

ORIGINAL ARTICLE

# The Usefulness of Water-drinking Ultrasonography Combined Test for Evaluating Patients with Functional Dyspepsia

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**Background/Aims:** The major causes of functional dyspepsia (FD) are motility dysfunction and visceral hypersensitivity. Despite the large number of diagnostic tests, there are no convenient methods for evaluation of gastric functions. Therefore, this study was conducted to assess the relationship between the degree of dyspepsia and gastric accommodation, emptying, and sensitivity.

**Methods:** A total of 120 FD patients that met the Rome III criteria and 30 healthy volunteers were included in this cross-sectional study. The mean cross-sectional area of the fornix was measured to investigate fundic accommodation and gastric emptying during and after water intake. During the test, abdominal symptoms were evaluated using the 4-point Likert scale.

**Results:** The water-drinking ultrasonography combined test revealed impairment of gastric accommodation in FD after 1,000 mL of water intake, delayed emptying after 5 min of water intake and statistically significant hyperesthesia after 400 mL of water intake in the FD group compared with healthy controls ( $p < 0.05$ ). Postprandial distress syndrome (PDS) and overlap syndrome were independently associated with gut motor disturbances instead of epigastric pain syndrome (EPS) ( $p < 0.01$ ).

**Conclusions:** The results of the present study suggest that the water-drinking ultrasonography combined test could be used for diagnosis of gastric motor and sensory dysfunction, particularly in PDS and EPS-PDS patients. This test is easy, well tolerated by the patient and can be widely applied in clinical practice. (*Korean J Gastroenterol* 2015;66:92-97)

**Key Words:** Accommodation; Gastric emptying; Visceral hypersensitivity; Early satiation

## INTRODUCTION

Functional gastrointestinal disorders are a common problem in modern gastroenterology. Dyspepsia occurs in the same structural and functional pathology. According to Suzuki and Moayyedi<sup>1</sup> upper gastrointestinal endoscopy findings appear normal in approximately 75% of patients with dyspepsia, and most of these individuals are diagnosed with functional dyspepsia (FD). FD is extremely common, influencing 15-20% of the population, and is associated with a marked decrease in quality of life and substantial health-care costs.<sup>2</sup> Understanding the particular qualities of FD patients provides important information concerning the various factors affecting consultation choice, which will clarify

the etiology of FD patients.<sup>3</sup>

FD is determined based on the presence of dyspeptic symptoms in the absence of any organic cause that can explain them. The Rome III consensus divides FD into postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS). Epidemiological studies in the United States and Europe confirmed the presence of both subgroups, with great overlap between EPS and PDS.<sup>4</sup> The available treatment options for FD are of limited effectiveness, which reflects its poorly understood pathogenesis. Studies indicate that FD is a heterogeneous disorder in which different pathophysiological mechanisms underlie specific symptom patterns.<sup>5</sup> Traditionally, gut abnormalities such as impaired accommodation, delayed emptying and hypersensitivity are be-

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lieved to be involved in the pathophysiology of FD.<sup>2</sup> Tests of motility and sensory gastric functions are available in health service, but there is no gold standard. Gastric barostat is not widely used because the procedure is extremely invasive.<sup>6</sup> The results of electrogastrography are dependent on the location of electrodes, acid secretion or duodenal reflux. Imaging methods such as X-ray and scintigraphy with <sup>99</sup>Tc or <sup>111</sup>In cannot be extensively applied because of radiation exposure and long examination time. Video capsule endoscopy is a very expensive method that is not applicable in routine practice.<sup>13</sup> <sup>13</sup>C-urea breath tests for evaluation of gastric emptying are only available in specialized clinics.<sup>7</sup> Conversely, ultrasonography does not require radiation, expensive chemical substances or unusual equipment. In terms of money and timesaving, the water-drinking ultrasonography combined test (WDUCT) is useful for examination of FD patients.<sup>6</sup>

## SUBJECTS AND METHODS

### 1. Protocol

This cross-sectional study was conducted in the Department of Internal Medicine, Central Clinical Hospital No. 3, Donetsk, Ukraine, between November 2013 and November 2014. The study protocol was approved by the Ethics committee of the Central Clinical Hospital No. 3 on 11 November 2013 (No. 169), and carried out in accordance with the Declaration of Helsinki.

### 2. Subjects

This study included 120 patients with a diagnosis of FD. Patients were divided into three groups according to the Rome III criteria based on responses to Russian language-validated questionnaires from the Ukrainian Gastroenterology Association (member of World Gastroenterology Organisation). Subjects were eligible to enter the study if all of the following criteria were met: male or female subjects aged 18-75 years; Rome III Criteria fulfilled for the 3 months prior to informed consent with symptom onset at least 6 months prior to informed consent; normal endoscopy results within 6 months; female subjects of childbearing potential must provide a negative pregnancy test. Exclusion criteria included: subjects taking drugs that affect gut motility, gut sensitivity and/or acid secretion or NSAIDs; organic gastrointestinal disease; history of surgery that can affect gastrointestinal mo-

tility including endoscopic surgery for gastroesophageal reflux disease (GERD) and obesity; irritable bowel syndrome; chronic idiopathic nausea; Type I or Type II diabetes; active uncontrolled psychiatric and/or psychosomatic disorders; BMI over 30 kg/m<sup>2</sup>; clinically significant renal, hepatic, cardiovascular, pulmonary, endocrine, metabolic, or hematological condition.

Healthy subjects did not have dyspepsia symptoms or drug allergy. All subjects recruited in the study were subjected to upper gastrointestinal endoscopy, biochemistry analyses and abdominal ultrasound to exclude organic alimentary tract diseases. Written informed consent was obtained from all study participants.

### 3. Procedures

During the water-drinking period, subjects ingested 200 mL of water at 3-min intervals five times (total 1,000 mL) by ingesting water through a straw. The test was discontinued if subjects felt any discomfort. Examination of gastric emptying was conducted 5 and 10 min after completion of drinking 1,000 mL of water (or discontinuation). The mean cross-sectional area of the fornix during and after water intake was measured to investigate the fundic accommodation and gastric emptying. All ultrasonographic examinations were conducted using an Ultima PA (1-5 MHz convex-type probe; Radmir, Kharkiv, Ukraine). The patient was asked to grade the intensity (0, absent; 1, mild; 2, relevant; and 3, severe) of the pain during water intake.

### 4. Statistical analysis

Data were evaluated with Medstat (Donetsk, Ukraine), which is a commercially available statistical analysis software package. All values were expressed as the mean±SD. The normal range of the cross-sectional area of the fornix was set using dates of 30 healthy volunteers. Cases outside the normal range were diagnosed with a motor or sensory disorder. Student's t-test and Wilcoxon's tests were conducted to evaluate continuous variables and the chi-squared test was used to measure frequency variables. p-values of less than 0.05 were considered to indicate statistical significance. RR with a 95% CI was computed. Biochemical results displayed normal distribution.

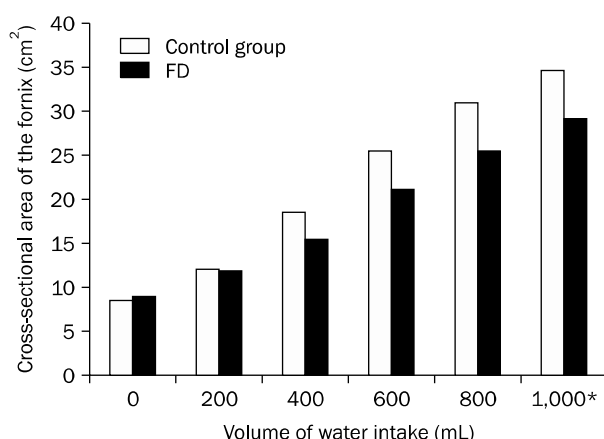
## RESULTS

### 1. Demographics

The first group consisted of 56 (46.7%) patients with PDS, the second contained 44 (36.7%) patients with overlapping EPS and PDS, and the third 20 (16.7%) patients with EPS. The age limits of the patients were 18-67 years (mean age  $39.4 \pm 4.3$  years). The study group consisted of 41 men (34.2%) and 79 women (65.8%). The mean BMI of the group was  $24.8 \pm 6.3$  kg/m<sup>2</sup>. The healthy control group consisted of 30 subjects (14 males and 16 females) with a mean age of  $39.2 \pm 14.8$  (18-59) years and a mean BMI of  $22.8 \pm 4.3$  kg/m<sup>2</sup>. There was no significant difference between groups in the distribution of sex, age, BMI, height and weight.

### 2. Gastric accommodation

We developed a novel WDUCT to assess gastric motility and sensory functions of FD patients compared with healthy controls. First, we studied gastric accommodation (Fig. 1).



**Fig. 1.** Impairment of gastric accommodation in the functional dyspepsia (FD) patients. \* $p=0.031$ .

**Table 1.** Gastric Accommodation and Visceral Hypersensitivity in Healthy Subjects and Functional Dyspepsia (FD) Patients

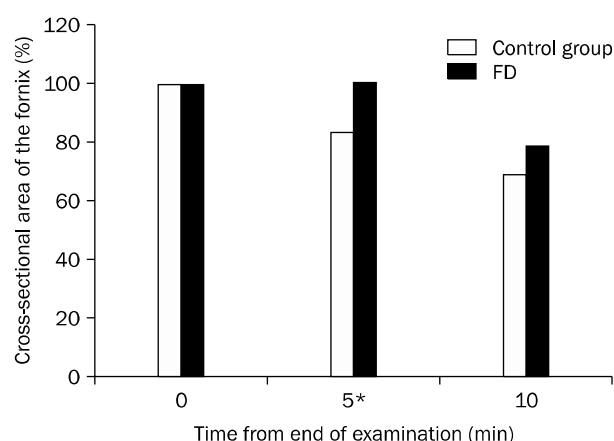
Water intake (mL)	Gastric accommodation (cm <sup>2</sup> )		Visceral hypersensitivity	
	FD	Control	FD	Control
0	8.98±1.8	8.64±1.78	0	0
200	11.9±2.1	12.21±2.94	0.4±0.63	0.1±0.31
400	15.76±2.14	18.57±4.6	0.8±1.01	0.1±0.31*
600	21.37±3.0	25.75±5.92	1.4±1.05	0.2±0.42
800	25.7±4.21	31.21±7.69	1.53±1.12	0.2±0.42
1,000	29.34±4.9	34.92±7.2*	1.8±1.08	0.3±0.48

\* $p<0.05$ .

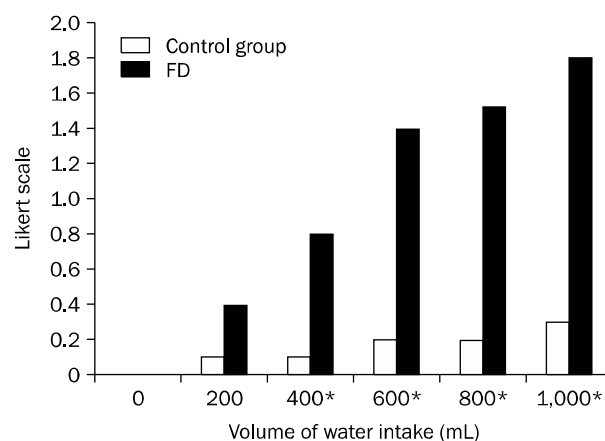
The values of the mean cross-sectional area of the fundus before and after intake of 200, 400, 600, 800, and 1,000 mL of water in the control and FD groups were expressed in Table 1. The mean cross-sectional area of the fundus after intake of 1,000 mL of water was significantly lower in the FD group, suggesting impairment of the gastric accommodation in FD.

### 3. Gastric emptying

We also experienced delayed emptying in the FD group (Fig. 2). The percentage of the cross-sectional area of the fundus after 5 min was  $100.4 \pm 15.1\%$  in the FD group and  $83.47 \pm 8.44\%$  in the control ( $p=0.002$ ). The percentage of the cross-sectional area of the fornix after 10 min was  $78.2 \pm 16.7\%$ , while it was  $69.4 \pm 8.8\%$  in the control group, ( $p=0.131$ ). The mean value of the cross-sectional area of the fundus 5 min after drinking water in the FD group was higher



**Fig. 2.** Delayed emptying in the functional dyspepsia (FD) patients. \* $p=0.002$ .



**Fig. 3.** Visceral hypersensitivity in the functional dyspepsia (FD) patients. \* $p=0.047$ .

than that in the control group, suggesting delayed emptying in FD.

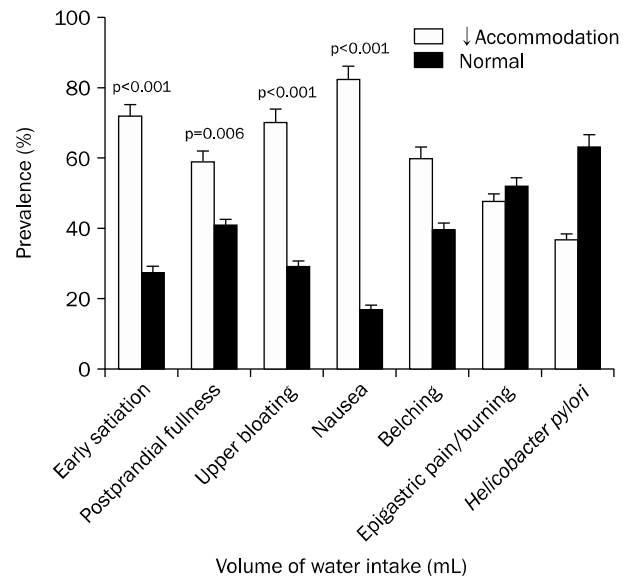
#### 4. Visceral hypersensitivity

In the FD group, marked symptoms such as abdominal fullness and epigastric pain developed immediately after the initiation of water intake, and the Likert scale was higher than the controls (Fig. 3). The Likert scale differed significantly between the control and FD groups after ingestion of 400 mL (after 200 mL of water  $0.4 \pm 0.63$  vs.  $0.1 \pm 0.31$ ,  $p=0.189$ ; after 400 mL  $0.8 \pm 1.01$  vs.  $0.1 \pm 0.31$ ,  $p=0.047$ ; after 600 mL  $1.4 \pm 1.05$  vs.  $0.2 \pm 0.42$ ,  $p=0.004$ ; after 800 mL  $1.53 \pm 1.12$  vs.  $0.2 \pm 0.42$ ,  $p=0.04$ ; after 1,000 mL  $1.8 \pm 1.08$  vs.  $0.3 \pm 0.48$ ,  $p=0.02$ ), suggesting hyperesthesia in the FD group.

#### 5. Relationship between symptoms and results of WDUCT

Comparison of the prevalence of individual symptoms in subjects with normal and reduced accommodation, normal and delayed gastric emptying, and normal and hypersensitivity are summarized in Table 2. This study has revealed connections between dyspeptic symptoms and gut motor function. Impairment of accommodation was found in

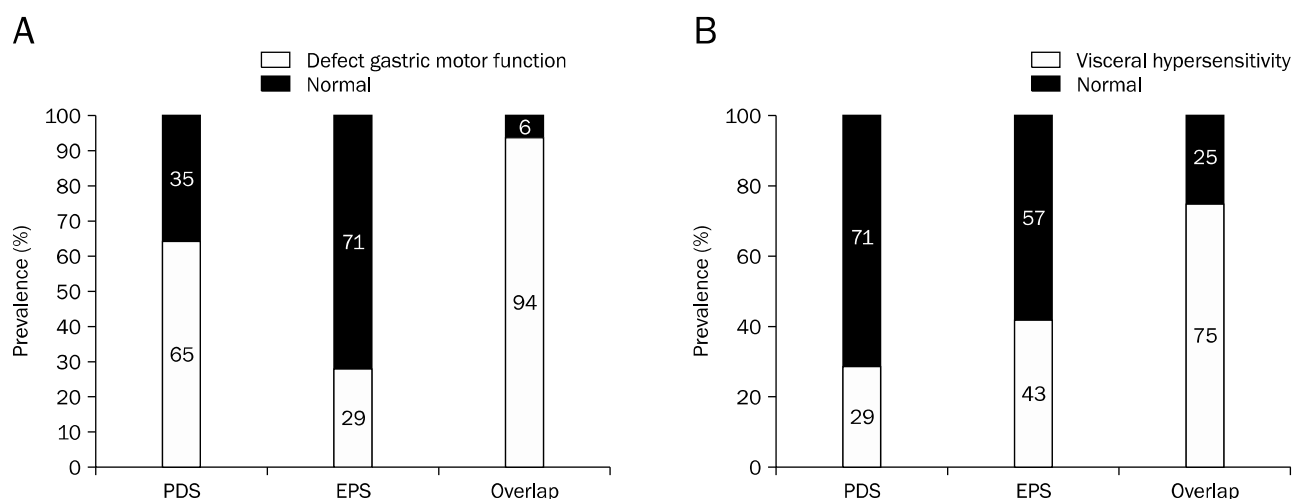
50.0% of FD patients and was typical for patients with postprandial symptoms,  $p < 0.001$  (Fig. 4). Delayed gastric emptying was typical for 37.5% of the FD patients and 52.2% of patients with epigastric pain. This type has hyperacid pH-



**Fig. 4.** Prevalence of dyspeptic symptoms and *Helicobacter pylori* (%) in patients diagnosed with normal and impaired gastric accommodation.

**Table 2.** Symptoms and Results of Water-drinking Ultrasonography Combined Test

Symptom	Impaired accommodation (%)	RR (95% CI)	p-value	Delayed emptying (%)	RR (95% CI)	p-value	Visceral sensitivity (%)	RR (95% CI)	p-value
Early satiation			<0.001			0.221			0.045
Yes (54)	39 (72.2)	2.45 (1.55-3.89)		24 (44.4)			33 (61.1)	1.52 (1.03-2.24)	
No (66)	21 (31.8)			21 (31.8)			27 (40.9)		
Postprandial fullness			0.006			0.392			0.697
Yes (81)	48 (59.2)	1.7 (1.21-2.38)		33 (40.7)			42 (51.9)		
No (39)	12 (30.7)			12 (30.8)			18 (46.2)		
Upper bloating			<0.001			0.811			0.010
Yes (51)	36 (70.6)	2.33 (1.45-3.75)		18 (35.3)			33 (64.7)	1.72 (1.14-2.62)	
No (69)	24 (34.8)			27 (39.1)			27 (39.1)		
Nausea			<0.001			0.921			0.076
Yes (46)	38 (82.6)	3.57 (1.86-6.88)		17 (36.9)			29 (63.1)		
No (74)	28 (37.8)			28 (37.8)			33 (44.6)		
Belching			0.134			0.086			0.705
Yes (45)	27 (60.0)			12 (26.7)			24 (53.3)		
No (75)	33 (44.0)			33 (44.0)			36 (48.0)		
Epigastric pain/burning			0.712			0.003			<0.001
Yes (69)	33 (47.8)			36 (52.2)	1.6 (1.20-2.14)		45 (65.2)	2.03 (1.40-2.93)	
No (51)	27 (52.9)			12 (23.5)			15 (29.4)		
Helicobacter pylori			0.001			0.921			0.001
Yes (46)	17 (36.9)	0.49 (0.33-0.74)		17 (36.9)			17 (36.9)	0.49 (0.33-0.74)	
No (74)	51 (68.9)			28 (37.8)			51 (68.9)		



**Fig. 5.** Comparison of the prevalence defect motor gastric function (A) and visceral hypersensitivity (B) in patients with different functional dyspepsia subtypes using the  $\chi^2$ -test. Postprandial distress syndrome (PDS) and overlap have defective accommodation and/or significantly higher frequency of emptying than epigastric pain syndrome (EPS) ( $p < 0.05$ ). Visceral hypersensitivity is increased in overlap relative to PDS ( $p < 0.001$ ).

gram frequently. It is assumed that acidification of the duodenum promotes mechanisms such as impaired gastric accommodation, delayed gastric emptying and hypersensitivity, which contributes to the appearance of symptoms. Visceral hypersensitivity occurred in half of the FD individuals and prevailed among patients with early satiety ( $p=0.045$ ), bloating ( $p=0.010$ ) and pain ( $p < 0.001$ ). The disturbances of gastric motor-evacuation function were dependent on the clinical subtype of FD (Fig. 5). Impairment of the accommodation and/or emptying were encountered more frequently in the PDS and overlap group than in the EPS,  $p < 0.05$ . Visceral hypersensitivity prevailed in the overlap group ( $p < 0.001$ ).

## DISCUSSION

The pathophysiological mechanisms of FD include gastrointestinal dysmotility, perception disturbance, acid hypersensitivity, psychological factors, duodenal dysfunction, and abnormalities within the brain-gut axis. WDUCT revealed abnormalities in gastric motility and sensation in patients with FD when compared with healthy controls. However, most diagnostic tests of gastric motility only characterize gastric emptying. Therefore, we investigated the relationship between accommodation and postprandial symptoms.

Several studies have reported that the prevalence of impaired gastric accommodation in patients with FD is around 40-60%, whereby proximal adequate relaxation occurs.<sup>8</sup> The

origin of impaired accommodation in FD is not known, but it is likely caused by abnormalities of the vago-vagal reflex, the intrinsic inhibitory innervation (myenteric plexus) or smooth muscles of the proximal stomach.<sup>2</sup> Delayed gastric emptying also plays an important role in the pathogenesis of FD. Depending on the different study design, the prevalence ranges from 20% to 50%.<sup>2,9</sup> Visceral hypersensitivity to gastric distension is detected in 34-65% of patients with FD and correlated with the severity of dyspeptic symptoms.<sup>8</sup> Van Ouden-hove et al.<sup>10</sup> first found a significant and independent influence of gastric sensitivity and abuse history on gastric sensation scores in FD. Additionally, brain imaging revealed differences in the activity of homeostatic-afferent, emotional-arousal and cortical-modulatory regions, most of which are involved in cognitive/affective aspects of visceral pain.

FD is one of the most common gastrointestinal disorders encountered in clinical practice. Keeping in mind the high human and economic burden, more effective treatment is badly needed. The wide variety of FD symptoms indicates multiple pathophysiological mechanisms. Progress in its understanding might lead to better symptom control through the development of targeted therapy.<sup>2</sup> Impaired accommodation of the proximal stomach has been observed in FD, but its relevance to postprandial symptoms is unclear. We demonstrated that impaired gastric accommodation causes early satiety, postprandial fullness, bloating and nausea, but not delayed gastric emptying. Despite the large number of proki-

netic agents represented in our market, they are assigned blindly because physicians do not know about modification of gastric motility during treatment. The WDUCT can be readily performed, is well tolerated and widely applied in routine clinical practice. However, further studies are necessary to clarify the strategy of FD treatment. Promotion of gastric accommodation may be an effective therapy for patients with FD who report early satiety and postprandial fullness.

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