FNB), which revealed the following diagnoses: GIST n=4 (10%), NET n=1 (2.5%), leiomyoma n=28 (70%), granular cell tumor n=2 (5%), lipoma n=1 (2.5%), and non diagnostic biopsy n=4 (10%).

The main indications for endoscopic resection were the presence of symptoms (58%), potential for malignancy (21%), and patient preference for resection over surveillance (21%). Among symptomatic lesions, dysphagia was reported in 82% of cases, bleeding in 7% and pain in 11%. The mean lesion size was significantly larger in symptomatic compared to asymptomatic patients (38.3 mm vs. 18.6 mm, $P<0.001$). Among the 6 patients classified as ASA III-IV, the median lesion size was 30 mm (range: 8-50). Three of these patients presented with dysphagia. Final histopathological examination revealed 2 NETs, 3 leiomyomas, and 1 granular cell tumor. The high ASA classification in this subgroup indicates that esophagectomy would be particularly challenging in such patients.

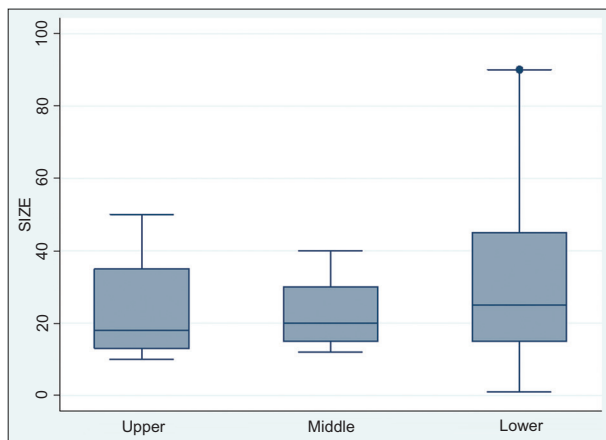
Lesion morphology, based on endoscopy, EUS or CT scan, was classified as purely endoluminal in 62 cases (64%), combined endoluminal and extraluminal in 22 cases (23%), and purely extraluminal in 10 cases (10%).

A total of 48 patients (49%) underwent ESD and 49 (51%) underwent STER, with a mean procedure time of 95 minutes. *En bloc* resection was achieved in 92 of 97 cases (95%). Histopathological examination of the resected tumors revealed leiomyomas in 52%, granular cell tumors in 22% and GISTs in 6%. Less common histologies included lipomas (4%), schwannomas (2%), and NETs (2%).

Table 1 Baseline characteristics of the study population (n = 97)

Variable, n (%) or median (range)	STER n=49	ESD n=48
Type of center	45 (92%)	36 (75%)
University	4 (8%)	12 (25%)
Non-university		
Male sex	26 (53%)	27 (56%)
Age, years	48 (20-80)	48 (19-72)
ASA score		
I	24 (49%)	29 (60%)
II	21 (43%)	17 (36%)
III	4 (8%)	1 (2%)
IV	0	1 (2%)
Indication		
Symptoms (dysphagia, pain, bleeding)	36 (73%)	21 (44%)
Potential for malignancy	6 (12%)	14 (29%)
Patient's wish and diagnosis purpose	7 (15%)	13 (27%)
Symptoms		
Dysphagia	30 (84%)	17 (81%)
Pain	3 (8%)	3 (14%)
Bleeding	3 (8%)	1 (5%)
Histology		
GIST	4 (10%)	2 (5%)
NET	1 (2%)	1 (2%)
Leiomyoma	36 (82%)	14 (34%)
Schwannoma	1 (2%)	1 (2%)
GCT	1 (2%)	20 (49%)
Lipoma	1 (2%)	3 (8%)

ESD, endoscopic submucosal dissection; STER, submucosal tunneling endoscopic resection; GIST, gastrointestinal stromal tumors; NET, neuroendocrine tumors; GCT, granular cell tumors

**Figure 2** Mean lesion size (mm) according to esophageal location

Procedure-related details and outcomes

Of the 97 patients, 48 underwent ESD (mean size 21 mm) and 49 lesions were resected using STER (mean size 33 mm; $P=0.018$). STER required longer procedures (116 vs. 72 min; $P=0.002$). The majority of resections were carried out in

endoscopy suites, with only 5 ESD and 8 STER cases performed in surgical theaters.

The lesion's layer of origin on preprocedural EUS guided the technique selection. STER was more common in lesions arising from deeper layers, particularly those originating from the *muscularis propria*. Regarding the depth of dissection in STER cases, intramuscular dissection was performed in 53% of patients, while full-thickness dissection was required in 27%. Mucosal defect closure was performed in all cases involving muscular layer dissection and in 28% of cases without muscle involvement. Among the cases where closure was performed, endoscopic clips or a combination of clips and loop were used in 80%. Procedural details by technique are shown in Table 2.

En bloc resection was achieved in 98% of ESD and 92% of STER cases, with no significant difference. Likewise, type of center, sex, age, ASA score, histology, lesion size and distance from incisors were not associated with *en bloc* resection.

Transmural dissection (perforation) occurred in 5 STER and 4 ESD cases, of which only 1 case in the STER group and 3 in the ESD group were considered unintentional. Closure methods included endoscopic clips, a combination of clips and loop, and, in the STER group, use of the mucosal flap at the end of the tunnel. No patient required surgical intervention for perforation due to failure of endoscopic closure methods, or admission to an intensive care unit (ICU) following the procedure. Notably, 80% of procedures were conducted in centers with esophageal surgeons capable of performing esophagectomies (87% in university hospitals), and in 45% of cases a standby surgeon had been pre-notified.

No cases of significant intraoperative bleeding, defined as bleeding lasting more than 5 minutes, were reported. Gas-related adverse events included subcutaneous emphysema in 3 STER cases, mild asymptomatic pneumothorax in 1 STER case, pneumomediastinum in 3 STER cases, and pneumoperitoneum in 2 ESD cases. These findings were detected on the postoperative CT esophagogram, and neither altered the clinical management nor resulted in any symptoms. One case of mild post-procedural stricture after ESD was recorded, occurring in a patient with a lower esophageal lesion required no dilation. Hospital stay was longer following STER (median 3 vs. 2 days; $P<0.001$).

Regarding recurrence, follow-up endoscopy between 3 and 12 months post-procedure was available for 63 patients. One case of local recurrence was identified at 3 months in a patient with a 50-mm lower esophageal leiomyoma, previously resected via STER, and was managed with endoscopic surveillance. No case required immediate additional treatment, such as surgery, chemotherapy or radiotherapy. Clinical outcomes by resection technique are summarized in Table 3.

Discussion

This multicenter retrospective cohort study evaluated ESD and STER for the treatment of ESTs in non-East Asian centers

Table 2 Procedure-related details by endoscopic technique (ESD vs. STER)

Variable, n (%)	STER n=49	ESD n=48	P-value
Size (mm), mean±SD	33±17	21±16	0.018
Location			0.680
Upper	5 (10%)	6 (13%)	
Middle	16 (33%)	14 (29%)	
Lower	28 (57%)	28 (58%)	
Distance from incisors (mm), mean±SD	31±7.3	32±6.4	0.573
EUS layer			
MM	3 (6%)	15 (39%)	<0.001
SM	5 (11%)	22 (58%)	
MP	40 (83%)	1 (3%)	
Morphology			0.006
Endoluminal	32 (66%)	30 (66%)	
Endo- and extraluminal	14 (29%)	8 (17%)	
Extraluminal	2 (5%)	8 (17%)	
Muscle dissection			<0.001
SM dissection	8 (17%)	40 (85%)	
MP dissection	26 (55%)	5 (11%)	
FTD	13 (28%)	2 (4%)	
Duration (min), mean±SD	116±88	72±85	0.002
Procedure location			0.491
Endoscopy room	41 (84%)	42 (89%)	
Surgical theater	8 (16%)	5 (11%)	

Note: Totals may be lower than the overall cohort due to missing data in some subgroups

ESD, endoscopic submucosal dissection; STER, submucosal tunneling endoscopic resection; SD, standard deviation; EUS, endoscopic ultrasound; MM, muscularis mucosa; SM, submucosa; MP, muscularis propria; FTD, full-thickness dissection

Table 3 Primary and secondary outcomes by endoscopic technique (ESD vs. STER)

Variable, n (%)	STER n=49	ESD n=48	P-value
<i>En bloc</i> resection	45 (92%)	47 (98%)	0.176
Perforation	42 (89%)	44 (92%)	
No	4 (9%)	1 (2%)	
Intentional	1 (2%)	3 (6%)	
Unintentional			
Gas adverse events			
Subcutaneous emphysema	3 (6%)	0	
Pneumothorax	1 (2%)	0	
Pneumomediastinum	3 (6%)	0	
Pneumoperitoneum	0	2 (4%)	
Stricture	0	1 (2%)	
Hospital stay (days), median (range)	3 (1-7)	2 (0-5)	<0.001
Local recurrence	1 (2%)	0	

ESD, endoscopic submucosal dissection; STER, submucosal tunneling endoscopic resection; SD, standard deviation

with expertise in third-space endoscopy. While most existing literature on ESD and STER originates from high-volume East Asian centers, especially China [13], this study is the first that draws from a diverse group of 15 institutions across 9 countries. This geographic diversity strengthens the external validity of our findings, and reflects the growing global adoption of advanced endoscopic resection techniques and third-space endoscopy.

Overall, the *en bloc* resection rate was 95%, with comparable outcomes for ESD (98%) and STER (92%), demonstrating that both techniques may achieve complete tumor removal. This aligns with prior data. A recent meta-analysis of 2161 lesions reported a pooled STER R0 resection rate of 91.4% (95% confidence interval 82.3-96.0; $I^2=81\%$; $P<0.001$) for ESTs [14]. ESD results are also consistent with recent studies reporting 93.3-100% *en bloc* resection rates for ESTs [9,15].

The choice of technique depended on tumor size and depth. ESD was mainly used for submucosal or *muscularis mucosae* tumors (mean size 21 mm), while STER was applied to larger tumors (mean size 33 mm) and/or those from the *muscularis propria*. This reflects their technical strengths. STER is preferred for *muscularis propria* tumors, as it allows *en bloc* resection via a submucosal tunnel, enabling full-thickness dissection and enucleation while preserving mucosal and esophageal lumen integrity [16,17].

Procedure time was longer for STER than ESD (116 vs. 72 min), probably because of the complexity of submucosal tunnel creation. Furthermore, the greater frequency of ESD utilization may be indicative of greater operator familiarity, as most endoscopists have broader ESD training, while STER is newer and requires prior third-space endoscopy expertise. However, this did not result in more unfavorable clinical outcomes.

Histological analysis of lesions identified leiomyomas as the most common type of tumor resected (52%), followed by granular cell tumors (22%) and GISTs (6%). This distribution aligns with previous epidemiological data indicating that most esophageal submucosal tumors are benign, with malignant potential present in a minority [1].

A recent meta-analysis of >2900 patients undergoing STER for upper gastrointestinal subepithelial tumors reported a recurrence rate of 2.3% [14]. In our cohort, there was only 1 recurrence, in a 50 mm lesion treated with STER, suggesting that tumor size may be a contributing factor to recurrence risk. However, a study of 133 large ESTs (≤ 3 cm: 69; 3-5 cm: 31; >5 cm: 33) reported no recurrence or metastasis, indicating STER is effective for lesions of all sizes [18].

The rate of adverse events was low in our study. Gas-related complications were more commonly associated with STER, consistently with prior reports [19,20]. These events are usually self-limiting, and related to the prolonged insufflation and deeper dissection involved in tunneling. Nine perforations were recorded, of which 5 were intentional,

performed as part of full-thickness resections. Only 4 unintentional perforations occurred (1 in STER and 3 in ESD). All complications were managed conservatively without the need for surgery or ICU admission, underscoring the safety of both techniques and their favorable outcome when recognized and effectively managed at an early stage. Our findings demonstrate the shift from what was previously considered a disastrous event towards an acceptable event that has no clinical consequences, provided that it is managed endoscopically with efficient closure. The largest study to date evaluating adverse events in patients undergoing STER for ESTs, involving 1701 cases, demonstrated an overall adverse event rate of 18.8%, with only 5.0% classified as major events requiring intervention [21].

One important aspect to note is the role of EUS in guiding both diagnosis and management. Our data showed that the layer of origin, as determined by EUS, significantly influenced the choice of procedure: 82% of tumors resected through STER originated from the *muscularis propria*, whereas only 2% of tumors in the ESD group originated from this layer. This highlights the critical role of EUS in pre-procedural planning, especially in distinguishing lesions that arise from deeper layers. The European Society of Gastrointestinal Endoscopy and the American Gastroenterological Association both recommend EUS as the most accurate method for diagnosing ESTs [22,23]. EUS is the best tool for characterizing various features of ESTs, including size, location, originating layer, echogenicity and shape. However, EUS alone cannot distinguish among all types of ESTs. Preoperative EUS-guided FNA/FNB enhances diagnostic accuracy by providing tissue for histopathological and immunohistochemical analysis, thereby improving the ability to distinguish benign from malignant subepithelial tumors [24]. Nonetheless, these procedures have limitations, including lower yield in small lesions (<2 cm), potential for non-diagnostic samples, delay in definitive therapy, and higher healthcare costs. Although rare, this procedure carries risks such as bleeding or perforation, which may complicate subsequent endoscopic resection; additionally, it may induce fibrosis that hinders mucosal separation from the tumor and makes STER more challenging [25]. Tissue sampling is recommended for ESTs suspected to be GISTs if they are ≥ 20 mm, have high-risk features, or require treatment [22]. In our study, EUS was performed in 86 of 97 cases (89%).

Notably, 21% of resections were patient-preferred, reflecting the desire for definitive diagnosis and avoidance of long-term surveillance. This highlights the psychological and practical burden of ongoing endoscopic monitoring, especially in cases of uncertain pathology. As most resected lesions were benign, careful selection is needed to avoid unnecessary procedures. Pre-resection EUS-FNA/FNB is particularly valuable for lesions larger >20 mm, where histological confirmation can better guide management. While patient

preference is important and should be respected, symptom-based indications are subjective, and are often influenced by malignancy-related anxiety. Thus, individualized decisions are essential to balance diagnostic certainty, patient expectations and the risk of overtreatment.

Our findings support the feasibility and safety of performing ESD and STER in standard endoscopy suites. The study included 15 hospitals, of which 10 were university and 5 non-university centers. In terms of sector distribution, 39 cases were managed in the private sector and 58 in the public sector. Notably, 86% of procedures were conducted in non-surgical endoscopy rooms, demonstrating that these techniques can be performed safely and effectively outside the operating theater by experienced teams with appropriate equipment, including in non-university hospitals.

Endoscopic techniques such as STER and ESD may transform the management of ESTs, particularly those arising from the *muscularis propria*. While these lesions were traditionally managed surgically, many can now be resected endoscopically with comparable efficacy. Comparison of STER with video-assisted thoracoscopic surgery has shown comparable resection success rates, but with shorter procedure times, less blood loss, faster recovery and lower costs [26-28].

However, some limitations of the study should be considered. First, as a retrospective analysis, it carries the risk of selection and recall bias. Patient selection and choice of ESD or STER were not randomized, relying on center practice and endoscopist discretion, introducing potential confounding. Variability in equipment, operator experience and perioperative protocols mean that, although all centers had documented expertise in third-space endoscopy, differences in technique and clinical management may have affected outcomes and comparability. Third, follow-up times ranged from 3-12 months, limiting conclusions about long-term recurrence and complications. Lastly, patient-reported outcomes (e.g., pain, functional impairment) were not systematically assessed—an important limitation for minimally invasive techniques.

In conclusion, this multicenter retrospective study shows that ESD and STER are safe and effective for esophageal submucosal tumors, with high *en bloc* resection rates, few complications and rare recurrence, even outside East Asia. STER was primarily used for larger, deeper lesions, while ESD was applied to more superficial lesions. These findings support the growing global adoption of advanced endoscopic techniques, which are progressively transforming the management of ESTs from surgical to minimally invasive endoscopic approaches. Nonetheless, as many resected lesions were small and benign, and follow up was limited, careful patient selection is required, and further studies are needed to clarify the role of these techniques as alternatives to surveillance and surgery.

Summary Box

What is already known:

- Esophageal submucosal tumors (ESTs) are increasingly managed with endoscopic resection techniques, such as endoscopic submucosal dissection (ESD) and submucosal tunneling endoscopic resection (STER), which have shown promising results in East Asian centers
- ESD allows *en bloc* resection of superficial lesions, but carries a higher risk of perforation for deeper tumors
- STER enables removal of tumors originating from the *muscularis propria* with preserved mucosal integrity and fewer complications
- Existing data are largely limited to high-volume tertiary centers in Japan and China, with scarce evidence from western or international settings

What the new findings are:

- Both techniques achieved high *en bloc* resection rates (95%) and low complication rates, in non-East Asian centers with advanced endoscopic expertise
- STER was primarily used for larger and deeper lesions, while ESD was reserved for more superficial tumors, reflecting their complementary roles
- The results support the feasibility and safety of advanced endoscopic resection in standard endoscopy units across diverse healthcare systems, including non academic hospitals

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