

Endoscopic submucosal tunnel dissection for large superficial esophageal squamous cell neoplasms

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Abstract

Endoscopic submucosal dissection (ESD) is a well-established treatment for superficial esophageal squamous cell neoplasms (SESCNs) with no risk of lymphatic metastasis. However, for large SESCns, especially when exceeding two-thirds of the esophageal circumference, conventional ESD is time-consuming and has an increased risk of adverse events. Based on the submucosal tunnel conception, endoscopic submucosal tunnel dissection (ESTD) was first introduced by us to remove large SESCns, with excellent results. Studies from different centers also reported favorable results. Compared with conventional ESD, ESTD has a more rapid dissection speed and R0 resection rate. Currently in China, ESTD for large SESCns is an important part of the digestive endoscopic tunnel technique, as is peroral endoscopic myotomy for achalasia and submucosal tunnel endoscopic resection for submucosal tumors of the muscularis propria. However, not all patients with SESCns are candidates for ESTD, and postoperative esophageal strictures should also be taken into consideration, especially for lesions with a circumference greater than three-quarters. In this article, we describe our experience, review the literature of ESTD, and provide detailed information on indications, standard procedures, outcomes, and complications of ESTD.

Key words: Endoscopic submucosal tunnel dissection; Esophageal squamous cell neoplasms; Digestive endoscopic tunnel technique; Endoscopic submucosal dissection

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Core tip: The digestive endoscopic tunnel technique

(DETT) innovatively broke the traditional boundaries between medicine and surgery and has been a recent research hotspot. Based on the submucosal tunnel concept, endoscopic submucosal tunnel dissection (ESTD) was introduced by us to treat large superficial esophageal squamous cell neoplasms, with excellent results. Studies from different centers also achieved favorable results, and ESTD has become an important part of DETT in China. Therefore, we conducted a literature review and provided detailed information on indications, standard procedures, outcomes, and complications of ESTD.

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INTRODUCTION

Endoscopic submucosal dissection (ESD) is acknowledged as the standard treatment for superficial esophageal squamous cell neoplasms (SERCNs)^[1-3]. Compared with conventional endoscopic mucosal resection (EMR), ESD enables *en bloc* resection and precise pathological assessment, leading to a lower local recurrence rate^[4]. However, with respect to large SERCNs, some frustrating problems arise, especially for tumors with a circumference that exceeds two-thirds of the esophageal lumen. During submucosal injection, rapid diffusion of submucosal liquid cushion after circumferential incision made the lifting-effect unsatisfactory. The submucosal endoscopic view was also not clear because the resected mucosa shrank and blocked the confined lumen^[5,6]. Consequently, the ESD procedure is time consuming, has a high risk of adverse events, and requires highly skilled endoscopists. To overcome these problems, some endoscopic innovations were introduced, such as modified fishing-line traction system^[6], peroral traction-assisted technique^[7], clip-band technique^[8], and medical ring system^[9], but these were not suitable for extensive standardized application.

Early in 2009, Linghu *et al.*^[10,11] attempted to dissect a submucosal tunnel and successfully achieved *en bloc* removal of an 8 cm long circumferential SERCN. The results were presented as the "tunnel technique for circumferential esophageal lesions", at the 2009 Beijing Annual Meeting of Digestive Endoscopy. The innovative technique was termed endoscopic submucosal tunnel dissection (ESTD)^[5]. Although derived from ESD, ESTD with the submucosal tunnel concept changed the traditional procedures for ESD: marking-injection-circumferential incision-submucosal dissection became a new treatment strategy for superficial esophageal neoplasms.

The submucosal tunnel formed a bridge between medical treatment and surgery, which was a long-held ambition of endoscopists. Peroral endoscopic myotomy (POEM) for achalasia launched a new field in endoscopy of digestive endoscopic tunnel technique (DETT)^[12]. Inspired by POEM, submucosal tunnel endoscopic resection (STER) was developed for the treatment of submucosal tumors of the muscularis propria (MP)^[13,14]. Since we first reported our experience in ESTD^[5], an increasing number of endoscopists have focused on the new treatment strategy for SERCNs^[15-20]. Some believe that standardized ESTD has made esophageal ESD straightforward and less difficult, especially for Western endoscopists^[15]. Currently in China, ESTD has become an important part of DETT, together with POEM and STER^[10].

In this review, we describe the indications, procedures, outcomes, complications, advantages, and future perspectives of ESTD for SERCNs.

INDICATIONS

Generally, whether endoscopic resection is preferred for patients with SERCNs is determined by risk of lymph node metastasis and technical resectability^[21]. Postoperative quality of life also should be taken into consideration. According to 2012 Japan Esophageal Society (JES) guidelines for treatment of esophageal carcinoma^[22], lesions limited to the mucosal epithelium (m1) or the lamina propria mucosa (m2) have a low risk of lymph node and distant metastasis, and radical resection can be achieved endoscopically, with similar long-term survival to surgery. Therefore, these lesions are considered to be an absolute indication for endoscopic resection. As the risk of lymphatic metastasis increases to 10%-15%, endoscopic resection is relatively indicated for lesions invading the muscularis mucosae (m3) or submucosal layer < 200 μ m (sm1), although Western endoscopists remain cautious and conservative (Figure 1)^[1].

Technical resectability is often determined by circumferential extension of lesions, which is an important risk factor for postoperative stenosis^[23,24]. As a result of advances in endoscopic techniques, the 2012 JES guidelines removed the restriction of lesion circumference in the 2007 edition, by which endoscopic resection was only indicated for m1 or m2 lesions not exceeding two-thirds of the esophageal circumference (absolute indication)^[22,25]. We believe that it was the standardized ESTD that enabled lesion size no longer to be a barrier to endoscopic resection and significantly improved efficacy. Double-tunnel ESTD could further minimize operation duration for whole circumferential lesions^[20]. Despite that, patients with lesions larger than three-quarters of the circumference should be informed of the risk of esophageal stenosis and prophylactic measures should be taken^[23,24,26]. Lesions < 15 mm in diameter are not recommended for ESTD, although the technique is reported to be feasible^[15].

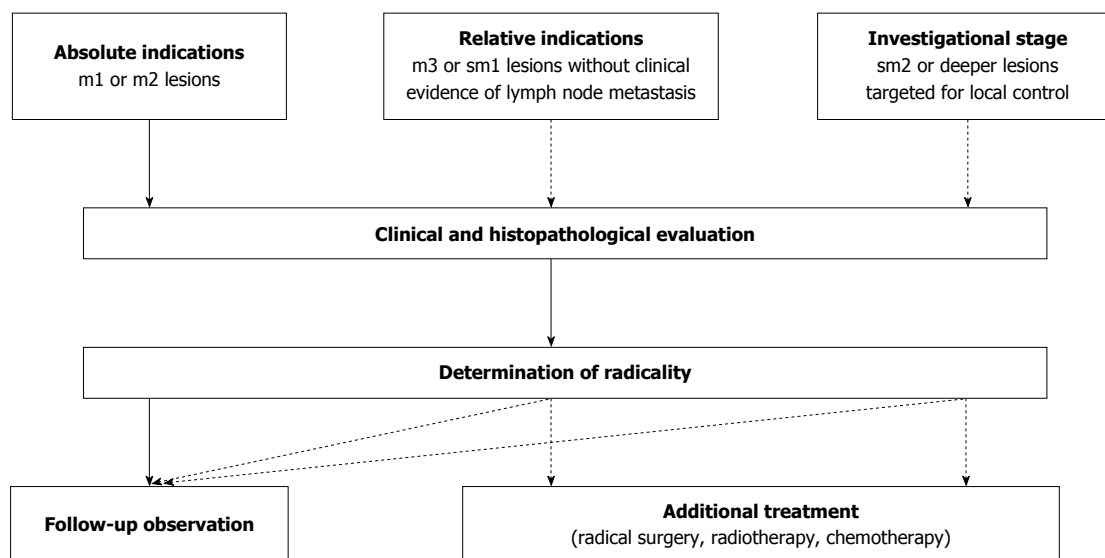


Figure 1 Indications for endoscopic resection by 2012 Japan Esophageal Society guidelines.

The reasons are as follows: (1) EMR is easy to perform and achieves a favorable *en bloc* resection rate; and (2) excess normal mucosa is resected by the creation of a submucosal tunnel and is followed by more trauma and longer recovery. Based on calculation and our experience, the diameter of the submucosal tunnel should be ≥ 10 mm, and the resected area should be ≥ 20 mm in diameter, or one-third of the circumference^[10,27].

Therefore, ESTD is indicated for: (1) lesions not invading deeper than sm1 and without clinical evidence of lymph node metastasis; and (2) lesions at least one-third of the esophageal circumference and ≥ 20 mm in diameter.

EQUIPMENT REQUIRED

A forward-viewing gastroscope (GIF 260J; Olympus, Tokyo, Japan) with a water-jet function is used, with a 9.8 mm outer diameter and a single 3.2 mm working channel. A transparent cap (D201-11804; Olympus) is fitted to the tip of the endoscope to provide a clear submucosal view. It also facilitates entering the tunnel and blunt dissection. Similar to ESD, an electro-surgical energy generator (ICC-200 or VIO 300D; Erbe, Tübingen, Germany) is connected to provide cutting or coagulation when needed. Various electro-surgical knives are available, including the dual knife, insulated-tip (IT) knife, the triangle-tip (TT) knife, and hook knife. The hybrid or flush knife, with a combined function of submucosal injection and electro-surgical knife, avoids frequent changing of tools, making the procedure simpler and more efficient. Selection of knives depends on the preference and specialty of the endoscopist. We prefer the dual knife for marking and mucosal incision and the IT knife for submucosal dissection and lateral resection.

A hemostatic forceps is used to handle active

bleeding or large exposed vessels when a hand-held knife is insufficient. CO₂ insufflation is strongly suggested because it decreases the risk of air-related adverse events, such as subcutaneous or mediastinal emphysema and even pneumothorax, and for its rapid absorption rate, around 150 times higher than air^[28-30].

ESTD PROCEDURES

Patients are placed in the left lateral position. General anesthesia with mechanical ventilation is required in view of lesion location and long operation time. Endotracheal intubation prevents aspiration, and positive pressure ventilation reduces the risk of air-related adverse events^[5,31]. ESTD procedures differ from ESD in the following ways (Figures 2 and 3)^[5].

Marking lesion margin

Magnifying narrow-band imaging and lugol staining are carried out to delineate the lesion. Dots are made around 5 mm outside the margin with argon plasma coagulation (APC) or electro-surgical knives. For circumferential lesions, circular dots reveal the anal and oral margins.

Submucosal injection and mucosal incision

In the anal-oral sequence, the anal side of the mucosa is first cut open transversely with a dual knife after the submucosal fluid cushion reaches an acceptable level. In China, the frequently used injection fluid is a mixture of 100 mL normal saline solution or glycerol-fructose injection, 1 mg epinephrine, and indigo carmine or methylene blue, for its ease of application and low cost. Highly viscous hyaluronic acid can maintain a thick fluid cushion for a long time and is widely used by Japanese endoscopists. Subsequently, the same procedure is performed for incision of the oral side of the mucosa along the marked dots.

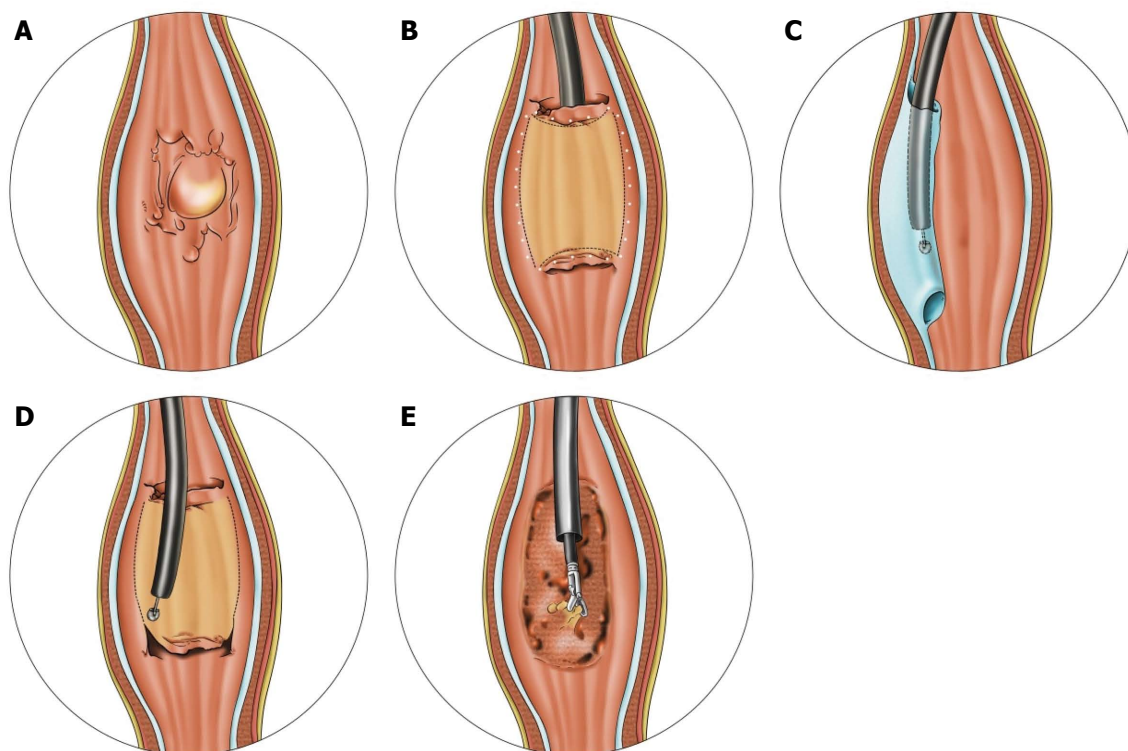


Figure 2 Schema of endoscopic submucosal tunnel dissection. A: Evaluating and delineating the neoplasm; B: After marking the lesion margin, mucosal incision was performed in the anal-oral sequence; C: A submucosal tunnel was created from the oral to anal side; D: Lateral resection with an insulated-tip knife for complete removal of the lesion; E: Preventive coagulation on artificial ulcer.

The anal side of the incision is a useful indicator of submucosal tunnel endpoint. More importantly, communication between the submucosal tunnel and esophageal lumen prevents gas accumulation and sharply rising tunnel pressure during dissection, avoids excessive normal mucosal separation, and reduces risk of air-related adverse events^[5,32].

Creation of submucosal tunnel

Submucosal dissection was used to create a tunnel from the oral side to the anal side. Repeated submucosal injection is necessary to separate the mucosa from the MP to maintain an adequate space. IT knife (IT 2 or IT nano) with a small ceramic ball is a safe and efficient tool, offering both lateral and backward dissection. Submucosal dissection should be conducted close to the MP, where rich vascular networks are absent, which differs from the upper submucosal layer and muscularis mucosae. According to basic principles of DETT, at least one side of the submucosal tunnel should be intact as the only barrier to the mediastinum. Therefore, the blade should be parallel to the MP as much as possible and catch the submucosal fibers to the center of tunnel for electric cut to avoid MP injury. During lateral dissection of the tunnel, mucosal dots are a reminder of the tunnel boundary, and constant withdrawal of the endoscope from the tunnel also ensures that the tunnel is a consistent size, to avoid postoperative stenosis caused

by excessive dissection.

Lateral resection

After completion of the tunnel, the endoscope is withdrawn, and the IT knife is used for lateral mucosal resection close to the markings from the anal to the oral side, until complete removal of the lesion. The resection is carried out simultaneously on the both sides of the tunnel. In this way, traction of the contralateral mucosa makes the procedure easier.

Management of artificial ulcer

After removal of the lesion, hemostatic forceps and APC are applied to coagulate the visible vessels on the surface of the artificial ulcer to prevent delayed bleeding. More attention should be given to vessels on the edge of the ulcer. Preventive clips should be placed when the MP layer is injured. Fibrin sealant or sucralfate can be used to protect the ulcer. For lesions more than three-quarters of the circumference, a fully covered esophageal metallic stent is conventionally placed to prevent postoperative stenosis in our endoscopy center.

As for double-tunnel ESTD, the difference is that circular incisions are successively performed at the anal and oral margin after marking. Then, the two opposite tunnels are dissected one after another from the oral to anal side. The procedures of double-tunnel ESTD are detailed in Figure 4.

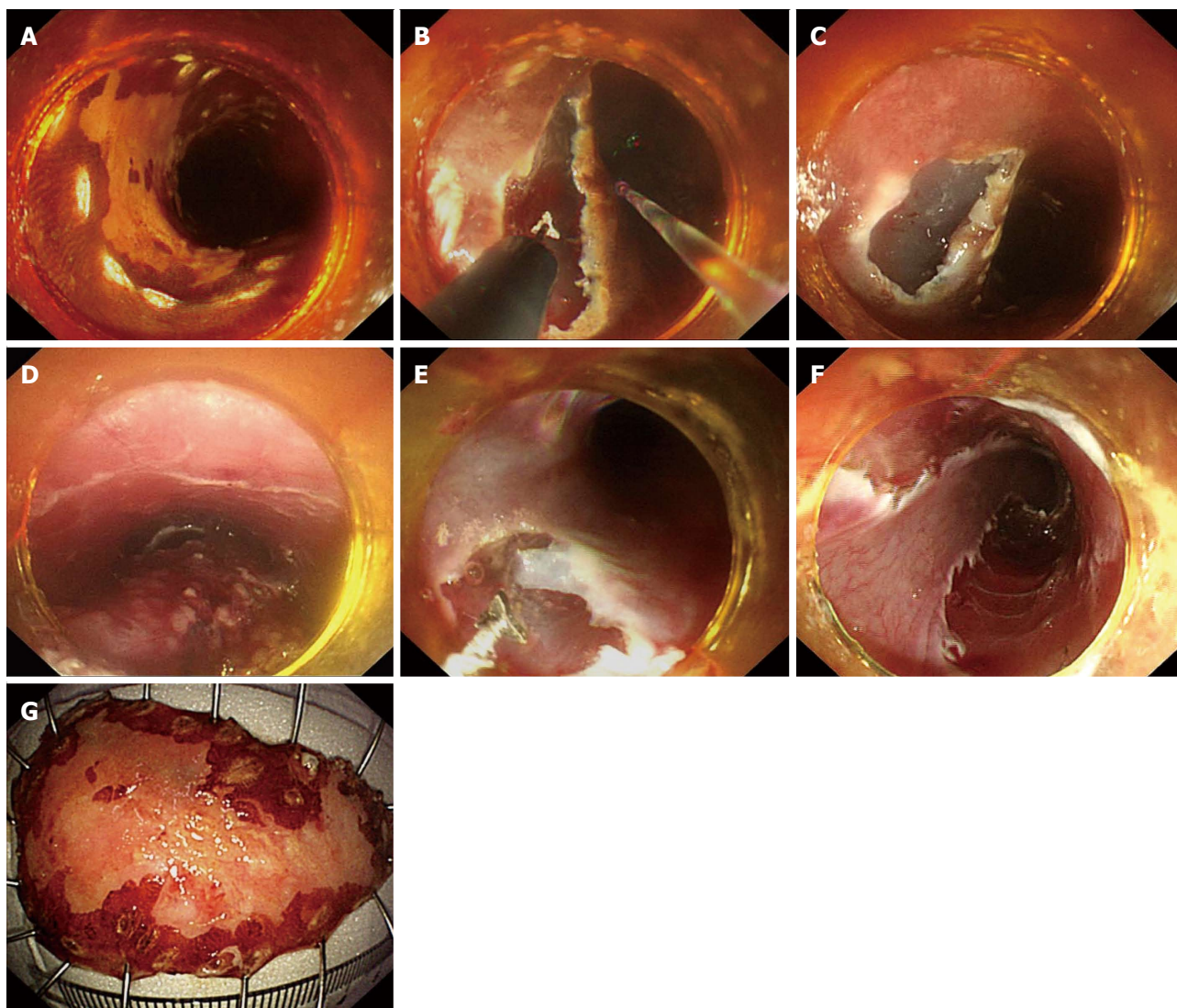


Figure 3 Endoscopic submucosal tunnel dissection with a single triangle-tip knife. A: Lugol staining to delineate the lesion, occupying almost half of the esophageal lumen. The margin was marked by argon plasma coagulation; B, C: Anal and oral incision was performed successively with a triangle-tip (TT) knife. Water jet helped entry into the submucosal tunnel; D: Submucosal tunnel was created from the oral to anal side; E: Lateral resection with a TT knife from the oral to anal side until reaching the anal incision; F: Complete *en bloc* resection was achieved in 52 min; G: The specimen, around 55 mm × 35 mm in size, was retrieved. Histopathological examination revealed a microinvasive squamous carcinoma limited in the lamina propria mucosa, free of lateral and vertical margin.

OUTCOMES AND COMPARATIVE RESULTS

In our first report of ESTD, five SESCNS with a mean diameter of 57 mm (range: 40-80 mm) were *en bloc* and R0 resected without any complications^[5]. Mean operation duration was 78.6 min (34-120 min) and no recurrence of SESCNS was observed with a mean follow-up of 7.4 mo (3-13 mo), preliminarily showing the feasibility and efficiency of ESTD. Several studies from different centers achieved similar favorable results. Xiong *et al.*^[19] reported that *en bloc* and R0 resection were achieved in all seven SESCNS treated with ESTD. In another retrospective study of 11 ESTD procedures by Pioche *et al.*^[17], *en bloc* and R0 resection rate were 100% and 81.8% (2/11), respectively. One patient (9.1%) experienced recurrence. Arantes

et al.^[15] treated 25 esophageal neoplasms from 23 patients, ranging from 10 to 60 mm, with ESTD. *En bloc* resection was successfully performed in 23 lesions, and R0 resection was achieved in 22 lesions. Two of 23 patients experienced local recurrence, and one patient underwent reoperation, with supplementary EMR and radiofrequency ablation.

We performed a systematic literature review of ESTD from Chinese databases (CBM, Wanfang Data, CMJD and CNKI) and English databases (PubMed, EMBase and Cochrane Library). The review identified a total of 90 lesions (88 patients) from nine studies, with a mean size of 37.8 mm (range: 10-80 mm) (Table 1). The pooled *en bloc*, R0 resection and local recurrence rates were 97.8% (92%-100%), 85.6% (81.8%-100%), and 3.3% (0%-9.1%), respectively, which were at least comparable to those for ESD. In

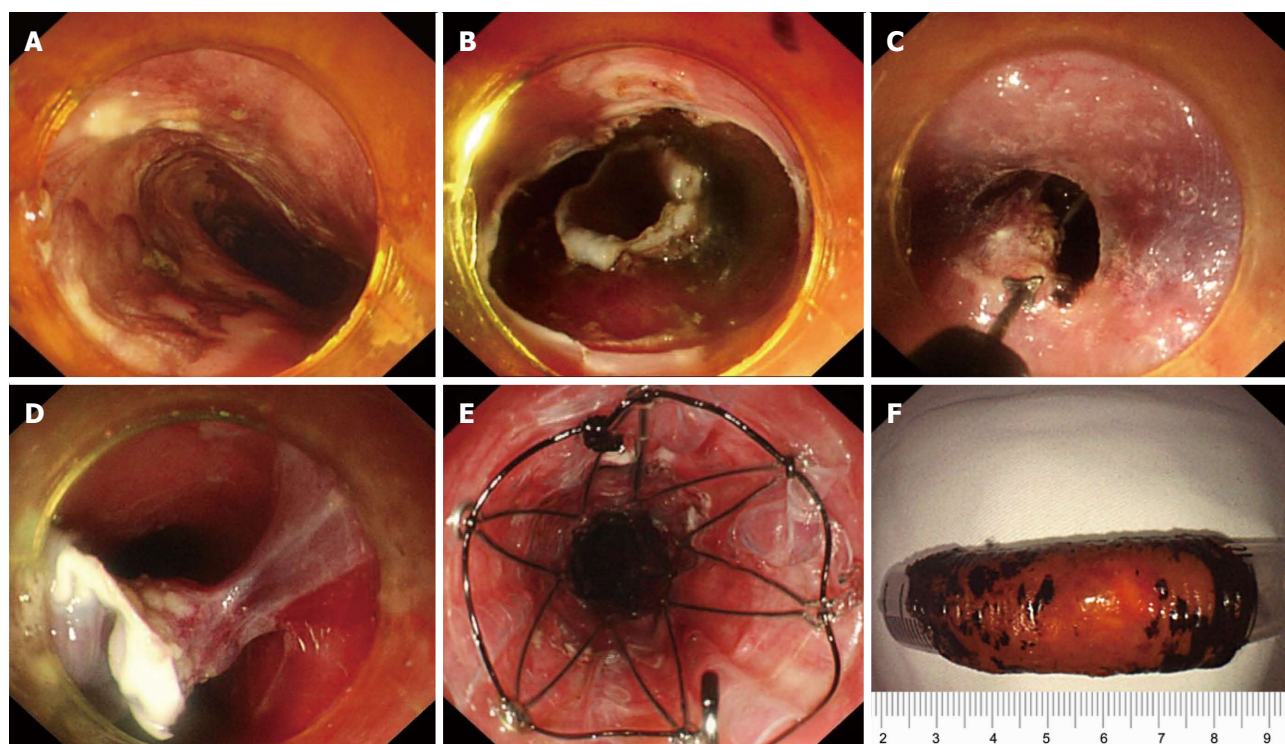


Figure 4 Double-tunnel endoscopic submucosal tunnel dissection for circumferential superficial esophageal neoplasms. A: An 8 cm circumferential superficial esophageal cancer was showed by iodine staining, at 28–36 cm from the incisors; B: Circular incisions were successively performed at the anal and oral margins after marking; C, D: Two submucosal tunnels were created opposite each other. Two tunnels nearly covered the whole esophageal lumen, and the borders were narrow enough to be resected easily; E: A 14 cm retrievable, fully-covered esophageal stent was placed to prevent postoperative stenosis. F: The lesion was resected circumferentially, about 60 mm in length. From Zhai *et al*^[20].

Table 1 Systematic literature review of endoscopic submucosal tunnel dissection for superficial esophageal squamous cell neoplasms *n* (%)

Ref.	Year	Lesions/cases	Mean size (mm)	Operation time (min)	<i>En bloc</i> resection	R0 resection	Complications	follow-up (mo)	Local recurrence
Linghu <i>et al</i> ^[5]	2011	11/11	48.2 (30-80)	78.6 (34-120)	100%	81.8%	Stenosis: 6 (54.5)	13.5 (3-30)	0%
Linghu <i>et al</i> ^[11]	2013								
Zhai <i>et al</i> ^[32]	2014								
Gao <i>et al</i> ^[18]	2012	17/17	24 (20-50)	128 (60-180)	100%	82.4%	Delayed bleeding: 1 (5.9)	NA	0%
Xiong <i>et al</i> ^[19]	2013	7/7	35.7 (20-40)	61 (37-110)	100%	100%	Immediate bleeding: 2 (28.6)	12	0%
Arantes <i>et al</i> ^[15]	2013	25/23	25 (10-60)	85 (60-210)	92%	84%	SE and ME: 2 (8)	21.4 (3-36)	2 (8)
							Perforation: 1 (4)		
Pioche <i>et al</i> ^[17]	2013	11/11	45 (27-80)	76 (35-150)	100%	81.8%	SE: 9.1%	NA	1 (9.1)
							Stenosis: 4 (36.4)		
Tan <i>et al</i> ^[65]	2014	1/1	50	NA	100%	100%	None	6	0%
Zhou <i>et al</i> ^[66]	2014	18/18	58 (45-74)	54.5 (32-85)	100%	100%	Immediate bleeding: 1 (5.6)	6	0%
							SE: 1 (5.6)		
							Stenosis: 3 (16.7)		
Total		90/88	37.8 (10-80)	83.3 (32-180)	88 (97.8)	77 (85.6)	Immediate bleeding: 4 (4.4)	NA	3 (3.3)
							Delay bleeding: 1 (1.1)		
							Perforation: 1 (1.1)		
							SE or ME: 3 (3.3)		
							Stenosis: 9 (10)		

SE: Subcutaneous emphysema; ME: Mediastinal emphysema.

our retrospective comparative study^[32], among 29 consecutive patients, 11 patients underwent ESTD and 18 ESD for lesions that were at least one-third the circumference and ≥ 20 mm in diameter. ESTD had a more rapid dissection speed, almost twice that of ESD (22.4 mm²/min vs 12.2 mm²/min). Curative resection

was more likely to be achieved with ESTD (81.8% vs 66.7%). These advantages of ESTD may be attributed to the following factors^[5,32]: (1) counter-traction of bilateral mucosae provides a clear submucosal vision for dissection; (2) the transparent cap and gas cushion created by CO₂ insufflation can play a role in blunt

dissection, accelerating the operation; (3) submucosal injection solution is retained longer because ESTD avoids conventional circumferential incision, and there is less need for repeated injection; and (4) because the dissection is deeper in the submucosa, close to the muscularis mucosae, and the mucosa together with most of the submucosa can be removed, making for more precise pathological assessment.

COMPLICATIONS

Bleeding and perforation are the common adverse events of ESTD, with a pooled incidence of 4.4% and 1.1%, respectively. These incidences do not differ significantly from those of ESD, which were reported as 0%-5.2% and 0%-6.9%, respectively^[26,33-37]. Submucosal dissection is performed in the deeper submucosa, where transversed vessel trunk prevails. After exposure of the vessel trunk, prophylactic coagulation with hemostatic forceps should be undertaken in soft mode. For minor oozing bleeding, an electrosurgical knife in coagulation mode is usually sufficient, while for massive active bleeding, identification of bleeding spots with a water jet is more advisable than blind coagulation with hemostatic forceps. Clips are reserved for the last resort because they may hinder the next dissection procedure. Unstopped hemorrhage is rare and is mostly caused by delayed bleeding in the first 24 h postoperatively. In 17 patients with ESTD^[18], one patient had delayed bleeding and was transferred to surgery after failed endoscopic hemostasis. Proton pump inhibitors are routinely administered, and emergency endoscopy should be performed once delayed bleeding is suspected during close surveillance.

Perforation during operation is usually < 10 mm, and endoscopic clips are the standard method for closing such perforations. Generally, multiple clips are required in a zipper fashion to ensure complete closure. Recently, a new over-the-scope clip has become clinically available and can successfully seal esophageal perforation up to 20 mm in size with high compression force^[38-42]. For larger perforations, fully-covered self-expandable metal stents (FCSEMs) are effective, although they have a potential risk of stent migration^[43]. For delayed perforation, early recognition determines treatment option and outcome. As a result of minor inflammation and content egression, delayed perforations within 12 h can be treated conservatively, including endoscopic closure with clips and percutaneous drainage. However, surgery is mandatory for patients with unstable hemodynamics, with perforations that are recognized after > 24 h, or who fail conservative treatment^[44].

Although one tries to avoid touching the MP during dissection, air-related adverse events frequently occur; partly due to increased air pressure in the submucosal tunnel and thin MP without compact serosa. In 25 ESTDs with room-air insufflation by Arantes *et*

al^[15], two patients experienced subcutaneous and mediastinal emphysema, while 11 patients reported by us were uneventful with CO₂ insufflation during ESTD^[32]. Consensus has been reached that CO₂ insufflation is strongly recommended in DETT^[5,10,14,31,45]. The pooled incidence is 4.4% (0%-9.1%), which is lower than that of POEM or STER. All the emphysema was minor and could be absorbed spontaneously without additional treatment.

Postoperative esophageal stricture is of most concern for large mucosal defects after ESTD because it reduces quality of life. Circumference extent and histological depth are reliable predictors of postoperative stricture^[23,24,46]. In a retrospective study of 84 esophageal ESDs by Ono *et al*^[34], the incidence of lesions less than half, less than three-quarters, and more than three-quarters of the circumference was 2% (1/49), 20% (5/25), and 90% (9/10), respectively. Shi *et al*^[24] also reported similar results in a review of 362 ESDs, in which lesions that were more than three-quarters of the circumference had a 93.3% (32/34) risk of stricture. Therefore, preventive intervention should be implemented for lesions that exceed three-quarters of the circumference or are less than three-quarters of the circumference but invade to a greater depth than m2^[24,32,47].

Endoscopic pneumatic dilation (EPD) is taken as the standard treatment for postoperative esophageal strictures^[48,49]. However, refractory strictures caused by large defects usually demand up to dozens of EPDs. This increases the risk of perforation as well as the treatment cost. In a study of 121 patients with 1337 EPD procedures for post-ESD stenosis^[50], the incidence of perforation was 4.1% (5/121) per patient and 0.4% (5/1337) per procedure. Patients with perforations required more sessions of EPD than those without perforations [37 times (6-57) vs 7 times (1-70)]. Takahashi *et al*^[51] also reported that seven patients developed perforation during 648 dilation procedures for post-EMR/ESD stricture, and multiple dilations and lower esophageal site were independent risk factors for perforation. Systemic administration or local endoscopic injection of steroid is effective, which not only lowers incidence of stricture, but also decreases extension of stricture and numbers of required endoscopic dilations^[52-56]. In a recent randomized controlled trial by Takahashi *et al*^[57], 32 patients with post-ESD defects more than three-quarters of the circumference were randomized to single triamcinolone acetonide injection ($n = 16$) and conventional EPD ($n = 16$). The steroid group required fewer dilatation sessions than the control group (6.1 sessions vs 11.5 sessions), without an increased risk of perforation. With respect to circumferential ESD, Sato *et al*^[56] reported that oral steroid therapy with EPD was more effective than single EPD for the prevention of esophageal stricture. Given possible multiple local injections and mistaken deep injection into the MP, convenient oral steroid therapy with EBD

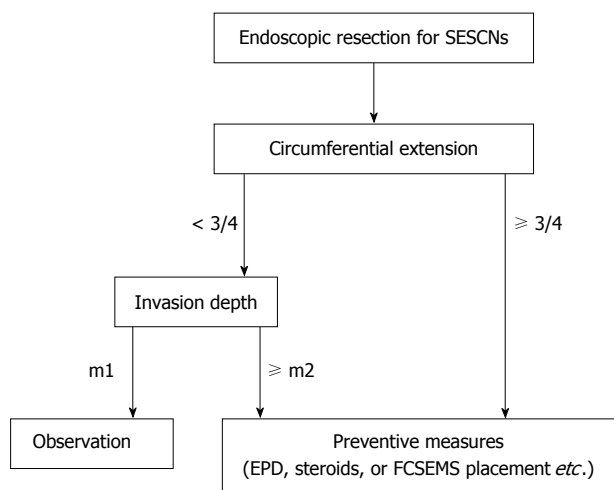


Figure 5 Proposed flow diagram of postoperative stricture prevention for superficial esophageal squamous cell neoplasms after endoscopic resection.

on demand may be a preferred option for prevention and treatment of post-ESD stricture, in spite of a lack of studies comparing oral and local steroid injection. In our endoscopy center, FCSEMs are routinely placed for lesions more than three-quarters of the circumference with a period of 4-8 wk, which has been shown to decrease incidence of stricture and reduce the need for dilation^[58]. Therefore, we suggest an algorithm for the prevention of postoperative stricture after endoscopic resection of SESCNS (Figure 5). Recently, other approaches, such as bioabsorbable poly-L-lactic acid stent placement^[59], polyglycolic acid sheet with fibrin glue^[60], and transplantation of tissue-engineered cell sheets^[47,61], have shown promising results, but these approaches require further studies with large samples prior to extensive clinical use.

PERSPECTIVES AND OTHER APPLICATIONS

ESTD has established a new strategy for large SESCNS, which is different from that of traditional ESD, namely marking-circumferential incision-submucosal dissection. ESTD is derived from submucosal dissection techniques and advances in endoscopic equipment. As an important branch of DETT, ESTD is another good reflection of the submucosal tunnel concept, like popular POEM and STER. Compared with the latter procedures, ESTD does not have any operative difficulties and may be safer due to maintaining the MP layer untouched. Hence, we believe that endoscopists with experience of POEM or STER will find it easy to adopt ESTD, along with its parallel learning curve and training. Arantes *et al.*^[15] described their ESTD learning process, which involved several sessions of hands-on practice on animals; experience as first-assistant in human procedures; unsupervised ESD operations for gastric and rectal tumors (25 cases);

and ESTD operations. With the excellent performance in 25 patients, Arantes *et al.*^[15] proposed ESTD as a standardized approach to facilitate ESD learning for Western endoscopists. Moreover, the promising results from both Asian and Western endoscopy centers and the advantages of ESTD over conventional ESD enable us to speculate that ESTD will replace ESD as a standardized method for large SESCNS. A multicenter prospective study of ESTD by us is ongoing, and other large-sample research from different centers is awaited. A prospective randomized study comparing ESTD with ESD is also eagerly anticipated.

ESTD can be also used for superficial lesions in other parts of the digestive tract. We have reported initial experience of ESTD for gastric lesions (three in the cardia and one in the lesser curvature), which were successfully removed in *en bloc* and R0 fashion without any complications^[62]. The mean diameter was 43 mm (40-50 mm), and the mean operation time was 65 min (34-97 min). However, it is easy to miss lesions in the gastric tunnel by submucosal dissection, because the lesions are not always in a straight line, and superficial marks are invisible from the tunnel view. Frequent withdrawal of the endoscope from the tunnel is necessary. To overcome the limitations of submucosal fibrosis, Choi *et al.*^[63] utilized ESTD as a salvage technique to treat two patients with ulcerative early gastric cancer with fibrosis. The salvage technique made some modifications, by which the oral incision was 2-3 cm distal to lesions, and the anal was cut open in an arcuate style. To resect a large sessile duodenal adenoma in the bulb adjacent to a scar, Jin *et al.*^[16] created a submucosal tunnel through the pyloric ring for its removal. *En bloc* resection was achieved, and two minor perforations during hemostasis were completely clipped after submucosal dissection. The postprocedural course was uneventful, and the patient was discharged 8 d after ESTD. Hu *et al.*^[64] reported successful application of STER to resect eight rectal submucosal tumors. Despite absence of clinical use of ESTD in the colorectum, we still believe it is feasible to remove large, laterally spreading tumors from the rectum and distal colon. In our experience, given different anatomical features and potential risk, ESTD is currently indicated for lesions limited to the gastric cardia, lesser curvature of the gastric body, antrum, and rectum.

CONCLUSION

In conclusion, as a new treatment strategy, ESTD is an effective and safe method for large SESCNS. ESTD can thoroughly remove the obstacle of endoscopic resection due to lesion size and is recommended for lesions that do not invade deeper than sm1 and without clinical evidence of lymph node metastasis and at least one-third of the circumference of the esophagus and ≥ 20 mm in diameter. Postoperative esophageal stricture has received much attention, and preventive

intervention should be implemented for lesions that exceed three quarters of the circumference, or lesions that are less than three-quarters of the circumference but invading deeper than m2. Although studies to date have been limited and larger studies with a high level of evidence are required, the promising results so far enable us to speculate that ESTD will replace traditional ESD as the standard treatment for large SESCNS in the near future.

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