INTRODUCTION

Abdominal bloating is one of the most common functional symptoms. However, functional bloating is not a part of functional bowel or gastroduodenal disorder. A recent study showed that the prevalence of functional bloating in Korea, according to Rome III criteria, was 6.9%, after excluding other overlapping functional gastrointestinal (GI) diseases. In another study, abdominal bloating symptom was present in 26.9% of the health screening cohort. An epidemiologic sur-
A survey in the United States revealed that sex and age-adjusted overall prevalence of abdominal bloating was 19.0%.3 Moreover, another study showed that 82.5% of patients with irritable bowel syndrome (IBS) reported abdominal bloating, which may be a more bothersome symptom than abdominal pain or discomfort.4 In that study, abdominal bloating was the third most common reason for IBS patients to visit the doctors, and more than half of these patients reported regular use of anti-gas medications. In spite of this high prevalence, the pathophysiology of bloating is complicated and poorly understood.

Four factors, including volume of intra-abdominal contents, subjective sensation of abdominal bloating, objective abdominal dimensional changes, and muscular activities of the abdominal walls, were included in the pathophysiology of abdominal bloating.5 Of all the intra-abdominal elements, intestinal gas has been the most likely candidate to explain bloating. Although many studies have been performed to prove excessive amounts of gas in the GI tract for patients with bloating using washout techniques,6,7 simple X-ray,8 and computed tomography (CT) image analysis,9,10 bloating remains contentious.

Abdominal bloating might also result from increased abdominal fat. However, previous studies that evaluated the association between body mass index (BMI) and abdominal symptoms showed inconsistent results. In one study, no relationship between BMI and abdominal symptoms was found.11 Another study found that increasing BMI was associated with increasing vomiting, upper abdominal pain, bloating, and diarrhea.12 Therefore, the relationship between increased BMI and bloating remains unclear. Additionally, no study on intra-abdominal fat contents and bloating can be found in the literature.

Based on these data, we hypothesized that excessive gas, abnormal distribution, and abdominal fat could account for abdominal bloating. The aim of this study was to determine whether increased intestinal gas or increased fat content in the abdominal cavity or relevant to abdominal bloating, using three-dimensional abdominal CT scan, which is a validated method for measuring intra-abdominal gas and fat.9,10,13

SUBJECTS AND METHODS

1. Participants

 Twenty-nine healthy individuals without abdominal bloating and organic disease (15 women and 14 men; mean age, 49 years; range of age, 23-73 years) and 30 patients diagnosed with functional bloating experiencing chronic recurrent abdominal bloating (10 women and 20 men; mean age, 53 years; range of age, 35-75 years) participated in this study. All participants received a list of symptoms by validated Korean version of the bowel disease questionnaire (Rome III-K)14 according to the Rome III criteria.1 Subjects diagnosed with other functional GI disorders, including IBS, functional diarrhea, functional constipation, and functional dyspepsia, were excluded. Moreover, blood tests and colonoscopy were performed to exclude participants with organic bowel disease. This study was approved by the institutional review board of the university hospital (AJIRB-MED-MDB-12-018). Before participation, all subjects provided written informed consent and were informed of their right to discontinue participation at any time.

2. Determination of the sample size

 In a previous study that used plain abdominal radiography to determine the amount of abdominal gas,8 the mean gas volume score of patients with IBS and controls were 0.069 (standard deviation 0.039) and 0.033 (standard deviation 0.013), respectively. The number of participants in each arm of this study was calculated to obtain a satisfactory result with \( \alpha = 0.05 \) and a power of 0.90. Therefore, we calculated that 34 subjects, including 17 subjects and 17 controls, were necessary. We chose to enroll 60 subjects to allow for about 30% no-show on the day of the scheduled procedure. Only one healthy participant did not participate in this study.

3. CT technique

 Abdominal imaging was performed using a Somatom Sensation 16-channel multidetector CT (Siemens, Forchheim, Germany). Subjects fasted for at least 6 h before the CT scan. No glucagon or anticholinergic agents were administered. First, pre-contrast CT scan was performed. Second, 150 mL of iopromide (Ultravist 300; Schering, Berlin, Germany) or iomepr (Iomeron 300; Bracco, Milan, Italy) was injected intravenously through an 18-gauge angiographic catheter inserted into an antecubital vein using a LF CT 9000 power injector (Liebel-Flarsheim, Ohio, USA) at a rate of 2.5 mL/sec. Third, combinations of arterial and portal phase scans were acquired for 35 sec (arterial phase) and 90 sec (delayed
phase), respectively. Arterial phase and delayed phase CT images were obtained using the following protocol: detector collimation of 16×1.5, pitch of 1.0, section width of 5 mm, reconstruction increment of 5 mm as 5 mm-thick sections, 120 kVp, and 160 mAs. The scanning range included the region from the liver to pelvic cavity in the precontrast and arterial phase, and from the lower chest to the symphysis pubis for the delayed phase.

4. Imaging and analyses

Two certified experienced abdominal radiologists blindly reviewed the CT images by consensus on a picture archiving and communication system (Starpacs; infinitt, Seoul, Korea) picture and communication system workstation (Infinitt, Seoul, Korea). The morphologic features on CT images were measured and calculated on the PACS workstation.

Air volume measurement was also performed using the interactive image processing workstation software. With automatic thresholds between -400 and -1024 Hounsfield Unit, manually defined multiple regions of interest were selected, and the total air volume in the bowel segment was measured in the stomach, ascending (A) colon, transverse (T) colon, descending (D) colon, and rectosigmoid (RS) colon (Fig. 1).

To evaluate the volume of small bowel and non-gas intraluminal contents in the colon, maximal diameter of ascending colon, transverse colon, descending colon, and rectosigmoid colon, as well as the maximal diameter of small bowel in the left upper quadrant abdomen and right lower abdomen were measured. The measurement of small bowel gas distribution using CT scan was not definite yet. The division point between the small bowel parts is arbitrary. As a general rule, the jejunum includes about 40% of the small intestine proximally and the ileum includes about 60% of the small intestine distally, except the duodenum. The jejunum lies mainly in the left upper and lower quadrants and the ileum in the lower abdomen and the right iliac fossa. Hence, the alternative way to assume intra-abdominal volume was used in this study.

Subcutaneous fat and visceral fat were measured via Syngo interactive image processing workstation software (Siemens, Erlangen, Germany). With automatic thresholds of Hounsfield Units between -30 and -120, manually-defined subcutaneous fat area was selected, and the total amounts of abdominal fat and visceral abdominal fat were measured (Fig. 2). The amount of subcutaneous fat was calculated from the total abdominal fat amount and the visceral fat amount, according to the following equation: Subcutaneous fat amount=total abdominal fat amount-visceral fat amount.

5. Statistical analyses

All data were expressed as the mean±standard error for each group. The mean values of the measured parameters were compared using Student’s t-test or Mann-Whitney U-test. P values of less than 0.05 were considered statistically significant. SPSS for Windows version 11 (SPSS Inc., Chicago, USA) was used for all statistical analyses.
RESULTS

1. Intra-abdominal gas volume and distribution

The results of intra-abdominal gas volume and distribution are summarized in Fig. 3. The mean volume of the total colon gas in patients with bloating was not significantly different from that in control subjects (90.6±12.6 vs. 75.5±9.8 mm³; p=0.353). Moreover, the mean volumes of stomach, A colon, D colon, and RS colon of patients with bloating were similar to those of controls (38.7±6.0 vs. 28.8±3.9 mm³; p=0.174, 12.2±1.4 vs. 10.6±1.3 mm³; p=0.433, 7.2±2.1 vs. 5.2±1.4 mm³; p=0.446, 19.0±5.0 vs. 27.7±6.0 mm³; p=0.271, respectively). However, the amount of gas in the transverse colon tended to be higher in patients with bloating than in controls (52.0±8.9 vs. 31.8±4.7 mm³; p=0.051). The distribution ratio of the intra-abdominal gas was calculated. The gas ratio of the T colon in the total colon was significantly higher in patients with bloating compared with the controls (p=0.009). The gas ratio of the stomach, A colon, D colon, and RS colon in the total colon of patients with functional bloating did not significantly differ from those detected in control subjects.

According to the analysis of male and female subgroups, there was no significant intra-abdominal gas difference between patients and controls in women. In men, however, intra-abdominal gas was higher in patients, especially in the transverse colon (57.6±12.0 vs. 26.9±6.8 mm³; p=0.058).

2. Maximal diameter of intestinal segment

Fig. 4 shows the maximal diameter distribution of intestine between the two groups. The mean maximal diameter of A colon, T colon, D colon, and RS colon in patients with bloating was similar to those in controls (5.1±1.7 vs. 4.8±1.5 cm; p=0.171, 3.1±1.5 vs. 3.0±1.3 cm; p=0.858, 3.3±1.1 vs. 3.1±0.9 cm; p=0.135, 3.1±1.9 vs. 3.2±1.7 cm; p=0.661 by t-test). Moreover, the mean maximal diameter of ileum in patients with bloating was similar to that in controls (1.9±0.9 vs. 1.7±0.6 cm; p=0.187 by t-test). However, the maximum diameter of jejunum in the left upper quadrant was significantly greater in patients with bloating compared with controls (2.0±0.7 vs. 1.8±0.6 cm; p=0.031 by t-test). Also, the jejunal diameter ratio of ileum was calculated. The diameter ratio was not significantly different between the two
Table 1. Comparison of Body Mass Index and Fat Contents between Patients with Bloating and Control Subjects

| Variables                        | Bloating (n=29) | Controls (n=30) | p-value | Subgroup            | Male (n=20) | p-value | Female (n=10) | p-value |
|----------------------------------|----------------|----------------|---------|---------------------|-------------|---------|---------------|---------|
| Body mass index (kg/m²)          | 23.4 (3.2)     | 22.3 (3.1)     | 0.175   |                     | 24.0 (3.1)  | 0.364   | 22.1 (3.1)    | 0.652   |
| Circumferential area (mm²)       | 509.5 (113.0)  | 482.3 (120.2)  | 0.373   | Male (n=20)         | 536.8 (110.2)| 0.632   | 454.9 (102.5) | 0.894   |
| Subcutaneous fat (mm)            | 20.5 (6.5)     | 19.8 (6.6)     | 0.684   |                     | 19.3 (5.8)  | 0.450   | 22.8 (7.5)    | 0.682   |
| Visceral fat area (mm²)          | 76.5 (38.1)    | 62.6 (32.8)    | 0.136   | Female (n=10)       | 85.4 (40.1) | 0.483   | 58.7 (27.2)   | 0.430   |
| Total fat area (mm²)             | 158.3 (96.3)   | 129.6 (57.9)   | 0.173   |                     | 72.2 (16.1) | 0.617   | 167.0 (136.9) | 0.220   |

Values are presented as mean (standard deviation).

groups (p=0.750 by Mann-Whitney U-test). According to the analysis of male and female subgroups, there was no significant difference with respect to the mean diameter in women. In men, however, the mean diameter of intestine was significantly higher in the jejunum (2.1±0.6 vs. 1.7±0.6 cm; p=0.001) and ileum (2.0±1.2 vs. 1.6±0.7 cm; p=0.020), compared with control.

3. Abdominal fat contents

Table 1 shows the abdominal fat content of the two groups. BMI in patients with bloating (23.4±3.2 kg/m²) was higher than that in controls (22.3±3.1 kg/m²), but the difference was not statistically significant (p=0.175). The circumferential area, subcutaneous fat, visceral fat area, and total fat area were slightly higher in patients with functional bloating than in control subjects, but the difference was not statistically significant.

DISCUSSION

Abdominal bloating is common and frequently associated with IBS. Many patients with IBS with complaint of abdominal
bloating are convinced that these symptoms might have originated from excessive intra-abdominal gas.\textsuperscript{16,17} It was reported that patients with IBS can show large abdominal girth increase, as high as up to 12 cm without gas infusion.\textsuperscript{18} In addition, colonic gas production appear to be greater in patients with IBS than in controls.\textsuperscript{19} Therefore, patients with bloating symptom are generally considered to have excessive intra-abdominal gas. Although many imaging studies that used simple radiography demonstrated the presence of excessive gas in patients with bloating symptom, many recent imaging studies, including multidetector CT studies, have not confirmed this fact.\textsuperscript{10,20} Therefore, this present study verified whether the total amount of GI gas in patients with functional bloating was significantly different from that in control subjects. Moreover, the use of gas challenge technique, while not involving imaging, has provided supporting results. For example, although infusion of a large amount of gas into the intestinal tract in healthy individual produces only an incrementally small change in abdominal girth, patients with IBS develop gas retention, abdominal girth increment, and increased GI symptoms.\textsuperscript{7} This suggests that bloating might not just be the result of excess GI gas. Symptom perception did not correlate with the degree of abdominal distension, but with the mechanism of retention and gut motor activity.\textsuperscript{21}

The second issue in this present study was gas distribution about the intra-abdominal gas in abdominal bloating. The amount of gas in the transverse colon tended to be higher in patients with bloating than in controls, indicating a difference in gas distribution between the two groups. These results correlated well with those of a study that used magnetic resonance imaging to assess the bowel volume in patients with bloating symptom, further investigations will be needed.

To the best of our knowledge, this is the first study to demonstrate the relationship between abdominal fat content and abdominal bloating. Obesity is a risk factor for some GI diseases, such as gastro-esophageal reflux disease, and is suggested to be linked to common GI functional disorders.\textsuperscript{28} This association suggests the possibility that obesity and functional GI disorders may be pathologically linked. The results of the current study correlated well with those of a recent meta-analysis, showing no relationship between bloating and BMI.\textsuperscript{29} Interestingly, several studies showed that patients with abdominal bloating were more prone to recent weight gain than controls, irrespective of BMI.\textsuperscript{30,31} The suggested hypothesis of these studies was that excessive accumulation of intra-abdominal fat content could alter visceral sensation. However, no studies have compared the intra-abdominal fat content between patients with functional bloating and control subjects. The present study showed that the circumferential area, subcutaneous fat, visceral fat area, and total fat area in patients with functional bloating were slightly higher than in control subjects, but the difference was not statistically significant. Since a recent increase in intra-abdominal fat might be associated with the development of abdominal bloating, further investigations will be needed.

According to gender sub-analysis, there was no significant difference in gas or maximal intestinal diameter between patients and controls in females. However, in the males, the amount of gas and maximal intestinal diameter was higher in patients than in controls. This is presumed to be due to the involvement of visceral hypersensitivity in females.\textsuperscript{27}
and day-to-day variation of bloating and distension were not considered. Fourth, cases and controls were not matched. However, the baseline characteristics, including age and BMI, did not differ between patients and control. In the future, matched control studies, including more patients, will be needed to confirm the results of this study.

In conclusion, bloating might not just be the result of excess intra-abdominal gas, but may involve other factors, such as localized abnormality in gas handling and visceral hypersensitivity. Moreover, bloating appears to not be related with intra-abdominal fat content.

REFERENCES

1. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. Gastroenterology 2006; 130:1480-1491.
2. Ryu MS, Jung HK, Ryu JI, Kim JS, Kong KA. Clinical dimensions of bloating and day-to-day variation of bloating and distension were not associated with intra-abdominal fat content. Am J Gastroenterol 2001;96:3341-3347.
3. Lembo T, Nailiboff B, Munakata J, et al. Symptoms and visceral perception in patients with pain-predominant irritable bowel syndrome. J Am Gastroenterol 1999;14:1320-1326.
4. Houghton LA, Lea R, Agrawal A, Reilly B, Whorwell PJ. Relationship of abdominal bloating to distention in irritable bowel syndrome and effect of bowel habit. Gastroenterology 2006;131:1003-1010.
5. King TS, Elia M, Hunter JO. Abnormal colonic fermentation in irritable bowel syndrome. Lancet 1998;352:1187-1189.
6. Mc Williams SR, Mc Laughlin PD, O’Connor OJ, et al. Computed tomography assessment of intestinal gas volumes in functional gastrointestinal disorders. J Neurogastroenterol Motil 2012;18:419-425.
7. Serra J, Azpiroz F, Malagelada JR. Mechanisms of intestinal gas retention in humans: impaired propulsion versus obstructed evacuation. Am J Physiol Gastrointest Liver Physiol 2001;281:G138-G143.
8. Lam C, Chaddock G, Marciani Laurea L, et al. Distinct abnormalities of small bowel and regional colonic volumes in subtypes of irritable bowel syndrome revealed by MRI. Am J Gastroenterol 2017;112:346-355.
9. Kellow JE, Phillips SF, Miller LJ, Zinsmeister AR. Dysmotility of the small intestine in irritable bowel syndrome. Gut 1988;29:1236-1243.
10. Kellow JE, Phillips SF. Altered small bowel motility in irritable bowel syndrome is correlated with symptoms. Gastroenterology 1987;92:1885-1893.
11. Hernando-Harder AC, Serra J, Azpiroz F, et al. Colonic responses to gas loads in subgroups of patients with abdominal bloating. Am J Gastroenterol 2010;105:876-882.
12. Agrawal A, Whorwell PJ. Review article: abdominal bloating and distension in functional gastrointestinal disorders—epidemiology and exploration of possible mechanisms. Aliment Pharmacol Ther 2008;27:2-10.
13. Luidsi S, Mujagic Z, Jonkers D, et al. Markers for visceral hypersensitivity in patients with irritable bowel syndrome. Neurogastroenterol Motil 2014;26:1104-1111.
14. Lee KJ. Obesity and functional gastrointestinal disorders. Korean J Gastroenterol 2012;59:1-7.
15. Eslick GD. Gastrointestinal symptoms and obesity: a meta-analysis. Obes Rev 2012;13:469-479.
16. Sullivan SN. A prospective study of unexplained visible abdominal bloating. N Z Med J 1994;107:428-430.
its relation to functional gut symptoms. Neurogastroenterol Motil 2016:28:849-854.
33. Accarino A, Perez F, Azpiroz F, Quiroga S, Malagelada JR. Abdominal distention results from caudo-ventral redistribution of contents. Gastroenterology 2009;136:1544-1551.