EUS-guided tissue samples for the diagnosis of patients with a thickened gastric wall and prior negative endoscopic biopsies

F.I. Téllez-Ávila, G. Duarte-Medrano, G. Lopez-Arce, D. Herrera-Mora, M.Á. Ramírez-Luna, F. Valdovinos-Andraca, J. Elizondo-Rivera

Gastrointestinal Endoscopy Department of the National Institute of Medical Sciences, Mexico City, Mexico.

Abstract

Aim : **Evaluate the diagnostic yield of biopsies obtained by EUS guidance in patients with gastric wall thickening and prior negative endoscopic biopsies.**

Material and methods **: Data collected from October 2008 to January 2016 were analyzed in a retrospective manner. All included patients had undergone at least one endoscopy with a negative biopsy and showed evidence of gastric wall thickening by tomography, confirmed by endoscopy. All patients gave their written informed consent before the procedure. Demographics and baseline characteristics, including age, sex, number of previous endoscopies, and histopathological diagnosis were recorded. Follow-up data were obtained from a review of the electronic medical records.**

Result : **In total, 22 patients with previous negative endoscopic biopsies and gastric wall thickening were included. Using EUS-FNA/FNB, the diagnosis was made in the first procedure in 19/22 (86.30%) cases, while in 1/22 (4.5%) patients the diagnosis was made in the second EUS-FNA. A total of 18 (81.82%) patients with EUS-FNA were assessed using a standard Echo-tip, while the remaining four (18.18%) patients underwent EUS-FNB and using a ProCore needle. All patients with a final diagnosis of malignancy had a thickened gastric wall with impaired gastric distension and a loss of wall structure determined by EUS. Of patients with a benign final diagnosis, all (n=8) showed a thickened gastric wall by EUS but with preservation of the deep layers**

Conclusion : **EUS-FNA/FNB is necessary in patients with a thickened gastric wall and prior negative biopsy on endoscopy. The procedure is safe and has a good diagnostic.** (Acta gastroenterol. belg., **2019**, 82, **359-362**).

Keywords : Endoscopic ultrasound, FNA, Wall thickening, Biopsy

Introduction

The study of patients with gastric wall thickening is one of the most challenging scenarios for the endoscopist. Sometimes, it is difficult to obtain an appropriate tissue sample for histopathological evaluation by endoscopy. In some patients, endoscopy is limited for diagnosis mainly because the obtained tissue sample is only from the mucosa (1).

Today, ultrasonographic features can be identified in gastric lesions with thickening (1). When these patients have at least one previous negative endoscopic biopsy, EUS could be a good alternative diagnostic tool to evaluate the gastric wall and to obtain biopsies (2,3,4,5). However, the evidence for this is still limited (3,4,5,6,7).

The aim of this study was to evaluate the diagnostic yield of tissue samples obtained by EUS guidance in patients with thickening of the gastric wall and a prior negative endoscopic biopsy.

Material and methods

Data collected from October 2008 to January 2016 were analyzed in a retrospective manner. All included patients had undergone at least one endoscopy with a negative biopsy and showed evidence of gastric wall thickening by CT, confirmed by endoscopy. All patients gave their written informed consent before the procedure. Demographics and baseline characteristics, including age, sex, number of previous endoscopies, and histopathological diagnosis were recorded. Follow-up data were obtained from a review of the electronic medical records. The definition of gastric wall thickness on CT, for this study, was a wall thickness ≥ 5 mm persistent in more of two increments in the presence of good GI distension (qualitative evaluation by a radiologist). A 64-slice multidetector CT (Somatom, Sensation 64 ; Siemens Munchen, Germany) was used in the CT examination, and images were obtained with a section thickness of 3-5 mm with a reconstruction interval of 2-2.5 mm. All cases were analyzed on a workstation with the ability to produce coronal reformatted images. For patients who received IV contrast, 120 ml of Conray (Mallinckrodt Baker Inc., St. Louis, MO, USA) was given 45 s prior to CT examination. Forty milliliters of ioditrast M60 (Justesa Imagen Mexicana) was diluted in 1,000 ml of water and given to all patients orally 1 h prior to CT. All patients received IV and oral contrast except for those whose serum creatinine was 1.4 mg/dl, who did not receive IV contrast. All CT images were analyzed by at least two certified radiologists and discussed with the endoscopic team before the procedure. All CT and endoscopic studies were carried out in the same center (INCMNSZ)

EUS-FNA/FNB was performed using a FUJI EG-530UT linear array echoendoscope with the SU-8000 console (Fujifilm Corporation, Minato-Ku, Tokyo, Japan), or the GF-UCT 140 linear echoendoscope (Olympus

Correspondence to : Félix I Téllez-Ávila, MD, MSc, PhD Department of Gastrointestinal Endoscopy, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Vasco de Quiroga #15. Col. Sección XVI. Del. Tlalpan. CP 14000, Mexico City, Mexico. Tel. : +525 54870900. Fax : +525 54870900
E-mail : felixtelleza@gmail.com

Submission date : 20/03/2018
Acceptance date : 24/02/2019

Corporation, Center Valley, Pennsylvania) with the Aloka SSD 5500 console by two echoendoscopists. All patients were observed for at least 4 hours after the procedure for possible complications. The gastric lumen was filled with 300-600 ml of water. The gastric wall was imaged as a five-layered structure with the histologic correlation previously described (1) : layers 1 and 2 = superficial and deep mucosa; layer 3 = submucosa and interface; layer 4 = muscularis propia; layer 5 = serosa and subserosal fat. Layers 1 and 2 were considered to be the superficial gastric wall, whereas layers 3, 4, and 5 were considered the deep layers (3). In EUS, the gastric wall is considered thickened if the maximum thickness from the luminal to the extraluminal border is more than 5 mm, irrespective of the contribution of individual layers or whether there is asymmetrical thickening of one segment of the wall compared to the rest of the circumference (3-4).

EUS-FNA technique (EUS fine-needle aspiration, standard needle)

All procedures were performed with standard EchoTip Ultra (Cook medical Inc., Winston Salem, North Carolina, USA) or ProCore (Cook Medical Inc., Limerick, Ireland) 22-gauge or 19-gauge needles. However, in our center, ProCore needles were available only until May 2012; thus, we had a small number of procedures with this kind of needle.

At first, the transducer was brought into a stable position in front of the targeted area. The metal spiral was then introduced into the biopsy channel while ensuring that the needle piston was securely locked and the needle was completely retracted. The spiral was inserted completely and the handle with the Luer-lock was firmly screwed into the biopsy channel. To ensure that the sheath was protecting the entire length of the working channel, we used the optics of the endoscope. With the stylet retracted but still inside the needle, the biopsy needle was moved forwards into the lesion under full real-time ultrasound control. After penetration into the gastric wall, the stylet was completely removed. Upon reaching the optimal needle position, a 10-ml syringe with a locking device was firmly screwed onto the needle, while pulling on the syringe piston to create low pressure. The syringe piston was locked into this position for permanent suction. The needle was moved to and fro 10-15 times inside the gastric wall under complete ultrasonic control. With the needle tip still in the gastric wall, suction was released and the needle was safely retracted inside the needle sheath and locked in a secure position.

EUS fine-needle biopsy (Procore needle)

Fine-needle biopsy using a ProCore needle was performed in a similar fashion to EUS-FNA but without aspiration, instead using capillary aspiration without suction, whereby the stylet was slowly removed over 40 seconds as the needle was moved to and fro.

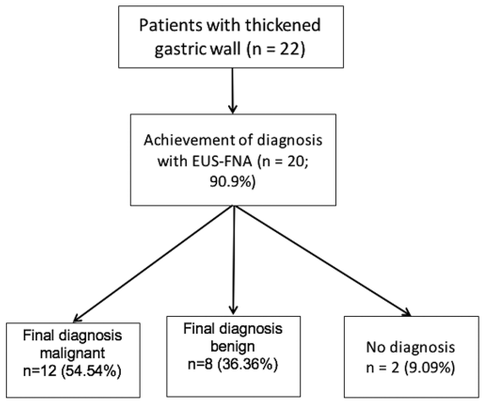

Fig. 1

All specimens were recovered, fixed in formalin and processed for histological and cytological analysis. A single expert pathologist evaluated the tissue samples. The cytological diagnoses of material obtained by EUS-FNA or EUS-FNB were then categorized into the following groups: positive for malignancy, benign/reactive process, or non-diagnostic. For the purposes of this study, material reported as suspicious for malignancy or atypical cells indeterminate for malignancy were considered negative (failures) for EUS-FNA/FNB. The final diagnosis (the gold standard) used to conclude a malignant or benign condition was pathology (obtained either by surgery, EUS-FNA/FNB or macrobiopsy with a diathermic snare) or clinical follow-up in the remaining patients. In this second group, patients were considered to be free of malignancy if they were alive and without clinical signs of progression of disease (absence of pain, vomiting or weight loss, or repeated imaging techniques precluding malignancy) after at least one year of follow-up.

Complications were defined as any of the following: excessive bleeding at the puncture site, perforation, hypotension, and the need for reversal medication. Acute pancreatitis was defined as upper abdominal pain associated with nausea or vomiting, and accompanied by at least a three-fold elevation in serum amylase or lipase. Immediate (intraprocedural and in the recovery area) complications were evaluated in all patients.

Statistical analysis

The results were evaluated using descriptive statistics for non-parametrically distributed data: median and minimum-maximum, as well as absolute and relative frequencies. Sensitivity, specificity, positive and negative predictive values were calculated based on the final results of the gold standard. All analyses were conducted using Statistical package for the Social Sciences (SPSS) V20 for Mac.

Results

A total of 22 patients with previous negative endoscopic biopsies and a thickened gastric wall were included. Of the included patients, 12 (54.5%) were women with a mean age of 57.8± 14.7 years. The median number of endoscopic procedures with biopsies before EUS-FNA/FNB was 2 (1-3). Twenty patients underwent (previous to EUS-FNA/FNB) macrobiopsy with a diathermic snare. In all cases (n = 22), the histological diagnoses in the endoscopic biopsies were of chronic gastritis.

A total of 18 (81.82%) patients with EUS-FNA were performed using a standard Echo-tip, while the remaining 4 (18.18%) patients underwent EUS-FNB performed using a ProCore needle. In Table 1, the final histologic diagnosis of the tissue samples obtained by EUS-FNA/FNB are shown. According to EUS, the median gastric wall thickness was 15 (6-50) mm. During sampling with EUS guidance, 1-10 needle passes (median 2) were made. Of the patients in whom the diagnosis was obtained by EUS-FNA/FNB, in 19/22 (86.3%) cases, the diagnosis was made in the first procedure, and in 1/22 (4.5%) patients the diagnosis was made in the second EUS-FNA. In 2/22 (9%) patients, it was not possible to make a diagnosis by EUS-FNA/FNB (specifically, these patients underwent EUS-FNA). The patients without a diagnosis were lost to follow-up.

All patients with a final diagnosis of malignancy had a thickened gastric wall with impaired gastric distension and a loss of wall structure determined by EUS. Ascites were reported in 4 (30.7%) patients, and 6 (46.15%) patients had pathological lymph nodes. Of patients with a benign final diagnosis, all (n=8) showed a thickened gastric wall by EUS but with preservation of the deep layers. In Table 2, the univariate and multivariate analysis for predictors of malignant disease are shown. There were no immediate or late complications.

Table I. — **Definitive histology of tissue samples obtained by EUS guidance in patients with malignancy**

Final Histology	n (%)
Adenocarcinoma	8 (61.5%)
Lymphoma	2 (5.3%)
Stromal tumor	1 (7.69%)
Poorly differentiated tumor cells	1 (7.69%)

Table II. — **Univariate and multivariate analyses for malignancy results on the histological evaluation of tissue samples obtained by EUS guidance**

	OR (95%CI)	P-value
Univariate		
Age >60, *years*	1.56 (0.8-3)	0.36
Sex, *female*	1.2 (0.6-2.5)	0.65
Impaired gastric distension	7.6 (2-27)	0.001
Loss of wall structure	7.6 (2.01-26)	0.001
Ascites	1.6 (0.2-4.5)	0.5
Pathologic lymph nodes	1.8 (036-10.5)	0.8
Multivariate		
Loss of wall structure	6 (1.6-23)	0.026
Impaired gastric distension	5.6 (1.2-20)	0.026

Discussion

According to our results, EUS-FNA/FNB is necessary in patients with a thickened gastric wall and a prior negative biopsy by endoscopy.

Little information exists on the usefulness of EUS in the evaluation of patients with large gastric folds, and much less is available in the subgroup of patients with prior negative endoscopic biopsies. In Table 3, previous studies that have evaluated the usefulness of EUS in patients with large gastric folds are shown. In the study by Thomas et al 2009; 4/31 cases, attempted Trucut biopsy technically failed or was difficult (needle malfunction after first puncture in three patients and needle distortion after first puncture in one patient) and inadequate samples were obtained in three patients in whom the procedure technically failed. In another study Zohu et al 2015; the deep (bite-on-bite) and large biopsy technique (EMR) provided a definitive diagnosis in 29 (80.6%) of the 36 patients. In the remaining seven patients, diagnosis was by surgery.

Achievement of a histological diagnosis sometimes is difficult with endoscopic biopsies only. In 2006, Gines et al. reported the usefulness of radial EUS for diagnosis in this group of patients. They reported that enlargement of the deep layers was the only variable that independently predicted malignancy. In the present study, the loss of wall structure and impaired gastric distension were independent predictors of malignancy. Is important to mention that, in the study by Gines et al., EUS-FNA/FNB was not performed and the "gold-standard" they used was the pathology results of surgery or macrobiopsy with a diathermic snare; this study included 61 patients, but only 19 patients had tissue samples (surgery, n = 11; macrobiopsy, n = 8). In our patients, we used a linear echoendoscope and we obtained tissue samples in all patients. The advantages of EUS-FNA/FNB during the EUS procedure are: (i) the possibility of avoiding surgery, (ii) achieving a diagnosis more quickly and safely compared with surgery or clinical follow-up, and (iii) cost saving. Although there is scarce information specifically on patients with a thickened gastric wall, the safety of EUS-FNA/FNB in different areas has been reported previously, (8,9,10,11 including one recently published paper with EUS-FNB of the gastric wall of patients with gastroparesis but without a thickened gastric wall (12).

Although, to the best of our knowledge, there have been no studies comparing costs in this setting, we think that the differences in cost regarding EUS-FNS/FNB

Table III. — **Previous studies on EUS and EUS tissue samples in patients with a thickened gastric wall and negative endoscopic biopsies**

Author/year	n/patients with EUS-FNA	Sensitivity of EUS-FNA (%)	Malignant pathology n (%)	Benign pathology n (%)	Previous neg-biopsies by endoscopy (yes/no)
Mendis 1994	28/0	NA	4 (16)	17 (71)	Yes
Songur 1995	35/0	NA	23 (65.7)	12 (34.2)	No
Gines 2006	61/0	95	21 (34.4)	40 (65.6)	Yes
Thomas 2009	31/31	85	16 (51.6)	11 (35.4)	Yes
Zhou 2015	36/0	NA	28 (77.7)	1 (2.7)	Yes

vs. surgery must be favorable to the EUS procedure. In addition to these reasons, all oncological practice guidelines insist on cytological/histological evidence of cancer prior to the consideration of definitive treatment (13). Therefore, in practical terms, obtaining a tissue diagnosis is crucial to determining the management strategy in this group of patients.

In this study, EUS had a sensitivity of 86% with the first EUS-FNA/FNB. Table 3 shows sensitivities reported in other studies; our results are similar.

We have to mention some limitations of our study. The first is the retrospective design, and the second is the small sample size. Previous studies have been mainly retrospective or, in the case of prospective studies, they have not provided information on tissue samples and only included EUS images. In this study, all included patients had tissue samples collected with the available needles. The Trucut biopsy needle (Quick-Core, Cook Medical, Ireland) for EUS is not currently available in our country.

In conclusion, EUS-FNA/FNB is necessary in patients with a thickened gastric wall and negative biopsy by endoscopy. The procedure is safe and has a good diagnostic yield.

Author contributions : Téllez-Ávila FI design the report; Téllez-Ávila FI, Duarte-Medrano G, Lopez-Arce G, Herrera D, and Ramírez-Luna M were attending doctors for patients; Téllez-Ávila FI and Ramírez-Luna M performed endoscopies; Téllez-Ávila FI, Duarte-Medrano G, Lopez-Arce G, Herrera D, Elizondo-Rivera J, Valdovinos-Andraca F organized the report; and Téllez-Ávila FI and Duarte-Medrano G wrote the paper.

All authors declare no conflicts of interest. No funding was received for the study.

Disclosure : All authors disclosed no financial relationship relevant to this publication.

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