



# Per oral endoscopic tumor (POET) resection for treatment of upper gastrointestinal subepithelial tumors

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## Abstract

**Background** Endoscopic submucosal tunneling has evolved to allow endoscopic resection of subepithelial tumors of gastrointestinal tract without full-thickness perforation. This study aimed to investigate safety and efficacy of submucosal tunnel resection for these tumors.

**Method** Patients with subepithelial tumors (SET) located in esophagus, gastric cardia, lesser curvature, and antrum were recruited. The size of tumor was limited to <40 mm. The procedures were performed under general anesthesia. A mucosal entrance was created 2 cm proximal to the SET after submucosal injection. Submucosal tunnel was then extended and the tumor was dissected and mobilized with intact overlying mucosa. After complete dissection, the tumors would be retrieved per orally and mucosal entrance closed by endoclips.

**Results** From June 2012 to December 2016, 51 patients with subepithelial tumors received POET. 39 patients had SET in stomach, 11 located in esophagus, and 1 in duodenum. The mean operative time was  $90.46 \pm 46.49$  min, while the mean size of the tumors was  $20.71 \pm 14.05$  mm. The POET was converted to endoscopic full-thickness resection (EFTR) in three patients with gastric subepithelial tumors located at greater curvature. The overall complication rate was 4.0%, and there was no bleeding, mucosal dehiscence, or leakage. The time to resume diet was 1.7 days, while the average hospital stay was  $3.2 \pm 1.0$  days. The mean follow-up period was  $19 \pm 16$  months, and only 1 patient developed recurrence of leiomyoma.

**Conclusion** Per oral endoscopic tumor resection is safe and effective treatment for esophageal and gastric SET located at cardia, lesser curvature, and antrum. Currently, POET for treatment of upper GI SET is limited by the size and location of the tumor.

**Keywords** Subepithelial tumors · Upper gastrointestinal tract · Submucosal tunnel endoscopic resection · Per oral endoscopic tumor resection · Therapeutic endoscopy

Gastric subepithelial tumors (SET) are increasingly recognized upon upper gastrointestinal endoscopy [1]. One of the commonest SET found in stomach is gastrointestinal stromal tumors (GIST). Recently, guidelines recommended surgical

resection for treatment of GIST 20 mm or larger [2]. The current standard surgical treatment ranged from laparoscopic wedge resection, distal gastrectomy, proximal gastrectomy, or even total gastrectomy. The decision to different surgical procedures depends on the location and size of the GIST. Gastric GIST are commonly located at the greater curvature and fundus where laparoscopic wedge resection served as the standard treatment [3, 4]. However, surgical resection becomes difficult for subepithelial tumors located at the cardia, lesser curvature, and antrum [4, 5]. For tumors located at the cardia, proximal or total gastrectomy may be necessary to achieve en bloc resection due to limitation in the luminal resection margin, but wedge resection at these locations imposed significant limitation due to the concerns on stricture after surgery [5].

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Numerous studies reported the application of ESD techniques to achieve endoscopic resection for gastric subepithelial tumors [6–8]. However, endoscopic resection with ESD techniques for subepithelial tumors is limited by the likelihood of full-thickness perforation leading to difficulties in closure of the sizable defect. The development of peroral endoscopic myotomy (POEM) opens a novel space—the submucosa for potential development in diagnostic and therapeutic endoscopy [9, 10]. Submucosal endoscopic tunneling creates an alternative access to pathology in the submucosa, muscularis propria, serosa, or beyond the gastrointestinal tract. Previous attempts on endoscopic resection for subepithelial tumors using ESD techniques generally resulted in high rate of perforation and endoscopic full-thickness resection. Submucosal endoscopic tunneling allows access to subepithelial tumors of the gastrointestinal tract without inducing full-thickness perforation. In this cohort study, we attempted to refine the techniques of peroral endoscopic tunneling for resection of subepithelial tumors of upper gastrointestinal tract.

## Method

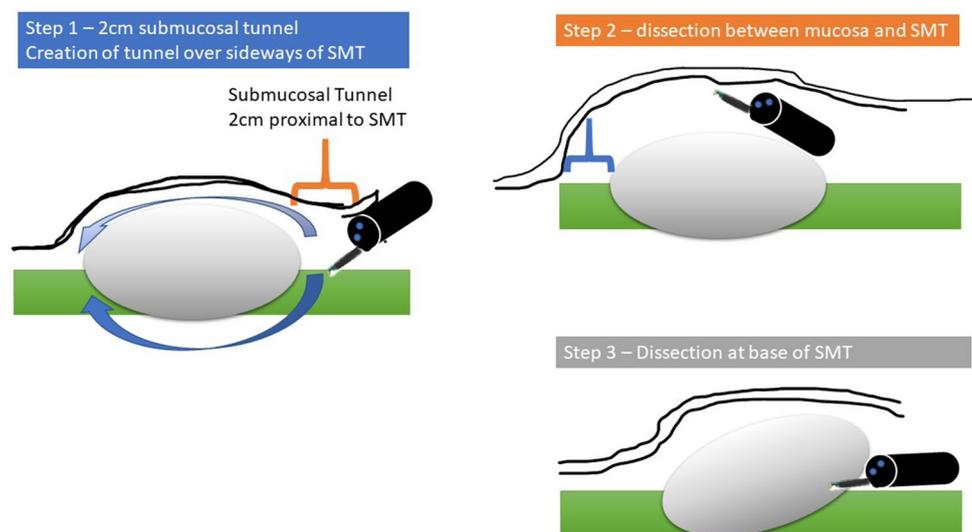
This is a retrospective review of a prospective collected database on patients with gastroesophageal subepithelial tumors (SET) located at gastric cardia, lesser curvature, and antrum treated by POET. Consecutive patients who were diagnosed to have gastric SET were assessed by combination of endoscopy and endoscopic ultrasonography (EUS) to determine the location and size of the SET. Patients received preoperative contrast CT abdomen or thorax to investigate for extraluminal components. We included patients with subepithelial tumors size of <40 mm for POET and informed consent were obtained from all patients. We excluded those

larger than 40 mm or those located over fundus and proximal gastric body at greater curvature. The reasons for exclusion of these subepithelial tumors were (1) development of submucosal tunnel is difficult over high proximal body, and impossible for tumors located at fundus; (2) tumors larger than 40 mm in size may not be able to retrieve through the oral route.

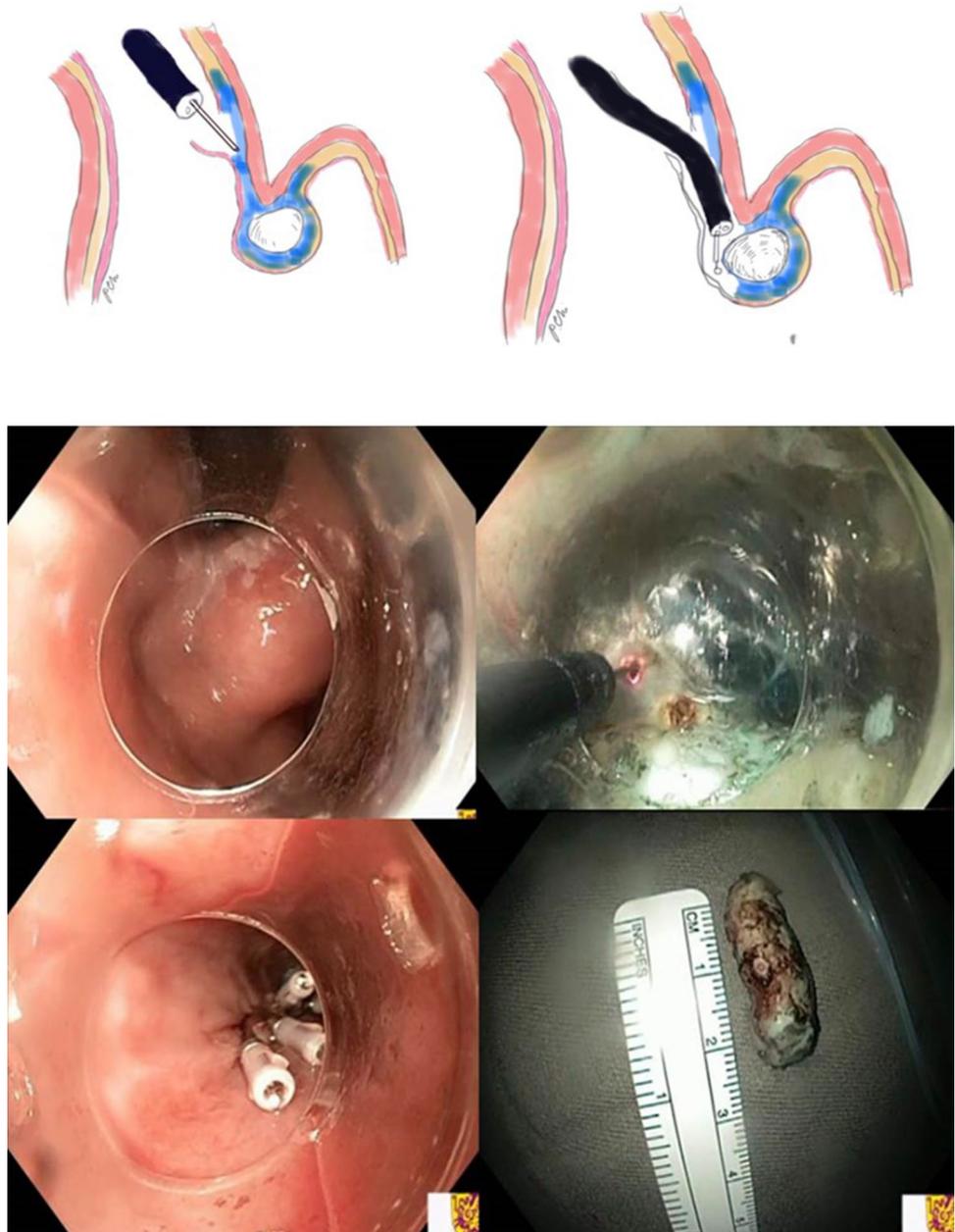
## Techniques of per oral endoscopic tumor resection (POET)

The techniques and approaches of POET varied with different locations of the subepithelial tumors. Generally, the approach for submucosal endoscopic tumor resection would be decided according to the following locations: (1) esophagus; (2) gastric cardia; (3) lesser curvature; and (4) antrum. A mucosal entrance was created using Triangle tip (TT) or Dual knife jet (Olympus Co Ltd, Tokyo, Japan) at 2–3 cm proximal to the SET after submucosal injection with a mixture of normal saline and indigocarmine. The submucosal tunnel was then developed in straight alignment to the SET until positive identification of the proximal part of SET. Further tunneling would be developed over the lateral sides of the SET until 1–2 cm distal to the tumor (Figs. 1, 2, 3). The SET would then be dissected circumferentially using TT jet, Dual knife jet, or IT nano (Olympus Co Ltd, Tokyo, Japan), while the overlying mucosa was kept intact. The final dissection would be focusing on the base of the tumor, and a full-thickness resection of the muscularis propria would be expected. Caution would be exercised at this stage on CO<sub>2</sub> insufflation to prevent induction of extensive pneumoperitoneum or pneumomediastinum. After complete dissection, the tumor would be retrieved per orally and the mucosal entrance was closed using endoclips. The same technique

**Fig. 1** Techniques of POET resection



**Fig. 2** POET resection at the gastroesophageal junction (ante-grade approach) (video 1)



was applied for per oral endoscopic tumor resection in stomach and esophagus (Fig. 4) (videos 1 and 2).

### Technical modification to POET

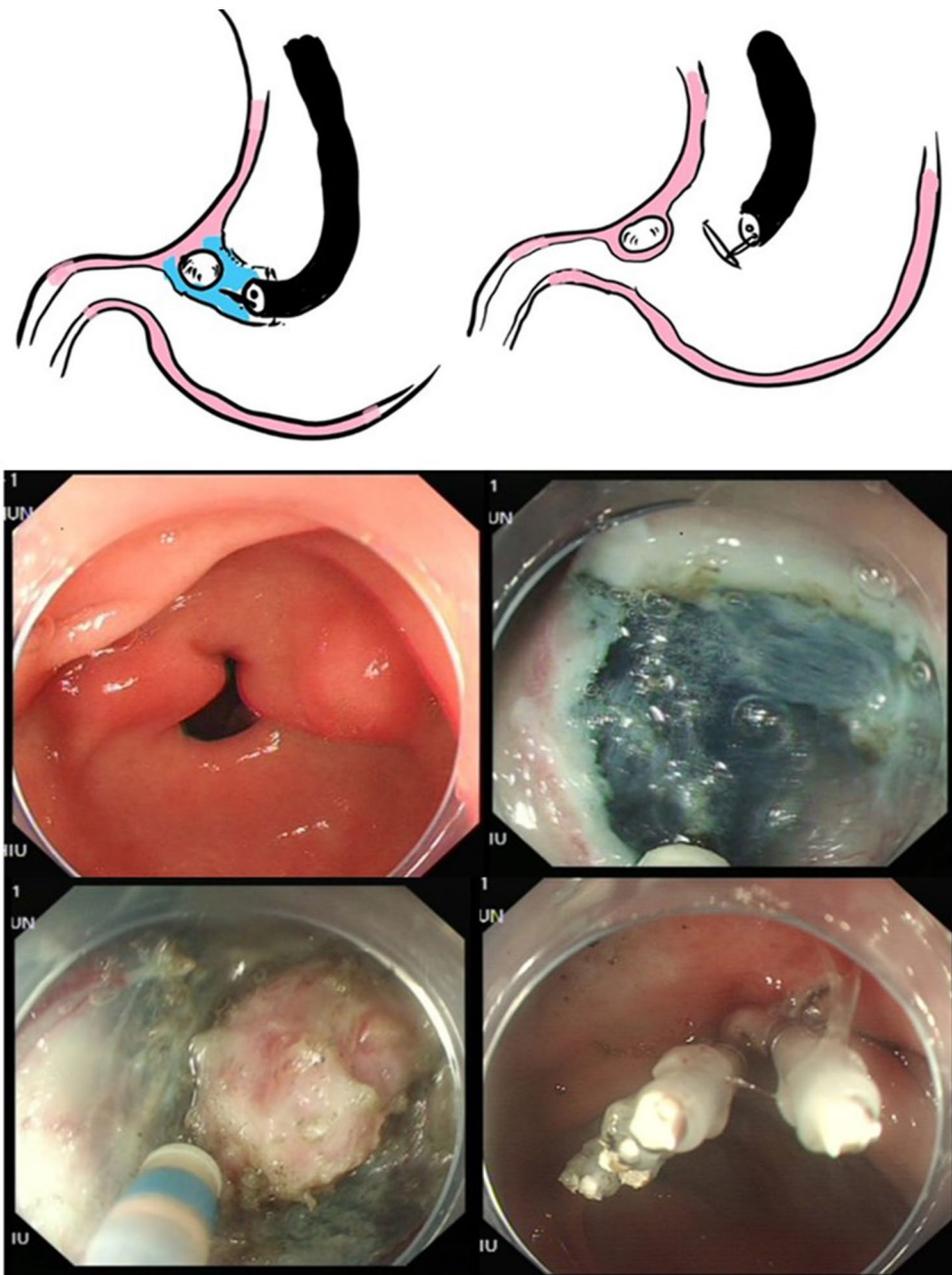
An entrance and exit technique would be used to retrieve large size SET that had difficulties in passing through the mucosal entrance [11]. A mucosal exit site would be created distal to the location of the SET where full-thickness resection of muscularis propria was induced. The SET would then be pushed from the submucosal space into the gastrointestinal lumen via the exit mucosal site. After endoscopic

retrieval of the SMT, both the entrance and exit sites would be closed by endoclips (video 1).

### Conversion

The criteria to convert to salvage procedures included the following: (1) SET were not able to be retrieved per orally due to large size; (2) full-thickness perforation during endoscopic resection; (3) unstable clinical condition of the patient. The salvage procedures included endoscopic full-thickness resection (EFTR) and laparoscopic wedge resection of the gastric subepithelial tumor.

**Fig. 3** POET resection of GIST at gastric antrum



### Endoscopic full-thickness resection (EFTR)

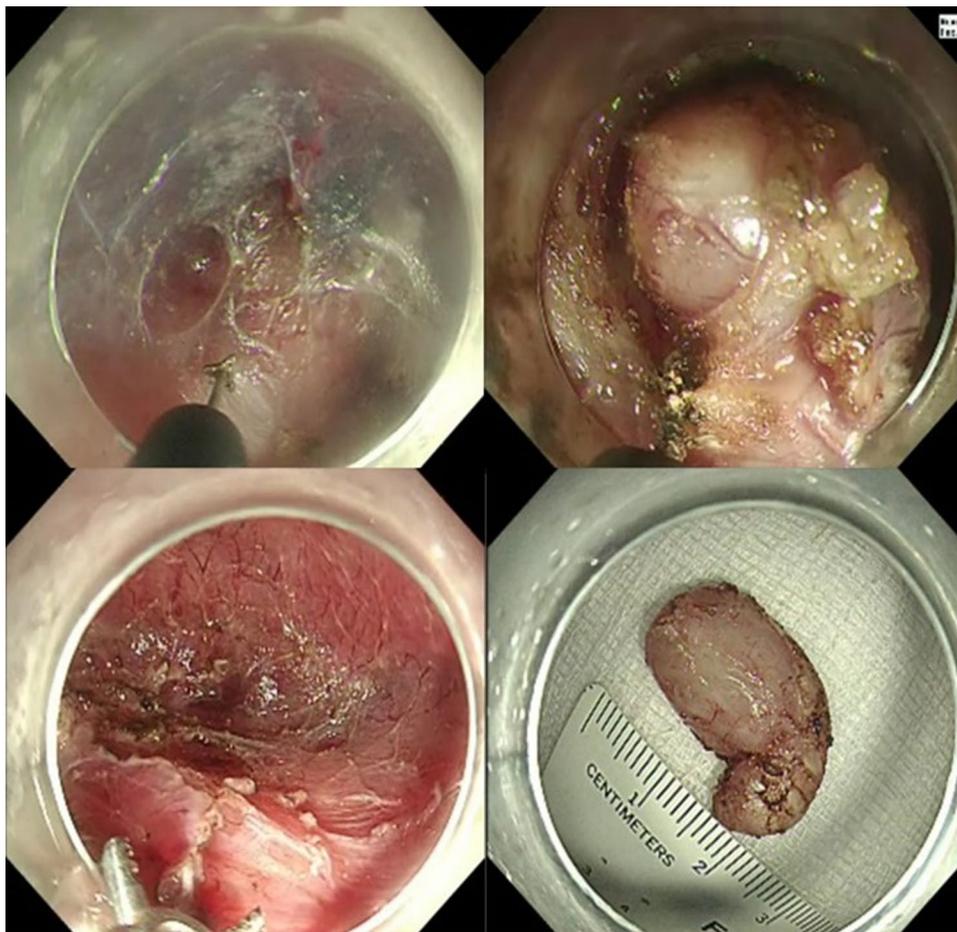
The procedure would be converted to EFTR when (1) submucosal tunnel was difficult to perform and reach the tumor within the stomach, including those subepithelial tumors located at greater curvature and high proximal body of stomach; (2) the mucosal entrance could not be developed due to dense fibrosis in the submucosa. EFTR would be performed using ordinary ESD devices including Dual Knife jet and Insulated tip (IT) knife. After circumferential incision, submucosal dissection was performed around the tumors. After mobilization of the SET from the submucosa, the tumor would be dissected from the muscularis propria.

A full-thickness perforation would be expected during this step, and after entering into the peritoneal cavity the dissection would be completed with the use of IT knife. The tumor would be retrieved, and the full-thickness defect would be closed by Overstitch (Apollo Endosurgery Inc., US) (video 3).

### Postoperative management

Patients would be resumed on regular diet day 1 after operation. They would receive intravenous esomeprazole 40 mg every 12 h for 3 days, and then changed to oral esomeprazole 40 mg daily for 8 weeks after procedure.

**Fig. 4** POET resection for esophageal leiomyoma (video 3)



Follow-up endoscopy or endoscopic ultrasonography would be performed 12 months after POET to confirm no local recurrence.

## Results

From June 2012 to December 2016, 51 patients who were diagnosed to have subepithelial tumors of the upper gastrointestinal tract received POET. 39 patients had subepithelial tumors located in stomach, 11 had tumors located in esophagus, while 1 was in duodenum (Table 1). For the stomach, most of the subepithelial tumors were located at the cardia, lesser curvature, and proximal body, as those located at the fundus were treated by laparoscopic wedge resection. The mean operative time was  $90.46 \pm 46.49$  min, while the mean size of the tumors was  $20.71 \pm 14.05$  mm (range 5–66 mm). In one patient, the esophageal subepithelial tumor was too large to be retrieved through the submucosal tunnel and required laparoscopic transhiatal retrieval of specimen after complete dissection. The POET procedure was converted to EFTR in three patients with gastric subepithelial tumors. All these subepithelial tumors resected by

EFTR were located over the greater curvature of mid-body of stomach. The overall complication rate was 4.0% with two patients having self-limiting fever after the procedure. There was no bleeding, mucosal dehiscence, or leakage after the procedure. There was no gas-related complication including pneumoperitoneum, pneumomediastinum, or surgical emphysema. The time to resume diet was 1.7 days, while the average hospital stay was  $3.2 \pm 1.0$  days. The en bloc resection rate was 94.1% (48/51) and the complete resection rate was 98.0% (50/51). 15 of the subepithelial tumors were gastric GIST, while 20 were leiomyoma. 12 of the 15 GIST had mitotic figure of  $< 1$  per 10 high power field. The mean follow-up period was  $19 \pm 16$  months, and only 1 patient developed recurrence of leiomyoma.

## Discussion

Subepithelial tumors of the upper gastrointestinal tract represent a wide range of pathologies arising from mesenchymal layer with different malignant potentials [12, 13]. Gastrointestinal stromal tumors (GIST) are among those with high variation in the malignant potential, which can be predicted

**Table 1** Baseline demographics and perioperative outcomes for 51 patients with upper gastrointestinal subepithelial tumors treated by POER resection

Parameters	Per oral endoscopic tumor resection ( <i>n</i> = 51)
Age	54.1 ± 11.3
Gender (male/female)	20/31
Location	
Cardia	17
Lesser curvature	8
Greater curvature	3
Antrum	11
Esophagus	11
Duodenum	1
Size of subepithelial tumor (mm)	20.71 ± 14.05 mm (range 5–66 mm)
Mean operative time (min)	90.46 ± 46.49 min
Mean hospital stay (days)	3.2 ± 1.0
Technological variation/conversion	
Conversion to laparoscopic tumor retrieval	1 (esophagus due to large size)
Conversion to endoscopic full-thickness resection	3 (stomach—located at antrum and greater curvature)
Double mucosal entrance for resection and extraction	2
Time to resume diet (days)	1.7 ± 0.77
Overall complication rate (%)	2 (4.0%)
Postop fever day 1	2
Bleeding	0
Leakage	0
Mean follow-up period (months)	19 ± 16 months
En bloc resection	48 (94.1%)
Complete resection	50 (98.0%)
Recurrence	1 (1.96%)
Pathologies	
Gastrointestinal stromal tumor	15
Leiomyoma	20
Ectopic pancreas	5
Poorly differentiated carcinoma	1
Neuroendocrine tumor	1
Lipoma	1
Other (including fibrofatty scar, lymphectasia)	8
Mitotic figures among GIST	
< 1/10 HPF	12
> 1/10 HPF	3

*HPF* high power field

by the large tumor size, higher number of mitotic figures per high power field, and the non-gastric location. Though leiomyoma is generally considered as benign, it can lead to significant symptoms like pain and dysphagia when it becomes sizable in the upper gastrointestinal tract. The recent NCCN guidelines recommended resections for gastrointestinal stromal tumors of larger than 20 mm [14]. Conventional treatment for upper gastrointestinal subepithelial tumors is either laparoscopic gastric wedge resection or thoracoscopic enucleation of esophageal SET [15, 16]. However, surgical

resection can sometimes be technically challenging [17]. For gastric subepithelial tumors located at the cardia, lesser curvature, and antrum, laparoscopic wedge resection could lead to significant narrowing of the stomach. Classical resections for tumors around the cardia and gastroesophageal junction could lead to significant morbidities of up to 24%. Thoracoscopic enucleation of esophageal leiomyoma required one lung ventilation which imposes significant risks of pulmonary collapse and pneumonia after surgery [18].

Recently, the development of per oral endoscopic myotomy opens a new approach to treatment of gastrointestinal diseases beyond mucosa [9]. Submucosal endoscopy allowed a novel approach for resection of subepithelial tumors while avoiding a full-thickness perforation [19]. Numerous cohort studies reported on the application of endoscopic submucosal dissection (ESD) for resection of upper gastrointestinal subepithelial tumors [19–21]. Though the results demonstrated a reasonable rate of en bloc resection, the risks of gastrointestinal perforation varied between 10 and 15%. The report of submucosal tumor endoscopic resection (STER) and per oral endoscopic tumor resection (POET) in 2012, which were similar in techniques, achieved high en bloc resection and significantly reduced the risks of perforation [22, 23]. We reported our experience in performance of POET for treatment of upper gastrointestinal subepithelial neoplasia, the difficulties encountered during dissection of these subepithelial tumors, as well as the alternative techniques to salvage these conditions. From results of the current study, STER and POET can achieve high rate of en bloc resection for upper GI subepithelial tumors of < 40 mm safely, except for those tumors located over higher body at greater curvature or those at the fundus where creation of submucosal tunnel would be quite challenging. Hence, for the three subepithelial tumors located over greater curvature of stomach, submucosal tunnel was difficult due to misalignment of the endoscope to the tumor and were converted to EFTR. The lumen defect was closed by endoscopic suturing using overstretch [24].

Technical challenges for POET and STER included the management of unexpected large size subepithelial tumors discovered during the dissection. The completeness of dissection may not be easily confirmed, especially over the anal side of the tumor due to the limited space for manipulation and inspection [11, 25]. Hence, we recommended the extension of at least 1-cm submucosal tunnel distal to the tumor, as well as adequate dissection on both sides of the subepithelial tumor before further dissection at base to allow adequate space for manipulation. Moreover, the mucosal entrance may not be large enough for retrieval of the tumor. In our study, we tackled this issue by opening an exit mucosal site distal to the dissection area and push the tumor into the normal lumen before retrieval [11]. This is an effective method as the remnant attachment of the tumor could be exposed after pushing the main bulk of SMT into the normal lumen.

This study has several limitations. Firstly, the average follow-up period for this study was only  $19 \pm 16$  months. Although a follow-up endoscopy or EUS would be performed for all the patients, the follow-up period might not be long enough to detect local recurrence. Secondly, four patients required either additional laparoscopic procedure or conversion to endoscopic full-thickness resection, and all these conversions were related to tumor characteristics

including the location and sizes. We advise for large subepithelial tumors, POET or STER should be conducted in the operation theater under general anesthesia with surgeons, and patients should be prepared for the possibility of conversion.

In summary, subepithelial tumors of the upper gastrointestinal tract can be safely resected by per oral endoscopic tumor resection through submucosal tunneling. The endoscopic tunneling resection is especially indicated for subepithelial tumors less than 40 mm located at esophagus, cardia, lesser curvature, and antrum of stomach.

## Compliance with ethical standards

**Disclosures** Philip Wai Yan Chiu, Hon Chi Yip, Anthony Yuen Bun Teoh, Vivien Wai Yin Wong, Shannon Melissa Chan, Simon Kin Hung Wong, and Enders Kwok Wai Ng have no conflicts of interest or financial ties to disclose.

## References

- Hwang JH, Rulyak SD, Kimmey MB (2006) American Gastroenterological Association Institute technical review on the management of gastric subepithelial masses. *Gastroenterology* 130:2217–2228
- von Mehren M, Randall RL, Benjamin RS, Boles S, Bui MM, Casper ES, Conrad EU 3rd, DeLaney TF, Ganjoo KN, George S, Gonzalez RJ, Heslin MJ, Kane JM 3rd, Mayerson J, McGarry SV, Meyer C, O'Donnell RJ, Pappo AS, Paz IB, Pfeifer JD, Riedel RF, Schuetze S, Schupak KD, Schwartz HS, Van Tine BA, Wayne JD, Bergman MA, Sundar H (2014) Gastrointestinal stromal tumors, version 2.2014. *J Natl Compr Cancer Netw* 12(6):853–862
- Choi SM, Kim MC, Jung GJ, Kim HH, Kwon HC, Choi SR, Jang JS, Jeong JS (2007) Laparoscopic wedge resection for gastric GIST: long-term follow-up results. *Eur J Surg Oncol* 33(4):444–447
- Honda M, Hiki N, Nunobe S, Ohashi M, Kiyokawa T, Sano T, Yamaguchi T (2014) Long-term and surgical outcomes of laparoscopic surgery for gastric gastrointestinal stromal tumors. *Surg Endosc* 28(8):2317–2322
- Okumura S, Kanaya S, Hosogi H, Ito T, Miura S, Okada T, Shimoike N, Akagawa S, Kawada H, Arimoto A (2017) Our experience with laparoscopic partial gastrectomy by the 'lift-and-cut method' for gastric gastrointestinal stromal tumor with maximal preservation of the remnant stomach. *Surg Endosc* 31(8):3398–3404
- Yu C, Liao G, Fan C, Yu J, Nie X, Yang S, Bai J (2017) Long-term outcomes of endoscopic resection of gastric GISTs. *Surg Endosc*. <https://doi.org/10.1007/s00464-017-5557-2>
- He Z, Sun C, Zheng Z, Yu Q, Wang T, Chen X, Cao H, Liu W, Wang B (2013) Endoscopic submucosal dissection of large gastrointestinal stromal tumors in the esophagus and stomach. *J Gastroenterol Hepatol* 28(2):262–267
- Li QL, Yao LQ, Zhou PH, Xu MD, Chen SY, Zhong YS, Zhang YQ, Chen WF, Ma LL, Qin WZ (2012) Submucosal tumors of the esophagogastric junction originating from the muscularis propria layer: a large study of endoscopic submucosal dissection (with video). *Gastrointest Endosc* 75(6):1153–1158

9. Inoue H, Minami H, Kobayashi Y, Sato Y, Kaga M, Suzuki M, Satodate H, Odaka N, Itoh H, Kudo S (2010) Peroral endoscopic myotomy (POEM) for esophageal achalasia. *Endoscopy* 42(4):265–271
10. Chiu PW, Wu JC, Teoh AY, Chan Y, Wong SK, Liu SY, Yung MY, Lam CC, Sung JJ, Chan FK, Lau JY, Ng EK (2013) Peroral endoscopic myotomy for treatment of achalasia: from bench to bedside (with video). *Gastrointest Endosc* 77(1):29–38
11. Ng JJ, Chiu PW, Shabbir A, So JB (2015) Removal of a large, 40-mm, submucosal leiomyoma using submucosal tunneling endoscopic resection and extraction of specimen using a distal mucosal incision. *Endoscopy* 47(Suppl 1):E232–E233
12. American Gastroenterological Association Institute (2006) American Gastroenterological Association Institute medical position statement on the management of gastric subepithelial masses. *Gastroenterology* 130(7):2215–2216
13. Koo DH, Ryu MH, Kim KM, Yang HK, Sawaki A, Hirota S, Zheng J, Zhang B, Tzen CY, Yeh CN, Nishida T, Shen L, Chen LT, Kang YK (2016) Asian consensus guidelines for the diagnosis and management of gastrointestinal stromal tumor. *Cancer Res Treat* 48(4):1155–1166
14. Demetri GD, von Mehren M, Antonescu CR, DeMatteo RP, Ganjoo KN, Maki RG, Pisters PW, Raut CP, Riedel RF, Schuetz S, Sundar HM, Trent JC, Wayne JD (2010) NCCN Task Force report: update on the management of patients with gastrointestinal stromal tumors. *J Natl Compr Cancer Netw* 8(Suppl 2):S1–S41 (**quiz S42–S44**)
15. Kim KH, Kim MC, Jung GJ, Kim SJ, Jang JS, Kwon HC (2012) Long term survival results for gastric GIST: is laparoscopic surgery for large gastric GIST feasible? *World J Surg Oncol* 10:230
16. Coccolini F, Catena F, Ansaloni L, Lazzareschi D, Pinna AD (2010) Esophagogastric junction gastrointestinal stromal tumor: resection vs enucleation. *World J Gastroenterol* 16:4374–4376
17. Correa-Cote J, Morales-Urbe C, Sanabria A (2014) Laparoscopic management of gastric gastrointestinal stromal tumors. *World J Gastrointest Endosc* 6(7):296–303
18. von Rahden BHA, Stein HJ, Feussner H, Siewert JR (2004) Enucleation of submucosal tumors of the esophagus: minimally invasive versus open approach. *Surg Endosc* 18:924–930
19. Chiu PW, Inoue H, Rösch T (2016) From POEM to POET: applications and perspectives for submucosal tunnel endoscopy. *Endoscopy* 48(12):1134–1142
20. Liu BR, Song JT, Qu B et al (2012) Endoscopic muscularis dissection for upper gastrointestinal subepithelial tumors originating from the muscularis propria. *Surg Endosc* 26:3141–3148
21. He Z, Sun C, Wang J et al (2013) Efficacy and safety of endoscopic submucosal dissection in treating gastric subepithelial tumors originating in the muscularis propria layer: a single-center study of 144 cases. *Scand J Gastroenterol* 48:1466–1473
22. Inoue H, Ikeda H, Hosoya T, Onimaru M, Yoshida A, Eleftheriadis N, Maselli R, Kudo S (2012) Submucosal endoscopic tumor resection for subepithelial tumors in the esophagus and cardia. *Endoscopy* 44(3):225–230
23. Xu MD, Cai MY, Zhou PH, Qin XY, Zhong YS, Chen WF, Hu JW, Zhang YQ, Ma LL, Qin WZ, Yao LQ (2012) Submucosal tunneling endoscopic resection: a new technique for treating upper GI submucosal tumors originating from the muscularis propria layer (with videos). *Gastrointest Endosc* 75(1):195–199
24. Chiu PW, Chan FK, Lau JY (2015) Endoscopic suturing for ulcer exclusion in patients with massively bleeding large gastric ulcer. *Gastroenterology* 149(1):29–30
25. Zhang Q, Cai JQ, Xiang L, Wang Z, de Liu S, Bai Y (2017) Modified submucosal tunneling endoscopic resection for submucosal tumors in the esophagus and gastric fundus near the cardia. *Endoscopy* 49(8):784–791

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