Forward-viewing versus oblique-viewing echoendoscopes in the diagnosis of upper gastrointestinal subepithelial lesions with EUS-guided fine needle aspiration: a prospective, randomized, crossover study

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Abstract

Background: The role of the forward-viewing echoendoscope compared with the oblique-viewing echoendoscope for endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) of upper gastrointestinal subepithelial lesions has not been defined.

Objective: To compare the diagnostic yield and clinical efficacy of EUS-FNA using the two echoendoscopes in the same upper gastrointestinal subepithelial lesion.

Design: Prospective, randomized**,** crossover study.

Setting: Tertiary medical center.

Patients: Forty-one patients with an upper gastrointestinal subepithelial lesion.

Interventions: All patients first underwent EUS-FNA with a 19-gauge needle using both echoendoscopes based on random selection. When required, 22- or 25-gauge needles were used additionally.

Main outcome measurements: Comparison of diagnostic yield, tissue sample area, puncture success rates, procedure time, and adverse events.

Results: Forty-one patients **(**median lesion size 22 mm; range 15-63 mm) were enrolled. Rates of histological diagnosis were 80.5% (33/41) and 73.2% (30/41) (*P*= 0.453) using forward and oblique-viewing echoendoscopes, respectively. Median tissue sample area in gastrointestinal stromal tumors (n=22) obtained with the forward-viewing echoendoscope was larger than with the oblique-viewing echoendoscope (2.46 mm^2 vs. 1.00 mm^2; *P* = 0.046). Puncture success rates were 39/41 (95.1%) and 35/41 (85.4%), (*P* = 0.289) with forward and oblique-viewing echoendoscopes, respectively. Median procedure time was 21 min with the forward-viewing echoendoscope and 27 min with the oblique-viewing echoendoscope (*P* = 0.009). An infectious adverse event occurred in a patient and was treated with antibiotics.

Limitations: Small sample size.

Conclusions: Diagnostic yield did not differ between the two echoendoscopes. However, tissue sample area and procedure time was superior with the forward-viewing echoendoscope.

Main text

Most subepithelial lesions harbor a very low risk of progression. However, gastrointestinal stromal tumors (GISTs) have malignant potential, and surgical resection is recommended [1-5]. Endoscopic ultrasonography (EUS) is considered the first choice for evaluating subepithelial lesions and is used to differentiate GISTs from other subepithelial lesions [6-8]. However, a definitive diagnosis based on imaging alone is insufficient and tissue sampling is necessary [9-11]. Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) has become an accurate method for obtaining tissue samples from upper gastrointestinal subepithelial lesions. In several retrospective studies, the diagnostic yield of EUS-FNA in upper gastrointestinal subepithelial lesions ranged from 43 to 91% [10,12-16]. At present, the oblique-viewing echoendoscope is the standard instrument for EUS-FNA. Recently, a new forward-viewing echoendoscope was developed to overcome the major disadvantages of the former instrument: lack of a forward endoscopic view and difficulty in fixing the target. The advantages of the forward-viewing echoendoscope for the treatment of pancreatobiliary disease were noted in several reports [17-25]. A few reports described the diagnostic accuracy of forward-viewing echoendoscopes compared with oblique-viewing echoendoscopes [20,23,26]. More recently, Larghi *et al*. reported extraordinary results using the forward-viewing echoendoscope for subepithelial lesions [27]. To date, a comparative study of forward-viewing and oblique-viewing echoendoscopes has not been reported. We therefore hypothesized that the forward-viewing echoendoscope would increase the diagnostic yield and facilitate EUS-FNA.

The aim of this study was to compare the diagnostic yield and clinical efficacy of EUS-FNA between the newly developed forward-viewing echoendoscopes and conventional oblique-viewing echoendoscopes for the same upper gastrointestinal subepithelial lesions.

Patients and Methods

This study was a prospective, randomized, crossover trial, and was conducted at the Nagoya University Hospital in Japan. Between January 2013 and May 2014, all 78 patients with upper gastrointestinal subepithelial lesions were examined with a radial scanner (GF-UM2000; Olympus Medical Systems Corp., Tokyo, Japan) before EUS-FNA.

The inclusion criterion for the study was the presence of an upper gastrointestinal subepithelial lesion. Exclusion criteria were as follows: age >80 y; tumor size <1.5 cm; diagnosis of lipoma, cyst, or ectopic pancreas by EUS; hemodynamic instability or

severe coagulopathy (international normalized ratio: INR >1.5 or platelet count <60000/ml), and lack of patient's consent. This study was approved by the institutional review board of the Nagoya University (IRB No. 2012-0257), and written informed consent was obtained from all patients.

Equipment

Echoendoscope

All EUS procedures were performed by experienced endosonographers (I.M., R.M., K.F.) who had performed EUS for more than 200 upper gastrointestinal lesions using the newly developed forward-viewing echoendoscope (GIF-Y0007-UCT or TGF-UC260J; Olympus) and oblique-viewing echoendoscope (GF-UCT240AL-5; Olympus) (Table 1). These echoendoscopes were used with an ultrasound processor with color Doppler function (EU-ME1; Olympus). All patients underwent EUS-FNA with both echoendoscopes. The echoendoscopic order was selected randomly using computer-generated numbers.

Forward-viewing echoendoscope

The prototype forward-viewing echoendoscope (GIF-Y0007-UCT; Olympus) was used in 33 patients between January 2013 and January 2014, and the commercially available forward-viewing echoendoscope (TGF-UC260J; Olympus) was used in 8 patients between February and May 2014. Specifications for these echoendoscopes did not differ significantly (Table 1). The forward-viewing echoendoscopes were used with the attachment of a transparent hood (D-201-16403; Olympus) to the tip for fixing the lesion (Fig. 1). This echoendoscope provides a forward endoscopic view, allows device deployment along the axis of the scope, and has a larger tip angulation compared with the oblique-viewing echoendoscope. However, it has no elevator function for the accessory channel and has a narrower ultrasound scanning range.

FNA needle

The puncture was carried out using disposable 19-, 22- and 25-gauge puncture needles (EZ Shot2: NA-220H-8019, NA-220H-8022, NA-220H-8025; Olympus). EUS-FNA was basically performed using a 19-gauge needle. If the puncture was not successful within 3 tries, or the lesions were highly vascularized, a 22- or 25-gauge needle was used. The choice of needle size was left to the discretion of the endosonographers. If the needle had broken, including bending, or there was loss of handle maneuverability, a new needle of the same size was used.

EUS-FNA procedure

All patients were placed in the left lateral position under conscious or deep sedation

with intravenous anesthesia using midazolam and pentazocine. Once the originating layer and echo characteristics of the lesion were observed and color flow mapping was applied to avoid puncturing vessels, the needle was advanced into the lesion under EUS visualization. After the mass was punctured, the stylet was completely removed. The needle was positioned at different areas within the mass and 15 uniform to-and-fro needle movements were made with 20-ml syringe suction applied during each puncture session. The puncture needle was removed and the aspirated tissue samples were ejected into saline solution. The aspiration procedure was repeated until whitish tissue was obtained macroscopically, with a maximum of 3 passes in each echoendoscopy. If macroscopic examination determined that a sufficient specimen was present, the echoendoscope was changed and EUS-FNA was performed using the other echoendoscope. On-site pathologists were not present to determine the adequacy of specimens.

Histological assessment

Pathological results from EUS-FNA were categorized as diagnostic or non-diagnostic. The collected specimens were immediately placed in formalin and embedded in paraffin for histological examination. The pathological diagnosis was made on the basis of hematoxylin-eosin staining and immunopathological stains by expert pathologists (A.N., Y.S.) blinded to the echoendoscopes and needle size used. Cases with insufficient material for immunopathological diagnosis were included in the non-diagnostic group.

Outcome measures

Primary endpoint: diagnostic yield

The primary endpoint was comparison of diagnostic yield from EUS-FNA with the forward-viewing echoendoscope and oblique-viewing echoendoscope. If the yield was sufficient for a pathological diagnosis, the patient was classified as a diagnostic case while if the yield was insufficient the patient was classified as a non-diagnostic case. In some cases, puncture was unsuccessful.

Secondary endpoints: clinical efficacy

Diagnostic accuracy

Diagnostic accuracy was calculated after the EUS-FNA results were confirmed by additional available modalities, including surgical pathology, additional EUS-FNA, and biopsy with a thin endoscope. Technical failures and insufficient samples for histological evaluation were considered false negatives even if the final diagnosis was benign.

Tissue sample area

In GIST cases (n=22), the maximum total area of the specimen obtained with each echoendoscope was measured and compared under a photomicroscope using imaging software (cellSens; Olympus). Data were expressed as a median of lower quartile (LQ) and upper quartile (UQ) values (Fig. 2).

Technical efficacy

Total puncture success rates and success rate with 19-gauge needles were evaluated. Furthermore, the number of passes and procedure times were calculated. Procedure time was defined as the time from oral insertion of the endoscope to retrieval of the endoscope.

Adverse events

Adverse events were defined as any deviation from the clinical course after EUS-FNA as observed by endosonographers. All patients were contacted within 1 month of the procedure to assess if there were any late adverse events.

Statistical analysis

Continuous variables such as patients' age and tumor size were reported as median and range. Comparisons of proportions such as diagnostic yield, diagnostic accuracy, and technical success were expressed as frequencies and proportions and were tested using the McNemar's test. Furthermore diagnostic yield in relation to endoscopic order was tested using the Fisher's exact test. Tissue sample area, number of passes, and procedure time were reported as median and interquartile range and tested with the Wilcoxon signed-rank test. *P* value <.05 was considered statistically significant. Based on an anticipated diagnostic yield by EUS-FNA of 90% for forward-viewing echoendoscopes and 70% for oblique-viewing echoendoscopes, we calculated that 40 patients would be needed to detect significant differences ($P < .05$) with 80% power. SPSS software version Statistics20 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

Results

During this study period, 78 patients with upper gastrointestinal subepithelial lesions were identified as potentially eligible for participation. Thirty-seven patients were excluded for the following reasons: age >80 y (n=3), lesion <1.5 cm (n=20), cyst (n=4) and ectopic pancreas (n=6) diagnosed by EUS, and lack of patient consent (n=4). Thus, 41 patients were enrolled in this study and underwent EUS-FNA with both echoendoscopes. Based on random selection, 21 patients underwent the procedure first with the forward-viewing echoendoscope (Fig. 3). There were 21 males and 20 females, and the median age was 64 y (range 25-80 y). Tumor locations were esophagus, 7 cases; stomach, 32 cases; and duodenum, 2 cases. The median tumor size was 22 mm (range

15-63 mm). The layers of origin were the submucosa, 2 cases; muscularis propria, 38 cases; and undetermined, 1 case (Table 2). All of the tumors were endoscopically apparent within the lumen of the gastrointestinal tract.

The overall rates of histological diagnosis using the forward-viewing and oblique-viewing echoendoscopes were 80.5% (33/41) and 73.2% (30/41), respectively, a difference that was not significant (Table 3). Furthermore, in relation to endoscopic order, the diagnostic yield using the forward-viewing echoendoscope firstly and secondly were 81.0% (17/21) and 80.0% (16/20) (P = 1.000), respectively, and the diagnostic yield using oblique-viewing echoendoscope firstly and secondly were 85.0% (17/20) and 61.9% (13/21) (P = 0.273), respectively. The combined results of forward-viewing and oblique-viewing echoendoscopes established the diagnosis in 35 of 41 (85.4%) lesions. The histologic results of EUS-FNA with both echoendoscopes were GIST (n = 22), leiomyoma (n = 9), carcinoma (n = 1), malignant lymphoma (n = 1), ectopic pancreas (n = 2), and non-diagnostic (n = 6) including spindle cell tumor (n = 2). Details of the 4 indeterminate cases are provided below.

In one patient, a 16 mm leiomyoma was located in the cardia and the lesser curvature and was diagnosed by repeat EUS-FNA. The second lesion was highly vascularized and located in the second portion of the duodenum. The bite-on-bite forceps technique allowed the diagnosis of a GIST. The third lesion was 15 mm and located in the fornix and greater curvature, and was resected laparoscopically with the final diagnosis of a GIST. The fourth case had an esophageal stricture due to a tumor. Puncture could be performed with the forward-viewing echoendoscope, but the materials obtained were insufficient. Bite-on-bite forceps technique using a thin endoscope allowed the diagnosis of a tubular adenocarcinoma.

At the time of the current follow-up, a definitive diagnosis was established in 22 of the 41 cases: surgical pathology in 20 GIST cases, additional EUS-FNA in 1 leiomyoma case and biopsy with a thin endoscope in 1 carcinoma case. Among the 19 remaining cases for whom there was not a definitive diagnosis, one GIST case underwent tyrosine-kinase inhibitor treatment and a metastasis of breast cancer was treated by chemotherapy and esophageal mucosa-associated lymphoid tissue was treated by radiation therapy. Tumors in the other 16 cases, including 3 GIST cases, did not show changes in size during a median follow-up of 11 months (range 3-18 months). In 17 of the 22 patients in which an EUS-FNA diagnosis with the forward-viewing endoscope was made a definitive diagnosis was confirmed while in the 16 cases that were diagnosed using the oblique-viewing echoendoscope, a definitive diagnosis was confirmed. The diagnostic accuracy of the forward-viewing echoendoscope was not

significantly different from that of the oblique-viewing echoendoscope (Table 3).

The total median tissue sample area in the GIST cases (n=22) obtained with the forward-viewing echoendoscope was significantly larger than that obtained with the oblique-viewing echoendoscope, 2.46 mm^2 and 1.00 mm^2 (P = 0.046), respectively (Fig. 4). Furthermore, total puncture success rates were 39/41 (95.1%) and 35/41 (85.4%) (P = 0.289), and the 19-gauge needle puncture success rates were 29/41 (70.7%) and 24/41 (58.5%) (P = 0.180) using the forward-viewing and oblique-viewing echoendoscopes, respectively. Significant differences were not found (Table 3). In all cases of total puncture failure, puncture was successful using the alternative echoendoscope.

With regard to puncture failure, puncture could not be performed by the forward-viewing echoendoscope in 2 patients, one with a 16 mm lesion in the cardia and lesser curvature and the other with a hypervascular tumor in the duodenum. With the oblique-viewing echoendoscope the tumor could not be visualized in 3 patients, 2 with esophageal stricture due to a tumor and scarring from endoscopic submucosal dissection and 1 with a cervical esophageal lesion. In another 3 cases the tumors were <20 mm and were visualized on the puncture route before the needle was passed into the accessory channel; however, puncture was impossible due to the strong resistance encountered when the needle was advanced with the oblique-viewing echoendoscope.

Median number of passes was 2 (P = 0.212) with both the forward viewing echnoendoscope and the oblique-viewing echoendoscope. The median procedure times were 21 min with the forward-viewing echoendoscope and 27 min with the oblique-viewing echoendoscope (P = 0.009) and the median procedure times in cases in which puncture was successful with a 19-gauge needle (n=22) were 17 min with the forward-viewing echoendoscope and 25 min with the oblique-viewing echoendoscope (P = 0.004) (Table 3). An infectious adverse event occurred in a patient with an esophageal leiomyoma who developed a fever 2 days after EUS-FNA. Computer tomography showed a possible abscess in the tumor. This case was treated successfully with broad spectrum antibiotics.

Discussion

This is the first prospective, randomized, crossover trial comparing the forward-viewing echoendoscope and oblique-viewing echoendoscope for EUS-FNA of upper gastrointestinal subepithelial lesions. Differences in diagnostic yields were not found between the two echoendoscopes. However, the tissue sample area in GIST cases was larger and the procedure time was shorter with the forward-viewing echoendoscope than with the oblique-viewing echoendoscope with statistical significance.

Subepithelial lesions comprise a diverse group of histologic diagnoses, including benign or potentially malignant lesions [3,4]. EUS is considered the first choice for evaluation of subepithelial lesions in the upper gastrointestinal tract [6,7,8]. Therefore, definitive histology is important to guide further management [9-11]. Furthermore, certain neoplasms such as lymphomas and gastrointestinal stromal tumors are usually difficult to assess by evaluation of cytologic material and often require histologic confirmation for a definitive diagnosis [28].

Because a biopsy examination by conventional forceps is not helpful in most cases, jumbo biopsy forceps and bite-on-bite forceps techniques have been reported. However, the diagnostic yields were low and most lesions were located in the submucosa, with significant bleeding occurring that required endoscopic hemostasis [29-32]. On the other hand, some techniques using endoscopic mucosal resection and endoscopic submucosal dissection are thought to be useful for obtaining a histological diagnosis even with small lesions. However, it might be more difficult to obtain tissue from a lesion located in extraluminal regions [29,33-35].

Recently, new endoscopic resection techniques, including laparoscopic endoscopic cooperative surgery [36], endoscopic full-thickness resection, and endoscopic submucosal tunnel dissection were developed. These techniques are safe and effective for small GISTs [37-40].

EUS-FNA is an accurate method for obtaining histopathological specimens, including those for immunopathological diagnosis, from upper gastrointestinal subepithelial lesions [9.10,12]. Gastric lesions <2 cm appear to have a low risk of malignant behavior and may be considered for EUS surveillance without resection [1,2,5]. However, rapid growth of such tumors was also reported and accurate prediction remains difficult [41]. Management strategies, including tissue sampling of subepithelial lesions <2 cm, may need to be revised [27]. Therefore, tumors <20 mm (n=15) were included in our study.

In several retrospective studies, the diagnostic yield of EUS-FNA with the use of a 22-gauge needle ranged from 43 to 91% [10,12-16]. To increase the yield of histological specimens, the Tru-cut needle (Quick-Core; Wilson-Cook Medical Inc., Winston-Salem, NC, USA) was developed. Moderate diagnostic yields of 63-90% were found by several studies [42-47]. The Tru-cut needle might be suitable to puncture larger lesions because the needle tray is designed to advance at least 20 mm into the lesion. Recently, a forward-viewing echoendoscope was developed to facilitate the EUS-FNA procedure. Several studies have reported the advantages of the forward-viewing echoendoscope for the diagnosis and treatment of pancreatobiliary disease and celiac plexus neurolysis [17-26]. The advantage of the forward-viewing echoendoscope is that the target is

punctured in a straight line with the endoscope and the puncture site can be readily visible, especially in the pancreatic head from the bulb and the pancreatic uncinate and ampulla from the second portion of the duodenum [17-27]. Also, our results showed that the use of the forward-viewing echoendoscope facilitated the puncture of lesions associated with strictures by lesions and of lesions that were located at the fornix, which are sites difficult to access with the oblique-viewing echoendoscope. In addition, attaching a transparent hood to the tip was shown to expand the capabilities of the endoscope by fixing the target, especially small gastrointestinal subepithelial lesions [48]. In our study, the transparent hood was used in almost all cases except for the esophageal stricture due to scarring, and good fixation between the target and endoscope was obtained. On the other hand, the distal end of the outer diameter of the forward-viewing echoendoscope was larger than that in the oblique-viewing echoendoscope. However, the forward endoscopic view allowed a safe esophageal insertion and ease in detection of the lesion.

A large-caliber needle may help overcome the limitation of a 22-gauge needle by acquiring a larger tissue sample. On the other hand, the increased diameter of the needle made penetration of subepithelial lesions more difficult [49]. To resolve this problem, from the recent study by Larghi *et al*., it was suggested that the forward-viewing echoendoscope and 19-gauge needle was a good combination [27]. Histological assessment, including immunostaining, could be completed in 93.4% (113/121) of the patients. Twenty-seven lesions (22.3%) had a mean diameter of 14 mm (range 7-19). A definitive diagnosis could be made in 22 of these patients (81.5%). In our study, the overall rates of histological diagnosis were 80.5%, 73.2%, and 85.4% of all lesions using the forward-viewing, oblique-viewing, and both echoendoscopes, respectively. If cytological assessments were made and on-site pathologists were available, the overall diagnostic yield might have been higher.

Small tumor size was thought to be one of the factors related to a nondiagnostic result of EUS-FNA [13, 15, 27]. The design of the forward-viewing echoendoscope with the frontal exit of the needle and a transparent hood allowed for fixing the target, especially small and mobile lesions [27,48]. There was no resistance when a mass was punctured, which enabled back-and-forth movement of the needle within the mass easily with the forward-viewing echoendoscope. However, significant differences in puncture success rates were not found between forward-viewing and oblique-viewing echoendoscopes in our study. Our study clarified that in GIST cases larger samples were obtained with the forward-viewing echoendoscope than with the oblique-viewing echoendoscope and the procedure time was shorter. A larger tissue sample area would be theoretically useful to

increase diagonostic yield including that for immunopathological diagnosis. However, significant differences in diagnostic yields were not found between forward-viewing and oblique-viewing echoendoscopes. Furthermore, detecting the target with a forward endoscopic view might be easier than with an oblique endoscopic view.

On the other hand, because of lack of an elevator function, it is difficult in some cases to penetrate different areas in a tumor, the so-called fanning technique, with a forward-viewing echoendoscope compared to the oblique-viewing echoendoscope. As a result, some of specimens might include unsuitable materials, like a blood clot [50].

In this study, on-site pathologists were not present during the procedure to verify the adequacy of specimens as in the study of Larghi *et al*. There were methodological differences between our study and theirs: the type of FNA needle, number of to-and-fro needle movements, pressure of syringe suction, and use or non-use of a transparent hood [27]. Nevertheless, the tumors in our study were relatively small and diagnostic yields were modest although useful. For adequate tissue acquisition, the combination of a forward-viewing echoendoscope and a 19-gauge needle would be reasonable.

The main risks related to the use of a 19-gauge needle are hemorrhage and infectious adverse events. Actually, we experienced only self-limited hemorrhages. In our study, one patient had fever and was treated with broad spectrum antibiotics. Similarly, severe septic adverse events were reported using the Tru-cut needle with a 19-gauge needle [43,45,49]. Peri-interventional antibiotics might be recommended.

There are a few limitations to this study. One is the small sample size, and the lack of a definitive diagnosis to confirm the findings of EUS-FNA in a major portion of cases.

In conclusion, differences in diagnostic yields were not confirmed between forward-viewing and oblique-viewing echoendoscopes. However, this study clearly demonstrated that the tissue sample area and procedure time of EUS-FNA with the forward-viewing echoendoscope were better than those with the oblique-viewing echoendoscope in upper gastrointestinal subepithelial lesions.

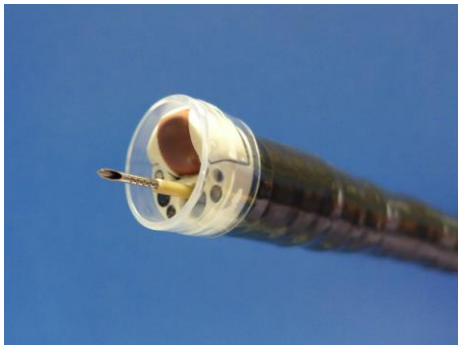

Fig. 1 Forward-viewing echoendoscope with a transparent hood and 19-gauge needle

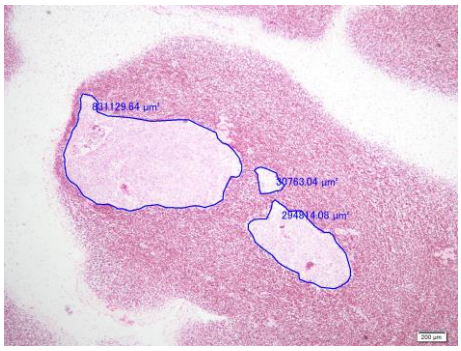

Fig. 2 Example of gastrointestinal stromal tumor. Area of specimen measured under a photomicroscope using imaging software. (hematoxylin and eosin, mag. ×40)

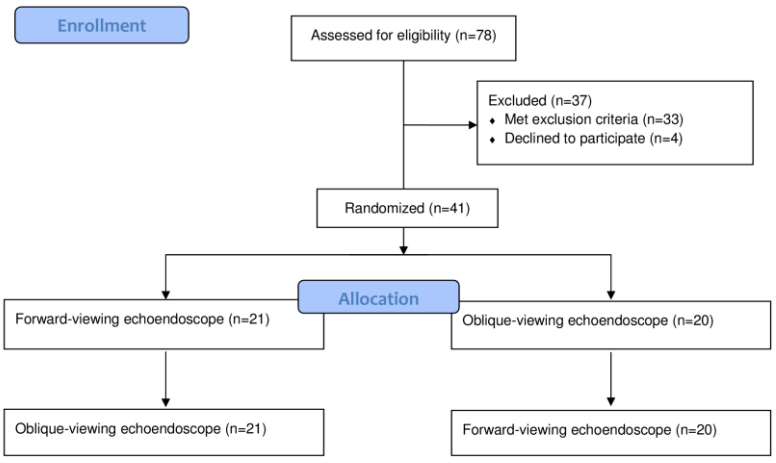

Fig. 3 Flow chart of the prospective, randomized, crossover study design.

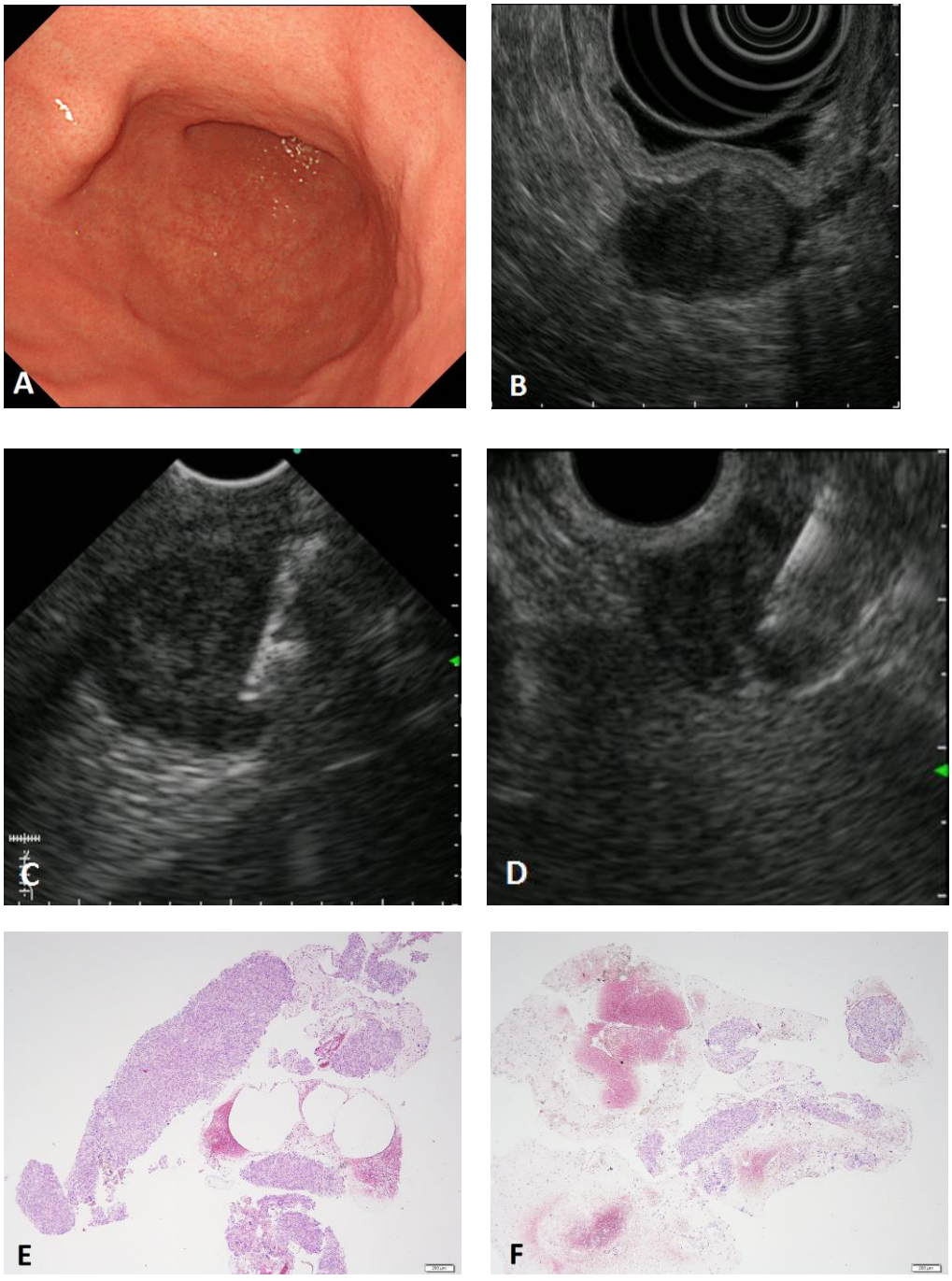

Fig. 4 Representative case of a gastrointestinal stromal tumor. A, Endoscopy showing subepithelial lesion in the lower body of stomach. B, Endoscopic ultrasound image with radial scanner. The hypoechoic tumor was 17 mm and had a heterogeneous echo pattern, irregular border, and was localized in the muscularis propria. C, Puncture of the tumor under direct endosonographic visualization with a 19-gauge needle using the forward-viewing echoendoscope. D, Puncture of the tumor with 22-gauge needle using the oblique-viewing echoendoscope. E, Abundant tissue fragments were obtained using

the forward-viewing echoendoscope (hematoxylin and eosin, mag. ×40). F, Small tissue fragments were obtained using the oblique-viewing echoendoscope (hematoxylin and eosin, mag. ×40).

Table 1. Specifications of the forward-viewing echoendoscope and oblique-viewing echoendoscope

Endoscope details	Forward-viewing echoendoscope		Oblique-viewing echoendoscope
	GIF-Y0007-UCT	TGF-UC260J	GF-UCT240AL-5
Distal end outer diameter (mm)	14.2 (16.7*)	14.6 (16.7*)	14.6
Insertion tube outer diameter (mm)	11.8	12.6	12.6
Channel inner diameter (mm)	3.7	3.7	3.7
Elevator	Not available	Not available	Available
Angulation range (degree) Up/Down Right/Left	 180/100 100/100	 180/90 90/90	 130/90 90/90
Possible US frequencies (MHz)	5, 6, 7.5, 10, 12	5, 6, 7.5, 10, 12	5, 6, 7.5, 10
Scanning range (degree)	90	90	180

*size of transparent hood (D-201-16403)

Table 2. Patients' characteristics and indications for the performance of EUS-FNA

Patients' characteristics	
N (male/female)	41 (21/20)
Age, median (range), y	64 (25-80)
Tumor location	
Esophagus, no.	7
Stomach, no. Upper/middle/lower AW/PW/LC/GC	32 24/7/1 5/6/10/11
Duodenum, no.	2
Tumor size on EUS, median (range), mm	22 (15-63)

Wall layer of origin on EUS	
Submucosa/Muscularis propria/Undetermined	2/38/1

Abbreviations: LC, lesser curvature; PW, posterior wall; GC, greater curvature; AW, anterior wall

Table 3. Outcome of EUS-FNA

	Forward-viewing echoendoscope	Oblique-viewing echoendoscope	P value
Diagnostic yield, no. (%)			
Total	33/41 (80.5%)	30/41 (73.2%)	0.453
Tumor <20 mm	12/15 (80.0%)	11/15 (73.3%)	1.000
Diagnostic accuracy, no. (%)	17/22 (77.2%)	16/22 (72.7%)	1.000
Tissue sample area*, median, (IQR), mm^2	2.46 (0.908-8.095)	1.00 (0.477-4.764)	0.046
Puncture success, no. (%)			
Total	39/41 (95.1%)	35/41 (85.4%)	0.289
Tumor ≥20 mm	25/26 (96.2%)	23/26 (88.5%)	0.625
Tumor <20 mm	14/15 (93.3%)	12/15 (80.0%)	0.625
19 gauge	29/41 (70.7%)	24/41 (58.5%)	0.180
Tumor ≥20 mm	20/26 (76.9%)	19/26 (73.1%)	1.000
Tumor <20 mm	9/15 (60.0%)	5/15 (33.3%)	0.219
Number passes, median, (IQR)	2 (2-3)	2 (1-3)	0.212
Procedure time, median, (IQR), min	21 (15-30)	27 (17-35)	0.009
Procedure time, 19 gauge puncture success cases, median, (IQR), min	17 (13-31)	25 (16-33)	0.004

*Tissue sample area was measured in GIST cases.

DISCLOSURE

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References

1. Fletcher CD, Berman JJ, Corless C et al. Diagnosis of gastrointestinal stromal tumors: A consensus approach. Hum Pathol 2002; 33: 459-465
2. Miettinen M, Lasota J. Gastrointestinal stromal tumors: pathology and prognosis at different sites. Semin Diagn Pathol 2006; 23: 70-83
3. Lim YJ, Son HJ, Lee JS et al. Clinical course of subepithelial lesions detected on upper gastrointestinal endoscopy. World J Gastroenterol 2010; 16: 439-444
4. Kim MY, Jung HY, Choi KD et al. Natural history of asymptomatic small gastric subepithelial tumors. J Clin Gastroenterol 2011; 45: 330-336
5. Dumonceau JM, Polkowski M, Larghi A et al. Indications, results, and clinical impact of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy 2011; 43: 897-912
6. Boyce GA, Sivak MV, Rösch T et al. Evaluation of submucosal upper gastrointestinal tract lesions by endoscopic ultrasound. Gastrointest Endosc 1991; 37: 449-454
7. Chak A, Canto MI, Rösch T et al. Endosonographic differentiation of benign and malignant stromal cell tumors. Gastrointest Endosc 1997; 45: 468-473
8. Sakamoto H, Kitano M, Kudo M. Diagnosis of subepithelial tumors in the upper gastrointestinal tract by endoscopic ultrasonography. World J Radiol 2010; 2: 289-297
9. Matsui M, Goto H, Niwa Y et al. Preliminary results of fine needle aspiration biopsy histology in upper gastrointestinal submucosal tumors. Endoscopy 1998; 30: 750-755
10. Ando N, Goto H, Niwa Y et al. The diagnosis of GI stromal tumors with EUS-guided fine needle aspiration with immunohistochemical analysis. Gastrointest Endosc 2002; 55: 37-43
11. Hwang JH, Saunders MD, Rulyak SJ et al. A prospective study comparing endoscopy and EUS in the evaluation of GI subepithelial masses. Gastrointest Endosc 2005; 62: 202-208
12. Okubo K, Yamao K, Nakamura T et al. Endoscopic ultrasound-guided fine-needle aspiration biopsy for the diagnosis of gastrointestinal stromal tumors in the stomach. J Gastroenterol 2004; 39: 747-753
13. Akahoshi K, Sumida Y, Matsui N et al. Preoperative diagnosis of gastrointestinal stromal tumor by endoscopic ultrasound-guided fine needle aspiration. World J Gastroenterol 2007; 13: 2077-2082
14. Hoda KM, Rodriguez SA, Faigel DO. EUS-guided sampling of suspected GI stromal tumors. Gastrointest Endosc 2009; 69: 1218-1223

15. Mekky MA, Yamao K, Sawaki A et al. Diagnostic utility of EUS-guided FNA in patients with gastric submucosal tumors. Gastrointest Endosc 2010; 71: 913-919
16. Watson RR, Binmoeller KF, Hamerski CM et al. Yield and performance characteristics of endoscopic ultrasound-guided fine needle aspiration for diagnosing upper GI tract stromal tumors. Dig Dis Sci 2011; 56: 1757-1762
17. Voermans RP, Eisendrath P, Bruno MJ et al. Initial evaluation of a novel prototype forward-viewing US endoscope in transmural drainage of pancreatic pseudocysts (with videos). Gastrointest Endosc 2007; 66: 1013-1017
18. Larghi A, Lecca PG, Ardito F et al. Evaluation of hilar biliary strictures by using a newly developed forward-viewing therapeutic echoendoscope: preliminary results of an ongoing experience. Gastrointest Endosc 2009; 69: 356-360
19. Trevino JM, Varadarajulu S. Initial experience with the prototype forward-viewing echoendoscope for therapeutic interventions other than pancreatic pseudocyst drainage (with videos). Gastrointest Endosc 2009; 69: 361-365
20. Kida M, Araki M, Miyazawa S et al. Fine needle aspiration using forward-viewing endoscopic ultrasonography. Endoscopy 2011; 43: 796-801
21. Eloubeidi MA. Initial evaluation of the forward-viewing echoendoscope prototype for performing fine-needle aspiration, Tru-cut biopsy, and celiac plexus neurolysis. J Gastroenterol Hepatol 2011; 26: 63-67
22. Voermans RP, Ponchon T, Schumacher B et al. Forward-viewing versus oblique-viewing echoendoscopes in transluminal drainage of pancreatic fluid collections: a multicenter, randomized, controlled trial. Gastrointest Endosc 2011; 74: 1285-1293
23. Iwashita T, Nakai Y, Lee JG et al. Newly-developed, forward-viewing echoendoscope: a comparative pilot study to the standard echoendoscope in the imaging of abdominal organs and feasibility of endoscopic ultrasound-guided interventions. J Gastroenterol Hepatol 2012; 27: 362-367
24. Larghi A, Capurso G, Carnuccio A et al. Ki-67 grading of nonfunctioning pancreatic neuroendocrine tumors on histologic samples obtained by EUS-guided fine-needle tissue acquisition: a prospective study. Gastrointest Endosc 2012; 76: 570-577
25. Hara K, Yamao K, Hijioka S et al. Prospective clinical study of endoscopic ultrasound-guided choledochoduodenostomy with direct metallic stent placement using a forward-viewing echoendoscope. Endoscopy 2013; 45: 392-396
26. Larghi A, Verna EC, Ricci R et al. EUS-guided fine-needle tissue acquisition by using a 19-gauge needle in a selected patient population: a prospective study. Gastrointest Endosc 2011; 74: 504-510

27. Larghi A, Fuccio L, Chiarello G et al. Fine-needle tissue acquisition from subepithelial lesions using a forward-viewing linear echoendoscope. Endoscopy 2014; 46: 39-45
28. Philipper M, Hollerbach S, Gabbert HE et al. Prospective comparison of endoscopic ultrasound-guided fine-needle aspiration and surgical histology in upper gastrointestinal submucosal tumors. Endoscopy 2010; 42: 300-305
29. Hunt GC, Smith PP, Faigel DO. Yield of tissue sampling for submucosal lesions evaluated by EUS. Gastrointest Endosc 2003; 57: 68-72
30. Cantor MJ, Davila RE, Faigel DO. Yield of tissue sampling for subepithelial lesions evaluated by EUS: a comparison between forceps biopsies and endoscopic submucosal resection. Gastrointest Endosc 2006; 64: 29-34
31. Ji JS, Lee BI, Choi KY et al. Diagnostic yield of tissue sampling using a bite-on-bite technique for incidental subepithelial lesions. Korean J Intern Med 2009; 24: 101-105
32. Buscaglia JM, Nagula S, Jayaraman V et al. Diagnostic yield and safety of jumbo biopsy forceps in patients with subepithelial lesions of the upper and lower GI tract. Gastrointest Endosc 2012; 75: 1147-1152
33. Kojima T, Takahashi H, Parra-Blanco A et al. Diagnosis of submucosal tumor of the upper GI tract by endoscopic resection. Gastrointest Endosc 1999; 50: 516-522
34. Lee CK, Chung IK, Lee SH et al. Endoscopic partial resection with the unroofing technique for reliable tissue diagnosis of upper GI subepithelial tumors originating from the muscularis propria on EUS (with video). Gastrointest Endosc 2010; 71: 188-194
35. Kataoka M, Kawai T, Yagi K et al. Mucosal cutting biopsy technique for histological diagnosis of suspected gastrointestinal stromal tumors of the stomach. Dig Endosc 2013; 25: 274-280
36. Hiki N, Yamamoto Y, Fukunaga T et al. Laparoscopic and endoscopic cooperative surgery for gastrointestinal stromal tumor dissection. Surg Endosc 2008; 22: 1729-1735
37. Lee IL, Lin PY, Tung SY et al. Endoscopic submucosal dissection for the treatment of intraluminal gastric subepithelial tumors originating from the muscularis propria layer. Endoscopy 2006; 38: 1024-1028
38. Schlag C, Wilhelm D, von Delius S et al. EndoResect study: endoscopic full-thickness resection of gastric subepithelial tumors. Endoscopy 2013; 45: 4-11
39. Inoue H, Ikeda H, Hosoya T et al. 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

40. Mitsui T, Niimi K, Yamashita H et al. Non-exposed endoscopic wall-inversion surgery as a novel partial gastrectomy technique. Gastric Cancer 2013:

41. Tanaka J, Oshima T, Hori K et al. Small gastrointestinal stromal tumor of the stomach showing rapid growth and early metastasis to the liver. Dig Endosc 2010; 22: 354-356

42. Levy MJ, Jondal ML, Clain J et al. Preliminary experience with an EUS-guided trucut biopsy needle compared with EUS-guided FNA. Gastrointest Endosc 2003; 57: 101-106

43. Varadarajulu S, Fraig M, Schmulewitz N et al. Comparison of EUS-guided 19-gauge Trucut needle biopsy with EUS-guided fine-needle aspiration. Endoscopy 2004; 36: 397-401

44. Storch I, Jorda M, Thurer R et al. Advantage of EUS Trucut biopsy combined with fine-needle aspiration without immediate on-site cytopathologic examination. Gastrointest Endosc 2006; 64: 505-511

45. Polkowski M, Gerke W, Jarosz D et al. Diagnostic yield and safety of endoscopic ultrasound-guided trucut [corrected] biopsy in patients with gastric submucosal tumors: a prospective study. Endoscopy 2009; 41: 329-334

46. Fernández-Esparrach G, Sendino O, Solé M et al. Endoscopic ultrasound-guided fine-needle aspiration and trucut biopsy in the diagnosis of gastric stromal tumors: a randomized crossover study. Endoscopy 2010; 42: 292-299

47. DeWitt J, Emerson RE, Sherman S et al. Endoscopic ultrasound-guided Trucut biopsy of gastrointestinal mesenchymal tumor. Surg Endosc 2011; 25: 2192-2202

48. Irisawa A, Imaizumi H, Hikichi T et al. Feasibility of interventional endoscopic ultrasound using forward-viewing and curved linear-array echoendoscope: a literature review. Dig Endosc 2010; 22 Suppl 1: S128-131

49. Eckardt AJ, Adler A, Gomes EM et al. Endosonographic large-bore biopsy of gastric subepithelial tumors: a prospective multicenter study. Eur J Gastroenterol Hepatol 2012; 24: 1135-1144

50. Bang JY, Magee SH, Ramesh J et al. Randomized trial comparing fanning with standard technique for endoscopic ultrasound-guided fine-needle aspiration of solid pancreatic mass lesions. Endoscopy 2013; 45: 445-450