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ORIGINAL ARTICLE

Proximal and Overall Gastric Emptying of Solids in Patients with Reduced Gastric Volume Accommodation Compared to Matched Controls

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Abstract
Background Interventions such as gastric surgery and erythromycin result in displacement of solids to the distal stomach and acceleration of overall and proximal gastric emptying. The effect of non-surgical impairment of gastric accommodation on gastric emptying is unclear. Non-surgical impairment of gastric accommodation is associated with accelerated gastric emptying.
Aim To compare measurements of proximal and overall gastric emptying in patients with reduced postprandial gastric volume accommodation with the emptying rates in age- and gender-matched controls with normal postprandial gastric volume accommodation.
Methods We evaluated overall and proximal gastric emptying in nine patients with impaired gastric accommodation and age-equivalent and gender-matched controls. Gastric volumes and emptying were measured using validated SPECT and dual gamma camera scintigraphy, respectively. We compared group differences in overall and proximal gastric emptying $t_{1/2}$ by t test.
Results Patients with impaired postprandial gastric volume accommodation had greater fasting gastric volume. The proportion of food emptied from the proximal stomach immediately after meal ingestion was lower and $t_{1/2}$ of proximal gastric emptying correspondingly longer in the group with reduced postprandial gastric accommodation. In contrast, differences were not detected in overall gastric emptying in the two groups, and the ratio of overall to proximal gastric emptying $t_{1/2}$ was greater in the group with impaired volume accommodation.
Conclusions Proximal stomach emptying is reduced in patients with impaired postprandial volume accommodation; this difference occurs predominantly during the time of meal ingestion. Compensatory mechanisms that result in normal overall gastric emptying require further elucidation.

Keywords Stomach · Volume · Dyspepsia · Distal · Surgical · SPECT

Introduction

Surgical fundoplication, gastric banding and intragastric balloon result in displacement of solids to the distal stomach and acceleration of overall and proximal gastric emptying. Impaired gastric accommodation is an important mechanism in dyspepsia [1]. Some patients with impaired gastric volume accommodation also have impaired gastric emptying. In a prior study of patients with low gastric volume accommodation, 12.9% of functional dyspepsia and 10% of postfundoplication patients had accelerated gastric emptying, whereas 27.6 and 35%, respectively, had normal gastric emptying of solids [2]. These findings contrast with the effects of surgical models of impaired accommodation, such as sleeve gastrectomy and Roux-Y gastric bypass, which reduce anatomical gastric volume and induce accelerated proximal and overall gastric emptying [3–5], and with pharmacological models demonstrated with intravenous erythromycin, which increases gastric fasting and postprandial tone, reducing gastric accommodation [6] and accelerating proximal and total gastric emptying [7].

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The effect of reduced gastric accommodation on gastric emptying is unclear. The study hypothesis is that non-surgically reduced gastric accommodation is associated with accelerated gastric emptying. Our aim was to compare proximal and overall gastric emptying in patients with reduced postprandial gastric volume accommodation with the emptying rates in age- and gender-matched controls with normal postprandial gastric accommodation.

Methods

Participants and Study Design

Participants for the study were selected from a database of patients who have undergone measurements of gastric volume and emptying in research studies in our laboratory. We identified nine patients with postprandial gastric volume accommodation (delta postprandial minus fasting volume) below 428 ml, which was previously demonstrated to be the 5th percentile for normal controls. Having identified those patients who had not undergone any prior gastric surgery, we used the database to identify two controls with normal postprandial gastric volume accommodation for every patient with reduced gastric volume accommodation. Thus, the study design was a case-controlled study with age-equivalent and gender-matched controls. The study was approved by Mayo Clinic's Institutional Review Board.

Gastric Emptying of Solids

After an overnight fast, participants ingested a radiolabeled meal: 0.75 mCi ^{99m}Tc-sulfur colloid was added to two raw eggs during the scrambling, cooking process. The eggs were served on one slice of bread with 240 ml of 1% milk (total calories: 296 kcal, 32% protein, 35% fat, 33% carbohydrate). All participants were instructed to ingest the meal in about 10 min or less. Anterior and posterior gamma camera images were obtained immediately after ingestion of the radiolabeled meal, every 15 min for the first 2 h, then every 30 min for the next 2 h (total 4 h after the radiolabeled meal), and analyzed as in previous studies [8–10].

Geometric means of decay-corrected counts in anterior and posterior gastric regions of interest were used to estimate the proportion of ^{99m}Tc emptied at each time point (gastric emptying). Intra-individual and inter-individual coefficients of variation in gastric emptying of solids are ~12 and 24%, respectively [11]. To measure emptying of the proximal stomach, we drew a region of interest horizontally across from the incisura of the stomach and extended the region of interest around the stomach orad to this line. Identification of the incisura was facilitated by study of the initial or subsequent scans that identified the angle of the stomach. The same region of interest was then applied to all subsequent gastric images to assess emptying of the proximal stomach; a separate analysis issuing a variable region of interest drawn around the whole stomach was used to assess emptying of the whole stomach (referred to henceforth as overall emptying).

Assessing Gastric Volume by ^{99m}Tc-SPECT Imaging

We used a noninvasive method to measure gastric volume during fasting and after 300 ml of Ensure® (316 kcal) using single photon emission computed tomography (SPECT). The method has been validated in detail elsewhere [12, 13]. Intravenous injection of ^{99m}Tc-sodium pertechnetate, which is taken up by the parietal and non-parietal cells of the gastric mucosa, allows visualization of the stomach wall. Tomographic images of the gastric wall were obtained using a dual-head gamma camera (SMV SPECT System™, Twinsburg, OH, USA) that rotates around the body, and imaging processing (AVW 3.0, Biomedical Imaging, Mayo Foundation) was used to render a three-dimensional reconstruction of the stomach to measure its volume (ml). We have previously validated the method in vitro and in vivo [14]. There is high intra-observer reproducibility to measure gastric volume with this technique [15]. Intra- and inter-individual coefficients of variation (at average 9 months) are ~20% [16]. Therefore, all measurements of gastric accommodation were performed by an experienced investigator (DB).

Data and Statistical Analysis

The primary endpoints of interest were postprandial change in gastric volume, fasting gastric volume, and overall and proximal gastric emptying $t_{1/2}$. The $t_{1/2}$ for overall and proximal gastric emptying was measured by linear interpolation of scintigraphic images obtained every 15 min, as shown in Fig. 1. This frequency of imaging incorporates the time for half emptying and allows for very accurate estimation without the need for modeling or other mathematical analysis. We compared overall and proximal gastric emptying $t_{1/2}$, as well as the differences and ratio between the emptying times by Student's t test.

Results

Participants

We studied nine patients with impaired gastric volume accommodation postprandially and 19 controls; each group had the same proportion of females and males (5:4), and

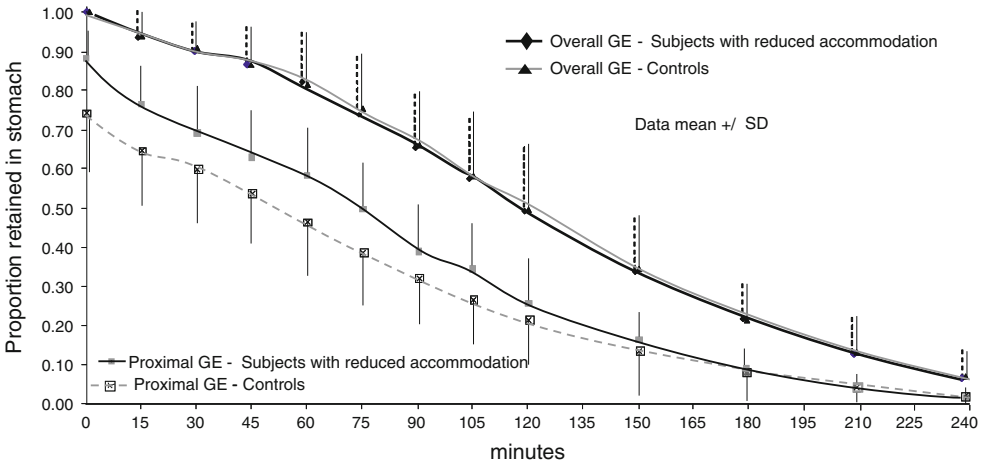

Fig. 1 Overall and proximal gastric emptying of solids in human subjects with reduced gastric accommodation and controls with normal accommodation. Note that patients with reduced accommodation have initial acceleration that is slower than in controls

the ages of the two groups were equivalent, as dictated by the study design. The data were derived from participants in two prior Mayo Clinic IRB approved studies in which participants receiving placebo were analyzed (from which the primary data have been published [17–19]). The demographic information of the participants and the time taken for ingestion of the meal (Table 1) in the two groups were not different.

Gastric Volumes

As expected from the selection of participants, there was a significant difference in the whole gastric volume between those with impaired gastric volumes and the matched controls. Patients with impaired postprandial gastric volume accommodation (<428 ml) had greater fasting gastric volume (Table 1).

Gastric Emptying of Solids

Contrary to expectations, the patients with impaired postprandial gastric volume accommodation had a lower proportion of food emptied from the proximal stomach immediately after meal ingestion compared to controls (Table 1). In addition, the $t_{1/2}$ of proximal gastric emptying was numerically longer ($p = 0.058$) in the group with reduced postprandial gastric accommodation. Figure 1 indicates that the slopes of proximal emptying curves were similar, and the main difference appears to be in the amount emptied during the very earliest phase (see proportion emptied at time 0 in Table 1) that includes the period when food was being ingested, which was not significantly different in the two groups of participants.

In contrast, differences were not detected in overall gastric emptying in the two groups, and the difference in overall to proximal gastric emptying $t_{1/2}$ was smaller in the group with reduced volume accommodation (Table 1).

Discussion

This study shows that non-interventional reduction in gastric accommodation does not accelerate proximal gastric emptying. Rather, we observed a slowing of proximal

Table 1 Characterization of overall and proximal gastric emptying in patients with impaired postprandial gastric volume

Data: mean ± SD	Reduced postprandial volume accommodation	Normal postprandial volume accommodation	*p* value
Age, years	39.0 ± 12.6	39.0 ± 10.8	0.864
Gender (F:M)	5:4	10:8	
Time for meal ingestion (min)	8.8 ± 1.61	8.4 ± 0.7	0.83
Postprandial gastric volume accommodation, ml	379.2 ± 41.4	539.0 ± 47.2	<0.0001
Fasting gastric volume	273.8 ± 72.1	219.0 ± 48.1	0.028
Overall gastric emptying, $t_{1/2}$ min	122.9 ± 32.5	126 ± 33.9	0.837
Proximal gastric emptying, $t_{1/2}$ min	74.3 ± 29.8	53.0 ± 32.9	0.109
Difference overall—proximal gastric emptying, $t_{1/2}$ min	48.6 ± 27.2	73.0 ± 33.5	0.059
Proportion proximal gastric emptying at time 0	0.12 ± 0.09	0.26 ± 0.18	0.012

gastric emptying and a normal rate of emptying of the entire stomach. Thus, the difference of overall to proximal gastric emptying is shorter in those with reduced postprandial gastric accommodation. This suggests that compensatory mechanisms result in acceleration in the distal gastric emptying in order to result in overall normal gastric emptying in those with reduced gastric accommodation.

We had previously observed that some patients with dyspepsia (non-diabetic, non-surgical etiology) had both reduced gastric accommodation and overall retardation of gastric emptying [2]. These features may represent vagal dysfunction, as previously reported in some patients with dyspepsia and antral motor dysfunction [20]. On the other hand, the normal overall gastric emptying of solids suggests that antral motor and vagal cholinergic functions are normal in the patients included in this study. Several prior studies had noted the redistribution of the ingested meal to the distal stomach in patients with dyspepsia [21–23], but this typically affects only a subset of patients or affects one phase (typically the liquid phase) of the meal. None of the prior studies actually documented impaired gastric accommodation [24] in the same study of gastric meal distribution and emptying. Piessevaux et al. [25] did not observe significant differences in the intra-gastric meal distribution between functional dyspepsia and healthy controls; however, they did observe that, on both univariate and multivariate analysis, distal gastric distribution of the liquid phase of the meal was associated with relevant or severe early satiety, a symptom which is usually attributed to impaired gastric accommodation. Our main focus was therefore to assess whether reduced postprandial gastric accommodation resulted in impaired distribution of the meal, and alteration in proximal and overall emptying of the stomach. A dimension of gastric function which was not evaluated in the prior studies (that predominantly used a barostatically controlled balloon to evaluate gastric tone) is the fasting gastric volume. In fact, our results do not concur with those of Troncon et al. [23] who did not appraise fasting gastric volume. Our data are consistent with the hypothesis that the greater fasting gastric volume in our patients resulted in greater reservoir capacity of the fasting stomach and, therefore, reduced transfer from the proximal to the distal stomach during the very early postprandial period, and slower proximal gastric emptying.

In view of the results in our current study, the data suggest that interventions like fundoplication, vagotomy, sleeve gastrectomy, and intragastric balloons, or pharmacological agents such as erythromycin or ghrelin (that impair gastric accommodation) cannot be used to predict the effects of non-interventional impairment of gastric accommodation on gastric emptying. Vagotomy reduces gastric accommodation and impairs gastric emptying, causing dumping of liquid food and retention of solid food [26, 27]. On the other hand, operations that reduce the gastric reservoir capacity, such as sleeve gastrectomy (3) and fundoplication without vagal injury [28], typically accelerate gastric emptying of liquids and, in some reports, the emptying of solids also.

Pharmacologically induced increase in fundic tone and decreased gastric accommodation increase gastric emptying rate. Thus, pharmacologically induced increase in fundic tone [29, 30] by erythromycin [7], motilin, and ghrelin [31] similarly accelerate gastric emptying of liquids and, with erythromycin, the emptying of solids [32]. The reduction in gastric accommodation is assumed to increase intragastric pressure and to result in displacement of the meal into the distal stomach for earlier emptying. However, increasing intragastric pressure by placement of an intragastric balloon at low or high intragastric pressure levels (2 or 4 mmHg, respectively, above intra-abdominal pressure) showed there were no significant effects on emptying of solids; however, there was modest but significant acceleration of emptying of liquids [33]. These data suggest that the effects of these pharmacological agents on gastric emptying may have reflected actions on function other than gastric accommodation (e.g., stimulation of antral motility) that resulted in acceleration of gastric emptying.

Conversely, hyperglycemia reduces proximal gastric tone, increasing gastric accommodation [34, 35] and is associated with retardation of gastric emptying [36, 37]. The effects of hyperglycemia are complex, and cannot be attributed solely to the effects on fundic tone. Thus, in the setting of hyperglycemia, there is evidence of increased phasic contractions in the proximal stomach [38], failed coupling of the proximal and distal stomach [39], and reduced and uncoordinated antral contractile activity [40].

The mechanism of the impaired gastric accommodation was not the focus of the current study. It is conceivable that some obese patients had borderline blood glucose or hyperinsulinism. However, it has been shown that physiological changes in blood glucose do not affect gastric compliance [41] or gastric emptying [38].

We conclude that, in the absence of a surgical or pharmacological intervention, reduced postprandial gastric volume accommodation does not necessarily impair gastric emptying. In circumstances associated with reduced postprandial accommodation without surgical or pharmacological intervention, the stomach appears to have the ability to compensate for the impaired accommodation, and to empty solids at a normal rate. The compensatory mechanisms that accelerate overall gastric emptying despite the delayed proximal gastric emptying require further study.

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Conflicts of interest The authors have no conflicts of interest.

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