Reduction in Gastroesophageal Reflux Disease Symptoms Is Associated with Miso Soup Intake in a Population-Based Cross-Sectional Study: The Nagahama Study

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Summary Dietary habits and lifestyles are considered to affect the frequency of epigastric symptoms. In our previous study, we found that three amino acids in Japanese broth promoted gastric emptying. We hypothesized that a higher consumption of miso soup which was mainly composed of Japanese broth and miso paste would be associated with a lower frequency of epigastric symptoms. We conducted a cross-sectional study of the association between frequency of miso soup intake and reflux or dyspepsia symptoms in a general Japanese population. Sixteen items of dietary habits were assessed using a self-reported questionnaire, and epigastric symptoms were evaluated using the Frequency Scale for Symptoms of Gastroesophageal Reflux Disease (FSSG). We fitted generalized linear models to analyze the association between miso soup intake and FSSG, reflux, or dyspepsia scores adjusted by age, sex, body mass index (BMI), another 15 dietary habits, smoking, drinking alcohol, and unfavorable dietary behaviors. A total of 9,364 subjects were included in the analysis. Trend analysis revealed that higher frequency of miso soup intake was associated with lower FSSG scores (p<0.001). In a generalized linear model, daily intake of miso soup was associated with lower FSSG, reflux, and dyspepsia scores independent of age, sex, BMI, other 15 dietary habits, smoking, drinking alcohol, and unfavorable dietary behaviors (estimate=−0.46, −0.22, and −0.27, respectively; 95% CI=−0.83, −0.12; −0.38, −0.07; and −0.47, and −0.08, respectively). Dairy intake of miso soup was associated with lower epigastric symptoms.

Key Words Japanese diet, miso soup, gastric emptying, Frequency Scale for Symptoms of Gastroesophageal Reflux Disease (FSSG), dietary habit

Upper gastrointestinal disorders, such as gastroesophageal reflux disease (GERD) and functional dyspepsia (FD), are common throughout the world. The prevalence of GERD symptoms in Asia has increased to around 20% (1–4), and the prevalence of FD is approximately 10% to 20% of the general population in Japan and worldwide (5). The symptoms of GERD and FD have some overlap, and are associated with a poor health-related quality of life (6–9).

Both dietary and lifestyle habits are generally considered to affect the frequency of reflux or dyspepsia symptoms, and patients with GERD or FD are advised to refrain from certain food and lifestyle choices (10, 11). For example, unfavorable dietary behaviors are reported to be associated with GERD symptoms (12, 13). Fat intake provokes reflux symptoms in patients with GERD or FD (14–17). Tobacco, chocolate, carbonated beverages, and a postprandial right lateral decubitus position decrease pressure on the lower esophageal sphincter in patients with GERD (18). These studies, however, mainly included patients with GERD, and few population-based studies have evaluated the role of dietary behaviors in GERD or FD symptoms (11, 18, 19).

The Japanese dietary pattern is composed of the dietary staple, side dishes, and soup (20, 21). Miso soup is the most basic soup of Japanese daily meals, and it is made with miso paste dissolved in Japanese broth and various ingredients such as vegetables, mushrooms, seaweed, or tofu, depending on regional and seasonal recipes (21). A bowl of miso soup usually contains a tablespoon of miso paste that has about 32 kcal of energy, 2.1 g of protein, 1.1 g of fat, and 3.5 g of carbohydrate (http://www.mext.go.jp/en/policy/science_technology/policy/title01/detail01/1374030.htm), and the salt content of miso soup is 0.5–1.2% (22). Japanese broth

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contains amino acids, but has virtually no calories (23). The nutrients contained in miso soup can differ between the ingredients used; basically, however, miso soup has low fat and low energy. The influence of the consumption of miso soup on salt intake and blood pressure are often studied (22, 24, 25). But, there is no study to focus on the relationship between frequency of miso soup intake and frequency of epigastric symptoms. In our previous study, we found that levels of three amino acids (histidine, glutamate, and aspartate) and sodium chloride that closely parallel those in Japanese broth promote gastric emptying (23). We hypothesized that higher consumption of miso soup would be associated with a lower frequency of reflux or dyspepsia symptoms.

In this study, we investigated the associations between frequency of miso soup intake and reflux and dyspepsia symptoms in a general Japanese population using cross-sectional data obtained in the Nagahama Prospective Cohort for Comprehensive Human Bioscience study (the Nagahama Study).

MATERIALS AND METHODS

Study subjects. Study subjects were participants of the baseline survey in the Nagahama Study. The Nagahama Study is an ongoing community-based cohort study conducted by the Kyoto University Graduate School of Medicine and Nagahama City. The participants are members of the general population living in Nagahama City, a rural city of 125,000 inhabitants in Shiga Prefecture located in central Japan, aged 30 to 74 years recruited from 2008 to 2010. Among the total of 9,764 study participants, subjects who did not complete the Frequency Scale for Symptoms of Gastroesophageal Reflux Disease (FSSG) (n=1), who were pregnant (n=42), who received GERD treatment (n=105) or who reported a medical history of upper gastrointestinal cancer (n=71) or Helicobacter pylori infection (n=181) were excluded from this study (Fig. 1). The Ethics Committee of Kyoto University Graduate School and Faculty of Medicine, the Ethical Review Board of the Nagahama Study, and the Nagahama Municipal Review Board of Personal Information Protection approved all study procedures.

Data collection. At the baseline survey in the Nagahama Study, physical and biochemical parameters were measured. Data regarding medical history; medications; epigastric symptoms; smoking status; and dietary habits, including alcohol consumption, were obtained using a self-reported questionnaire. An individual who consumed alcohol more than 4 drinks per week was defined as a frequent drinker (12).

Epigastric symptoms. Epigastric symptoms were evaluated using the FSSG, a well-established and widely used questionnaire in Japan for evaluating the symptoms of GERD (26) and the response to treatment of GERD (16) or FD (27). The FSSG comprises 12 questions: 7 questions (#1, 4, 6, 7, 9, 10, and 12) about acid-reflux related symptoms (reflux score) and 5 questions (#2, 3, 5, 8, and 11) about dyspepsia symptoms (dyspepsia score), which were scored to indicate the frequency of symptoms, as follows: never=0, occasionally=1, sometimes=2, often=3, and always=4 (26) (Supplemental Online Material, Table S1). At a cutoff score of 8 points, the FSSG shows 62% sensitivity, 59% specificity, and 60% accuracy for an endoscopic diagnosis of GERD (26).

Dietary habits. Dietary habits were assessed using a simple 16-item questionnaire about the frequency of intake of 1) meat dishes; 2) fish dishes; 3) tofu (soy bean curd) dishes (or soy bean dishes); 4) egg dishes; 5) milk; 6) vegetable dishes; 7) fruits; 8) deep-fried foods; 9) cakes or Japanese confectioneries, 10) juice or isotonic drinks; 11) junk foods; 12) sweets like candies and chocolates; 13) miso (fermented soybean paste) soup; 14) pickles; 15) ham, sausage, or kamaboko (boiled fish paste); and 16) frozen foods or precooked foods. Subjects answered

9764 subjects from the Nagahama Study

- Incomplete FSSG n = 1
- Pregnant women n = 42
- GERD treatment n = 105
- Medical history of upper gastrointestinal cancer n = 71
- Medical history of Helicobacter pylori infection n = 181

9364 eligible subjects

Fig. 1. Flowchart detailing the process of obtaining subjects for analysis. FSSG, Frequency Scale for Symptoms of Gastroesophageal Reflux Disease.

Table 1. Characteristics of subjects.

<table>
<thead>
<tr>
<th>Factors</th>
<th>All (n=9,364)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>3,048 (32.6)</td>
</tr>
<tr>
<td>Age, y (SD)</td>
<td>53.4 (13.4)</td>
</tr>
<tr>
<td>BMI, kg/m² (SD)</td>
<td>22.3 (3.3)</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>1,369 (14.6)</td>
</tr>
<tr>
<td>Frequent drinker, n (%)</td>
<td>2,123 (22.7)</td>
</tr>
<tr>
<td>FSSG scores (95% CI)</td>
<td>4.6 (4.5–4.7)</td>
</tr>
<tr>
<td>Reflux scores (95% CI)</td>
<td>2.1 (2.0–2.1)</td>
</tr>
<tr>
<td>Dyspepsia scores (95% CI)</td>
<td>2.5 (2.5–2.6)</td>
</tr>
<tr>
<td>8 points or more, n (%)</td>
<td>2,049 (21.9)</td>
</tr>
<tr>
<td>Medication, n (%)</td>
<td></td>
</tr>
<tr>
<td>Steroid</td>
<td>63 (0.7)</td>
</tr>
<tr>
<td>Antithrombotic drugs</td>
<td>370 (4.0)</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>307 (3.3)</td>
</tr>
<tr>
<td>Antihypertensive drugs</td>
<td>1,560 (16.7)</td>
</tr>
<tr>
<td>Medical history, n (%)</td>
<td>201 (2.1)</td>
</tr>
</tbody>
</table>

Continuous variables are described as mean (SD or 95% CI), and categorical variables are expressed as numbers (%).

An individual who consumed alcohol more than 4 times per week was defined as a frequent drinker.

CI, confidence interval; GERD, gastroesophageal reflux disease; NSAIDS, non-steroidal anti-inflammatory drugs; SD, standard deviation.
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Dietary behaviors which are supposed to be closely correlated with GERD symptoms (12, 13) were assessed by the following four questions that are used in the standard health checkup program performed by the Japanese government: 1. Do you have dinner within 2 h before going to bed more than 3 d a week? 2. Do you snack after dinner more than 3 d a week? 3. Do you have a habit of eating rapidly? 4. Do you skip breakfast more than 3 d a week? Subjects answered each item by choosing “yes” or “no.” A score of one was assigned to each “yes” response.

Unfavorable dietary behaviors. Dietary behaviors which are supposed to be closely correlated with GERD symptoms (12, 13) were assessed by the following four questions that are used in the standard health checkup program performed by the Japanese government: 1. Do you have dinner within 2 h before going to bed more than 3 d a week? 2. Do you snack after dinner more than 3 d a week? 3. Do you have a habit of eating rapidly? 4. Do you skip breakfast more than 3 d a week? Subjects answered each item by choosing “yes” or “no.” A score of one was assigned to each “yes” response.

Continuous variables are described as mean (95% CI).

For trend testing, we assigned variables to each category of dietary habits as follows: less than once per week = 1, two to three times per week = 2, four to five times per week = 3, every day = 4. Three dummy variables corresponding to each category of dietary habit frequency with 0 and 1 as possible values were then constructed. “Less than once per week” category was selected as the reference category. Sex was coded as male = 1, female = 0.

A two-tailed p < 0.05 was considered statistically significant. All statistical analyses were performed using JMP Pro version 13.0.0 (2016 SAS Institute).

RESULTS

A total of 9,364 subjects was included in the analysis (Fig. 1). Approximately one-third of the subjects were male (Table 1). Mean age (SD) was 53.4 (13.4) y old. Among the subjects, 201 subjects (2.1%) reported a medical history of GERD, and 2,049 subjects (21.9%) had FSSG scores ≥ 8. The mean FSSG score was 4.5, and its 95% CI was 4.5–4.7. The mean FSSG scores, reflux scores, and dyspepsia scores decreased with an increase in miso soup intake (Table 2). Differences in the mean scores between the “less than once per week” and “every

Table 2. Mean FSSG scores, reflux scores, and dyspepsia scores by the frequency of intake of miso soup.

<table>
<thead>
<tr>
<th>Miso soup</th>
<th>n</th>
<th>FSSG scores (95% CI)</th>
<th>Reflux scores (95% CI)</th>
<th>Dyspepsia scores (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1/wk</td>
<td>1,081</td>
<td>5.3 (5.0–5.6)</td>
<td>2.3 (2.2–2.4)</td>
<td>3.0 (2.8–3.2)</td>
</tr>
<tr>
<td>2–3/wk</td>
<td>2,510</td>
<td>4.9 (4.7–5.1)</td>
<td>2.2 (2.1–2.2)</td>
<td>2.7 (2.6–2.8)</td>
</tr>
<tr>
<td>4–5/wk</td>
<td>2,524</td>
<td>4.5 (4.3–4.7)</td>
<td>2.0 (2.0–2.1)</td>
<td>2.5 (2.4–2.6)</td>
</tr>
<tr>
<td>Every day</td>
<td>3,249</td>
<td>4.2 (4.0–4.3)</td>
<td>2.0 (1.9–2.0)</td>
<td>2.2 (2.1–2.3)</td>
</tr>
</tbody>
</table>

CI, confidence interval; FSSG, Frequency Scale for Symptoms of Gastroesophageal Reflux Disease.

For trend testing, we assigned variables to each category of dietary habits as follows: less than once per week = 1, two to three times per week = 2, four to five times per week = 3, every day = 4. Three dummy variables corresponding to each category of dietary habit frequency with 0 and 1 as possible values were then constructed. “Less than once per week” category was selected as the reference category. Sex was coded as male = 1, female = 0.

A two-tailed p < 0.05 was considered statistically significant. All statistical analyses were performed using JMP Pro version 13.0.0 (2016 SAS Institute).
and age and BMI were significantly associated with higher reflux scores (Table 4). With dyspepsia scores as the dependent variable, male sex, age, BMI and everyday intake of miso soup were all significantly associated with lower dyspepsia scores (Table 5).

### DISCUSSION

The present findings suggest that a higher frequency intake of miso soup is associated with fewer epigastric symptoms in the general population. The difference in the mean FSSG scores between “less than once per week” intake of miso soup and “every day” intake of miso soup was 1.1, which corresponds to the difference of the frequency between “occasionally” and “never” of one epigastric symptom. This inverse trend was evident in the FSSG scores. These results are consistent with previous findings that levels of three amino acids (histidine, glutamate, and aspartate) and sodium chloride corresponding to those found in Japanese broth promote gastric emptying (28). Promoted gastric emptying is a possible mechanism for less reflux and less dyspepsia. Glutamate accelerates gastric emptying when added to a liquid meal with protein, but has no significant effect on gastric emptying when added to water or a liquid meal with only carbohydrates in humans (29). Based on the fact that miso soup comprises both Japanese broth and miso paste, which contains soybean protein, miso soup is likely to promote gastric emptying. In addition, some studies suggest that soybean-derived products ameliorate gastroparesis (30) and decrease regurgitation (31).

In the present study, male sex was associated with lower FSSG, reflux, and dyspepsia scores. The same sex differences have been reported in previous Japanese studies (13, 32, 33). Younger age was associated with
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higher FSSG scores in the present study. Previous studies among Japanese have also demonstrated that younger subjects have higher FSSG scores in the general population (13, 32). When reflux and dyspepsia symptoms were analyzed separately, younger age was associated with fewer reflux symptoms, and more dyspepsia symptoms. BMI was not associated with lower FSSG scores. In a separate analysis of reflux scores and dyspepsia scores, however, BMI was associated with more reflux symptom and fewer dyspepsia symptoms.

GERD, which is mainly based on reflux symptoms, has a multifactorial pathogenesis, including the presence of excess gastric acid (34), hiatal hernia (35), lower esophageal sphincter (LES) dysfunction (36, 37) and esophageal motility dysfunction (38). Aging is a major risk factor for GERD (39). The age-related increase of GERD is mainly caused by the higher prevalence of hiatal hernia (35) and esophageal motility dysfunction (38). Increased BMI is also associated with reduced esophageal body contractility (36) and impaired LES function (36, 37), and causes erosive esophagitis (4, 40). Our results that aging and increased BMI were associated with higher reflux scores were in accordance with these data.

The pathogenesis of FD, which is mainly based on dyspepsia symptoms, is more heterogeneous. Psychological distress, particularly anxiety, is associated with FD (41). A disturbance of gastric physiologic factors, such as slow gastric emptying, failure of the gastric fundus to relax after a meal, or gastric hypersensitivity with distension of the stomach are also involved in FD (42). Several population-based studies demonstrated that FD is more common in younger subjects (43, 44). There have been no studies that revealed any association between BMI and FD. Our results which revealed an association of aging with lower dyspepsia scores was consistent with previous data (43, 44).

A limitation of the current study is that endoscopic assessment to diagnose esophagitis was not performed. However, we focused on the frequency of the epigastric symptoms with or without endoscopic esophagitis, and found significant associations between miso soup intake and epigastric symptoms. Because of the limitation of a cross-sectional study, the results of the current study do not mean that miso soup intake has any preventive or therapeutic effects on GERD. Further longitudinal research is required to clarify the protective effect of miso soup against deterioration of epigastric symptoms. One strength of the current study is the simple questionnaire for dietary assessment. Study subjects readily answered the question regarding the frequency of intake of miso soup per week, even those that do not cook for themselves.

In conclusion, daily intake of miso soup was associated with the lower FSSG, reflux, and dyspepsia scores in a Japanese community-based cohort population.

Acknowledgments

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Authors contributions

The authors’ contributions were as follows: F.M., K.I., and T.S. designed and conducted research; F.M., K.I., T.S., D.T., E.J., and N.I. analyzed data; T.N., Y.T., S.K., A.S., Y.T., and F.M. mainly conducted the Nagahama Study; F.M., K.I., and T.S. wrote the paper. N.I. had primary responsibility for final content. All authors read and approved the final manuscript.

Supporting information

Supplemental Online Material is available on J-STAGE.

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