# Measurement of Gastric Emptying by Standardized Real-Time Ultrasonography in Healthy Subjects and Diabetic Patients

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The aim of this study was to simplify and standardize a reproducible, well-tolerated and clinically applicable method for the assessment of gastric emptŷing rate by real-time ultrasonography. A total of 33 subjects were examined, including 19 healthy subjects and 14 patients with insulin-dependent diabetes mellitus and clinically suspected delayed gastric emptying. Measurements of the gastric antrum were taken in the supine position and in relation to internal landmarks to obtain a standardized cross-sectional image producing the area of a selected slice of the antrum. Diabetic patients were examined on the condition that the fasting blood glucose level was 3.5 to 9.0 mmol/l. Gastric emptying rate was estimated and expressed as the percentage reduction in antral cross-sectional area from 15 to 90 min after the ingestion of a standardized semisolid breakfast meal (300 g rice pudding, 330 kcal). Interobserver and intraobserver measurement errors were assessed, as was the significance of age and sex on gastric emptying. In comparison to healthy subjects, diabetic patients showed significantly wider median values of the 90 min postprandial antral area, but only a mild tendency toward greater dilation of the gastric antrum prior to and 15 min after meal ingestion. The median value of gastric emptying rate in these diabetic patients was estimated at 29%, which was less than half of that in the healthy subjects (63%). Statistically the difference was highly significant. Interpersonal variability of gastric emptying rate and antral areas was large for both groups. Measurements of gastric emptying rate gave highly reproducible results on separate days and from different observers (interobserver systematic measurement error 0.3% and random measurement error 10.9%; intraobserver systematic measurement error 3.6% and random measurement error 9.5%). No difference in gastric emptying rate was found related to age or sex. We conclude that the use of standardized real-time ultrasonography to determine gastric antral cross-sectional area in a single section of the stomach is a valid method for estimating gastric emptying rate. KEY WORDS: Stomach, emptying rate; Diabetes mellitus; Emptying, gastric.

# ABBREVIATIONS

GER, Gastric emptying rate; IDDM, Insulin-dependent diabetes mellitus; BMI, Body mass index; SD, Standard deviation; HBA $_{\rm lc}$  Hemoglobin A $_{\rm lc}$ 

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everal methods have been used to assess gastric emptying in humans.<sup>1,2</sup> Barium contrast examinations, scintigraphy, manometric techniques, and intubation methods have the disadvantages of being invasive and potentially harmful. An alternative safe, reproducible, and reliable noninvasive technique would be preferable. Scintigraphy is still regarded as the gold standard for clinical measurement of gastric emptying.<sup>1–3</sup> Realtime ultrasonography provides another method for dynamic imaging of the gastric peristaltic activity and its effect on stomach emptying. Sonographic measurements of the total gastric volume and determination of postprandial changes in total gastric vol

ume, reflecting gastric emptying, can be obtained by adding cross-sectional areas of a series of slices through the stomach.<sup>4,5</sup> This method, however, also has disadvantages. It is time-consuming and can be done only with liquids; moreover, the technique cannot be performed when it is difficult to visualize the total stomach as a result of excessive air6 or when the gastric fundus is located behind the costal margin. Gastric emptying time also can be determined by restricting the measurements to the changes in the volume of the gastric antrum, which is visible in almost all subjects before and after meals.<sup>7,8</sup> Good correlation has been seen in simultaneous studies of gastric emptying by ultrasonography and scintigraphy.5,6,9,10 Sonographic measurements of antral volumes are reproducible and linearly correlated to the amount of ingested or administered liquids and consequently are representative of the entire gastric contents.11 Thus, by estimating the antral volume, it is possible to measure gastric emptying reliably irrespective of the ingestion of a liquid or solid meal, the presence of air in the fundus, or the anatomic location of the fundus. An even easier way to determine gastric emptying time indirectly, using single scan measuring of the changes in the cross-sectional area or dimensions of the gastric antral region at one selected level, has been proposed.8,9

This study was aimed at simplifying the ultrasonographic method, making it more clinically applicable, and evaluating if the assessment of GER by this simplified real-time sonographic method could be reproducible in a Swedish population consisting of healthy subjects and patients with IDDM and symptoms of delayed gastric emptying.

#### MATERIALS AND METHODS

#### Subjects

# Healthy Subjects

Nineteen healthy subjects (eight men, 11 women; mean age,  $37 \pm 18$  years [range, 18 to 77 years]; BMI,  $23.4 \pm 3.1$  kg/m² [range, 18.1 to 27.2 kg/m²]) without symptoms of gastrointestinal disease, abdominal surgery (except for appendectomy), or diabetes mellitus were recruited from the population in a southern county of Sweden (Table 1). None of the subjects smoked or used snuff. The subjects had no psychiatric diseases or connective tissue, cerebrovascular, or endocrine diseases, nor were they receiving any drugs affecting gastrointestinal motility. On each

study day any current symptoms attributable to the gastrointestinal tract were noted. If the subject reported symptoms indicating constipation or diarrhea, the examination was postponed.

## Diabetic Patients

Fourteen patients with IDDM (eight women, six men; mean age,  $55 \pm 9$  years [range, 40 to 71 years]; BMI,  $22.8 \pm 3.2 \text{ kg/m}^2$  [range, 17.2 to  $28.5 \text{ kg/m}^2$ ]; diabetes mean duration,  $34 \pm 10$  years [range, 20 to 51 years]) and suspected clinically of having delayed gastric emptying were recruited among diabetic patients of the Malmö University Hospital (Table 2). The patients had symptoms suggestive of diabetic gastroparesis (postprandial early satiety, abdominal fullness, nausea, vomiting, or early postprandial hypoglycemia despite the ingestion of food and correctly taken insulin doses). All patients had poor control of glycemia (the mean value of HbA<sub>1c</sub> for the preceding year was 8% or greater despite good compliance) and neuropathy. Twelve had retinopathy and seven showed signs of nephropathy, without uremia. The patients had no evidence of prior gastric outlet obstruction, connective tissue disease, or gastrointestinal surgery (except for appendectomy). Three were snuff-users and one was a smoker (Table 2, patients 2, 4, 10, and 9, respectively). No patients had received drugs affecting gastrointestinal motility<sup>12</sup> for at least 7 days before examination. On each study day, any current symptoms attributable to the gastrointestinal tract were noted. Patients reporting temporary abnormal defecation, such as constipation or diarrhea, were examined on another day on the condition that the abnormal defecation was normalized. Patients with chronic constipation (in our study defined as symptoms for 1 year or longer) were not excluded, as this was assumed to be their basal state, possibly owing to autonomic neuropathy.<sup>13</sup> All subjects were given written information prior to the study and were aware of their option to withdraw from the study any time they desired.

#### Procedure

The subjects were examined between 8:00 and 9:00 a.m. after an 8 h fast. Smoking and snuff-taking were prohibited for 8 h before and during the test. On the day of the study, each healthy subject was checked for normal fasting blood glucose concentration. Measurements of gastric emptying in the diabetic group were done on the condition that the fasting blood glucose concentration was 3.5 to 9.0 mmol/l. Each subject was given 300 g of rice pudding to be ingested within 5 min. Total caloric value was 330

Table 1: Data on Healthy Subjects

Subject No.		Sex			Gastri	Gastric Antral Cross-Sectional Area (mm²)					
			Smoker	Snuff User	BMI (kg/m²)	Fasting	Postprandial				
	Age (yr)						15 min	90 min	Gastric Emptying (%)		
1	18	F	_	_	18.2		315	127	60		
2	19	F	_	****	25.4		545	94	83		
3	20	F	_	_	9.9	269	475	166	65		
4	21	F	_	none.	18.5		812	133	84		
5	22	M	_	_	24.9		377	170	55		
6	23	M			25.4		267	103	61		
7	24	F	_	_	26.8		387	149	62		
8	26	F	_	***	24.7	191	242	129	47		
9	6	M	_	_	23.5		292	124	58		
10	28	M	_	***	25.1		406	124	69		
11	36	F	_	-	24.4		645	192	70		
12	40	M	water .	_	19.2	106	719	68	91		
13	44	M	_	_	23.7	293	577	341	41		
14	45	F	_		27.2	97	489	167	66		
15	54	F		_	18.1	246	<i>7</i> 54	282	63		
16	58	M	_		22.0		777	292	62		
17	59	F		_	23.7		1040	389	63		
18	68	M	_	_	25.9	232	887	279	69		
19	77	F	_	eour	27.1	195	487	223	54		

kcal, provided as 10% protein, 58% carbohydrate, and 32% fat. The temperature of 10 randomly selected test meals was measured immediately prior to ingestion (mean temperature,  $20.7 \pm 2.1$ °C). All subjects were studied in a supine position with the ultrasound transducer applied with minimal abdominal compression. Between examinations the

subjects rested seated in a chair. The measurements of the gastric antrum were performed by two radiologists (C.C., O.B.), who were blinded with regard to the subjects' diagnoses. The diabetic patients' usual oral medications were given after the examination; insulin, however, was taken by the patients before the examination.

Table 2: Data for Diabetic Patients

Subject No.	Age (yr)	Sex	Smoker	Snuff User	BMI (kg/m²)	Diabetes Duration (yr)	Gastric Antral Cross-Sectional Area (mm²)						
							HbA1c(%)	Fasting	Postprandial			Gastric	
									15 min	90 min	120 min	Emptying (%)	
1	40	F		_	24.8	26	9.1	293	1082	477		56	
2	42	M	-	+	22.0	28	9.5	432	815	402		51	
3	46	F		-	23.2	30	8.7		193	58		70	
4	48	M	_	+	23.1	38	8.4		431	409	357	5	
5	51	M		_	24.0	24	8.1		1155	1232	1052	0	
6	52	F	_		19.5	24	8.4		220	211		4	
7	54	F		_	24.2	42	8.6		478	337	309	29	
8	55	F	_	_	25.5	20	8.3	114	1761	754		57	
9	58	F	+	-	17.2	28	8.5		573	305	188	47	
10	59	M		+	27.2	51	8.2		634	470	404	26	
11	62	M	_	_	21.4	36	8.1		898	647	487	28	
12	64	M	_		28.5	39	8.9	365	737	355		52	
13	65	F		_	18.8	48	8.1		473	485	448	0	
14	71	F			20.1	46	9.8		915	767	870	16	

# Reproducibility of the Sonographic Measurements

To evaluate the reliability and reproducibility of the method, interobserver and intraobserver measurement errors were assessed, as was the significance of age and gender on gastric emptying. The interobserver and intraobserver variability of the GER was evaluated by examining both healthy subjects and diabetic patients. To determine the interobserver variability, seven subjects (three healthy subjects and four diabetic patients) were assessed. The measurements were done under identical conditions on two separate days by one examiner each day in a random order. The previous results were masked for each investigator. Intraobserver variability was evaluated by examining nine subjects (four healthy subjects and five diabetic patients). The subjects were examined measured under identical conditions twice on separate days by the same investigator in a blinded fashion.

## Ultrasonographic Examination Technique

The sonographic examination was performed using a Hitachi EBU 400 (Hitachi, Tarrytown, NY) realtime ultrasound instrument with a transcutaneous 3.5 MHz transducer. Gastric emptying was monitored indirectly by determining the longitudinal (D<sub>1</sub>) and anteroposterior (D<sub>2</sub>) diameters of a single section of the gastric antrum, using the abdominal aorta and the left lobe of the liver as internal landmarks to obtain the same standardized scanning level consistently (Fig. 1A, B). At each observation three measurements were done using the mean values of the longitudinal ( $D_{1mean}$ ) and anteroposterior ( $D_{2mean}$ ) diameters to calculate the antral area. At this level, the scan showed the stomach shaped as either a circle or an ellipse, so the antral cross-sectional area (A<sub>Antrum</sub>) was calculated in all subjects using the following formula:

$$A_{Antrum} = \pi \times D_{1 \text{ mean}} \times D_{2 \text{ mean}} / 4$$

The measurements of the gastric antrum (on average lasting between 1 and 3 min) were taken from the outer profile of the wall and obtained between antral contractions to provide a measure of the relaxed width of the antrum. Depending on what would optimize the quality of the image in each subject, the subjects consistently either held their breaths in inspiration or breathed normally (during all measurements, to avoid changes in antral diameters related to inspiration and expiration). In all subjects measurements were taken 15 and 90 min after the end of meal ingestion. The times for the measure-

ments were chosen with regard to our previous results on examining healthy subjects at more frequent time intervals (prior to and immediately after meal ingestion, subsequently at regular 15 to 30 min intervals over a period of 120 min). These results indicated a postprandial maximal antral area at 15 min, continuously decreasing with time and reaching a plateau 90 min after the end of meal ingestion (close to the value of the fasting antral area). Only modest further reduction of the gastric antral cross-sectional area was noted after that time. GER was estimated and expressed as the percentage reduction in antral cross-sectional area from 15 to 90 min, calculated as follows:

GER = 
$$[(A \text{ area } 90 \text{ min}/A \text{ area } 15 \text{ min})-1] \times 100$$

The patients in whom antral area was not reduced over 50% were examined one more time, 120 min after the end of the meal. In 12 randomly selected subjects (eight healthy subjects and four diabetic patients), the antral area also was measured prior to meal ingestion as a reference.

#### Statistical Analysis

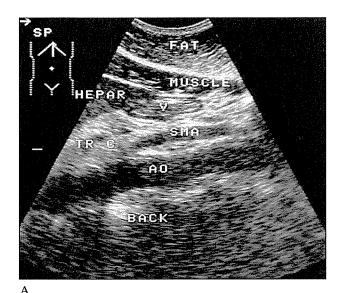
Median values with quartiles (q1 to q3) are presented for the antral cross-sectional areas and the GER. Intergroup and intragroup comparisons were assessed with the Mann-Whitney U test, using a two-sided test. Linear correlations were sought between GER and age in healthy subjects and diabetic patients using Pearson's correlation coefficient. Correlations also were sought between GER and the 15 and 90 min postprandial antral areas. Values of P < 0.05 were considered significant. Interobserver and intraobserver variability were assessed using the systematic measurement error, calculated as the mean difference between the two examinations, and the random measurement error, calculated as the SD of the differences.

### **RESULTS**

# Interpersonal Variability in Gastric Emptying

#### Healthy Subjects

In eight randomly selected healthy subjects the median antral area prior to meal ingestion was 214 mm<sup>2</sup> (range, 126 to 263 mm<sup>2</sup>). In the 19 healthy subjects the median values of the antral cross-sectional area were



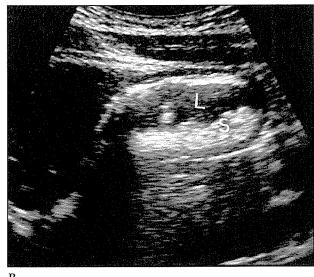


Figure 1 A, Longitudinal ultrasonogram of the gastric antral cross-sectional area (V) in a fasting healthy subject visualized by a scan passing through the abdominal aorta (AO) and the left lobe of the liver (HEPAR). The layers of the anterior abdominal wall (FAT, MUSCLE), the celiac trunk (TR C), and the superior mesenteric artery (SMA) also are shown. B, Postprandial longitudinal ultrasonogram of the gastric antral cross-sectional area in a healthy subject shows the liquid (L) and solid (S) parts of the gastric content.

489 mm<sup>2</sup> (range, 377 to 754 mm<sup>2</sup>) and 166 mm<sup>2</sup> (range, 124 to 279 mm<sup>2</sup>) at 15 and 90 min, respectively, after the end of the meal. The median value of GER was estimated at 63% (range, 58 to 69%).

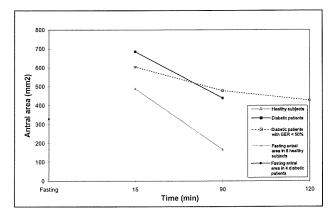
## Patients with Diabetes

In four randomly selected diabetic patients the median antral area prior to meal ingestion was 329 mm<sup>2</sup> (range, 159 to 415 mm<sup>2</sup>). In the 14 patients with diabetes the median antral areas were 685 mm<sup>2</sup> (range, 473 to 915 mm<sup>2</sup>) and 439 mm<sup>2</sup> (range, 337 to 647 mm<sup>2</sup>) at 15 and 90 min, respectively, after the end of the meal. In nine patients the antral area was not reduced to at least 50% from 15 to 90 min after the ingestion of the meal (the median GER in these patients = 16%, q1 = 2%, q3 = 29%). For that reason eight of these patients with slow emptying also were examined 120 min after the end of the meal (one patient missed this examination), and the median antral areas in this subgroup were 604, 478, and 426 mm<sup>2</sup> after 15, 90, and 120 min, respectively (Fig. 2). The median value of GER in the diabetic patients was estimated at 29% (range, 5 to 52%). The difference in the median GER between the entire group of diabetic patients and the subgroup of diabetic patients using nicotine (three snuff users and one smoker) was interpreted as insignificant.

A highly significant difference could be shown between the GER in healthy subjects and diabetic

patients (P < 0.001) (Fig. 3). A tendency to greater dilation of the gastric antrum was observed in diabetic patients in comparison with healthy subjects prior to meal ingestion (P = 0.106, with diabetic persons having 53% larger median antral area) and at 15 min after meal ingestion (P = 0.190, with diabetic patients having 40% larger median antral area). However, the diabetic patients showed significantly greater antral dilation 90 min after meal ingestion (P < 0.001, with diabetic persons having 164% larger median antral area). In absolute dimensions this means a median difference of about 200 mm²

Figure 2 Antral areas (fasting and postprandial) of healthy subjects and diabetic patients.



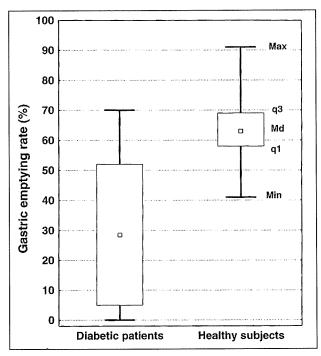


Figure 3 GER in healthy subjects and diabetic patients. The median (Md), minimum (Min), and maximum (Max) values and the values of the first (q1) and third (q3) quartiles are shown.

(15 min) and almost 300 mm² (90 min) between the antral areas of the two groups. No significant correlation was found between the 15 min postprandial antral areas and the GER in healthy subjects (r = 0.41, P = 0.083) or diabetic patients (r = 0.22, P = 0.459). Also, no significant correlation was found between the 90 min postprandial antral areas and the GER in healthy subjects (r = -0.42, P = 0.071) or diabetic patients (r = -0.39, P = 0.165). Assuming that the GER in healthy subjects was normally distributed (mean GER  $64 \pm 12\%$  and median GER 63%), a limit could be calculated using a one-sided 95% confidence interval (mean GER  $-1.64 \times SD$ ), indicating that a GER of less than 45% should be regarded as delayed.

### Significance of Age and Gender

#### Healthy Subjects

No significant correlation could be found between age and GER in healthy subjects (r = -0.15, P = 0.547) (Fig. 4). In addition, no significant difference was noted between the GER for men (mean age,  $39 \pm 17$  years; median GER, 62%; q1 = 56%; q3 = 69%) and women (mean age,  $36 \pm 20$  years; median GER, 63%; q1 = 60%; q3 = 70%) (P = 0.591).

### Diabetic patients

No significant correlation could be found between age and GER in diabetic patients (r = -0.34, P = 0.239) (Fig. 4), nor was a significant difference noted between the GER for diabetic men (mean age,  $54 \pm 9$  years; median GER, 27%; q1 = 4%; q3 = 51%) and women (mean age,  $55 \pm 10$  years; median GER, 38%; q1 = 13%; q3 = 57%) (P = 0.477).

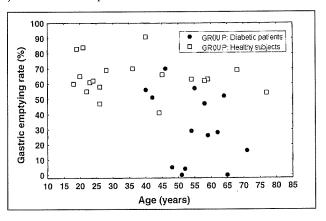
### Reproducibility of Ultrasonographic Measurements

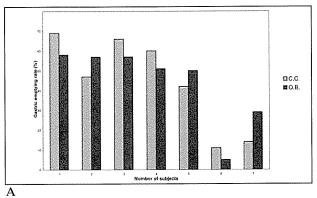
Interobserver variability showed a systematic measurement error of 0.3% and a random measurement error of 10.9% between different observers (Fig. 5A, B). Intraobserver variability showed a systematic measurement error of 3.6% and a random measurement error of 9.5% when measured on two separate days by the same investigator in a blinded study (Fig. 6A, B).

#### DISCUSSION

At present the diabetic population in Sweden is over 300,000 and globally it is about 200 million. Considering these numbers and the high prevalence of delayed gastric emptying in persons with diabetes, a less expensive technique than the currently used methods for measuring gastric emptying should be available. Because the predictive value of symptoms of this condition is poor, objective measurement is required for the diagnosis of disordered gastric motility. Scintigraphy is still the method of choice when measuring gastric emptying, although it is considerably more expensive than ultrasonography and involves exposure to ionizing radiation. Until now, the sonographic technique for measuring

Figure 4 Correlation between age and GER in healthy subjects and diabetic patients.





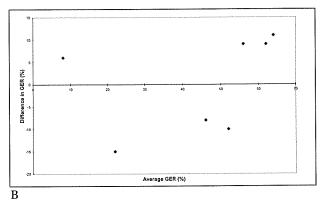


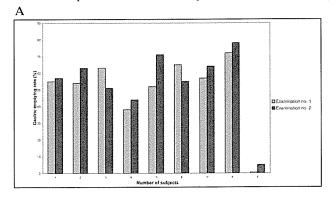
Figure 5 A, Interobserver variability for two independent observers of the same subjects. B, Differences in means for GER data from repeated measurements by two independent observers of the same subjects.

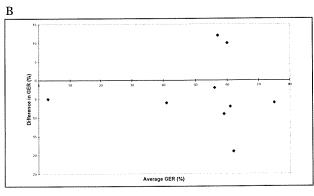
gastric emptying has been quite time-consuming.<sup>1,6,10</sup> We have been able to simplify the procedure using only two, or in some cases three, measurements during the entire examination.

A variety of different test meals have been used to visualize the stomach on ultrasonographic examinations. The test meal should be appetizing, easy to ingest, and an ordinary meal since the gastric motor response could be influenced by the cephalic phase. Furthermore, it is important to choose an echogenic test meal to achieve clear images for reliable measurements of the gastric contents and delimit the stomach (including the posterior wall of the antrum). The volume of the meal should be limited with regard to postprandial early satiety, which occasionally occurs with as little as 1.5 dl in some patients with delayed gastric emptying. Considering these points, rice pudding works as an excellent test meal for gastric measurements with ultrasonography.

We chose to study patients with long-standing diabetes and poor glycemic control because gastroparesis is more likely to occur in these patients.14-19 Measurements of gastric emptying in the diabetic group were done on condition that the fasting blood glucose level was 3.5 to 9.0 mmol/l, since hyperglycemia slows<sup>20–22</sup> and hypoglycemia increases the rate of gastric emptying.23,24 Changes in meal temperature also influence gastric emptying.25 Postprandial antropyloroduodenal motility in healthy subjects is retarded if the drink temperature is either raised or lowered (from 37°C to 50°C and 4°C, respectively).26 As the mean temperature of the test meals, measured immediately prior to ingestion, showed slight variation (20.7°  $\pm$  2.1°C), a possible influence of temperature on gastric emptying was interpreted as insignificant in our study. Between the examinations the subjects rested seated in a chair since gastric emptying may be affected by the posture and gravity (observed in patients after truncal vagotomy with pyloroplasty)<sup>27</sup> as well as exercise.<sup>28</sup> Each subject's usual defecation frequency was taken into consideration as a reference before evaluating the

Figure 6 A, Intraobserver variability for measurements of the same observer in repeat studies. B, Differences in means for GER data from repeated measurements by the same observer in duplicate studies.





presence of constipation or diarrhea.<sup>13,29–31</sup> Voluntary suppression of defecation delays gastric emptying in normal subjects,<sup>32</sup> and this "cologastric brake" is believed to be involved in the pathogenesis of upper abdominal symptoms in constipated patients.

After ingestion or intragastric administration of equal amounts of liquid, antral volumes determined by ultrasonography show a wide intersubject variability.<sup>11</sup> Therefore, it should be more important to evaluate changes in the antral area over time, as a measure of GER, instead of comparing the antral area at a fixed time between subjects. To assess the normal range (interpersonal variability) in gastric emptying, healthy subjects as well as patients with IDDM and clinically suspected delayed gastric emptying were examined. In our study the sonographic antral areas differed widely from subject to subject prior to and after meal ingestion in the healthy group as well as in the diabetic group (Tables 1, 2). The interpersonal differences of the gastric antral area are to a great extent attributed to anatomic differences in the stomach and its intraabdominal location. This affects the position of the gastric antrum in relation to the internal landmarks used in our standardized ultrasonographic technique. However, in each subject, measurements of the distance between the pylorus and the aorta during the examination showed only a minor alteration in the position of the stomach as it empties.33 A fairly great range in GER also was noted in the healthy group (41 to 91%) and in the diabetic group (0 to 70%). High intersubject variability in GER measured by real-time ultrasonography in healthy subjects have been reported previously.34 Gastric emptying of carbohydratecontaining liquids is normally regulated at about 2 kcal/min as a result of feedback from mucosal receptors in the small intestine.35 Several observations indicate that feedback from these receptors can be influenced by patterns of prior nutrient intake, 36,37 resulting in adaptive changes in gastric emptying. Thus, gastric emptying of glucose is faster after dietary supplementation with glucose for 3 days in healthy subjects.<sup>36</sup> This could be an underlying factor that partially explains day-to-day variability of gastric emptying within subjects. Probably other factors exist that could affect day-to-day variability, such as acute stress and phase of the menstrual cycle.38,39 During our measurements, prior to meal ingestion, fluid was noted in the antrum in most of the subjects, possibly as a result of secretion of gastric juice partially due to the cephalic phase. This assumption could explain the fact that 90 min after ingestion the antral area was smaller than it was prior to meal ingestion in a few cases.

As compared to healthy subjects, diabetic patients showed a highly significant larger median value for antral areas 90 min postprandially, but nonsignificant larger median values for the antral areas at 15 min postprandially and after fasting (Fig. 2). Observations have been made previously, showing a wide gastric antrum in patients with long-standing diabetes mellitus type 1.40 This difference could represent a loss of gastric tone in the diabetic group. Possible differences in the gastric antral content of liquid during fasting between healthy subjects and diabetic patients also could influence the results. It has been stated that a wide antral area reflects increased amounts of gastric juice in fasting.11,41 Postprandially, wider antral areas also could be due to impaired antral contractility, increased duodenogastric reflux, increased production of saliva, delayed gastric emptying, or insufficient postprandial accommodation of the proximal stomach (impaired reservoir function) causing abnormal distribution of food in the stomach. When the proximal part of the stomach does not adapt normally, abnormal amounts of food are forced into the antrum immediately after ingestion, leading to abnormal antral filling and a wider area. This could be a consequence of poor vagal tone.42 In other words, vagal impairment due to autonomic neuropathy could not only cause a generally more "slack" stomach with poor postprandial motility but also disturb the intragastric food distribution and thereby gastric emptying, since the reservoir capacity of the stomach is controlled mainly by the vagus nerve. This vagal reflex, called adaptive relaxation, makes it possible to ingest fairly great amounts of food, multiplying the volume of the stomach (for example, from 300 to 1500 ml), without raising the intragastric pressure considerably.<sup>43,44</sup> Impaired adaptive relaxation is seen after vagotomy.45

The median value of GER in diabetic patients was estimated to be 29%, which is less than half the rate in healthy subjects (63%). No significant correlations were found between the antral areas at 15 and 90 min postprandially and the GER in either healthy subjects or diabetic patients. This strongly indicates that the size of the antral area 15 and 90 min postprandially cannot predict the GER. Using the results in our study and assuming a normal distribution of GER in the healthy subjects, it was possible to calculate a limit, indicating that a GER of less than 45% should be regarded as delayed. Accordingly, about 57% (8 of 14) of the diabetic patients in this study had a more or less pronounced delays in GER. The difference in the median GER between the subgroup of diabetic patients using nicotine and the entire group of diabetic patients was interpreted as insignificant. Several studies have indicated that the acute effect of cigarette smoking slows gastric emptying,46,47 whereas other studies have shown an increase in gastric emptying related to smoking.39,48 It has also been shown that habitual heavy smokers, when abstaining from smoking (at least 10 h before and during the examination), exhibit shorter gastric emptying half-times than nonsmokers.49 No difference in GER related to age could be found in this or previous studies.<sup>11,34</sup> These results do not exclude the fact that older subjects (for example, older than 70 years) might have different gastric emptying times than younger persons, as older subjects often have abnormal autonomic function. Our study did not evaluate this aspect. We did not find an influence of sex on gastric emptying, as was noted in some other studies.11,34 This contrasts with results reporting a prolonged gastric emptying time in healthy women as compared to men<sup>39,50,51</sup> as a possible result of sexrelated differences in levels of estradiol or progesterone. Both interobserver and intraobserver variability showed good agreement, indicating that this is a useful method for evaluating gastric emptying. Actually, owing to intrapersonal day-to-day variability, these measurement errors would be expected to be even less than presented here because the repeated measurements in the same subject were done on different days.

We conclude that the use of standardized real-time ultrasonography to determine gastric antral cross-sectional area in a single section of the stomach 15 and 90 min postprandially is a valid method for estimating GER. It precludes exposure to ionizing radiation and is a potentially useful, reliable, cost effective, and relatively simple method of measuring gastric emptying that shows good intraobserver and interobserver agreement. Significant differences in GER between healthy subjects and patients with IDDM and clinically suspected delayed gastric emptying could be demonstrated with this method.

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