Management of gastric subepithelial tumors: The role of endoscopy

Su Young Kim, Kyoung Oh Kim

Su Young Kim, Kyoung Oh Kim, Division of Gastroenterology, Department of Internal Medicine, Gachon University, Gil Medical Center, Incheon 405-760, South Korea

Author contributions: Kim SY and Kim KO contributed equally to this work.

Conflict-of-interest statement: No author has any personal or financial conflict of interest.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY -NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

Manuscript source: Invited manuscript

Correspondence to: Kyoung Oh Kim, MD, PhD, Division of Gastroenterology, Department of Internal Medicine, Gachon University, Gil Medical Center, 21, Namdong-daero 774beon-gil, Namdong-gu, Incheon 405-760, South Korea. kkoimge@naver.com
Telephone: +82-32-4603778
Fax: +82-32-4603408

Received: March 26, 2016
Peer-review started: March 27, 2016
First decision: April 19, 2016
Revised: April 28, 2016
Accepted: May 17, 2016
Article in press: May 27, 2016
Published online: June 10, 2016

Abstract

With the wide use of esophagogastroduodenoscopy, the incidence of gastric subepithelial tumor (SET) diagnosis has increased. While the management of large or symptomatic gastric SETs is obvious, treatment of small (≤ 3 cm) asymptomatic gastric SETs remains inconclusive. Moreover, the presence of gastrointestinal stromal tumors with malignant potential is of concern, and endoscopic treatment of gastric SETs remains a subject of debate. Recently, numerous studies have demonstrated the feasibility of endoscopic treatment of gastric SETs, and have proposed various endoscopic procedures including endoscopic submucosal dissection, endoscopic muscularis dissection, endoscopic enucleation, endoscopic submucosal tunnel dissection, endoscopic full-thickness resection, and a hybrid approach (the combination of endoscopy and laparoscopy). In this review article, we discuss current endoscopic treatments for gastric SETs as well as the advantages and limitations of this type of therapy. Finally, we predict the availability of newly developed endoscopic treatments for gastric SETs.

Key words: Subepithelial tumor; Endoscopy; Stomach; Treatment; Complication

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Recently, technical advances in endoscopic treatment, including diverse endoscopic procedures, have been performed for the resection of gastric subepithelial tumors (SETs). However, the presence of gastrointestinal stromal tumors with malignant potential is of concern and endoscopic treatment of gastric SETs remains subject of debate. In this review article, we discuss current endoscopic treatments for gastric SETs as well as the advantages and limitations of this type of therapy. The information presented in this review should be taken into consideration when making decisions concerning endoscopic treatment for gastric SETs.
INTRODUCTION

The majority of subepithelial tumors (SETs) are considered to be benign in origin; however, some lesions may be malignant, especially if they originate in the muscularis propria (MP) layer. Gastrintestinal stromal tumors (GIST), the most common mesenchymal neoplasms originating in the MP layer of the stomach, are malignant in 10%-30% of cases. According to the National Comprehensive Cancer Network guidelines, all GISTs larger than 2 cm should be resected. For GISTs smaller than 2 cm without high-risk features on endoscopic ultrasonography (EUS), endoscopic follow-up may be recommended. However, endoscopic surveillance has limitations, including delayed diagnosis of malignancy, high cost, hazards associated with repeated endoscopic procedures, patient discomfort related with long-term follow up examinations, and concerns associated with missing the optimum treatment window. Therefore, even for small sized gastric SETs originating in the MP layer, histological confirmation should be obtained if the tumor was not definitely differentiated as benign.

In the past, the standard treatment for gastric SETs was surgical resection, including laparotomy or laparoscopic partial gastrectomy, and endoscopy was used for diagnostic purposes, and was rarely used for treatment. However, surgical resection is invasive and associated with possible surgical complications. Recently, numerous reports have proposed that endoscopic resection can be applied to gastric SETs, including GIST. The purpose of this article was to examine all practical endoscopic methods that should be taken into consideration when deciding whether to perform endoscopic treatment for gastric SETs. Through this process, we provide orientation for endoscopic treatment of gastric SETs.

WHY IS GASTRIC SET DIFFICULT TO TREAT WITH ENDOSCOPY?

Gastric SETs should be treated using endoscopic procedures; however, they remain challenging to treat. Several factors underlie the difficulties associated with endoscopic treatment. First, determining the possibility of malignancy for gastric SETs is difficult before resection. EUS and computed tomography (CT) can aid in but are by no means satisfactory for accurate diagnosis, and are limited in their ability to evaluate tumor size, fibrosis, and MP layer invasion. Thus, establishing a treatment strategy with endoscopy may be difficult. Endoscopic treatments alone do not guarantee complete resection and prevention of cancer recurrence for gastric SETs. Secondly, when endoscopic resection was performed in patients with gastric SETs originating from the MP layer, the complication rate was relatively high, especially for perforation. Furthermore, endoscopic resection removes only the tumor without excision of the surrounding normal tissue; therefore, the tumor is likely to be incompletely resected. Third, it is difficult to eliminate large or predominantly extraluminal growth of SETs by endoscopy. Even the endoscopic full-thickness resection (EFTR) technique that enables treatment of relatively large gastric SETs cannot be used to treat tumors larger than 4 cm with an extraluminal pattern. Lastly, the effectiveness of endoscopic treatment is highly affected by the location of the gastric SET. For instance, endoscope retroflexion should be maintained for gastric SETs located on the fundus or cardiac region, which has been shown to be difficult and to have a high perforation risk.

CONVENTIONAL AND MODIFIED ENDOSCOPIC SUBMUCOSAL DISSECTION FOR TREATMENT OF GASTRIC SETS

Endoscopic submucosal dissection (ESD) is an effective and safe tissue resection method for the treatment of early gastric cancer (EGC). Although the focus of this technique has been the treatment of EGC, its use has recently been expanded for the treatment of gastric SETs. According to a recent study concerning endoscopic resection of SETs using ESD, the overall rate of R0 resection was 81.1% (30/37) and no recurrence was observed in patients with R0 resections during the follow up period. In lesions that were incompletely resected, the tissue acquired was sufficient for all immunohistochemistry studies and, as a result, ESD can aid in confirming SET diagnosis. In a large study published in China, ESD was an effective and feasible treatment option for gastric SETs with diameters no greater than 50 mm originating in the MP layer. The en bloc complete resection rate was 92.4% (134/145) and no recurrence was detected during the follow-up period. In our previous study, we discovered that tumors ≤ 2 cm in size or with a positive rolling sign, which indicates that the SET originated from the submucosal layer or has a narrow connection to the MP layer, had high complete resection rates. Moreover, we found that fixed tumor mobility and neurogenic tumors were significantly associated with perforation. We anticipated that lower tumor mobility was associated with broad muscular connections or intramural-type or subserosal-type tumors, for which it is difficult to dissect the SET from adjacent muscle tissue. To treat gastric SETs, conventional ESD is feasible. However, complete resection rates were inconsistent for the MP layer (68.2%-92.4%), and perforation risk was high. Specifically, endoscopic resection without perforation is challenging in the gastric fundus compared with other locations in the stomach. In a prospective study, conventional ESD using the “Resolution clip” was a feasible and easy method to prevent perforation of gastric fundus SETs. However, this study...
in a relatively small number of patients showed a high perforation rate of 30%\(^\text{[20]}\). Therefore, conventional ESD is limited for removing SETs originating from the MP layer; modified ESD was introduced to solve these problems.

Various modified ESD techniques exist, consisting of a combination of ESD and endoscopic muscularis dissection (EMD). Depending on the degree of connection between the tumor and the muscularis layer, the application ratio of ESD and EMD can be determined. According to Liu et al\(^\text{[22]}\), EMD was effective for treatment of gastric SETs originating in the MP layer. In their study, a longitudinal incision was made to cut the overlying mucosa, and electrical or blunt dissection was then used to dissect the SET from the submucosa and MP layers. Finally, the wound was closed with endoscopic clips\(^\text{[22]}\). Using this method, the complete resection rate was as high as 96.8%, but perforation was also high, at 12.9%. Many trials of SET endoscopic resection using conventional and modified ESD exist (Table 1). In a study published in South Korea, in which the mucosa covering the SETs was eliminated using a coagulation snare to reveal the hidden tumors, the successful complete resection rate by endoscopic enucleation was 92.3% (60/65)\(^\text{[14]}\), however, the perforation rate was comparatively high (12.3%). The most common location of perforation was the fundus, as it has a thin wall and is difficult to approach endoscopically. Moreover, all perforations occurred in schwannomas and GISTs; these tumors do not have intact tumor capsules and have tight adhesions\(^\text{[14]}\). Another study demonstrated the feasibility of modified ESD with enucleation for treatment of gastric SETs\(^\text{[8]}\). Two incisions were performed (longitudinal and transverse), which resulted in more obvious exposure of the tumor and its underlying MP layer, and an easier resection\(^\text{[8]}\). All tumors were larger than 2 cm, and the complete resection rate was 93.8% (15/16) with no perforation or overt bleeding\(^\text{[8]}\). This method demonstrates the beneficial results of endoscopic resection compared with surgical resection. Open or laparoscopic surgery can lead to late stenosis and gastroesophageal reflux after surgery, resulting in decreased patient satisfaction. Despite the advantages of endoscopic enucleation, several limitations, including the difficulty of complete removal of tissue with a large enough margin around the tumor\(^\text{[14]}\), are associated with this method. Therefore, if the histologic diagnosis of a SET is highly malignant, clinicians should consider additional treatment. Moreover, in many studies, the follow-up period was short and research was performed at a single center.

### ENDOSCOPIC SUBMUCOSAL TUNNEL DISSECTION FOR GASTRIC SETS

Inoue et al\(^\text{[23]}\) (2010) investigated peroral endoscopic myotomy (POEM) for endoscopic treatment of achalasia. This method involves creating a submucosal tunnel to create space for endoscopic treatment under the mucosal layer, and can also be used to remove muscle layer lesions. The POEM procedure was applied to SETs originating in the MP layer, and was named endoscopic submucosal tunnel dissection (ESTD), which was introduced in 2012\(^\text{[10,24]}\). A mucosal incision was made proximal to the lesion, and a submucosal tunnel was created to resect the tumor completely using an electrosurgical knife. After removing the tumor, the mucosal layer was sutured using endoscopic clips. Compared with ESD, this method has several benefits, including fast wound healing and maintaining an intact mucosal layer, thus preventing leakage of bowel contents\(^\text{[10,25]}\). A Japanese study with a small sample size demonstrated that ESTD resulted in safe resection of SETs without complications\(^\text{[26]}\). Since then, other studies have shown the efficacy of ESTD for removal of SETs in the esophagus and the cardia, with competitive resection rates of 100% (Table 2)\(^\text{[10,24]}\). According to Liu et al\(^\text{[26]}\), esophageal and cardiac SETs originating

---

**Table 1** Publications reporting conventional and modified endoscopic submucosal dissection for upper gastrointestinal subepithelial tumors originating in the muscularis propria

| Ref.     | No. of patients | Location               | Mean tumor diameter (mm) | Mean procedure time (min) | Resection method       | Complete resection rate (%) | Total complication rate (%) | Mean follow-up period (mo)/recurrence in complete resection patients |
|----------|-----------------|------------------------|--------------------------|----------------------------|------------------------|-----------------------------|-----------------------------|---------------------------------------------------------------------|
| Lee et al\(^\text{[26]}\) (2006) | 11               | Cardia/body            | 20.7                     | 60.9                       | ESD                    | 75.0                        | 0                          | 10.9/N                                                              |
| Jeong et al\(^\text{[14]}\) (2011) | 64               | Cardia/fundus/body/antrum | 13.8                  | 34.7                       | Endoscopic enucleation | 92.3                        | 12.3                       | 10.0/N                                                              |
| Liu et al\(^\text{[22]}\) (2012) | 31               | Esophagus/cardia/stomach | 22.1                  | 76.8                       | EMD                    | 96.8                        | 12.9                       | 17.7/N                                                              |
| He et al\(^\text{[1]}\) (2013)   | 144              | Cardia/fundus/body/antrum | 15.1                  | 63.4                       | ESD                    | 92.4                        | 14.5/4.8                  | 19.1/N                                                              |
| Chu et al\(^\text{[8]}\) (2012)  | 16               | Cardia/fundus/body/antrum | 26.1                  | 52.0                       | Modified ESD with enucleation | 93.8                        | 0                          | 14.8/N                                                              |
| Li et al\(^\text{[20]}\) (2013)  | 11               | Fundus                | 18.8                     | 81.0                       | ESD                    | 90.9                        | 27.2                       | 6.4/N                                                               |
| Chun et al\(^\text{[26]}\) (2013) | 35              | Cardia/fundus/body/antrum | 18.0                  | 32.3                       | ESD                    | 74.3                        | 5.7                        | 6.1/N                                                               |

\(^1\)Median follow-up period; \(^2\)Perforation; \(^3\)Bleeding; ESD: Endoscopic submucosal dissection; N: None; EMD: Endoscopic muscularis dissection.
in the MP layer were more easily dissected using ESTD than with EMD. Treatment of SET at the esophagogastric junction is difficult due to the interference of esophageal peristalsis and respiration with a detailed endoscopic view and control. ESTD allows for the endoscope to enter into the submucosal tunnel, improving visibility and enabling direct cutting. Moreover, SETs originating from the MP layer can be removed without damage to the mucosa around the lesion, diminishing procedure-related strictures and scars. In another prospective study, ESTD was successful for the treatment of SETs located in the upper gastrointestinal tract, and revealed GIST and lesions in deeper MP layers as risk factors for complications. The ESTD method is relatively safe and results in a high rate of complete resection; however, it is not without limitations. In the majority of studies, ESTD was performed for SETs of the esophagogastric junction, while few studies have been performed to determine the effect of ESTD on SETs of the stomach. Because the stomach mucosa is thick and has greater curvature, submucosal tunneling can be challenging in regions including the gastric fundus and the proximal corpus. Therefore, it is difficult to perform consistent tunneling of the stomach. In addition, large SETs (> 3 cm) are difficult to remove with ESTD because confines of tunneling space may give rise to poor endoscopic visualization and insufficient en bloc resection.

### EFTR FOR GASTRIC SETS

Many gastric SETs originate in the deep MP layer. EFTR allows for en bloc resection of such SETs, including those tightly connected to the MP layer (Table 3), which was first reported in 2001 in Japan. In the past, EFTR was only applied to small lesions. The usefulness of EFTR with laparoscopy was reported in animals in 2006 study; however, it also demonstrated the risk for perforation-induced intraperitoneal infections. In 2011, Zhou et al. showed the feasibility of EFTR without laparoscopy for gastric SETs originating in the MP layer. This strategy was effective in treating deep gastric SETs with a complete resection rate of 100% (26/26) and no severe complications. These results were mirrored in another study published in China, in which EFTR resulted in successful complete resection (98.0%) without severe complications. However, this study used clip closures and endoloop ligatures as additional closure devices, which may have strengthened the suturing technique to avoid gastric perforation. Moreover, endoloop ligatures are simple and do not require specific equipment. Recently, a new technique was introduced using endoscopic suturing devices in EFTR; full-thickness sutures were deployed underneath the subepithelial mass and the SET was removed using an endoscopic electrocautery snare. This technique, explained by Schmidt et al. as “suture first, cut later”, has several advantages including the fact that it is applicable to large tumors (up to 4 cm), it can be applied to tumors at all stomach sites, and it does not require laparoscopic assistance.

While EFTR is effective in treating gastric SETs originating in the MP layer, EFTR without laparoscopy has several limitations, as it is not suitable for the removal of very large tumors, it requires advanced endoscopic skills, and it has a high risk for perforation or peritonitis. Two reports published in Japan investigated the efficacy and feasibility of laparoscopic and endoscopic cooperative surgery (LECS) (Table 3). In this procedure, three-quarters of the tumor submucosal layer was dissected circumferentially using the ESD technique. Then, laparoscopic seromuscular dissection was performed at the three-quarter cut line around the tumor. Finally, the tumor was raised using laparoscopic forceps, and the resection was performed using laparoscopic stapling devices. This method is applicable to gastric SETs irrespective of tumor dimension and site. Additionally, this procedure only requires a minimal area of the stomach to be resected. To avoid excessive normal gastric tissue removal, Abe et al. studied laparoscopy-assisted

| Ref. | No. of patients | Location | Mean tumor diameter (mm) | Mean procedure time (min) | Resection method | Complete resection rate (%) | Total complication rate (%) | Mean follow-up period (mo)/recurrence in complete resection patients |
|------|----------------|----------|--------------------------|--------------------------|----------------|-----------------------------|-----------------------------|------------------------------------------------------------------|
| Inoue et al. (2012) | 7 | Esophagus/cardia | 19.0 | 152 | Submucosal endoscopic tumor resection | 100 | 0 | 5.5/N |
| Gong et al. (2012) | 12 | Esophagus/cardia | 19.5 | 48.3 | ESTD | 83.3 | 16.7 | NA |
| Liu et al. (2013) | 12 | Esophagus/cardia | 18.5 | 78.3 | tEMD | 100 | 66.7 | 7.1/N |
| Ye et al. (2014) | 85 | Esophagus/cardia/stomach | 19.2 | 57.2 | STER | 100 | 9.4 | 8'/N |
| Zhou et al. (2015) | 21 | Esophago gastric junction | 23.0 | 62.9 | STER | 100 | 42.9 | 6'/N |

1Median follow-up period. ESTD: Endoscopic submucosal tunnel dissection; N: None; NA: Not available; tEMD: Tunneling endoscopic muscularis dissection; STER: Submucosal tunneling and endoscopic resection.

**Table 2 Publications reporting endoscopic submucosal tunnel dissection for upper gastrointestinal subepithelial tumors originating in the muscularis propria**

---

Kim SY et al. Endoscopic treatment for gastric subepithelial tumor
endoscopic full-thickness resection (LECS) or LAEFR could prevent these side effects, as the complications such as stenosis or deformity can occur. Indeed, methods including LECS and LAEFR is that these methods are appropriate for the treatment of intraluminal gastric SETs in the MP layer. Another recent study showed that indications for endoscopic assistance during laparoscopic resection included growing type (intraluminal) tumors and a tumor size ≤ 18 mm[34]. It is difficult to determine the correct location and proper resection margin of these tumors by laparoscopy, which could result in excessive tissue elimination. Indeed, complications such as stenosis or deformity can occur. LECS or LAEFR could prevent these side effects, as the resection margin is determined through endoscopy[17].

Some researchers have developed new combinations of endoscopic and laparoscopic treatments for full-thickness resection. A combination of laparoscopic and endoscopic approaches to neoplasia using the non-exposed endoscopic wall-inversion surgery (NEWS) were developed[26,27,28]. The CLEAN-NET and NEWS procedure are effective novel hybrid techniques. However, these methods are rarely applied to treat gastric SETs. Therefore, further studies of these methods are needed for application to gastric SET treatment.

CONCLUSION

To expand the role of endoscopy for the treatment of gastric SETs, several problems must be resolved. First, it is important to determine ways in which to reduce complications associated with endoscopic treatment, focusing specifically on perforation. Carbon dioxide insufflation during endoscopic procedures could be considered as it may reduce the risk of emphysema and pneumoperitoneum[9,27]. Several closing devices for the prevention of procedure-induced perforation have been also described[19,20]. Indeed, methods including OTSC and the “Resolution clip” are efficient in reducing perforation. However, these only apply to a few patients with small perforations and specific lesions sites, and
are not suitable for larger SETs. Thus, the development of new methods to address this limitation is warranted. Secondly, the mean follow-up period of the majority of the studies presented in this review was under 2 years. Although complete resection was preceded by endoscopic treatment, gastric SETs with malignant potential have a risk of recurrence. Therefore, further studies with longer-term follow-up periods and appropriate follow-up duration guidelines after endoscopic SET treatment are required. Next, until now, most studies were performed at a single institute, were retrospective in nature, and only included a small number of participants. Due to the characteristic of SETs, recruitment of a large sample size can be difficult and, thus, may introduce statistical errors including selection bias. Therefore, larger prospective multicenter studies or meta-analyses studying the effects of endoscopic treatment in gastric SETs are warranted. Moreover, the limitations involving large gastric SETs or tumors of the esophagogastric junction or posterior wall must be resolved. As ESTD showed promising results for the treatment of gastric SETs located on the esophagogastric junction, appropriate procedures for other difficult locations should be developed. Finally, a hybrid approach combining endoscopy and laparoscopy should be considered. This method has the advantage of preserving the volume and function of the stomach, and may increase a patient’s satisfaction with the procedure. In addition, novel hybrid techniques (CLEAN- NET and NEWS) avoid exposing malignant SETs to the peritoneal cavity. In conclusion, technical modifications and improvements are required to define the role of endoscopy for treating gastric SETs.

REFERENCES

1. Hwang JH, Rulyak SD, Kimmey MB. American Gastroenterological Association Institute technical review on the management of gastric subepithelial masses. Gastroenterology 2006; 130: 2217-2228 [PMID: 16762644 DOI: 10.1053/j.gastro.2006.04.033]

2. Chun SY, Kim KO, Park DS, Lee JJ, Park JW, Moon SH, Baek IH, Kim JH, Park CK, Kwon MJ. Endoscopic submucosal dissection as a treatment for gastric subepithelial tumors that originate from the muscularis propria layer: a preliminary analysis of appropriate indications. Surg Endosc 2013; 27: 3271-3279 [PMID: 23519491 DOI: 10.1007/s00464-013-2904-9]

3. Demetri GD, von Mehren M, Antoncscu CR, DeMatteo RP, Ganjoo KN, Maki RG, Pisters PW, Raut CP, Riedel RF, Schuetze S, Sundar HM, Trent JC, Wayne JD. NCCN Task Force report: update on the management of patients with gastrointestinal stromal tumors. J Natl Compr Canc Netw 2010; 8 Suppl 2: S1-41; quiz S42-44 [PMID: 20547867]

4. Ponsaing LG, Hansen MB. Therapeutic procedures for submucosal tumors in the gastrointestinal tract. World J Gastroenterol 2007; 13: 3316-3322 [PMID: 17659670 DOI: 10.3748/wjg.v13.i24.3316]

5. Lee CM, Kim HH. Minimally invasive surgery for submucosal (subepithelial) tumors of the stomach. World J Gastroenterol 2014; 20: 13035-13043 [PMID: 25278697 DOI: 10.3748/wjg.v20.i36.13035]

6. He Z, Sun C, Wang J, Zheng Z, Yu Q, Wang T, Chen X, Liu W, Wang B. 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 2013; 48: 1466-1473 [PMID: 24131359 DOI: 10.3109/03005652013.045796]

7. Bialek A, Wiegowska-Kozłowska A, Pertkiewicz J, Polkowski M, Mlikiewicz P, Karpińska K, Ławniczak M, Starzyńska T. Endoscopic submucosal dissection for treatment of gastric subepithelial tumors (with video). Gastrointest Endosc 2012; 75: 276-286 [PMID: 20203280 DOI: 10.1016/j.gie.2011.08.029]

8. Chu YY, Lien JM, Tsai CH, Chiu CT, Chen TC, Yang KC, Ng SC. Modified endoscopic submucosal dissection with enucleation for treatment of gastric subepithelial tumors originating from the muscularis propria layer. BMC Gastroenterol 2012; 12: 124 [PMID: 22978262 DOI: 10.1186/1471-230X-12-124]

9. Zhang Y, Ye JY, Zhou XD, Mao XL, Zhu LH, He BL, Huang Q. Safety and efficacy of endoscopic excavation for gastric subepithelial tumors originating from the muscularis propria layer: results from a large study in China. J Clin Gastroenterol 2013; 47: 689-694 [PMID: 23632361 DOI: 10.1097/MCG.0b013e3182908295]

10. Inoue H, Ikeda H, Hosoya T, Onimaru M, Yoshida A, Eleftheriadis N, Maselli R, Kudo S. Submucosal endoscopic tumor resection for subepithelial tumors in the esophagus and cardia. Endoscopy 2012; 44: 225-230 [PMID: 22354622 DOI: 10.1055/s-0031-1291659]

11. Schmidt A, Bauer M, Riecken B, von Renteln D, Muehelesen H, Caca K. Endoscopic full-thickness resection of gastric subepithelial tumors: a single-center series. Endoscopy 2015; 47: 154-158 [PMID: 25380509 DOI: 10.1055/s-0034-1390786]

12. Mullady DK, Tan BR. A multidisciplinary approach to the diagnosis and treatment of gastrointestinal stromal tumor. J Clin Gastroenterol 2013; 47: 578-585 [PMID: 23751846 DOI: 10.1097/MCG.0b013e3182936c57]

13. Faigel DO, Abulhawa S. Gastrointestinal stromal tumors: the role of the gastroenterologist in diagnosis and risk stratification. J Clin Gastroenterol 2012; 46: 629-636 [PMID: 22858511 DOI: 10.1097/MCG.0b013e3182548f6c]

14. Jeong ID, Jung SW, Bang SJ, Shin JW, Park NH, Kim do H. Endoscopic enucleation for gastric subepithelial tumors originating in the muscularis propria layer. Surg Endosc 2011; 25: 468-474 [PMID: 20589510 DOI: 10.1007/s00464-011-1957-7]

15. Lee HH, Lin PY, Tung SY, Shen CH, Wei KL, Wu CS. Endoscopic submucosal dissection for the treatment of intraluminal gastric subepithelial tumors originating from the muscularis propria layer. Endoscopy 2006; 38: 1024-1028 [PMID: 17058168 DOI: 10.1055/s-2006-948141]

16. Li QL, Yao LQ, Zhou PH, Xu MD, Chen SY, Zhong YS, Zhang YQ, Chen WF, Ma LL, Qin WZ. Submucosal tumors of the esophagogastric junction originating from the muscularis propria layer: a large study of endoscopic submucosal dissection (with video). Gastrointest Endosc 2012; 75: 1153-1158 [PMID: 22459663 DOI: 10.1016/j.gie.2012.01.037]

17. Abe N, Takeuchi H, Ooki A, Nagao G, Masaki T, Mori T, Sugiyama M. Recent developments in gastric endoscopic submucosal dissection: towards the era of endoscopic resection of layers deeper than the submucosa. Dig Endosc 2013; 25 Suppl 1: 64-70 [PMID: 23368096 DOI: 10.1111/den.12087]

18. Ye LP, Yu Z, Mao XL, Zhu LH, Zhou XB. Endoscopic full-thickness resection with defect closure using clips and an endoloop for gastric subepithelial tumors arising from the muscularis propria. Surg Endosc 2014; 28: 1978-1983 [PMID: 24619327 DOI: 10.1007/s00464-014-3421-1]

19. Schlag C, Wilhelm D, von Delius S, Feussner H, Meining A. EndoResect study: endoscopic full-thickness resection of gastric subepithelial tumors. Endoscopy 2013; 45: 4-11 [PMID: 23254401 DOI: 10.1055/s-0032-125760]

20. Li L, Wang F, Wu B, Wang Q, Wang C, Liu J. Endoscopic submucosal dissection of gastric fundus subepithelial tumors originating from the muscularis propria. Exp Ther Med 2013; 6: 391-395 [PMID: 24137915 DOI: 10.3989/etm.2013.1181]

21. Chung IK, Lee JH, Lee SH, Kim SJ, Cho JY, Cho WY, Hwangbo Y, Keum BR, Park JJ, Chun HJ, Kim JJ, Ji SR, Seol SY. Therapeutic outcomes in 1000 cases of endoscopic submucosal dissection for early gastric neoplasms: Korean ESD Study Group
multicenter study. Gastrointest Endosc 2009; 69: 1228-1235
[PMID: 19249769 DOI: 10.1016/j.gie.2008.09.027]

22 Liu BR, Song JT, Qu B, Wen JF, Yin JB, Liu W. Endoscopic muscularis dissection for upper gastrointestinal subepithelial tumors originating from the muscularis propria. Surg Endosc 2012; 26: 3141-3148 [PMID: 22580875 DOI: 10.1007/s00464-012-2305-5]

23 Inoue H, Minami H, Kobayashi Y, Sato Y, Kaga M, Suzuki M, Satodate H, Odaka N, Itoh H, Kudo S. Peroral endoscopic myotomy (POEM) for esophageal achalasia. Endoscopy 2010; 42: 265-271 [PMID: 20354937 DOI: 10.1055/s-0029-1244080]

24 Gong W, Xiong Y, Zhi F, Liu S, Wang A, Jiang B. Preliminary experience of endoscopic submucosal tunnel dissection for upper gastrointestinal subepithelial tumors. Endoscopy 2012; 44: 231-235 [PMID: 22354823 DOI: 10.1055/s-0031-1291720]

25 Ye LP, Zhang Y, Mao XL, Zhu LH, Zhou X, Chen JY. Submucosal tunneling endoscopic resection for small upper gastrointestinal subepithelial tumors originating from the muscularis propria layer. Surg Endosc 2014; 28: 524-530 [PMID: 24013472 DOI: 10.1007/s00464-013-3197-8]

26 Liu BR, Song JT, Kong LJ, Pei FH, Wang XH, Du YJ. Tunneling endoscopic muscularis dissection for subepithelial tumors originating from the muscularis propria of the esophagus and gastric cardia. Surg Endosc 2013; 37: 4354-4359 [PMID: 23765425 DOI: 10.1007/s00464-013-3023-3]

27 Zhou DJ, Dai ZB, Wells MM, Yu DL, Zhang J, Zhang L. Submucosal tunneling and endoscopic resection of submucosal tumors at the esophagogastric junction. World J Gastroenterol 2015; 21: 578-583 [PMID: 25593479 DOI: 10.3748/wjg.v21.i2.578]

28 Zhou PH, Yao LQ, Qin XY, Cui MY, Xu MD, Zhong YS, Chen WF, Zhang YQ, Qin WZ, Hu JW, Liu JZ. Endoscopic full-thickness resection without laparoscopic assistance for gastric submucosal tumors originated from the muscularis propria. Surg Endosc 2011; 25: 2926-2931 [PMID: 21424195 DOI: 10.1007/s00464-011-1644-y]

29 Suzuki H, Ikeda K. Endoscopic mucosal resection and full thickness resection with complete defect closure for early gastrointestinal malignancies. Endoscopy 2001; 33: 437-439 [PMID: 11396763 DOI: 10.1055/s-2001-1429]

30 Ikeda K, Mosse CA, Park PO, Fritscher-Ravens A, Bergström M, Mills T, Tajiri H, Swain CP. Endoscopic full-thickness resection: circumferential cutting method. Gastrointest Endosc 2006; 64: 82-89 [PMID: 16813808 DOI: 10.1016/j.gie.2005.12.039]

31 Hiki N, Yamamoto Y, Fukunaga T, Yamaguchi T, Nunobe S, Tokunaga M, Miki A, Ohyama S, Seto Y. Laparoscopic and endoscopic cooperative surgery for gastrointestinal stromal tumor dissection. Surg Endosc 2008; 22: 1729-1735 [PMID: 18074180 DOI: 10.1007/s00464-007-9696-8]

32 Tsujimoto H, Yaguchi Y, Kuman I, Takahata R, Ono S, Hase K. Successful gastric submucosal tumor resection using laparoscopic and endoscopic cooperative surgery. World J Surg 2012; 36: 327-330 [PMID: 22187132 DOI: 10.1007/s00268-011-1387-x]

33 Abe N, Takeuchi H, Yanagida O, Masaki T, Mori T, Sugiyama M, Atomi Y. Endoscopic full-thickness resection with laparoscopic assistance as hybrid NOTES for gastric submucosal tumor. Surg Endosc 2009; 23: 1908-1913 [PMID: 19184206 DOI: 10.1007/s00464-008-0317-y]

34 Dávila JS, Monblán D, Ginés Á, Sánchez-Montes C, Araujo I, Saavedra-Pérez D, Lucy AM, Fernández-Esparregó G. Endoscopic-assisted laparoscopic resection for gastric subepithelial tumors. Surg Endosc 2016; 30: 199-203 [PMID: 25860952 DOI: 10.1007/s00464-015-4183-0]

35 Inoue H, Ikeda H, Hosoya T, Yoshida A, Onimaru M, Suzuki M, Kudo SE. Endoscopic mucosal resection, endoscopic submucosal dissection, and beyond: full-layer resection for gastric cancer with nonexposure technique (CLEAN-NET). Surg Oncol Clin N Am 2012; 21: 129-140 [PMID: 22098836 DOI: 10.1016/j.soc.2011.09.012]

36 Mitsui T, Niimi K, Yamashita H, Goto O, Aikou S, Hatao F, Wada I, Shimizu N, Fujishiro M, Koike K, Seto Y. Non-exposed endoscopic wall-inversion surgery as a novel partial gastrectomy technique. Gastric Cancer 2014; 17: 594-599 [PMID: 23974429 DOI: 10.1010/j.s10120-013-0291-5]

37 Nabeshima K, Tomiku M, Nakamura K, Yasuda S. Combination of Laparoscopic and Endoscopic Approaches to Neoplasia with Non-exposure Technique (CLEAN-NET) for GIST with Ulceration. Tokai J Exp Clin Med 2015; 40: 115-119 [PMID: 26369265]

38 Ntourakis D, Mavrogenis G. Cooperative laparoscopic endoscopic and hybrid laparoscopic surgery for upper gastrointestinal tumors: Current status. World J Gastroenterol 2015; 21: 12482-12497 [PMID: 26604655 DOI: 10.3748/wjg.v21.i43.12482]

39 Maehata T, Goto O, Takeuchi H, Kitagawa Y, Yahagi N. Cutting edge of endoscopic full-thickness resection for gastric tumor. World J Gastrointest Endosc 2015; 7: 1208-1215 [PMID: 26566427 DOI: 10.4253/wjge.v7.i16.1208]

40 Kim DW, Kim JS, Kim BW, Jung YJ, Kim GJ, Kim JJ. Non-Exposed Endoscopic Wall-Inversion Surgery for Gastrointestinal Stromal Tumor of the Stomach: First Case Report in Korea. Clin Endosc 2016 Mar 15; Epub ahead of print [PMID: 26975860 DOI: 10.5946/ece.2016.002]

P- Reviewer: Arigami T  S- Editor: Ji FF  L- Editor: A  E- Editor: Lu YJ
