Reflux Esophagitis and *Helicobacter pylori* Infection in Patients with Scleroderma

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**Abstract**

**Objective** This study aimed to evaluate the possible effects of *Helicobacter pylori* (*H. pylori*) infection in reflux esophagitis with scleroderma.

**Patients and Methods** There were a total of 138 patients with scleroderma in our hospital between October 1998 and June 2005. Among these patients, 64 consecutive patients of scleroderma, who did not receive medication for gastrointestinal diseases, underwent endoscopy after informed consent. *H. pylori* was examined using an *H. pylori* IgG ELISA. The endoscopists graded esophageal mucosal breaks according to the Los Angeles Classification of Esophagitis.

**Results** Among the 64 patients, 37 patients (57.8%) were positive for *H. pylori* infection. Reflux esophagitis was observed in 10 of 37 *H. pylori*-positive patients and in 19 of 27 *H. pylori*-negative patients. Significantly fewer *H. pylori*-infected patients had reflux esophagitis than *H. pylori*-negative patients (*p*<0.01). The odds ratio for *H. pylori* infection and reflux esophagitis was 0.16 (95%CI; 0.052-0.47).

**Conclusion** These findings suggest an important role for *H. pylori* infection in reflux esophagitis with scleroderma.

**Key words:** collagen disease, gastroesophageal reflux disease, Los Angeles Classification, endoscopy, *Helicobacter pylori* IgG

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**Introduction**

Scleroderma, which is a collagen disease, causes fibrosis or sclerosing lesions in the skin and internal organs. The gastrointestinal tract is most commonly affected among the internal organs, and peristaltic disorders induced by fibrosis in the smooth muscle are the main cause for developing symptoms in esophagitis (1). Previous reports have shown that reflux esophagitis was observed in 50%-60% of patients with scleroderma (2-4). Esophageal involvement affects 75-90% of patients with scleroderma (5).

This high prevalence of reflux esophagitis associated with scleroderma is due to several factors including a mortality disorder of the upper gastrointestinal tract. The influence of *Helicobacter pylori* (*H. pylori*) infection on reflux esophagitis is still controversial (6-8), and the relationship between *H. pylori* and reflux esophagitis with scleroderma is currently unknown. This study aimed to evaluate the possible effects of *H. pylori* infection in reflux esophagitis with scleroderma.

**Materials and Methods**

**Subjects**

Subjects with a diagnosis of scleroderma were recruited from Saga Medical Hospital between October 1998 and  

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June 2005. Among the 138 patients with scleroderma, patients were excluded from the study if they had received medication for gastrointestinal disease or had a laparotomy. Finally, 64 consecutive patients underwent endoscopy with informed consent. The presence or absence of *H. pylori* infection was confirmed in the subjects who underwent endoscopy. There were 12 males and 52 females who were 24 to 85 years of age, with an average age of 60.7 years. Subjects with *H. pylori* eradication were also excluded from the study. The study was conducted according to the provisions of the Declaration of Helsinki, and all subjects were informed about the basic concept of the present study and of gastrointestinal endoscopy and detection of serum antibody to *H. pylori*.

**Upper endoscopic examination**

Routine upper gastrointestinal examination for the evaluation of reflux esophagitis was performed in this study. Endoscopists graded esophageal mucosal breaks with esophagitis according to the Los Angeles Classification of Esophagitis (9). The criteria for the diagnosis of esophagitis were as follows: grade A, one or more mucosal breaks, each no longer than 5 mm; grade B, at least one mucosal break more than 5 mm long; grade C, at least one mucosal break continuous between the tops of two or more mucosal folds; and grade D, a circumferential mucosal break.

**Detection of serum antibody to *H. pylori***

Serum samples were frozen at -20°C until assayed. Antibodies to *H. pylori* were examined using an *H. pylori* IgG ELISA (HM-CAP; Kyowa Medex, Enteric Products, Inc., Westbury, NY, USA). All samples were measured using the manufacturer’s instructions and results were interpreted as follows: an antibody titer ELISA value (EV) of less than 1.7 was considered negative, an EV of 1.8-2.2 was considered undetermined, and an EV greater than or equal to 2.3 was considered positive.

**Statistical analysis**

Analysis of the relationships between reflux esophagitis and *H. pylori* infection, herniation, gastroesophageal flap valve grading (10), reflux esophagitis in the disease pattern of scleroderma, distribution of age, complications of malignant diseases, treatment of scleroderma, inflammatory findings, smoking, drinking and the disease period of scleroderma was evaluated by χ² test. We used a logistic regression model to compute the odds ratio and the 95% confidence interval (CI). Two-tailed P values <0.05 were considered significant. Statistical analyses were performed using Statview (Version 5.0, SAS Institute Inc., Tokyo, Japan).

**Results**

The overall proportion of esophagitis in the subjects was 45% (29/64). Figure 1 shows the proportions of the grades of reflux esophagitis as evaluated by endoscopy, which were as follows in all 64 subjects according to the Los Angeles classification: grade A, 20% (n=13); grade B, 13% (n=8); grade C, 8% (n=5); grade D, 5% (n=3). Of the 64 patients tested for serum antibody to *H. pylori*, 37 patients (57.8%) were found to have *H. pylori* infection. Of these 37 *H. pylori*-positive patients, reflux esophagitis was observed in 10 patients. According to the Los Angeles classification, 5 patients were defined as grade A, 3 patients as grade B, no patients as grade C, and 2 patients as grade D (Fig. 2). Among 27 *H. pylori*-negative patients, reflux esophagitis was observed in 19 patients. According to the Los Angeles classification, 8 patients were defined as grade A, 5 patients as grade B, 5 patients as grade C, and one patient as grade D. The prevalence of reflux esophagitis among *H. pylori*-positive patients was significantly fewer than that in *H. pylori*-negative patients (P<0.01).
As shown in Table 1, analysis of the relationship between *H. pylori* infection and reflux esophagitis showed a negative correlation (odds ratio; 0.16, 95%CI; 0.052-0.47). The odds ratio for severe esophagitis (grades C and D) was 0.10 (95%CI; 0.017-0.56), which was lower compared to the odds ratio of mild esophagitis (grades A and B, odds ratio; 0.18, 95%CI; 0.06-0.60). There was no relationship between age distribution and *H. pylori* infection because there were only a small number of subjects.

There was no association of reflux esophagitis with herniation (p=0.08), gastroesophageal flap valve grading (11) (p=0.10), reflux esophagitis in the disease pattern of scleroderma (diffuse cutaneous or limited cutaneous, p=0.18), distribution of age (p=0.71), complications of malignant diseases (p=0.80), use of corticosteroids (p=0.30), inflammatory findings (p=0.43), smoking (p=0.95), drinking (p=0.25) or disease period of scleroderma (p=0.59, Table 2).

**Discussion**

*H. pylori* infection causes many gastric diseases, including chronic gastritis, peptic ulceration, gastric lymphomas and gastric cancer (11-13). The influence of *H. pylori* infection on reflux esophagitis with scleroderma is still controversial (6-8). According to previous reports, scleroderma patients have an accelerated frequency of *H. pylori* infection com-
pared to the average incidence of gastric *H. pylori* in white, healthy, asymptomatic subjects (14-16). Another report showed that scleroderma patients have a higher incidence of IgG antibodies to *H. pylori* compared to the general population in Japanese people (17). However, there are no reports about the relationship between *H. pylori* infection and reflux esophagitis associated with scleroderma. This study showed that *H. pylori* infection decreased the risk of reflux esophagitis in scleroderma patients.

Although the effect of *H. pylori* infection on reflux esophagitis is controversial, studies from Japan have demonstrated a negative correlation between *H. pylori* infection and the presence of reflux esophagitis (18-21). These studies indicated that a decrease in gastric acid secretion with *H. pylori* infection-induced gastritis was the main mechanism of reduced prevalence in reflux esophagitis. A meta-analysis of 20 observational studies examining the association between *H. pylori* and gastro-esophageal reflux disease symptoms was published in 2003, which included twenty studies with 4,134 subjects (22). This meta-analysis showed a 38.2% prevalence of *H. pylori* in gastro-esophageal reflux disease subjects, compared with 49.5% in subjects without gastro-esophageal reflux disease (22). In the same study, the pooled odds rate was 0.60 (95% confidence interval; 0.47 to 0.78) (22). In another cohort study, 6,125 patients with gastro-esophageal reflux disease were recruited, in which multivariate logistic regression identified the characteristics of erosive and non-erosive esophagitis (23). Independent predictors of erosive esophagitis were males (odds rate: 1.5), increased body mass index (BMI; odds rate: 1.4), regular alcohol intake (odds rate: 1.3), duration of disease (odds rate: 1.2), and *H. pylori* (odds rate: 0.85). The protective effect of *H. pylori* was greater in the subgroup analysis of patients with more severe Los Angeles C and D disease (odds rate: 0.61) (23).

In this study, *H. pylori* infection was more protective in scleroderma patients with grades C and D compared to grades A and B. We evaluated the effect of several factors on reflux esophagitis. There were no significant differences for reflux esophagitis and the disease pattern of scleroderma (diffuse cutaneous or limited cutaneous), distribution of age, complications of malignant diseases, use of corticosteroids, inflammatory findings, smoking, drinking or disease period of scleroderma.

Previous studies have indicated that motility disorders in scleroderma are the main reason for developing reflux esophagitis (24-27). The current study did not evaluate motility disorders directly. However, hiatus herniation and gastroesophageal flap valve grading, which might be caused by motility disorders, were not correlated with reflux esophagitis in scleroderma.

In conclusion, our results indicate that *H. pylori* infection plays an important role in the prevalence of endoscopic reflux esophagitis associated with scleroderma in Japan. The infection rate of *H. pylori* in Japan decreases in an age-related manner (28, 29), which might change the morbidity state of reflux esophagitis in scleroderma.

References


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