Comparison of FNA and fine-needle biopsy for EUS-guided sampling of suspected GI stromal tumors (CME)

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Background and Aims: Subepithelial lesions are found in about 1% of all EGD procedures, and GI stromal tumors are a type of subepithelial lesion commonly encountered. Although the majority of subepithelial lesions are benign, GI stromal tumors have malignant potential, making a definitive diagnosis important. Currently, the criterion standard for the diagnosis of GI stromal tumors is EUS-directed FNA (EUS-FNA). The definitive diagnosis of GI stromal tumors relies on immunohistochemical staining, which depends on enough tissue being submitted to the pathologist. Achieving adequate tissue acquisition from suspected GI stromal tumors by EUS-FNA remains a limitation. Advancements in needle design, however, have improved tissue acquisition and therefore may improve the definitive diagnosis of GI stromal tumors by EUS-FNA. The goal of this study is to compare a fine-needle biopsy (FNB) needle (SharkCore, Medtronics) with FNA needles in definitively diagnosing suspected GI stromal tumors.

Methods: This is a retrospective, single-center study of consecutive patients with suspected GI stromal tumors by EUS characterization who underwent EUS-FNA or EUS-FNB.

Results: A total of 106 patients (53 men, mean [± standard deviation {SD}] age 62.19 ± 16.33 years) were included in the study undergoing EUS-FNA or EUS-FNB of suspected GI stromal tumors. The needle size that was used most often was 22 gauge in both groups. The average size of the lesions was 27.68 ± 15.70 mm; 71.7% of lesions were located in stomach, 19.8% in the esophagus, 5.7% in the duodenum, and 2.8% in the rectosigmoid colon. Ninety-one patients underwent EUS-FNA and 15 patients underwent EUS-FNB. Adequate tissue was procured, allowing immunohistochemical staining in 59 (64.8%) patients in the FNA group and 15 (100%) patients in the FNB group; $P = .006$. A diagnosis was reached by immunohistochemical staining in 48 (52.7%) patients in the FNA group and 13 (86.7%) patients in the FNB group; $P = .01$. Tissue was insufficient to make a cytologic diagnosis in 22 (24.2%) patients in the FNA group compared with none in the FNB group; $P = .03$. Adequate tissue was procured on the first pass of the FNB needle in the majority of patients (83.3%), whereas only 23.5% of patients had adequate tissue on the first pass by the FNA needle, with a median of 3 passes; $P = .00$. Tissue was insufficient to perform immunohistochemical staining, and thus a diagnosis could not be confirmed before surgery in 8 of the 34 surgical patients in the FNA group. Ten of 15 patients in the EUS-FNB group underwent surgery, all of whom were correctly diagnosed by FNB. There were no reported immediate adverse events or technical difficulties in either group.

Conclusions: EUS-FNB by using a SharkCore needle for suspected GI stromal tumors is technically similar and equally safe as FNA, with better tissue acquisition, which was achieved with fewer needle passes and an improved diagnostic yield by immunohistochemical staining. (Gastrointest Endosc 2017;86:510-5.)

Abbreviations: EUS-FNA, EUS-guided FNA; FNB, fine-needle biopsy.

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Subepithelial lesions of the GI tract are increasingly encountered, given the widespread use of GI endoscopy. The vast majority of these subepithelial lesions are discovered incidentally in 0.3% to 1% of all EGD procedures.[1,2] The most frequently encountered subepithelial lesions are lipomas, GI stromal tumors, carcinoid tumors, leiomyomas, or heterotopic pancreas tissue. Although the majority of these lesions are benign, a significant percentage have the potential to undergo malignant transformation.[3] Accordingly, management can vary from reassurance for benign lesions with no malignant potential to surgical resection in patients with premalignant subepithelial lesions. Thus, distinguishing between different types of subepithelial lesions and obtaining a definitive diagnosis is clinically important. GI stromal tumors are the most common subepithelial lesion in the upper GI tract and the most common GI mesenchymal tumor, constituting up to 3% of all GI tract tumors.[4] All GI stromal tumors have malignant potential and in many cases are a diagnostic challenge, given low procured cellular material when sampled. The definitive diagnosis of GI stromal tumors depends on immunohistochemical staining that can be achieved only when enough tissue is submitted to the pathologist. Currently, EUS is considered the criterion standard diagnostic tool for subepithelial lesions owing to its ability to determine the layer of origin, provide accurate measurements of lesion size, and enable tissue acquisition for diagnosis. When EUS-guided FNA (EUS-FNA) was used, the diagnostic yield for GI stromal tumors was improved as compared with other available techniques but remained suboptimal, ranging from 58% to 82%.[5-9] EUS-guided fine-needle biopsy (EUS-FNB) needles were developed to improve tissue acquisition, maintain histologic architecture, and increase diagnostic yield. The literature, however, is scarce and inconclusive as to whether EUS-FNB improves the diagnostic yield for GI stromal tumors. The goal of this retrospective study is to compare EUS-FNA with EUS-FNB for histopathologic examination of suspected GI stromal tumors.

METHODS

Study population

This is a retrospective, single-center study that was approved by the Institutional Review Board at Thomas Jefferson University. Consecutive patients with suspected GI stromal tumors by EUS characterization who underwent EUS-FNA or EUS-FNB were added to a database that was prospectively maintained between 2008 and September of 2016. The following data were gathered from the database: patient age, patient sex, lesion long axis dimension, lesion location, needle type used (FNA/FNB), total number of needle passes, number of passes necessary to obtain an adequate sample, overall cytology result, immunohistochemical staining result, and surgical pathology if surgical resection was performed.

Our approach for tissue acquisition changed from EUS-FNA to EUS-FNB in January 2015. All procedures were performed by using a curvilinear array echoendoscope (GF-UC140P, Olympus America, Center Valley, Pa). Tissue acquisition was performed by using either an FNA needle (Echotip Ultra, Cook Endoscopy, Winston-Salem, NC, before March 2011, and mostly Expect, BSCI, Marlborough, Mass, with few Echotip Ultra thereafter) or FNB needle (SharkCore, Medtronics, Dublin, Ireland). The SharkCore FNB needle is an FDA-approved device for sampling subepithelial lesions, mediastinal masses, lymph nodes, solid pancreatic masses, and intraperitoneal masses within or adjacent to the GI tract.

Technique of EUS-FNA/EUS-FNB

Before tissue sampling, color Doppler was used to confirm the absence of intervening vessels. Tissue sampling was achieved by using the slow-pull technique for all patients starting March 2011. Before that date, dry suction was the technique used. We performed the slow-pull technique by moving the needle to-and-fro 15 to 20 times within the lesion, while an assistant slowly pulled the stylet a distance of approximately 90 cm over 20 to 40 seconds.

Preparation for histologic analysis

A cytotechnologist was present in the procedure room during all cases to process the specimens. The obtained specimen was placed onto slides by advancement of the stylet into the needle. The first slide was air dried and dipped in Diff-Quik stain to determine adequacy of the specimen. A second slide was sprayed with 95% ethyl alcohol and polyethylene glycol and dipped into Papanicolaou stain for more detailed cytologic examination. More passes were obtained as needed to obtain a representative specimen and to perform a cell block. Immunohistochemical staining was performed on the cell block. Pathology results were categorized as follows: (1) diagnostic if confirmed by immunohistochemical staining, (2) suspicious if cytology demonstrated spindle cells but without sufficient quantity to perform immunohistochemical staining, or (3) insufficient specimen and/or nondiagnostic.

Statistical analysis

For comparison of categorical data, a chi-square test was used as indicated. Continuous variables were expressed as mean ± standard deviation (SD). For comparison of continuous data, a 2-sample t test was used, if normal distribution was likely, and the Mann-Whitney test was used, if normality could not be demonstrated. Statistical significance was set at $P < .05$. Statistical calculations were performed by using SPSS version 21.0 for Windows (SPSS Inc, Chicago, Ill).

TABLE 1. Patient demographic and lesion characteristics

Characteristics	All patients N = 106	Type of needle		*P* value
		FNA N = 91	FNB N = 15	
Age, mean ± SD, y	64.85 ± 15.28	64.82 ± 15.71	65.00 ± 12.77	.52
Sex, male:female	53:53	44:47	9:6	.40
Size of mass, average ± SD, mm	27.68 ± 15.70	28.05 ± 16.50	25.48 ± 9.68	.18
Lesion location, no. (%)				.45
Esophagus	21 (19.8%)	20 (22.0%)	1 (6.7%)	
Stomach	76 (71.7%)	64 (70.3%)	12 (80.0%)	
Duodenum	6 (5.7%)	5 (5.5%)	1 (6.7%)	
Rectosigmoid colon	3 (2.8%)	2 (2.2%)	1 (6.7%)	
Lesion EUS features, no. (%)				.55
Irregular border	2 (1.9%)	2 (2.2%)	0	
Echogenic foci	6 (5.7%)	5 (5.5%)	1 (6.7%)	
Cystic foci	13 (12.3%)	11 (12.1%)	2 (13.3%)	
Lesions with surgical resection, no. (%)	44 (41.5%)	34 (37.4%)	10 (66.7%)	.36
GI stromal tumor	25 (56.8%)	20 (58.8%)	5 (50.0%)	
Leiomyoma	10 (22.7%)	7 (20.6%)	3 (30.0%)	
Other	9 (20.45%)	7 (20.6%)	2 (20.0%)	

FNB, Fine-needle biopsy; *SD*, standard deviation.

RESULTS

Patient and tumor characteristics

A total of 106 patients (53 men, mean [± SD] age 62.19 ± 16.33 years) were included in the study undergoing EUS-FNA or EUS-FNB of subepithelial lesions (Table 1). The needle size that was used most was a 22 gauge, and there was no significant difference in the size of the needle between the FNA and FNB groups ($P = .14$) (Table 2). The average size of the lesions was 27.68 ± 15.70 mm; 71.7% of lesions were located in stomach, 19.8% in the esophagus, 5.7% in the duodenum, and 2.8% in the rectosigmoid colon. The lesions in the FNB group were insignificantly smaller than those in the FNA group (25.48 mm vs 28.10 mm; 95% confidence interval [CI], -6.15 to 11.28; $P = .56$). The outer border was irregular in 2 lesions (1.9%), echogenic foci were seen in 6 lesions (5.7%), and cystic foci were found in 13 lesions (12.3%).

Tissue acquisition and diagnostic yield

Ninety-one patients underwent EUS-FNA, and 15 patients underwent EUS-FNB. Adequate tissue was procured, allowing immunohistochemical staining in 59 (64.8%) patients in the FNA group and 15 (100%) patients in the FNB group; $P = .006$. A diagnosis was reached by immunohistochemical staining in 48 (52.7%) patients in the FNA group and 13 (86.7%) patients in the FNB group; $P = .01$. The diagnosis was suspected but not confirmed by immunohistochemical staining because of lack of enough tissue in the FNA group in 11 (12.1%) patients. Tissue was insufficient to make a cytologic diagnosis in 22 (24.2%) patients in the FNA group compared with none in the FNB group; $P = .03$. The final diagnosis by immunohistochemical staining of the lesions is presented in Table 3. Lesions for which tissue acquisition via FNA was insufficient to make a diagnosis were similar in size to lesions for which tissue acquisition was adequate by FNB (22.2 mm vs 25.48 mm; 95% CI, -9.9 to 3.4; $P = .33$) and were insignificantly smaller than lesions for which tissue acquisition was adequate in the FNA group (22.2 mm vs 29.9 mm; 95% CI, -15.6 to 0.2; $P = .06$). Adequate tissue was procured on first pass of the FNB needle in the majority of patients (83.3%), whereas only 23.5% of patients had adequate tissue on the first pass by the FNA needle, with a median of 3 passes; $P = .00$ (Table 2). Other factors such as tumor size, location, and sonographic feature variables (border irregularity, hyperechoic foci, and presence of cystic foci) were not associated with diagnostic yield. There were no reported immediate adverse events or technical difficulties in either group. There was no significant difference between the FNA needles (Echotip Ultra, Cook vs Expect, BSCI) used in terms of lesions size (29.1 mm ± 18.8 vs 26.9 mm ± 12.1; $P = .55$), obtaining adequate tissue allowing immunohistochemical staining (64.3% vs 69.7%; $P = .60$), and adequate tissue procured on the first pass (10.7% vs 18.2%; $P = .32$). Using the slow-pull technique in FNA needles compared with a dry suction

TABLE 2. Fine-needle size and performance

Characteristics	All patients N = 106	Type of needle		*P* value
		FNA N = 91	FNB N = 15	
Needle size, gauge, no. (%)				.14
19		3 (3.5%)	1 (6.7%)	
22		77 (90.6%)	11 (73.3%)	
25		5 (5.9%)	3 (20.0%)	
No. of passes to obtain adequate tissue, median	2	3	1	.00
Adequate tissue on first pass	22 (34.9%)	12 (23.5%)	10 (83.3%)	
Correct preoperative diagnosis (N =44)		26 (76.5%)	10 (100.0%)	.42

FNB, Fine-needle biopsy.

technique improved adequate first-pass procurements (20.5% vs 6.4%; $P = .05$) but not overall tissue adequacy (70.5% vs 59.6%; $P = .27$). FNB was still superior to the subgroup of FNA with the slow-pull technique in terms of obtaining adequate tissue, allowing immunohistochemical staining (100% vs 70.5%; $P = .02$) and adequate tissue procured on the first pass (83.3% vs 20.5%; $P = .00$).

Comparison with resection pathology

Surgery was performed in 44 patients with surgical pathology as follows: GI stromal tumors 25, leiomyomas 10, schwannomas 3, metastatic cancer 3, granular cell tumor 1, carcinoid tumor 1, and duplication cyst 1. In all schwannomas and 7 of the leiomyomas that were resected, GI stromal tumor could not be ruled out by cytopathology, and the lesion size was >2 cm. The other 3 leiomyomas were resected secondary to presumed related GI symptoms such as dysphagia and abdominal pain. None of the lesions that were resected were malignant other than 3 lesions that were found to be metastatic cancer (Table 3). The primary malignancies of the 3 metastatic lesions were renal cell carcinoma, hepatocellular carcinoma, and esophageal cancer. EUS-FNA was performed in 34 patients of those who later underwent surgery (Table 1). Tissue was insufficient to perform immunohistochemical staining, and thus diagnosis could not be confirmed before surgery in 8 of the 34 surgical patients in the FNA group. Ten of 15 patients in the EUS-FNB group underwent surgery, all of whom were correctly diagnosed by FNB (Table 2).

TABLE 3. Final diagnosis based on surgical pathology or cytopathology via FNA or FNB

Location	Final diagnosis	Surgical pathology N = 44	Cytopathology N = 61
Esophagus			
	Leiomyoma	5 (11.4%)	6 (9.8%)
	Duplication cyst	1 (2.3%)	
	Granular cell tumor	1 (2.3%)	1 (1.6%)
	Metastatic lesion	1 (2.3%)	1 (1.6%)
Stomach			
	GI stromal tumor	24 (54.5%)	40 (65.6%)
	Leiomyoma	5 (11.4%)	7 (11.5%)
	Metastatic lesion	1 (2.3%)	1 (1.6%)
	Schwannoma	3 (6.8%)	2 (3.3%)
Duodenum			
	GI stromal tumor		1 (1.6%)
	Carcinoid tumor	1 (2.3%)	2 (3.3%)
	Metastatic lesion	1 (2.3%)	
Rectosigmoid colon			
	GI stromal tumor	1 (2.3%)	

FNB, Fine-needle biopsy.

DISCUSSION

Certain types of subepithelial lesions such as GI stromal tumors are associated with significant malignant potential and therefore require surveillance or surgical resection. As a consequence, it is essential to confirm the subepithelial lesion type by histopathology before committing patients to such management strategies. In our practice, we follow GI stromal tumors that are <2 cm with EUS surveillance at 1 year, then every other year, if stable. GI stromal tumors that are >2 cm are referred to surgery for possible resection. GI stromal tumors that are symptomatic; harbor high risk features such as irregular borders, echogenic foci, or cystic components; or demonstrate progression on follow-up examination are referred to surgery. EUS-FNA of suspected GI stromal tumors has been reported to achieve a diagnostic yield of 52% to 82%.[5-9] EUS-FNB needles were introduced to improve tissue acquisition, maintenance of histologic architecture, and diagnostic yield. Studies, however, have been conflicting with respect to the expected superiority. The EUS Tru-Cut needle (QuickCore; Wilson-Cook

Inc, Winston-Salem, NC) was a spring-activated 19-gauge needle that allowed preservation of tissue architecture and provided enough sample to perform immunohistochemical staining. The needle was associated with technical difficulties and failed to show superiority to FNA needles.[2,10] The release of the ProCore FNB needle (Cook Endoscopy, Winston-Salem, NC) with a reverse bevel design prompted new comparisons to the existing FNA needles.[8,11-14] In a large, multicenter study of mass lesions within and outside of the intestine, the diagnostic yield of the ProCore FNB needle was 89.4%.[11] On the other hand, Bang et al[12] demonstrated in their randomized controlled trial of solid pancreatic masses that yield of a histologic core and the diagnostic yield of the ProCore FNB needle were equivalent to those of the FNA needle. Three studies have addressed the efficacy of the ProCore FNB needle for subepithelial lesions, with a diagnostic yield reaching 86%.[8,13,14] In the study by Kim et al,[8] the yield of obtaining a histologically optimal tissue core was significantly higher with the ProCore FNB needle as compared with the EUS-FNA needle (75% vs 20%). The diagnostic yield of EUS-FNA in this study, however, was much lower than what is reported in the medical literature. This was related to the methodology of the study in which core samples were considered optimal on macroscopic visual inspection by the endosonographer and not through cell block and immunohistochemical stain analysis.

Our study compared the efficacy of the SharkCore FNB needle (Medtronic) with EUS-FNA for suspected GI stromal tumors. The needle tip of the SharkCore needle is designed with 6 distal cutting edge surfaces and an opposing bevel to catch tissue as it is sheared. In this study, 64.8% of patients who underwent EUS-FNA had enough specimen to perform immunohistochemical staining, a rate that is comparable to that reported in the literature.[5-9] By using the SharkCore FNB needle, we were able to procure enough tissue to perform immunohistochemical staining in all patients, exceeding what Kim et al[8] achieved by using the ProCore FNB needle. When compared with the criterion standard of surgical pathology on resected specimens in 44 of our patients, FNB was 100% accurate in predicting the diagnosis superior to FNA, which achieved a correct diagnosis in 76.5% of cases.

An equally important finding was that specimens were adequate for cytopathologic analysis on the first FNB needle pass in the majority of cases (83.3%) as compared with a median of 3 FNA needle passes. This outcome logically translates into fewer passes, shorter procedure duration, less risk to the patient, and increased operational efficiency for both the endoscopy unit and the cytopathology laboratory. In addition, if these data are reproducible in larger studies, the use of the SharkCore needle may preclude the need for an on-site cytopathologist or technician to assess sample adequacy. In fact, Rodrigues-Pinto et al[15] recently conducted a retrospective study showing that FNB sampling without rapid on-site evaluation performed similarly to FNA with rapid on-site evaluation in terms of diagnostic accuracy.

Our study had expected limitations arising from the retrospective design and given that the data were collected from a single tertiary-care referral center. Suspected GI stromal tumors that were found on EUS but not sampled were not included. In addition, we used 2 different FNA needles (Expect, BSCI and Echotip Ultra, Cook), both of which are expected to perform similarly. Our results are impacted by the presence of an on-site cytotechnologist to determine specimen adequacy. The major strengths of our study compared with previous ones is the larger number of patients included and having a subset of patients who underwent surgery, with available surgical pathology for comparison.

In summary, our study shows that EUS-FNB using a SharkCore needle for suspected GI stromal tumors is technically similar and has equal safety as that of an FNA, with better tissue acquisition achieved by fewer needle passes and improved diagnostic yield by immunohistochemical staining.

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