



Association Between Body Mass Index and Functional Dyspepsia in Young Japanese People

Yasunori Yamamoto,¹ Shinya Furukawa,^{2*} Junichi Watanabe,³ Aki Kato,² Katsunori Kusumoto,² Eiji Takeshita,⁴ Yoshio Ikeda,¹ Naofumi Yamamoto,⁵ Katsuhiko Kohara,⁶ Yuka Saeki,^{1,7} and Yoichi Hiasa⁸

¹Endoscopy Center, Ehime University Hospital, Toon, Ehime, Japan; ²Health Services Center, Ehime University, Matsuyama, Ehime, Japan; ³Department of Rehabilitation, Ehime Prefectural Central Hospital, Matsuyama, Ehime, Japan; ⁴Department of Inflammatory Bowel Diseases and Therapeutics, Ehime University Graduate School of Medicine, Ehime, Japan; ⁵Faculty of Collaborative Regional Innovation, Ehime University, Matsuyama, Ehime, Japan; ⁶Department of Internal Medicine, Anbiru Hospital, Kagoshima, Japan; ⁷Community Health Systems for Nursing, Ehime University Graduate School of Medicine, Toon, Ehime, Japan; and ⁸Department of Gastroenterology and Metabolism, Ehime University Graduate School of Medicine, Shitsukawa, Toon, Ehime, Japan

Background/Aims

Evidence regarding the association between body mass index (BMI) and functional dyspepsia (FD) in the Asian population is limited. Further, no study has evaluated this issue in young people in Asian and Western populations. Thus, we aim to investigate this issue among young Japanese people.

Methods

The study subjects comprised of 8923 Japanese university students. BMI was divided into 4 categories (quartiles) on the basis of the study subjects' distribution (lowest, low, moderate, and high [reference]). The definition of lean, normal, overweight, and obese was BMI < 18.5 kg/m², 18.5 ≤ BMI < 25 kg/m² (reference), 25 kg/m² ≤ BMI < 30 kg/m², and 30 kg/m² ≤ BMI, respectively. The definition of FD was based on the Rome III criteria.

Results

The prevalence of FD was 1.9% in this cohort. The lowest BMI was independently associated with FD after adjustment (adjusted odds ratio [OR], 2.88; 95% confidence interval [CI], 1.46-3.67); *P* for trend = 0.001). The lowest BMI was independently associated with FD in women but not in men (OR, 2.94; 95% CI, 1.59-5.77; *P* for trend = 0.001). Leanness was independently associated with FD in total and in women but not in men (total: adjusted OR, 2.01; 95% CI, 1.40-2.86) and women (OR, 2.19; 95% CI, 1.35-3.45). However, interaction analysis showed no significant difference for sex.

Conclusions

Among young Japanese people, BMI may be independently inversely associated with FD. Leanness may be an independent associated factor for FD in the young Japanese women.

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Key Words

Body mass index; Functional dyspepsia; Gender; Young

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*Correspondence: Shinya Furukawa, MD, PhD

Health Services Center, Ehime University, Bunkyo, Matsuyama, Ehime 790-8577, Japan

Tel: +81-89-927-9198, Fax: +81-89-927-9196, E-mail: shinya.furukawa@gmail.com

Yasunori Yamamoto and Shinya Furukawa equally contributed to this work.

Introduction

Functional dyspepsia (FD) is characterized by postprandial fullness, early satiation, epigastric pain, or epigastric burning despite the absence of organic digestive or metabolic disorders.¹ FD is one of the most common gastrointestinal disorders and has a high prevalence worldwide. FD can limit affected individuals' social life and affect their quality of life.² The reported risk factors for FD are female, current smoker, nonsteroidal anti-inflammatory drug (NSAID) use, and *Helicobacter pylori*-positive status.^{3,4}

In epidemiologic studies from Iceland, Taiwan, and 3 other countries (United Kingdom, Canada, and United States), the prevalence of FD in a young population was higher than that in middle-aged and older people.⁵⁻⁷ FD can impair patient work productivity and increase their medical costs. In the overall United States population, the estimated medical costs (including indirect costs) related to FD were reported to be 18.4 billion dollars.⁸ There is little information on FD in young people, however. Previous cohorts mainly consist of middle-aged subjects and/or patients with gastrointestinal symptoms.

Body mass index (BMI) is a well-known risk factor for gastroesophageal reflux disease (GERD) and erosive esophagitis.^{9,10} The association between BMI and FD in Western countries remains inconsistent, however. Several studies reported that BMI including obesity positively associated with dyspepsia symptoms mainly in Europe, the United States, and Latin American countries.¹¹⁻¹⁶ In a

large 10-year population-based study in Iceland, weight loss positively associated with the development of FD.⁵ In other studies, no association between BMI and FD was found.¹⁷⁻²¹

In the Asian population, 5 studies showed an inverse association between BMI and FD,²²⁻²⁶ and visceral adiposity was associated with FD in a Korean study.²⁷ In an Iranian study of the general population, no association between BMI and FD was found.²⁸ The association between BMI and FD in the Asian population remains unclear. Further, to date, no study has evaluated this issue in young people in Asian and Western populations. The primary aim of the present study is to investigate the association between BMI and FD based on the Rome III criteria in young Japanese people.

Materials and Methods

Study Population

We enrolled 10 104 university students who had no missing health check-up examination data at university between April 2015 and April 2017 in this study. A specific questionnaire pertaining to FD based on the Rome III criteria classification^{29,30} was sent to all subjects who underwent a health check-up. Information that was consistent with the Rome III criteria was collected from each subject's digestive medical history, which focused on the diagnosis of organic conditions and concerning symptoms. The exclusion criteria were as follows: medication for digestive disorders within 6 months, use of NSAIDs and steroids, and concerning signs (recur-

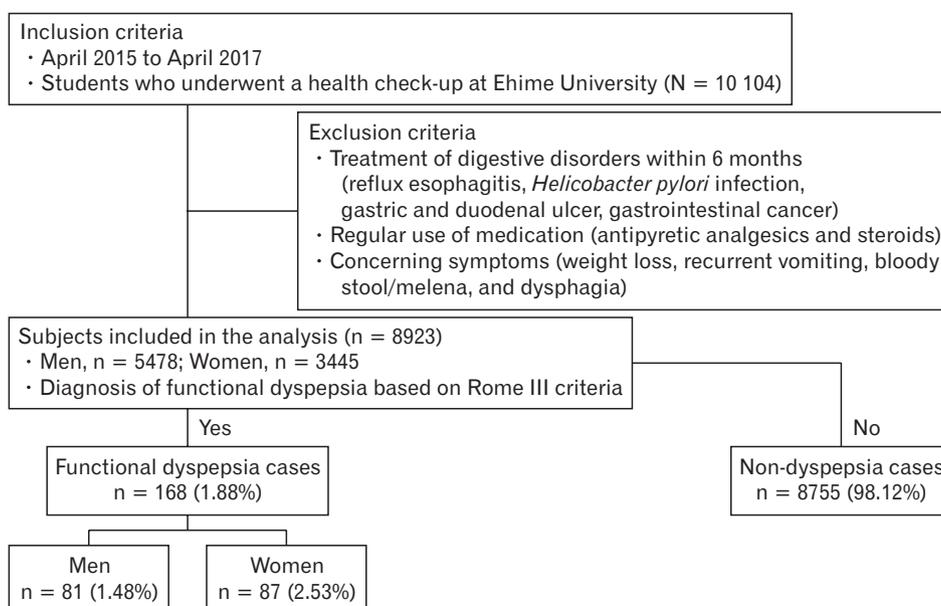


Figure. Study population.

rent vomiting, weight loss, bloody stool/melena, and dysphagia). Subjects were also excluded if they reported organic diseases such as GERD, gastritis, peptic ulcers, *H. pylori* infection, gastrointestinal cancers, or non-gastrointestinal diseases, such as those of the liver, pancreas, and gallbladder. After 1181 subjects were excluded due to incomplete data, medication for diseases within 6 months, use of NSAID and/or steroid, and concerning signs, the final analysis sample comprised 8923 subjects who were assessed for FD and BMI (Figure). This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of our university (No. 1610012). All subjects were provided an opt-out option.

Measurements

Using a self-administered questionnaire, information was collected and the following definitions were used for smoking, drinking, and regular exercise habit, and medical history. Current smoking was defined as smoking 1 cigarette or more per day. Current

drinking was defined as drinking alcohol, regardless of the amount or frequency. Regular exercise was defined as exercising 1 or more times per week.

Definition of Functional Dyspepsia

FD was defined as the subject reporting 1 or more symptoms, such as postprandial fullness, early satiation, or epigastric pain or burning. The definition of FD in this study was based on the Rome III criteria.^{29,30} Subjects with digestive symptom onset within 6 months prior to this study's survey were excluded from this cohort.

Statistical Methods

BMI was classified into 4 categories (quartiles) on the basis participant distribution, as follows: (1) lowest BMI, < 19.36 kg/m²; (2) low BMI, 19.36 kg/m² to 20.90 kg/m²; (3) moderate BMI, 20.90 kg/m² to 22.74 kg/m²; and (4) high BMI, > 22.74 kg/m² (reference). On the basis of the men's and women's BMI distribution, men's and women's BMI were classified into 4 categories (quartiles):

Table 1. Clinical Characteristics of 8923 Study Participants

Variable	Total (N = 8923)	Men (n = 5478)	Women (n = 3445)	P-value
Age (yr)	20.10 ± 2.80	20.20 ± 2.59	20.00 ± 3.10	0.003
BMI (kg/m ²)	21.35 ± 3.05	21.68 ± 3.24	20.84 ± 2.63	0.001
BMI < 18.5	1241 (13.9)	656 (12.0)	585 (17.0)	0.001
18.5 ≤ BMI < 25	6778 (76.0)	4131 (75.4)	2647 (76.8)	
25 ≤ BMI < 30	747 (8.3)	558 (10.2)	189 (5.5)	
30 ≤ BMI	157 (1.8)	133 (2.4)	24 (0.7)	
Smoking	527 (5.9)	492 (9.0)	35 (1.0)	0.001
Drinking	973 (10.9)	736 (13.4)	237 (6.9)	0.001
Exercise habit	3408 (39.3)	2415 (44.1)	1093 (31.7)	0.001
Medical history				
Irregular pulse	83 (0.9)	52 (1.0)	31 (0.9)	0.810
Heart murmur	47 (0.5)	30 (0.6)	17 (0.5)	0.730
ECG abnormality	63 (0.7)	33 (0.6)	30 (0.9)	0.140
Kidney disease	7 (0.1)	4 (0.1)	3 (0.1)	0.810
Anemia	239 (2.7)	52 (1.0)	187 (5.4)	0.001
Traffic accident	115 (1.3)	75 (1.4)	40 (1.2)	0.390
Sports injury	273 (3.1)	219 (4.0)	54 (1.6)	0.001
Frequency of symptoms				
Postprandial fullness	74 (0.8)	39 (0.7)	35 (1.0)	0.120
Early satiation	111 (1.2)	51 (0.9)	60 (1.7)	0.001
Epigastric pain or epigastric burning	36 (0.4)	12 (0.2)	24 (0.7)	0.001
Functional dyspepsia, %	168 (1.9)	81 (1.5)	87 (2.5)	0.001
EPS	33 (0.4)	12 (0.2)	21 (0.6)	0.003
PDS	146 (1.6)	74 (1.4)	72 (2.1)	0.007
Overlap	14 (0.2)	5 (0.1)	9 (0.3)	0.048

BMI, body mass index; ECG, electrocardiogram; EPS, epigastric pain syndrome; PDS, postprandial distress syndrome. Data are presented as mean ± SD or n (%).

men's BMI: (1) lowest BMI, < 19.56 kg/m²; (2) low BMI, 19.56 kg/m² to 21.12 kg/m²; (3) moderate BMI, 21.12 kg/m² to 23.12 kg/m²; and (4) high BMI, > 23.12 kg/m² (reference), and women's BMI: (1) lowest BMI, < 19.10 kg/m²; (2) low BMI, 19.10 kg/m² to 20.53 kg/m²; (3) moderate BMI, 20.53 kg/m² to 22.18 kg/m²; and (4) high BMI, > 22.18 kg/m² (reference). The definitions of lean, normal, and overweight and obese were < 18.5 kg/m², 18.5 kg/m² ≤ BMI < 25 kg/m² (reference), and 25 kg/m² ≤ BMI < 30 kg/m², and 30 ≤ BMI kg/m², respectively. Estimations of crude odds ratios (ORs) and their 95% confidence intervals (CIs) for FD in relation to BMI, leanness, and obesity were performed using a logistic regression analysis. We selected the following potential confounding factors: age, drinking, smoking, exercise habits, anemia, and sports injury. Trend of an association was assessed using a logistic regression model assigning consecutive integers to the categories of BMI variables. For tests of quadratic trend, we including linear and quadratic terms in the model. SAS software package version 9.4 (SAS Institute Inc, Cary, NC, USA) was used to perform the statistical analyses.

Results

Table 1 shows the characteristics of the 8923 study partici-

pants. The percentage of men was 61.4% in this cohort. The mean age and BMI were 20.1 years and 21.35 kg/m², respectively. The frequency of smoking, drinking, exercise habit, and sports injury in men was higher than that in women (*P* < 0.001). Anemia in women was higher than that in men (*P* < 0.001). The prevalence of FD in total, women, and men was 1.9%, 2.5%, and 1.5%, in this cohort, respectively. The prevalence of FD, epigastric pain syndrome (EPS), postprandial distress syndrome (PDS), and overlap in women was higher than that in men. The frequency of postprandial fullness, early satiation, and epigastric pain or epigastric burning, EPS, PDS, and overlap was 0.8%, 1.2%, 0.4%, 0.4%, 1.6%, and 0.2%, respectively.

Table 2 shows the crude and adjusted ORs and 95% CIs for FD compared to BMI. The prevalence of FD among the lowest, low, moderate, and in high BMI groups was 3.1%, 1.9%, 1.3%, and 1.2%, respectively. After adjustment for age, sex, drinking, smoking, exercise habits, anemia, and sports injury, the lowest BMI was independently associated with FD (adjusted OR, 2.28; 95% CI, 1.46-3.67; *P* for trend = 0.001). In men, no association between BMI and FD was found. In women, however, the prevalence of FD in the lowest, low, moderate, and high BMI groups was 4.5%, 2.2%, 1.7%, and 1.2%, respectively. The lowest BMI was independently associated with FD after adjustment (low: OR, 2.94; 95%

Table 2. Crude and Adjusted Odds Ratios and 95% Confidence Intervals for Functional Dyspepsia in Relation to Body Mass Index

Variable	Prevalence (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
FD			
Total			
BMI ≤ 19.36 kg/m ²	70/2231 (3.1)	2.75 (1.77-4.40)	2.28 (1.46-3.67)
19.36 kg/m ² < BMI ≤ 20.90 kg/m ²	42/2230 (1.9)	1.63 (1.001-2.70)	1.44 (0.88-2.39)
20.90 kg/m ² < BMI ≤ 22.74 kg/m ²	30/2232 (1.3)	1.16 (0.68-1.97)	0.98 (0.48-1.19)
22.74 kg/m ² ≤ BMI	26/2230 (1.2)	1.00	1.00
<i>P</i> for trend			0.001
Men			
BMI ≤ 19.56 kg/m ²	28/1369 (2.1)	1.66 (0.91-3.11)	1.48 (0.81-2.78)
19.56 kg/m ² < BMI ≤ 21.12 kg/m ²	22/1370 (1.6)	1.30 (0.69-2.49)	1.19 (0.63-2.28)
21.12 kg/m ² < BMI ≤ 23.12 kg/m ²	14/1370 (1.0)	0.82 (0.40-1.67)	0.77 (0.37-1.57)
23.12 kg/m ² ≤ BMI	17/1369 (1.2)	1.00	1.00
<i>P</i> for trend			0.100
Women			
BMI ≤ 19.10 kg/m ²	39/861 (4.5)	3.10 (1.69-6.07)	2.94 (1.59-5.77)
19.10 kg/m ² < BMI ≤ 20.53 kg/m ²	20/861 (2.3)	1.55 (0.77-3.22)	1.53 (0.76-3.17)
20.53 kg/m ² < BMI ≤ 22.18 kg/m ²	15/847 (1.7)	1.16 (0.55-2.48)	1.18 (0.55-2.53)
22.18 kg/m ² ≤ BMI	13/861 (1.5)	1.00	1.00
<i>P</i> for trend			0.001

Odds ratios adjusted for age, drinking, smoking, exercise habit, anemia, and sports injury. BMI, body mass index; FD, functional dyspepsia.

Table 3. Crude and Adjusted Odds Ratios and 95% Confidence Intervals for Functional Dyspepsia in Relation to Lean, Overweight, and Obese

Variable	Prevalence (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
FD			
Total			
BMI < 18.5 kg/m ²	44/1241 (3.6)	2.19 (1.52-3.09)	2.01 (1.40-2.86)
18.5 kg/m ² = BMI < 25 kg/m ²	112/6778 (1.7)	1.00	1.00
25 kg/m ² = BMI < 30 kg/m ²	10/747 (1.3)	0.81 (0.40-1.47)	0.87 (0.43-1.60)
30 kg/m ² = BMI	2/157 (1.2)	0.77 (0.13-2.45)	0.95 (0.16-3.06)
<i>P</i> for trend			0.001
Men			
BMI < 18.5 kg/m ²	16/656 (2.4)	1.85 (1.02-3.18)	1.74 (0.96-3.01)
18.5 kg/m ² = BMI < 25 kg/m ²	55/4131 (1.3)	1.00	1.00
25 kg/m ² = BMI < 30 kg/m ²	8/550 (1.4)	1.08 (0.47-2.15)	1.15 (0.51-2.30)
30 kg/m ² = BMI	2/133 (1.5)	1.13 (0.18-3.69)	1.35 (0.22-4.45)
<i>P</i> for trend			0.35
Women			
BMI < 18.5 kg/m ²	28/585 (4.8)	2.28 (1.42-3.59)	2.19 (1.36-3.45)
18.5 kg/m ² = BMI < 25 kg/m ²	57/2647 (2.2)	1.00	1.00
25 kg/m ² = BMI < 30 kg/m ²	2/189 (1.1)	0.49 (0.08-1.57)	0.50 (0.08-1.63)
30 kg/m ² = BMI	0/24 (0.0)	N/A	N/A
<i>P</i> for trend			0.001

Odds ratios adjusted for age, drinking, smoking, exercise habit, anemia, and sports injury. BMI, body mass index; FD, functional dyspepsia; N/A, not applicable.

CI, 1.59-5.77; *P* for trend = 0.001). However, interaction analysis showed no significant difference for gender (*P* = 0.210).

The association between leanness (BMI < 18.5 kg/m²), overweight (25 ≤ BMI < 30 kg/m²), obesity (30 ≤ BMI kg/m²), and FD is shown in Table 3. In crude analysis, leanness was associated with FD in men and women (OR, 1.85; 95% CI, 1.02-3.18 and OR, 2.28; 95% CI, 1.42-3.59, respectively). After adjustment, leanness was independently associated with FD in women (OR, 2.19; 95% CI, 1.35-3.45; *P* for trend = 0.001). After adjustment, the association between leanness and FD in men disappeared. No association between being overweight or obese and FD was found. In men, the relationship between BMI categories and FD was not a U-shaped curve (*P* for quadratic trend = 0.130).

Discussion

This study evaluated the association between BMI and the prevalence of FD in young Japanese people. In the present study, BMI was independently inversely associated with FD based on the Rome III criteria. This is the first study to show the inverse association between BMI and FD in a young population.

There is limited evidence on the relationship between BMI and the prevalence of FD in Asian people. In a Japanese web-based

study of 8038 participants who had no history of severe illness, FD based on the Rome III criteria with constipation was associated with a lower BMI among women.²² In another Japanese study of 7112 participants who underwent upper endoscopy examination for health screening, PDS, which is an FD subgroup, was significantly inversely associated with BMI.²³ In a Taiwanese study of patients with GERD, BMI was independently inversely associated with FD.²⁴ An Iranian cross-sectional study of 18 180 participants showed that the prevalence of FD without GERD was higher in subjects with a lower BMI.²⁵ In a Malaysian cross-sectional study of 1002 young adults, leanness (BMI < 18.5 kg/m²) was significantly positively associated with FD.²⁶ The findings in the present study were consistent with the results in previous studies that found an inverse association between BMI and FD.

In contrast, in the Asian population, some studies did not show the inverse association between BMI and FD. In a Korean case control study of 363 subjects that included 90 subjects with FD, higher visceral adiposity, not BMI, was associated with an increased risk of FD.²⁷ In an Iranian cross-sectional study of 790 patients with gastrointestinal symptoms (mean age, 49.9 years; mean BMI, 25.4 kg/m²), BMI was not associated with FD.²⁸ The Domestic/International Gastroenterology Surveillance Study showed that BMI positively associated with the prevalence of dyspepsia symp-

toms using an original questionnaire of the general population, including Japan.³¹ Discrepancies for BMI and FD in Asian people may be partially explained by differences in age, sex, distributions of BMI, prevalence of obesity, definition of FD, sample size, and confounding factors.

The underlying mechanism that links low BMI and FD remains unclear. In a study of patients with FD, weight loss was associated with visceral hypersensitivity and delayed gastric emptying.³² Similarly, delayed gastric emptying was found in participants with low BMI.³³ In several animal models, activation of corticotrophin releasing factor (CRF) receptors may inhibit gastric emptying.³⁴ Peripheral injection of CRF and related peptides inhibit gastric emptying in lean mice.³⁵ A low BMI may cause FD via visceral hypersensitivity and delayed gastric emptying due to CRF.

The strengths of the present study were the sample size and the definition of FD based on the Rome III criteria. Our study had several limitations, however. First, this was a cross-sectional analysis. Second, we did not have access to medical records, including those related to medication and endoscopy. Therefore, an unknown digestive disease such as GERD, cancer, or ulcer may have caused FD. The exclusion of any reported organic disorder or concerning signs likely limited this bias, however. Third, due to several exclusion criteria, the prevalence of FD in this cohort may be lower than that in previous studies. FD in this cohort was symptomatic but untreated. Therefore, the severity of FD may be milder than that in previous studies. Fourth, nutritional evaluation data was not available in this cohort. As diet varies among cultures, further research is needed to examine the influence of nutrition on the association between BMI and FD. Fifth, the association between psychological disorders and FD has been reported.^{36,37} Data on psychological disorders, including depression and anxiety, were not collected in this cohort. Finally, the subjects in this study were not representative of Japanese young people. Notably, the prevalence of FD was far lower in this study than in previous population-based studies that have found inverse associations between exercise habits and FD. Similarly, the rates of smoking and drinking were lower in this cohort than in previous cohorts. The percentage of obese subjects was low in this cohort, and the distribution of BMI may affect the association between BMI and FD. Given that the present cohort consisted solely of university students, it is possible that the relatively high educational status of our population affected health behaviors, and that this was partly responsible for the low prevalence of FD in this study.

In conclusion, among Japanese young people, BMI may be independently inversely associated with FD. Leanness may be an independent associated factor for FD in young Japanese women.

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