

# 学位論文の要旨

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学位論文名 Barrett's Esophagus in Japanese Patients: Its Prevalence, Form and Elongation

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## INTRODUCTION

Barrett's esophagus, which is a well-known acquired condition resulting from gastro-esophageal reflux disease (GERD), is a pre-cancerous condition. The incidence of Barrett's cancer has recently increased not only in the cases with long-segment Barrett's esophagus (LSBE) but also in those with short-segment Barrett's esophagus (SSBE), which is a major type of Japanese case with Barrett's esophagus. However, exact prevalence of SSBE in Japan has not been confirmed and it is also still unknown whether Barrett's esophagus develops gradually over time in patients with GERD. To address these issues, we investigated the change in prevalence and length of Barrett's esophagus over time by newly proposed diagnostic criteria.

## MATERIALS AND METHODS

**Study 1:** From January 2005 to March 2007, we enrolled 5338 patients who received upper gastrointestinal endoscopy. Prevalence and length of endoscopically identified SSBE were evaluated within groups divided on the basis of 10-year age intervals. The factors possibly influencing SSBE length such as acid reflux symptoms, antacid use (proton pump inhibitors or H2 receptor antagonists), endoscopic findings (presence or absence of reflux esophagitis, hiatal

hernia and gastric mucosal atrophy) and *Helicobacter pylori* infection were also evaluated. The criterion for endoscopic diagnosis of Barrett's esophagus was the observation of columnar-appearing mucosa between the squamo-columnar and the esophago-gastric junction. The esophago-gastric junction was defined as the proximal margin of the gastric folds, and the length of Barrett's esophagus was categorized according to Prague C&M criteria. In the present study, the endoscopically detected columnar-appearing mucosa was diagnosed as endoscopic Barrett's esophagus when the mucosa was longer than 5 mm.

**Study 2:** From July 2003 to June 2004, consecutive 500 patients with endoscopically identified SSBE were examined for the presence of specialized columnar epithelium by targeting biopsy. Specialized columnar epithelium was found in 261 out of 500 patients with SSBE. In this group of patients, the length of Barrett's esophagus was measured twice, separated by a 2-year interval, and the change in its length was calculated. The subpopulation consisted of patients who were continuously taking PPI or H2RA and those who never took them during the whole follow-up period. Patients with ambiguous history of PPI or H2RA administration were excluded from the present study. Subsequently, 236 patients (M: F=155:81, median age 68, 24-92) with histologically confirmed SSBE who fulfilled the study protocol were retrospectively enrolled to this follow up study. At the second endoscopy, the endoscopists were blinded to the results of the first endoscopy and the data concerning PPI or H2RA administration of enrolled patients.

## **RESULTS AND DISCUSSION**

**Study 1:** Out of 5338 patients, 1997 (37.4%) with SSBE and 10 (0.2%) with LSBE were endoscopically identified, and 1997 patients with SSBE were enrolled in the present study. The prevalence of endoscopically identified SSBE was significantly higher and its length was significantly longer in the elderly patients with over 70 years old. Multiple regression analysis showed that age ( $t = 2.78, p = 0.011$ ), presence of reflux symptom ( $t = 2.55, p = 0.012$ ), reflux esophagitis ( $t = 2.46, p = 0.006$ ), and hiatal hernia ( $t = 2.55, p = 0.004$ ) were positively correlated

with length of SSBE.

**Study 2:** Analysis of 2-year follow-up study of the histologically confirmed SSBE revealed significant extension of Barrett's length in 28.0% of 236 patients. Presence of reflux symptom (OR 2.18, 95%CI 1.16-4.70) and hiatal hernia (OR 2.11, 95%CI 1.27-3.48) were identified as positive predictors and administration of proton pump inhibitor as a negative predictor of SSBE elongation (OR 0.56, 95%CI 0.33-0.98).

As an alternative to the theory of "upward creeping of Barrett's mucosa," Cameron et al. have proposed the "stem cell" theory that Barrett's esophagus develops following the loss of a long segment of squamous epithelium initiated by reflux-induced ulceration at the esophagogastric junction, and it develops within a short time period with little subsequent change. However, this theory is somewhat controversial. SSBE was found to elongate gradually during two years of follow-up in the present study, supporting the "upward creeping" theory of Barrett's esophagus, although its elongation was very small. Moreover, presence of hiatal hernia and reflux symptom were positive predictors for the extension of SSBE, and PPI but not H2RA administration was a negative one. Neither presence nor grading of reflux esophagitis had a link with the extension of Barrett's esophagus in the present study. These discrepancies may be originated from the different subjects for the analysis, LSBE vs. SSBE.

### **CONCLUSION**

A longer Barrett's esophagus was found in elderly Japanese patients with SSBE, and SSBE elongated in approximately 30% of patients over a two-year period. SSBE may chronologically extend although the elongation was very small. In patients with SSBE, the positive predictors for the axial extension of Barrett's esophagus were presence of hiatal hernia and reflux symptom, and the negative predictor was administration of proton pump inhibitor.