

Pain: The Overlooked Symptom in Gastroparesis

W. A. Hoogerwerf, M.D., P. J. Pasricha, M.D., A. N. Kalloo, M.D., and M. M. Schuster, M.D.

The Marvin M. Schuster Center for Digestive and Motility Disorders, Johns Hopkins Bayview Medical Center, and the Division of Gastroenterology, Johns Hopkins Hospital, Baltimore, Maryland

OBJECTIVE: Abdominal pain has not been reported generally as a significant feature of the clinical presentation of patients with gastroparesis.

METHODS: Using a standardized questionnaire, we analyzed the clinical features of 28 consecutive patients referred with established or suspected gastroparesis over a 4-yr period. The diagnosis of gastroparesis was supported by abnormalities in gastric emptying studies (GES), electrogastrography (EGG), or upper endoscopy (EGD). Diagnostic tests were reviewed.

RESULTS: A total of 12 male (mean age 39.5 yr) and 18 female patients (mean age 39.6 yr) were included in this study. These patients had been symptomatic for an average of 37.8 months before their referral to our center. Seven of these patients had insulin-dependent diabetes. Idiopathic gastroparesis was present in more than half of the patients. The symptom profile of the 28 patients was as follows: nausea, 92.9%; abdominal pain, 89.3%; early satiety, 85.7%; and vomiting, 67.9%. The pain was described as burning, vague, or crampy in nature. Only 36% localized to the upper abdomen. In all, 60% of patients complained of postprandial pain, whereas 80% complained of nocturnal pain that interfered with their normal sleeping pattern. In general, pain responded poorly or not at all to prokinetic agents.

CONCLUSIONS: Nausea and abdominal pain are the most common complaints of patients with gastroparesis. In 80% of patients, GES and EGG correlated positively. (Am J Gastroenterol 1999;94:1029–1033. © 1999 by Am. Coll. of Gastroenterology)

INTRODUCTION

Classically, delayed gastric emptying (gastroparesis) has been a diagnosis made on the basis of clinical symptoms such as early satiety, nausea, and vomiting (1). Currently, scintigraphy is the most commonly used objective test to demonstrate delayed gastric emptying, although electrogastrography has been recognized as a valuable tool (2, 3).

The most common, known cause of gastroparesis is diabetes mellitus. Presumably this is the result of visceral

autonomic neuropathy. Other causes of gastroparesis include inflammatory, endocrine, collagen, and infiltrative diseases that affect the gastric mucosa and the underlying muscular layer, as well as muscular dystrophies; however, approximately one-third of patients are classified as idiopathic. Gastroparesis can have devastating complications, such as malnutrition, psychological distress, and depression (4). In this study, the clinical features of 28 patients with established gastroparesis were assessed, as were the results of diagnostic tests used to establish their diagnoses. These included gastric emptying scan (GES), electrogastrography (EGG), and esophagogastroduodenoscopy (EGD).

MATERIALS AND METHODS

Charts were reviewed from a 4-yr period (1991–1995). The 32 patients screened as possible candidates were those who presented to our institution with a preliminary diagnosis of gastroparesis. The inclusion criteria for patients selected from this larger group were: 1) a clinical suspicion of gastroparesis based on symptoms of early satiety, or long standing nausea, or vomiting of food >3 h postprandially; 2) absence of mechanical obstruction secondary to underlying pathology such as cancer by EGD or upper GI series; 3) demonstration of gastric retention on the basis of GES, EGD, or EGG to support the clinical diagnosis of gastroparesis. A total of 28 patients met these criteria (12 men and 16 women). Delayed GES was defined as T1/2 being >100 min for solids.

EGG was defined as abnormal if >30% of the cyclic electrical activity was outside of the normal 2.5–3.5 cycles/min in the fasting state. We used a standardized questionnaire which for many years has been given to all of our patients on their first visit. Topics covered were: 1) pain and its qualifiers—presence, location, quality, and duration, as well as aggravating and alleviating factors, and the presence of nocturnal pain; 2) presence of other GI symptoms—i.e., early satiety, nausea, vomiting, or heartburn; 3) general review of systems; 4) family history; 5) surgical history; 6) past medical history; and 7) medications. A section of the questionnaire allowed for additional comments by the patients if they felt certain topics were not covered by the standardized questions. In addition to the questionnaire, the history and physical examination notes from the medical record were reviewed.

Table 1. Results From GES and EGG Studies

	Delayed	Rapid	Normal	
GES	91% (20/22)	4.5% (1/22)	4.5% (1/22)	
	Tachygastria	Bradygastria	Tachy/Brady	Normal
EGG	80.8% (21/26)	7.7% (2/26)	3.8% (1/26)	7.7% (2/26)

GES = gastric emptying scan; EGG = electrogastrography; Tachy = tachygastria; Brady = bradygastria.

Most of the GES, EGG, and EGD studies were performed at the Johns Hopkins Bayview Motility Center; however, GES and EGD in some instances had been performed by the outside referring physicians and therefore were not repeated. All EGGs were done at The Johns Hopkins Bayview Motility Center.

RESULTS

GES, EGD, and EGG Studies

All 28 patients underwent GES or EGG: 26 of the 28 patients underwent EGG, 22 underwent GES, and 20 underwent both. In all patients, the diagnosis of gastroparesis was supported by abnormalities in GES, or EGG, or EGD. Of the 22 patients who underwent GES, 95% had abnormal transit. The vast majority (91%) had delayed emptying, and only 4.5% had a normal gastric emptying scan (Table 1). Among the patients for whom the exact GES figures were available, the T1/2 ranged from 120 min to 12 h. For the remaining patients the report simply indicated that gastric emptying was delayed.

In 92% of the patients who underwent EGG, the study was abnormal, (bradygastria or tachygastria), whereas the remaining 8% of patients had normal findings (Table 1). Of the 20 patients who underwent both GES and EGG, 90% showed delayed gastric emptying and 90% showed EGG abnormalities. A total of 80% showed abnormalities on both studies, with 20% showing a discrepancy between the findings on GES and EGG (Fig. 1). Of the 28 patients with a positive GES or EGG, 26 underwent EGD. Of these, 50% had a normal EGD; 34% had signs of inflammation (either esophagitis, gastritis, or duodenitis) and only 8% showed

evidence of gastric retention (Fig. 2). Two of the 28 patients had a normal upper GI series.

Analysis of Clinical Features

Seven of the 28 patients carried a diagnosis of insulin-dependent diabetes mellitus (IDDM). One patient had Schmidt's syndrome (which includes diabetes mellitus) and one patient had systemic lupus erythematosus/mixed connective tissue disorder (SLE/MCTD). Five patients had a significant history of GI surgery including vagotomy (for peptic ulcer disease [PUD]), pancreaticojejunostomy and vagotomy, Nissen fundoplication (for chronic reflux), Billroth 2 operation (for PUD), and liver transplantation. Fifteen of the 28 patients were labeled as idiopathic. Thus, no detectable cause was present in more than half of the patients, and diabetes was the most common known cause.

The average age was 39.5 yr, remarkably similar for both men and women. The average duration of symptoms for all patients was 37.8 months. Weight loss was reported in 64% of the patients. The weight loss was documented as reported by the patients on their initial visit. A wide range of weight loss was reported with 5–70 lb spread over .5 to 120 months.

Among the patients, 75% had a history of prokinetic medication use. The major upper gastrointestinal complaints were nausea (92.9%), abdominal pain (89.3%), and early satiety (85.7%). Altered bowel habits and fatigue were more common than the remaining upper gastrointestinal complaints such as vomiting (67.9%), postprandial pain (53.5%), and heartburn (42.9%).

Pain

Of all patients, 76% had localized pain. Although only 36% had upper abdominal pain, this was the most common site. The nature of the pain varied. It was constant in 28%. The remainder complained of intermittent pain. The pain was felt to be burning, vague, or crampy in 64% of patients. Of the 25 patients with complaints of pain, 80% had nocturnal pain that interfered with their normal sleep pattern. Sixty percent reported that eating made the pain worse, 15% that it decreased the pain, and 8% that it had no impact on their pain; 17% did not comment on the effect of eating on their pain.

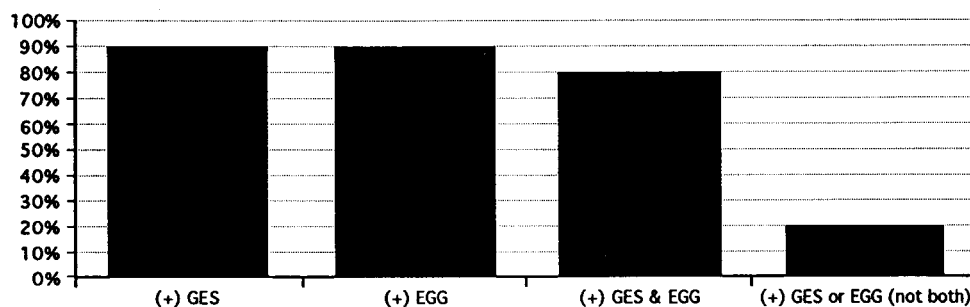


Figure 1. Concordance of gastric emptying scan (GES) and electrogastrography (EGG).

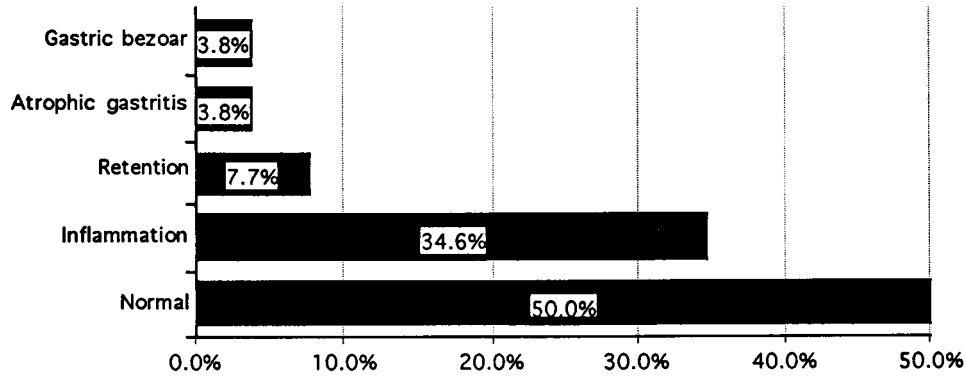


Figure 2. Esophagogastroduodenoscopy (EGD) findings in patients with positive findings on gastric emptying scan (GES) or electrogastrography (EGG).

Altered Bowel Habits

Diarrhea was reported in 75% (21) of patients. However, in 76% (16) of those reporting diarrhea, it occurred only “occasionally” (defined here as less than once every 4 wk). Still, 24% reported diarrhea that was more frequent than “occasional.” Among all patients, 80% (24) of patients reported occasional constipation; 43% of the 28 patients complained of heartburn; four of these 12 patients had gastritis by EGD; and 71% of all patients reported a significant increase in fatigue.

Drug Use

Of the study group 75% were taking prokinetic drugs for ≥3 wk before their first visit (Table 1). Eighty-one percent were on metoclopramide, 43% were on cisapride, and 19% were on erythromycin; 33% of the patients were on multiple medications. Only one patient reported symptomatic improvement with prokinetics.

Relationship of Pain to

Findings on GES, EGG, and EGD

There was no correlation between the presence or absence of pain and findings on GES, EGG, or EGD (Table 2).

DISCUSSION

Using the generally accepted clinical criteria for the diagnosis of gastroparesis, early satiety, nausea, and vomiting,

supported by findings on GES, EGD, or EGG, we assessed the frequency of symptoms (*e.g.*, pain and its qualifiers, weight loss, etc.) outside of the classic profile. In addition, we determined concordance between current physiologic testing (GES or EGG).

Study Group

Our group, reflecting the reported prevalence, consisted mostly of patients with idiopathic gastroparesis, but also included those patients with diabetes as well as gastroparesis secondary to a connective tissue disorder or to surgery (postsurgical gastroparesis). Nonidiopathic gastroparesis is most commonly due to diabetes, but may accompany collagen vascular disease, postradiation treatment, or drugs. Regardless of the underlying etiology of gastroparesis, the symptom profile of the 28 study patients seemed similar.

Overview of GES, EGG, and EGD Studies

GES is currently the gold standard for quantitating gastric emptying (3, 4, 10, 11), but was no better than EGG in this study. Of our patients who underwent GES, 91% showed delayed gastric emptying. Of the patients who underwent EGG, 92% had abnormal findings with tachygastria being the predominant finding; and 80% of the patients showed abnormalities on both EGG and GES, suggesting a high positive concordance between these two studies in delayed gastric emptying.

EGG has been recognized as a valuable tool in the diag-

Table 2. The Relationship of Pain to the Findings on GES, EEG, and EGD

	GES			EGG			EGD		
	% With Study	% Abnormal	% Normal	% With Study	% Abnormal	% Normal	% With Study	% Abnormal	% Normal
No pain (3)	66% (2)	100% (2/2), delayed	0%	100% (3)	100% (3/3), tachy	0%	100% (3)	0%	100% (3/3)
Pain (25)	80% (20)	90% (18/20), delayed; 5% (1/20), rapid	5% (1/20)	92% (23)	78% (18/23), tachy; 8.6% (2/23), brady; 4.3% (1/23), tachy/brady	8.6% (2/23)	92% (23)	57% (13/23)	43% (10/23)

GES = gastric emptying scan; EGG = electrogastrography; EGD = esophagogastroduodenoscopy; tachy = tachygastria; brady = bradygastria.

nosis of gastroparesis, although it is mainly available at academic research centers. A variety of gastric dysrhythmias have been associated with gastroparesis. EGG is considered abnormal when there is bradygastria or tachygastria >30% of the time (2, 6, 13). However, controversial findings are reported in the literature. Koch *et al.* (5) showed no association between EGG and gastric emptying, whereas Abell *et al.* (6) did find a good correlation between EGG and gastric emptying. Chen and McCallum suggested that a normal EGG recording may not guarantee normal gastric emptying, but that an abnormal EGG may predict delayed gastric emptying (2). The high concordance between EGG and GES found in this study supports the previous findings of a correlation between EGG and gastric emptying.

Only 34.6% (nine of 26) of the study patients had abnormal findings on EGD, mainly esophagitis, gastritis, and duodenitis. Three of the 28 patients had undergone surgery for PUD/chronic reflux, but gastroparesis presented only after their surgery. This suggests that the inflammation found on EGD may be a complication of gastric stasis rather than a primary cause of delayed gastric emptying.

Relationship of Pain to Findings on GES, EGG, and EGD

Pain was second only to nausea as a major symptom of gastroparesis. It should therefore be considered one of the cardinal symptoms of this disorder. Of the patients with pain and EGG studies, 91% had a gastric dysrhythmia on EGG. These findings might suggest that underlying gastric dysrhythmias are a cause of pain. However, all patients with normal findings on EGG had pain, and all patients without pain had an abnormal EGG and GES. Therefore, we cannot draw conclusions as to the relationship of EGG findings and the presence of pain. Part of the difficulty may be in the small numbers of patients.

Of the patients with pain and GES studies, 90% had delayed gastric emptying. Although delay in gastric emptying is considered a marker for gastroparesis or a result of gastroduodenal abnormality, abnormal motility does not always correlate with clinical symptoms and *vice versa* (7). One new hypothesis to explain functional abdominal pain and motility disorders is that of a neurogenic disturbance at the enteric nervous system level or spinal/brain level (9, 13–16). This neurogenic disturbance can cause visceral hypersensitivity to regional stimuli. This might explain the difference in sensitivity to perception of pain between normal individuals, as there is among patients with different diseases. Diabetic patients often have decreased perception to pain stimuli, whereas patients with nonulcer dyspepsia, as a group, have increased sensitivity to gastric distention, as shown by Coffin *et al.* (8).

The pain, as reported by the patients in this study, presented in a variety of locations. That the pain did not localize to any particular region, especially the epigastric region, suggests that it is either referred pain or it is not exclusively

caused by gastric distention. In gastroparesis, pain may therefore represent a more generalized derangement of the enteric nervous system such as visceral hypersensitivity, or it may represent sensory referred pain. To what extent motility and abnormal visceral sensitivity are associated remains to be determined.

Selection Bias

In this study there is a risk of selection bias because the setting is a tertiary GI referral center for motility disorders. We could be reporting a high incidence of abdominal pain in a self-selected group of patients who failed to respond to standard prokinetic therapy; 75% of the patients were on prokinetic drugs, with only one patient reporting a favorable response. This, too, may reflect a referral bias, with only nonresponsive patients being referred. Additionally, the patients in our study group probably represent the more severe cases in the spectrum of gastroparesis.

In conclusion, abdominal pain and nausea, are the most common complaints of patients with gastroparesis, including those with gastroparesis secondary to diabetes. In 80% of the patients, GES and EGG correlated positively. Potential therapeutic approaches to this syndrome need to address this symptom carefully.

Reprint requests and correspondence: Marvin M. Schuster, M.D., F.A.C.P., F.A.P.A., F.A.C.G., Professor of Medicine and Psychiatry, Johns Hopkins Bayview Medical Center, 4940 Eastern Avenue, Baltimore, MD 21224.

Received May 6, 1998; accepted Nov. 23, 1998.

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