

Diagnostic ability of a 22G Franseen needle in endoscopic ultrasound-guided fine needle aspiration of subepithelial lesions

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Abstract. The differential diagnosis of gastrointestinal subepithelial lesions (SELs) such as gastrointestinal stromal tumors from other benign tumors is important. In the present study, adequate sample rates of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) with a 22G Franseen needle for SELs were evaluated. The present study included 57 consecutive lesions (61 sessions) of EUS-FNA using a 22G needle to evaluate SELs between July 2013 and October 2017. Adequate sample rates were compared retrospectively between a 22G conventional needle group (C group) and a 22G Franseen needle group (F group). The overall adequate sample rate was 80.3%. The adequate sample rates in the C and F groups were 75.0% (33/44) and 94.1% (16/17), respectively ($P=0.15$). For lesions ≥ 20 mm, the adequate sample rates were 82.8% (24/29) in the C group and 91.7% (11/12) in the F group, 8.9% higher in the F group. However, for lesions <20 mm, the adequate sample rates were 60% (9/15) in the C group and 100% (5/5) in the F group, 40% higher in the F group ($P=0.65$, 0.26). In conclusion, the results of the present study suggested that using a 22G Franseen needle for EUS-FNA evaluation of SELs may improve adequate sample rates in small lesions <20 mm in diameter.

Introduction

Gastrointestinal subepithelial lesions (SELs) are often found incidentally on esophagogastroduodenoscopy (EGD) (1). Gastrointestinal stromal tumors (GISTs) may require treatment intervention, whereas benign lesions such as leiomyomas and

neurilemmomas can often be followed up. Therefore, the differential diagnosis of GISTs from benign lesions is important in deciding treatment strategy (2,3).

Follow-up observation has previously been recommended for GISTs <20 mm in diameter, but because of possible occult malignancy, surgery for smaller lesions <20 mm is now recommended in principle (4,5). Diagnosis of a small GIST by conventional endoscopic biopsy and imaging can be difficult. Thus, endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) to acquire tissue samples for immunohistological diagnosis is essential (6).

EUS-FNA to evaluate SELs is useful (7), and although tissue collection from small lesions <20 mm has been reported, the adequate sample rates have been slightly low (8). EUS-FNA with a 19G needle can be valuable for histologic diagnosis, since an adequate tissue sample is likely to be obtained for immunostaining (9,10). However, because a 19G needle is stiffer than a 22G needle, the difficulty of adequately positioning the scope, and in particular, the angulation of the needle relative to the scope, makes lesion puncture more difficult (11). This led to design of a thin needle to acquire adequate tissue, and in 2016, the Franseen needle was developed to improve diagnostic performance (12).

This study evaluated diagnostic accuracy rates of EUS-FNA for SELs and compared adequate sample rates between a 22G conventional needle and a 22G Franseen needle. In particular, utility for lesions <20 mm in diameter was compared.

Materials and methods

The present study was approved by the Ethical Review Board at Saitama Medical University International Medical Center (Saitama, Japan) and complied with the Declaration of Helsinki, as revised in Brazil 2013. All patients provided written, informed consent for EUS-FNA. This study included 57 consecutive lesions (61 sessions) of EUS-FNA using a 22G conventional needle or a 22G Franseen needle to evaluate SELs at our medical center between July 2013 and October 2017. Patient data were retrospectively analyzed. The primary endpoint of this study was to compare adequate sample rates between a 22G conventional needle group and a 22G Franseen needle group. The secondary endpoint was to compare

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other data, including tumor size, procedure time, number of punctures, and tumor site.

EUS-FNA procedures. EUS-FNA procedures were performed using a convex linear-array echoendoscope (GF-UCT260; Olympus Optical Co Ltd, Tokyo, Japan) paired with an ultrasound machine (EU-ME2 Premier Plus; Olympus Optical Co Ltd). EUS was performed with the patient under conscious sedation using intravenous midazolam and pethidine hydrochloride. After excluding regional or collateral vasculature, the mass was punctured. The stylet was removed, and continuous suction was applied with a 20-ml syringe.

Then, 20–30 rapid strokes were made within the lesion, suction was released, and the needle was removed. The aspirated samples were smeared onto glass slides by inserting the stylet and applying air pressure. The samples were examined visually for white color and then fixed in formalin for histologic examination.

Because on-site cytological examination was not performed, EUS-FNA was repeated whenever the procedure could be continued under our supervision with a cytology technician until there was visual confirmation of an adequate sample for histopathology and immunostaining.

The puncture needles used were a 22G conventional needle (C group) and a 22G Franseen needle (F group). Expect® (Boston Scientific Japan, Tokyo, Japan) was used in the C group, and Acquire® (Boston Scientific Japan) was used in the F group (Fig. 1). The C needle was primarily used in patients between July 2013 and December 2016, and the F needle was primarily used in patients thereafter. EUS-FNA procedures were performed by five endoscopists. Three endoscopists were trainees, and two were experienced in performing EUS-FNA. The three trainee endoscopists had sufficient experience, having conducted more than 1,000 regular EGDs, 500 colonoscopies, and 20 EUS procedures. They had also attended 20 EUS-FNA procedures performed by EUS-FNA experts as assistants. The two expert endoscopists had performed regular EGD, colonoscopy, and EUS procedures. They had performed more than 50 EUS-FNA procedures before the beginning of this study.

Histological evaluation. EUS-FNA specimens were fixed in 10% formalin and embedded in paraffin. Sections were stained with hematoxylin and eosin (H&E) for histologic examination, and immunostaining was performed. These were examined by two pathology technicians and two pathologists. Only the histologic diagnosis was analyzed in this study. Immunohistochemical (IHC) staining was subsequently performed. A diagnosis of GIST was made by positive c-kit staining, with or without positive CD34 and DOG-1 IHC staining. Leiomyoma was diagnosed by positive desmin staining, and schwannoma was diagnosed by positive S-100 staining. The results of IHC were described as positive or negative. Positive IHC staining was defined as staining of >50% of the tumor cells. Negative IHC staining was defined as either focal positivity or staining of <50% of the tumor cells.

Study definitions. Adequate samples were defined as samples sufficient for immunohistological examination. The final diagnosis was based on postoperative histopathology of lesions



Figure 1. A novel 22-gauge Franseen needle with 3 tips for puncture.

that were surgically resectable. When a diagnosis could not be made on the first examination, EUS-FNA was performed in the second session if the patient agreed.

Statistical analysis. Categorical variables are expressed as absolute (*n*) and relative (%) frequencies, and they were compared using Fisher's exact test. For comparisons of continuous data, a 2-sample t-test was used if a normal distribution was likely, and the Mann-Whitney test was used if normality could not be demonstrated. $P < 0.05$ was considered to indicate a statistically significant difference. Statistical calculations were performed using SAS 9.4 and SAS JMP 12.2.0 for Windows (SAS Institute Inc, Cary, NC, USA).

Results

Median age, tumor size, number of punctures, and procedure time were 67.0 years, 23.9 mm, 3 times, and 25.0 min, respectively (Table I). Among the 57 lesions, the most common FNA diagnosis was GIST in 32 patients, followed by leiomyoma in 9 patients. In 10 patients, there was insufficient material for an FNA diagnosis (Table II). Among the 10 lesions without a definitive diagnosis, 5 were <20 mm in size.

Consent for surgery was obtained from 26 patients who had a preoperative FNA diagnosis of GIST or other suspected malignancy. The postoperative diagnosis in these patients was GIST in 22, schwannoma in 2, lymph node metastases from esophageal cancer in 1, and other in 1 patient. None of the patients had any EUS-FNA-related complications.

The diagnostic accuracy rate of EUS-FNA for GIST was 95.5% (Table III). The overall adequate sample rate was 80.3%; the rates by lesion site were esophagus 100% (5/5), stomach 78.2% (43/55), and rectum 100% (1/1).

A comparison of patient characteristics between the C group and the F group showed no significant differences in age, sex, tumor size, or tumor site (Table I). The overall adequate sample rates in the C group and the F group were 75.0% (33/44) and 94.1% (16/17), respectively. Although the difference was not significant, the adequate sample rate tended to be higher in the F group. It was possible to collect specimens in both groups even for tumors located on the greater curvature side in the stomach (Table IV).

The adequate sample rates were also compared based on tumor size. For lesions ≥ 20 mm, the adequate sample rates were 82.8% (24/29) in the C group and 91.7% (11/12) in the F group, 8.9 percentage points higher in the F group. However,

Table I. Clinical features of patients and outcomes of endoscopic ultrasound-guided fine needle aspiration.

Variable	All	C group	F group	P-value
Sex, male/female	37/24	27/17	10/7	>0.99
Age (years), median (IQR)	67.0 (58.0-74.5)	67.0 (55.0-74.8)	72.0 (58.5-74.5)	0.71
Tumor size (mm), median (IQR)	23.9 (17.3-33.0)	23.9 (16.4-30.8)	26.7 (19.7-40.2)	0.47
Number of punctures, median (IQR)	3 (3-4)	3 (3-4)	3 (3-4)	0.55
Procedure time (min), median (IQR)	25.0 (18.5-32.0)	25.5 (18.0-32.0)	23.0 (19.0-32.0)	0.96

IQR, interquartile range; C group, conventional needle group; F group, Franseen needle group.

Table II. Endoscopic ultrasound-guided fine needle aspiration diagnoses.

EUS-FNA diagnosis	No. of lesions (%)
GIST	56.1 (32)
Schwannoma	3.5 (2)
Leiomyoma	15.8 (9)
Ectopic pancreas	3.5 (2)
Lymph node metastasis	1.8 (1)
Lipoma	1.8 (1)
Insufficient material	17.5 (10)

EUS-FNA, endoscopic ultrasound-guided fine needle aspiration; GIST, gastrointestinal stromal tumor.

Table III. Final diagnoses.

Final diagnosis	Accuracy of EUS-FNA, % (n of total)
GIST	95.5 (21/22)
Other tumors	50 (2/4)
Overall	88.5 (23/26)

GIST, gastrointestinal stromal tumor; EUS-FNA, endoscopic ultrasound-guided fine needle aspiration.

for lesions <20 mm, the adequate sample rates were 60% (9/15) in the C group and 100% (5/5) in the F group, 40 percentage points higher in the F group ($P=0.65$, 0.26). Thus, the adequate sample rate was markedly higher in the F group for lesions <20 mm in diameter (Table IV). Although there were a few cases of examination, even trainee endoscopists could collect adequate samples (Table V).

Discussion

EUS-FNA is a useful, minimally invasive procedure for tissue acquisition from SELs, with reported diagnostic accuracy rates of 52-92% (13-18). GISTs ≥ 20 mm in diameter are associated with a high rate of metastases, and previous guidelines

recommended surgery only for lesions ≥ 20 mm (19). However, a more recent study of 43 surgical cases found that, even for tumors <20 mm, 23% were at intermediate risk for possible metastases based on modified Fletcher criteria (8). Liver metastases after surgery for GISTs <20 mm have also been reported (20).

Furthermore, with the increase in minimally invasive procedures such as laparoscopic and endoscopic cooperative surgery (LECS) (21), primary surgical resection is now being recommended for resectable GISTs without metastases regardless of size (22). Therefore, the need for diagnosis and treatment of smaller SELs is increasingly being recognized. This calls for improved diagnostic performance of EUS-FNA, but the sensitivity for lesions <20 mm has been insufficient (8).

Novel needles, including those with a side hole (23) and fork-tip (14), have recently been developed for use in EUS-FNA. Despite the increase in needle options, no specific needle has been uniformly adopted. The needle sizes mainly used are 19G, 22G, and 25G, and although a 19G needle may provide sufficient tissue, strong puncture resistance can make using a 19G needle very difficult, especially in smaller lesions. Therefore, a 22G needle is more commonly used for EUS-FNA.

The 22G Franseen needle used in the present study provided a high adequate sample rate and was particularly useful for lesions <20 mm. The Franseen needle has 3 tips to puncture and grip tissue and 3 cutting planes to cut tissue for sample acquisition. This enables acquisition of an adequate tissue sample (12).

In our view, EUS-FNA is indicated for SELs larger than 10 mm. Using the current EUS-FNA system including needles, it is difficult to puncture SELs smaller than 10 mm (8), and metastatic lesions have not been reported in a small tumor.

This study was a retrospective analysis of a single-center experience with EUS-FNA to evaluate gastrointestinal SELs at our medical center, including a comparison of utility between a conventional needle and Franseen needle to evaluate smaller SELs.

The overall adequate sample rate for FNA diagnosis of SELs at our medical center was 80.3%, which is similar to previously reported studies. In patients in whom sample acquisition was difficult, factors besides needle selection and lesion size, including differences in lesion site and differences in disease type, may have had an influence. Therefore, further investigation is needed. In an analysis limited to cases in which a final diagnosis was possible, the diagnostic accuracy

Table IV. Comparison of endoscopic ultrasound-guided fine needle aspiration outcomes between the Franseen needle group and the conventional needle group.

Obtaining an adequate specimen, n (%)	All (%)	C group (%)	F group (%)	P-value
Location				
Esophagus	5/5 (100)	5/5 (100)	-	>0.99
Stomach	43/55 (78.2)	28/39 (71.8)	15/16 (93.8)	0.15
Greater curvature side	19/22 (86.4)	11/14 (78.6)	8/8 (100)	0.27
Lesser curvature side	24/33 (72.7)	17/25 (68.0)	7/8 (87.5)	0.39
Rectum	1/1 (100)	-	1/1 (100)	>0.99
≥20 mm	35/41 (85.4)	24/29 (82.8)	11/12 (91.7)	0.65
<20 mm	14/20 (70.0)	9/15 (60)	5/5 (100)	0.26
Overall	49/61 (80.3)	33/44 (75.0)	16/17 (94.1)	0.15

n, number of sessions; C group, conventional needle group; F group, Franseen needle group.

Table V. Comparison of endoscopic ultrasound-guided fine needle aspiration outcomes using a Franseen needle between the trainee and expert groups.

Obtaining an adequate specimen, n (%)	All (%)	Trainee (%)	Expert (%)	P-value
Location				
Esophagus	-	-	-	-
Stomach	15/16 (93.8)	4/4 (100)	11/12 (91.7)	>0.99
Greater curvature side	8/8 (100)	2/2 (100)	6/6 (100)	>0.99
Lesser curvature side	7/8 (87.5)	2/2 (100)	5/6 (83.3)	>0.99
Rectum	1/1 (100)	-	1/1 (100)	>0.99
≥20 mm	11/12 (91.7)	3/3 (100)	8/9 (88.9)	>0.99
<20 mm	5/5 (100)	1/1 (100)	4/4 (100)	>0.99
Overall	16/17 (94.1)	4/4 (100)	12/13 (92.3)	>0.99

rate for GIST at our medical center was 95.5%. Although these are good results, in many cases of a final diagnosis of an SEL, surgery was not performed, and during follow-up observation, there were no changes in imaging findings. Thus, assessment based on the clinical course in these patients was difficult.

This study examined the utility of a 22G-Franseen needle in small SELs, for which it is increasingly being recognized that early diagnosis and treatment are important.

Comparison between the Franseen needle group and the conventional needle group showed no marked differences in patient age, sex, tumor size, or number of punctures. Although there was no significant difference in the F group, the findings suggest that the Franseen needle may be useful to improve adequate sample rates, particularly, for small lesions <20 mm in size. Although the possibility that puncture performance of the Franseen needle might be inferior to the C needle was considered due to the shape of the tip of the needle, the present results showed no significant difference. The reason for this may be that when we puncture, the up angle is used to fix the lesion firmly and to take a quick puncture.

Because this study was retrospective, some limitations must be considered when interpreting the results. Some influence of needle selection on each examination day cannot be

excluded. In addition, all data were retrospectively collected from a single center. A prospective study with many cases will be necessary. However, the utility of the Franseen needle has already been reported (12), so the present results are consistent for SELs. In particular, the utility of the Franseen needle tended to be higher for small lesions <20 mm in the present study. In conclusion, the current findings suggest that a Franseen needle may improve the adequate sample rate and diagnostic accuracy rate of EUS-FNA in small SELs.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

AF designed the study and drafted the article. AF, SR, MK, YT and TK performed all of the endoscopic ultrasound-guided fine needle aspiration procedures, and RA performed the statistical analysis. KM, MM, and KN critically revised the article for important intellectual content. SR supervised the study and gave final approval of the version to be published. The final version of the manuscript was read and approved by all of the authors.

Ethics approval and consent to participate

The present study was approved by the Ethical Review Board at Saitama Medical University International Medical Center (Saitama, Japan) and complied with the Declaration of Helsinki, as revised in Brazil 2013. All patients provided written informed consent.

Patient consent for publications

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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