

Correlation of Reflux Esophagitis and Obesity: Quantitative and Qualitative Analysis

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ABSTRACT

Obesity is a possible risk factor for reflux esophagitis. The aim of this study was to determine whether reflux esophagitis is associated with obesity and adiposity. We studied 579 consecutive men who underwent upper gastrointestinal endoscopy during health checkups at the Jikei University Hospital. Obesity was assessed with four indices: body mass index and body weight gain since 20 years of age as quantitative indices and waist circumference and percent body fat as qualitative indices. The grades of reflux esophagitis were assessed according to the Los Angeles classification. The subjects with reflux esophagitis had significantly higher body mass index, greater weight gain since 20 years of age, greater waist circumference, and greater percent body fat than did subjects without esophagitis. Multiple regression analysis revealed that body weight gain since 20 years of age was the only risk factor for esophagitis. In addition, waist circumference in subjects with grade A esophagitis was significantly higher than that in subjects with grade M esophagitis. Our results show that reflux esophagitis is associated with body weight gain since 20 years of age, suggesting that maintaining body weight after 20 years of age prevents reflux esophagitis.

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Key words : reflux esophagitis, body mass index, weight gain, waist circumference, percent body fat

INTRODUCTION

Reflux esophagitis, which progresses through Barrett's esophagus to adenocarcinoma^{1,2}, is common in Western countries. In Japan, however, its incidence was low but has been increasing since 1990³.

Studies of risk factors for reflux esophagitis have focused on age, sex, race, smoking, alcohol intake, diet, and obesity^{4,5}. Obese persons, particularly those with large amounts of visceral fat, are generally considered more likely to have gastroesophageal reflux disease than are lean subjects⁶, but evidence for

this relation is weak and contradictory⁷. Several studies have shown associations between obesity, as assessed with body mass index (BMI), and reflux esophagitis^{6,8}. However, evaluating obesity on the basis of accumulated body fat is also important because BMI does not always indicate the degree of fat accumulation. In the present study, we investigated the association between reflux esophagitis and obesity, which was evaluated on the basis of BMI, weight gain since the age of 20 years, waist circumference as an indicator of visceral fat⁹, and percent body fat.

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SUBJECTS AND METHODS

The subjects studied were 579 Japanese men ranging in age from 35 to 69 years (mean age, 57.4 ± 0.4 (standard deviation) years). All subjects underwent upper gastrointestinal (GI) endoscopy as part of medical checkups at the Jikei University Hospital from January 2000 through December 2000. Subjects were excluded if they had undergone upper GI surgery or were taking medication that could alter esophageal motility (e.g., nitrates, calcium antagonists), H₂-receptor antagonists, proton pump inhibitors, or nonsteroidal anti-inflammatory drugs. Reflux esophagitis was diagnosed on the basis of findings at endoscopy (XQ230 endoscope, Olympus Optical Co., Ltd., Tokyo), for which a local anesthetic, 2% lidocaine jelly, was administered to the throat and a sedative, 0.3 mg of flunitrazepam, was given intravenously. Scopolamine butylbromide was not used. Endoscopic examinations were performed by experienced endoscopists certified by the Japanese Board of Gastrointestinal Endoscopy. Esophagitis was graded in accordance with the modified Los Angeles classification system¹⁰. Control subjects were persons in whom reflux esophagitis was not found on endoscopic examination. We also assessed the association of hiatal hernia with obesity.

The subjects examined were requested to answer a questionnaire about GI symptoms, body weight at 20 years of age, and their smoking and drinking habits.

Obesity was assessed with four indices: BMI and weight gain since 20 years of age as quantitative indices, and waist circumference and percent body fat as qualitative indices. The BMI was calculated as (weight in kg)/(height in m)². Body weight gain since 20 years of age was calculated by subtracting the body weight at 20 years of age from that at the

time of the study^{11,12}. Waist circumference, an index of abdominal visceral adipose tissue deposition, was measured to the nearest millimeter with flexible tape, midway between the lowest rib and the iliac crest, and hip circumference was measured at the level of the greater trochanters^{10,12}. Measurements were performed by trained nurses in accordance with World Health Organization classification system¹³. Percent body fat was measured with bioelectrical impedance instrument (TBF-202, Tanita Co., Ltd., Tokyo).

Statistical analyses

Statistical analysis was performed with analysis of variance (ANOVA), the χ^2 test, the Mann-Whitney U-test, and one-factor ANOVA. Multivariate analysis was performed using logistic regression. Results are shown as means \pm standard deviations (SD). A difference was considered significant if the *p* value was less than 0.05. Analysis was performed with StatView 5.0 statistical software (Hulinks Co., Ltd., Tokyo) and STATA 7.0 statistical software (StataCorp LP, College Station, TX, USA).

RESULTS

The incidence of reflux esophagitis among all subjects was 20.0% (116 of 579 subjects). Reflux esophagitis was grade M in 9 subjects (7.8%), grade A in 93 subjects (80.1%), and grade B in 14 subjects (12.0%). No subjects had grade C or grade D esophagitis. No subjects had esophageal stricture, esophageal ulcer, or Barrett's esophagus.

Twenty-nine of 116 subjects with reflux esophagitis (25.0%) had heartburn or acid regurgitation. Subjects with reflux esophagitis and control subjects without esophagitis did not differ in mean age, rate of

Table 1. Age, heartburn, smoking and alcohol in subjects studied

| | Subjects with reflux esophagitis <i>n</i> = 116 | Control subjects <i>n</i> = 463 | <i>p</i> value |
|--------------------------|--|------------------------------------|----------------|
| Age (years) | 57.4 \pm 7.4 | 57.4 \pm 7.6 | 0.392 |
| Heartburn | 21 (18.1%) | 60 (13.2%) | 0.337 |
| No. of cigarette per day | 22.7 \pm 10.1 | 22.0 \pm 10.2 | 0.696 |
| Alcohol (g/week) | 207 \pm 155 | 214 \pm 161 | 0.642 |

Table 2. BMI, body weight gain since 20 years of age, waist circumference, and percent body fat in the subjects with or without esophagitis

| | Subjects with reflux esophagitis <i>n</i> = 116 | Control subjects <i>n</i> = 463 | <i>p</i> value |
|---|--|------------------------------------|----------------|
| BMI (kg/m ²) | 23.9±2.61 | 23.4±2.58 | 0.011 |
| Body weight gain since 20 years of age (kg) | 9.6±7.33 | 7.7±7.40 | 0.018 |
| Waist circumference (cm) | 86.0±6.82 | 84.4±7.23 | 0.012 |
| Percent body fat | 21.5±4.68 | 20.4±4.58 | 0.018 |

Grade of esophagitis

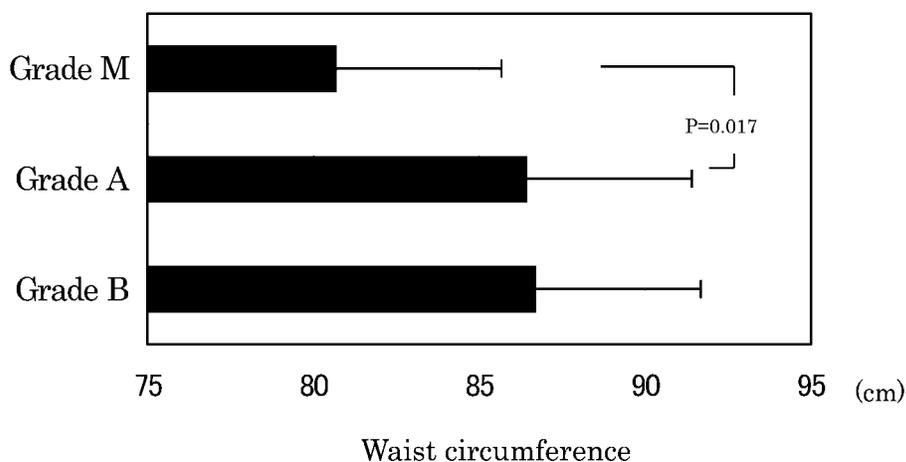


Fig. 1. Waist circumference and severity of reflux esophagitis according to the Los Angeles classification system. Each bar and error bar represent mean waist circumference and SD, respectively

heartburn, number of cigarettes per day, or weekly alcohol consumption (Table 1).

Subjects with reflux esophagitis had significantly higher BMI, more weight gained since 20 years of age, larger waist circumference, and higher percent body fat than did subjects without esophagitis (Table 2). The BMI at 20 years of age had been less than 25 kg/m² in almost all subjects (99.5%).

Multiple logistic regression analysis of indices of obesity showed that only weight gain since 20 years of age was significantly correlated with reflux esophagitis (odds ratio, 1.03; 95% confidence interval [CI], 1.006–1.063). Moreover, for each 10 kg of weight gain since 20 years of age, the risk of reflux esophagitis increased by a factor of 1.4 (odds ratio, 1.4; 95% CI, 1.058–1.837).

Grades of reflux esophagitis were not correlated with either BMI or weight gain since the age of 20 years, but waist circumference differed significantly

between grade A and grade M esophagitis ($p=0.017$; Fig. 1).

Of the upper GI tract disorders examined, only hiatal hernia was significantly more frequent in subjects with reflux esophagitis than in subjects without esophagitis ($p<0.0001$ Table 3). The BMI, body weight gain, waist circumference, and percent body fat were significantly greater in patients with hiatal hernia than in subjects without hiatal hernia (Table 4). Multiple logistic regression analysis showed that weight gain since 20 years of age was the only independent risk factor for hiatal hernia (odds ratio, 1.06; 95% CI, 1.029–1.086). Moreover, for each 10 kg of weight gain, the risk of hiatal hernia increased by a factor of 1.7 (odds ratio, 1.71; 95% CI, 1.280–2.286).

DISCUSSION

In Japan, the prevalence of reflux esophagitis has

Table 3. Upper GI tract disorders

| Upper GI tract disorders | Subjects with reflux esophagitis <i>n</i> = 116 | Control subjects <i>n</i> = 463 | <i>p</i> value |
|--------------------------|--|------------------------------------|----------------|
| Hiatal hernia | 42 (36.2%) | 60 (13.0%) | < 0.0001 |
| Gastric ulcer | 7 (6.0%) | 65 (14.0%) | 0.018 |
| Duodenal ulcer | 11 (9.5%) | 75 (16.2%) | 0.079 |

Table 4. BMI, body weight gain since 20 years of age, waist circumference and percent body fat in the subjects with or without hiatal hernia

| | Hiatal hernia <i>n</i> = 105 | Control <i>n</i> = 474 | <i>p</i> value |
|---|---------------------------------|---------------------------|----------------|
| BMI (kg/m ²) | 23.9 ± 2.59 | 23.3 ± 2.59 | 0.029 |
| Body weight gain since 20 years of age (kg) | 10.6 ± 7.64 | 7.4 ± 7.25 | < 0.001 |
| Waist circumference (cm) | 86.3 ± 6.88 | 84.3 ± 7.18 | 0.022 |
| Percent body fat | 21.7 ± 4.47 | 20.4 ± 4.60 | 0.009 |

been increasing since 1990³. This increase may be related to the increase in the elderly population and the Westernization of Japanese diets³. Diffusion of endoscopic tests in medical checkups performed regularly for persons older than 35 years may have also contributed to the increased prevalence of reflux esophagitis. In addition, the Los Angeles system for classification of esophagitis has improved the accuracy of diagnosis of esophagitis. Use of questionnaires has further increased the ease with which reflux esophagitis is diagnosed¹⁴.

Several studies have found an association of reflux esophagitis with obesity¹⁵, but the association has not been clearly established¹⁶. In these studies, only BMI was used to assess obesity¹⁷. Thus, we evaluated obesity with four indices: BMI and body weight gain since 20 years of age as quantitative indices, and waist circumference and percent body fat as qualitative indices. We found that increases in indices related to obesity and adiposity were closely associated with the development of reflux esophagitis. However, of these indices, only body weight gain since 20 years of age was identified as a risk factor for reflux esophagitis with multiple logistic regression analysis. Being an index of accumulation of mainly visceral fat, the weight gain since 20 years of age has been also shown to be a risk factor for hypertension, type 2 diabetes mellitus, coronary artery disease,

breast cancer, and osteoarthritis¹⁸.

Hiatal hernia is also closely associated with both obesity and age^{19–21}. Obesity (BMI ≥ 25 kg/m²) has been shown to impair function of the lower esophageal sphincter (LES) and esophageal acid clearance²². The present study found that body weight gain since 20 years of age, but not BMI, is associated with hiatal hernia.

Reflux esophagitis is closely associated with hiatal hernia^{7,23}. Hiatal hernia is also a causative factor in reflux esophagitis²⁴. Many conditions might induce both reflux esophagitis and hiatal hernia, including increased intra-abdominal pressure, abdominal diaphragmatic pinchcock, increased intragastric pressure, relaxation of the LES, and delayed acid clearance²⁵. Moreover, factors other than being overweight that weaken the LES include alcohol consumption, smoking, and diet. Weight gain since after 20 years of age may increase intra-abdominal pressure, in addition to weakening the LES, thereby increasing the risk of gastric esophageal reflux through hiatal hernia.

We found that gastric ulcer was significantly more frequent in subjects with reflux esophagitis than in subjects without esophagitis. Gastric ulcer induced by *Helicobacter pylori* (*H. pylori*) infection is common in Japanese adults, which suggests of *H. pylori* infection might also play an important role in reflux eso-

phagitis. Evaluation of the relationship between gastric ulcer and reflux esophagitis warrants further epidemiologic study. Reflux esophagitis progresses to adenocarcinoma through Barrett's esophagus^{1,2}. However, a recent report has found that although the incidence of reflux esophagitis has increased in Japan, the incidence of esophageal adenocarcinoma has not²⁶, perhaps because of racial differences. If the incidence of reflux esophagitis continues to increase in Japan, the incidence of esophageal carcinoma might also eventually increase.

In the present study, both reflux esophagitis and hiatal hernia correlated with both quantitative and qualitative indices of obesity, especially body weight since 20 years of age. Waist circumference correlated with progression from grade M to grade A. Weight reduction is associated with an improvement in reflux esophagitis²⁷.

Our study suggests that maintenance of body weight at 20 years of age can help prevent reflux esophagitis and esophageal adenocarcinoma.

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