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Original Article

Association Between Eating Behavior, Frequency of Meals, and Functional Dyspepsia in Young Japanese Population

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Background/Aims
Functional dyspepsia (FD) may be a common digestive disease worldwide and reduces the quality of life of patients. However, only a few studies have investigated the association between eating behavior and FD. The purpose of this cross-sectional study is to examine the association between eating behavior and prevalence of FD in a young Japanese cohort.

Methods
In this study, we enrolled 8923 Japanese university students. FD is diagnosed based on the Rome III criteria. Eating habits and frequency of meals were investigated using a self-administered questionnaire.

Results
The FD subjects had a younger mean age, a lower body mass index, and a lower proportion of men compared to the non-FD subjects. An independent positive association between skipping breakfast and/or lunch and FD was found (adjusted ORs were 1.60 [95% CI, 1.10-2.32] for breakfast and 2.52 [95% CI, 1.04-5.18] for lunch). Skipping dinner, extra meals (snacks) or midnight snacks was not associated with FD. The prevalence of FD in subjects eating 1, 2, and 3 meals per day was 4.8%, 2.2%, and 1.7%, respectively. The frequency of meals was independently inversely associated with prevalence of FD (adjusted ORs were 1 per day: 2.72 [95% CI, 1.19-5.42], and 2 per day: 1.69 [95% CI, 1.16-2.43], *P* for trend = 0.001).

Conclusions
In the young Japanese people, the frequency of meals may be independently inversely associated with prevalence of FD. In particular, skipping breakfast and/or lunch was associated with the prevalence of FD.
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Key Words
Dyspepsia; Japan; Meals

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Introduction

Despite the absence of organic disorders, epigastric pain, heart burn, early satiety, and postprandial fullness is found in patients with functional dyspepsia (FD).[1] FD has a high prevalence worldwide and worsens the quality of life of patients. In previous epidemiological studies, female, current smoking, use of NSAID, *Helicobacter pylori*-infection, low body mass index (BMI), and low physical activity are associated with prevalence of FD.[2-4]

Dietary intake is related with a variety of changes in gastrointestinal function.[5] Some studies of FD report that their FD-related digestive symptoms are associated with meal intake or worsening after meals.[5,6] However, most of the previous studies that have investigated food intolerance in FD and have not paid enough attention to the association between eating behaviors including skipping meals, snacking, and eating more meals per day and FD.[7-9]

An irregular meal pattern and eating quickly were independently associated with FD.[8,10-12] On the other hand, in case-control studies[9,13] eating pattern was not associated with FD. Although specific eating behaviors may be related to FD, such links are inconsistent. It is important to identify specific eating behaviors associated with FD in order to consider optimal dietary management strategies for patients with FD. In the present study, we aim to investigate possible associations between eating behaviors and FD in the young Japanese cohort.

Materials and Methods

The Cohort Population

From April 2015 to April 2017, in this cross-sectional study, the total 10 104 students who had no missing health check-up data were enrolled to this cohort. We sent questionnaires regarding FD based on the Rome III criteria[14,15] to all students at the time of their physical examination. The exclusion criteria are treatment for gastrointestinal disorders within the last 6 months, regular use of antipyretic analgesics and/or steroids, serious physical and gastrointestinal symptoms (loss of body weight, repeated vomiting, blood in the stools, and difficulty in swallowing). In addition, cases of reporting organic diseases such as gastritis, gastro-esophageal reflux disease, peptic ulcers including *Helicobacter pylori*-infection, gastrointestinal cancers, and liver/biliary/pancreatic disease were also excluded. The cohort of the present study consisted of 8913 subjects' data, after a total 1191 subjects were excluded due to missing data, medication, serious physical and gastrointestinal symptoms or organic digestive diseases (Figure). We created a protocol based on the Declaration of Helsinki's ethical guidelines and presented opt-outs to all subjects. The present study protocol was approved by the ethics committee of Ehime University of Medical Science (Approval No. 1610012).

Measurements

We used a self-administered web-based questionnaire to assemble information on daily habits and medical history. The definition of a current smoker were subjects who smoked regardless of the number of cigarettes per day. The definition of a current drinker were subjects with a habit of drinking alcohol, regardless of frequency or amount of alcohol intake. Height was measured in 1 mm increments using a stadiometer in a completely upright position. The calculation of BMI was performed by dividing body weight (kg) by height (m^2).

Definition of Functional Dyspepsia

Subjects were diagnosed as FD if they had one or more of the following symptoms within 6 months: postprandial fullness, early satiety, or epigastric pain or heart burn (the Rome III criteria[14,15]).

Definition of Eating Behavior

The definitions of eating habits and frequency of meals were

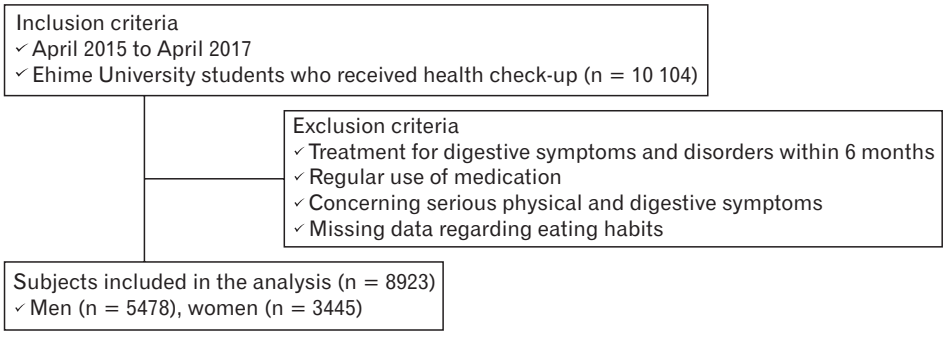

Figure. Study population.

based on the self-administered web-based questionnaire responses. Eating habits: in response to the question "Which meal do you eat (multiple answers possible)?," the following 5 options ("breakfast," "lunch," "dinner," "extra meals [snacks]," and "midnight snacks"). The frequency of meals was categorized based on the above question results (breakfast, lunch, and dinner) as follows: (1 per day, 2 per day, and 3 per day).

Statistical Methods

Two main patient characteristics were analyzed. The first was whether the patient habitually ate each meal; for each meal, each patient was classified as having answered no (reference) or yes. The second was the frequency of meals; patients were classified as having answered 1 per day, 2 per day, or 3 per day (reference). Multiple logistic regression analyses were adjusted by the potential confounding factors, such as sex, age, BMI, drinking, smoking, heart murmur, anemia, and exercise habit. We used SAS software package version 9.4 (SAS Institute Inc, Cary, NC, USA) for statistical analyses

Table 1. Characteristics of Study Cohort

Characteristics	Total (N = 8913)	FD (n = 168)	Non-FD (n = 8745)	*P*-value
Age (yr)	20.1 ± 2.8	19.4 ± 1.7	20.2 ± 2.80	0.001
Sex (men/women)	5474/3439	81/87	5393/3352	0.001
BMI	21.35 ± 3.05	20.44 ± 3.09	21.37 ± 3.04	0.001
Smoking	526 (5.9)	8 (4.8)	518 (5.9)	0.527
Drinking	972 (10.9)	14 (8.3)	958 (11.0)	0.280
Exercise habit	3507 (39.4)	46 (27.4)	3461 (39.6)	0.001
Medical history				
Heart murmur	47 (0.5)	3 (1.8)	44 (0.5)	0.023
ECG abnormality	63 (0.7)	2 (1.2)	61 (0.7)	0.450
Anemia	239 (2.7)	10 (6.0)	229 (2.6)	0.008
Traffic accident	115 (1.3)	2 (1.2)	113 (1.3)	0.908
Sport injury	273 (3.1)	2 (1.2)	271 (3.1)	0.155
Eating habits				
Eating breakfast	6475 (75.8)	121 (72.0)	6333 (75.9)	0.252
Eating lunch	8745 (98.1)	161 (95.8)	8584 (98.2)	0.028
Eating dinner	8597 (96.5)	158 (94.1)	8439 (98.2)	0.089
Eating extra meals (snacks)	1112 (12.5)	25 (14.9)	1087 (12.4)	0.309
Midnight snack	2757 (30.9)	58 (34.5)	2699 (30.9)	0.341
Frequency of meals (breakfast, lunch, and dinner)				0.058
One per day	217 (2.4)	8 (4.8)	209 (2.4)	
Two per day	2209 (24.8)	48 (28.6)	2161 (24.7)	
Three per day	6487 (72.8)	112 (66.7)	6375 (72.9)	
Functional dyspepsia	168 (1.9)			

FD, functional dyspepsia; SD, standard deviation; BMI, body mass index; ECG, electrocardiogram.
Data are presented as mean ± SD, n, or n (%).

Results

Subject Characteristics

The characteristics of this cohort are shown in Table 1. The FD subjects had a younger mean age, a lower BMI, and a higher proportion of women compared to the non-FD subjects. The frequencies of heart murmur, electrocardiogram abnormality, and anemia were higher in FD subjects. A higher proportion of FD subjects reported engaging in regular exercise compared to non-FD subjects. The proportion of participants who ate lunch and the proportion who ate dinner were significantly lower in FD subjects than in non-FD subjects (95.8% vs 98.2%, $P = 0.028$ for lunch and 94.1% vs 98.2%, $P = 0.089$ for dinner). There were no differences in the proportion of participants who ate extra meals (or snacks) or midnight snacks between FD and non-FD subjects.

Table 2. Crude and Adjusted Odds Ratios and 95% Confidence Intervals for Functional Dyspepsia in Relation to Eating Habits

Variable	Prevalence (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
Functional dyspepsia			
Breakfast			
No	47/2159 (2.2)	1.22 (0.86-1.70)	1.60 (1.10-2.32)
Yes	121/6754 (1.8)	1.00	1.00
Lunch			
No	7/168 (4.2)	2.32 (0.97-4.67)	2.52 (1.04-5.18)
Yes	161/8745 (1.8)	1.00	1.00
Dinner			
No	10/316 (3.2)	1.75 (0.85-3.17)	1.91 (0.93-3.49)
Yes	158/8597 (1.8)	1.00	1.00
Snack			
No	110/6156 (1.8)	0.85 (0.62-1.17)	0.98 (0.71-1.37)
Yes	58/2757 (2.1)	1.00	1.00
Midnight snack			
No	143/7801 (1.8)	0.81 (0.54-1.28)	0.73 (0.48-1.16)
Yes	25/1112 (2.3)	1.00	1.00

Adjusted for sex, age, body mass index, drinking, smoking, heart murmur, anemia, and exercise habit.

Association Between Eating Habits and Functional Dyspepsia

Table 2 shows the relationship between the eating habits and FD. Skipping breakfast and/or skipping lunch were independently inversely associated with prevalence of FD (breakfast: adjusted OR, 1.60 [95% CI, 1.10-2.32] and lunch: adjusted OR, 2.52 [95% CI, 1.04-5.18]). There was no association between FD and eating dinner, extra meals (snacks), or midnight snacks.

Association Between Frequency of Meals and Functional Dyspepsia

Table 3 shows the association between meals frequency and FD. The prevalence of FD in subjects who ate 1 meal, 2 meals, and 3 meals per day was 4.8%, 2.2%, and 1.7%, respectively. After adjustment for confounding factors, frequency of meals was independently inversely associated with prevalence of FD (1 per day: adjusted OR, 2.72 [95% CI, 1.19-5.42], and 2 per day: adjusted OR, 1.69 [95% CI, 1.16-2.43], P for trend $P = 0.001$).

Discussion

In the present cohort of a young Japanese population, frequency of meals was independently inversely associated with prevalence of FD. Skipping breakfast and/or skipping lunch were also associated with the prevalence of FD. There was no association, on the other hand, between FD and eating extra snacks or midnight snacks. This is 1 of only a few studies to show an independent inverse association between meal frequency and FD in a young Asian population.

Several previous studies have found associations between irregular eating behaviors and gastrointestinal diseases. A positive association between skipping breakfast and GERD was reported in a study conducted in China.[16] A positive relationship between skipping breakfast and the severity of GERD was found in a Japanese study of 19 864 people who underwent health examination.[17] Similarly, a positive association between skipping breakfast and self-reported constipation was found in Japanese university students. The evidence regarding the association between eating habits and FD specifically is more limited. An Irish case-control study of 40 outpatients reported that the proportion of FD patients who ate 3 meals per day was significantly lower than in non-FD patients.[10] In a cross-sectional Iranian study of 4763 subjects, an irregular meal pattern was significantly associated with chronic uninvestigated dyspepsia.[11] In a Serbian study of 180 FD patients aged 20-79, skipping meals and fasting was associated with a certain subset of FD symptoms.[8]

On the other hand, in a case-control Irish study (50 patients with FD and 50 healthy subjects), there were no differences on eating patterns between patients and healthy subjects.[13] A case-control study in Brazil reported that the association between their symptoms and the consumption of certain foods was found, but maintained regular eating patterns nevertheless.[9] Thus, the available data on the association between eating behavior including regular meal patterns and FD remain inconsistent. This inconsistency between eating behavior and FD may be explained at least in part by variation among the studies design, sex, age, BMI, sample size, definitions of eating behavior, and questionnaires.

The underlying mechanism linking skipping breakfast and/or lunch, frequency of meals and FD remains unclear. The etiology of FD is thought to be impaired gastroduodenal motility, delayed gastric emptying, food distribution, visceral hypersensitivity, dysfunction of central nervous system, and psychological factors.[18-24] Fasting may alter gastric emptying and gastroduodenal motility or proximal gastric regulation. Fasting may cause dyspepsia by gastroesophageal acid reflux via abnormal fundic relaxation. However, not all studies agree on these possible causes.

The present cohort had some strengths, as well as several potential limitations. This study benefits from having a relatively uniform population in terms of age, educational, marital, and socioeconomic status. These factors may confound dietary behaviors.[25,26] Our large sample size is another strength. One limitation is that this study evaluated the frequency of meals, the skipping of meals, and the consumption of snacks, but did not investigate overall energy intake, dietary nutrient composition, certain foods that worsen FD symptoms, or speed of eating. It is possible that FD patients may avoid eating regularly and eat less frequently in an attempt to mini-

Table 3. Crude and Adjusted Odds Ratios and 95% Confidence Intervals for Functional Dyspepsia in Relation to Frequency of Meals

Variable	Prevalence (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
Functional dyspepsia			
Frequency of meals			
One per day	8/217 (4.8)	2.18 (0.97-4.25)	2.72 (1.19-5.42)
Two per day	48/2009 (2.2)	1.26 (0.89-1.77)	1.69 (1.16-2.43)
Three per day	112/6487 (1.7)	1.00	1.00
P for trend			0.001

Adjusted for sex, age, body mass index, drinking, smoking, heart murmur, anemia, and exercise habit.

mize their symptoms. A previous study has reported that irregular eating is associated with lower energy intake, especially in women, as assessed in a seven-day dietary history.[10] In that study, however, snacks were not included in the dietary history, and FD patients were more likely to report recent weight gain compared to the control group. In our study, snacks between meals or at night was not associated with FD. This cannot be explained by attempts to avoid eating due to symptoms. However, the cross-sectional nature of our study means that we cannot infer causal relationships between eating behavior and FD from the findings in the present study. To identify the true association between symptoms of dyspepsia and dietary behaviors, further prospective cohort studies are warranted in the future. In addition, the participants in the present study were young university students. Compared to non-students of the same age, they may have had more regular access to healthier meals, as meals are provided for students in the school cafeteria. The proportion of males and the rates of drinking, smoking, and exercise habit were similar between the total population and the analysis group, while 1191 subjects were excluded. However, the participants analyzed in this study may not represent the young Japanese population in general. Thus, any extrapolation of the present findings to the other population should be undertaken with caution.

In conclusion, in the young Japanese people, the inverse association between meal frequency and FD was found. In particular, skipping breakfast and/or lunch was associated with the prevalence of FD. This finding may be helpful in recommending optimal dietary management strategies for patients with FD.

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