

学 位 論 文 の 要 旨

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学 位 論 文 名 PREVALENCE OF ENDOSCOPICALLY NEGATIVE AND
POSITIVE GASTROESOPHAGEAL REFLUX DISEASE IN
THE JAPANESE

発 表 雑 誌 名 Scandinavian Journal of Gastroenterology
(巻, 初頁~終頁, 年) 40: 1005-1009, 2005

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論 文 内 容 の 要 旨

INTRODUCTION

Gastroesophageal reflux disease (GERD) is characterized by the presence of esophageal mucosal injury or by symptoms associated with the abnormal reflux of gastric contents into the esophagus. Patients with GERD are divided into two groups: those with and without endoscopically proven reflux esophagitis. Patients with GERD symptoms but without erosive esophagitis are classified as having endoscopically negative GERD (NERD). In Western countries, the majority of patients with GERD have been reported to have NERD, not erosive esophagitis, even in cases where symptoms are severe. However, the prevalence of NERD has not been investigated in Japan. Therefore, we performed this study to investigate the prevalence of NERD and erosive esophagitis in the Japanese.

MATERIALS AND METHODS

This prospective, randomized, multi-center study was carried out in accordance with the Declaration of Helsinki. We prospectively enrolled in the study 2760 people (mean age 50.4 yr, range 24-84 yr) who visited Masuda Medical Association Hospital, Shimane Institute of Health Science, or Masuda Red Cross Hospital for their annual medical check-ups over the

1-year study period. Individuals with a history of gastric surgery or eradication therapy for *Helicobacter pylori* infection were not included in this study. Patients who had taken proton pump inhibitors or H₂ receptor antagonists in the preceding 2 months were also excluded. After written informed consent for enrollment in this study had been obtained, a precise medical history was taken, followed by a physical examination. GERD symptoms were assessed by the Japanese version of the Carlsson-Dent self-administered questionnaire (QUEST), and upper gastrointestinal endoscopy was performed on all study participants. We defined subjects whose QUEST scores were over 6 as positive for GERD symptoms. Cases with endoscopically proven erosive esophagitis and/or GERD symptoms were defined as having GERD. After the assessment by QUEST, we asked all subjects whether their symptoms were influenced by eating foods such as Japanese sweet cakes and rice cakes (for example, bean-paste buns or baked sweet potato) or sour foods such as orange. The endoscopic findings of esophagitis in the lower esophagus were assessed with the Los Angeles classification, and hiatal hernia and gastric mucosal atrophy were also assessed endoscopically.

Statistical analyses were performed by the chi-squared test for comparison between the groups, and by the Mann-Whitney U test when the Kruskal-Wallis test showed a significant difference. Multiple logistic regression analysis was also performed to calculate odds ratios. Differences at $P < 0.05$ were considered statistically significant.

RESULTS AND DISCUSSION

Of the 2760 subjects investigated, 495 (17.9%) were diagnosed with GERD by the presence of erosive esophagitis and/or GERD symptoms. A total of 195 (7.1% of the total) were endoscopically diagnosed with erosive esophagitis, and 351 (12.7%) had typical GERD symptoms and scored more than 6 on QUEST. Only 51 patients (1.8%) had both erosive esophagitis and typical GERD symptoms. Therefore, 300 of the 351 symptomatic patients

were considered to have NERD. By multiple logistic regression analysis, male gender, presence of hiatal hernia, and mild degree of gastric mucosal atrophy were significant predictive factors for the presence of erosive esophagitis. On the other hand, the presence of hiatal hernia was the only significant predictive factor for the presence of GERD symptoms. When we analyzed the factors that worsened GERD symptoms in symptomatic patients, Japanese sweet cakes and rice cakes worsened GERD symptoms more frequently than did spicy foods.

We demonstrated for the first time that the prevalence of NERD in the Japanese is 10.9%, which is higher than that of erosive esophagitis. The rate of symptomatic GERD is 10% to 30% in Western countries, and more than half of these patients lack endoscopically proven erosive esophagitis. NERD is therefore the most prevalent form of GERD in both Western countries and Japan. The presence of endoscopically identifiable gastric mucosal atrophy is associated with a significant decrease in the basal and stimulated secretion of gastric acid, as repeatedly reported previously. Thus, NERD may be caused by reflux of gastric contents, even if they are not acidic enough to induce erosive esophagitis. In addition, our study confirmed that, even in a country such as Japan, where traditional Oriental foods are eaten, NERD is still the most frequently encountered type of GERD in the non-hospital population.

CONCLUSION

The prevalence of GERD in the Japanese was 17.9%, and 61% of subjects with GERD had NERD. NERD is more frequently found in females than erosive esophagitis. The maintenance of a highly acidic gastric secretion is not necessarily important for the development of NERD. Eating traditional Japanese sweets may worsen GERD symptoms.