# 学位論文の要旨

氏名 渡邊 正章

学 位 論 文 名 Oral Soft Tissue Disorders are Associated with Gastroesophageal Reflux Disease: Retrospective Study

 発表
 雑誌
 名
 BMC Gastroenterology

 (巻,初頁~終頁,年)
 (17,92,2017)

著 名 Masaaki Watanabe, Eiji Nakatani, Hiroo Yoshikawa,

Takahiro Kanno, Yoshiki Nariai, Aya Yoshino, Michael Vieth,

Yoshikazu Kinoshita, Joji Sekine

# 論文内容の要旨 INTRODUCTION

Salivary flow volume and swallowing function in gastroesophageal reflux disease (GERD) were revealed to be significantly reduced in our preliminary study. According to the Montreal Definition and Classification of GERD, dental erosion (DE) is a major oral symptom caused by acid reflux in patients with GERD. In our previous study, we found that DE, as an extraoesophageal symptom of GERD, was caused by acid reflux, which resulted in reduced salivary flow volume and swallowing function.

The oral cavity consists of teeth, periodontal tissue including gingiva and other oral mucosal regions. The oral cavity disorders include dental caries, periodontal diseases including gingivitis and periodontitis, and inflammatory oral mucosal regions such as redness, erosion, and ulcer. Although we have already revealed the relationships between DE and GERD in our previous preliminary study, complete edentulous patients are included in the GERD patients. Understandably, DE is not in the edentulous GERD patients. Then, we focused on oral soft tissues to detect the edentulous GERD patients from oral findings. Oral soft tissue disorders (OSTDs) were defined as gingivitis and inflammatory oral mucosal regions. Few studies have evaluated and discussed these co-relationships between OSTDs and GERD. OSTDs are not mentioned as the extraesophageal syndromes of GERD in the Montreal Definition and Classification.

We hypothesized that OSTDs would be related to GERD. This retrospective clinical study aimed to evaluate the prevalence of OSTDs in GERD patients in the context of salivary flow volume and swallowing function, to test the above hypothesis.

### MATERIALS AND METHODS

# **Participants characteristics**

GERD outpatients were consecutively selected from the Department of Internal Medicine, Shimane University Hospital between February 2009 and March 2015. A GERD diagnosis was made based in the presence of typical reflux symptoms, such as heartburn and acid regurgitation that occurred more than twice weekly, according to the Montreal definition of GERD. A gastrointestinal fiberscope (GIF) procedure was performed to detect the possible presence of mucosal breaks. GERD patients were divided into two groups, which included a non-erosive reflux disease (NERD) group and a reflux oesophagitis (grades A–D by the Los Angeles classification) group based on the endoscopy findings. Control groups were outpatients without symptoms or medical histories of gastrointestinal or respiratory system disorders and volunteered in the Department of Oral and Maxillofacial Surgery, Shimane University Hospital, between February 2009 and March 2015. The control group was divided into older and younger subgroups. The older controls were set as the age-matched with GERD patients. Because aging affects the results of oral examinations, the younger controls were also set.

#### **Oral examination**

GERD patients (105 cases), older and younger controls (25 cases each) were retrospectively examined for oral symptoms, salivary flow volume (Saxon test), swallowing function (repetitive saliva swallowing test [RSST]), teeth (decayed, missing, and filled [DMF] indices), and soft tissues (as evaluation of OSTDs, gingivitis; papillary, marginal, and attached [PMA] gingival indexes, simplified oral hygiene indices [OHI-S], and inflammatory oral mucosal regions).

# **Clinical history**

Clinical histories, which included body mass index [BMI], the existence of alcohol and tobacco use, and bruxism, were also investigated. The relationships between GERD grading, NERD and reflux oesophagitis via the Los Angeles classification: (grades A-D), and results of the evaluated variables were also compared.

#### Statistical analysis

Continuous and categorical variables were summarized by mean  $\pm$  standard deviation (SD) and frequency (and percent), respectively. To compare continuous variables the between two and three groups, Wilcoxon rank-sum test and Kruskal-Wallis test were performed, respectively. Fisher's exact test was performed for comparison of categorical variables. A P value of < 0.05 was defined as statistically significant. All statistical analyses were performed using SAS® version 9.3 (Cary, NC, USA) and R version 3.2.2 (R Foundation, Vienna, Austria).

The study protocol was approved by the Ethics Committee of Shimane University and written informed consent was obtained from all subjects.

# **RESULTS AND DISCUSSION**

# **Participants characteristics**

GERD patients, older and younger controls participated and aged  $66.4 \pm 13.0$ ,  $68.3 \pm 8.2$  and  $28.7 \pm 2.6$  years old, respectively.

#### **Oral examination**

The most common oral symptom in the GERD patients was oral dryness. Salivary flow volume and swallowing function in the GERD patients were significantly lower than in either of the controls (all P < 0.05). The DMF indices, as a measure of dental caries, in the GERD patients were higher than in the younger controls (P < 0.001), but lower than in the older controls (P = 0.033). The PMA gingival indexes, as a measurement for gingival inflammation, and OHI-S, as a measure for oral hygiene, in the GERD patients were significantly higher than in either of the controls (all P < 0.05). Inflammatory oral mucosal regions were found only in the GERD patients. The numbers of NERD and reflux oesophagitis (grade A–D) instances were 62 and 43, respectively. No significant difference was found in any of the evaluated items by GERD grading. Notably, inflammation severity in the oral mucosa and esophagus showed negative correlations.

### **Clinical history**

Though no significant differences in BMI, the existence of alcohol and tobacco use were found, bruxism, as an exacerbation factor of periodontal disease, in the GERD patients was significantly more frequent than in either control group (P = 0.041).

## Relationship between OSTDs and GERD

OSTDs were observed as one of the oral symptoms in the GERD patients. Salivary flow volume in the GERD patients was significantly reduced, as was observed in our preliminary study, which suggested that this was a cause for the oral dryness. Swallowing function in the GERD patients was also significantly reduced. The refluxing gastric acid may be induced by both of reduced salivary flow volume and swallowing function. OSTDs were induced by damage from gastric acid reflux, similar to DE. The saliva prevents the oral infection by antimicrobial action, cleansing and maintaining mucosal integrity. Therefore, OSTDs were also induced by reduced salivary flow volume. Furthermore, the GERD patients showed a significantly higher frequency of bruxism than the controls. Therefore, gingivitis in some GERD patients may be accelerated by bruxism. The bruxism can also be co-cause of inflammatory oral mucosal regions.

#### CONCLUSION

OSTDs were associated with GERD, similar to what was observed for DE.