EUS-guided FNA biopsy of the muscularis propria of the antrum in patients with gastroparesis is feasible and safe

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Background and Aims: EUS-guided FNA biopsies of the muscularis propria of the gastric wall in patients with gastroparesis could replace the routine use of surgical full-thickness biopsies for assessing the loss of the interstitial cells of Cajal (ICCs) and cellular infiltrates in the myenteric plexus. We investigated the efficacy and safety of EUS-guided FNA biopsies of the muscularis propria of the gastric antrum in gastroparesis and compared the tissue with a surgically obtained full-thickness biopsy specimen in the same patient.

Methods: This was a prospective, nonrandomized, feasibility trial. Patients with gastroparesis who were undergoing gastric neurostimulator placement were enrolled. Patients had a gastric wall measurement by radial EUS in the body and antrum of the stomach followed by linear EUS examination and FNA of the muscularis propria in the antrum by using a 19-gauge core needle. Within 24 hours, a full-thickness biopsy specimen of the antrum was obtained surgically during neurostimulator placement. Endoscopic and surgical specimens were compared for tissue morphology, number of ICCs (c-kit stain) and enteric neurons (S-100 stain), and fibrosis (trichome) for each patient. The correlation coefficient of the ICC count per high-power field was used to compare both specimens. Continuous data were compared by using a *t* test.

Results: Eleven patients (10 female, 1 male), with a mean age of 40.6 years, were enrolled in the trial. EUS-guided core biopsies were successful in obtaining sufficient tissue for the histologic assessment of ICCs in 9 patients (81%) and for the myenteric plexus in 6 patients (54%). There was a good correlation coefficient (0.65) when both surgical and endoscopic groups were compared for the loss of ICCs. Mild serosal bruising and/or localized hematoma formations were noted at the sites of EUS biopsies, but there were no serosal tears, perforations, or adverse effects on the hospitalization and outcomes.

Conclusions: EUS-guided FNA of the gastric muscularis propria in patients with gastroparesis is safe and provides adequate tissue for full histologic assessment. (Clinical trial registration number: NCT01916460.) (Gastrointest Endosc 2016;83:327-33.)

Gastroparesis is a chronic disorder of gastric motility characterized by delayed gastric emptying of solids without evidence of mechanical obstruction. Gastroparesis presents with early satiety, postprandial fullness, nausea, vomiting, and abdominal discomfort. In severe cases, gastroparesis can significantly diminish quality of life because of chronic nausea and vomiting, malnutrition, and multiple hospital admissions.[1-3] Diabetes and idiopathic etiologies represent

Abbreviations: EUS-FNA, EUS-guided FNA; H&E, hematoxylin and eosin; HPFs, high power fields; ICC, interstitial cells of Cajal; IRB, institutional review board.

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the two major causes of gastroparesis.[4] Recent data indicate several structural changes associated with gastroparesis. Loss of interstitial cells of Cajal (ICCs) and decreased number of enteric neurons as well as increased number of immune infiltrates in the myenteric plexus of the muscularis propria were seen in patients with gastroparesis who underwent full-thickness gastric body biopsy.[5-7] In addition to the loss of ICCs, studies suggest that there is an accompanying loss of the expression of neuronal nitric oxide in enteric neurons in animal models of gastroparesis.[8]

The utility of echoendoscopy in examining the structural changes of the gastric wall in patients with gastroparesis has not been reported previously. Core biopsy of the gastric wall by using a linear echoendoscope and a 19-gauge needle was feasible in patients with gastric wall thickening.[9] The primary aims of our study were (1) to investigate the efficacy and safety of EUS-guided FNA (EUS-FNA) biopsies of the muscularis propria of the antrum in patients with gastroparesis and to compare the tissue obtained endoscopically to a surgically obtained full-thickness biopsy in the same patient and (2) to map the total wall thickness as well as specifically measure smooth muscle dimensions in the gastric body and antrum of patients with gastroparesis.

BACKGROUND

EUS can visualize the 5 layers of the gastric wall that correlate with specific histology. The first 2 layers are the superficial and deep mucosa, the third layer is the submucosa, the fourth hypoechoic layer represents the muscularis propria, and the fifth hyperechoic layer represents the serosa.[10] ICCs can be seen on a histologic specimen of the fourth layer (muscularis propria). Echoendoscopes and endoscopic miniprobes have various frequencies (5-20 MHz). Although high-frequency miniprobes can better visualize the GI wall, their use is hampered with the loss of acoustic coupling and the need for constant water instillation to achieve better visualization of the GI lumen.[11] Radial and linear echoendoscopes have been used for years in assessing gastric wall thickness for different pathologies, with high accuracy.[12] Although radial and linear echoendoscopes involve low frequencies (5-10 MHz), the acoustic coupling between the probe and the stomach wall is obtained by placing a water-filled balloon on the tip of the echoendoscope, resulting in clear, stable images of the gastric wall. In addition, the linear echoendoscope provides an opportunity to obtain core biopsy specimens of the gastric wall.

METHODS

Study design

This was a prospective, nonrandomized, pilot trial. The study was approved by the Institutional Review Board (IRB) of Texas Tech University Health Science Center on March 3, 2013. The study was registered at Clinicaltrial.gov under this identifier number: NCT01916460. The study was funded by a seed grant from the Paul L. Foster School of Medicine at Texas Tech University Health Science Center. The authors and the coauthors of this study had access to the study data and approved the final version of this manuscript. Inclusion criteria included patients (aged 18-80 years) with objective evidence of gastroparesis who were undergoing gastric neurostimulator placement because they had failed all standard and/or research treatment approaches to control their symptoms. Subjective evidence of gastroparesis included the following: documented symptoms of gastroparesis for >6 months, >7 episodes of vomiting per week, refractoriness, or intolerance to antiemetics and prokinetic medications. Objective evidence was supported by the documentation of delayed gastric emptying of solid meals (>60% gastric retention at 2 hours and >10% at 4 hours postprandial) by using a 4-hour scintigraphic method with a standard egg booster meal. Exclusion criteria were documented organic or intestinal pseudoobstruction, primary eating or swallowing disorders, rumination syndrome, psychogenic vomiting, cyclic vomiting syndrome, systemic sclerosis, thyroid and adrenal disease, psychiatric diagnosis of chemical dependency, cancer, peritoneal dialysis, and pregnancy. In addition, patients with a history of gastric surgery such as partial gastric resection, vagotomy, or bariatric procedures were excluded.

Technique

After careful reading and discussion, each patient gave written, informed consent. Demographics and clinically relevant data were obtained along with the results of a 4-hour gastric emptying test, EGD results, *Helicobacter pylori* status, and basic laboratory tests (Hb A_{1c}, blood cell counts, and coagulation parameter). The clinical evaluation of gastroparesis symptoms was through the PAGI-SYM standard questionnaire.

Patients with gastroparesis who met the criteria for enrollment in the study had been evaluated by a gastroenterologist (R.W.M.), and they were scheduled to undergo gastric neurostimulator placement. On the morning of the planned surgery, they underwent radial and linear EUS examination of the stomach wall as per IRB protocol. A radial Olympus GF-UE160-AL5 echoendoscope (Olympus America Inc, Center Valley, Pa) was used to measure the total wall thickness and muscularis propria thickness of the body, antrum, and pylorus by using harmonic echo. The tip of the echoendoscope was covered with a balloon; balloon distension with water was used to improve the visualization of the gastric wall by the echoendoscope. The 5 layers of the gastric wall were visualized, and the measurement of the total wall thickness and the thickness of the fourth layer (muscularis propria) was obtained (Fig. 1) Three measurements were obtained from each site. After that, the linear EUS was used to obtain a core biopsy specimen of the stomach wall in the antrum with a 19-gauge core biopsy needle under

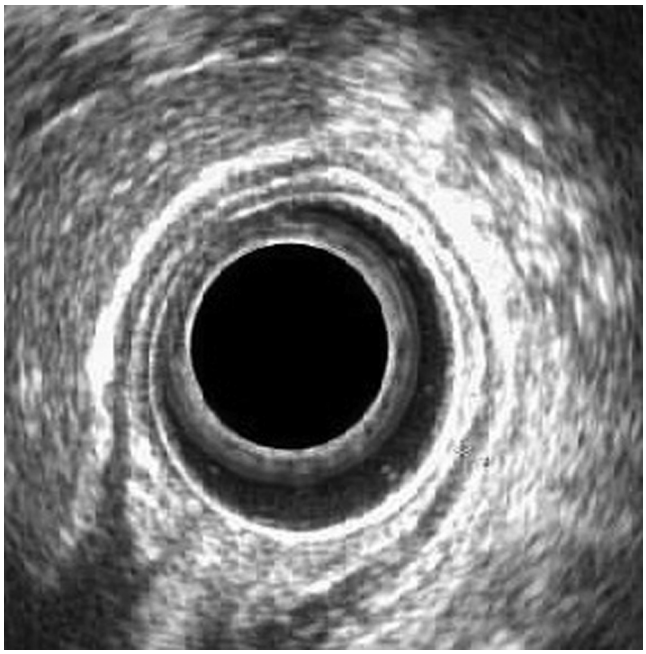

Figure 1. Total thickness of the gastric wall and muscularis propria measured with a radial echoendoscope.

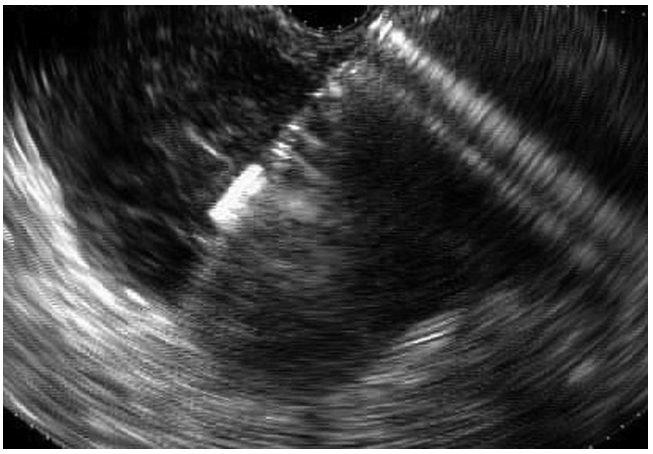

Figure 2. EUS-guided FNA of the gastric wall (zoomed-in view).

EUS guidance. The needle was allowed to completely pass through the wall of the stomach beyond the serosa to permit tissue acquisition within the needle core on withdrawal. The site of the biopsy was chosen at the posterior wall of the stomach in the antrum to avoid inadvertent sampling of the liver, pancreas, or gallbladder (Fig. 2). All procedures were performed by a single endoscopist (M.O.), who had performed more than 1700 EUS procedures in the previous 4 years. A linear Olympus GF-UC140P echoendoscope (Olympus) with a ProSound SSD 5000 processor (Aloka, Wallingford, Conn) was used in all cases. The procedure was performed with patients under propofol sedation administered by an anesthesiologist.

After the site of puncture in the antral wall was chosen, a 19-gauge Procore needle (Cook Endoscopy, Winston-Salem, NC) was used to obtain the core biopsy specimen. The FNA technique is as follows: once the antral area is selected, the needle was advanced into the stomach wall under EUS guidance to achieve the depth of insertion within the muscularis propria. The stylet was then removed and a 10-mL syringe was attached to the hub of the needle. Ten uniform to-and-fro needle movements were made for each of the passes with a 10-mL syringe suction applied. After aspiration, the needle was retracted into the catheter and removed. A pathologist on site assessed the adequacy of each sample for histologic examination. A visible core of at least 1 cm in length is generally adequate for histologic evaluation. No more than 5 passes with the FNA needle were performed. Five milliliters of methylene blue were injected at the site of puncture to mark it before surgery. The core specimen was submitted for histologic evaluation. The patient was taken to surgery within 24 hours for gastric neurostimulator placement and to obtain a full-thickness stomach biopsy. The site of the EUS puncture identified by the tattoo was specifically examined by one the investigators (B.D.) for bleeding, perforation, or tear during the surgery. The hospital course and follow-up of patients were monitored.

Specimens obtained endoscopically and surgically were evaluated for (1) Counting ICCs: This was performed by fixing the specimen in formalin, embedding it in paraffin, followed by immunohistochemical staining with antibodies to CD117. Any elongated cell was considered an ICC and was counted at high modification (×40 objectives). Round cells, corresponding to mast cells were not counted. The cell count obtained by surveying 10 high power fields (HPFs) was averaged, and the number of ICCs was expressed as cells per HPF.[13] (2) Smooth muscle morphology: This was assessed by hematoxylin and eosin (H&E) staining as well as trichrome staining for inflammation and fibrosis. (3) Enteric nerve and myenteric plexus: This was stained by standard H&E preparation in addition to S-100 immunostaining. In contrast to ICCs, there is no cutoff number for myenteric plexus per HPF to suggest gastroparesis, so we calculated the total number of myenteric plexus nerve bundles. Correlation between surgical and endoscopic biopsies for the total number of myenteric plexus nerve bundles was not done because the sampling success of the myenteric plexus is dependent on the surface area. Because the surgical samples were larger than samples obtained by EUS, the total number of nerve bundles was higher in the surgical sample.

The pathologist evaluating the specimen (A.T.) was not blinded to the means of tissue acquisition (EUS vs surgery).

Statistical analysis

As a proof of concept, we planned to include 7 to 12 patients in this trial as per approval from the IRB. Correlation coefficient of the ICC count per HPF was used to compare

TABLE 1. Characteristics of gastric wall muscle biopsy specimens obtained by EUS compared with surgical full-thickness biopsy

Case	Age, y	Sex	EUS cells of Cajal (c-kit+) per HPF	Surgical sample cells of Cajal (c-kit+) per HPF	Total number of nerve bundles (S-100+) on EUS sample	Total number of nerve bundles (S-100+) on surgical sample
1	58	F	4-5/HPF (2 pieces of muscularis)	11/HPF	1	5
2	20	F	15/HPF (4 pieces of muscularis)	16/HPF	3-4	7
3	57	F	14/HPF (7 pieces of muscularis)	16/HPF	1	6
4	43	F	6-7/HPF (3 very small pieces of muscularis)	15/HPF	None	5
5	30	F	11/HPF (2 pieces of muscularis)	16/HPF	None	6
6	58	F	12/HPF (3 very small pieces of muscularis)	17/HPF	None	6
7	27	F	Inadequate sample	8/HPF	None	4
8	29	F	11/HPF (7 pieces of muscularis)	Inadequate sample	3	None
9	36	F	12/HPF (2 pieces of muscularis)	14/HPF	1	6
10	36	F	Inadequate sample	10/HPF	None	6
11	53	M	7/HPF (10 pieces of muscularis)	5/HPF	1	5

HPF, High-power field; *F,* female; *M,* male.

specimens obtained endoscopically and surgically. Continuous data were reported as mean and standard deviation (SD). Categorical data were reported as proportions. Continuous data were compared by using a *t* test.

RESULTS

Patient characteristics

Eleven patients (10 female, 1 male) were enrolled in the trial from June 2013 until July 2014. Seven patients had diabetic gastroparesis, and 4 had idiopathic gastroparesis. The mean age of the patients was 40.6 years (SD ± 4.1 years). The mean total wall thickness of the stomach body was 2.7 mm (SD ± 1.5 mm), whereas the mean total wall thickness of the antrum was 3.3 mm (SD ± 1.2 mm). The mean total wall thickness of the antrum was significantly higher than the mean total wall thickness of the stomach body ($P = .006$). Mean thickness of the muscularis propria in the stomach body was 0.9 mm (SD ± 0.08 mm), whereas the mean thickness of the muscularis propria in the antrum was 1.5 mm (SD ± 0.15 mm). The mean thickness of the muscularis propria in the antrum was significantly greater than the mean thickness of the muscularis propria in the stomach body ($P = .005$).

STUDY OUTCOMES

Success rate of EUS-guided core biopsies technique

Table 1 details the study outcomes. EUS-guided core biopsies were successful in obtaining sufficient tissue for histologic assessment of ICCs in 9 patients (81%) and for the myenteric plexus in 6 patients (54.5 %). Surgical full-thickness biopsy was successful in obtaining sufficient tissue for histologic assessment of ICCs and for the myenteric plexus in 10 patients (90%). In patients for whom EUS-guided biopsies were successful, the mean number of muscularis propria pieces obtained was 4.4 pieces per patient (SD ± 0.95), with a median number of 3 pieces per patients (range 2-10). There was a high correlation coefficient (0.76) between the thickness of the muscularis propria in the antrum and the number of pieces obtained. In patients for whom S-100 staining was successful in visualizing the myenteric plexus, the median number of nerve bundles observed was 1 (range 1-4).

Correlation between endoscopic and surgical biopsies

There was no difference between the success rate of the endoscopic technique versus the surgical approach for obtaining sufficient tissue for histologic evaluation ($P = 1.0$). There was a good correlation coefficient (0.65) between surgical and endoscopic biopsies for the number of ICCs in each sample. Figure 3 to Figure 7 show different types of immunostaining for endoscopic and surgical specimens.

Safety

Mild serosal bruising and/or localized hematoma formations were noted at the sites of EUS biopsies in all patients but no serosal tears or perforations were noted (Fig. 8). No after-procedure adverse events were reported in any patient, and no postoperative problems changed standard discharge planning.

DISCUSSION

In this pilot trial, EUS-guided core biopsy obtained sufficient tissue from the muscularis propria of the antral wall for histologic examination of ICCs in 9 of 11 examined

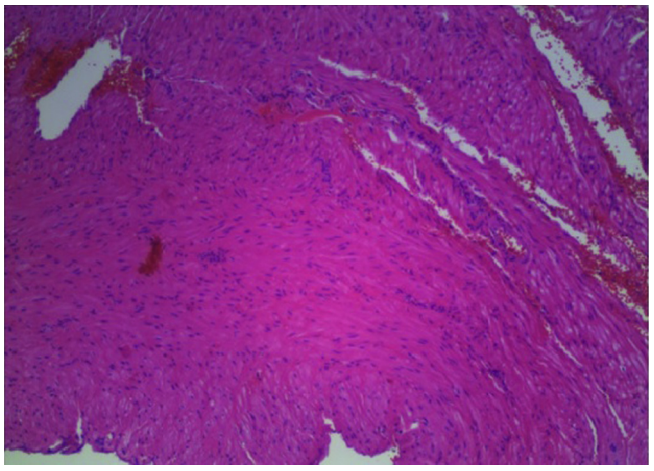

Figure 3. Hematoxylin and eosin staining of a surgically obtained biopsy specimen from the muscularis propria antrum (H&E, orig. mag. ×40).

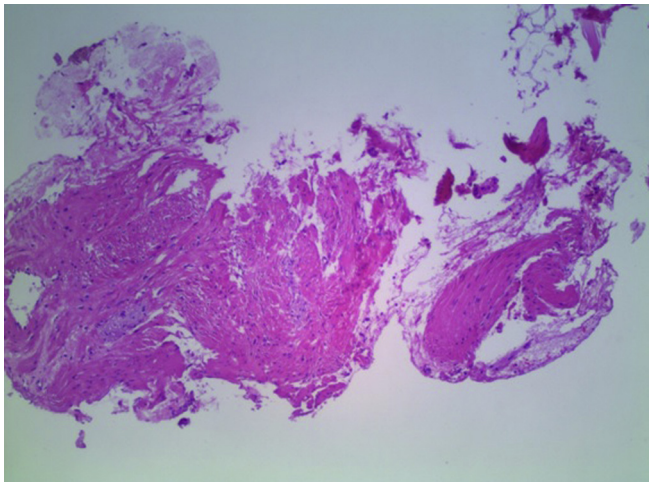

Figure 4. Hematoxylin and eosin staining of endoscopically obtained muscle biopsy specimen from the muscularis propria of the antrum (H&E, orig. mag. ×40).

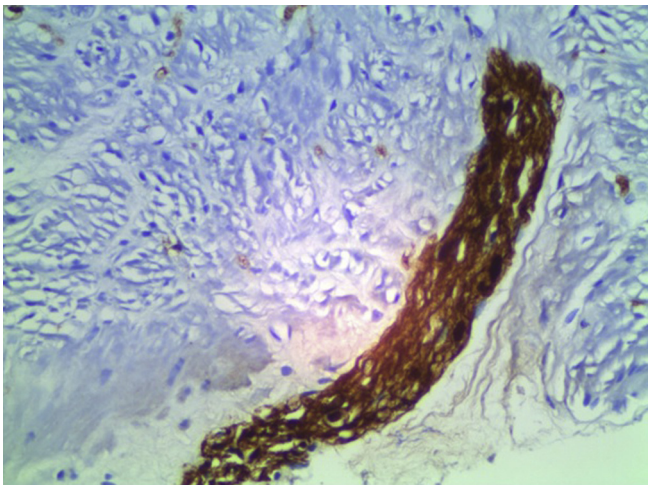

Figure 5. S-100 immunostaining of endoscopically obtained antrum muscle biopsy specimen showing myenteric plexus (S-100 immunostaining, orig. mag. ×40).

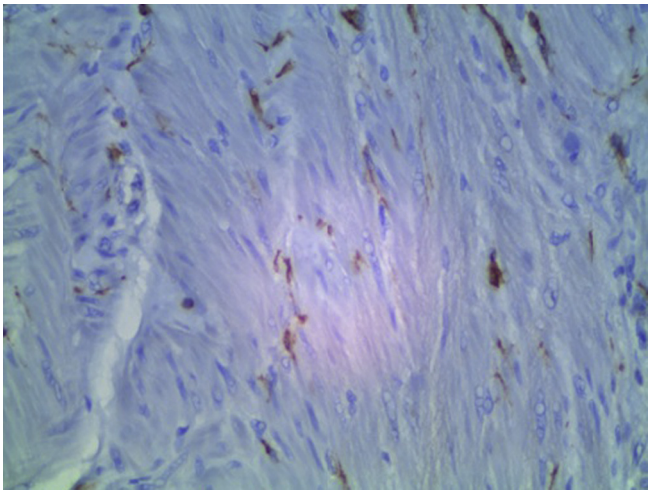

Figure 6. Interstitial cells of Cajal highlighted by c-kit staining in a surgically obtained antrum muscle biopsy specimen (C-Kit staining, orig. mag. ×40).

patients with gastroparesis. Myenteric plexus was seen in the tissue specimen of 6 patients. To our knowledge, this is the first study to use EUS in an attempt to obtain sufficient tissue for histologic evaluation of the muscularis propria in patients with gastroparesis without relying on full-thickness surgical biopsies. We also found a good correlation between the tissue obtained by surgery and by endoscopy technique. Core biopsy of the gastric wall yielded enough tissue to permit histologic assessment for the loss of ICCs and for identifying the myenteric plexus and changes in smooth muscle pathology. These specific tissue changes can be potential markers for grading gastroparesis in addition to predicting treatment outcomes and prognosis. The ability to assess the myenteric plexus regarding cellular infiltration and decreased number of neurons as well as smooth muscle inflammation and fibrosis will lead to better treatment approaches and more therapeutics options. To advance research in this area, the fundamental requirement is easier access to this tissue with a low-risk approach that overcomes reliance on an invasive surgical technique. We describe a safe technique that provides a potential alternative to surgical full-thickness biopsies.

We believe that the less-invasive nature of this technique may foster further research in the area of the pathophysiology of gastroparesis. Targeting the underlying defects in idiopathic and diabetic gastroparesis could lead to therapies aimed at the repair and restoration of cell function. Using the less-invasive EUS technique to gain gastric smooth muscle tissue and to identify these molecular defects in the earlier course of the disease sets the stage for new therapies to prevent and/or minimize the early cellular changes of gastroparesis. Recently, defects in several molecular pathways

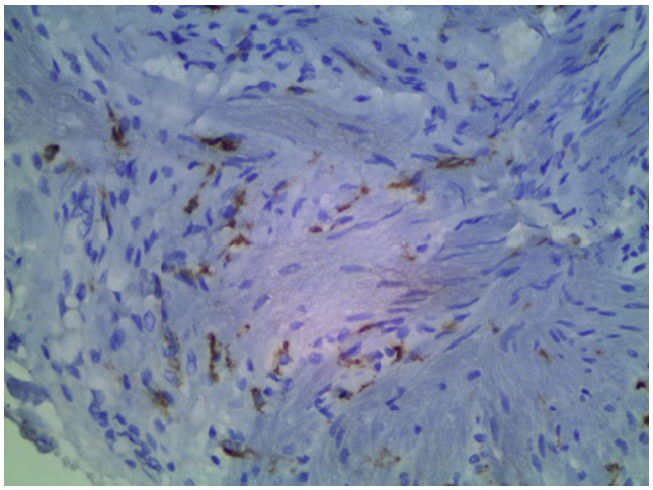

Figure 7. Interstitial cells of Cajal highlighted by c-kit staining in an endoscopically obtained muscle biopsy specimen of the muscularis propria of the gastric antrum.

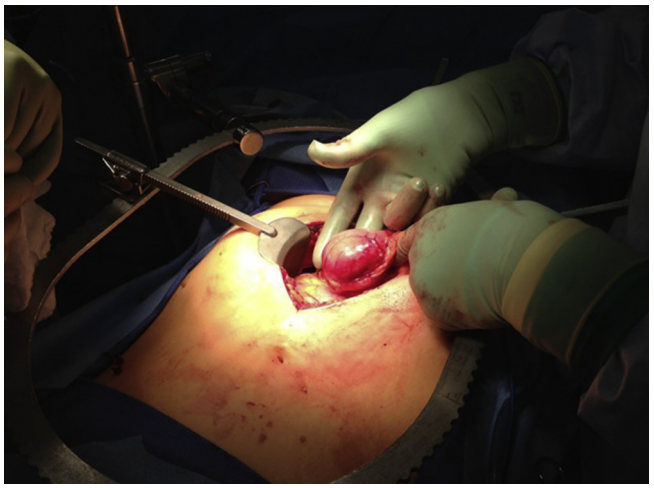

Figure 8. Open laparotomy for gastric neurostimulator placement showing the serosal surface of the stomach after EUS-guided FNA without any perforation or tear or significant hematoma formation.

linked to the pathophysiology of gastroparesis have been discovered. A good example is the defect in the heme oxygenase pathway, which has been addressed by treatment with hemin, something that is available already. Hemin treatment restored neuronal nitric oxide[14] in an animal model of diabetic gastroparesis. Interleukin-10 also can induce hemin and has been effective in restoring neuronal nitric oxide in some studies.[15]

Based on currently available publications and scientific discussions, there has been a poor correlation between symptoms of gastroparesis and results of the gastric emptying test.[16] This observation creates challenges in evaluating patients with gastroparesis and highlights the need for new options for the diagnosis of this debilitating condition. Potentially, our study could revolutionize the clinical investigation and care of patients with suspected gastroparesis by providing a more comprehensive profile of their pathophysiology through a procedure with demonstrated low risk for adverse events and no evidence for resulting in infection or peritonitis (ie, EUS-guided core biopsy).

Measurement of the thickness of the muscularis propria in idiopathic and diabetic gastroparesis also may be beneficial in explaining why a subset of patients with gastroparesis can benefit from botulinum injection into the pylorus via the endoscope.[17] Patients with idiopathic gastroparesis may have increased pyloric tone and phasic contractions known as *pylorospasm* or could have chronic impairment of pyloric sphincter relaxation.[18,19] Another possibility is pyloric sphincter muscle hypertrophy limiting the size of the pyloric opening. The increased force of the contractions required to overcome this pyloric resistance could lead to hypertrophy of the body and/or antrum, and therefore the thickness of the muscle could be regarded as a biomarker for this condition. By measuring the wall of the stomach, particularly the antrum, as well as the pylorus, information regarding whether there is wall thickening or hypertrophy could be obtained, providing evidence for treatment strategies in a subset of patients with idiopathic gastroparesis. This subset once identified by thickening of the muscularis propria of the gastric body, and/or antrum and/or pylorus could be considered for a treatment trial with injection of botulinum toxin into the pyloric sphincter as the first step. This clinical algorithm could lead to a period of symptom improvement. If this result could be reproduced with a second injection of botulinum toxin into the pyloric sphincter, then this could be sufficient evidence to consider a role for surgical pyloroplasty. Recently, evidence has accumulated for an important role of pyloroplasty in subsets of patients with gastroparesis.[20,21]

Our study has several limitations. First, it is a single-center study, with only one endoscopist performing the procedure. It is possible that other endoscopists with less experience with the EUS-FNA technique could have lower yields. However, we believe that the technique can be mastered by any well-trained endoscopist with advanced experience. Correlation between the number of myenteric plexus nerve bundles per HPF in endoscopic and surgical biopsies was not done. Unlike the number of ICCs, the relationship between the number of myenteric plexus nerve bundles per HPF and gastroparesis is not explored fully. Although myenteric plexus nerve bundles were seen in only 60% of patients, the possibility of staining for myenteric plexus nerve bundles on EUS samples will allow further exploration of different types of nerve-specific immunostaining to study its relationship with gastroparesis. Another limitation is the relatively small number of patients included in this pilot trial. This was influenced by the need to schedule the surgical procedure to place the gastric neurostimulator device within 24 hours of the EUS-guided biopsies to assure the safety of our patients as initially mandated by our IRB. The extended use of this technique will provide more confirmation of the

safety of the procedure. We hope that EUS-FNA of the antral wall in patients with gastroparesis will be part of the gastroparesis diagnosis algorithm in the future. EUS-FNA biopsies showing depleted ICCs may triage patients for early implementation of gastric electrical stimulator therapy because those patients with depleted ICCs respond well to gastric electrical stimulation. In the future, EUS-guided biopsies can be used to stain for novel gastroparesis markers and to help in assessing the response to medical therapy.

In conclusion, this pilot trial showed that it is feasible with the EUS-FNA technique to obtain adequate and histologically meaningful muscularis propria biopsies of the gastric antrum, obviating the need for surgical full-thickness biopsy. Further data from other centers are needed to confirm the safety and the efficacy of this technique.

REFERENCES

1. Soykan I, Sivri B, Sarosiek I, et al. Demography, clinical characteristics, psychological and abuse profiles, treatment, and long-term follow-up of patients with gastroparesis. Dig Dis Sci 1998;43:2398-404.
2. Parkman HP, Hasler WL, Fisher RS. American Gastroenterological Association technical review on the diagnosis and treatment of gastroparesis. Gastroenterology 2004;127:1592-622.
3. Zeidan A, Gan XT, Thomas A, et al. Prevention of RhoA activation and cofilin-mediated actin polymerization mediates the antihypertrophic effect of adenosine receptor agonists in angiotensin II- and endothelin-1-treated cardiomyocytes. Mol Cell Biochem 2014;385: 239-48.
4. McCallum RW, Sarosiek I, Parkman HP, et al. Gastric electrical stimulation with Enterra therapy improves symptoms of idiopathic gastroparesis. Neurogastroenterol Motil 2013;25: 815-e636.
5. Faussone-Pellegrini MS, Grover M, Pasricha P, et al. Ultrastructural differences between diabetic and idiopathic gastroparesis. J Cell Mol Med 2012;16:1573-81.
6. Grover M, Farrugia G, Lurken MS, et al. Cellular changes in diabetic and idiopathic gastroparesis. Gastroenterology 2011;140:1575-1585, e8.
7. Pasricha PJ, Pehlivanov ND, Gomez G, et al. Changes in the gastric enteric nervous system and muscle: a case report on two patients with diabetic gastroparesis. BMC Gastroenterol 2008;8:21.
8. Camilleri M, Bharucha AE, Farrugia G. Epidemiology, mechanisms, and management of diabetic gastroparesis. Clin Gastroenterol Hepatol 2011;9:5-12; quiz e7.
9. Thomas T, Kaye PV, Ragunath K, et al. Endoscopic-ultrasound-guided mural trucut biopsy in the investigation of unexplained thickening of esophagogastric wall. Endoscopy 2009;41:335-9.
10. Odegaard S, Nesje LB, Hoff DA, et al. Morphology and motor function of the gastrointestinal tract examined with endosonography. World J Gastroenterol 2006;12:2858-63.
11. Hirano I, Pandolfino J. New technologies for the evaluation of esophageal motility disorders: impedance, high-resolution manometry, and intraluminal ultrasound. Gastroenterol Clin North Am 2007;36:531-51, viii.
12. Tsuzuki T, Okada H, Kawahara Y, et al. Usefulness and problems of endoscopic ultrasonography in prediction of the depth of tumor invasion in early gastric cancer. Acta Med Okayama 2011;65:105-12.
13. Lin Z, Sarosiek I, Forster J, et al. Association of the status of interstitial cells of Cajal and electrogastrogram parameters, gastric emptying and symptoms in patients with gastroparesis. Neurogastroenterol Motil 2010;22:56-61, e10.
14. Choi KM, Gibbons SJ, Nguyen TV, et al. Heme oxygenase-1 protects interstitial cells of Cajal from oxidative stress and reverses diabetic gastroparesis. Gastroenterology 2008;135:2055-64, 2064, e1-2.
15. Kashyap P, Farrugia G. Enteric autoantibodies and gut motility disorders. Gastroenterol Clin North Am 2008;37:397-410, vi-vii.
16. Hejazi RA, Sarosiek I, Roeser K, et al. Does grading the severity of gastroparesis based on scintigraphic gastric emptying predict the treatment outcome of patients with gastroparesis? Dig Dis Sci 2011;56:1147-53.
17. Friedenberg FK, Palit A, Parkman HP, et al. Botulinum toxin A for the treatment of delayed gastric emptying. Am J Gastroenterol 2008;103: 416-23.
18. Ramkumar D, Schulze KS. The pylorus. Neurogastroenterol Motil 2005;17(suppl 1):22-30.
19. Mearin F, Camilleri M, Malagelada JR. Pyloric dysfunction in diabetics with recurrent nausea and vomiting. Gastroenterology 1986;90:1919-25.
20. Toro JP, Lytle NW, Patel AD, et al. Efficacy of laparoscopic pyloroplasty for the treatment of gastroparesis. J Am Coll Surg 2014;218:652-60.
21. Hibbard ML, Dunst CM, Swanstrom LL. Laparoscopic and endoscopic pyloroplasty for gastroparesis results in sustained symptom improvement. J Gastrointest Surg 2011;15:1513-9.