EUS-FNA WITH 19 OR 22 GAUGES NEEDLES FOR GASTRIC SUBEPITHELIAL LESIONS OF THE MUSCLE LAYER

Punção aspirativa ecoguiada com agulhas de 19 e 22 gauges para lesões subepiteliais gástricas da camada muscular própria

César Vivian LOPES1, Antônio Atalibio HARTMANN2, Everson Luiz de Almeida ARTIFON3

ABSTRACT - Background: Tissue diagnosis is required for gastric subepithelial lesions for differential diagnosis of GISTs. However, there has not been consensus about the best needle for EUS-guided sampling of these lesions. Aim: To evaluate the diagnostic yield of EUS-FNA for gastric subepithelial lesions of the proper muscle layer with large-bore 19 gauge needles. Methods: A prospectively maintained database was retrospectively reviewed to identify consecutive patients who underwent EUS-FNA with 19 and 22 gauge needles for gastric subepithelial lesions of the fourth endosonographic layer in a tertiary care referral center. EUS-FNA was performed by the same endosonographer, using the fanning technique, without on-site cytopathologist. Specimens were analysed by cell blocks by the same pathologist. Procedure results were categorized into diagnostic, defined as enough material for histopathology and immunohistochemistry, or nondiagnostic. Results: Eighty-nine patients (mean age: 59 years, 77% women) underwent 92 EUS-FNA with 19 (75) or 22 (17) gauge needles. Mean lesion size was 22.6 mm. Overall diagnostic yield was 88%. The diagnostic yield of 19 gauge was higher than that of 22 gauge needle (92%x70.6%; p=0.0410), and similar for lesions >2 cm and ≤2 cm (93.7%x90.7%; p=0.9563). The best performance for 19 gauge needles was obtained performing <3 needle passes. Complication rate was 2.8%. Conclusions: Diagnostic yield of EUS-FNA with 19 gauge needles is 92% for gastric subepithelial lesions of the proper muscle layer. It is safe and highly valuable for differentiation between GIST and leiomyoma, no matter the size of the lesion.

INTRODUCTION

Endoscopic ultrasonography-guided fine-needle aspiration (EUS-FNA) is a minimally invasive technique for sampling gastric subepithelial lesions (SELs), which are a challenge for the differential diagnosis of gastrointestinal stromal tumors (GISTs). The yield of EUS-FNA for diagnosis of these lesions ranges from 49-73% with 22 gauge needles10,16, but often the specimens are insufficient for immunostaining. Regarding the needle size, the literature about large-bore needles is too limited.
The objective of this study was to review the results of EUS-FNA with 19 gauge needles for gastric SELs of the proper muscle layer performed under the same routine technique, and with specimens evaluated through cell blocks.

METHODS

Study design
Eligible patients included those referred for EUS-FNA at a single tertiary-referral center. Inclusion criteria were patients with hypoechochogenic gastric SELs of the proper muscle layer (Figures 1A e 1B). Exclusion criteria were an INR>1.5 or platelet count <50,000, lesions from the submucosa (ectopic pancreas) and cysts. The first 25 EUS-FNA of SELs were also excluded, of which 18 gastric and seven esophageal SELs, in order to reach the minimum number of EUS-FNA procedures before competency can be assessed according to the guidelines from American and European Societies of Gastrointestinal Endoscopy\(^2\). All patients signed informed consent before enrollment.

EUS-FNA technique
All procedures were performed by the same endosonographer with a curvilinear array echoendoscope (Olympus GF-UCT140-ALS, Olympus America Inc., New York, USA), coupled to an ultrasound unit Aloka Prosound alfa-5 SX. Needles for EUS-FNA were 19 or 22 gauge (EchoTip Ultra Echo-19 or 22, Cook Medical, Winston-Salem, USA) until July 2015, and only 19 gauge needles after that time. EUS-FNA was performed under deep sedation with the assistance of an anesthesiologist. The needle was advanced under EUS guidance into the target lesion, the stylet was removed, 10 ml of suction was applied, and the needle was moved back and forth 10 to 20 times in a fan-like motion within the lesion during each needle pass. After removal of the needle, the specimens were placed in 20% buffered formalin. Pathological specimens were regarded as adequate in the presence of whitish cores (tumor tissue) and reddish cores (coagula with tumor tissue, Figure 1C). On-site cytopathologist was not available. No smears were prepared. Patients were monitored for 1 h after the procedure.

Pathology
The histological analysis of the specimens were made through cell blocks by the same experienced gastrointestinal pathologist. The material was stained with H&E (Figure 1D), and immunohistochemistry stain for actin antibodies, c-kit, and DOG-1 was performed in the presence of white cores (tumor tissue) and reddish cores (coagula with tumor tissue, Figure 1C). On-site cytopathologist was not available. No smears were prepared. Patients were monitored for 1 h after the procedure.

Statistical analysis
Categorical variables were compared by chi-square test or Fisher’s exact test. Continuous variables were compared by Student’s t-test. Statistical analyses were performed using SPSS software (version 15.0, SPSS, Chicago, IL).

RESULTS

Patients demographics
From September 2009 to January 2017, a total of 129 patients who underwent 132 EUS-FNA procedures were studied. Twenty-two lesions were excluded from the analysis, of which 13 submucosal lesions and nine duplication cysts. After excluding the first 18 EUS-FNA of gastric SELs, the final study group was composed of 89 patients with hypoechochogenic gastric SELs of the proper muscle layer, which were submitted to 92 EUS-FNA with 19 (n=75) or 22 gauge (n=17) needles. Repeated EUS-FNA procedures were performed in two patients. The baseline characteristics of the patients and lesions are summarized in Table 1.

TABLE 1 - Demographics and characteristics of the patients/lesions

|                          | TOTAL | 19 gauge needles | 22 gauge needles | P       |
|--------------------------|-------|-----------------|-----------------|---------|
| n                        | 89    | 72              | 17              |         |
| Sex (F/M)                | 69/20 | 57/15           | 12/5            |         |
| Age, mean ± SD (range), yr | 58.7 ± 14.5 (17-94) | 59.2 ± 13.5 (25-94) | 56.3 ± 18.4 (17-86) | 0.4611 |
| EUS-FNA                  | 92    | 75              | 17              |         |
| Size, mean ± SD (range), mm | 22.6 ± 18.6 (5-140) | 23.8 ± 19.7 (6.5-140) | 17.4 ± 12.0 (5-50) | 0.2027 |
| Size > 2 cm              | 34    | 32              | 2               |         |
| Size ≤ 2 cm              | 58    | 43              | 15              |         |
| Needle passes, mean ± SD (range) | 2.9 ± 1.13 (1-6) | 2.8 ± 1.0 (1-5) | 3.4 ± 1.41 (1-6) | 0.0341 |
| ≤ 3 needle passes        | 69    | 59              | 10              |         |
| > 3 needle passes        | 23    | 16              | 7               |         |
| Diagnosis                | 81 (88%) | 69 (92%)   | 12 (70.6%) | 0.0410 |
| Adenocarcinoma/Adenomatosis | 1 (1%) | 0                | 1               |         |
| Complications            | 2 (2.2%) | 2 (2.8%) | 0               |         |
Diagnostic yield of EUS-FNA: 19x22 gauge needles

Needle punctures were successful in all cases irrespective of lesion location. The overall diagnostic yield of EUS-FNA was 88% (81/92). The diagnostic yield of EUS-FNA with 19 gauge needles was higher than that of 22 gauge needles [92% (69/75) x70.6% (12/17); p=0.0410].

Diagnostic yield of EUS-FNA with 19 gauge needles according to the lesion size and number of needle passes EUS-FNA with 19 gauge needles revealed the same diagnostic yield for lesions >2 cm and <2 cm [93.7% (30/32) x90.7% (39/43); p=0.9563]. The mean number of needle passes for gastric SELs of the proper muscle layer with 19 gauge needles was 2.8±1. For lesions >2 cm and <2 cm, the mean number of needle passes were, respectively, 2.84±0.95 and 2.72±1.09, with median of three needle passes. The diagnostic yields for EUS-FNA with 19 gauge needles were, respectively, 98.3% (58/59) and 68.7% (11/16) when performing <3 or >3 needle passes (p=0.00082).

The diagnostic yields of EUS-FNA for lesions >2 cm with 19 gauge needles were similar when performing <3 or >3 needle passes [96.1% (25/26)x83.3% (5/6); p=0.8145]. On the other hand, for lesions <2 cm, EUS-FNA with 19 gauge needles and <3 needle passes offered the best diagnostic yield [100% (33/33)x60% (6/10); p=0.0014].

Complications

The complication rate was very low. Two (2.8%) cases developed epigastric pain due to hematoma of the gastric wall after EUS-FNA with 19 gauge needles, one of them with a 5 cm exofitic GIST requiring surgical intervention. The other case was managed conservatively, with no need of blood transfusion.

DISCUSSION

In our experience, EUS-FNA was performed with 19 gauge needles for 75 gastric SELs of the proper muscle layer, which represents the largest study published to date with this needle for this kind of lesions. Its diagnostic yield was higher than that of 22 gauge needles (92%±70.6%; p=0.0410), and revealed results higher than 90% despite the size of the lesions. Its diagnostic yields were, respectively, 98% and 68.7% when performing <3 or >3 needle passes (p=0.00082).

Concerning the different types of needles for EUS-guided sampling of SELs, Zhang et al.24 did not demonstrate difference in diagnostic rate for any kind of needle. However, among 17 studies included in this meta-analysis, 14 used EUS-FNA needles, but only three with 19 gauge needles,6,12,13, corresponding to less than 9% of the evaluated cases. Other seven studies evaluated EUS-FNB needles, five with trucut needles4,8,14,19, and two with a core trap needle (ProCore®)9,12. There was only five comparative studies8,9,11,12,22, and only one of them evaluating EUS-FNA with 19 gauge needles6. The number of evaluated cases for different types of needles was very small in six studies, each one with less than 20 cases for every type of needle2,6,9,12. In regard to the type of SELs, six of 14 studies were not restricted to gastric SELs4,8,11,13,22, and three other studies were not restricted to SELs, but also included lesions from other organs, especially pancreatic ones10,11. In reference to the wall layer evaluated, 10 of 17 studies were not restricted to the proper muscle layer1,2,6,8,12,14,16,18,19,22, this information was unclear in four studies4,10,11,23, and only three analyzed specifically the proper muscle layer14,19,20, but two of them were not restricted to gastric SELs14, and none of them evaluated EUS-FNA with 19 gauge needles. At last, relating to histopathology, cell blocks were used in only nine (53%) studies, two of eight them evaluating EUS-FNA4,8,10,12,22, but only a single study with 19 gauge needles22. This way, with significant heterogeneity among the selected studies, the best needle for EUS-guided sampling of gastric SELs of the proper muscle layer has not been already defined.

The experience already published for the EUS-FNA with 19 gauge needles for gastric SELs is constituted of four studies. In the experience by Larghi et al.13, using a forward-viewing linear echoendoscope, adequate specimens for histological examination and immunohistochemistry were obtained in 93% of the cases. Our results were very similar to that study, but we used a curvilinear array echoendoscope. Watson et al.22 provided adequate specimens for diagnosis in 79% of the cases. This group counted on on-site cytopathologist in 65% of the procedures, and cell block was used. The diagnostic yields for SELs >20 and <20 mm were, respectively, 80% and 45%, but this difference was not significant in multivariate analysis. Besides, EUS-FNA with 19 gauge needles and a higher number of needle passes were not associated with improved yield. In our experience, we demonstrated better results with the large-bore needle, and the best yield was obtained with up to three needle passes. Eckardt et al.4, without on-site cytopathologist, using a combined evaluation with cyto and histopathology, with median lesion size of 24 mm, and an average number of two needle passes, obtained diagnostic material in 52% of the cases. Nonetheless, this material allowed immunohistochemistry stain in 91% of the cases. Unlike our study, these authors evaluated gastric SELs of the proper muscle layer in only 61% of the cases, which could explain the high rate of non-diagnostic cases, in spite of the needle caliber, lesion size, and number of needle passes have been similar to ours. At last, a study evaluating the specimens by means of cytopathology, without on-site cytopathologist, obtained adequate material in only 58% of the cases17. The 19 gauge needle may obtain a hemorrhagic specimen, which can difficult or even make unfeasible the cytopathologic evaluation. This needle must be used if the intention is to obtain tissue cores, and not only a group of cells.

Our diagnostic yield with a large-bore needle, with no restriction regarding the lesion size, with three or less needle passes, without on-site cytopathologist, with specimens evaluated through cell blocks is higher than that obtained with trucut needles, and as good as that obtained with Procore needles. Beshir et al.3 comparing the trucut needle (EUS-TCB) to the EUS-FNA, demonstrated a diagnostic yield of EUS-TCB and EUS-FNA for SELs of the proper muscle layer of 64% and 66%, respectively. The literature is scarce on comparative studies between EUS-TCB and EUS-FNA with 19 gauge needles. Nevertheless, it is unlikely a study like this to be undertaken, as it is well know the higher incidence of technical failures which not allow the puncture in up to 15% of the cases6,14,17,19, and the absence of higher diagnostic yield even when compared to EUS-FNA with smaller caliber needles. Concerning the Procore® needles, Kim et al.17 conducted a study comparing EUS-FNB to EUS-FNA, both with 22 gauge needles, for SELs >2 cm, neither restricted to the stomach nor to the proper muscle layer. The Procore® needle established the diagnosis with fewer number of passes, with median of two passes, and revealed an important difference in the diagnostic yield (92%±30%). However, the literature has not any comparative study between EUS-FNB with Procore® needles and EUS-FNA with 19 gauge needles for gastric SELs of the proper muscle layer.

Our complication rate was very low (2.8%) for EUS-FNA with 19 gauge needles. This rate is a little higher than the bleeding of 2.2% described by Eckardt et al.4, but lower than 8% described by Na et al.17 with 22 gauge needles. With a better diagnostic yield, our complication rate is lower than the rates of 3-4% for trucut needles14,17,19, and there has not been complication report with Procore® needles for SELs.

This study is subject to the limitations inherent to its retrospective design, and the experience of a single endosonographer in solely a referral center. Furthermore, the diagnoses obtained by means of EUS-FNA were not compared to surgery15. However, as most patients were asymptomatic and their median lesion
size was 16 mm, it would not be possible to submit all GISTs to resection.

On the other hand, this study has many strengths as well. After an initial experience with 22 gauge needles, all EUS-FNA procedures were performed with 19 gauge needles for all gastric SELs of the proper muscle layer despite their presumptive EUS diagnosis, location and size. EUS-FNA with 19 gauge needles obtained a definitive diagnosis in most cases. The routine histopathology processing for the specimens was the same, and a single experienced gastrointestinal pathologist evaluated the material. The small sample sizes of previous studies, inclusion of suspected diagnoses, SELs from various sites of the gastrointestinal tract, and only lesions >2 cm might have led to an overestimation of the diagnostic yield of different needles in those studies. With a scarcity of studies comparing the yield of EUS-FNA for gastric SELs of the proper muscle layer using different needle calibers, our experience with 19 gauge needles is the largest when compared to other studies. We found a significant higher diagnostic yield with the 19 gauge needle even in the absence of on-site cytopathologists.

The question about the best needle for EUS-guided biopsy for these lesions is still unclear. Further comparative, randomized and multicentric studies are necessary to define whether this approach is the best and most cost-effective diagnostic strategy for gastric SELs of the proper muscle layer.

**CONCLUSION**

Endoscopic ultrasonography-guided fine-needle aspiration of subepithelial gastric lesions of the own muscular layer in the absence of cytopathologist in the room, with up to three punctures with 19 gauge needles and evaluation of the material through cell blocks, allows a diagnostic gain of more than 90%. It is safe and highly valuable for differentiation between GIST and leiomyoma, no matter the size of the lesion.

**REFERENCES**

1. Akahoshi K, Oya M, Koga T, Koga H, Motomura Y, Kubokawa M, et al. Clinical usefulness of endoscopic ultrasound-guided fine-needle aspiration for gastric subepithelial lesions smaller than 2 cm. J Gastrointestin Liver Dis 2014;23:25-31.
2. Arantes V, Logrono R, Farug S, Ahmed J, Waxman L, Bhatuni M. Endoscopic sonographically guided fine-needle aspiration yield in submucosal tumors of the gastrointestinal tract. J Ultrasound Med 2004;23:1141-50.
3. Beshir MAL, Alawamy M, Wels MM, Rahman A, Morkobrada M, Yar J, et al. Gastrointestinal Stromal Tumors: a Systematic Review of Diagnostic Efficacy of Endoscopic Ultrasound-Guided Fine Needle Aspiration. Scand J Gastroenterol 2014;49:347-54.
4. Camellini L, Carlinfanne G, Azzolini F, Ioni V, Cavina M, Sereni G, et al. A randomized clinical trial comparing 22 G and 25 G needles in endoscopic ultrasound-guided fine-needle aspiration of solid lesions. Endoscopy 2011;43:709-15.
5. DeWitt J, Emerson RE, Sherman S, Al-Haddad M, McHenry L, Cote GA, et al. Endoscopic ultrasound-guided Trucut biopsy of gastrointestinal mesenchymal tumors. Surg Endosc 2011;25:2192-202.
6. Eckardt AJ, Adler A, Gomes EM, Jensen C, Siebert C, Gottschalk U, et al. Endosonographic large-bore biopsy of gastric subepithelial tumors: a prospective multicenter study. Eur J Gastroenterol Hepatol 2012;24:1135-44.
7. EisenGM, DominitzJA, FaiqeldDO, GoldsteinJA, PetersenBT, RaddawiHM, et al. Guidelines for credentialing and granting privileges for endoscopic ultrasound. Gastrointest Endosc 2001;54:811-4.
8. Fernandez-Esparrach G, Sendino O, Sole M, Pellise M, Colomo L, Pardo A, et al. Endoscopic ultrasound-guided fine-needle aspiration and trucut biopsy in the diagnosis of gastrointestinal tumors: a randomized crossover study. Endoscopy 2010;42:292-9.
9. Hoda KM, Rodriguez SA, Faiqeld DO. EUS-guided sampling of suspected GI stromal tumors. Gastrointest Endosc 2009;69:1218-23.
10. Iglesias-Garcial, Polkowski M, Larghi A, Weynand B, Boustière C, Giovannini M, et al. Feasibility and yield of a new EUS histology needle biopsy versus a multicenter, pooled, cohort study. Gastrointest Endosc 2011;73:1189-96.
11. Imazu H, Uchiyama Y, Kakatani H, Ikeda KI, Sumiyama K, Kaise M, et al. A prospective comparison of EUS-guided FNA using 25-gauge and 22-gauge needles. Gastroenterol Res Pract 2009;2009:546390.
12. Kim GH, Cho KY, Kim EY, Kim HK, Cho JW, Lee TH, et al. Comparison of 22-gauge aspiration needle with 22-gauge biopsy needle in endoscopic ultrasonography-guided subepithelial tumor sampling. Scand J Gastroenterol 2014;49:347-54.
13. Larghi A, Verna EC, Ricci R, Seredt CN, Galasso D, Carnuccio A, 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;74:504-10.
14. Lee JH, Choi KD, Kim MY, Choi KS, Kim DH, Park YS, et al. Clinical impact of EUS-guided Trucut biopsy results on decision making for patients with gastric subepithelial tumors >2 cm in diameter. Gastrointest Endosc 2011;74:1010-8.
15. Loureiro-MdeP, AlmeidaRA, ClausCM, BoninEA, Cury-FilhoAM, Dimbarte D, Costa MA, Vital ML. Laparoscopic resection of gastrointestinal stromal tumors (GIST). Arq Bras Cir Gastroenterol 2016;23:1-4.
16. Melkkaya MA, Yamao K, Sawaki A, Mizuno N, Hara K, Nafeh MA, et al. Diagnostic utility of EUS-guided FNA in patients with gastric submucosal tumors. Gastrointest Endosc 2010;71:1913-9.
17. Na HK, Lee JH, Park YS, Ahn JY, Choi KS, Kim DH, et al. Yields and Utility of Endoscopic Ultrasound-Guided 19-Gauge Trucut Biopsy versus 22-Gauge Fine Needle Aspiration for Diagnosing Gastric Subepithelial Tumors. Clin Endosc 2015;48:152-7.
18. Philipper M, Hollerbach S, Gabbert HE, Heikaus S, Bücking A, Pomjanski N, et al. Prospective comparison of en-doscopic ultrasound-guided fine-needle aspiration and trucut, GI histology diagnosis in upper gastrointestinal submucosal tu-mors. Endoscopy 2010;42:300-5.
19. Polkowski M, Gerke W, Jarosz D, Nasierowska-Guttmejer A, Rutkowski P, Nowecki ZJ, et al. Diagnostic yield and safety of endoscopic ultrasound-guided trucut biopsy in patients with gastric submucosal tumors: a prospective study. Endoscopy 2009;41:329-34.
20. Polkowski M, Larghi A, Weynad B, Bouetiere C, Giovannini M, Pujol B, et al. Learning, techniques, and complica-tions of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Technical Guideline. Endoscopy 2012;44:190-206.
21. Suzuki T, Arai M, Matsumura T, Arai E, Hata S, Maruoka D, et al. Factors associated with inadequate tissue yield in EUS-FNA for gastric SMT. ISRN Gastroenterol 2011:619128.
22. Watson RR, Binmoeller KF, Harneski CM, Shergill AK, Shaw RE, Jaffee IM, et al. Prospective comparison of endoscopic ultrasound-guided trucut biopsy in the diagnosis of gastric subepithelial tumors. Gastrointest Endosc 2011;73:860-6.
23. Zhong X, Li QL, Yu YF, Yao LQ, Xu MD, Zhang YG, et al. Diagnostic efficacy of endoscopic ultrasound-guided fine-needle aspiration cytology for gastrointestinal stromal tumors: a meta-analysis. Surg Endosc 2016;30:2431-41.