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Proximal stomach function in obesity with normal or abnormal oesophageal acid exposure

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Abstract *There is an increased prevalence of gastro-oesophageal reflux and symptoms in obese patients. Information about the proximal stomach in obese patients with reflux is lacking. Gastric volume and compliance are similar between obese and lean subjects. To study the proximal stomach function and perception in obese patients with normal or abnormal oesophageal acid exposure, thirty-one obese patients, with normal or abnormal oesophageal acid exposure, underwent medical evaluation of oesophageal and gastrointestinal symptoms by a questionnaire and measurement of proximal stomach function and perception by an electronic barostat and a standardized questionnaire. Nineteen obese patients had abnormal oesophageal acid exposure. The percentage of total time with pH <4 is significantly related to the presence of hiatal hernia, the oesophageal intensity-frequency symptom score and gender, i.e. higher percentage in men. The perception cumulative score was significantly different between patients with normal and abnormal oesophageal acid exposure after adjusting for covariates (gender, body mass index, age, minimal distending pressure, gastric tone and gastric compliance). Gastric tone and compliance were significantly related to the perception cumulative score. In conclusion, patients with abnormal oesophageal acid exposure have increased gastric perception. A significant relation among gastric tone, gastric compliance and upper gastrointestinal sensations was shown.*

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INTRODUCTION

Obesity is a major health hazard in developed countries, and morbid obesity is associated with serious, debilitating and life-threatening sequelae.[1,2] Epidemiological studies demonstrated an increased prevalence of gastro-oesophageal reflux (GORD) in obese patients,[3] but the basic underlying mechanisms involved are still debated. We have already demonstrated that oesophageal symptoms, abnormal oesophageal exposure and a decreased lower oesophageal sphincter (LOS) pressure are more frequent in obese patients.[4] In lean patients with GORD an increased gastric sensitivity with normal compliance of proximal stomach at fasting and delayed recovery of gastric tone after food was shown,[5] which may explain, at least in part, the delayed gastric emptying and an higher association of transient (LOS) relaxations with reflux, whereas both abnormalities may contribute to a greater level of perception of symptoms.

No differences in gastric volume or in gastric compliance between obese and lean subjects were shown as measured by the barostat and single photon emission computer tomography (SPECT) techniques[6,7] respectively. On the other hand, some authors suggested that obese and bulimic individuals would have a higher gastric capacity that may explain the tolerance of higher gastric volume loads.[8] Recently greater body mass index (BMI) has been independently associated with reduced satiation and decreased postprandial fullness. Gastric volume at fasting significantly influences time and caloric intake to reach maximum satiation so it has been hypothesized that the differences in fasting gastric volume could be correlated with differences in gastric tone.[9] In contrast to the observation of decreased satiation in obese individuals, the same authors and others reported an increased prevalence of different gastrointestinal (GI) symptoms in obese patients compared with community controls.[10,11]

Despite these findings, informations about proximal gastric function in obese patients with reflux disease are lacking. We hypothesized that an increase of upper abdominal symptoms in obese patients could reflect either an increased gastric sensitivity or disordered motility causing impaired proximal stomach function as documented in patients with reflux disease.

Our aim was to study the proximal stomach function and perception in obese patients with normal or abnormal oesophageal acid exposure.

MATERIALS AND METHODS

Participants

Thirty-nine individuals participated in the study after giving their informed consent. The study protocol has previously been approved by the Ethical Committee of Federico II University of Naples, Italy.

Obese population

This study enrolled 31 consecutive obese patients (27 women, range: 17–51 years; Table 1). All these patients were referred for bariatric surgery as had a BMI of >35–40 kg m^{-2} and also had obesity-related comorbidities or had a BMI of >40 kg m^{-2} even without comorbidities if the weight adversely affected their life and could show that dietary attempts at weight control had been ineffective.[12] A patient underwent cholecystectomy and another was hypertensive and on treatment with enalapril. None of them used medications that could alter GI sensorimotor function, and altered recently their food intake. The diagnostic workup included an upper gastrointestinal (UGI) endoscopy and an UGI barium meal also with the patients in Trendelenberg position to exclude anatomic lesions of the oesophagus and the stomach and to assess for the presence of oesophagitis and hiatal hernia (HH).

The medical evaluation included a structured questionnaire on the presence/absence of GI symptoms – fullness, abdominal pressure, abdominal pain, nausea and vomiting.[13]

Control subjects

Eight lean healthy volunteers (six women, range: 21–65 years) with normal weight (no one was under 18.5 or above 25 kg) were selected from the general and medical staffs of the medical centre and from the workers and staff of Federico II University of Naples as healthy control (HC; Table 1). Exclusion criteria included history of GI surgery (except for appendectomy), concurrent significant medical conditions, use of medication that could alter GI sensory motor function. None of them had either oesophageal or GI symptoms as assessed by questionnaires. The gender and age distribution of HC was similar to obese patients (χ^2: $P = 0.4$, t-test: $P = 0.8$).

Table 1 Demographic and clinical parameters of obese patients and HC

	Obese patients ($n = 31$)	Obese patients with abnormal acid exposure ($n = 19$)	Obese patients with normal acid exposure ($n = 12$)	HC ($n = 8$)
Gender (M/F)	27/4	4/15	0/12	6/2
Age (years)	31.9 ± 11.0	31.3 ± 10.9	32.8 ± 11.4	32.9 ± 11.3
Weight (kg)	122.6 ± 22.0	126.7 ± 23.4	115.9 ± 18.6	63.8 ± 9.4
BMI (kg m^{-2})	45.4 ± 5.5	46.2 ± 6.1	44.2 ± 4.4	22.3 ± 1.9
Oesophageal symptoms	14/31	11/19	3/12	0/8
Oesophageal symptoms score	2.13 ± 3.0	3.2 ± 3.4	0.5 ± 0.9	0.0 ± 0.0
Presence of upper GI symptoms				
Bloating	8/23	5/14	3/9	0/8
Abdominal pressure	2/29	1/18	1/11	0/8
Fullness	10/31	6/13	4/8	0/8
Nausea	1/30	1/18	0/12	0/8
Abdominal pain	1/30	1/18	0/12	0/8
Vomiting	5/26	3/16	2/10	0/8

Values are expressed as mean ± SD.
HC, healthy controls; BMI, body mass index; GI, gastrointestine.

Protocol

All participants were studied after overnight fast without any medication for at least 72 h. Examinations were performed in a calm room, at 9 AM. The participants underwent an assessment of oesophageal symptoms, but only obese patients underwent an assessment of GOR pattern. They were then divided into two groups according to the presence of normal oesophageal acid exposure (pH < 4 for <4.75% of the total time) or abnormal oesophageal acid exposure (pH < 4 for more than 4.75% of the total time).[4] On a separate day (median 4, range: 2–8 days) each participant fulfilled the structured GI questionnaire and underwent a measurement of the proximal stomach function and perception.

Assessment of the oesophageal symptoms

The oesophageal symptom score was calculated by giving obese patients and HC a validated questionnaire dealing with the frequency and the intensity of heartburn, regurgitation, and dysphagia and chest pain retrospectively.[4] For each obese patient and HC, the score of frequency and intensity of each symptom was calculated. When more than one symptom was present, the cumulative total score was calculated.[4]

Assessment of gastro-oesophageal reflux pattern

Oesophageal pH measurements were performed on ambulatory basis over 24 h as previously described.[4] Briefly, a monoglass pH electrode (Mettler-Toledo AG, Greifensee, Switzerland) was passed through and secured to the nose with the electrode positioned 5 cm above the LOS previously detected manometrically and, connected to a data logger (LEM, Bologna, Italy). The patients were encouraged to adhere to their usual diet, to their normal mealtimes. They were carefully instructed to activate the event marker and to record on a diary card the timing of symptoms, meals, drinks and body position. A computer program (GENESI 4 version 8.0) was used to analyse all pH data. The time that oesophageal pH was below 4 (oesophageal acid exposure time) was expressed as a (percentage) fraction of the total registration period. Abnormal oesophageal acid exposure was considered to be present when >4.75% of the total time showed a pH < 4.[4] Mean oesophageal acid clearance time (EAC) per subject was defined as total reflux time (in min) divided by total number of reflux episodes.

Proximal stomach function

Proximal stomach function was investigated using an electronic barostat (ABS, Saint-Rosny-sous-Bois, France). A detailed description of the electronic barostat has been reported previously.[13] Briefly, the barostat maintains a constant pressure on the inside of a bag containing air by means of feedback. The feedback mechanism consists of a strain-gauge connected to an injection/aspiration system by means of a relay. Both the strain-gauge and the injection/aspiration system are independently connected by a double-lumen polyvinyl tube (12F, Vygon, Brussels, Belgium) to a spherical ultrathin bag (capacity 750 mL; max diameter 17 cm). A dial allows the selection of the desired pressure level. Pressure and volume within the bag are continuously recorded on a paper polygraph (model R611, Beckman, SensorMedics, Milan, Italy) at 1 mm s^{-1}. The carefully folded gastric bag was introduced through the mouth into the stomach. To unfold the intragastric bag, one lumen of the connecting tube was connected to a pressure transducer and the bag was slowly inflated through the other lumen of the tube with 300 mL of air under controlled pressure (<20 mmHg). The bag was then completely deflated and connected to the barostat. Firstly, the pressure in the bag was increased stepwise by 1 mmHg every 2 min to measure the minimal distending pressure (MDP) of the stomach, defined as the first pressure inducing an intragastric volume >30 mL. This pressure level accounted for intra-abdominal pressure. Afterwards, intrabag pressure was increased stepwise by 2 mmHg every 3 min until intrabag volume was >600 mL or when the participants reported discomfort.

After the distensions, the bag was deflated completely and the participants allowed moving about for 10 min. The barostat was then set again at 1 mmHg above MDP and fasting recordings performed for 20 min. If rhythmic volume waves were detected, the start of the fasting recording was postponed until they had stopped.[14]

At each pressure step intrabag volume was averaged over the last minute of stepwise increments before the next pressure step. The volume at each pressure level was corrected for air compressibility using Boyle's Law ($P_1V_1 = P_2V_2$). The volume–pressure curve was constructed starting from MDP and the compliance ($\Delta V/\Delta P$) was used for analysis.[13]

Mean barostat volume or baseline volume named as fasting gastric tone was determined over the 20-min observation period by counting the mean intrabag volume over that period, excluding variations attributable to volume waves were excluded.[14] A volume wave was defined as a change of bag volume >30 mL, which reverted in <2 min to a volume within 50% of the previous level.

In each participant we calculated the responses to the same isobaric distensions. Minimal distending preseuure, gastric tone and gastric compliance were used for statistical comparisons.

Assessment of gastrointestinal sensations

At each pressure step the perception of the upper abdominal sensations (pressure, fullness and nausea) was scored using a validated questionnaire.[13] The participants were also asked to specify any other sensation perceived in an open choice box on the questionnaire. Any sensation was independently evaluated on a graphic rating scale that combines visual descriptors on a visual analogue scale graded from 0 to 6. Each participant received standard instructions, specifying that score 0 represented absence of perception, score 5 represented a sensation of discomfort and score 6 represented a sensation of pain that was not expected and that signalled an immediate interruption of the stimulus. Any sensation was evaluated on the scale, on the basis of its perceived intensity, and orientative descriptors were provided indicating that score 1 represented vague perception of light intensity, score 2 represented definite perception of light intensity, scores 3 and 4 represented vague and definite perception of moderate sensation respectively. The participants were also told that if needed, they could indicate half unit scores on the scale, in such a way that scores of intensity were really 12. When more than one sensation was scored, the cumulative perception score was computed for comparisons.

Statistical analysis

Computation was carried out by the SPSS software package for Windows (release 11.5.1; SPSS Inc., Chicago, IL, USA). Data are presented as mean ± SD unless otherwise indicated. $P < 0.05$ was used for statistical significance. Chi-squared test, Pearson's correlation, Multiple ANOVA and linear regression analyses were used as appropriate.

RESULTS

Demographic and clinical parameters

The demographic and clinical parameters are shown in Table 1. Obese patients had BMI ranging from to 36 to 57 kg m^{-2}. Eight obese patients evidenced HH and two of them showed also oesophagitis (Grade A Los Angeles).

Gastro-oesophageal reflux pattern

Table 2 showed the influence of morbid obesity on 24 h pH measurements. On an individual basis 19 of 31 (61%) had abnormal oesophageal acid exposure. The percentage of total time with pH < 4 was 1.7 ± 1.5 and 8.9 ± 3.6 (mean ± SD) in patients with normal and abnormal oesophageal exposure respectively. Patients with abnormal oesophageal acid exposure had higher significant prevalence of HH than patients with normal oesophageal acid exposure (χ^2: eight of 19 *vs* one of 12, $P = 0.04$).

Oesophageal symptoms

The prevalence of oesophageal and GI symptoms is reported in Table 1. In all obese patients heartburn and regurgitation were reported more frequently than dysphagia. The intensity-frequency symptom score was significantly higher in obese patients with abnormal than normal acid exposure (ANOVA, $P < 0.01$; Table 1). Gastrointestinal symptoms were present in 19 obese patients and six patients had more than one symptom (Table 1).

Multiple linear regression analysis in obese patients showed that the percentage of total time with pH < 4 is significantly related to the presence of HH, the oesophageal intensity-frequency symptom score and gender, i.e. higher percentage in men (Table 3).

Table 2 Reflux parameters of obese patients ($n = 31$)

Time (%) for pH < 4	Mean ± SD (range)
Total time	6.1 ± 4.6 (0.0–15.1)
Time supine	7.6 ± 7.9 (0.0–30.9)
Time upright	6.0 ± 5.0 (0.0–16.9)
EAC	1.9 ± 1.1 (0.0–4.0)

	Weight		BMI	
Reflux variables	*r*	*P*-value	*r*	*P*-value
Time (%) for pH < 4				
Total time	0.226	0.111	0.131	0.241
Supine	0.095	0.315	0.009	0.481
Upright	0.217	0.134	0.166	0.199

Values are expressed as mean ± SD.

Table 3 Multiple regression analysis: the percentage of total time with pH < 4 by gender, age, BMI, presence or absence of hiatal hernia, presence of gastrointestinal symptoms and oesophageal intensity-frequency symptom score

	Unstandardized coefficients		Standardized coefficients			
	β	SE	*β*	*t*-test	Significance	95% CI
Constant	8.64	6.08		1.42	0.17	−3.91 to 21.19
Presence or absence of HH	4.05	1.38	0.40	2.93	0.01	1.20–6.90
Presence of upper GI symptoms	−0.23	0.58	−0.05	−0.39	0.70	−1.42 to 0.97
Oesophageal symptom score	0.63	0.22	0.41	2.83	0.01	0.17–1.09
Gender	−6.46	2.16	−0.48	−2.99	0.01	−10.92 to −2.00
Age	0.03	0.06	0.08	0.60	0.56	−0.08 to 0.15
BMI	−0.09	0.11	−0.11	−0.84	0.41	−0.33 to 0.14

Dependent variable: the percentage of total time with pH < 4.
CI, confidence interval; HH, hiatal hernia; GI, gastrointestine, BMI, body mass index.

Proximal stomach function

The volume–pressure relationship in response to stepwise increments in intragastric pressure was linear in obese patients and HC (individual *r* from 0.88 to 0.99 for both groups). Minimal distending pressure was significantly higher in obese patients compared with lean HC (11.8 ± 2.2 *vs* 6.4 ± 3.0 mmHg, ANOVA, $P < 0.001$). Because four patients and one HC experienced discomfort and/or showed an intrabag volume >600 mL at 8 mmHg above MDP, which was used as upper limit for the calculation of compliance. The volume–pressure curves for obese patients and HC are illustrated in Fig. 1. Gastric tone and compliance were not significantly different between obese and lean HC (ANOVA, $P = 0.1$ and 0.4 respectively). No difference was found in MDP, gastric tone and gastric compliance between obese patients with abnormal or normal oesophageal acid exposure (ANOVA, $P > 0.05$; Table 4). No relationship was found between EAC and MDP in obese patients ($r = 0.004$).

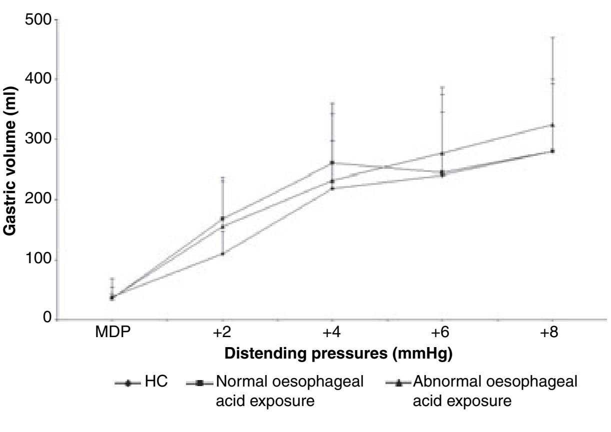

Figure 1 Volume–pressure relationship in obese patients with normal or abnormal oesophageal acid exposure and healthy control (HC).

Symptomatic response to gastric distension

Isobaric gastric distensions induced increased perception of UGI symptoms in obese patients and HC. The cumulative perception score positively skewed was borderline significantly higher in obese patients than in HC (0.57 ± 0.48 *vs* 0.14 ± 0.31, $P = 0.06$, ANOVA). Fig. 2 shows mean values for the cumulative perception score positively skewed in obese patients with normal or abnormal oesophageal acid exposure. The cumulative perception score positively skewed was significantly different between patients with normal or abnormal oesophageal acid exposure after adjusting for covariates: gender, BMI, age, MDP, gastric tone and gastric compliance. Gastric tone and compliance were significantly related to the perception cumulative score positively skewed (Table 5).

DISCUSSION

The ambulatory 24-h oesophageal pH monitoring is the most sensitive and objective means to assess reflux. Nineteen of our obese patients presented an abnormal oesophageal acid exposure according to criteria of the Italian multicentre GISMAD Study Group[15] and, the percentage of total time with pH < 4 is found to be positively related to intensity-frequency of oesophageal symptoms score, to presence of HH and to gender, i.e. men had higher percentage of total time with pH < 4. So far no pathophysiological mechanisms can completely explain the increased association between reflux and obesity.[3] One of the possibilities was an increased intra-abdominal pressure.[16] The elevated MDP in obese patients compared with lean subjects, showed by Klatt *et al.*[6] and, confirmed in this study, can be explained assuming an elevated intra-abdominal pressure. Alternatively, it is conceivable that an increased

Table 4 MDP*, gastric tone and compliance in obese patients and HC

	Obese patients ($n = 31$)	Obese patients with abnormal acid exposure ($n = 19$)	Obese patients with normal acid exposure ($n = 12$)	HC ($n = 8$)
MDP (mmHg)	11.7 ± 2.1	12.3 ± 2.0	10.8 ± 2.1	6.4 ± 3.0
Tone (mL)	97.5 ± 52.9	98.5 ± 62.6	96.0 ± 35.0	65.0 ± 19.3
Compliance (mL mmHg^{-1})	35.5 ± 14.3	36.5 ± 15.5	34.0 ± 12.6	30.7 ± 16.3

Values are expressed as mean ± SD.
MDP, minimal distending pressure; HC, healthy controls.
See Results for the statistical significance.

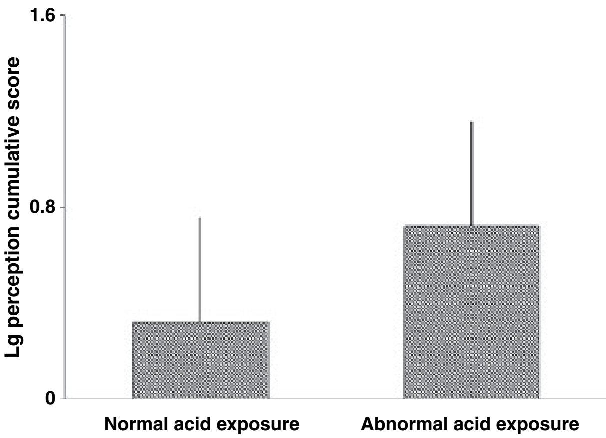

Figure 2 Base-10 logarithm (Lg) of perception cumulative score in patients with normal or abnormal oesophageal acid exposure (mean ± SD).

BMI predisposes to the development of a HH and explains the link to reflux symptoms.[17,18] A higher prevalence of HH was also found in our obese patients with abnormal oesophageal acid exposure.

Our novel findings are that the cumulative perception score in response to isobaric gastric distensions using a barostat is higher in obese patients with abnormal oesophageal acid exposure compared to obese patients with normal oesophageal acid exposure adjusted for age, BMI, gender, MDP, gastric tone and compliance. No significant difference was found in gastric tone and pressure–volume relationship (compliance) between obese patients with normal or abnormal oesophageal acid exposure and HC, but the multiple ANOVA showed a significant effect of gastric tone and compliance on the cumulative perception score.

Table 5 Base-10 logarithm (Lg) of perception cumulative score by normal = 1 or abnormal = 2 oesophageal acid exposure with gender, BMI, age, MDP*, gastric tone, gastric compliance

	Experimental method				
	Sum of squares	d.f.	Mean square	F	Significance
ANOVA					
Lg perception cumulative score					
Covariates (combined)	2.497	6	0.416	2.834	0.032
Gender	0.245	1	0.245	1.670	0.209
BMI	0.291	1	0.291	1.985	0.172
Age	0.004	1	0.004	0.024	0.878
MDP*	0.000	1	0.000	0.003	0.957
Gastric tone	1.113	1	1.113	7.577	0.011
Gastric compliance	0.653	1	0.653	4.449	0.046
Main effects					
normal = 1 or abnormal = 2 oesophageal acid exposure	1.009	1	1.009	6.870	0.015
Model	3.506	7	0.501	3.411	0.012
Residual	3.378	23	0.147		
Total	6.884	30	0.229		

BMI, body mass index.
*Minimal distending pressure (MDP; mmHg), gastric tone (mL), gastric compliance (mL mmHg^{-1}).

Previous studies of proximal gastric function using an electronic barostat in lean GORD patients demonstrated that compared with HC they had a similar gastric compliance, a prolonged gastric relaxation after meal ingestion and an increased visceral sensitivity.[5]

It may be considered that in patients with reflux disease the distension of the proximal stomach results in a higher number of postprandial transient LOS and increases reflux episodes, and then the perception.[5] We cannot exclude that by distending very proximal stomach anatomical changes might affect the distal oesophageal anatomy, but to date, in our knowledge, no data *in vivo* about anatomical modifications of these complex region to proximal stomach distension are available. These observations suggest that chemical stimulation of intestinal afferents by acid exerts a sensitizing effect on the stomach and increases perception of gastric distensions. This suggestion is supported by previous animal studies showing that chemical stimulation is able to induce sensitization at the peripheral or the central level.[19] In keeping with these studies, acid perfusion in the oesophagus, stomach, or duodenum was found to result in enhanced mechanosensitivity of the same region.[20] Furthermore, it has been shown that acid perfusion in the distal oesophagus is associated with the development of mechanical hyperalgesia in the proximal oesophagus, which has not been exposed to acid.[21] Accordingly, chemical irritation with acid appears to increase sensory input to interneurones and/or projection neurones in the dorsal horn of the spinal cord, resulting in a secondary hyperalgesia in adjacent, undamaged visceral tissue and a central hyperexcitability.[19] Thus, increased oesophageal acid exposure presented in our obese patients might potentiate perception of a different concurrent stimulus, expanding the whole spectrum of GORD-related symptoms. In fact, patients with reflux disease often report also dyspeptic symptoms as epigastric pain, bloating and nausea.[22,23] Our results are consistent with previous population-based studies of increased GI symptoms in overweight and obese subjects,[11] and in the same population a positive linear relationship between BMI and self-reported frequent heartburn or acid regurgitation has previously been reported.[24] Contrary to an increase of GI symptoms a decreased satiation was found in obese patients with no association between BMI and increased gastric volume as measured by SPECT techniques.[7] In fact, gastric volume at fasting significantly influences time and caloric intake to reach maximum satiation so it has been hypothesized that the differences in fasting gastric volume are more likely to be related to gastric morphological differences or differences in gastric tone.[9] During fasting a vagal cholinergic input maintains a high gastric tone, which is a particular type of sustained contraction exerted by the wall of the proximal stomach. We confirmed in this study that basal gastric tone and compliance measured by an electronic barostat are not altered in obesity as a previous study has already demonstrated,[6] adding the novel datum of no difference in gastric tone and compliance between obese patients with normal or abnormal oesophageal acid exposure. Nevertheless, either gastric tone or gastric compliance were significantly related to the cumulative perception score during isobaric distensions in our obese patients. Either technique aspect or population studied could be considered. The barostat has limitations and potential technical pitfalls that require proper attention. At constant pressure barostat measures variations of tone, but not absolute tone levels. Baseline volume depends on the operating pressure, which cannot be standardized so precisely, as to grant absolute measurements of basal tone.[25] One could expect a stronger correlation between gastric tone and UGI perception, but one of the limits of our study is that we investigated only the extreme spectrum of obese patients with BMI >36. Gastric emptying, another potentially relevant factor, was not tested in this study. However, studies of gastric emptying in obese patients compared with lean subjects are contradictory, with some showing accelerated[26,27] and others slower[28] emptying rates. This may be attributable to the lack of standardization of dietary habits (e.g. calorie restricted *vs* calorie excess) immediately preceding the studies[29] that we carefully avoided.

In conclusion, this is the first study that demonstrated an increased gastric perception only in obese patients with abnormal oesophageal acid exposure and a significant relation among gastric tone, gastric compliance and UGI sensations, which could not be due to the immediate effects of reflux, but involve more elaborate mechanisms that might be further investigated.

REFERENCES

1 Kuczmarski RJ, Flegal KM, Campbell SM, Johnson CL. Increasing prevalence of overweight among US adults: the National Health and Nutrition Examination Surveys, 1960 to 1991. *JAMA* 1994; **272**: 205–11.
2 Formiguera X, Canton A. Obesity: epidemiology and clinical aspects. *Best Pract Res Clin Gastroenterol* 2004; **18**: 1125–46.
3 Murray L, Johnston B, Lane A *et al.* Relationship between body mass and gastro-oesophageal reflux symptom: The

Bristol *Helicobacter* Project. *Int J Epidemiol* 2003; **32**: 645–50.
4 Iovino P, Angrisani L, Tremolaterra F *et al.* Abnormal esophageal acid exposure is common in morbidly obese patients and improves after a successful Lap-band system implantation. *Surg Endosc* 2002; **16**: 1631–5.
5 Penagini R, Hebbard G, Horowitz M *et al.* Motor function of the proximal stomach and visceral perception in gastro-oesophageal reflux disease. *Gut* 1998; **42**: 251–7.
6 Klatt S, Pieramico O, Gurthmen C *et al.* Proximal gastric motility functions are normal in severe obesity. *Digestion* 1997; **58**: 1115–9.
7 Kim DY, Camilleri M, Murray JA, Stephens DA, Levine JA, Burton DD. Is there a role for gastric accommodation and satiety in asymptomatic obese people? *Obes Res* 2001; **9**: 655–61.
8 Geliebter A, Hashim SA. Gastric capacity in normal, obese, and bulimic women. *Physiol Behav* 2001; **74**: 343–6.
9 Delgado-Aros S, Cremonini F, Castillo JE *et al.* Independent influences of body mass and gastric volumes on satiation in humans. *Gastroenterology* 2004; **126**: 432–40.
10 Crowell MD, Cheskin LJ, Musial F. Prevalence of gastrointestinal symptoms in obese and normal weight binge eaters. *Am J Gastroenterol* 1994; **89**: 387–91.
11 Delgado-Aros S, Locke CR, Camilleri M *et al.* Obesity is associates with increased risk of gastrointestinal symptoms: a population-based study. *Am J Gastroenterol* 2004; **99**: 1801–6.
12 SAGES. Guidelines for laparoscopic and open surgical treatment of morbid obesity. American Society for Bariatric Surgery. Society of American Gastrointestinal Endoscopic Surgeons. *Obes Surg* 2000; **10**: 378–9.
13 Iovino P, Valentini G, Ciacci C *et al.* Proximal stomach function in systemic sclerosis. *Dig Dis Sci* 2001; **46**: 723–30.
14 Azpiroz F, Malagelada JR. Physiological variations in canine gastric tone measured by an electronic barostat. *Am J Physiol* 1985; **248**: G229–37.
15 Pace F, Annese V, Ceccatelli P, Fei L. Ambulatory oesophageal pHmetry. Position paper of the Working Team on oesophageal pHmetry by the GISMAD (Gruppo Italiano di Studio sulla Motilità dell'Apparato Digerente). *Dig Liver Dis* 2000; **32**: 357–64.
16 Mercer CD, Wren SF, DaCosta LR, Beck IT. Lower esophageal sphincter pressure and gastroesophageal pressure gradients in excessively obese patients. *J Med* 1987; **18**: 135–46.
17 Stene-Larsen G, Weberg R, Froyshov Larsen I, Bjortuft O, Hoel B, Berstad A. Relationship of overweight to hiatus hernia and reflux oesophagitis. *Scand J Gastroenterol* 1988; **23**: 427–32.
18 Wilson LJ, Ma W, Hirschowitz BI. Association of obesity with hiatal hernia and esophagitis. *Am J Gastroenterol* 1999; **94**: 2840–4.
19 Mayer EA, Gebhart GF. Basic and clinical aspects of visceral hyperalgesia. *Gastroenterology* 1994; **107**: 271–93.
20 Mehta A, Caestecker JS, Camm AJ, Northfiels TC. Sensitization to painful distention and abnormal sensory perception in the esophagus. *Gastroenterology* 1995; **108**: 311–9.
21 Sarkar S, Aziz Q, Woolf CJ, Hobson AR, Thompson DG. Contribution of central sensitization to the development of noncardiac chest pain. *Lancet* 2000; **30**: 1154–9.
22 Klauser A, Schindlbeck N, Muller-Lissner S. Symptoms gastro-oesophageal reflux disease. *Lancet* 1990; **335**: 205.
23 Shi G, Bruley des Varannes S, Scarpignato C *et al.* Reflux related symptoms in patients with normal oesophageal exposure to acid. *Gut* 1995; **37**: 457.
24 Locke GR 3rd, Talley NJ, Fett SL, Zinsmeister AR, Melton LJ 3rd. Risk factors associated with symptoms of gastroesophageal reflux. *Am J Med* 1999; **106**: 642–9.
25 Azpiroz F. Gastric tone and the barostat: comprehend and compromise. *Neurogastroenterol Motil* 1997; **9**: 5.
26 Johansson E, Ekelund K. Relation between body weight and the gastric and intestinal handling of an oral caloric load. *Gut* 1976; **17**: 456–62.
27 Wright RA, Krinsky S, Fleeman C, Trujillo J, Teague E. Gastric emptying and obesity. *Gastroenterology* 1983; **84**: 747–51.
28 Maddox A, Horowitz M, Wishart J, Collins P. Gastric and oesophageal emptying in obesity. *Scand J Gastroenterol* 1989; **24**: 593–8.
29 Corvilain B, Abramowicz M, Fery F *et al.* Effect of short-term starvation on gastric emptying in humans: relationship to oral glucose tolerance. *Am J Physiol* 1995; **268**: G512–7 (*Gastrointest Liver Physiol* **31**).