Simple and non-invasive assessment of the accommodation reflex of the proximal stomach

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Abstract

Background: Impaired gastric accommodation of the proximal stomach is one of the major pathophysiological mechanisms in functional dyspepsia (FD). However, no useful method exists for the clinical evaluation of this phenomenon. Aim: The aim of the present study was to establish a simple and non-invasive method for evaluating the accommodation reflex of the proximal stomach. Methods: Nine healthy subjects received up to 1,700 mL of water (stepwise administration in 100-mL increments) using a nasogastric tube while they were in a supine position. To assess the meal-induced gastric accommodation reflex, we measured the cross-sectional area of the proximal stomach via ultrasonography (US) at 3-min intervals after administration of water. We also measured the pressure of the water column using the same tube. Then, we administered up to 400 mL of water in 100-mL increments and measured the area of the proximal stomach in 44 FD patients with early satiation (the measurements were performed at intervals of 3-min), and we compared the results with those for 44 healthy subjects. Results: The incremental changes in the area of the proximal stomach corresponded well with the amount of water administered. The area of the proximal stomach increased, but the antral area and the intragastric pressure remained relatively stable. After administration of more than 100 mL water, the area of the proximal stomach in healthy subjects was significantly greater than that in FD patients. Conclusion: US can be used to assess the isotonic expansion of the proximal stomach. We were able to distinguish FD patients with impaired accommodation reflex from healthy individuals by using this simple and easy method.

Key words: ultrasound, gastric accommodation, proximal stomach, functional dyspepsia
Introduction

Functional dyspepsia (FD) is defined by the presence of symptoms such as epigastric pain, epigastric burning, postprandial fullness, and early satiation. These symptoms are thought to originate in the gastroduodenal region without any predisposing organic, systemic, or metabolic disease.

On the basis of the Rome III criteria (Tack et al., 2006), FD is subdivided into 2 diagnostic categories: (1) meal-induced postprandial distress syndrome (PDS), which is characterized by postprandial fullness and early satiation, and (2) epigastric pain syndrome (EPS), which is characterized by epigastric pain and burning. Although the Rome III subdivisions were proposed under the assumption that the subgroups would be characterized by different underlying pathophysiological mechanisms, impaired accommodation reflex of the proximal stomach and delayed gastric emptying may play a major role in the pathogenesis of the PDS subgroup (Karamanolis et al., 2006). According to previous reports, impaired accommodation reflex of the proximal stomach and delayed gastric emptying are seen in 15–50% of FD patients (Quartero et al., 1998; Van Den Elzen and Boeckxstaens, 2006). Moreover, some studies have reported that the impaired gastric accommodation reflex was significantly associated with early satiation and weight loss (Tack et al., 1998; Tack et al., 2004).

In previous studies, magnetic resonance imaging (Ajaj et al., 2004), three-dimensional computed tomography, and single-photon emission computed tomography (SPECT) (Bouras et al., 2002) were used to assess the gastric accommodation reflex of the proximal stomach. However, no simple and useful method exists for the clinical evaluation of this phenomenon. Although a barostat study is the gold standard for the assessment of the gastric accommodation reflex (Van Den Elzen and Boeckxstaens, 2006), this test is invasive and cannot be used to evaluate the gastric accommodation reflex under normal conditions in the stomach.

To establish a simple and non-invasive method for the evaluation of the accommodation reflex in the proximal stomach by using ultrasonography (US), we performed the following 2 experiments.

Materials and Methods

Experiment 1

Nine healthy subjects (male, age range: 22–35 years, median age: 27 years) who had no abdominal symptoms volunteered for this study. The subjects had not taken any medication or undergone gastrectomy before the study. Volunteers with Helicobacter pylori infection were excluded from the study.

To assess the meal-induced gastric accommodation reflex, we administered up to 1,700 mL water (in 100 mL increments) through a nasogastric tube (8 Fr) and measured the cross-sectional area of the proximal stomach and antrum via US. The measurements were performed after every 100 mL administration within one minute at intervals of 3 min with the patients in a supine position. We considered the oral side from the gastric angle as the “proximal stomach” and inserted the nasogastric tube into the gastric fundus. We used X-ray analysis and US imaging to
confirm the position of the tube and to ensure that it remained in place inside the gastric fundus. We measured the water column pressure using this nasogastric tube after every administration of 100 mL of water within one minute. The water level from the surface of the bed in the nasogastric tube was considered to represent the intragastric pressure. To obtain the cross-sectional area of the proximal stomach, a US probe was positioned and maintained stationary in an intercostal space of the left axilla (Fig. 1); the spleen and hilum of the spleen served as the landmarks. The cross-sectional area of the proximal stomach was estimated by tracing its mucosal side with a built-in caliper within 3 min after incremental administration of water. After the assessment of the gastric accommodation reflex, the US probe was positioned vertically to permit simultaneous visualization of the antrum, the superior mesenteric artery, and the abdominal aorta. The antral area was estimated by tracing the mucosal side of the antrum with a built-in caliper. All US images were recorded on videotape to confirm the measurements.

All examinations were performed by the same researcher. The equipment used was an SSA-770A US system (Toshiba, Nasu, Japan) with a 3.75-MHz curved-array scanner.

Experiment 2

In experiment 1, we found that the water was partially distributed in the proximal stomach after administration of up to 400 mL of water via a nasogastric tube. On the basis of this observation, we decided to assess the isotonic expansion of the proximal stomach after
administration of up to 400 mL of fluid with the patient in a supine position. To assess the usefulness of this method for evaluating the impaired accommodation reflex in patients with FD, we measured the area of the proximal stomach in 44 FD patients with meal-induced early satiation. We administered up to 400 mL of water via a nasogastric tube (5 Fr) and conducted the measurements after every 100 mL administration within one minute at intervals of 3 min with the patients in a supine position. We compared the obtained areas with those measured in 44 healthy subjects. The measurements were performed using the method described earlier in the paper.

**Results**

**Experiment 1**

Changes on the US images of the cross-sectional area of the proximal stomach after incremental administration of up to 1,700 mL water through a nasogastric tube are shown in Fig. 2. The incremental changes in the area of the proximal stomach corresponded with the differences in water intake. The area of the proximal stomach increased, but the pressure remained relatively stable (Fig. 3). Water distribution was restricted to the proximal stomach when the administered volume was within 400 mL. Therefore, the size of the antrum did not increase until we infused more than 400 mL of water.
Experiment 2

Figure 4 shows the changes on US images of the cross-sectional area of the proximal stomach after stepwise administration of up to 400 mL water. The comparison of the changes in the area of the proximal stomach between patients with early satiation and healthy subjects is shown in Figure 5. In healthy subjects, the area increased proportionally to the amount of administered water (100 mL, 14.8 [1.2] cm²; 200 mL, 25.8 [1.5] cm²; 300 mL, 37.0 [1.5] cm²; 400 mL, 47.5 [1.8] cm²). In contrast, FD patients showed impaired gastric accommodation after administration of more than 100 mL water (100 mL, 11.2 [0.5] cm²; 200 mL, 19.8 [1.2] cm²; 300 mL, 25.0 [1.6] cm²; 400 mL, 31.0 [2.0] cm²).

Discussion

The accommodation reflex of the proximal stomach is the reflex that reduces the gastric mural tone and reserves the meal after ingestion. Its function consists of 2 reflexes stimulated by the vagus nerve: one is a reflex that occurs in a short period and is called “receptive relaxation”, and
Fig. 4. US images of the cross-sectional area of the proximal stomach after incremental administration of up to 400 mL water: the spleen served as a landmark for the measurement of the cross-sectional area, which was estimated by tracing the mucosal side of the proximal stomach with the built-in caliper.

Fig. 5. Comparison of changes in the largest cross-sectional area of the proximal stomach after incremental administration of up to 400 mL of water between patients who experienced early satiation and healthy subjects: after administration of more than 100 mL water, FD patients showed impaired gastric accommodation in comparison with the healthy subjects.
the other is a reflex that occurs for more than 30 minutes and is called “adaptive relaxation”. These differences can be distinguished physiologically; however, it is actually difficult to distinguish “adaptive relaxation” from “receptive relaxation”. Therefore, we considered these 2 reactions together as “accommodation reflex.”

Several pathophysiological causes of FD have been identified, such as delayed gastric emptying (Gilja et al., 1996; Quartero et al., 1998; Kusunoki et al., 2010; Karamanolis et al., 2006), abnormal antroduodenal motility (Stanghellini et al., 1992; Kusunoki et al., 2000), altered sensitivity to duodenal acid or lipid exposure (Burbera et al., 1995; Samson et al., 1999), visceral hypersensitivity (Mertz et al., 1998; Undeland et al., 1998), and impaired accommodation reflex (Salet et al., 1998; Tack et al., 1998). Among these, an impaired accommodation reflex is the most frequently observed pathophysiological condition in patients with FD. Several methods such as scintigraphy, barostat, SPECT, and magnetic resonance imaging (Jian et al., 1989; Tack et al., 1998; Kim et al., 2001; Bourat et al., 2002; Van Den Elzen et al., 2003) have been used to evaluate the gastrointestinal function, including the meal-induced gastric accommodation reflex. However, these techniques often have technical limitations and are too expensive or complex for daily use. Hence, the barostat-based technique is the standard method for the assessment of the accommodation reflex in the proximal stomach and has been used in several studies (Tack et al., 1998; Caldarella et al., 2003; Tack et al., 2003; Lee et al., 2004; Tack et al., 2004; Van Den Elzen and Boecxstaens, 2006). However, this method is invasive and because the presence of food in the stomach would interfere with the expansion of the balloon of the barostat, the postprandial gastric volume may be lesser than that recorded before consuming the test meal (Tutuian et al., 2008). To establish a simple and non-invasive method for the evaluation of the accommodation reflex in the proximal stomach by using ultrasonography (US), we performed the 2 experiments.

In previous studies (Gilja et al., 1995; Gilja et al., 1996), US has been confirmed to be a simple and non-invasive technique for the assessment of gastric motility, including gastric accommodation. The authors of these reports chose the sagittal section and the maximal diameter in an oblique frontal section to evaluate gastric accommodation of the proximal stomach. However, in the experiment 1, we selected the cross-sectional area of the proximal stomach for the assessment of gastric accommodation reflex. This study told us that changes in the cross-sectional area of the proximal stomach significantly correlate with changes in the volume after administration of water. In the experiment 1, we also found that the water was partially distributed in the proximal stomach after administration of up to 400 mL of water via a nasogastric tube. On the basis of this observation, the measurement of this area has been confirmed to be suitable for assessment of the isotonic expansion of the proximal stomach. In a previous study, Matsumoto et al. (2009) reported that US and a pressure sensor can be used to assess the isotonic expansion of the proximal stomach.

In the present study, we measured the area of the proximal stomach 3 min after administration of water. In some studies, the volume of the proximal stomach reached a peak value at about 2–5 min after ingestion of the test meal (Gilja et al., 1995; Gilja et al., 1996; Undeland et al., 1998; Lunding et al., 2006). In contrast, in the standard procedure using a barostat, the volume of the intragastric bag connected to the barostat increases every 2–3 min (Mearin et al., 1991; Kim et al., 2001). Therefore we thought that 3 min was the enough time to assess the expansion phenomenon...
induced by the intragastric pressure of water. If we would like to assess the secondary accommodation reaction including "receptive relaxation" and "adaptive relaxation" we needed more than 3 min period and the subjects needed to eat a test meal including some nutrients orally.

Although US is the simple and non-invasive method for assessment of the accommodation reflex of the proximal stomach, this method has some disadvantages, i.e., it requires the patients to be in the supine position for partial distribution of the liquid test meal in the proximal stomach. Therefore, the US method also cannot be used to evaluate the accommodation reflex with normal gastric distribution of a liquid test meal. In addition, US has some limitations because it requires sonographic skills and a certain level of expertise to fully interpret the information from the images. However, we used US for easy assessment of the accommodation reflex. In the present study, all evaluations were performed by the same researcher to prevent interobserver variation. The US probe was suitably positioned and was kept in the same position for all patients to avoid inconsistencies in the results. However, the reproducibility of the measurements was not adequately evaluated. In this regard, we selected and confirmed some landmarks to ensure that the same portion of the stomach was analyzed throughout all the measurements (Hara et al., 2002; Kusunoki et al., 2010). Therefore, we believe that there is very little possibility of inconsistencies caused by human errors in this method.

Impaired gastric accommodation reflex of the proximal stomach is one of the major pathophysiological mechanisms in FD. On the basis of the results of experiment 1, we believed that this method can be used to distinguish FD patients with impaired gastric accommodation reflex from healthy subjects without impaired gastric accommodation reflex by using ultrasonographic measurements of the cross-sectional area of the proximal stomach after administration of 400 mL of water while the patient is in a supine position. In experiment 2, after administration of more than 100 mL of water, the gastric accommodation reflex in FD patients with early satiation was more impaired than that in healthy subjects. These results supported some previous findings (Tack et al., 1998; Tack et al., 2004). Furthermore, our results revealed that this method is useful for the assessment of the gastric accommodation reflex. Our results also revealed that this method could be used to determine whether the accommodation reflex of the proximal stomach was sufficient. Therefore this method does not need to be a completely quantitative method.

Impaired gastric accommodation reflex of the proximal stomach occurs because of "underproductivity" and release disorder of nitric oxide (NO), which is the last neurotransmitter of the gastric accommodation reflex (Hayama et al., 1999). We believe that this method is useful in pharmacometrics associated with NO-related drug developments in the future.

In summary, US can be used to assess the isotonic expansion of the proximal stomach. We were able to distinguish FD patients with impaired accommodation reflex from healthy individuals by using this simple and easy method.

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