Dynamic Antral Scintigraphy to Characterize Gastric Antral Motility in Functional Dyspepsia

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We evaluated intragastric food distribution and antral motor activity in patients with functional dyspepsia. **Methods:** A standard gastric emptying test and dynamic imaging of the antrum were used to characterize gastric antral motility disturbances and to correlate them with total and compartmental gastric emptying in 25 dyspeptic patients. **Results:** We found a 40% prevalence of gastroparesis in functional dyspepsia. Solid gastric emptying delay is indicated by a prolonged lag phase and an increase in frequency and amplitude of gastric contractions, resulting in nonexpulsive antral contractions and/or antropyloric dyscoordination. Food retention in the distal stomach and antral distention appears to account for patients' dyspeptic symptoms. **Conclusion:** This study demonstrates that scintigraphy not only detects abnormalities of food distribution in the stomach but also provides information on antral motor activity noninvasively. Dynamic antral scintigraphy and compartmental gastric emptying are useful tools to define the pathophysiology of dyspeptic patients with or without gastroparesis.

Key Words: scintigraphic gastric emptying; food distribution; antral motility; functional dyspepsia

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Dyspepsia is common in the normal adult population, with 38% reporting a history of dyspeptic symptoms in the last 6 mo; dyspepsia also accounts for 3%–4% of consultations to general practitioners (*1*). The clinical description of dyspepsia includes a constellation of symptoms such as abdominal pain or discomfort, early satiety, fullness, distension, bloating, nausea, vomiting, belching and epigastric or retrosternal burning. Based on the presence or absence of underlying structural and/or biochemical abnormalities, dyspepsia is categorized as either organic or functional (idiopathic). Patients with dyspeptic symptoms but normal physical examination, blood tests, biliary tree ultrasonography and endoscopic findings fit into this latter category.

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The pathophysiology of functional dyspepsia remains unclear. Complex and objective detailed evaluation of patient symptoms does not necessarily establish a dominant etiologic factor. Postprandial antral hypomotility (*2,3*), nonexpulsive antral contractions (*4*), alterations to gastric pacemaker function and abnormal myoelectric activity (*5*) may contribute to patient symptoms and explain the delay in gastric emptying of solids observed in these patients.

The dominant role of the antrum in the emptying of solid food and the manometric observations that few low-amplitude contractions are detected in response to a meal in patients with various stomach disorders have led to the conclusion that delayed gastric emptying of a solid meal is synonymous with antral hypomotility in functional dyspepsia (*6,7*).

We have previously demonstrated that dynamic gastric scintigraphy allows visualization and characterization of antral contractions in healthy subjects and diabetic patients with or without gastroparesis (*8,9*). We have also shown that scintigraphy can be used simultaneously to evaluate the compartmentalization of food inside the stomach and to quantify the emptying of a radiolabeled test meal from each compartment (*10*).

The purpose of this scintigraphic study was threefold: to investigate food distribution in the stomach in patients with functional dyspepsia; to characterize, in those patients, antral motility; and to correlate gastric emptying parameters with antral motor activity.

MATERIALS AND METHODS

Subjects

We studied 25 patients with idiopathic dyspepsia (17 women, 8 men; mean age 44 ± 11 yr) and compared their results with 10 healthy controls (5 women, 5 men; mean age 43 ± 12 yr) who were studied previously (*9*). Patient selection was based on the presence of at least two of the following symptoms for more than 3 mo: abdominal pain or discomfort, early satiety, bloating, distension, belching, nausea, vomiting. None of the patients had prior gastrointestinal surgery, peptic ulcer disease, scleroderma, gastric outlet obstruction, biliary abnormality or metabolic disease. In addition, no patient was taking any pharmaceutical likely to influence gastric emptying. Control subjects were free of any gastrointestinal symptoms, had no history of gastrointestinal surgery

and were not taking any medication. All patients and control subjects had normal esophageal and gastric endoscopy. The study was approved by our local institutional review boards and informed consent was obtained from each subject.

Scintigraphic Test Procedure

All controls and patients were studied after an overnight fast of at least 12 hr. Gastric emptying was evaluated after ingestion of a standardized test meal consisting of 50 g scrambled egg labeled with 74 MBq (2 mCi) ^{99m}Tc-sulfur colloid, 2 slices of regular white bread and 150 ml water labeled with 75 μCi ^{111}In-DTPA. Simultaneous 1-min anterior and posterior static images (128 × 128 pixels) of the stomach were acquired on the 140-keV ^{99m}Tc and 247-keV ^{111}In peaks with the subjects sitting between the two detectors of a dual-head gamma camera. Images were taken every 10 min for 1 hr and every 15 min for the second hour and, if needed, until 50% of the meal had emptied from the stomach. Anterior dynamic (64 × 64 pixels) frames of 1 sec each were also acquired for 4 min at 11, 31, 41, 61, 91 and 121 min. In four patients, dynamic images were obtained up to 150 min after meal completion to reach 50% emptying.

Data Analysis

Static Images. After correction for technetium decay and indium down scatter, regions of interest (ROIs) were drawn around the total, proximal and distal stomach at each time interval. Geometric mean counts were determined for each region and isotope and percentages of meal retention were calculated. Total stomach data for solids were analyzed using the power exponential function

$$y(t) = 1 - (1 - e^{-kt})^{\beta},$$

which permits determination of the solid lag phase (TLAG), emptying rate (ER) and half-emptying time (*10*). The parameters k and β of this function were determined by a nonlinear least-squares fitting algorithm. Total stomach liquid emptying data were fit to a single exponential function to determine the emptying rate and half-emptying time.

The methodology used to process dynamic images has been described elsewhere (*9*). Briefly, to allow for precise outlining of the antrum, each set of dynamic images was first reframed in a single 4-min image and a ROI was drawn around the horizontal portion of the stomach between the incisura angularis and the pylorus. A time-activity curve was then generated for each dynamic set of images. Curves were first normalized to their respective mean count. The auto correlation function

$$A(T) = \int C(t) \cdot C(t + T)\, dt,$$

where t is the time and T the lag time of the correlation, was then applied to each set of normalized data. This function eliminates the background noise and the nonperiodical events in the defined time interval. The frequency (in contractions per minute) and amplitude (in percent variation around the mean) in the time domain of the antral contractions were obtained for each set of dynamic acquisition using Fourier transform analysis:

$$F(w) = \Delta t \int A(T) \cdot \cos(wT)\, dT,$$

where w is the pulsation frequency. A scintigraphic antral motility index (SAMI) equal to the frequency times the amplitude of the antral contractions was also determined by analogy to manometric recordings. The average frequency, amplitude and motility index for the whole gastric emptying course were calculated for each subject.

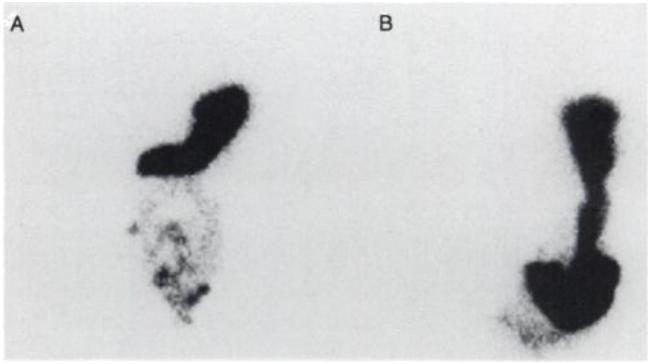


FIGURE 1. Image of the stomach in a normal subject (A) and in a patient with dyspepsia (B) 30 min after ingestion of the test meal. The patient's stomach has an elongated J-shape and the antrum is distended.

Statistical Analysis

Statistical computation was performed on a computer using the Statview® 4.0 software package (Abacus Concepts, Berkeley, CA). Unpaired t-tests were used to compare the percentages of meal retention, lag phase, emptying rate and half-emptying time values, as well as the antral contractions' amplitude and frequency and motility indices between dyspeptic patients and healthy controls. One-way analysis of variance was performed to compare these parameters between controls, idiopathic patients with delayed emptying and idiopathic patients with normal emptying. Differences were considered significant when $p < 0.05$. A linear correlation analysis was used to determine the relation between gastric emptying parameters and the amplitude and motility indexes.

RESULTS

No significant difference in age distribution and meal ingestion time was observed between patients and controls. Compared to control subjects, each patient with dyspepsia had a bizarre configuration of the stomach, which had either an elongated J-shape or an entirely horizontal position (Fig. 1A, B).

Global Analysis

Total Gastric Emptying (Table 1). Gastric emptying of solids was significantly delayed in patients with dyspepsia compared to control subjects (Fig. 2A). This was accounted for by both a prolonged lag phase, a slower emptying rate and, consequently, a longer half-emptying time.

No significant difference was observed for any parameter of liquid emptying between patients with dyspepsia and control subjects (Fig. 2B).

Compartmental Gastric Emptying. During the first 10 min, the percentage of solid retained in the proximal portion of the stomach was higher in patients with dyspepsia than in control subjects. After the initial retention, proxi-

TABLE 1
Gastric Emptying Parameters in Control Subjects and Idiopathic Patients with and without Gastroparesis

	Solids			Liquids	
	Lag Phase (min)	Emptying rate (%/min)	$T_{1/2}$ (min)	Emptying rate (%/min)	$T_{1/2}$ (min)
Controls	22.3 ± 12.8	1.74 ± 0.5	62 ± 13	2.1 ± 0.7	36 ± 11
Patients	47.3 ± 25.9*	1.58 ± 0.6*	88 ± 28*	2.03 ± 0.6	37 ± 13
DN	34.4 ± 22†	1.63 ± 0.6†	72 ± 11†	2.23 ± 0.7	36 ± 11
DD	67.4 ± 23‡	1.32 ± 0.7‡	116 ± 19‡	1.74 ± 0.5	43 ± 14

*$p < 0.005$ dyspeptic patients versus control subjects.
†$p < 0.05$ DD versus DN.
‡$p < 0.05$ DD versus control subjects.
DD = delayed solid emptying; DN = normal gastric emptying.

mal stomach emptying for solids and liquids was faster in patients than in control subjects (Fig. 2C, D).

Compared to controls, distal stomach retention of solid food was significantly increased in patients with dyspepsia (Fig. 2E). In contrast, liquid retention in the distal stomach was the same in patients and control subjects (Fig. 2F).

Antral Motor Activity. Beyond 10 min after meal ingestion, the frequency of antral contractions was significantly higher in patients compared to control subjects (Fig. 3A). Normal subjects showed a significant decrease in frequency over the 2-hr test period.

The strength of antral contractions was also remarkably increased in patients with dyspepsia compared to controls (Fig. 3B) for the entire postprandial period, with a peak at 41 min. The scintigraphic antral motility index was significantly increased in patients with dyspepsia compared to controls subjects.

Correlation between Antral Motor Activity and Gastric Emptying Parameters. In control subjects, an inverse correlation was found between the lag phase and the motility indices ($r = -0.673$ and $r = -0.666$; $p < 0.05$), i.e., the higher the motor activity of the antrum, the shorter the lag phase and the faster the emptying. In patients, no correlation could be found between any of these parameters.

Subgroup Analysis

In an attempt to further refine the analysis of gastric emptying abnormalities in the patient group and based on the common observation that distribution of gastric half-emptying times of patients with symptoms of gastroparesis is usually normal, we divided the dyspeptic population into two groups according to the solid gastric emptying result. Using the cutoff value of $T_{1/2}$ + 2 s.d. obtained in control subjects, 10 of the 25 patients (40%) had delayed solid emptying and 15 patients had normal gastric emptying.

Total and Compartmental Gastric Emptying for Solids. Figure 4A shows total gastric emptying for controls and dyspeptic patients with and without gastroparesis. Although the lag phase was prolonged, there was no statistically significant difference in half-emptying times between patients with dyspepsia but no gastroparesis compared to control subjects. Both a prolonged lag phase and a slower emptying rate accounted for delayed emptying in patients with dyspepsia and gastroparesis compared to controls and patients with normal half emptying times.

Food distribution in the stomach was different between controls and patients immediately following meal ingestion: 64% of the test meal was retained in the proximal stomach in healthy controls versus 81% in patients with normal gastric emptying, and 84% in patients with gastroparesis (Fig. 4C). The initial retention of food in the proximal stomach in patients with delayed gastric emptying was followed by rapid emptying. In patients with normal emptying, the proximal emptying course was faster than in control subjects.

Solid food retention in the distal stomach was higher in patients with gastroparesis compared to controls and patients with normal gastric emptying. It was also higher in patients with normal gastric emptying compared to controls. Maximal filling of the distal stomach (Fig. 4E) was obtained at ±10 and 25 min in healthy subjects and normal patients with dyspepsia, respectively. Distal stomach filling in patients with delayed gastric emptying occurs at ±50 min.

Total and Compartmental Gastric Emptying of Liquids. Emptying of liquids was slightly but significantly delayed in dyspeptics with gastroparesis compared to control subjects and dyspeptic patients without gastroparesis (Table 1). This delay was essentially related to retention in the distal stomach (Fig. 4B,D,F).

Antral Motor Activity. Beyond 10 min, the frequency of antral contractions in both patient groups remained higher than that in control subjects for the entire postprandial period (Fig. 5A). No statistical difference was observed between patients with and without gastroparesis. A striking increase in amplitude of antral contractions (Fig. 5B) was seen during the entire gastric emptying course in patients with normal gastric emptying compared to control subjects. A statistically significant, but inconstant, increase was observed in patients with gastroparesis. Starting at 30 min, the SAMI was higher in patients with normal empty-

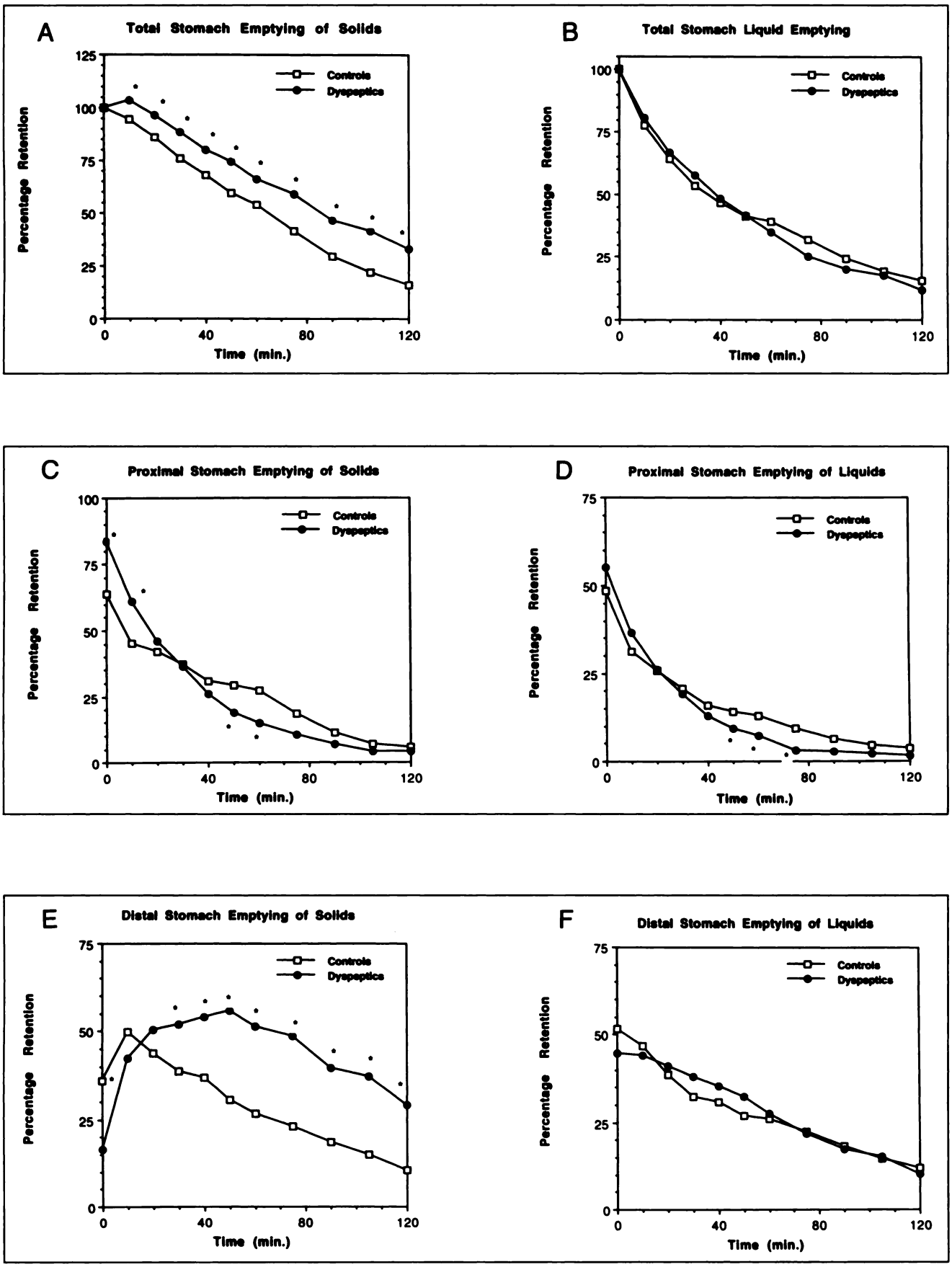


FIGURE 2. Solid and liquid meal retention in the total (A, B), proximal (C, D) and antral (E, F) portions of the stomach in controls and patients. Gastric emptying of solids is significantly delayed in patients compared to the control group. *$p < 0.05$ patients versus controls.

ing times and patients with gastroparesis compared to controls (Fig. 5C).

Correlation between Antral Motor Activity and Gastric Emptying Parameters. No correlation could be found between any gastric emptying parameter or dynamic motility index in either patient group, suggesting that hypermotility induces a disruption of normal gastric emptying mechanics.

DISCUSSION

Depending on patient selection and the methodology used to assess gastric emptying, the frequency of gastroparesis in patients with functional dyspepsia has been found to vary from 28% (*11*) up to 75% (*2*). This broad range reflects the absence of current consensus on how to categorize dyspepsia based on specific pathophysiologic abnormalities (*12–14*). Most authors still prefer to use the standard classification which differentiates organic from functional dyspepsia based on the presence or the absence of a well-recognized underlying process responsible for patient symptoms such as esophagitis, gastritis, peptic ulcer and biochemical abnormalities.

Using this latter definition and the scintigraphic gastric emptying technique, we observed a 40% prevalence of gastroparesis in idiopathic dyspepsia. This is in agreement with studies showing between one-third and two-thirds of patients with functional dyspepsia have delayed solid gastric emptying, while liquid emptying is normal or slightly delayed (*7,11,15–18*). Our results also confirm that the delay in solid emptying is accounted for by prolongation of the lag phase and slowing of the emptying rate (*18*). The compartimentalization of the stomach into its two distinctly functional portions, namely the proximal and distal stomach, further demonstrates that the distal stomach is responsible for food retention while the proximal stomach emptying appears to be normal in functional dyspepsia. This later finding correlates with the observation that the receptive relaxation and accommodation reflexes of the proximal stomach are intact in idiopathic dyspepsia (*17,19–20*) and contrasts with the impairment of the proximal stomach observed in diabetic gastroparesis (*9,21*). Retention of ingested food in the distal stomach has been demonstrated by others using scintigraphic (*22–23*) and ultrasonographic (*24–25*) studies. These studies suggest an impairment of antral motor activity.

Pathophysiologic information is limited in functional gastroparesis. Based on manometric and static scintigraphic studies, Camilleri suggested that antral hypomotility is the major cause of gastric emptying delay (*6–7*). Functional gastroparesis can be accounted for by both fasting and postprandial hypomotility (*2–3,15–16,26*), bradygastria and tachygastria (*5,27–28*), nonexpulsive antral contractions (*4*), defective proximal small bowell motility (*15,29–30*) and, potentially, abnormal coordination of antropyloric contractions (*31–32*). It is now clear that normal gastric emptying requires the concerted and finely tuned action of the proximal stomach, antrum, pylorus, and duodenum (*32–35*). Our observation of an increased antral motility index in functional dyspepsia generating different patterns of gastric emptying contrasts with the literature and is puzzling. With the current limited knowledge of the pathophysiologic mechanisms of dyspepsia, explanations can only be partial and, to some extent, speculative. The increased antral motor activity observed in our study relates to both an increase in frequency and amplitude of antral contractions. It is well known that the frequency of antral contractions is, among other factors, under control of the excitatory and inhibitory impulses from the vagus nerve.

It is likely that the increased frequency we observed in our dyspeptic population reflect the impairment of vagal tone, which is a characteristic of patients with functional dyspepsia (*23*). Also, the retention of food in the distal stomach we observed has been described previously and generates antral distention (*36,37*). This retention-distention is reflected by a prolongation of the lag phase (*10*) and probably explains the elongated shape of the stomach seen in our dyspeptic patients. The increase in amplitude of antral contractions might therefore represent the physiological response of the antral smooth muscle to the outstretching wall and correspond to changes in muscle activity based on the force-length relation mechanism (*38*). Differences in gastric emptying times between patients with and without gastroparesis could then be explained by the fact that the response of antral muscle to distention is impaired in patients with gastroparesis and already on the descending portion of the force-length relationship curve. This phenomenon is well known in cardiac pathophysiology and seems to be corroborated in this study by the greater distention of the distal stomach as well as lower amplitude of antral contractions in dyspeptic patients with delayed emptying.

The apparent discrepancy between our findings of increased antral amplitude and the hypomotility state described previously in functional dyspepsia could also be explained by the fact that our dyspeptic population had only moderate gastroparesis. If our patients had had more severe gastroparesis, we would have found a decrease in antral motility. Finally, one can also hypothesize that there was an impairment of antroduodenal coordination, which is required for normal gastric emptying, in our patients with gastroparesis (*33,39*). It has been shown that delayed gastric emptying might be caused by a preponderance of nonexpulsive antral contractions (*28,30*), pyloric dysmotility (*32*) and abnormal small bowel motor patterns (*7,16*). Verification of this hypothesis requires simultaneous recording of antro-pyloro-duodenal pressure and dynamic antral scintigraphy, which was not performed in this study.

The temporal relationship between symptoms and meal ingestion and abnormal gastric and/or duodenal motility patterns observed in patients with idiopathic dyspepsia has led to the conclusion that their symptoms are related to delay in gastric emptying and abnormal gastric and/or

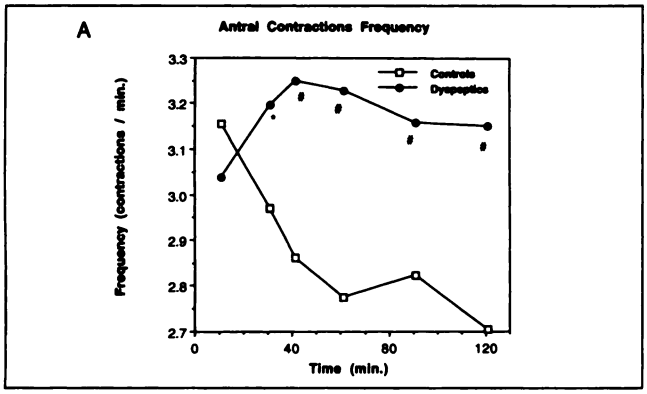


FIGURE 3. Average antral contraction frequency (A), amplitude (B) and motility indices (C) during the gastric emptying course for control subjects and patients. Beyond 10 min, frequency is and remains higher in patients compared to control subjects. The amplitude and motility index are constantly and significantly higher in patients than in controls. *p < 0.05, #p < 0.01 patients versus control subjects.

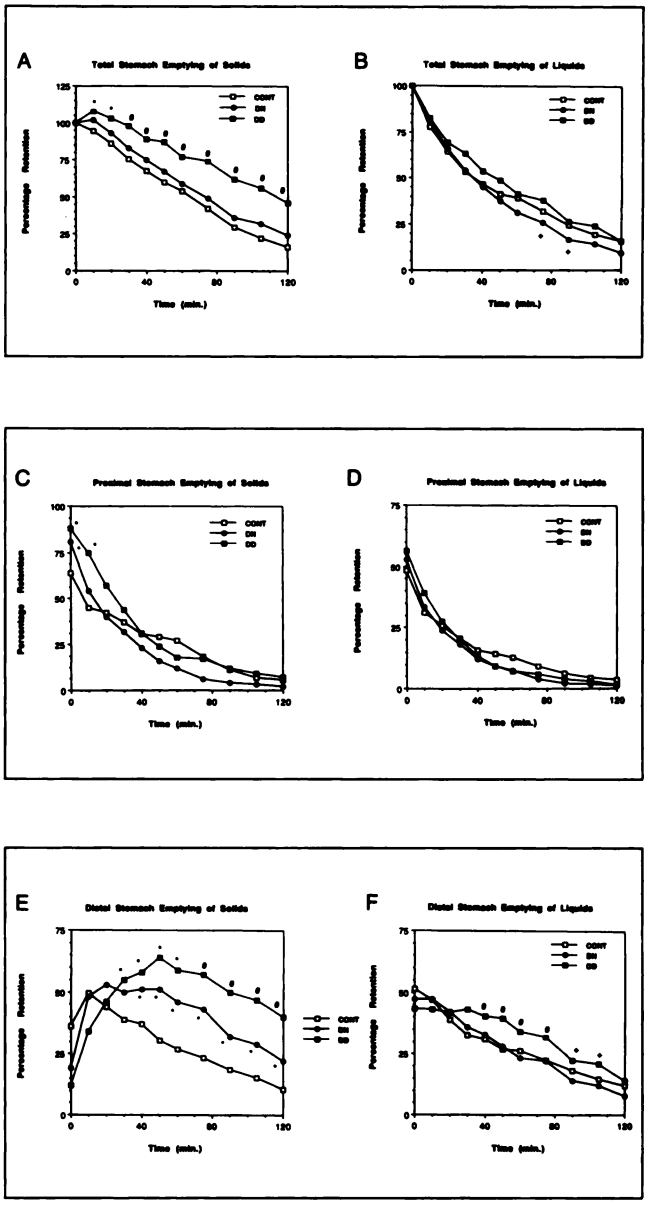
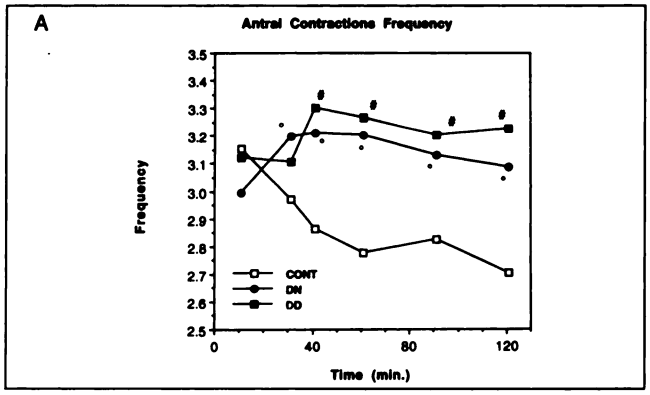
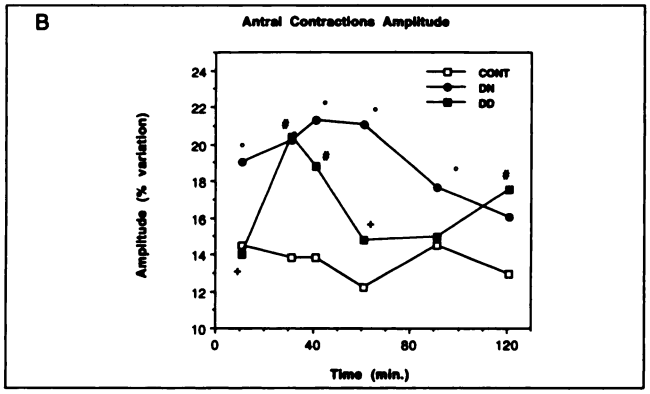


FIGURE 4. Meal retention in the total (A, B), proximal (C, D) and antral (E, F) portions of the stomach in control subjects (CONT), patients with normal gastric emptying (DN) and patients with delayed gastric emptying (DD). *p < 0.05 delayed emptying versus control subjects; #p < 0.05 delayed emptying versus control subjects and normal emptying; °p < 0.05 normal emptying versus control subjects; +p < 0.05 delayed versus normal emptying.

duodenal motility patterns (*40–44*). This assumption does not explain, however, the discrepancy between patients' symptoms and the incidence of gastric emptying delay and the absence of a relationship between symptom severity and the degree of delay in emptying (*41–43*). Emotional and psychological factors such as anger, depression, hysteria, hypochrondriasis have been implicated in the pathogenesis of functional dyspepsia (*46–47*), but these factors seem insufficient to explain the whole cohort of patient symptoms (*48*). In addition to psychological patterns, recent studies on gastric accommodation and distention have demonstrated that patients with functional dyspepsia have a lower threshold to recognition and perception of pain secondary to gastric distention (*17,20*). There is also a correlation between antrum width and abdominal bloating (*36*). Although our study was not aimed at correlating patient symptoms to scintigraphic findings, it is tempting to relate the altered visceral perception abnormality described in functional dyspepsia to the distal stomach dis-





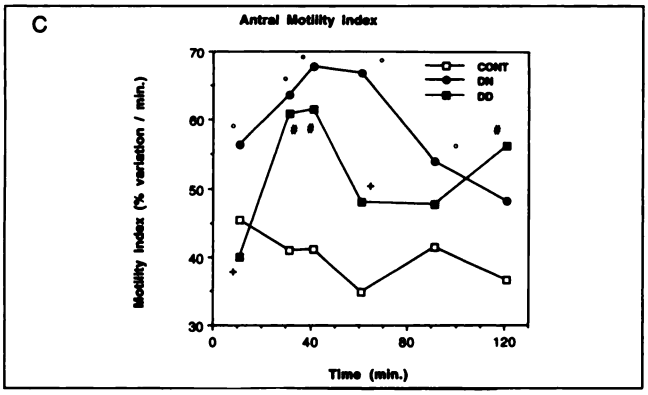


FIGURE 5. Average antral contraction amplitude (A), frequency (B) and motility indices (C) during the gastric emptying course for control subjects (CONT), patients with normal gastric emptying (DN) and patients with delayed gastric emptying (DD). $^{\#}p < 0.05$ delayed versus control subjects; $^{\circ}p < 0.05$ normal emptying versus control subjects; $^{+}p < 0.05$ delayed versus normal emptying.

tention and increased gastric wall tension observed in our patients with and without gastroparesis.

CONCLUSION

This study shows a 40% prevalence of gastroparesis in patients with functional dyspepsia. Gastric emptying delay for solid emptying is accounted for by a prolonged lag phase and antral hypermotility. The hypermotility state is probably related to outstretching of the gastric wall and might generate nonexpulsive antral contractions and/or antro-pyloric dyscoordination. Patient symptoms are likely to correspond to distal stomach distention and altered visceral perception. Dynamic gastric scintigraphy and compartmental gastric emptying are useful tools to define the pathophysiology of dyspeptic patients, with or without gastroparesis. To standardize terminology and to separate scintigraphic studies from manometric recordings, we propose the name dynamic antral scintigraphy for dynamic acquisition and processing of antral images.

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