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Functional Gastrointestinal Disorders and Abdominal Visceral Fat in Children and Adolescents

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The authors have no financial conflicts of interest.

ABSTRACT

Purpose: Few reports have investigated the correlation between functional gastrointestinal disorders (FGIDs) and the degree of obesity in children and adolescents. Thus, this study aimed to examine the relationship between FGIDs and the degree of obesity in children and adolescents.
Methods: Children and adolescents (<19 years old) who had undergone abdominopelvic computed tomography and had been diagnosed with FGIDs from 2015 to 2016 were included in this retrospective case-control study in a ratio of 1:2. Abdominal visceral fat was measured using an image analysis software.
Results: The mean age of all 54 FGID patients was 12.9±3.4 years, and the male: female ratio was 1:1.2. We observed no difference in body mass index (BMI) between the FGID and control groups (19.5±4.6 vs. 20.6±4.3 kg/m^2, p=0.150). However, the FGID group had less abdominal visceral fat than that of the control group (26.2±20.0 vs. 34.4±26.9 cm^2, p=0.048). Boys in the FGID group had lower BMI (18.5±3.5 vs. 20.9±4.3 kg/m^2, p=0.019) and less abdominal visceral fat (22.8±15.9 vs. 35.9±31.8 cm^2, p=0.020) than those of boys in the control group. However, we found no difference in BMI (20.5±5.3 vs. 20.4±4.2 kg/m^2, p=0.960) and abdominal visceral fat (29.0±22.9 vs. 33.1±22.1 cm^2, p=0.420) between girls in both groups.
Conclusion: Our study revealed a difference in the relationship between FGID and the degree of obesity according to sex, which suggests that sex hormones influence the pathogenesis of FGIDs. Multicenter studies with larger cohorts are required to clarify the correlation between FGID subtypes and the degree of obesity.

Keywords: Functional gastrointestinal disorders; Obesity; Abdominal visceral fat; Child

INTRODUCTION

Functional gastrointestinal disorders (FGIDs) are characterized by chronic and repeated gastrointestinal symptoms that cannot be traced to any organic disease [1]. FGIDs are common diseases that affect approximately 40% of the world's population. Moreover, FGIDs reduce the quality of life of patients and increase the burden of medical costs [2]. The prevalence of FGIDs and their effect on the quality of life is similar between adults and children and adolescents. The prevalence of FGIDs in adolescents is approximately 23.1%.

FGIDs may reduce the quality of life of children and adolescents in various aspects, such as physical, emotional, social, and school life [3,4].

The pathology of FGIDs is unclear; however, various hypotheses have been proposed, such as genetic predisposition, mental health issues, dietary habits, changes in intestinal microorganisms, and obesity-related changes in gastrointestinal tract motion and hormones [5-8]. Research on the relationship between FGIDs and obesity has revealed that patients with FGIDs are often obese or overweight. In particular, some studies have shown that patients with FGIDs have higher body mass indices (BMIs) than those of control individuals [9,10]. However, some other recent studies have shown that patients with FGIDs have lower BMI than that of controls [11,12], and that FGIDs and BMI are not correlated [13,14]. Moreover various studies have segregated their results by sex and FGID subtypes [15-17]. Although few studies have assessed children and adolescents with FGIDs in comparison with adults, they indicated that the BMI of children with FGIDs can be higher, lower, or unrelated to that of healthy children, a finding that is similar to the results for adults [5,18-20].

Because BMI is calculated based only on height and weight, it may be affected by external factors such as race, age, and sex, and may not accurately predict obesity and its accompanying diseases [21-23]. Abdominal visceral fat is not affected by external factors; thus, it is more objective than BMI for the prediction of obesity and its accompanying diseases [24,25]. Therefore, this study aimed to examine the effect of obesity on FGIDs in children and adolescents by evaluating the correlation of FGIDs with BMI and abdominal visceral fat.

MATERIALS AND METHODS

Participants and methods

This was a 1:2-matched retrospective case-control study. Pediatric patients (<19 years old) who had undergone abdominopelvic computed tomography (APCT) for abdominal pain and trauma and had been diagnosed with FGIDs according to the ROME IV criteria in the outpatient Department of Pediatrics and Emergency Medicine at Gachon University Gil Hospital between 2015 and 2016 were screened for inclusion into this study. Among them, patients with underlying disease or those who had undergone APCT for surgery were excluded. Healthy individuals with same sex distribution as patients with FGIDs and an age difference <1 year were randomly selected for inclusion as controls. Electronic medical records, age, sex, height, weight, and imaging data of patients were retrospectively reviewed. BMI was calculated as weight divided by height squared (kg/m^2).

The study was approved by the Institutional Review Board of Gil Medical Center (GDIRB 2019-367). Informed consent was not obtained due to the retrospective design of the study.

Measurement of abdominal visceral fat using abdominopelvic computed tomography

APCT images of abdominal visceral fat were analyzed using the semi-automatic image split software in the Open-Source Software (BMI_CT) available in MATLAB Version R2014A (Mathworks Inc.) [26]. Abdominal visceral fat is an area of adipose tissue surrounded by the peritoneum, except for the spine and the muscles around it. The surface area of abdominal visceral fat was calculated in cm^2 and measured in an L4-L5 transverse section [27,28].

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Three investigators used BMI_CT to independently measure the L4-L5 cross-section of the abdominal visceral fat area. Pixels in the abdominal visceral fat were identified in the inner computed tomography image using Hounsfield unit thresholds of –190 to –30 [29].

Statistical analyses

Categorical variables are presented as numbers and percentages, whereas continuous variables are presented as mean±standard deviation. Data were analyzed using the paired *t*-test. Statistical significance was set at $p<0.05$. All analyses were performed using PASW Statistics for Windows, Version 18.0 (SPSS Inc.).

RESULTS

A total of 1,044 patients <19 years old underwent APCT for abdominal pain and trauma during the study period. Of these, 54 pediatric patients (25 male and 29 female) with FGIDs who met the inclusion criteria were included in the FGID group. Additionally, 108 control individuals with similar sex distribution and age difference of less than one year were randomly selected as the control group. The mean age of the FGID group was 12.9±3.4 years and the male:female ratio was 1:1.2 (**Table 1**).

The FGID subtypes included functional abdominal pain (FAP, 29 [53.7%] patients), functional dyspepsia (FD, 11 [20.4%] patients), functional nausea and functional vomiting (FNVD, 6 [11.1%] patients), cyclic vomiting syndrome (CVS, 2 [3.7%] patients), and functional constipation (FC, 1 [1.9%] patients). Of the 25 boys in the FGID group, 12 (48.0%) had FAP, 5 (20.0%) had FD, 3 (12.0%) had FNVD, 3 (12.0%) had irritable bowel syndrome (IBS), 1 (4.0%) had CVS, and 1 (4.0%) had FC. Of the 29 girls in the FGID group, 17 (58.6%) had FAP, 6 (20.7%) had FD, 2 (6.9%) had IBS, and 1 (3.4%) had CVS (**Table 2**).

We found no difference in the BMI between the FGIDs and control groups (19.5±4.6 vs. 20.6±4.3 kg/m^2, $p=0.146$). However, the FGID group had less abdominal visceral fat than the control group did (26.2±20.0 vs. 34.4±26.9 cm^2, $p=0.048$). Boys in the FGID group had lower BMI (18.5±3.5 vs. 20.9±4.3 kg/m^2, $p=0.019$) and less abdominal visceral fat (22.8±15.9 vs. 35.9±31.8 cm^2, $p=0.020$) than those of boys in the control group. However, BMI (20.5±5.3 vs.

Table 1. Baseline characteristics of children and adolescents with functional gastrointestinal disorders

Variable	FGIDs (n=54)	Control (n=108)	*p*-value
Sex			
Male	25 (46.3)	50 (46.3)	
Female	29 (53.7)	58 (53.7)	
Age (yr)			
Total	12.9±3.4	13.0±3.3	0.763
Male	12.6±3.6	12.8±3.4	0.712
Female	13.2±3.2	13.3±3.2	0.955
Height (m)			
Total	1.5±0.2	1.5±0.2	0.513
Male	1.5±0.2	1.6±0.2	0.342
Female	1.5±0.2	1.5±0.1	0.943
Weight (kg)			
Total	46.9±17.7	50.4±16.5	0.224
Male	45.2±16.7	53.4±18.4	0.066
Female	48.4±18.6	47.8±14.5	0.863

Values are presented as number (%) or mean±standard deviation.
FGID: functional gastrointestinal disorders.

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Table 2. Subtypes of functional gastrointestinal disorders in children and adolescents

Subtypes	Total (n=54)	Male (n=25)	Female (n=29)
Functional abdominal pain – NOS	29 (53.7)	12 (48.0)	17 (58.6)
Functional diarrhea	11 (20.4)	5 (20.0)	6 (20.7)
Functional nausea and functional vomiting	6 (11.1)	3 (12.0)	3 (10.3)
Irritable bowel syndrome	5 (9.2)	3 (12.0)	2 (6.9)
Cyclic vomiting syndrome	2 (3.7)	1 (4.0)	1 (3.4)
Functional constipation	1 (1.9)	1 (4.0)	0 (0.0)

Values are presented as number (%).
NOS: not otherwise specified epidemiology.

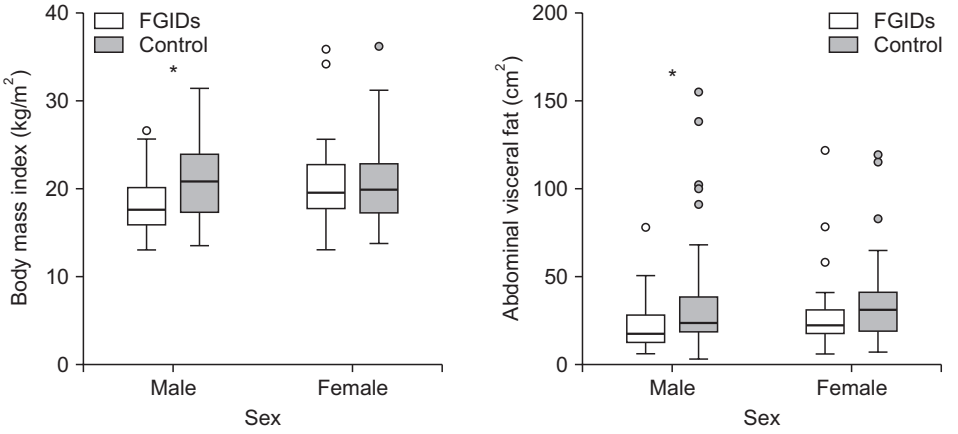

Fig. 1. Box plots showing the obesity indices of children and adolescents with functional gastrointestinal disorders.
*p<0.05.
FGID: functional gastrointestinal disorders.

20.4±4.2 kg/m², p=0.964) and abdominal visceral fat (29.0±22.9 vs. 33.1±22.1 cm², p=0.423) of the girls were not significantly different between the FGID and control groups (**Fig. 1**).

DISCUSSION

In this study, we investigated the relationship between FGIDs and the degree of obesity in children and adolescents. Although we observed no difference in BMI between the FGID and control groups, children in the FGID group had less abdominal visceral fat than those of children in the control group, suggesting that abdominal visceral fat is more a useful marker than BMI for the prediction of pediatric FGIDs. Moreover, boys in the FGID group had lower BMI and less abdominal visceral fat than those of boys in the control group. This suggests that male children and adolescents with FGIDs are not obese or overweight. Consistent with the results of previous large-scale studies with adults, the sex-specific differences in the relationship between FGIDs and obesity in the present study appear to be influenced by sex hormones in children and adolescents.

Several cases of high BMI were noted in the FGID groups in previous studies on FGIDs and BMI [9,10]. However, some studies showed that patients with FGIDs had lower BMI than that of control individuals [11,12], and that FGIDs and BMI were not correlated [13,14].

Furthermore, previous studies have presented their results according to FGID subtypes [15-17]. The present study also revealed no significant difference in BMI between children in the FGID and control groups. Several factors may influence the various correlations

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between FGIDs and BMI. First, changes in eating habits that occur after symptom onset may be considered. Cogliandro et al. [30] and Tack et al. [31] reported that gastrointestinal symptoms, such as abdominal pain, in patients with FGIDs caused a decrease in food intake, which may lead to weight loss. This may account for the low BMI observed in patients with FGIDs. Second, it has been suggested that cultural eating habits (e.g., Asians eat a lot of dietary fiber compared to those consumed by Westerners), and specific defecation postures among different cultures may affect the occurrence of FGIDs [32,33]. These cultural factors may account for the various degrees of relationships observed between FGIDs and BMI. Third, suitability of BMI as a variable should be re-considered. Because BMI is calculated based only on weight and height, it cannot reflect the influence of external factors such as race, sex, or age. Several studies have demonstrated that abdominal visceral fat varied in people of different sexes and races, albeit with the same BMI, and that BMI does not reflect age-related changes in height, muscle mass, and fat mass [21-23]. According to Okorodudu et al. [34], BMI is not suitable for distinguishing obesity, due to its low sensitivity. On the other hand, abdominal visceral fat is not affected by external variables, rendering it as a useful marker for predicting diseases related to obesity. In fact, abdominal visceral fat is better than BMI for the prediction of some diseases [24,25]. Moreover, a study on the correlation between FGIDs and abdominal visceral fat in adults showed that patients with IBS and FD had a high amount of abdominal visceral fat, despite that their BMIs were comparable [35,36]. In the present study, children in the FGID group had less abdominal visceral fat than that of children in the control group. However, we observed no difference in BMI between the two groups, consistent with the findings from a previous study. These results suggest that abdominal visceral fat may be a more objective indicator than BMI when evaluating the correlation between FGIDs and obesity.

In the present study, the relationship between FGIDs and the degree of obesity differed according to sex. Previous large-scale studies on adults with FGIDs also showed that the relationship between FGIDs and BMI varied according to sex. In a large-scale study on the correlation between FGIDs and BMI in adults, which was conducted in 2015, only women in underweight and obesity groups showed a high incidence of FD. Moreover, only women in the obesity group showed a high incidence of functional diarrhea, whereas only men in the underweight group showed a high incidence of IBS compared to those exhibited by the other groups [16]. In a recent Japanese study with young adults, the prevalence of FD was high only in females in the underweight group [11]. The relationship between FGIDs and the degree of obesity, which varies according to sex, may be attributed to the influence of sex hormones. According to a Jiang et al. [37], estrogen, a female hormone, was involved in the motility and sensitivity of the gastrointestinal tract. People with higher estrogen levels were more likely to develop FGIDs than were those with lower estrogen levels; hence, women are more susceptible than men to the development of FGIDs. Another study also showed that female children and adults with obesity have elevated estrogen levels [38,39]. In other words, compared to men with the same degree of obesity, women with obesity may have a relatively higher likelihood to develop FGIDs. This effect is thought to cause sex-specific differences in the relationship between FGIDs and obesity. In fact, boys with FGIDs in the present study had lower BMI and less abdominal visceral fat than those of boys in the control group, whereas BMI and abdominal visceral fat were comparable between girls in the FGID and control groups. This relationship can also be explained by the effect of excessive estrogen in girls with obesity.

The present study has several strengths. First, FGIDs were diagnosed by an experienced medical professional using the ROME IV criteria. Second, this was a 1:2 matching case-

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control study, which reduces variability as much as possible by limiting the influence of age and sex.

This study has some limitations as well. First, recruitment of patients with FGIDs was limited, because APCT for pediatric patients may be challenging due to radiation exposure [40]. As a result, the number of patients included in this study was insufficient for analysis according to FGID subtypes. Since the relationship between FGIDs and BMI varies according to FGIDs type [15-17], future studies with larger cohorts are required to evaluate the correlation between FGIDs and obesity according to FGID subtypes. Second, as this study included children and adolescents who visited a tertiary center in Incheon, South Korea, it may not fully represent pediatric patients with FGIDs in the general population. It is expected that unbiased results will be acquired in multicenter studies in various regions and institutions.

In conclusion, this study revealed the importance of abdominal visceral fat and sex in the relationship between FGIDs and obesity in children and adolescents. Future studies on the relationship between FGIDs and obesity in children and adolescents should include a comprehensive sex-stratified evaluation using abdominal visceral fat and BMI as indicators of obesity.

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