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ORIGINAL ARTICLE

Retrospective Study

Submucosal tunneling and endoscopic resection of submucosal tumors at the esophagogastric junction

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Abstract

AIM: To evaluate the safety and efficacy of submucosal tunneling and endoscopic resection (STER) for treating submucosal tumors (SMTs).

METHODS: Between August 2012 and October 2013, 21 patients with SMTs originating from the muscularis propria (MP) layer at the esophagogastric junction were treated by STER of their tumors. Key steps of the procedure include: (1) mucosal incision: a 2-cm longitudinal mucosal incision was made 5 cm proximal to the tumor; (2) submucosal tunneling: a submucosal tunnel was created 5 cm proximal to and 1 to 2 cm distal to the tumor; (3) tumor resection: the SMT was resected under direct endoscopic viewing; (4) hemostasis: while finishing the tumor resection, careful hemostasis of the MP defect and the tunnel was performed; and (5) mucosal closure: the mucosal incision site was closed by using hemostatic clips. During the operation, equipment used included a cap-fitted endoscope, an insulated-tip knife, a hook knife, hemostatic forceps, an injection needle, a snare, an endoclip, and a high-frequency generator. Carbon dioxide (CO_2) insufflation was achieved by using a CO_2 insufflator.

RESULTS: The median age of the patients was 46.2 years (range, 35-59 years), and the majority were male (18 male *vs* 3 female). Complete resection rate was 100% (21/21). Eighteen lesions were resected *en bloc*. Mean tumor size was 23 mm (range, 10-40 mm), and mean procedure time was 62.9 min (range, 45-90 min). Pathological diagnosis of these tumors included leiomyoma (15 out of 21) and gastrointestinal stromal tumor (6 out of 21). Full-thickness MP resection was performed in 9 of 21 patients (42.9%), with mediastinal and subcutaneous emphysema occurring in all nine. At the completion of the procedure, all patients received closure of the incision with hemoclips. One patient required percutaneous drainage. The remaining 20

patients required no further endoscopic or surgical intervention. There were no incidents of massive or delayed bleeding. The median follow-up period after the procedure was 6 mo (range, 2-14 mo). During follow-up, no patients were found to have residual or recurrent tumor or esophageal stricture.

CONCLUSION: STER is safe, effective and feasible, which provides accurate histopathologic evaluation and curative treatment for SMTs originating from the MP layer at the esophagogastric junction.

Key words: Submucosal tunneling and endoscopic resection; Esophagogastric junction; Subepithelial tumor; Muscularis propria layer; Submucosal tunneling

Core tip: Submucosal tunneling and endoscopic resection (STER) has emerged as a new technique for resecting upper gastrointestinal subepithelial tumors (SETs). This new endoscopic technique has advantages over conventional endoscopic muscularis excavation in terms of maintaining the integrity of the digestive tract mucosa and submucosa, promoting rapid wound healing, and reducing the risk of pleural/abdominal infection. The present study was conducted to evaluate the safety and efficacy of STER for SETs at the esophagogastric junction originating from the muscularis propria layer.

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INTRODUCTION

Most esophageal and gastric cardia subepithelial tumors (SETs) are benign, but the possibility of transformation to malignancy considerably influences the attitude towards the entire group, especially when SETs originate from the muscularis propria (MP) layer[1-3]. Asymptomatic gastrointestinal submucosal tumors (SMTs) which are < 3 cm could be followed by periodic endoscopy and/or EUS or resection[4]. Conventional endoscopic muscularis excavation of tumors originating from the MP layer has been reported to be feasible and safe. However, SETs at the esophagogastric junction are often irregular and lobulated. Therefore, conventional endoscopic muscularis excavation results in larger mucosal defects which are difficult to close. Moreover, perforation is the common complication when SETs originating from the MP layer are treated by endoscopic resection. Submucosal tunneling and endoscopic resection (STER) has emerged as a new technique for resecting upper gastrointestinal SETs[5-7]. This new endoscopic technique has advantages over endoscopic submucosal dissection (ESD) in terms of maintaining the integrity of the digestive tract mucosa and submucosa, promoting rapid wound healing, and reducing the risk of pleural/abdominal infection. The present study was conducted to evaluate the safety and efficacy of STER for SETs at the esophagogastric junction originating from the MP layer.

MATERIALS AND METHODS

Participants

The current study was a retrospective study conducted at a single center in China. The study protocol was approved by the hospital's Internal Review Board and Ethics Committee. Informed consent was obtained for all procedures. Between August 2012 and October 2013, 21 patients with SETs originating from the MP layer at the esophagogastric junction were treated by STER. Endoscopic ultrasound (EUS) using an echoendoscope (UM 240; Olympus Optical Co. Ltd., Tokyo, Japan) and esophageal air-insufflation CT were performed to determine the size, layer of origin, margin, interval growth pattern of SETs, and the anatomical features of the adjacent structures (Figure 1B).

STER procedure

Patients were sedated with intravenous propofol (2 mg/kg). Endotracheal intubation was performed for positive pressure ventilation. Endoscopic equipment and accessories were sterilized in a standard manner. The esophagus and stomach were lavaged with levofloxacin (0.6 g/200 mL). Equipment used included a cap-fitted endoscope (GIF-H260, D-201-11802; Olympus, Tokyo, Japan), an insulated-tip knife (KD-611L, IT2; Olympus), a hook knife (KD-620LR, Olympus), hemostatic forceps (FD-410LR, Olympus), an injection needle (NM-4L-1, Olympus), a snare (SD-9L-1, Olympus), an endoclip (HX-600-135, Olympus), and a high-frequency generator (ICC-200, Erbe, Tu¨bingen, Germany). Carbon dioxide (CO_2) insufflation was achieved by using a CO_2 insufflator (UCR; Olympus, Tokyo, Japan).

The STER procedure was performed as follows. The lesion and potential location of the submucosal tunnel were injected with methylene blue or indigo carmine. A fluid cushion was created 5 cm proximal to the SET by injecting several milliliters of a solution containing 100 mL saline, 2 mL indigo carmine, and 1 mL epinephrine. A 2 cm longitudinal mucosal incision was made and a submucosal tunnel between the submucosal and muscular layers was created. Endoscopic resection of the SET was then performed through the created tunnel. When the lesion was completely resected, it was removed with a snare or forceps. All visible blood vessels were coagulated with hot biopsy forceps or by argon plasma coagulation. The mucosal incision site was closed with hemoclips (Figure 1).

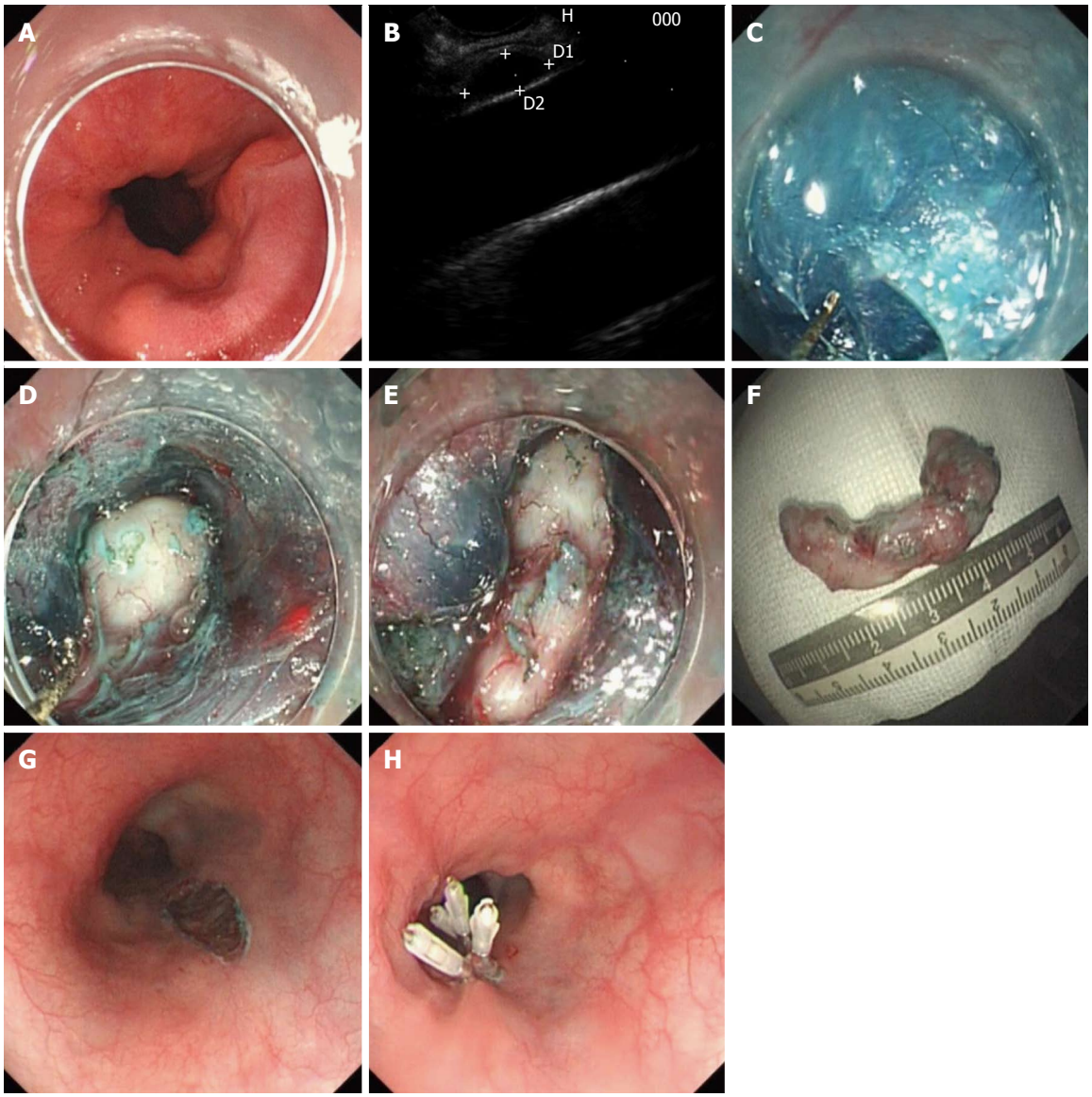

Figure 1 Submucosal tunneling and endoscopic resection of subepithelial tumors at the esophagogastric junction originating from the muscularis propria layer. A: Endoscopic view of subepithelial tumors; B: Endoscopic ultrasonographic evaluation of the same lesion; C: Submucosal tunnel to the lesion (with a hook knife); D: The exposed tumor; E: Annular growth of the tumor; F: The resected specimen; G: The mucosal entry incision; H: The closure of the mucosal entry incision (with several clips).

Definitions

During the procedure, any bleeding affecting the field of view and that could not be managed by endoscopic methods is considered a complication[8]. Delayed bleeding is defined as active post-procedure bleeding diagnosed by endoscopy[9]. Perforation is considered to be present if there is: endoscopic visualization of an extragastric structure during the procedure, subcutaneous emphysema, pneumothorax, pneumoperitoneum, or retroperitoneal gas with signs of peritonitis[10]. Resection is deemed incomplete when negative margins could not be established[10]. *En bloc* resection refers to resection in one piece. Procedure time is calculated from the beginning of the mucosal incision until the withdrawal of the endoscope.

Postoperative management

If there were no complications, an oral diet was restarted 1-2 d after the STER. Esomeprazole 40 mg twice daily (Astra Zeneca, Soderalje, Sweden) was administered intravenously during the patient's hospital stay, and then orally for another 4 wk. When pneumothorax, pneumoperitoneum, or subcutaneous emphysema occurred, patients were treated by gastrointestinal decompression, intravenous infusion of esomeprazole, intravenous antibiotics and suspension of oral diet for 2-3 d. When the patient had no abdominal pain and their vital signs were stabilized, they were progressed to a full fluid diet.

Pathological evaluation

Paraffin-embedded tissue sections were immunohistochemically

Table 1 Conditions of patients and effects of submucosal tunneling and endoscopic resection

Variable	Value
Age (yr)	46.2 yr (range, 35-59 yr)
Sex	
Male	18
Female	3
Tumor size (mm)	23 mm (range, 10-40 mm)
Pathological diagnosis	
Leiomyoma	15
GIST	6
Methods of resection	
Partial-thickness MP resection	12
Full-thickness MP resection	9
Complications	
Perforation	9
Bleeding	0
Delayed bleeding	0
Hospital stay (d)	4.3 (range, 3-7)
Follow-up period (mo)	6 (range, 2-14)

MP: Muscularis propria.

stained with DAKO antibodies (Dako Poland LTD, Gdynia, Poland). Tumors with positive staining for CD117 or DOG-1, as well as CD34 were considered diagnostic of a gastrointestinal stromal tumor. Tumors that were positive for smooth muscle actin and desmin were diagnosed as leiomyomas[7].

Follow-up

Surveillance endoscopy was performed to observe healing of the wound at 1, 3, and 6 mo. Surveillance EUS was performed at 3 mo.

RESULTS

The median age of the patients was 46.2 years (range, 35-59 years), and the male/female ratio was 6 (18 male *vs* 3 female). Complete resection rate was 100% (21/21). Eighteen lesions were resected *en bloc*. The mean size of tumors was 23 mm (range, 10-40 mm). Mean procedure time was 62.9 min (range, 45-90 min). Pathological diagnosis of these tumors included leiomyoma (15 out of 21) and gastrointestinal stromal tumor (6 out of 21). All patients had successful closure with hemoclips, which maintained the integrity of the digestive tract mucosa and submucosa. Full-thickness MP resection was performed in 9 of 21 patients (42.9%), with mediastinal and subcutaneous emphysema occurring in all nine. Nine patients receiving full-thickness MP resection were treated with anti-inflammatory therapy as well as fasting. Eight of nine patients had successful closure with hemoclips and required no further treatment. Mediastinal effusions were found in one patient, with obvious fever occurring. After treatment with anti-inflammatory therapy as well as percutaneous drainage, the patient was discharged 7 d later with normal temperature. There were no episodes of massive or delayed bleeding.

The median hospital stay after procedure was 4.3 d (range, 3-7 d). The median follow-up period after the procedure was 6 mo (range, 2-14 mo). No patients had residual or recurrent tumors detected and no patients had esophageal or gastric strictures during the follow-up period (Table 1).

DISCUSSION

Management of submucosal gastrointestinal tract lesions continues to be a challenging and controversial topic. Recent studies have reported that gastric SETs originating from the MP layer could be successfully removed by endoscopic full-thickness resection[11,12]. Management of SETs at the esophagogastric junction provides further difficulties. First, the esophagogastric junction is adjacent to the diaphragm, complicating the endoscopic resection with movement from breathing as well as esophageal peristalsis. Second, the shape of SETs of the esophagogastric junction is often irregular and lobulated. Moreover, SETs at the esophagogastric junction originating from the MP layer always grow annularly. Conventional endoscopic muscularis excavation causes large mucosal defects which are difficult to close and often result in strictures. Although conventional endoscopic submucosal excavation (ESE) and endoscopic full-thickness resection (EFR) are very effective methods for the removal of esophageal or cardial SETs originating from the MP, they are found to have difficulty in closing the mucosal incision site by using hemostatic clips and have the possibility of resulting in strictures after the formation of scar.

The submucosal tunneling technique was originally described by Sumiyama as an access for natural orifice transluminal endoscopic surgery[13]. This technique was later modified by Pasricha and Inoue, who started to use the submucosal tunnel as a working space for endoscopic myotomy in patients with achalasia[14,15]. Motivated and encouraged by this technique, Xu *et al*[6] used a similar submucosal tunnel as a working space for endoscopic muscularis dissection to resect esophageal or cardial SETs involving the MP layer, and named it STER.

Compared with the other conventional ESD techniques, the STER procedure differs in some aspects, although resection could be performed completely by both ESD and STER. First, a submucosal tunnel to the lesion is created between the submucosal and muscular layers. There is a certain distance between proximal mucosal incision and SETs, so the mucosal incision is regular and closed easily. Second, the gastroscope enters into the tunnel, providing an improved endoscopic view for the resection. Last but not least, when SETs originating from the MP layer are successfully removed, part of the MP layer is resected at the same time without harming the mucosa at the lesion, which reduces the risk of post-procedure stricture in theory.

In the present study, 21 patients with SETs at the esophagogastric junction originating from the MP layer underwent STER, and complete resection was achieved

in all 21 cases. Eighteen lesions were resected *en bloc*. Results have shown no significant difference in complete resection rate between ESE/EFR and STER. However, when endoscope enters submucosal tunnel, it has little effect on respiration during the procedure. What's more, a good field of view during the procedure contributes to more accurate operation.

Although conventional endoscopic muscularis excavation is a very effective method for the removal of esophageal or cardial SETs originating from the MP, perforation is frequently observed, especially in patients who have a full-thickness MP resection. In this study, considering that submucosal tumors were irregular and lobulated, and there was a close relationship between submucosal tumors and deep longitudinal muscle, 9 patients were treated by full-thickness MP resection. Of the 9 patients who had a full-thickness MP resection, the mucosal entry site was completely closed with endoscopic clips at the end of the procedure, preventing leakage of the gastrointestnal contents into the mediastinum or thoracoabdominal cavity. Although the mucosal layer becomes the only barrier between the gastrointestinal lumen and the visceral cavity, a similar situation is observed after the widely used Heller myotomy for achalasia, where a full-thickness myotomy is covered only by the esophageal mucosal layer[16]. All 21 patients recovered with conservative treatment without further endoscopic or surgical intervention. In this study, it was observed that all patients were diagnosed with mediastinum and subcutaneous emphysema. However, mediastinal effusions were found in only one patient, with obvious fever occurring. After treatment with anti-inflammatory therapy as well as percutaneous drainage, the patient was discharged 7 d later with normal temperature. No massive bleeding, delayed bleeding, or other severe complications occurred during or after the procedure. When it comes to recurrence after resection, it should be attached great importance to, especially for invasive tumors like gastrointestinal stromal tumors. In this study, no residual or recurrent tumors were detected and no strictures were identified during the follow-up period (median, 6 mo; range, 2-14 mo). Due to the limitation of short follow-up period, it requires further clinical observation. All in all, STER may provide a feasible, safe, and effective treatment strategy for providing accurate histopathologic evaluation and curative treatment for SETs at the esophagogastric junction originating from the MP layer.

COMMENTS

Background

Management of submucosal gastrointestinal tract lesions continues to be a challenging and controversial topic. Recent studies have reported that gastric subepithelial tumors (SETs) originating from the muscularis propria (MP) layer could be successfully removed by endoscopic full-thickness resection. Management of SETs at the esophagogastric junction provides further difficulties. First, the esophagogastric junction is adjacent to the diaphragm, complicating the endoscopic resection with movement from breathing as well as esophageal peristalsis. Second, the shape of SETs of the esophagogastric junction is often irregular and lobulated. Moreover, SETs at the esophagogastric junction originating from the MP layer always grow annularly. Conventional endoscopic muscularis excavation causes large mucosal defects which are difficult to close and often result in strictures. Therefore, the development of new technique for resecting upper gastrointestinal SETs remains attractive.

Research frontiers

The submucosal tunneling technique was originally described by Sumiyama as an access for natural orifice transluminal endoscopic surgery. This technique was later modified by Pasricha and Inoue, who started to use the submucosal tunnel as a working space for endoscopic myotomy in patients with achalasia. Motivated and encouraged by this technique, Xu used a similar submucosal tunnel as a working space for endoscopic muscularis dissection to resect esophageal or cardial SETs involving the MP layer, and named it submucosal tunneling and endoscopic resection (STER).

Innovations and breakthroughs

Conventional endoscopic muscularis excavation results in larger mucosal defects which are difficult to close. Moreover, perforation is the common complication when SETs originating from the MP layer are treated by endoscopic resection. However, STER has emerged as a new technique for resecting upper gastrointestinal SETs. This new endoscopic technique has advantages over endoscopic submucosal dissection (ESD) in terms of maintaining the integrity of the digestive tract mucosa and submucosa, promoting rapid wound healing, and reducing the risk of pleural/abdominal infection.

Applications

Submucosal tunneling and endoscopic resection is a safe, effective and feasible method, which provides accurate histopathologic evaluation and curative treatment for submucosal tumors (SMTs) originating from the MP layer at the esophagogastric junction.

Terminology

ESD is known as a kind of treatment modality for gastrointestinal epithelial lesions.

Peer review

This paper describes the whole procedure of STER for treating SMTs. The main thrust of the paper is that the authors aim to demonstrate its clinical efficacy for the treatment of SMTs at the esophagogastric junction. This paper is well written and reports an important study.

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