

# Evaluation of gallbladder motility in patients with irritable bowel syndrome

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## Summary

**Background:** Abnormalities involving smooth muscle function in different systems of the body have been reported in irritable bowel syndrome (IBS). There are a few studies on gallbladder function in this disorder with conflicting results.

**Objectives:** To investigate the motility of gallbladder in patients with IBS.

**Patients and methods:** Forty-eight patients (15 male and 33 female) with IBS and 48 healthy volunteers (15 male and 33 female) were included into the study. Thirty-four patients (70.8%) had constipation predominant and 14 patients (29.2%) had diarrhoea predominant type of IBS. Fasting and postprandial gallbladder volumes were studied using real time ultrasonography and ejection fraction (EF) of gallbladder was calculated.

**Results:** While fasting gallbladder volume

(FGV) was similar between IBS and control groups ( $18.0 \pm 4.0$  ml vs.  $17.8 \pm 4.9$  ml,  $p > 0.05$ ), postprandial gallbladder volume (PGV) was lower in IBS group than in the control group ( $5.5 \pm 1.4$  ml vs.  $6.2 \pm 1.9$  ml,  $p = 0.03$ ). Accordingly, the mean EF of gallbladders was found to be higher in IBS group than in the control group (69.1% vs. 64.1%,  $p = 0.0001$ ). There were no difference in FGV, PGV and EF of gallbladders between constipation predominant and diarrhoea predominant IBS patients ( $p > 0.05$ ).

**Conclusion:** The results of this study indicated that IBS patients have increased emptying of gallbladder compared to healthy subjects.

**Key words:** irritable bowel syndrome; gallbladder; motility

## Introduction

Irritable bowel syndrome (IBS) is a symptom complex characterized by abdominal discomfort or pain associated with defecation or a change in bowel habit [1, 2]. IBS is a common disorder with a prevalence of 15–20% [3] in the general population and it constitutes 50% of the cases in outpatient clinics of gastroenterology [3, 4]. Health related quality of life is poor in patients with IBS [5, 6]. Moreover, this disorder can lead to lost of time from work or increased health care costs [7].

Although the basic symptoms of IBS belong to colon, there are also some extra colonic gastrointestinal symptoms such as nausea, vomiting, early satiety and heartburn [8, 9], somatic symptoms such as fibromyalgia [10], headache [11], backache [8], genitourinary symptoms [8, 12], autonomic cardiovascular dysfunction [13], and psychosocial dysfunction [14]. Recently, it has been demonstrated that asthma is more common in IBS patients than in normal population [15]. The existence of a generalized abnormality involving smooth muscle and/or autonomic nervous system has been suggested to explain all these associations

[16]. Reports on gallbladder function in patients with IBS are scant, with conflicting results varying from normal [17, 18] to impaired [19, 20] contractility. We therefore aimed to investigate whether the gallbladder motility is different in patients with IBS than in healthy subjects using real time ultrasonography.

### Abbreviations:

BMI	body mass index
CCK	cholecystokinin
C-IBS	constipation predominant irritable bowel syndrome
D-IBS	diarrhoea predominant irritable bowel syndrome
EF	ejection fraction
FGV	fasting gallbladder volume
GB	gallbladder
IBS	irritable bowel syndrome
PGV	postprandial gallbladder volume
SD	standard deviation

## Patients and methods

### Patients

Forty-eight consecutive patients with IBS (15 males and 33 females), all in symptomatic period, and 48 healthy volunteers (15 males and 33 females) were included into the study. Diagnosis of IBS was based on Rome II criteria [1]. Thirty-four patients (70.8%) had constipation predominant (C-IBS) and 14 patients (29.2%) had diarrhoea predominant (D-IBS) type of IBS. All subjects gave informed consent for the study and the Local Ethics Committee approved the study.

All subjects with IBS had normal results of the following tests: complete blood count, erythrocyte sedimentation rate, stool hemocult test, stool culture, stool test for ova and parasites, urinalysis, blood chemistry, thyroid function tests, and sigmoidoscopy in patients  $\leq 45$  years of age and colonoscopy in patients  $> 45$  years of age. Diarrhoea-prone patients were put on a 3-week trial of lactose-free diet for the exclusion of lactose intolerance and were studied for anti-tissue transglutaminase IgA and IgG antibodies for Coeliac Disease. Exclusion criteria were: i) gallstone disease, ii) history of cholecystectomy, iii) diseases that influence gallbladder functions (e.g. diabetes mellitus, thyroid diseases, electrolyte disturbances, and other systemic diseases), iv) use of drugs, that influence gallbladder functions (e.g. anti-cholinergics), and v) diseases that influence gastric emptying (e.g. diabetes mellitus, diseases affecting smooth muscles, neurologic disorders, gastric outlet obstruction). Cigarette smoking, alcohol and caffeine consumption were not allowed for 24 hours prior to study in order to avoid possible effects on gallbladder motility.

### Methods

Gallbladder measurements were performed by the same ultrasound machine with a 6–8 MHz active matrix array (convex) transducer (General Electric, model Logic 9, Milwaukee, USA) and tissue harmonic imaging (THI) modality was applied. Harmonic imaging is a technique

originally developed in contrast imaging, but it is now widely applied to native tissue imaging and thus is generally called THI. THI diminishes low frequency high amplitude noise and improves B-mode image quality without introducing a contrast agent. The gallbladder was measured in three dimensions, one longitudinal (D1) and two cross-sectional diameters (D2 and D3), and the volume was calculated by using the ellipse formula ( $\pi/6 \times D1 \times D2 \times D3$ ) [21]. The mean gallbladder volume was calculated from the consecutive measurements of three sequential gallbladder volumes. Premenopausal women (29 patients and 28 controls) were studied in the first phase of menstrual cycle, because it has been noted that gallbladder motility varies during the menstrual cycle [22].

All patients were studied after 12-hours of fasting and 45 min after eating a standard 100 g milky chocolate (Ulker AS, Istanbul, Turkey) containing 54.1 g carbohydrate, 9.2 g protein and 31.5 g fat, which provide a caloric intake of 536 kcal. The pre-meal and post-meal gallbladder volumes were substituted into the following formula to calculate the ejection fraction (EF) of the gallbladder (GB) [23].

$$EF (\%) = \frac{\text{fasting GB volume} - \text{postprandial GB volume}}{\text{fasting GB volume}} \times 100$$

### Statistical analysis

All statistical analysis was performed using SPSS for Windows version 10.0 (SPSS Inc., Chicago, Ill., USA). Comparisons of variables between groups were performed with independent sample *t* test, Mann-Whitney U test, and  $\chi^2$  test, where appropriate. The relationships between variables were calculated by Pearson's correlation coefficient. Data are expressed as mean  $\pm$  standard deviation (SD). P values of less than 0.05 were considered statistically significant.

## Results

The patient and control groups were comparable for age, gender, body mass index (BMI), and parity (table 1). The average duration of IBS was

similar for males ( $6.7 \pm 3.2$  yr) and females ( $8.0 \pm 3.4$  yr) in the study group (table 1).

### Comparisons for fasting gallbladder volumes (FGV) and for postprandial gallbladder volumes (PGV)

The FGV was similar in IBS and control groups ( $18.0 \pm 4.0$  ml vs.  $17.8 \pm 4.9$  ml,  $p > 0.05$ ), whereas the PGV was lower in IBS group than in the control group ( $5.5 \pm 1.4$  ml vs.  $6.2 \pm 1.9$  ml,  $p = 0.03$ ) (table 2). There was no gender difference in FGV and PGV between study and control groups and also within each group (table 2). Moreover, there was no difference in FGV and PGV between C-IBS and D-IBS patients (table 3).

Neither FGV nor PGV was found to correlate with age, parity, BMI or duration of IBS in the patient group (for FGV:  $r = 0.17$ ,  $r = -0.05$ ,  $r = 0.03$  and  $r = 0.24$ , respectively,  $p > 0.05$ ; for PGV:  $r = 0.09$ ,  $r = 0.03$ ,  $r = 0.09$  and  $r = 0.04$  respectively,  $p > 0.05$ ). Likewise, there was no correlation between FGV or PGV and age, parity, and BMI in

**Table 1**  
The characteristic features of study and control groups (mean  $\pm$  SD).

	patients	controls	P
Male/female (n/n)	15/33	15/33	NS <sup>1</sup>
Age (yr)	$37.2 \pm 6.5$	$37.4 \pm 6.6$	NS <sup>2</sup>
BMI (kg/m <sup>2</sup> )	$26.0 \pm 2.5$	$26.4 \pm 2.8$	NS <sup>2</sup>
Duration of IBS (yr)			
Male	$6.7 \pm 3.2$		NS <sup>3</sup>
Female	$8.0 \pm 3.4$		
Parity of women (median)	3	3	NS <sup>4</sup>

NS: not significant, BMI: body mass index, IBS: irritable bowel syndrome

<sup>1</sup> Statistical significance for the comparison between patients and controls,  $\chi^2$  test

<sup>2</sup> Statistical significance for the comparison between patients and controls, *t* test

<sup>3</sup> Statistical significance for the comparison between male and female patients, *t* test

<sup>4</sup> Statistical significance for the comparison between patients and controls, Mann-Whitney U test

**Table 2**

The mean FGV, PGV and EF values of gallbladder in patients and control subjects (mean  $\pm$  SD).

	patients			controls		
	males (n = 15)	females (n = 33)	total (n = 48)	males (n = 15)	females (n = 33)	total (n = 48)
Mean FGV (ml)	17.6 $\pm$ 3.3	18.2 $\pm$ 4.3	18.0 $\pm$ 4.0	16.6 $\pm$ 4.8	18.3 $\pm$ 4.9	17.8 $\pm$ 4.9
Mean PGV (ml)	5.3 $\pm$ 1.3	5.6 $\pm$ 1.4	5.5 $\pm$ 1.4 <sup>1</sup>	6.2 $\pm$ 2.4	6.3 $\pm$ 1.7	6.2 $\pm$ 1.9 <sup>1</sup>
Mean EF (%)	69.4 $\pm$ 7.3 <sup>2</sup>	69.0 $\pm$ 6.2 <sup>3</sup>	69.1 $\pm$ 6.5 <sup>4</sup>	63.2 $\pm$ 7.4 <sup>2</sup>	64.6 $\pm$ 5.9 <sup>3</sup>	64.1 $\pm$ 6.3 <sup>4</sup>

FGV: fasting gallbladder volume

PGV: postprandial gallbladder volume

EF: ejection fraction

<sup>1</sup> p = 0.03 for comparison between patient and control groups, *t* test.

<sup>2</sup> p = 0.03 for comparison of males between patient and control groups, *t* test.

<sup>3</sup> p = 0.004 for comparison of females between patient and control groups, *t* test.

<sup>4</sup> p = 0.0001 for comparison between patient and control groups, *t* test.

the control group (for FGV:  $r = 0.17$ ,  $r = 0.17$  and  $r = 0.11$  respectively,  $p > 0.05$ ; for PGV:  $r = 0.11$ ,  $r = 0.07$  and  $r = 0.03$  respectively,  $p > 0.05$ ).

### Comparisons for EF of gallbladder

The mean EF of gallbladder in IBS group was higher than that in the control group (69.1% vs. 64.1%,  $p = 0.0001$ ), and this was also true for the comparisons of males and females separately between patient and control groups (table 2). On the other hand, there was no gender difference in EF within each group (table 2). In addition, there was no difference in EF between C-IBS and D-IBS patients (table 3).

There was no correlation between EF and age, parity, BMI and duration of IBS ( $r = 0.03$ ,  $r = -0.12$ ,  $r = -0.04$  and  $r = 0.18$  respectively,  $p > 0.05$ ) in the patient group. Likewise, there was no correlation between EF and age, parity and BMI ( $r = -0.02$ ,  $r = 0.07$  and  $r = -0.02$  respectively,  $p > 0.05$ ) in the control group.

**Table 3**

The mean FGV, PGV and EF values of gallbladder in subgroups of IBS (mean  $\pm$  SD).

	C-IBS (n = 34)	D-IBS (n = 14)	P <sup>1</sup>
Mean FGV (ml)	17.8 $\pm$ 4.2	18.6 $\pm$ 3.4	NS
Mean PGV (ml)	5.3 $\pm$ 1.4	6.0 $\pm$ 1.1	NS
Mean EF (%)	69.9 $\pm$ 6.4	67.2 $\pm$ 6.4	NS

C-IBS: constipation predominant irritable bowel syndrome

D-IBS: diarrhoea predominant irritable bowel syndrome

FGV: fasting gallbladder volume

PGV: postprandial gallbladder volume

EF: ejection fraction

NS: not significant

<sup>1</sup> Statistical significance for the comparison between C-IBS and D-IBS subgroups, *t* test.

## Discussion

In this study, we investigated the motility of gallbladder by using real time ultrasonography in IBS patients. There was no significant difference in FGV between IBS patients and healthy subjects. However, the mean PGV was lower and the mean EF of gallbladder was higher in IBS patients than in controls. Moreover, the FGV, PGV and EF were similar in two subgroups of IBS.

Information on gallbladder function in patients with IBS is limited and variable results have been reported. The first study in which gallbladder motor function was evaluated in 12 patients with IBS [19] showed that the fasting gallbladder volume and the residual volume after maximal contraction were higher in IBS patients than in controls, but the maximum percent of gallbladder emptying and the time necessary for maximal contraction did not differ significantly from controls. Therefore, it was speculated that abnormalities of gallbladder function in these patients might promote stone formation with lithogenic bile. However, until now no study has reported an increased incidence of gallstones in patients with IBS. In another study of 20 patients with IBS [20] higher FGV but lower EF values compared to healthy

subjects were reported and no differences in FGV and EF of gallbladder between C-IBS and D-IBS patients were detected. There are a few studies, however, reporting no difference in gallbladder function between IBS patients and healthy subjects [17, 18]. In the present study, although FGV was not different, EF of gallbladder was significantly higher in IBS patients than in control subjects, and the FGV and the EF of gallbladder were similar in both subgroups of IBS. Our different results from the literature may be because our patients were all in symptomatic period or our study included a larger population of patients than the previous studies.

Normally, gallbladder emptying is regulated by both neural and hormonal factors. Gallbladder contraction is accompanied by relaxation of Oddi sphincter for egress of bile [24, 25] and abnormality of either may impair gallbladder emptying. CCK is the physiologic mediator of gallbladder contraction and relaxation of the sphincter of Oddi. Since CCK receptors are found throughout the gut, CCK has a physiological role not only in the stimulation of pancreatic and biliary secretions but also in the regulation of gastrointestinal motility.

ity by inhibiting gastric emptying and colonic transit mediated by CCK-1 receptors [25]. It was demonstrated that patients with IBS have exaggerated and prolonged postprandial release of CCK and it has been implicated in the pathophysiology of IBS [26–28]. It was also shown that gallbladders of C-IBS patients are more responsive but those of D-IBS patients are less responsive to CCK infusion compared to those of healthy subjects [29]. As small bowel transit was reported to be delayed in patients with C-IBS [30], but to be rapid in patients with D-IBS [31]; CCK-1 receptor antagonists are currently under development for the treatment of C-IBS. Clinical studies suggest that CCK-1 receptor antagonists are effective facilitators of gastric emptying and inhibitors of gallbladder contraction and can accelerate colonic transit time in healthy volunteers and in patients with IBS [32, 33].

The autonomic nervous system has an important influence on the regulation of gallbladder emptying [24]. It has also been postulated that the autonomic nervous system may play an important role in altered visceral sensations and changes in afferent reflex mechanisms modulating gastro-

intestinal motility in patients with IBS [16]. Increased frequency of dysmenorrhea, urinary frequency, and respiratory symptoms in patients with IBS suggests that these patients may have autonomic instability [8, 15].

In conclusion, our study demonstrated that IBS patients have increased emptying of gallbladder compared to healthy subjects. We think that altering motility of gallbladder may explain a part of the postprandial symptoms in patients with irritable bowel syndrome. Further studies with a larger number of patients are needed to better define the changes in gallbladder motility in patients with IBS and the relationships between gallbladder function and type of IBS.

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