J Korean Med Sci. 2022 Jun 13;37(23):e184
https://doi.org/10.3346/jkms.2022.37.e184
eISSN 1598-6357·pISSN 1011-8934

JKMS

Original Article
Gastroenterology & Hepatology

Check for updates

Natural History of Asymptomatic Esophageal Subepithelial Tumors of 30 mm or Less in Size

Seokin Kang,[1,2] **Do Hoon Kim**,[1] **Yuri Kim**,[1] **Dongsub Jeon**,[1] **Hee Kyong Na**,[1] **Jeong Hoon Lee**,[1] **Ji Yong Ahn**,[1] **Kee Wook Jung**,[1] **Kee Don Choi**,[1] **Ho June Song**,[1] **Gin Hyug Lee**,[1] **and Hwoon-Yong Jung**[1]

[1]Department of Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea
[2]Department of Internal Medicine, Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Korea

OPEN ACCESS

Received: Dec 19, 2021
Accepted: May 16, 2022
Published online: May 30, 2022

Address for Correspondence:
Do Hoon Kim, MD, PhD
Department of Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea.
Email: dohoon.md@gmail.com

ORCID iDs
Seokin Kang
https://orcid.org/0000-0003-2228-6479
Do Hoon Kim
https://orcid.org/0000-0002-4250-4683
Yuri Kim
https://orcid.org/0000-0003-4372-065X
Dongsub Jeon
https://orcid.org/0000-0003-0847-6030
Hee Kyong Na
https://orcid.org/0000-0001-6764-9099
Jeong Hoon Lee
https://orcid.org/0000-0002-0778-7585
Ji Yong Ahn
https://orcid.org/0000-0002-0030-3744

ABSTRACT

Background: No definite guidelines for the management of small esophageal subepithelial tumors (SETs) have been established, because there are limited data and studies on their natural history. We aimed to assess the natural history and propose optimal management strategies for small esophageal SETs.
Methods: Patients diagnosed as esophageal SETs ≤ 30 mm in size between 2003 and 2017 using endoscopic ultrasound (EUS) with a minimal follow-up of 3 months were enrolled, and their esophagogastroduodenoscopy (EGD) and EUS were retrospectively reviewed.
Results: Of 275 esophageal SETs in 262 patients, the initial size was < 10 mm, 10–20 mm, and 20–30 mm in 104 (37.8%), 105 (38.2%), and 66 (24.0%) lesions, respectively. Only 22 (8.0%) SETs showed significant changes in size and/or echogenicity and/or morphology at a median of 40 months (range, 4–120 months). Tissues of 6 SETs showing interval changes were obtained using EUS-guided fine needle aspiration biopsy; 1 was identified as a gastrointestinal stromal tumor (GIST) and was surgically resected, while the other 5 were leiomyomas and were regularly observed. Eight SETs showing interval changes were resected surgically or endoscopically without pathological confirmation; 1 was a GIST, 2 were granular cell tumors, and the other 5 were leiomyomas.
Conclusion: Regular follow-up with EGD or EUS may be necessary for esophageal SETs ≤ 30 mm in size considering that small portion of them has a possibility of malignant potential. When esophageal SETs ≤ 30 mm show significant interval changes, pathological confirmation may precede treatment to avoid unnecessary resection.

Keywords: Endosonography; Esophagus; Gastrointestinal Stromal Tumors; Subepithelial Tumors

INTRODUCTION

Subepithelial tumors (SETs) of the upper gastrointestinal tract, which were previously called submucosal tumors, originate from the layers under the epithelium such as the muscularis mucosa, submucosa, and muscularis propria. Although the precise incidence or prevalence

Kee Wook Jung
https://orcid.org/0000-0002-3771-3691
Kee Don Choi
https://orcid.org/0000-0002-2517-4109
Ho June Song
https://orcid.org/0000-0002-3195-8794
Gin Hyug Lee
https://orcid.org/0000-0003-3776-3928
Hwoon-Yong Jung
https://orcid.org/0000-0003-1281-5859

Disclosure

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: Kang S, Kim DH, Jung HY. Data curation: Jung KW, Choi KD, Song HJ, Lee GH. Formal analysis: Kang S, Kim Y, Jeon D. Methodology: Kim DH. Validation: Na HK, Lee JH, Ahn JY. Writing - original draft: Kang S. Writing - review & editing: Kim DH.

of SETs is unknown because of lacking epidemiologic data, the reported prevalences fall within 0.36–1.45%.[1-3] The stomach is the most frequently involved organ, and the esophagus is relatively less affected.[2,3]

Endoscopic ultrasound (EUS) is the most accurate modality for differentiating SETs since tumor size, echogenicity pattern, and the layer of origin can be evaluated.[4-6] Moreover, pathological diagnoses can be obtained using EUS-guided fine needle aspiration biopsy (EUS-FNAB).

Small esophageal SETs are often found in asymptomatic individuals in Japan and Korea where esophagogastroduodenoscopy (EGD) is performed during cancer screening examinations.[6] Esophageal SETs consist of various subtypes, such as gastrointestinal stromal tumor (GIST), leiomyoma, and granular cell tumor (GCT). Among these, leiomyomas are benign and are the most common subtype in the esophagus.[7] GISTs have malignant potentials and are commonly located in the stomach in 70% of cases, with approximately only 5% of cases encountered in the esophagus.[8] GCTs are rare and are considered benign, but a malignant transformation has been reported, specifically in tumors > 40 mm in size.[5]

The recent development of endoscopic procedures has allowed upper gastrointestinal SETs, including esophageal ones, to be removed through endoscopic resection (ER).[9-12] Nevertheless, GIST is very rare in the esophagus in contrast to its relatively high frequency in the stomach, and leiomyomas are the most common subtype of esophageal SETs.[6,7] Therefore, the need to resect asymptomatic esophageal SETs is controversial considering the risk of complications.[13]

Although several guidelines and management plans for gastric SETs have been published,[5,6,14] no definite guidelines for small esophageal SETs have yet been established owing to the lack of epidemiologic data and knowledge of their natural history. In this study, we assessed the natural course of esophageal SETs ≤ 30 mm in size to determine optimal therapeutic strategies.

METHODS

Patients

Between 2003 and 2017, a total of 464 patients underwent EUS for asymptomatic esophageal SETs ≤ 30 mm in size at the Asan Medical Center, a tertiary center in Seoul, Korea. The EGD and EUS images of 477 esophageal SETs in 464 patients were reviewed. Among these, 202 esophageal SETs (202 patients) were excluded; 33 lesions were extrinsic compressions; 152 were lost to follow-up; 17 underwent surgery or ER within 3 months of tumor diagnosis. Finally, 275 esophageal SETs in 262 patients with a minimal follow-up period of 3 months were enrolled (**Fig. 1**). None of these esophageal SETs had malignant features at the initial test.

EGD and EUS

EGD and EUS were performed at the Asan Medical Center by expert endoscopists (Kim DH, Na HK, Ahn JY, Lee JH, Choi KD, and Song HJ). The location, size, presence of the ulcer on the surface, layer of origin, and echogenicity pattern of SETs were evaluated using EUS at the initial diagnosis and either EGD or EUS were periodically performed during follow-up. A SET was defined as a mass covered with normal-appearing mucosa on EGD, which was located in the second, third, or fourth layer on EUS. Significant changes were defined as follows: ≥ 25%

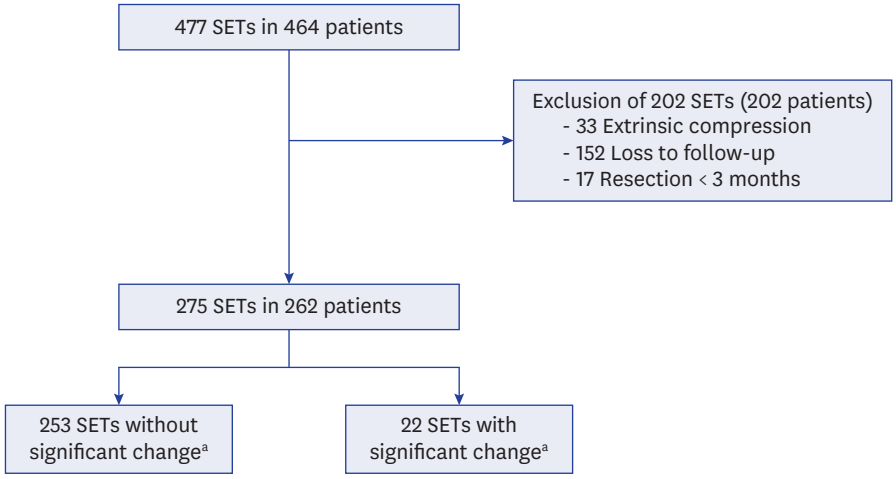

Fig. 1. Flowchart of the patient enrollment process.
SET = subepithelial tumor.
[a]Significant change: ≥ 25% increase in the longest diameter, changes in echogenicity indicating malignancy, or ulcerative changes.

increase in the longest diameter, echogenicity changes indicative of malignancy (irregular border, echogenic foci, cystic spaces, heterogeneity),[6] and ulcerative changes on the surface.

Follow-up

A total of 262 patients with 275 esophageal SETs ≤ 30 mm in size with benign echogenicity and no ulceration on the surface underwent EGD or EUS with a minimal follow-up period of 3 months after the initial evaluation. Patients without significant changes in size, echogenicity, and morphology received EGD or EUS every 12–24 months for surveillance. Furthermore, patients with one or more significant changes in their lesions were advised to undergo EUS-FNAB, ER, or surgery.

Pathologic review

Tissue samplings of esophageal SETs obtained using EUS-FNAB, ER, or surgery were reviewed to arrive at a pathological diagnosis. Specific immunohistochemical staining was used as follows: 1) leiomyoma: smooth muscle actin and desmin; 2) GIST: C-Kit (CD117) and CD34; and 3) GCT: CD68 and S100.[13,15] In addition, GISTs were classified as very low, low, intermediate, or high risk, according to the modified National Institutes of Health consensus criteria.[16]

Statistical analysis

Medical records and the EGD and EUS images were reviewed by a single investigator. Baseline characteristics were presented as medians and means with standard deviations for continuous variables and as numbers with percentages for categorical variables. Univariate Cox regression analysis was conducted to identify factors associated with significant changes of SETs. All statistical analyses were carried out using IBM SPSS Statistics for Windows version 24.0 (IBM Corp., Armonk, NY, USA). *P* values were two-sided and < 0.05 were considered as statistically significant.

Ethics statement

Ethical approval for this study was obtained from the Institutional Review Board (IRB) of the Asan Medical Center (IRB number: 2018-0884). Informed consent was waived because of the retrospective nature of the study.

https://doi.org/10.3346/jkms.2022.37.e184

RESULTS

Baseline characteristics

The baseline characteristics of the 262 patients with 275 asymptomatic esophageal SETs ≤ 30 mm in size are shown in **Table 1**. The male-to-female ratio was 1.82:1 (169/93) and the median patient age was 52.0 years (range, 16–78 years). The median follow-up period was 40 months (range, 3–158 months), and the median lesion size was 11.9 mm (range, 2.8–30.0 mm). The most common layer of origin was the fourth layer, and the initial size of tumor was < 10 mm, 10–20 mm, and 20–30 mm in 104 (37.8%), 105 (38.2%), and 66 (24.0%) lesions, respectively.

Natural courses of asymptomatic esophageal SETs ≤ 30 mm

Of the 275 esophageal SETs, 22 (8.0%) showed significant changes in size, echogenicity (suggesting malignant transformation), and/or morphology at a median follow-up period of 40 months (range, 4–120 months). Among them, 18 increased in size by ≥ 25% (1 tumor had changes in both size and echogenicity), and 4 showed ulcerative changes (**Table 1**). No consistent growth pattern was observed during follow-up in the SETs showing significant interval changes (**Supplementary Fig. 1A**).

Table 2 documents that age, sex, location, initial size, and the layer of origin were not statistically significant factors associated with tumor changes.

Esophageal SETs with significant interval changes

Fig. 2 indicates the flowchart of 275 small esophageal SETs during follow-up. Of the 22 SETs that had significant interval changes, 8 did not undergo further evaluation for tissue samplings because of loss to follow-up, patient refusal, or technical difficulties. Six underwent EUS-FNAB for pathological diagnosis (1 was identified as a GIST and was surgically resected, while the other 5 were leiomyomas and were regularly observed using

Table 1. Baseline characteristics of all included individuals

Characteristics	Total (262 patients)	With interval changes (22 patients)
No. of SETs	275	22
Age, yr	52.0 (52.7 ± 10.6)	47.5 (45.8 ± 12.4)
Sex (M:F)	169:93	14:8
Follow-up duration, mon	40.0 (51.7 ± 39.8)	51.0 (63.2 ± 39.5)
Location		
Upper third	48 (17.5)	1 (4.5)
Middle third	142 (51.6)	11 (50.0)
Lower third	85 (30.9)	10 (45.5)
Initial size, mm	11.9 (13.6 ± 7.0)	15.0 (13.9 ± 5.5)
< 10	104 (37.8)	6 (27.3)
10–20	105 (38.2)	10 (45.5)
20–30	66 (24.0)	6 (27.3)
Layer on initial EUS		
Second	94 (34.2)	7 (31.8)
Third	14 (5.1)	1 (4.5)
Fourth	167 (60.7)	14 (63.6)
Duration until interval change, mon		40.0 (47.0 ± 28.8)
Significant interval changes		
25–50% increase in size		10
> 50% increase in size		7
Surface ulcerations		4
Increase in size and echogenicity changes		1

Values are presented as median (mean ± standard deviation) or number (%).
SET = subepithelial tumor, M = male, F = female, EUS = endoscopic ultrasound.

https://doi.org/10.3346/jkms.2022.37.e184

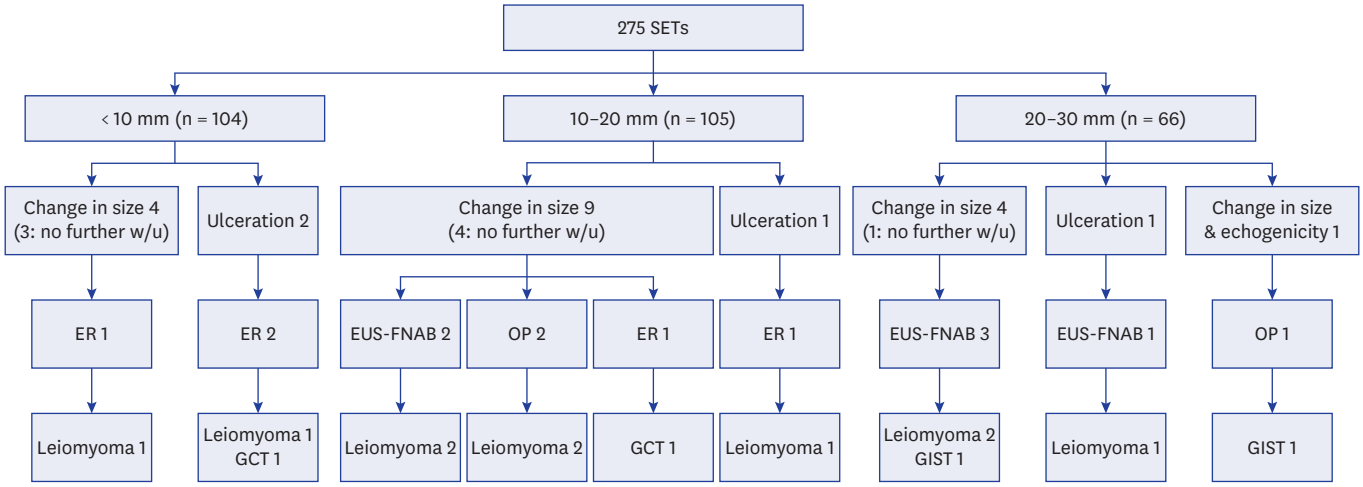

Fig. 2. Flowchart of 275 small esophageal SETs during follow-up.
SET = subepithelial tumor, w/u = work-up, ER = endoscopic resection, EUS-FNAB = endoscopic ultrasound-guided fine needle aspiration biopsy, OP = operation, GCT = granular cell tumor, GIST = gastrointestinal stromal tumor.

Table 2. Factors associated with significant tumor changes

Variables	HR	95% CI	*P* value
Age ≥ 60	0.291	0.068–1.246	0.096
Male	0.827	0.347–1.974	0.669
Location			
Upper third	1.000	Reference	
Middle third	3.334	0.430–25.834	0.249
Lower third	5.832	0.746–45.580	0.093
Initial size, mm			
< 10	1.000	Reference	
10–20	1.557	0.565–4.289	0.392
20–30	1.160	0.373–3.609	0.797
Layer of origin			
Second	1.000	Reference	
Third	0.757	0.093–6.162	0.794
Fourth	0.916	0.370–2.273	0.851

HR = hazard ratio, CI = confidence interval.

EGD or EUS), whereas 8 underwent ER or surgery without pathological confirmation (1 was a GIST, 2 were GCTs, and the other 5 were leiomyomas) (**Table 3**).

The resected SETs had no consistent growth patterns (**Supplementary Fig. 1B**).

DISCUSSION

Management and follow-up of small esophageal SETs are clinically important because some SETs, such as GISTs, have malignant potentials. Several guidelines or management plans for gastric SETs have been published. The American Gastroenterological Association recommended that gastric SETs > 30 mm in size, arising from the muscularis propria, showing hypoechoic echogenicity, and having patterns indicative of malignancy should be resected, whereas SETs ≤ 30 mm in size and without features indicative of malignancy can be observed regularly.[14] The American Society for Gastrointestinal Endoscopy suggested that gastric SETs > 20 mm with malignant features can be removed either surgically or

https://doi.org/10.3346/jkms.2022.37.e184

Table 3. Characteristics of 14 pathologically confirmed subepithelial tumors

No.	Initial size, mm	Duration until interval change, mon	Follow-up size, mm	Echogenicity change	Ulcerative change	Layer of origin	EUS-FNAB	Tx	Pathologic diagnosis
1	8.4	69	8.4	No	Yes	2	No	ER	Leiomyoma
2	20	51	25	Yes (heterogeneity, a cystic space)	No	4	No	OP	GIST, low risk
3	15	36	22	No	No	4	No	OP	Leiomyoma
4	23	4	33	No	No	4	Yes	OP	GIST, low risk
5	9.4	49	11	No	Yes	2	No	ER	GCT
6	11	29	18	No	No	4	No	OP	Leiomyoma
7	15	38	14	No	Yes	2	No	ER	Leiomyoma
8	10	11	13	No	No	2	No	ER	GCT
9	6.1	17	8	No	No	2	No	ER	Leiomyoma
10	20	56	43	No	No	4	Yes	obs	Leiomyoma
11	20	24	20	No	Yes	4	Yes	obs	Leiomyoma
12	15	42	22	No	No	4	Yes	obs	Leiomyoma
13	20	38	25	No	No	4	Yes	obs	Leiomyoma
14	12	24	22	No	No	4	Yes	obs	Leiomyoma

EUS-FNAB = endoscopic ultrasound-guided fine needle aspiration biopsy, Tx = treatment, ER = endoscopic resection, OP = operation, GIST = gastrointestinal stromal tumor, GCT = granular cell tumor, obs = observation.

endoscopically, and suggested surveillance EUS for SETs that were < 20 mm in size.[5] However, GISTs rarely occur in the esophagus, where leiomyomas are most often located; therefore, it is unclear whether these guidelines and management plans can be applied in the management of esophageal SETs.[6,13,17] Furthermore, studies focusing on esophageal SETs are limited.

In this study, we found that 92.0% of asymptomatic esophageal SETs ≤ 30 mm in size showed no significant changes in size, morphology, or echogenicity during a mean period of 51.7 months (median, 40.0 months; range, 3–158 months). Of 22 SETs that showed significant changes during follow-up, 14 were diagnosed pathologically using EUS-FNAB, ER, or surgery and only 2 (0.7%) were diagnosed with GISTs.

Our findings are consistent with previous studies of upper gastrointestinal SETs. Bruno et al.[17] showed that nearly 90% of small (< 30 mm) SETs did not change in size and echogenicity. Kim et al.[18] reported that 91.5% of small (≤ 30 mm) SETs showed no interval changes. However, these studies did not include esophageal SETs. Several studies for SETs containing esophageal tumors have been published. Tio et al.[19] studied 21 small (≤ 30 mm) SETs and reported that all tumors, including 6 esophageal SETs, showed no changes during a follow-up period of 1–3 years. Lim et al.[2] reported that 244 out of 252 SETs (< 30 mm in size), including 104 esophageal tumors, did not show interval changes during a mean period of 59.1 months. Unfortunately, these studies mainly focused on gastric SETs rather than esophageal ones.

Despite EUS being the most valuable diagnostic tool for SETs, as it can be used to evaluate their size, margin, the layer of origin, and echogenicity,[4-6] differentiating between benign and malignant lesions, especially between leiomyomas and GISTs, is challenging, and a pathological confirmation is often required.[5] The diagnostic value of EUS is also relatively lower in SETs < 30 mm in size.[20] EUS can allow tissue samples from SETs to be obtained using EUS-FNAB, which is the most widely used and established tissue sampling method.[5,21] EUS-FNAB can be used for all gastrointestinal tract lesions, with accuracy rates of approximately 80–90%.[22-26] Nevertheless, EUS-FNAB for SETs may often be non-diagnostic owing to insufficient quality or amount of specimen acquired. In our study, of the 22 SETs showing significant changes, 8 SET tissues were obtained using EUS-FNAB, all of which were

https://doi.org/10.3346/jkms.2022.37.e184

diagnostic. Among a total of 275 SETs, 25 EUS-FNAB were performed, and the diagnostic yield was 80.0% (20 out of 25), which were in accordance with findings of previous reports. Five cases whose EUS-FNAB results were non-diagnostic were observed regularly because malignancy was not highly suspected. All showed no significant interval changes at a median follow-up period of 26 months (range, 15–87 months). In cases where EUS-FNAB is non-diagnostic, there are several options as follows: observation if malignancy is not highly suspected, repeating EUS-FNAB, and the unroofing technique (also called deep biopsy after endoscopic mucosal resection or endoscopic submucosal dissection). The diagnostic yield of unroofing technique is reportedly comparable to that of EUS-FANB.[24,27,28] However, complications, such as bleeding and perforation, exist while performing the unroofing technique owing to its invasiveness.[21]

Recently, interest in ER of upper gastrointestinal SET has been increasing with the development of endoscopic techniques.[9-12] In contrast to the relatively high frequency of GISTs in the stomach, the most common subtype of esophageal SETs is leiomyomas. EUS alone is not enough to distinguish malignant from benign stromal cell tumors because it has a sensitivity and specificity of only 64% and 80%, respectively.[29] Since interpreting EUS images is operator-dependent, the interobserver agreement on significant changes was poor in terms of changes in echogenicity indicative of a malignancy (irregular border, echogenic foci, cystic spaces, heterogeneity). Hence, further pathological confirmation is required. Therefore, in many guidelines and algorithms, pathological confirmation is always recommended to establish the basis for tumor resection, and the indications for such pathological confirmation are a tumor size of > 20–30 mm and/or risk of malignant changes.[4,6,30-32] Based on our results, most asymptomatic esophageal SETs ≤ 30 mm in size that were managed by ER or surgery were benign lesions that did not require treatment. In addition, since only 2 out of 22 esophageal SETs that had significant interval changes were GISTs, pathological confirmation should be made prior to ER or surgery, even if significant changes were identified.

To the best of our knowledge, this is the largest single-center study specific to esophageal SETs rather than gastric ones; previous studies of gastrointestinal SETs have primarily focused on gastric ones. Furthermore, we showed that age, initial size, tumor location, and the layer of origin were not statistically significant factors associated with changes in esophageal SETs ≤ 30 mm in size (**Table 2**). Moreover, esophageal SETs ≤ 30 mm in size that had significant interval changes had no consistent growth patterns (**Supplementary Fig. 1**). Of 275 SETs, only 2 (0.7%) were diagnosed as GISTs and their initial sizes were ≥ 20 mm. This implies that endoscopic surveillance for esophageal SETs < 20 mm can be an appropriate management strategy.

Our study has some limitations. First, this was a single-center, retrospective, observational study; therefore, this may limit the generalizability of our findings. Second, not all SETs were followed up using EUS. However, the size of SETs was evaluated using EGD with open biopsy forceps, and this had a reasonable correlation with EUS.[33] Moreover EUS was performed in cases where significant changes were detected. Third, SETs were evaluated by multiple endoscopists. A single investigator reviewed the serial images of EGD and EUS in order to avoid interobserver variations. Finally, of the 22 SETs that showed significant changes during follow-up, 8 were not diagnosed pathologically. Some cases were technically difficult for EUS-FNAB owing to their small size. The other patients either became lost to follow-up or refused further evaluation.

https://doi.org/10.3346/jkms.2022.37.e184

In conclusion, most of esophageal SETs of 30 mm or less in size do not show significant interval changes during long-term follow-up. However, regular follow-up with EGD or EUS may be necessary considering that small portion of esophageal SETs ≤ 30 mm in size has a possibility of malignant potential. When esophageal SETs ≤ 30 mm show significant interval changes, pathological confirmation may precede treatment to avoid unnecessary resection.

SUPPLEMENTARY MATERIAL

Supplementary Fig. 1

Changes in the size of small esophageal SETs within the follow-up period. (**A**) Changes in the size of the 22 esophageal SETs in which significant interval changes were observed. At the initial diagnosis, 6, 10, and 6 measured ≤ 10 mm (black line), 10–20 mm (blue line), and 20–30 mm (red line), respectively. (**B**) Size changes of the 9 resected SETs, of which 2, 2, and 5 were diagnosed as gastrointestinal tumors (red line), granular cell tumors (blue line), and leiomyomas (black line), respectively.

Click here to view

REFERENCES

1. Papanikolaou IS, Triantafyllou K, Kourikou A, Rösch T. Endoscopic ultrasonography for gastric submucosal lesions. *World J Gastrointest Endosc* 2011;3(5):86-94.
PUBMED | CROSSREF
2. Lim YJ, Son HJ, Lee JS, Byun YH, Suh HJ, Rhee PL, et al. Clinical course of subepithelial lesions detected on upper gastrointestinal endoscopy. *World J Gastroenterol* 2010;16(4):439-44.
PUBMED | CROSSREF
3. Ko WJ, Song GW, Cho JY. Evaluation and endoscopic management of esophageal submucosal tumor. *Clin Endosc* 2017;50(3):250-3.
PUBMED | CROSSREF
4. Landi B, Palazzo L. The role of endosonography in submucosal tumours. *Best Pract Res Clin Gastroenterol* 2009;23(5):679-701.
PUBMED | CROSSREF
5. Standards of Practice Committee, Faulx AL, Kothari S, Acosta RD, Agrawal D, Bruining DH, et al. The role of endoscopy in subepithelial lesions of the GI tract. *Gastrointest Endosc* 2017;85(6):1117-32.
PUBMED | CROSSREF
6. Cho JW; Korean ESD Study Group. Current guidelines in the management of upper gastrointestinal subepithelial tumors. *Clin Endosc* 2016;49(3):235-40.
PUBMED | CROSSREF
7. Lee LS, Singhal S, Brinster CJ, Marshall B, Kochman ML, Kaiser LR, et al. Current management of esophageal leiomyoma. *J Am Coll Surg* 2004;198(1):136-46.
PUBMED | CROSSREF
8. Chandrasekhara V, Ginsberg GG. Endoscopic management of gastrointestinal stromal tumors. *Curr Gastroenterol Rep* 2011;13(6):532-9.
PUBMED | CROSSREF
9. Tu S, Huang S, Li G, Tang X, Qing H, Gao Q, et al. Submucosal tunnel endoscopic resection for esophageal submucosal tumors: a multicenter study. *Gastroenterol Res Pract* 2018;2018:2149564.
PUBMED | CROSSREF
10. Kim SY, Kim KO. Endoscopic treatment of subepithelial tumors. *Clin Endosc* 2018;51(1):19-27.
PUBMED | CROSSREF
11. 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(11):3141-8.
PUBMED | CROSSREF

12. Marcella C, Sarwar S, Ye H, Shi RH. Efficacy and safety of endoscopic treatment for gastrointestinal stromal tumors in the upper gastrointestinal tract. *Clin Endosc* 2020;53(4):458-65.
PUBMED | CROSSREF

13. Codipilly DC, Fang H, Alexander JA, Katzka DA, Ravi K. Subepithelial esophageal tumors: a single-center review of resected and surveilled lesions. *Gastrointest Endosc* 2018;87(2):370-7.
PUBMED | CROSSREF

14. Hwang JH, Rulyak SD, Kimmey MB; American Gastroenterological Association Institute. American Gastroenterological Association Institute technical review on the management of gastric subepithelial masses. *Gastroenterology* 2006;130(7):2217-28.
PUBMED | CROSSREF

15. Le BH, Boyer PJ, Lewis JE, Kapadia SB. Granular cell tumor: immunohistochemical assessment of inhibin-alpha, protein gene product 9.5, S100 protein, CD68, and Ki-67 proliferative index with clinical correlation. *Arch Pathol Lab Med* 2004;128(7):771-5.
PUBMED | CROSSREF

16. Joensuu H. Risk stratification of patients diagnosed with gastrointestinal stromal tumor. *Hum Pathol* 2008;39(10):1411-9.
PUBMED | CROSSREF

17. Bruno M, Carucci P, Repici A, Pellicano R, Mezzabotta L, Goss M, et al. The natural history of gastrointestinal subepithelial tumors arising from muscularis propria: an endoscopic ultrasound survey. *J Clin Gastroenterol* 2009;43(9):821-5.
PUBMED | CROSSREF

18. Kim MY, Jung HY, Choi KD, Song HJ, Lee JH, Kim DH, et al. Natural history of asymptomatic small gastric subepithelial tumors. *J Clin Gastroenterol* 2011;45(4):330-6.
PUBMED | CROSSREF

19. Tio TL, Tytgat GN, den Hartog Jager FC. Endoscopic ultrasonography for the evaluation of smooth muscle tumors in the upper gastrointestinal tract: an experience with 42 cases. *Gastrointest Endosc* 1990;36(4):342-50.
PUBMED | CROSSREF

20. Iwahashi M, Takifuji K, Ojima T, Nakamura M, Nakamori M, Nakatani Y, et al. Surgical management of small gastrointestinal stromal tumors of the stomach. *World J Surg* 2006;30(1):28-35.
PUBMED | CROSSREF

21. Akahoshi K, Oya M, Koga T, Shiratsuchi Y. Current clinical management of gastrointestinal stromal tumor. *World J Gastroenterol* 2018;24(26):2806-17.
PUBMED | CROSSREF

22. Vander Noot MR 3rd, Eloubeidi MA, Chen VK, Eltoum I, Jhala D, Jhala N, et al. Diagnosis of gastrointestinal tract lesions by endoscopic ultrasound-guided fine-needle aspiration biopsy. *Cancer* 2004;102(3):157-63.
PUBMED | CROSSREF

23. Bluen BE, Lachter J, Khamaysi I, Kamal Y, Malkin L, Keren R, et al. Accuracy and quality assessment of EUS-FNA: a single-center large cohort of biopsies. *Diagn Ther Endosc* 2012;2012:139563.
PUBMED | CROSSREF

24. Jung YS, Lee H, Kim K, Sohn JH, Kim HJ, Park JH. Using forceps biopsy after small submucosal dissection in the diagnosis of gastric subepithelial tumors. *J Korean Med Sci* 2016;31(11):1768-74.
PUBMED | CROSSREF

25. Hoda KM, Rodriguez SA, Faigel DO. EUS-guided sampling of suspected GI stromal tumors. *Gastrointest Endosc* 2009;69(7):1218-23.
PUBMED | CROSSREF

26. Çağlar E, Hatemi I, Atasoy D, Şişman G, Şentürk H. Concordance of endoscopic ultrasonography-guided fine needle aspiration diagnosis with the final diagnosis in subepithelial lesions. *Clin Endosc* 2013;46(4):379-83.
PUBMED | CROSSREF

27. Vaicekauskas R, Stanaitis J, Valantinas J. Efficacy of deep biopsy for subepithelial lesions in the upper gastrointestinal tract. *Wideochir Inne Tech Malo Inwazyjne* 2016;11(3):192-9.
PUBMED | CROSSREF

28. Choi CW, Hwang JH. Mucosal incision-assisted endoscopic biopsy as an alternative to endoscopic ultrasound-guided fine-needle aspiration/biopsy for gastric subepithelial tumor. *Clin Endosc* 2020;53(5):505-7.
PUBMED | CROSSREF

29. Ji JS, Lee BI, Choi KY, Kim BW, Choi H, Huh M, et al. Diagnostic yield of tissue sampling using a bite-on-bite technique for incidental subepithelial lesions. *Korean J Intern Med* 2009;24(2):101-5.
PUBMED | CROSSREF

30. Kongkam P, Devereaux BM, Ponnudurai R, Ratanachu-ek T, Sahai AV, Gotoda T, et al. Endoscopic ultrasound forum summary from the Asian pacific digestive week 2012. *Endosc Ultrasound* 2013;2(1):43-60.
CROSSREF

31. Nishida T, Blay JY, Hirota S, Kitagawa Y, Kang YK. The standard diagnosis, treatment, and follow-up of gastrointestinal stromal tumors based on guidelines. *Gastric Cancer* 2016;19(1):3-14.
PUBMED | CROSSREF

32. Yegin EG, Duman DG. Small EUS-suspected gastrointestinal stromal tumors of the stomach: an overview for the current state of management. *Endosc Ultrasound* 2016;5(2):69-77.
PUBMED | CROSSREF

33. Hwang JH, Saunders MD, Rulyak SJ, Shaw S, Nietsch H, Kimmey MB. A prospective study comparing endoscopy and EUS in the evaluation of GI subepithelial masses. *Gastrointest Endosc* 2005;62(2):202-8.
PUBMED | CROSSREF