


# Diagnostic yields of endoscopic ultrasound-guided fine-needle tissue acquisition according to the gastric location

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## Abstract

The diagnostic accuracy of endoscopic ultrasound-guided fine-needle tissue acquisition (EUS-FNTA) according to the gastric location of subepithelial tumors (SETs) has not been well established. We aimed to evaluate the efficacy of EUS-FNTA for the diagnosis of gastric SETs according to tumor location.

Thirty-three patients diagnosed with gastric SETs via EUS-FNTA from January 2016 to May 2018 were analyzed retrospectively. Patient demographics, diagnostic yields, and complications were evaluated.

Nineteen patients (57.6%) were female, with a mean age of 57.7 years. Endoscopic ultrasound revealed a mean longitudinal diameter of 25.6 mm. The most common location of SETs was in the gastric body (n = 18, 54.5%), followed by cardia and fundus (n = 10, 30.3%), and antrum (n = 5, 15.2%). A 20-gauge biopsy needle was most frequently used (90.9%). The diagnostic yield was obtained in 23 patients (69.7%). The most common diagnosis was gastrointestinal stromal tumor (73.9%), followed by leiomyoma (17.4%). The diagnostic yield of SETs in gastric antrum (0/5, 0%) was significantly lower than that in the gastric body and cardia (23/28, 82.1%,  $P = .001$ ). A case of immediate bleeding after EUS-FNTA occurred in 1 patient (3.0%) who recovered uneventfully. According to related literature, the overall diagnostic yield of SETs in gastric antrum was significantly lower than that in the gastric body, fundus, and cardia (29.7% vs 71.4%,  $P < .001$ , n = 191).

EUS-FNTA is ineffective in the diagnosis of SETs in the gastric antrum. Although EUS-FNTA is an advanced diagnostic tool for gastric SETs, it is essential to develop more effective methods for the diagnosis of antral SETs.

**Abbreviations:** EUS = endoscopic ultrasound, EUS-FNTA = EUS-guided fine-needle tissue acquisition, GIST = gastrointestinal stromal tumor, SET = subepithelial tumor.

**Keywords:** endoscopic ultrasound-guided fine needle aspiration, gastrointestinal stromal tumors, pyloric antrum, stomach

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## 1. Introduction

Gastric subepithelial tumors (SETs) encompass an extensive range of benign, premalignant, and malignant lesions. SETs are typically concealed by the mucosa. The word “submucosal tumor” is a misleading term, as these lesions are not always confined to the submucosa and instead may originate in both intramural and extramural locations.<sup>[1]</sup> Although these lesions are considered rare, gastric SETs are quite frequently seen as incidental findings in gastroscopy.<sup>[2,3]</sup> Many SETs are benign<sup>[4,5]</sup>; however, gastric SETs may be premalignant or malignant lesions, such as gastrointestinal stromal tumors (GISTs). Although endoscopic ultrasound (EUS) criteria have been used to differentiate GISTs from leiomyomas,<sup>[6]</sup> histopathology is still considered the gold standard.<sup>[7]</sup> GISTs are mesenchymal neoplasms with a characteristic immunohistological expression of c-kit (CD117) that distinguishes them from other benign spindle cell neoplasms, such as leiomyomas or schwannomas.<sup>[8,9]</sup>

Tissues from SETs within the second or third layer as seen in EUS can be acquired via large biopsies and endoscopic mucosal resection techniques. However, tissue acquisition is difficult for tumors within the fourth layer. EUS-guided fine-needle tissue acquisition (EUS-FNTA) is an advanced technique used for the differentiation of GISTs and leiomyomas, especially for those within the fourth layer.<sup>[10]</sup>

Each part of the stomach has a different wall thickness, and when a needle enters, the force required to penetrate the mucosal or submucosal layer also varies. In the case of the gastric antrum, tissues are often obtained when the stomach is pushed by an endoscope. This suggests that there may be a difference in the tissue acquisition rate when EUS-FNTA is performed for each gastric location.

Until now, the diagnostic accuracy of EUS-FNTA according to the gastric location of SETs has not been well established. Therefore, we investigated whether there is a difference in the tissue acquisition rate of EUS-FNTA for each part of the stomach.

## 2. Methods

### 2.1. Ethical considerations

This study was conducted in accordance with the ethical guidelines of the Declaration of Helsinki. This study was approved by the Institutional Review Board of Chonnam National University Hospital (IRB No: CNUH-2019-005, approval date: 2019-01-09).

### 2.2. Patients and study protocol

This study is a retrospective study involving 33 patients with gastric SETs who underwent EUS-FNTA at Chonnam National University Hospital from January 2016 to May 2018. Patient demographics, location and size of SETs, EUS findings, methods of EUS-FNTA, diagnostic yield, and complications were evaluated.

### 2.3. Definition

We divide the gastric location into 3 areas: upper third, middle third, and lower third. Fundus and cardia were classified in the upper third area of the stomach. Corpus was designated as the middle third area of the stomach. Antrum and pylorus were defined as the lower third of the stomach.

EUS-guided FNTA comprises both EUS-guided fine-needle aspiration and EUS-guided fine-needle biopsy.

### 2.4. Endoscopic procedure

The EUS Probe (UM-2R; Olympus, Tokyo, Japan) and probe driving unit (MAJ-935; Olympus) were used to map the lesion. The image frequency of the probe was 12 MHz. EUS-guided FNTA was performed with a linear array echoendoscope (GF-UCT260; Olympus) and probe driving unit (MAJ-1720; Olympus). Under ultrasound guidance, SETs were punctured with 19-, 20-, 22-, or 25-gauge needles (EchoTip ProCore, Cook Medical Inc, Bloomington, IN; EchoTip Ultra, Cook Medical; EZ Shot3 Plus, Olympus). After visualizing the tip of the catheter, the needle was advanced from the catheter sheath through the wall of the gastrointestinal (GI) tract and into the target lesions under ultrasound guidance. The stylet was removed, and the initial passes were performed by moving the needle back and forth within the target lesion for 15 to 30 seconds. No suction was applied during biopsy unless the biopsy failed to yield any material or if the lesion was cystic.

### 2.5. Histopathology

The biopsy specimens were transferred onto the glass slides by flushing air into the needle assembly. The needle was reintro-

duced until an adequate number of biopsy specimens were obtained, as determined by an endosonographic specialist based on gross inspection. The biopsy specimens were transferred into a formalin bottle. Cytological smears with aspirated specimens were also prepared. The smeared slides were fixed with alcohol. The biopsy and aspiration slides of all the cases were evaluated and reviewed by an experienced GI pathologist. Immunohistochemical staining was performed for the differential diagnosis of gastric SETs whenever necessary. An immunohistochemical study was performed to determine the expression of CD 34, CD 117, S100, and smooth muscle actin in the spindle cell lesion placed on the H&E slides. A diagnostic procedure, including immunohistochemical staining, was done depending on the adequacy of the number of biopsy specimens or cytological aspirates.

### 2.6. Statistical analysis

Statistical analysis was performed using IBM-SPSS version 23.0 (SPSS Inc, IBM, Chicago, IL). Continuous data are expressed as the mean  $\pm$  standard deviation or medians (ranges) and categorical data as absolute and relative frequencies. Continuous variables were analyzed using a Student *t* test. Categorical data were examined using Fisher exact test or  $\chi^2$  test with Yates correction.

## 3. Results

### 3.1. Baseline characteristics of the enrolled patients

Nineteen patients (57.6%) were female, with a mean age of 57.7  $\pm$  13.2 years. EUS revealed mean longitudinal diameters of 25.6 mm. The most common endoscopic finding was an intact mucosa (81.8%), followed by ulceration (9.1%), dimpling (6.1%), and erosion (3.0%). The fourth layer (muscularis propria, 54.5%) was the most common layer of SETs, followed by the third layer (submucosa, 21.2%) and the outer wall (serosa, 6.1%). The most common location of SETs in the stomach was the middle third ( $n=18$ , 54.5%) followed by the upper third ( $n=10$ , 30.3%) and the lower third ( $n=5$ , 15.2%). The longitudinal diameter of SETs was 25.6  $\pm$  12.8 mm (range, 11–52 mm). The transverse axis diameter of SETs was 19.3  $\pm$  12.8 mm (range, 10–45 mm). A 20-gauge needle (EchoTip ProCore) was used most frequently (90.9%), and 19-, 22-, and 25-gauge needles were used in each case.

A mild degree of immediate bleeding after EUS-FNTA occurred in 1 patient (3.0%), with which we performed endoscopic hemoclippping to achieve hemostasis.

The diagnostic yield was obtained in 23 patients (69.7%). The most common diagnosis was GIST (73.9%) followed by leiomyoma (17.4%). The diagnostic yield of SETs in the lower third area (0/5, 0%) was significantly lower than that in the upper third and middle third areas (23/28, 82.1%,  $P=.001$ ) (Table 1).

### 3.2. Comparative analysis of EUS, EUS-FNTA, and surgery or endoscopic resection

Using EUS, GIST was the most frequently observed ( $n=23$ , 69.7%), followed by neuroendocrine tumor ( $n=2$ , 6.1%), leiomyoma ( $n=2$ , 6.1%), and ectopic pancreas ( $n=2$ , 6.1%). Fine-needle biopsy resulted in a histopathologic diagnostic yield in 20 patients (60.6%), with GIST ( $n=14$ ), leiomyoma ( $n=3$ ),

**Table 1**  
**Comparison of patients with SETs according to gastric location.**

	Total (N=33)	Upper + middle third (N=28, %)	Lower third (N=5, %)
Age, yrs (mean ± SD)	57.7 ± 13.2	57.1 ± 13.1	60.8 ± 14.9
Female, n (%)	19 (57.6)	16 (57.1)	3 (60)
Male, n (%)	14 (42.4)	12 (42.9)	2 (40)
Endoscopic finding			
Intact mucosa	27 (81.8)	24 (85.7)	3 (60)
Ulceration	3 (9.1)	2 (7.1)	1 (20)
Dimpling	2 (6.1)	2 (7.1)	
Erosive mucosa	1 (3.0)		1 (20)
Layer			
3th layer	7 (21.2)	6 (21.4)	1 (20)
4th layer	18 (54.5)	16 (57.1)	2 (40)
Outer wall	2 (6.1)	2 (7.1)	
Not clearly identified	6 (18.2)	4 (14.3)	2 (40)
Location			
Cardia and fundus	10 (30.3)	10 (35.7)	
Corpus	18 (54.5)	18 (64.3)	
Antrum	5 (15.2)		5 (100)
Size (mm × mm)			
Longitudinal diameter	25.6 ± 12.8	25.8 ± 13.3	24.0 ± 10.7
Transverse axis	19.3 ± 12.8	19.6 ± 13.7	18.1 ± 7.3
Complications			
bleeding	1 (3.0)	1 (3.6)	0
Needle size			
20 gauge	30 (90.9)	26 (92.9)	4 (80)
19 gauge	1 (3.0)	1 (3.6)	
22 gauge	1 (3.0)	1 (3.6)	
25 gauge	1 (3.0)		1 (20)
Frequency of needle passage	2.78 ± 0.88	2.79 ± 0.88	3.6 ± 0.55

SD = standard deviation, SET = subepithelial tumor.

ectopic pancreas (n=2), and chronic gastritis (n=1) as the diagnoses. Fine-needle aspiration resulted in a histopathologic diagnostic yield in 7 patients (21.2%), with spindle cell lesions (n=4), epithelioid lesions (n=1), a benign epithelial cell (n=1), and an ectopic pancreas (n=1) as the diagnoses.

There was no statistical significance in the diagnostic yield between SETs measuring more than 2 cm (17/22, 77.3%) and SETs less than 2 cm (6/11, 54.5%,  $P=.181$ ). In addition, there was no statistical significance in the diagnostic yield between SETs larger than 3 cm (7/10, 70%) and those less than 3 cm (16/23, 69.6%,  $P=.98$ ).

Diagnostic concordance between EUS-FNTA compared with that of endoscopic or surgical resection was 100% (12/12). Concordance of EUS only compared with that of endoscopic or surgical resection was 82.4% (14/17). The concordance of EUS-FNTA compared with that of EUS only was 48.5% (16/33) (Table 2).

#### 4. Discussion

SETs can be identified via endoscopy or EUS. In endoscopy, the size of the tumor and presence of the pillow sign can be evaluated. Meanwhile, EUS can be used to distinguish intramural from extramural lesions, as well as see the specific layer where the tumors originated and their echogenicity. However, the diagnostic accuracy of EUS is relatively low, especially without histologic confirmation.<sup>[7,11]</sup> The concordance of EUS with histology is only about 43% to 66.7%.<sup>[7,11]</sup> In our study, the agreement between EUS-FNTA and EUS (48.5%, 16/33) was similar to that of a previous study.

SETs can be histologically diagnosed via both endoscopic and surgical resection.<sup>[12,13]</sup> Recently, new techniques such as endoscopic full-thickness resection and endoscopic submucosal tunnel resection were developed to remove SETs in deeper layers, which was normally difficult with conventional methods.<sup>[14,15]</sup> However, it is not always easy to perform histological diagnosis via endoscopic or surgical resection for all benign-looking lesions because of their invasiveness and considerable complication rates. Therefore, EUS-FNTA is a reasonable and viable option for histologic confirmation of SETs.<sup>[16,17]</sup>

Several studies have already confirmed the utility of EUS-FNTA.<sup>[18–21]</sup> EUS-guided fine-needle biopsy for suspected GI stromal tumors is technically similar and has an equivalent safety profile to that of simple fine-needle aspiration biopsy, with even better tissue acquisition.<sup>[18]</sup> Needles of various sizes ranging from 19- to 25-gauge are used to perform EUS-FNTA.<sup>[10,19,22,23]</sup> It was assumed that the large-bore needles, such as the 19-gauge needle, might increase the diagnostic yield of SETs compared with small-bore needles. However, in a previous study, the 19-gauge needle showed no superiority compared with 22-gauge needles.<sup>[10]</sup> Various needle passage frequencies (1 to 7) were used in other studies.<sup>[10,22]</sup> To date, however, no clear consensus is available regarding the optimal frequency. In the present study, the mean frequency of needle passage was 2.78, which is similar to that of other studies.

In this study, the histopathological diagnosis of gastric SETs based on FNTA in 33 cases was analyzed. GIST was identified as the most common cause of SETs. The diagnostic yield was 69.7% (23/33), with the reliability of the diagnostic yield with EUS-FNTA at 100% (12/12). EUS-FNTA was more accurate

**Table 2**  
**Comparison of cases diagnosed by EUS, EUS-FNTA, and surgery or ESD.**

Patient number	Site of SET	Size (mm × mm)	EUS	EUS-FNTA	Needle Gauge	Model of FNTA needle	Operation or ESD
1	Cardia	52 × 45	GIST	Leiomyoma	20	ProCore	Leiomyoma
2	Antrum	40 × 30	GIST	Undiagnostic	20	ProCore	Ectopic pancreas
3	Cardia	20 × 20	AGC, Bormann IV	Undiagnostic	19	Ultra	Chronic gastritis
4	Corpus	12 × 5	NET	Undiagnostic	20	ProCore	NET
5	Cardia	39 × 20	Leiomyoma	Undiagnostic	20	ProCore	Leiomyoma
6	Corpus	20 × 15	Leiomyoma	Undiagnostic	20	ProCore	Leiomyoma
7	Corpus	16 × 11	GIST	GIST	20	ProCore	GIST
8	Corpus	13 × 8	GIST	GIST	20	ProCore	GIST
9	Corpus	21 × 19	GIST	GIST	20	ProCore	GIST
10	Corpus	30 × 28	GIST	GIST	20	ProCore	GIST
11	Fundus	25 × 15	GIST	GIST	20	ProCore	GIST
12	Corpus	20 × 18	GIST	GIST	20	ProCore	GIST
13	Corpus	34 × 24	GIST	GIST	20	ProCore	GIST
14	Corpus	32 × 28	GIST	GIST	20	ProCore	GIST
15	Corpus	25 × 15	GIST	GIST	20	ProCore	GIST
16	Corpus	25 × 22	GIST	GIST	20	ProCore	GIST
17	Cardia	13 × 11	GIST	GIST	20	ProCore	GIST
18	Corpus	30 × 15	Pancreatic tail cancer	GIST	20	ProCore	N/A
19	Corpus	70 × 70	GIST	GIST	20	ProCore	N/A
20	Cardia	23 × 9	GIST	Leiomyoma	20	ProCore	N/A
21	Corpus	15 × 10	Early gastric cancer	Undiagnostic	20	ProCore	N/A
22	Cardia	23 × 12	GIST	Ectopic pancreas	20	ProCore	N/A
23	Antrum	15 × 15	Ectopic pancreas	Undiagnostic	20	ProCore	N/A
24	Corpus	29 × 11	NET	Leiomyoma	22	EZ Shot	N/A
25	Corpus	25 × 20	GIST	Leiomyoma	20	ProCore	N/A
26	Antrum	17 × 13	GIST	Undiagnostic	25	ProCore	N/A
27	Cardia	16 × 14	Ectopic pancreas	Chronic gastritis	20	ProCore	N/A
28	Antrum	18 × 12	GIST	Undiagnostic	20	ProCore	N/A
29	Antrum	30 × 20	Gastritis cystica profunda	Undiagnostic	20	ProCore	N/A
30	Cardia	48 × 44	GIST	GIST	20	ProCore	N/A
31	Corpus	21 × 14	GIST	GIST	20	ProCore	N/A
32	Corpus	16 × 15	GIST	GIST	20	ProCore	N/A
33	Cardia	11 × 10	GIST	GIST	20	ProCore	N/A

AGC=advanced gastric cancer, ESD=endoscopic submucosal dissection, EUS-FNTA=endoscopic ultrasound-guided fine-needle tissue acquisition, EZ Shot=EZ Shot3 Plus, GIST=gastrointestinal stromal tumor, N/A=not available, NET=neuroendocrine tumor, Procore=EchoTip ProCore, Ultra=EchoTip Ultra

compared with EUS only (82.4%, 14/17). The concordance between EUS and EUS-FNTA was relatively low (48.5%, 16/33).

In our study, the needle passage was more frequent in the lower third area (3.6) than that in the upper to middle third areas (2.79). However, the diagnostic yield of SETs obtained via EUS-FNTA in the lower third of the gastric region was very low (0/5). On the other hand, a considerable diagnostic yield of SETs was obtained with EUS-FNTA in the upper to middle third of the stomach (23/28, 82.1%). Three studies have previously reported the diagnostic yields of EUS-FNTA according to the gastric location.<sup>[10,24,25]</sup> Eckardt et al<sup>[10]</sup> showed lower diagnostic yield

in the lower third area (36.4%) compared with the upper to middle third of the stomach (75%,  $P=.008$ ). Lee et al (25% vs 59%,  $P=.183$ ) and Suzuki et al (33.3% vs 80.5%,  $P=.013$ ) also showed a lower diagnostic yield in the lower third area compared with the upper to middle third area of the stomach.<sup>[24,25]</sup> Similar to these studies, we have identified in our study that the diagnostic yield was significantly lower in the lower third area compared with the upper to middle third areas (29.7% vs 71.4%,  $P<.001$ ,  $n=191$ ) (Table 3).

The 2 most common causes of nondiagnostic EUS-FNTA were insufficient tissue acquisition and puncture failure in the gastric

**Table 3**  
**Review of 4 original studies showing diagnostic rates of EUS-FNTA by gastric location.**

Case (n)	Biopsy needle (gauge)	Size of SET (median) (mm)	Diagnostic rate depending on location of SET (%)			Upper + middle vs Lower	References
			Upper third	Middle third	Lower third		
46	19G	24	10/12 (83.3)	8/12 (66.7)	8/22 (36.4)	.008	Eckardt <sup>[10]</sup>
65	TCB	37	15/26 (57.7)	21/35 (60)	1/4 (25)	.183	Lee <sup>[24]</sup>
47	22G or Echo tip	N/A	22/26 (84.6)	11/15 (73.3)	2/6 (33.3)	.013	Suzuki <sup>[25]</sup>
33	20G (90%)	26	8/10 (80)	15/18 (83.3)	0/5 (0)	<.001	Our case
191			55/74 (74.3)	55/80 (68.8)	11/37 (29.7)	<.001	

EUS-FNTA=endoscopic ultrasound-guided fine-needle tissue acquisition, G=gauge, N/A=not available, SET=subepithelial tumor, TCB=true cut biopsy.

wall. The antral wall of the stomach is known to be relatively thicker than that of the corpus or cardia. Lee et al<sup>[24]</sup> reported that the puncture failure rate was relatively higher in the lower third area (50%) compared with the upper to middle third areas (11.4%) of the stomach. These results suggested that thickening of the gastric wall influences the diagnostic yields of EUS-FNTA. Adequate needle gauge and frequency of needling therefore vary depending on the location of the SETs. Suzuki et al<sup>[25]</sup> suggested that it was more difficult to stably maintain a scope in the lower third area of the stomach. In addition, it is known that ectopic pancreas is more frequently detected in the antrum than it is in the corpus or cardia.<sup>[26–29]</sup> Ectopic pancreas is a heterogeneous lesion associated with muscular wall thickening; therefore, it might be difficult to obtain adequate tissue from ectopic pancreas using EUS-FNTA.<sup>[30]</sup>

Recently, an electrocautery-enhanced delivery system was applied to facilitate self-expandable metal stent insertion under combined endoscopic and EUS guidance.<sup>[31–33]</sup> EUS-FNTA needle with an electrocautery function may enhance the penetration for thick gastric antral wall and reduce the mechanical force to the wall. The electrocautery function can also overcome the difficulty in sampling the gastric antrum procedure to obtain a better sample rate.

Our study has several limitations. First, the sample size included in our study was relatively small compared with previously reported studies.<sup>[10,24,25,34,35]</sup> Second, it was a single-center study with a retrospective design based on observational data. Therefore, the possibility of selection bias exists, and the quality of the data may not be sufficient to draw an appropriate conclusion. Lastly, in the absence of on-site cytopathologists during the EUS-FNTA procedure, the specimen adequacy was only assessed macroscopically by endosonographic specialists.

## 5. Conclusion

Although EUS-FNTA is a good method facilitating the diagnosis of gastric SETs, it is essential to develop more effective methods for the diagnosis of antral SETs.

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## Author contributions

All authors have read and approved this manuscript. DHK developed the concept of the study, analyzed electronic medical records, and wrote the manuscript. C-HP made substantial contributions to the conception and design of the study, interpreted data, wrote the paper, and revised it critically for intellectual contents. S-YP, EC, HSK, and SKC performed the literature review and collected clinical data. All authors (DHK, C-HP, S-YP, EC, HSK, and SKC) have read and approved the final manuscript.

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