A Study on the Relationship between Reflux Esophagitis and Periodontitis

Kyoichi Adachi¹, Tomoko Mishiro¹, Shino Tanaka¹, Hiroo Yoshikawa² and Yoshikazu Kinoshita³

Abstract

Objective Metabolic syndrome and dental erosion have been demonstrated to correlate with gastro-esophageal acid reflux disease (GERD), while periodontitis has been reported to have a positive relationship with metabolic syndrome. However, no correlation between periodontitis and GERD has yet been reported. We therefore investigated the relationship between periodontitis and GERD.

Methods The subjects consisted of 280 individuals who visited the Health Center for a detailed medical checkup examination. Each underwent upper endoscopy and periodontitis examinations, with the latter performed by measuring the concentrations of lactate dehydrogenase and hemoglobin in saliva. The subjects were divided into those with positive and negative periodontitis findings, and the prevalence rates of endoscopically proven reflux esophagitis, dyslipidemia, hypertension, and hyperglycemia were compared.

Results The number of subjects positive for periodontitis was 93, while 187 had negative findings. The prevalence of reflux esophagitis was not different between the positive and negative groups (8.6% vs. 8.0%). In addition, a multiple logistic regression analysis did not identify a positive relationship between the presence of periodontitis and reflux esophagitis. On the other hand, dyslipidemia and hypertension were more frequently observed in the subjects that were positive for periodontitis.

Conclusion We did not find an association between periodontitis and reflux esophagitis in the present study. On the other hand, the presence of periodontitis was found to correlate with hypertension and dyslipidemia.

Key words: gastro-esophageal reflux disease, reflux esophagitis, periodontitis, hypertension, dyslipidemia


Introduction

Gastroesophageal reflux disease (GERD) is characterized by the presence of esophageal mucosal injury or reflux symptoms caused by an abnormal reflux of the gastric contents into the esophagus (1, 2). An increased gastroesophageal pressure gradient and hiatal hernia development have been reported to be induced by a high intra-abdominal pressure due to abdominal fat accumulation (3-7), while obesity and a high body mass index (BMI) have repeatedly been demonstrated to be associated with the high prevalence of reflux esophagitis and GERD symptoms (8-15). In addition, metabolic syndrome, diagnosed by the presence of visceral fat accumulation, dyslipidemia, hypertension, and hyperglycemia, has been demonstrated to correlate with the occurrence of GERD (16-18).

Periodontitis is a common low-grade chronic inflammatory disease of microbial origin that affects humans and results in destruction of the tooth supporting apparatus. Signs and symptoms include swollen gums, deepening of gingival crevices leading to the formation of periodontal pockets, bleeding on brushing, increased spacing between teeth, and loose teeth. Recent studies have indicated that periodontitis is closely correlated with systemic disorders, such as obesity, metabolic syndrome and cardiovascular diseases (19, 20), which have also been demonstrated to have a positive relationship with GERD occurrence (3-18). In addi-

¹Health Center, Shimane Environment and Health Public Corporation, Japan, ²Shimane Dental Association, Japan and ³Second Department of Internal Medicine, Shimane University Faculty of Medicine, Japan

Received for publication November 26, 2015; Accepted for publication January 13, 2016

Correspondence to Dr. Kyoichi Adachi, adachi@kanhokou.or.jp
tion, periodontitis may induce or worsen GERD, since saliva secretion, which is influenced by oral hygiene including the periodontal status, has been demonstrated to be associated with GERD (21-23). Reflux of the gastric acidic contents into the oral cavity may also affect the local bacterial flora and the status of periodontitis, since several investigators have reported a close correlation between dental erosion and gastroesophageal acid reflux (24-27). However, the relationship between periodontitis and GERD has not been determined. In the present study, we investigated the relationship between the presence of periodontitis and endoscopically proven reflux esophagitis.

**Materials and Methods**

The subjects were individuals who visited the Health Center of Shimane Environment and Health Public Corporation for a detailed medical checkup examination between April 2014 and March 2015. The majority were socially active and productive, and considered to be socioeconomically middle class. Those with a history of gastric surgery were excluded from this study. Subjects who had taken medications, such as proton pump inhibitors and H2 receptor antagonists, were also excluded. As a result, 280 subjects (males 191, females 89; mean age 52.0 years) were examined simultaneously by the use of upper GI endoscopy and a screening test for periodontitis.

The body mass index (BMI) was calculated for all study subjects. We also evaluated the presence of dyslipidemia (LDL-cholesterol ≥140 mg/dL, HDL-C level <40 mg/dL, and/or triglyceride ≥150 mg/dL, or specific treatment for these lipid abnormalities), hypertension (systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg, or treatment of previously diagnosed hypertension), and hyperglycemia (fasting plasma glucose ≥126 mg/dL and/or HbA1c ≥6.5% or specific treatment for diabetes mellitus). The values for high-sensitivity C-reactive protein (HsCRP) and the peripheral leucocyte count were also assessed to estimate low grade inflammation.

All upper endoscopic examinations were performed by licensed experienced endoscopists (K.A., T.M., S.T.) using either an EG-530NW or EG-530NP endoscope (Fujifilm, Tokyo, Japan). The endoscopic findings in the lower esophagus were assessed using the Los Angeles (LA) classification (28) and patients with a grade of A, B, C, or D were diagnosed as positive for reflux esophagitis. The diametrical hiatus was assessed during endoscopic observation by comparing the width of the cardiac opening with the diameter of the shaft used for endoscopy at the cardiac portion, and the presence of a hiatal hernia was defined as positive when the size of the diametrical hiatus was 1.0 cm or greater. The degree of gastric mucosal atrophy was endoscopically evaluated using the classification of Kimura and Takemoto, according to which gastric mucosal atrophy was classified into six groups (C1, C2, C3, O1, O2, O3) (29). The degree of endoscopically evident gastric mucosal atrophy in all study subjects was simultaneously reviewed and determined by the same three licensed experienced endoscopists. For this study, we defined C1-C2 as mild, C3-O1 as moderate, and O2-O3 as severe gastric mucosal atrophy.

There are several methods to diagnose the degree of periodontitis. Symptoms, such as gingival bleeding, are helpful to identify the presence of periodontitis. However, the status of periodontium should be examined to diagnose periodontitis. Presently, dentists typically diagnose the degree of periodontitis by the community periodontal index (CPI) method. In CPI method, periodontal pocket probing depth is examined and the degree of periodontitis is determined by gingival bleeding, presence of tartar and depth of periodontal pocket. However, this method requires time, can be troublesome, and it is also occasionally not reliable, thus making it unsuitable for a large number of subjects (30-33). Recently, several biomarkers in saliva, such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), creatinine, blood urea nitrogen (BUN), urea and hemoglobin (Hb), have been demonstrated to be useful to evaluate the periodontal status (30-33). In this study, the concentrations of LDH and Hb in saliva were used to examine the periodontal status, since saliva concentrations of LDH and Hb have been demonstrated to correlate with the degree of periodontitis measured by the CPI method (32, 33). LDH and Hb concentrations in saliva are considered to reflect the degree of destruction of periodontal tissue and the grade of gingival bleeding due to periodontitis, respectively (32). In brief, saliva was collected after fasting by asking the subjects to chew an exclusive gum for 5 minutes and spit as necessary into a collection cup as part of a saliva collecting kit (Eiken Chemical, Tokyo, Japan). The concentrations of LDH and Hb in the collected saliva samples were examined using automatic chemical analyzers (LDH: Labospect 008, Hitachi High-Technologies, Tokyo, Japan; Hb: Diana OC-sensor, Eiken Chemical) according to the manufacturer’s instructions. A saliva concentration of LDH ≥350 U/L and/or Hb ≥2 μg/mL was defined as positive for periodontitis by the Shimane Dental Association based on the results of previous studies (31-33).

The status of *H. pylori* infection, including a past history of successful eradication therapy, in each subject was also determined by examining medical records. Individuals with post-eradication for *H. pylori* were included in *H. pylori*-positive cases in this study.

Statistical analyses were performed using chi-squared, Fisher’s exact, Mann-Whitney U, and Kruskal-Wallis tests, and a multiple logistic regression analysis. All calculations were performed using the Stat View 5.0 software program (Abacus Concepts, Berkeley, USA) for Macintosh, with differences of *p*<0.05 considered to be statistically significant.

This study was performed in accordance with the Declaration of Helsinki and the protocol was approved by the ethics committee of the Shimane Environment and Health Public Corporation. Written informed consent indicating that the clinical data would be used for a clinical study without the
Dyslipidemia and hypertension were more frequently observed in the positive group. There was no significant difference for the prevalence of hyperglycemia between positive and negative subjects, while the HsCRP value and the peripheral leucocyte count in the positive group were significantly higher.

The status of *H. pylori* infection could be determined in 228 of the 280 study subjects. The percentage of subjects that had a positive finding for the periodontitis test in *H. pylori*-positive cases tended to be higher than that in *H. pylori*-negative ones (Table 2).

The odds ratios for prevalence of reflux esophagitis as shown by a multiple logistic regression analysis are presented in Table 3. A high BMI was shown to be a significant predictive factor for the presence of reflux esophagitis. Furthermore, a male gender, the presence of hiatal hernia, habitual drinking, habitual smoking, hiatal hernia, and mild gastric mucosal atrophy were considered to be risk factors for the presence of reflux esophagitis, though the difference did not reach the level of statistical significance. There was no significant relationship found between the presence of periodontitis and occurrence of reflux esophagitis.

### Discussion

The occurrence of GERD, which is caused by an abnormal reflux of the gastric contents into the esophagus, is affected by multiple factors, including gastric acid secretion, the presence of a hiatal hernia, a lower esophageal sphincter (LES) function, esophageal motility, and esophageal perception (1, 2). Lifestyle factors, such as eating foods with high components of fat or in large portions, alcohol intake, smoking, obesity, and metabolic syndrome, have also been reported to be related to a high prevalence of reflux esophagitis and GERD symptoms (8-18). In addition, the factors shown to induce and/or worsen GERD have also been demonstrated to be associated with periodontitis.

Saliva promotes esophageal acid clearance not only by eliciting swallowing, but also by enhancing washout, dilution, and acid neutralization. Indeed, salivation secretion in patients with reflux esophagitis has been found to be lower than in normal control subjects (21-23). Therefore, poor oral hygiene in relation to periodontitis is considered to increase the occurrence of GERD, as it is one of the most important causes of hypo-salivation.

In the present study, we investigated the relationship between reflux esophagitis and the presence of periodontitis as served in the positive group. There was no significant difference for the prevalence of hyperglycemia between positive and negative subjects, while the HsCRP value and the peripheral leucocyte count in the positive group were significantly higher.

### Results

The number of subjects positive for periodontitis was 93, while 187 were negative. The subject characteristics are shown in Table 1. Those who were positive for the periodontitis test were significantly older. The prevalence of reflux esophagitis was not different between the positive and negative subjects (8.6% vs. 8.0%), whereas the degree of endoscopic gastric mucosal atrophy in the positive subjects was significantly higher. The following factors including gender, BMI, habitual smoking, habitual drinking, and presence of hiatal hernia were not different between the groups. Dyslipidemia and hypertension were more frequently observed in the positive group. There was no significant difference for the prevalence of hyperglycemia between positive and negative subjects, while the HsCRP value and the peripheral leucocyte count in the positive group were significantly higher.

The status of *H. pylori* infection could be determined in 228 of the 280 study subjects. The percentage of subjects that had a positive finding for the periodontitis test in *H. pylori*-positive cases tended to be higher than that in *H. pylori*-negative ones (Table 2).

The odds ratios for prevalence of reflux esophagitis as shown by a multiple logistic regression analysis are presented in Table 3. A high BMI was shown to be a significant predictive factor for the presence of reflux esophagitis. Furthermore, a male gender, the presence of hiatal hernia, habitual drinking, habitual smoking, hiatal hernia, and mild gastric mucosal atrophy were considered to be risk factors for the presence of reflux esophagitis, though the difference did not reach the level of statistical significance. There was no significant relationship found between the presence of periodontitis and occurrence of reflux esophagitis.

### Discussion

The occurrence of GERD, which is caused by an abnormal reflux of the gastric contents into the esophagus, is affected by multiple factors, including gastric acid secretion, the presence of a hiatal hernia, a lower esophageal sphincter (LES) function, esophageal motility, and esophageal perception (1, 2). Lifestyle factors, such as eating foods with high components of fat or in large portions, alcohol intake, smoking, obesity, and metabolic syndrome, have also been reported to be related to a high prevalence of reflux esophagitis and GERD symptoms (8-18). In addition, the factors shown to induce and/or worsen GERD have also been demonstrated to be associated with periodontitis.

Saliva promotes esophageal acid clearance not only by eliciting swallowing, but also by enhancing washout, dilution, and acid neutralization. Indeed, salivation secretion in patients with reflux esophagitis has been found to be lower than in normal control subjects (21-23). Therefore, poor oral hygiene in relation to periodontitis is considered to increase the occurrence of GERD, as it is one of the most important causes of hypo-salivation.

In the present study, we investigated the relationship between reflux esophagitis and the presence of periodontitis as

### Table 1. Characteristics of the Subjects with and without Periodontitis.

<table>
<thead>
<tr>
<th>Periodontitis test</th>
<th>Positive</th>
<th>Negative</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>93</td>
<td>187</td>
<td>0.349</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>60/33</td>
<td>131/56</td>
<td>0.283</td>
</tr>
<tr>
<td>Age (years)</td>
<td>54.0±0.8</td>
<td>50.9±0.8</td>
<td>0.002</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.2±0.4</td>
<td>22.5±0.2</td>
<td>0.283</td>
</tr>
<tr>
<td>Habitual drinking</td>
<td>54 (58.1)</td>
<td>97 (51.9)</td>
<td>0.327</td>
</tr>
<tr>
<td>Habitual smoking</td>
<td>9 (9.7)</td>
<td>17 (9.1)</td>
<td>0.874</td>
</tr>
<tr>
<td>Reflux esophagitis</td>
<td>8 (8.6)</td>
<td>15 (8.0)</td>
<td>0.868</td>
</tr>
<tr>
<td>Hiatal hernia</td>
<td>22 (23.7)</td>
<td>36 (19.3)</td>
<td>0.392</td>
</tr>
<tr>
<td>Gastric mucosal atrophy*</td>
<td>66 (71.0)</td>
<td>156 (83.4)</td>
<td>0.015</td>
</tr>
<tr>
<td>moderate &amp; severe</td>
<td>27 (29.0)</td>
<td>31 (16.5)</td>
<td>0.015</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>53 (57.0)</td>
<td>82 (43.9)</td>
<td>0.038</td>
</tr>
<tr>
<td>no therapy</td>
<td>38 (40.9)</td>
<td>69 (36.9)</td>
<td>0.007</td>
</tr>
<tr>
<td>with therapy</td>
<td>15 (16.1)</td>
<td>13 (7.0)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Hypertension</td>
<td>31 (33.3)</td>
<td>35 (18.7)</td>
<td>0.142</td>
</tr>
<tr>
<td>no therapy</td>
<td>14 (15.1)</td>
<td>13 (7.0)</td>
<td>0.007</td>
</tr>
<tr>
<td>with therapy</td>
<td>17 (18.3)</td>
<td>22 (11.8)</td>
<td>0.142</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>8 (8.6)</td>
<td>8 (4.3)</td>
<td>0.142</td>
</tr>
<tr>
<td>no therapy</td>
<td>3 (3.2)</td>
<td>3 (1.6)</td>
<td>0.142</td>
</tr>
<tr>
<td>with therapy</td>
<td>5 (5.4)</td>
<td>5 (2.7)</td>
<td>0.142</td>
</tr>
<tr>
<td>HsCRP (mg/dL)</td>
<td>0.117±0.021</td>
<td>0.062±0.010</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Leucocyte count (×10³/μL)</td>
<td>5.554±0.181</td>
<td>4.724±0.075</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Cases with *H. pylori* positive included 23 post-eradicated subjects. Values in parentheses indicate the percentages in *H. pylori* positive and negative subjects.

### Table 2. Status of Helicobacter pylori Infection and Periodontitis.

<table>
<thead>
<tr>
<th>Periodontitis test</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>H. pylori</em>-negative (n=140)</td>
<td>45 (32.1)</td>
<td>95 (67.9)</td>
</tr>
<tr>
<td><em>H. pylori</em>-positive* (n=88)</td>
<td>36 (40.9)</td>
<td>52 (59.1)</td>
</tr>
</tbody>
</table>

*Odds ratio calculated in comparison to subjects with mild atrophy.

### Table 3. Odds Ratios for the Prevalence of Reflux Esophagitis (multiple Logistic Regression Analysis).

<table>
<thead>
<tr>
<th>Odds ratio</th>
<th>95%CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male)</td>
<td>7.549</td>
<td>0.942-60.524</td>
</tr>
<tr>
<td>Age (1-year increments)</td>
<td>0.979</td>
<td>0.924-1.038</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>1.171</td>
<td>1.013-1.353</td>
</tr>
<tr>
<td>Habitual drinking</td>
<td>1.392</td>
<td>0.498-3.894</td>
</tr>
<tr>
<td>Habitual smoking</td>
<td>1.626</td>
<td>0.472-5.599</td>
</tr>
<tr>
<td>Hiatal hernia</td>
<td>1.600</td>
<td>0.603-4.248</td>
</tr>
<tr>
<td>Gastric mucosal atrophy* (moderate &amp; severe)</td>
<td>0.430</td>
<td>0.110-1.676</td>
</tr>
<tr>
<td>periodontitis</td>
<td>1.043</td>
<td>0.387-2.811</td>
</tr>
</tbody>
</table>

*Odds ratio calculated in comparison to subjects with mild atrophy.
diagnosed by a saliva test. Unfortunately, our results did not demonstrate a significant relationship between those, even after performing a multiple logistic regression analysis, for which we do not have any definitive explanation. Other factors besides salivation may affect the relationship between GERD and periodontitis. To resolve this issue, the influence of therapy for periodontitis on GERD prevalence should be investigated in collaboration with dentists in a future study. Several investigators have reported that dental erosion is correlated with the prevalence of GERD (24-27). Therefore, the relationship with GERD associated dental erosion is considered to be different than that between GERD and periodontitis, though those may have some effect on each other.

Recent studies have demonstrated that periodontitis is well correlated with the occurrence of lifestyle-associated systemic disorders, such as obesity, metabolic syndrome, and cardiovascular disease (19, 20), while the present results also showed that obesity, dyslipidemia, and hypertension were more frequently observed in subjects with periodontitis as compared to those without periodontitis. The precise mechanism of the association between periodontitis and systemic disorders has not been determined. Low grade persistent inflammation caused by periodontitis has been reported to produce inflammatory cytokines, such as tumor-necrosis factor-alpha and interleukin 6, from monocytes and macrophages, and these inflammatory cytokines are considered to induce several systemic disorders (19, 20, 34-36). Indeed, higher HsCRP and peripheral leucocyte counts were observed in our subjects who were positive in the periodontitis test. It was proposed that periodontitis is not only associated with the severity of lipid metabolism, but it also aggravates dyslipidemia via the up-regulation of serum and gingival inflammatory cytokines (37). In addition, systemic inflammation induced by periodontitis perpetuates atherosclerosis by impairing the elastic properties of the large arteries and thereby inducing a hypertensive state (38).

One of the interesting findings of this study is that the degree of endoscopic gastric mucosal atrophy in subjects with periodontitis was significantly higher as compared to those without. To our knowledge, the positive relationship between periodontitis and gastric mucosal atrophy was demonstrated for the first time in this study. In addition, the individuals with a positive finding for the periodontitis test were more frequently observed in H. pylori-positive cases as compared to H. pylori-negative ones, though no statistical significance was observed due to the small number of study subjects. Continuous H. pylori infection is a main cause of gastric mucosal atrophy and nearly all Japanese individuals with gastric mucosal atrophy are considered to be infected by H. pylori. In addition, eradication therapy for H. pylori infection was likely performed after long-term H. pylori infection in nearly all of the post-eradicated cases, since the original infection generally occurs during childhood (39-42). Several investigators have detected H. pylori in dental plaque and saliva, and also showed that periodontal pockets ≥5 mm in depth are associated with increased odds of H. pylori sero-

positivity (43-46). Therefore, long-term H. pylori infection is considered to cause not only gastric mucosal atrophy, but also periodontitis. It has been demonstrated that H. pylori infection induces several systemic disorders, such as dyslipidemia, hyperglycemia, and several types of cardiovascular disease (47-52), thus their occurrence may be affected by long-term continuous inflammation caused by H. pylori-induced gastritis and periodontitis.

There are several limitations associated with our study. It was not performed in a population-based manner, since the study subjects were individuals who visited a medical center for a medical checkup and a test was required for the diagnosis of periodontitis. In addition, the number of subjects was relatively small. Thus, our results should be confirmed by an additional large scale study. In this study, we investigated the concentrations of LDH and Hb in collected saliva for the diagnosis of periodontitis, and the presence of dental erosions was not examined. Therefore, further study with the collaboration of dentists is needed to more clearly determine the relationships among GERD occurrence, periodontitis and dental erosions.

In conclusion, we did not find a positive association between periodontitis and the prevalence of reflux esophagitis, though the presence of periodontitis was shown to be correlated with the occurrence of lifestyle-associated diseases, such as hypertension and dyslipidemia.

The authors state that they have no Conflict of Interest (COI).

References


