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Gastric function in diabetic gastroparesis assessed by ultrasound and scintigraphy

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Abstract

Background: Gastroparesis is a severe diabetes complication characterized by delayed gastric emptying. We examined patients with symptoms of diabetic gastroparesis using gastric emptying scintigraphy and ultrasound drink test. The primary aim was to investigate how ultrasound could provide information about gastric motility features in diabetic gastroparesis.

Material and methods: We prospectively included 58 patients with diabetes (48 type 1) with symptoms of gastroparesis and 30 healthy controls. Patients were examined with ultrasound of the stomach in a seated position after drinking 500 ml low-caloric meat soup, at the same time recording dyspeptic symptoms. The following day, they were examined with gastric emptying scintigraphy, defining gastroparesis as >10% retention after 4 h.

Key Results: We found motility disturbances in the proximal stomach measured by ultrasound in patients with diabetic gastroparesis. A linear mixed effects model including repeated ultrasound measurements revealed a slower decrease of the proximal stomach size in gastroparesis compared to healthy controls ($p < 0.01$), and the proximal diameter at 20 min was correlated to scintigraphy at 4 h ($r = 0.510$, $p = 0.001$). The antrum in patients with diabetic gastroparesis was twice as large compared to healthy controls ($p = 0.009$), and fasting antral size was correlated to gastric emptying scintigraphy ($r = 0.329$, $p = 0.013$). Both diabetes patients with and without gastroparesis had impaired accommodation ($p = 0.011$).

Conclusions and Inferences: On ultrasound, we found delayed reduction of proximal stomach size and impaired accommodation after a liquid meal in patients with gastroparesis, emphasizing the role of the proximal stomach. Furthermore, we found antral distention in gastroparesis patients.

KEYWORDS
diabetes complications, diagnostic imaging, gastric emptying, gastroparesis, nausea

1 | INTRODUCTION

Gastroparesis is a severe complication of diabetes associated with impaired quality of life, increased hospital admission, and high morbidity.[1,2] Gastroparesis is characterized by delayed gastric emptying without a mechanical obstruction. Cardinal symptoms are nausea and vomiting, early satiety, postprandial fullness, and bloating. Abdominal pain is another frequently reported symptom.[3,4] Many studies have shown that gastric emptying rate correlates poorly to the patients' symptoms and quality of life.[1,3,5] Evaluation of gastric emptying is important in relation to postprandial nutrient absorption and consequently blood glucose control in diabetes.[5] In addition to delayed gastric emptying, patients with diabetic gastroparesis are known to have impaired gastric accommodation, antral hypomotility, pylorospasm, and altered visceral sensation.[3,6-9]

While the diagnostic gold standard, scintigraphy, mainly measures gastric emptying, the ultrasound meal accommodation test (UMAT) provides additional information about real-time motility, pyloric function, accommodation, and visceral sensitivity.[10,11] Ultrasound of the antrum is an accepted method for evaluating gastric emptying, showing good correlation to radionuclide emptying rate estimates.[12] It is often used by anesthesiologists as a "Point of care" examination to assess preoperative gastric contents.[13,14] The association between proximal stomach size and gastric emptying is, however, insufficiently studied.

In this study, we investigated a cohort of diabetes patients with symptoms of gastroparesis using UMAT and 4 h scintigraphy. Our main hypothesis was that the UMAT could provide information about gastric motility features in diabetic gastroparesis. Our aims were as follows: (a) To assess the proximal gastric emptying rate in diabetic gastroparesis, compared to diabetic patients with normal gastric emptying and to healthy controls, (b) to investigate whether the antral area was enlarged in patients with gastroparesis compared to healthy controls and patients with normal gastric emptying, (c) to compare the dyspeptic symptoms in fasting and postprandial states in patients with gastroparesis to patients with normal gastric emptying and to healthy controls, and to explore whether the symptoms were associated with ultrasound measurements, and (d) lastly, to investigate gastric accommodation by ultrasound in patients with diabetes with or without gastroparesis, and to compare to healthy controls.

Key Points

- Fifty-eight patients with symptoms of diabetic gastroparesis were examined with gastric emptying scintigraphy and a liquid meal gastric ultrasound test.
- Patients with gastroparesis reported the same upper gastrointestinal symptom load as the diabetes patients with normal gastric emptying.
- Repeated ultrasound measurements revealed a slower proximal gastric emptying rate in gastroparesis patients, and the proximal stomach measurements correlated well to scintigraphy results.

2 | MATERIALS AND METHODS

2.1 | Subjects

This was a prospective cross-sectional study including diabetes patients who were referred to a tertiary center at Haukeland University Hospital, Bergen, Norway, because of symptoms indicative of gastroparesis. They were examined with both gastric emptying scintigraphy and the ultrasound meal accommodation test (UMAT) during 2014 to 2018 (N = 58 patients). Further description of the study population is published elsewhere.[15] As a control group for the ultrasound test, we included 30 healthy subjects.

Before admission, all patients were examined with upper endoscopy to rule out mechanical obstructions or other pathology explaining their symptoms. The patients were recruited consecutively and admitted to the hospital for an interview and examination by a physician. On two consecutive days, the patients were examined with ultrasound and gastric scintigraphy after an overnight fast. During the procedures, patients' blood glucose levels were controlled by infusion of glucose and insulin, aiming at a blood glucose level between 4 and 10 $mmolL^{-1}$. To avoid affection of gastrointestinal motility, the following medications were paused before and during the study: proton pump inhibitors (7 days in advance), opioid analgesics, histamine H_2-antagonists, non-steroidal anti-inflammatory drugs, prokinetic agents, antiemetic drugs, and antidiarrheal drugs (3 days), laxatives (2 days), and other antireflux medications (24 h). Exclusion criteria were age <18 years, previous major intra-abdominal surgery, breastfeeding or pregnancy, or inability to adhere to the study protocol.

The ultrasound procedure was performed prior to the scintigraphy procedure, thus ensuring blinding of the diagnostic outcome for the physicians performing the ultrasound.

2.2 | Healthy controls

Healthy controls were prospectively included during 2016–2018 (Table 1). They were all healthy and did not report symptoms of any GI disease or motility disorder in a physician interview. They did not use any medications potentially affecting gastric motility. Two subjects reported ovarian surgery, one had undergone appendectomy and one had undergone hysterectomy. One of the healthy subjects had an abnormal shape of the proximal stomach, and measurements of the proximal stomach from this subject were excluded from the material.

2.3 | The ultrasound meal accommodation test (UMAT)

UMAT combines a drink test with ultrasound imaging of the stomach, described in detail by Gilja et al.[11] The patients were seated, leaning slightly backward, and examined with transabdominal ultrasound

TABLE 1 Demographics and participants' characteristics. *p*-values are the results of Pearson's chi-square test and Student's *t* test

Participant's characteristics	Patients n = 58	Controls n = 30	*p*-value
Age (years)[a]	48.5 (11.7)	32.6 (12.0)	<0.001
Sex (Female)[b]	39 (66%)	20 (66%)	0.402
BMI (kg/m2)	26.8 (6.1)	23.5 (2.6)	<0.001
Diabetes Type I	48 (81%)	0	
Complications[c]			
1	16 (27%)		
>1	27 (46%)		
Gastroparesis[b]	23 (40%)		
Diabetes Type 1[d]	22 (47%)		
Diabetes Type 2	1 (9%)		

[a]Mean (SD).
[b]n (%).
[c]Complications such as retinopathy, peripheral neuropathy, nephropathy, or cardiovascular disease.
[d]OR (95%CI): 8.80(1.04, 74.34)

using a standard curvilinear probe of 3.5 MHz. The antral area was obtained in a sagittal section, and the patient reported symptoms, before drinking 500 ml commercial meat soup (Toro klar kjøttsuppe, Bergen, Norway. Contents: 1.8 g protein, 1.1 g carbohydrate, 0.9 g bovine fat, 84 kJ) in 4 min. Immediately after drinking, the patient reported his/her symptoms, and the stomach was measured in three standardized sections: an area of the proximal stomach in a sagittal section ("proximal area"), a diameter in an oblique frontal section ("proximal diameter), and the antral area obtained in a sagittal section (Figure 1). Measurements of the proximal stomach were performed in the phase mid respiration to normal expiration, avoiding deep inspiration. All measurements of the antrum were done between contractions. The real-time ultrasound scanning was frozen, and then the measurements were performed immediately thereafter. These measurements, as well as symptom scoring, were repeated at 10 and 20 min postprandially. Normal values for the UMAT are published in Steinsvik et al.[16] In this paper, we used fasting antral area >5.4 cm^2 as a cutoff value for enlarged fasting antral area, based on mean plus two standard deviations from the healthy controls study.

2.4 | Symptoms

To be able to evaluate dyspeptic symptoms simultaneous to ultrasound measurements, the patients reported symptoms on a visual analogue scale ranging from 0 to 100 mm, zero being "no symptoms" and 100 being "worst symptoms". In the case of hunger/satiety, 0 indicated "very hungry," 100 indicated "very full," and 50 indicated "neutral".

The reported symptoms were epigastric pain, nausea, fullness/bloating, hunger/satiety, and total discomfort of the upper part of the abdomen. Visual analogue scales have proven useful in monitoring gastroparesis-symptoms such as nausea and proven to be superior to integral scales such as Likert and Borg.[17]

2.5 | Gastric emptying scintigraphy

On the day after the UMAT, the patients were examined with gastric emptying scintigraphy. The nuclear radiologist responsible for performing the scintigraphy test and analyzing the test results was blinded for the outcome of the ultrasound test. The test meal consisted of a nutrient bar (260 kcal, 66% carbohydrate, 17% protein, 2% fat, and 3% fiber) and a boiled egg (90 kcal; 13% protein, 11% fat, and 1.1% carbohydrate) labeled with Tc-99m-nanocolloid.[18] They were allowed to drink 120 ml of water. Another six hours of fasting followed, but the patients were allowed to drink 100 ml of water during this period.

We performed simultaneous posterior and anterior planar scintigraphy of the upper abdomen (1 min per view) on a double-headed camera system (Siemens e.cam; Siemens Healthineers). In accordance with current guidelines, pictures were taken at 0, 30, 60, 120, 240, 360, and 480 min.[19] We used Segami Oasis 1.9.4.9 (Segami Corp., Inc) to quantify the images, by drawing a region of interest (ROI) around the stomach at 0 min. This was copied onto the following images, and gastric retention was calculated as the root mean square of the counts in posterior and anterior ROI relative to the 0 min acquisition.

Normal value for GES at 4 h is <10%,[20] and in this paper, we used this as a cutoff value for the diagnosis "Gastroparesis".

2.6 | Ethical considerations

All participants received oral and written information and signed consent forms before any study-related procedures. The study was conducted according to the Declaration of Helsinki and was approved by the Western Norway Regional Medical Ethics Committee (REK 2015/58) and South Eastern Norway Regional Medical Ethics Committee (REK 2014/222-20 (Healthy controls study)).

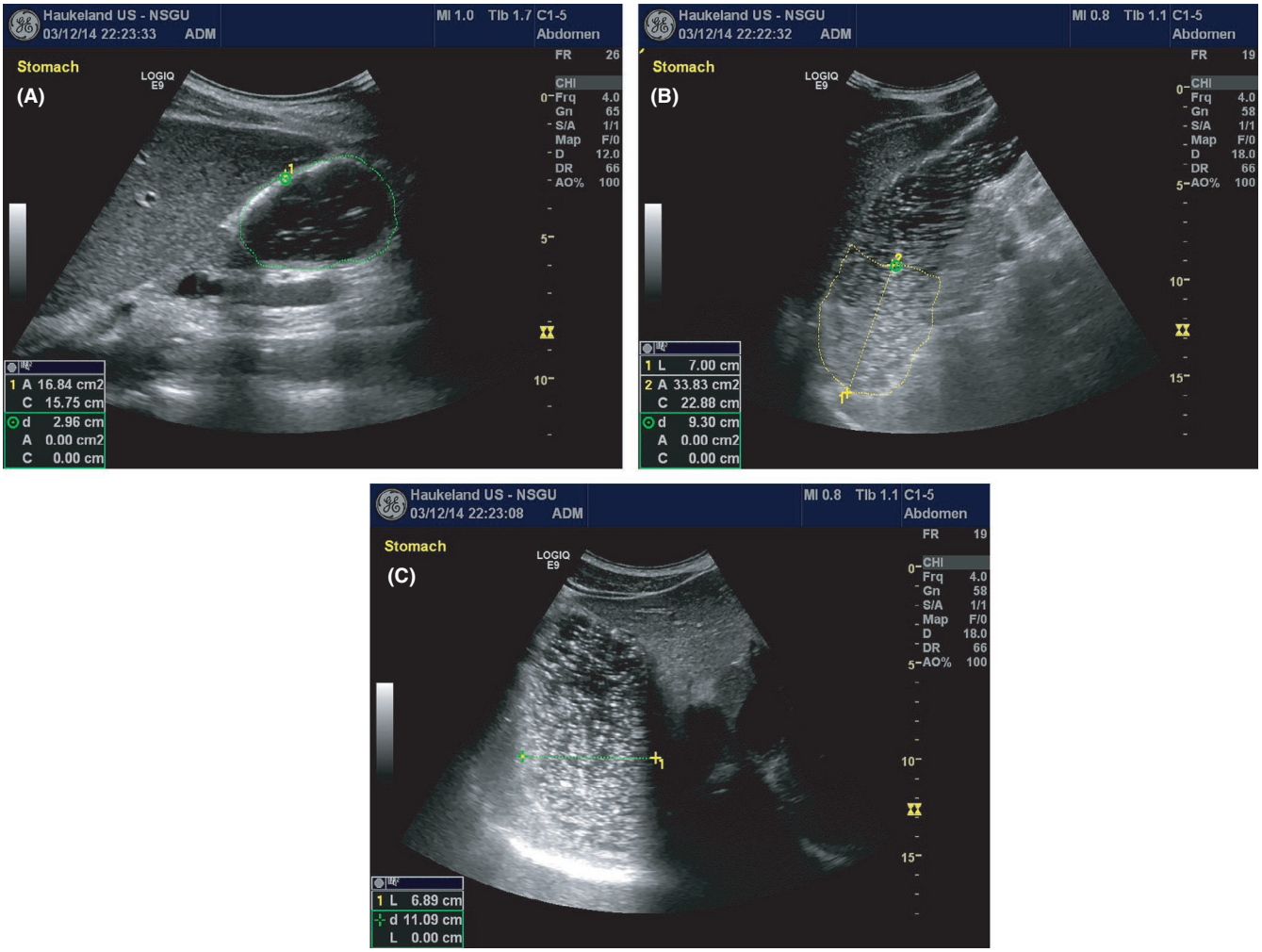

FIGURE 1 Examples of the ultrasound images obtained from the standardized sections used in the study. All images were obtained with the patient seated, after ingesting 500 ml soup: (A) Sagittal section of the antrum, using the aorta and superior mesenteric vein as landmarks. The liver is visible to the left. (B) The proximal diameter of the stomach was obtained from an oblique frontal section. (C) The proximal area was estimated from a sagittal section in the epigastrium near the midline, tilting the probe slightly upwards and to the left. The area was calculated after measuring 7 cm from the apex

2.7 | Statistical analysis

Descriptive methods were used to characterize the study participants. The association between the groups (gastroparesis, no gastroparesis, and healthy controls) and ultrasound measurements (antral area (AA), proximal area (PA), and proximal diameter (PD)) was assessed by linear mixed effects models (LME) for each of the outcomes as dependent variable depending on time, group, and their interaction with individual random intercept and simple contrasts.[21] The interaction term described the change of differences in the outcomes between the groups over time. All models were estimated both unadjusted and adjusted for age, sex, and the ability to finish the soup meal within given time limits.

The LME with symptoms as dependent and ultrasound, group and time point and all interactions as independent variables with individual random intercept including all follow-up time points was used to assess the association between symptoms and ultrasound. Since this full interaction model was too large with respect to the number of observations, we reduced it removing time and time-containing interactions.

The significance level was set to 0.05. All computation was done in SPSS 26 (IBM Corp.,) and R 4.0.2[22] with the packages nlme 3.1,[23] and the graphics was derived using Matlab 2020a (Mathworks Inc.,).

Furthermore, we used Pearson's correlations to evaluate associations between ultrasound and scintigraphy measurements. To compare incidences between different groups where the expected cell count was <5 we used Fisher's exact test. Student's *t* test was used to test for differences between men and women, and we used multiple logistic regression to adjust for gastric emptying where we found significant differences. Results are given as unadjusted and adjusted odds ratios (OR) with 95% confidence interval and *P*-values.

3 | RESULTS

An overview of participant characteristics is presented in Table 1. Twenty-three diabetes patients (40%) had delayed gastric emptying on scintigraphy and are in the following referred to as patients with gastroparesis. The diabetes patients with normal gastric emptying are referred to as patients without gastroparesis or "No gastroparesis." There were no gender differences concerning ultrasound measurements. Eleven patients had type 2 diabetes, and only 1 of them had delayed gastric emptying on scintigraphy.

3.1 | Slower proximal gastric emptying rate and antral distention

Results from the linear mixed effects (LME) model are presented in Figure 2. The complete LME model and ultrasound measurements are available in the Supplementary Material.

By repeated ultrasound measurements during 20 min, we found that patients with gastroparesis had a slower proximal gastric emptying rate compared to healthy controls ($p < 0.01$). The proximal diameter at 20 min correlated with gastric emptying scintigraphy at 4 h ($r = 0.510$, $p = 0.001$, Table 2) and 2 h ($r = 0.528$, $p = 0.001$).

Patients with gastroparesis had more than twice as large fasting antral area compared to healthy controls ($p = 0.009$, Figure 2). Looking at the LME model, we found that the gastric emptying profile of the antral area was the same for patients with gastroparesis as in healthy controls ($p < 0.3$) and patients without gastroparesis ($p < 0.4$).

The fasting antral area was enlarged in 45% of the gastroparesis patients compared to 12% of the non-gastroparesis patients, OR = 6.25(1.64, 23.8). The positive predictive value of an enlarged antral area was 71%. The fasting ultrasound antral area was positively correlated to the degree of gastric emptying measured by scintigraphy at 4 h ($r = 0.329$, $p = 0.013$) and 2 h ($r = 0.354$, $p = 0.008$) (Table 2).

3.2 | Dyspeptic symptoms associated with gastroparesis

Both diabetes patients with and without gastroparesis reported higher levels of fasting and postprandial dyspeptic symptoms compared to healthy controls (Figure 3). Upper abdominal discomfort and bloating/distention were the most pronounced symptoms, followed by nausea. We found no differences in reported symptoms between patients with delayed gastric emptying and patients with normal gastric emptying.

Women reported higher levels of postprandial bloating and satiety at all time points, and this remained significant when we adjusted for gastric emptying (Table 3).

A linear mixed effects model was used to explore the associations between symptoms and ultrasound measurements of the stomach. We found no significant associations between symptoms and ultrasound measurements in the gastroparesis patients. However, we found that patients with normal gastric emptying had a negative relationship between the ultrasound measurements and symptoms of discomfort and epigastric pain. The association was strongest for the proximal stomach (Figure 4 and Figure S1).

Fifteen patients were unable to complete the soup meal within the time limit of four min due to discomfort or nausea. The ability to complete the meal did not correlate to fasting antral area (OR = 1.097 (0.928, 1.296)) or gastric emptying by scintigraphy at 4 h (OR = 1.009 (0.981, 1.038)). We found no difference in fasting symptoms between the group that completed the meal and the group that did not complete.

3.3 | Impaired gastric accommodation

Overall, we found that diabetes patients with and without gastroparesis had lower proximal area on ultrasound at 1 and 10 min ($p = 0.011$), compared to healthy controls (Figure 2). There was, however, no difference between patients with gastroparesis and without gastroparesis at 1 and 10 min ($p = 0.153$).

3.4 | Missing data

Twelve patients were not able to complete the liquid meal within the time limit of 4 min. In this material, we have not included the postprandial ultrasound measurements for these patients, but have included their symptoms. In some cases, reduced visualization of the stomach made single measurements by ultrasound difficult, and caused missing data (n = 10). One patient had rapid gastric emptying and the proximal stomach was difficult to measure at 20 min. These factors account for varying numbers in different tables.

4 | DISCUSSION

In this study of 58 diabetes patients with symptoms of gastroparesis, we performed scintigraphy with a solid meal and repeated ultrasound measurements of the proximal and distal stomach after a liquid meal. Repeated ultrasound measurements of the proximal stomach demonstrated that gastroparesis patients had a slower decrease in proximal stomach size compared to healthy controls during 20 min ($p < 0.01$), suggesting delayed emptying of the proximal stomach, and a wider antrum in a fasting and postprandial state.

Previous studies have found a good correlation between stomach contents and antral area or a cross-section of the antrum measured by ultrasound,[24] and between ultrasound and scintigraphy after a liquid dextrose drink.[25] Thus, our results from antral measurements are well in agreement with previous studies.

Studies of the proximal stomach have traditionally been performed mainly to assess gastric accommodation. In the present study,

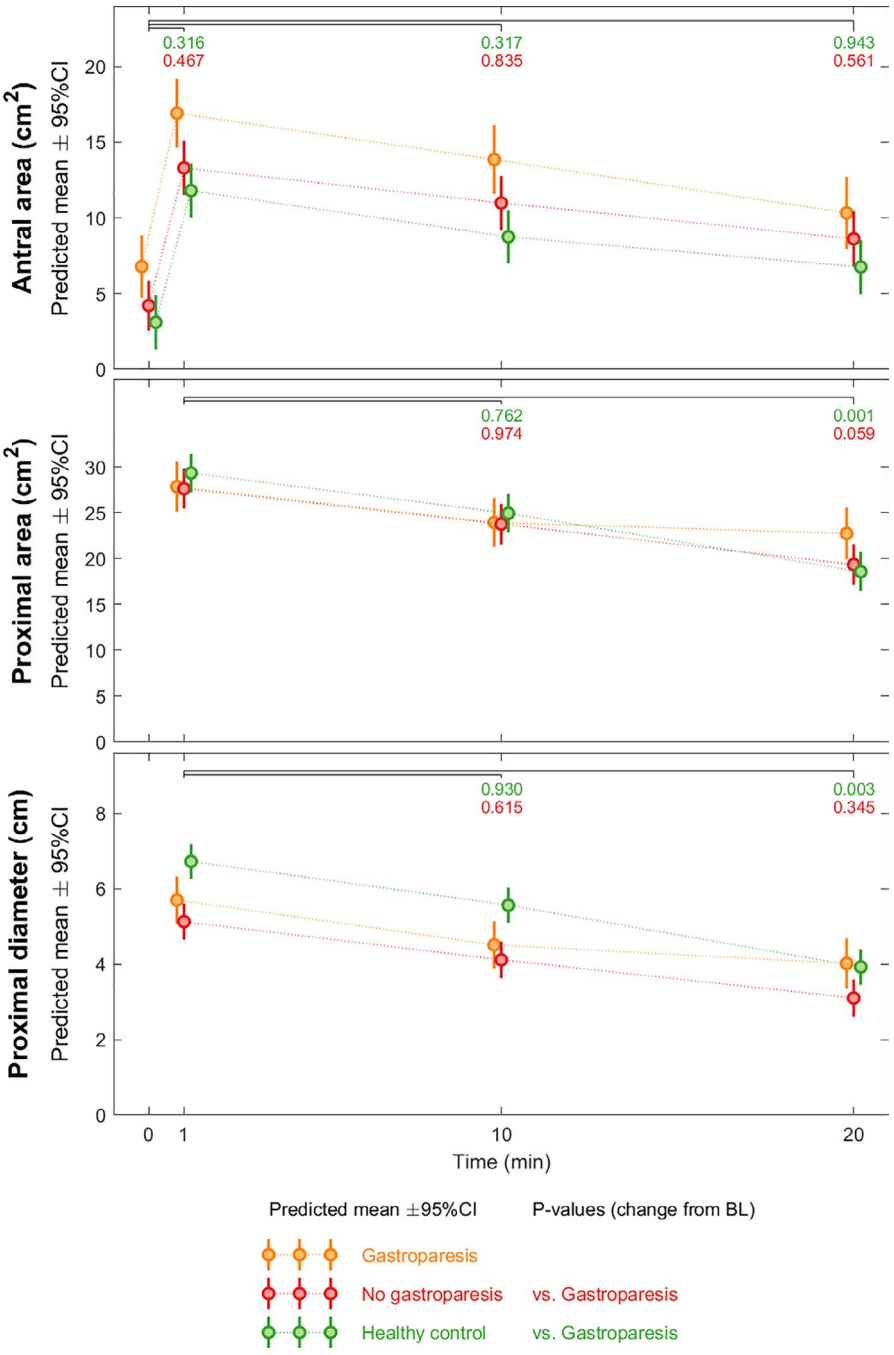

FIGURE 2 Ultrasound measurements of the stomach in a fasting and postprandial condition after ingestion of 500 ml low-calorie soup in diabetes patients with or without gastroparesis, and healthy controls. *p*-values represent the interaction in a linear mixed effects model, describing the change of differences in the outcomes between the groups over time. All models were estimated both unadjusted and adjusted for age, sex, and the ability to finish the soup meal within given time limits

we explored if a delay in overall gastric emptying could influence measurements of the proximal stomach and measurements of the antrum. Using a linear mixed effects model, we found that patients with diabetic gastroparesis had a slower decrease in proximal stomach size ($p < 0.01$), although separate measurements of the proximal stomach at 20 min were not different from healthy controls. Perlas et al.[24] described gastric emptying assessment by ultrasound of the antrum, body, and fundus of the stomach, but were unable to visualize the fundus adequately to evaluate gastric emptying. Orthey and co-workers presented a new method using enhanced gastric emptying scintigraphy to assess intragastric meal distribution, thus studying both gastric accommodation and proximal gastric emptying on healthy subjects in the same protocol,[26] but the method still needs more validation before being ready for clinical use.[27] In a study using scintigraphy by Edholm et al.[28] on healthy subjects, the gastric emptying process was divided into a proximal and a distal part, and they studied the effects of incretin hormones. They found that a low dose of glucose-dependent insulinotropic polypeptide (GIP) increased proximal emptying rate and decreased distal emptying rate, while a higher dose increased gastric emptying rate both proximally and distally. Furthermore, they found that glucagon-like peptide-1 decreased emptying from the proximal stomach before decreasing emptying in the antral part. Thus, a compartmentalization of the gastric emptying process has been described earlier and supports our findings.

The patients in our study as a group showed impaired accommodation of the proximal stomach. This finding is supported by a

TABLE 2 Correlations between gastric emptying scintigraphy at 2 and 4 h after ingesting a solid radiolabeled meal, and ultrasound measurements before and after ingesting a liquid low-calorie meal, in patients with diabetes and symptoms of gastroparesis, with and without delayed gastric emptying

	Scintigraphy 2 h		Scintigraphy 4 h		Patients
Ultrasound measurement	Correlation[a]	*p*-value	Correlation[a]	*p*-value	n
Antral area fasting	0.354	0.008	0.329	0.013	56
Antral area 1 min	0.247	0.097	0.150	0.327	45
Antral area 10 min	0.131	0.390	0.024	0.877	45
Antral area 20 min	0.141	0.374	0.060	0.710	41
Proximal area 1 min	−0.053	0.731	−0.049	0.754	44
Proximal area 10 min	−0.091	0.554	−0.188	0.221	44
Proximal area 20 min	0.228	0.551	0.170	0.295	40
Proximal diam. 1 min	0.406	0.006	0.333	0.029	43
Proximal diam. 10 min	0.323	0.035	0.312	0.044	42
Proximal diam 20 min	0.536	<0.001	0.510	0.001	38

[a]Pearson's correlation coefficient.

study on 108 diabetes patients by Chedid and co-workers. Gastric emptying for solids assessed by scintigraphy indicated rapid gastric emptying in 37% and delayed gastric emptying in 19% of the cases. Using single photon emission computed tomography before and after drinking 300 ml nutrient drink, they found that 40% of the patients had impaired accommodation.[29] In a study by Kumar et al.[8] on 18 patients with diabetic gastroparesis without clinical response to prokinetic therapy, accommodation was assessed by barostat. They found that 9 of 10 patients had impaired accommodation. The accommodation process depends on normal vagal function, and vagal nerve damage is an important factor in the pathogenesis of diabetic gastroparesis.[30,31] In future studies, it is of interest to investigate whether impaired accommodation in diabetes patients with normal gastric emptying may be an early sign of gastroparesis, explaining the similarity in proximal accommodation between the gastroparesis- and non-gastroparesis groups in our study. Furthermore, we found a negative association between measurements of the proximal stomach and epigastric pain and discomfort in the non-gastroparesis group. This indicates that impaired accommodation plays a role in symptom generation. We found no such association in the gastroparesis group. We believe this may be explained by the effect of the delayed gastric emptying on this group.

The patients in the present study were all included because they had symptoms consistent with gastroparesis. They all reported more upper abdominal discomfort, nausea, fullness, and epigastric pain than healthy controls. The patients reported highest level of fullness and upper abdominal discomfort (Figure 3), followed by nausea. Patients with gastroparesis had the same upper gastrointestinal symptom load as the diabetes patients with normal gastric emptying. This observation is in keeping with previous studies.[1,15] Cogliandro and co-workers did a study on 88 patients with symptoms of gastroparesis, and examined them with ^{13}C-octanoic acid breath test to assess gastric emptying, and small bowel manometry to evaluate enteric motility. They found that 80% of the patients had small bowel dysmotility, while only 28% had delayed gastric emptying.[32] We support Cogliandro's view that gastric emptying may not be the best biomarker of gastroparesis. Gastric emptying only accounts for a part of the pathophysiology of gastroparesis. Thus, a broader assessment of suspected gastroparesis patients is recommended, including testing of gastric accommodation and entire GI motility.[8,33]

The availability of gastric motility testing such as scintigraphy or wireless motility capsule varies from country to country. Given the unspecific nature of dyspeptic symptoms and the varying correlation to motility parameters, it is challenging to prioritize patients for further diagnostic testing. We have demonstrated that an enlarged antrum in fasting state assessed with transabdominal ultrasound is closely associated with delayed gastric emptying. Ultrasound of the antrum is frequently used to investigate gastric emptying, in particular in patients where scintigraphy is not advisable or available, such as in newborns,[34-36] children,[37] and pregnant women.[38,39] By adding a low-caloric liquid meal, it is possible to evaluate gastric accommodation, visceral sensitivity, and gastric emptying, all within a regular outpatient consultation.

Our study had some limitations. A weakness of our study design was the comparison of a low-caloric liquid meal to a solid meal of higher caloric content. Furthermore, a test using a low-calorie meal will not trigger the full cascade of gastrointestinal hormones and reflexes triggered by a proper meal. A caloric content of at least 250 Kcal is necessary to shift the gastric motoric activity from "fasting" to "fed".[3] The results must therefore be interpreted with some caution. While a solid meal can be visualized in the antrum by ultrasound, proximal measurements after a solid meal are difficult to obtain. In addition, if the liquid content contains high levels of fat or protein, it is harder to visualize by ultrasound. As we aimed to study both the proximal and distal stomach, we had to choose a liquid meal. Ultrasound of the antrum after both high- and low-calorie meals has shown to correlate well with gastric emptying scintigraphy.[40] As in most procedures, some intra-observer variation can be observed during ultrasound examinations. The overall coefficient of variance in a study of the antral area assessed by ultrasound was 6% in a study by Hveem et al.[41] In a study of the proximal stomach assessed by ultrasound, Gilja et al.[42] found correlations of 0.95 and 0.94 for measurements by two examiners. Visualization of the proximal stomach by ultrasound may be challenging due to subcutaneous

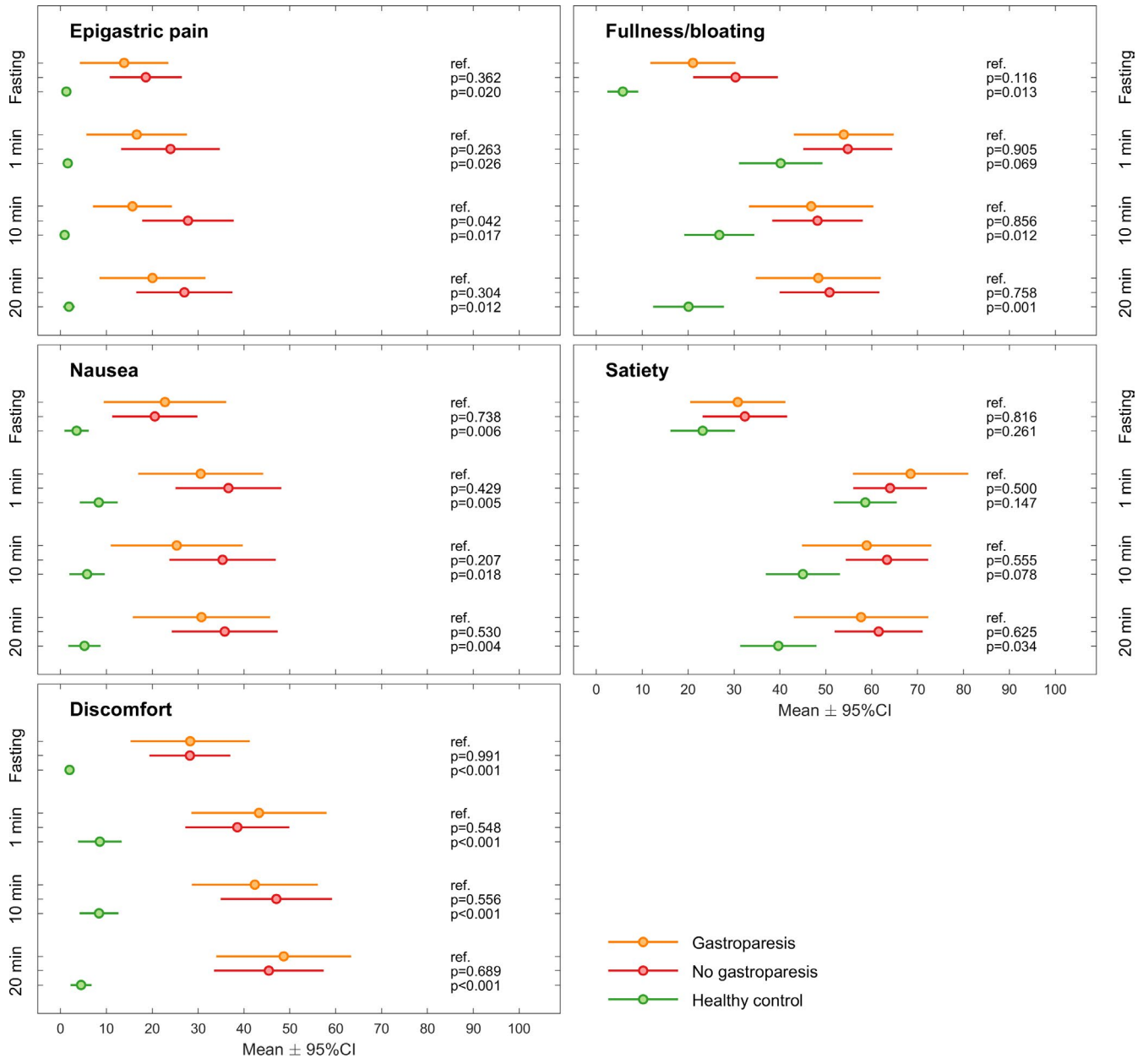

FIGURE 3 Forest plot presenting patient reported upper gastrointestinal symptoms in patients with diabetic gastroparesis (ref), diabetes without gastroparesis, and healthy controls, on a visual analogue scale (0–100 mm). The symptoms were recorded in a fasting condition, and after ingesting a 500 ml low-calorie soup meal

or intra-abdominal fat, or due to gas in the transverse colon. This was also the case in this study, resulting in missing data in 10 cases. However, the impaired visualization was equally distributed between the groups, hence unlikely to have an impact on the results. The healthy controls included in this study were originally recruited to be compared to another patient cohort, and were not matched for age and BMI in this study. However, we adjusted for age in the linear mixed effects models, finding no influence on our main results.

In this study, we have assessed both the proximal and distal stomach of patients with gastroparesis in a clinical setting, and compared to scintigraphic measurements. Relating proximal postprandial measurements on ultrasound to gastric emptying have, to our knowledge, not been done before, and we consider this one of the main strengths of our study.

5 | CONCLUSION

We found motility disturbances in the proximal stomach measured by ultrasound and scintigraphy in patients with diabetic gastroparesis. Repeated ultrasound measurements revealed a slower proximal gastric emptying rate in gastroparesis, and the proximal stomach measurements correlated well to scintigraphy results. The antrum in patients with diabetic gastroparesis was twice as large compared

TABLE 3 Sex differences in symptoms of satiety and bloating in patients with diabetes mellitus and symptoms of gastroparesis. Higher reported symptoms on a visual analogue scale (0–100 mm) in women than men in the ultrasound meal accommodation test. Results from logistic regression (OR) before and after adjusting for gastric emptying scintigraphy 4 h after a solid meal

Symptom	Men n=19 Mean (SD)	Women n=38 Mean (SD)	Unadjusted for GE[a] OR (95% CI)	*p*-value	Adjusted for GE[a] OR (95% CI)	*p*-value
Satiety						
Fasting	21.2 (29.1)	36.3 (23.1)	0.97 (0.92, 1.00)	0.044	0.98 (0.95, 1.00)	0.065
1 min	46.6 (26.4)	74.8 (22.3)	0.96 (0.93, 0.981)	0.001	0.96 (0.93, 0.98)	0.001
10 min	42.3 (27.2)	70.9 (26.1)	0.96 (0.94, 0.99)	0.001	0.96 (0.94, 0.99)	0.002
20 min	40.3 (28.2)	70.1 (27.0)	0.96 (0.94, 0.99)	0.001	0.97 (0.94, 0.99)	0.002
Bloating						
1 min	40.5 (28.1)	60.5 (25.9)	0.97 (0.95, 0.99)	0.014	0.97 (0.95, 1.00)	0.026
10 min	34.2 (32.8)	54.2 (25.7)	0.98 (0.96, 1.00)	0.021	0.98 (0.96, 1.00)	0.038
20 min	33.9 (31.5)	58.0 (28.2)	0.97 (0.95, 0.99)	0.009	0.97 (0.95, 0.99)	0.013

[a]Gastric emptying assessed by scintigraphy 4 h after a solid meal.

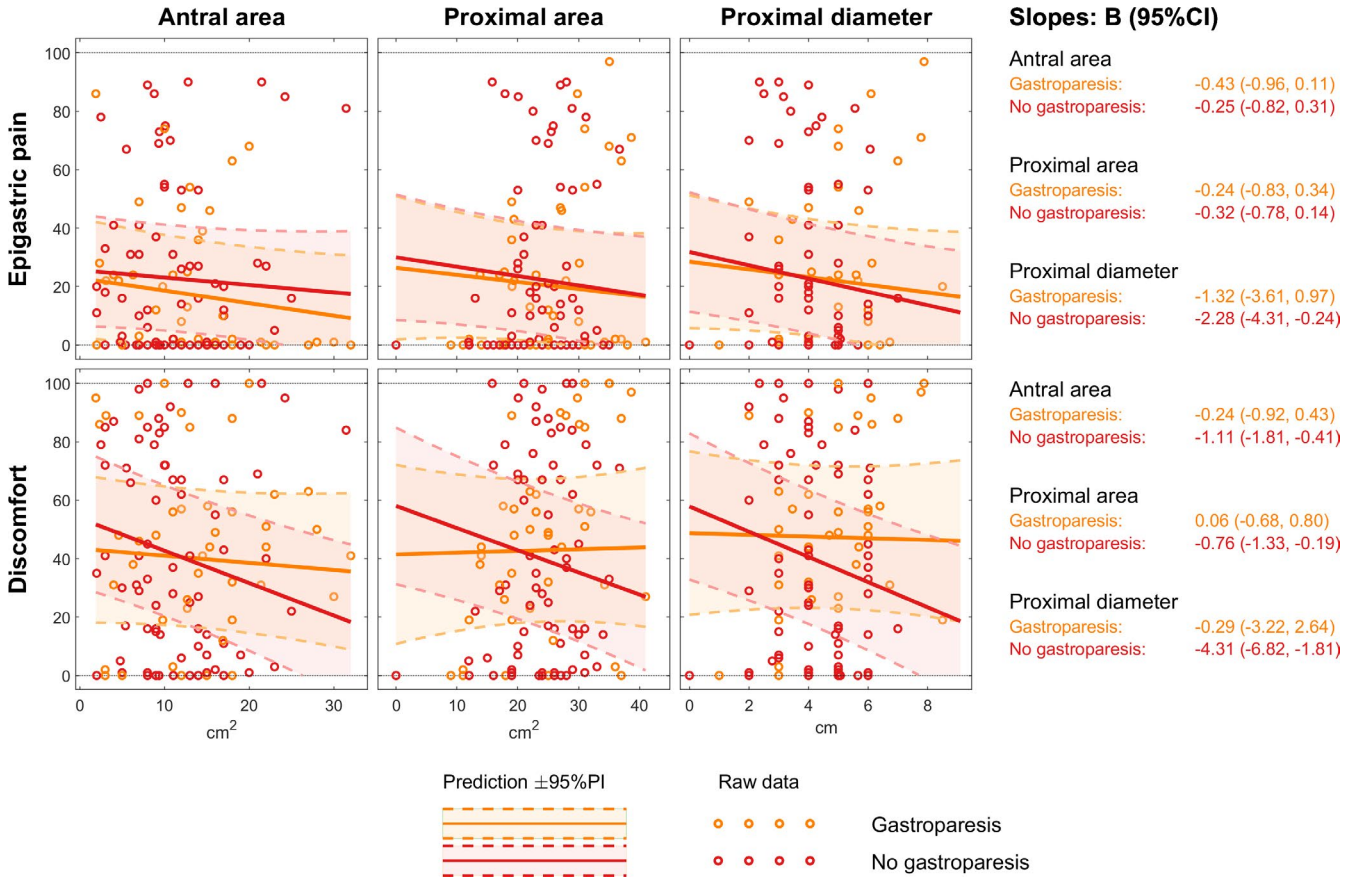

FIGURE 4 The association between upper GI symptoms (epigastric pain and upper abdominal discomfort) and ultrasound measurements from the antrum and the proximal stomach in diabetes patients with or without gastroparesis, with slope B (95% CI) of the estimated regression line. Results from a drink test of 500 ml low-calorie liquid meal analyzed by a linear mixed effects model

to healthy controls, and fasting antral size correlated with gastric emptying by scintigraphy. Both diabetes patients with and without gastroparesis had impaired accommodation and significantly more dyspeptic symptoms, both fasting and postprandially, suggesting a common cause of symptoms other than disturbed gastric emptying. Our findings suggest that the proximal stomach is affected by diabetic gastroparesis both in impaired accommodation and in delayed gastric emptying.

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CONFLICT OF INTEREST

No competing interests declared.

AUTHOR CONTRIBUTIONS

EKS performed 1/3 of the ultrasound examinations and basic statistical analyses, and wrote the paper. DS planned and organized the study and participated in writing and reviewing the manuscript. ES was principal investigator of the study and critically reviewed the manuscript. GD was involved in designing the study and reviewing the manuscript. MB was responsible for the scintigraphy analyses. OHG contributed with ultrasound images, was involved in the study design, and reviewed the manuscript. JA performed the linear mixed effects model statistical analyses and made Figures 2-4. TH performed 2/3 of the ultrasound examinations, was involved in the study design and in the writing of the paper.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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