

Comparison between submucosal tunneling endoscopic resection and video-assisted thoracoscopic surgery for large esophageal leiomyoma originating from the muscularis propria layer

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Abstract

Background Submucosal tunneling endoscopic resection (STER) has been proved to be safe and effective for removal of esophageal leiomyoma originating from the muscularis propria (MP) layer. However, there are still technical challenges for tumors ≥ 35 mm due to the limited space of the submucosal tunnel. The aim of the study was to estimate the safety and efficacy of STER for large esophageal leiomyoma originating from the MP layer as well as compare its efficacy with video-assisted thoracoscopic surgery (VATS), which is a standard procedure for treating esophageal leiomyoma.

Methods We retrospectively collected the clinical data of the patients with esophageal leiomyoma of 35–55 mm who underwent STER or VATS at our hospital between January 2010 and December 2014. Epidemiological data (gender, age), tumor location, tumor size, procedure-related parameters, complications, length of stay and cost were compared between STER and VATS.

Results A total of 31 patients were enrolled, and 18 patients underwent STER and the other 13 received VATS. There was no significant difference between the two groups in gender, age, tumor location, tumor size, complications and rate of en bloc resection ($P > 0.05$). However, patients

in the STER groups had a shorter operation time, a less decrease in hemoglobin level, a shorter length of hospital stay and a decreased cost ($P < 0.05$). No recurrence was noted in the STER and VATS groups during a mean follow-up of 10.9 and 30.8 months, respectively.

Conclusions The treatment efficacy was comparable between the STER and VATS for esophageal leiomyoma of 35–55 mm. However, STER is superior to VATS in a shorter operation time, a less decrease in hemoglobin level, a shorter length of hospital stay and a decreased cost.

Keywords Esophageal leiomyoma · Gastrointestinal surgical procedures · Submucosal tunneling endoscopic resection · Video-assisted thoracoscopic surgery

Introduction

Esophageal leiomyoma is one of the most common submucosal tumors (SMTs) and is usually benign and asymptomatic, but it should be resected if the tumor is too large or symptomatic [1]. Current methods to remove a leiomyoma include surgery and endoscopic resection [2]. Surgery via thoracoscopic approach is usually recommended because it has a shorter hospital stay and less invasive compared with thoracotomy [3]. Although endoscopic resection such as endoscopic submucosal dissection (ESD), endoscopic submucosal excavation (ESE) and endoscopic full-thickness resection (EFR) has been regarded as minimally invasive resection methods for leiomyoma [4, 5], they can be unsatisfactory sometimes due to incomplete resection or risk of perforation during procedure.

STER, also called submucosal endoscopic tumor resection (SET) or tunneling endoscopic muscularis

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dissection (tEMD), has emerged as a new technique for treating esophageal leiomyoma and shown exciting results [6–13]. This new endoscopic technique has advantages over ESD in terms of maintaining the integrity of the digestive tract mucosa, promoting rapid wound healing and reducing the operating time without any compromise in success rate or increase in complications [11]. For SMTs >10 mm, STER is a preferable choice in terms of preventing air leakage symptoms compared with ESE [12]. However, due to the limited space of the submucosal tunnel, most researchers recommended a maximum resectable lesion size of 35 mm [7–9]. What is more, little is known about the comparison between STER and surgical methods. We report our preliminary experience of STER for esophageal leiomyoma of 35–55 mm as well as compare its efficacy with video-assisted thoracoscopic surgery (VATS) in this study.

Patients and methods

Patients

This is a single center, retrospective study conducted in China. The study was approved by the ethics committee of the Second Xiangya Hospital of Central South University. The inclusion criteria for enrollment in the study were as follows: (a) The presence of an esophageal SMT originating from the MP layer confirmed by computerized tomography (CT) and EUS (UM-2R, 12 MHz; UM-3R, 20 MHz; Olympus, Tokyo, Japan), and diagnosed of leiomyoma histologically; (b) the diameter of the leiomyoma was 35–55 mm; (c) a Zubrod–ECOG performance status 0 or 1; and (d) patients consent to undergo an STER or VATS procedure at our hospital. Informed consent was obtained from all patients before the procedure was performed. All patients were informed of possible adverse events (pneumothorax, subcutaneous emphysema, massive bleeding, incomplete resection, postoperative leaks, etc.) and other possible treatment options.

Epidemiological data (gender, age), tumor location, tumor size, procedure-related parameters (operative time, en bloc resection rate), complications, decrease in hemoglobin level, length of stay and cost were recorded and analyzed between the two methods. Tumors were classified according to their location along the esophagus, relative to the incisor teeth: Upper esophageal lesions were defined as those 15–23 cm from the incisors, middle esophageal lesions as those 24–32 cm from the incisors and lower esophageal lesions as those >32 cm from the incisors.

STER procedure

STER was performed under general anesthesia via tracheal intubation using a single-channel endoscopy (GIF-Q260 J; Olympus, Tokyo, Japan) with a transparent cap (D-201-11802, Olympus, Japan) attached to the front. Carbon dioxide insufflator (UCR; Olympus, Japan) was used. STER was performed the same as in our previous reports [14]. Briefly, the procedure was as follows: (1) A fluid cushion was made by submucosal injection (a mix solution of 100 ml saline + 2 ml indigo carmine + 1 ml epinephrine) at about 3–5 cm proximal to the SMT; (2) to create tunnel entry, a longitudinal mucosal incision over 2 cm was made using a dual knife or a hybrid knife and then a following submucosal dissection for at least 0.5 cm along both sides of the longitudinal incision; (3) a submucosal tunnel was made with a dual knife between the submucosal and muscular layers; (4) dissecting the tumor with a hybrid knife, a IT knife or a dual knife; and (5) close the mucosal entry with several clips after the tumor was removed. Figures 1, 2 and video 1 depict an example of STER.

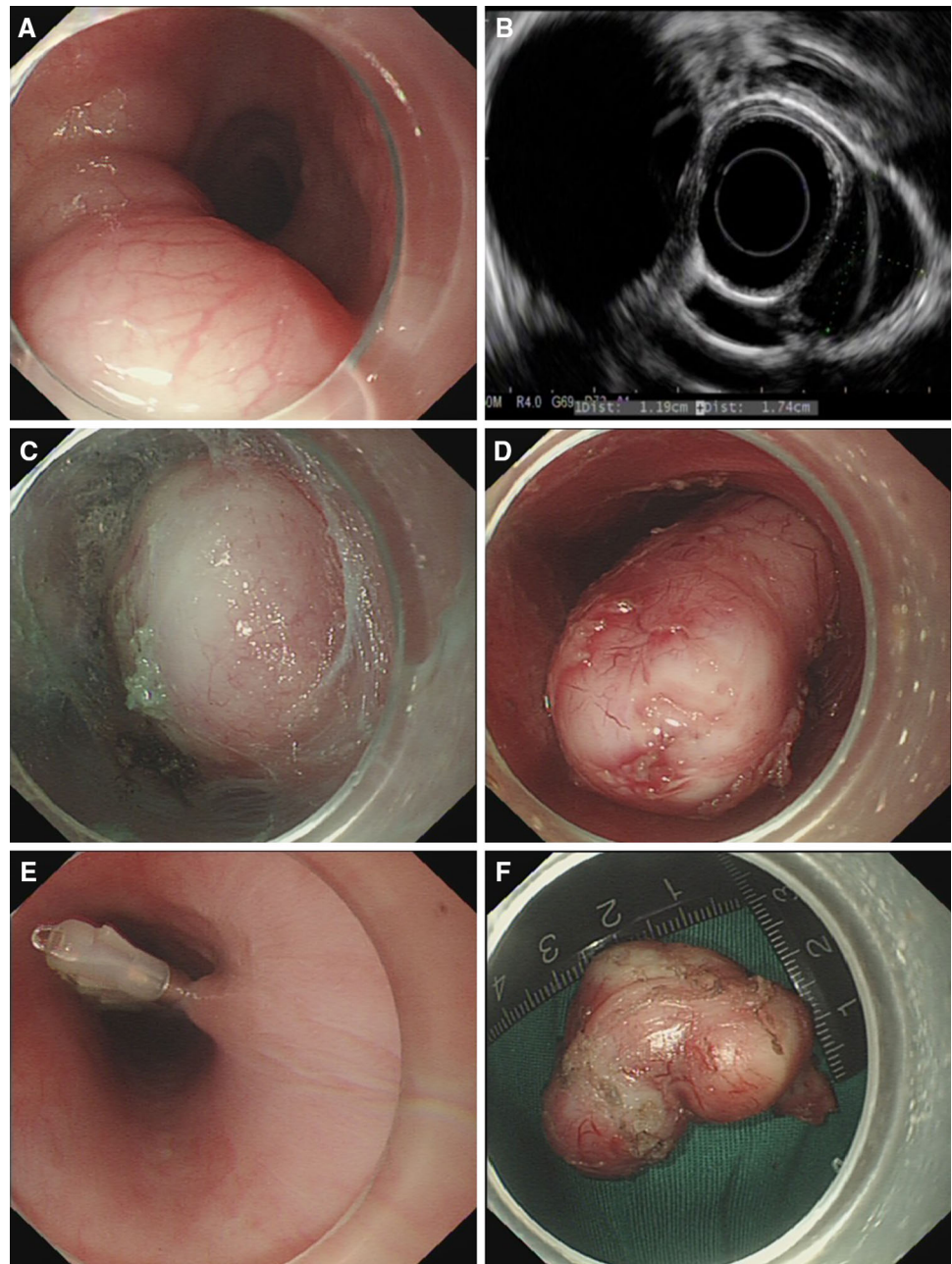
VATS procedure

The VATS procedure was performed under general anesthesia with double-lumen intubation. The patient is placed in a right or left lateral decubitus position at about a 15° frontal incline. A right VATS was performed for tumors located in the upper two-thirds of esophagus and a left VATS for those of the lower thirds of the esophagus. VATS was performed as reported [3] briefly: A 3- or 4-port placement was chosen based on the preference of the operator. After localization of the tumor, the mediastinal pleura was incised longitudinally, and a myotomy was performed over the tumor. The tumor was removed gently to prevent mucosal damage. The muscle layer is re-approximated, and a 28- or 32-Fr chest tube is placed through one of the ports for postoperative drainage.

Postoperative management

For patients received STER, they were kept NPO for 24 h, a liquid diet for 3 days and returning gradually to a normal diet within 2 weeks. At Day 2 post-operation, thoracoabdominal X-ray was performed to check for the occurrence of emphysema, pneumothorax, pneumoperitoneum, pleural effusion, etc. For patients received VATS, they were kept NPO for 48 to 72 h, a liquid diet for 3 days, a soft diet for 2 weeks and then a normal diet. An esophagography was performed at 5–7 days after surgery, and the chest tube was removed once we confirmed the mucosal integrity.

Fig. 1 Case illustration of STER. **a** Submucosal tumor located in the esophagus. **b** EUS showed a tumor originating from the muscularis propria layer. **c** Dissection was made along the margin of the tumor within the tunnel. **d** The entire exposed tumor after endoscopic dissection. **e** Tunnel entry was closed with several clips. **f** The specimen resected



Intravenous proton pump inhibitor (PPI) and antibiotics were used for at least 3 days for all patients.

Pathological evaluation

The specimens were fixed, embedded with paraffin and then sectioned. Hematoxylin and eosin and immunohistochemical staining (CD34, CD117, S-100, desmin, SMA, Ki67, Dog-1) were carried out. En bloc resection was defined as the intact fibrous capsule of the resected tumor and the absence of any remnant of tumor observed on endoscopy.

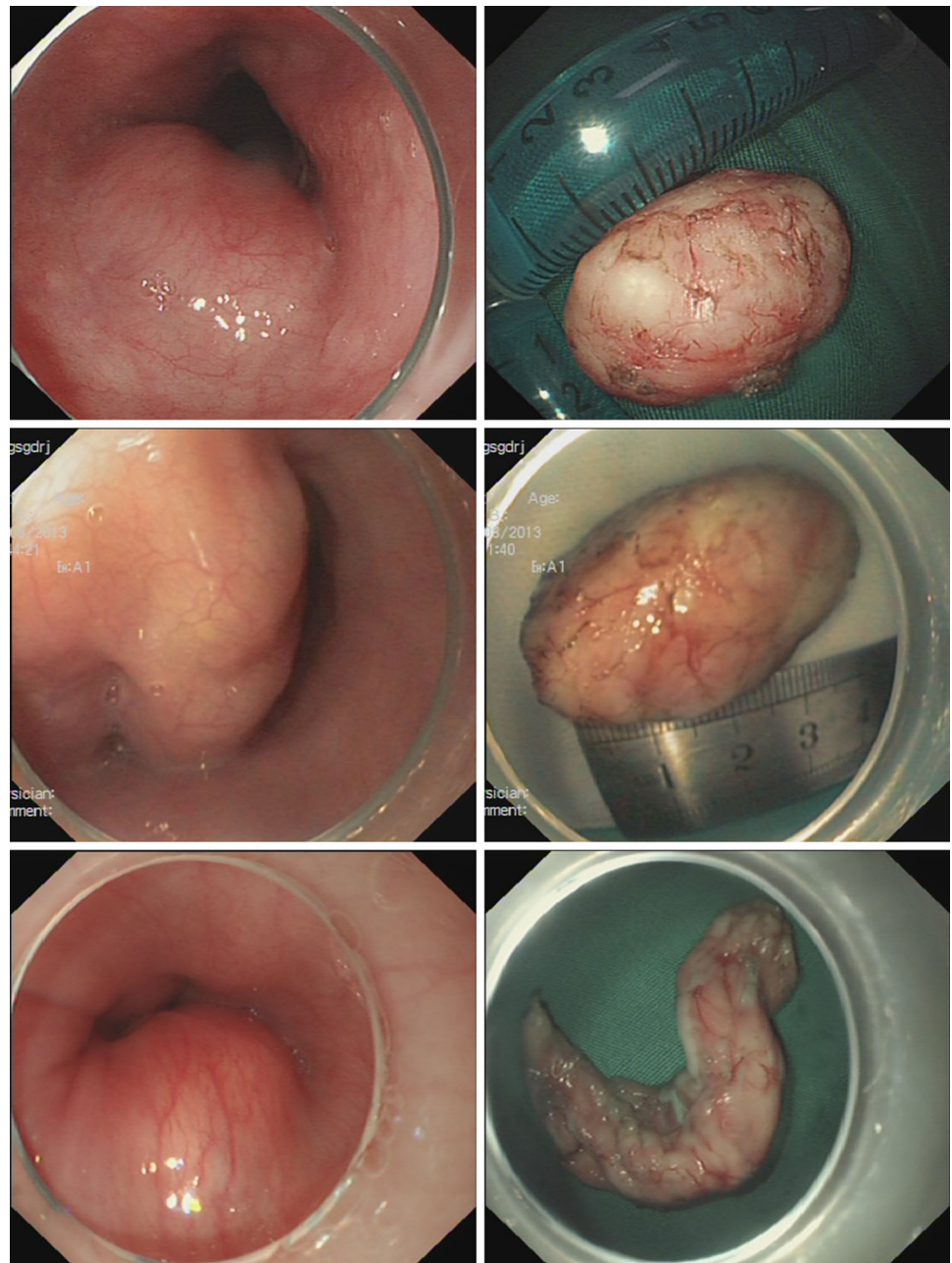
Follow-up

Surveillance endoscopy or barium swallow was performed at 1, 6 and 12 months and annually thereafter to observe healing of the wound and check for any residual tumor.

Statistical analysis

SPSS 17.0 software was applied for data analysis. Continuous variables were presented as mean \pm standard deviation and analyzed using Student's *t* test. And qualitative data were presented as frequencies and calculated

Fig. 2 Case illustration of STER for large esophageal leiomyoma



using the Chi-square test or Fisher's exact test. A two-tailed p value <0.05 was considered as statistically significant in all cases.

Results

Clinical characteristics and therapeutic outcome

A total of 31 patients were enrolled in this study from January 2010 to December 2014, of whom the mean age was 42.6 years (range 22–64 years), and the male/female

ratio was 21:10. Of the 31 SMTs, 4 were located in the upper esophagus, 16 in the middle esophagus and 11 in the lower esophagus. The mean tumor size was 40.6 mm (range 35–53 mm), and all of them were diagnosed of leiomyoma. Eighteen cases received STER and the other 13 cases received VATS. There was no significant difference between the two groups in gender, age, tumor location and tumor size ($P > 0.05$, Table 1). However, patients in the STER groups had a shorter operation time, a shorter length of hospital stay and a decreased cost ($P < 0.05$, Table 1). En bloc resection was achieved in 88.9 % (16/18) of the cases in the STER group and 100 % (13/13) in the

Table 1 Comparison of clinical features and treatment outcomes between STER and VATS

	STER (<i>n</i> = 18)	VATS (<i>n</i> = 13)	<i>P</i>
Gender (female/male)	5/13	5/8	0.530
Age, years	42.94 ± 8.56	42.15 ± 12.42	0.835
Tumor location, upper/middle/lower	2/10/6	2/6/5	0.864
Tumor size, mm	40.56 ± 5.17	40.69 ± 6.05	0.946
Operation time, min	75.00 ± 27.17	123.46 ± 50.18	0.002
Decrease in hemoglobin level, g/L	3.54 ± 1.81	9.33 ± 3.64	<0.001
Complications, %	16.7 (3/18)	15.4 (2/13)	1.000
En bloc resection, %	88.9 (16/18)	100 (13/13)	0.497
Length of stay, day	6.00 ± 1.19	8.85 ± 2.64	<0.001
Cost, USD	3379.4 ± 702.8	4614.7 ± 862.3	<0.001
Duration of follow-up, month	18.94 ± 8.19	38.77 ± 18.15	<0.001

VATS group, and there was no significance ($P > 0.05$). In case 2 and case 15 of STER, en bloc resection was failed because the tumor was too large ($53 \times 30 \times 18$ mm and $43 \times 25 \times 12$ mm, respectively), tumor fragmentation was needed for successful extraction of the two tumors. A total of 22 cases (13 in the STER group and 9 in the VATS group) had paired blood test before and within 48 h after surgery, and the decrease in hemoglobin level was greater in the VATS group ($P < 0.05$, Table 1).

Complications and follow-up

Three patients (16.7 %) in the STER group and 2 patients (15.4 %) in the VATS group had complications, and there was no significant difference ($P > 0.05$, Table 1). In the STER group, case 3 suffered from subcutaneous emphysema and it absorbed spontaneously within 3 days; case 7 suffered chest pain and it remitted within 3 days; case 14 encountered mucosa laceration while extracting the tumor and a metal stent was inserted. Repeated endoscopy and removal of the stent 7 days later revealed closure of the mucosal injury. In the VATS group, two cases suffered from mucosal injury intraoperatively and the mucosa were repaired with interrupted sutures. No esophageal leaks, delayed bleeding or other severe complications occurred during or after the procedure. No recurrence was noted during periodical follow-up.

Discussion

In the present study, we successfully managed 18 cases with esophageal leiomyoma of 35–55 mm by the STER technique without major complication. This indicates that STER is feasible, safe and effective for large esophageal leiomyoma originating from the MP layer. What is more, we demonstrated that STER takes advantages to VATS in a shorter operation time, a less decrease in hemoglobin level,

a shorter length of hospital stay and a decreased cost, although their efficacy was the same. As far as we know, this is the first study about comparison between STER and VATS.

However, concerning that some of the SMTs do have malignant potential, especially when they originate from the MP layer or with a large diameter [15], a comprehensive preoperative assessment is necessary for STER. In the present study, all the 18 patients underwent preoperative esophagogastrosocopy (EGD), EUS and CT. Because imagery, EGD and clinical examination suggested a benign tumor in all the 18 cases, we did not perform fine-needle aspiration in any of the cases [15–17]. In our experience, STER can be an alternative for large leiomyoma only when they adhere to the following characteristics: (a) EGD reveals an intact mucosal surface without ulceration or erosion at the site of tumor location; (b) EUS examination shows no high-risk features, such as irregular border, internal heterogeneity including anechoic area (i.e., necrosis) and echogenic loci (i.e., bleeding), heterogeneous enhancement and regional lymph node swelling; (c) no signs of metastasis are noted during a CT examination; and (d) patients consent to undergo a STER procedure and sign an informed consent. Those who are unwilling to do or intolerable to an open/laparoscopic surgery may have an attempt to STER as well.

The feasibility of STER for leiomyoma ≥ 35 mm was also reported by a few researchers. Kumbhari et al. [18] resected a giant esophageal leiomyoma ($60 \times 28 \times 22$ mm) by STER; fragmentation was needed for successful extraction of the lesion. Inoue et al. [6] failed to remove two large SMTs ($75 \times 42 \times 35$ mm and $60 \times 55 \times 45$ mm, respectively), and conversion to surgery was necessary. Gong et al. [10] reported a maximum diameter of 40 mm in their retrospective study; en bloc resection was failed. Wang et al. [11] reported a maximum diameter of 45 mm in their retrospective study. Tan et al. [19] reported a case of 52-mm esophageal leiomyoma en bloc resected

by STER. In the present study, the mean size of the lesion was 40.6 mm (range 35–53 mm), and en bloc resection was achieved in 16 of the 18 cases, and no recurrence was noted during periodical follow-up. In our opinion, there are several points that may facilitate an en bloc resection: (a) General anesthesia via tracheal intubation with muscle relaxants are recommended, as it can suppress the contraction of muscle and reduce the resistance of the upper esophagus, which may be helpful for removal of large SMTs through the narrow upper esophagus and esophagopharyngeal junction. (b) The tunnel orifice should be at least 2 cm and increased to the size of the short dimension of the tumor, after mucosal incision; a following submucosal dissection for at least 0.5 cm along both sides of the longitudinal incision is recommended to provide an ample submucosal space for tumor extraction as well as gas diffusion [20]. (c) We recommend a minimum tunnel width of 3 cm. The width of tunnel should expand according to the diameter of SMTs, which facilitates submucosal dissection and gas diffusion. (d) The tumor should be exposed clearly. The tunnel should extend at least 2 cm beyond the tumor, to ensure a satisfactory endoscopic view of the SMT and enough working space for resection. (e) Complete resection without interruption of the tumor capsule is recommended. For a SMT originates from deep MP layer or has a tight connection with the underlying MP or serosal layer, a full-thickness resection including the lesion, its underlying MP and serosa is generally performed. (f) After removal of SMTs, the wound surface should be washed repeatedly to reduce the chance of residual tumor cells. (g) While removing the tumor, the tumor is grasped in a fashion as to have its long dimension parallel to the long axis of the esophagus and its short dimension transversely and extract it from the tunnel through the tunnel orifice and the UES in a straightforward way as possible as we could. (h) If preoperative imagery, EGD and clinical examination suggested a benign tumor, we can use a snare after completion of the resection to cut the tumor in 2 or more pieces (while in the tunnel) so that it could then be easily extracted from the tunnel. (i) Another approach is to create a second “window” either in the area of tumor or by a distal mucosal incision to may facilitate en bloc extraction for large leiomyoma [21, 22].

Limitations of the present study include its retrospective design and relative small sample, thus warranting a prospective, large and randomized study. In conclusion, this preliminary study has shown that the STER technique is feasible and appears to be safe and effective for esophageal leiomyoma of 35–55 mm. The treatment efficacy was comparable between the STER and VATS for esophageal leiomyoma of 35–55 mm. However, STER is superior to VATS in a shorter operation time, a less

decrease in hemoglobin level, a shorter length of hospital stay and a decreased cost.

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Compliance with ethical standards

Disclosures Deliang Liu, Yuyong Tan, Liang Lv, Tianying Duan, Junfeng Zhou, Yao Tang and Dongzi Peng declare no conflict of interests for this article.

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