Prevalence of Laryngopharyngeal Reflux Symptoms: Comparison between Health Checkup Examinees and Patients with Otitis Media

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Abstract

Objective. To investigate the prevalence of laryngopharyngeal reflux (LPR) symptoms in health checkup examinees and in patients with otitis media with effusion (OME) of undetermined etiology and the significance of age, body mass index (BMI), and pepsinogen (PG) concentration in middle ear effusions (MEEs).

Study Design. Cross-sectional study.

Setting. Health checkup and private clinics.

Subjects and Methods. A total of 410 subjects who had undergone a health checkup were asked to respond to the reflux symptom index (RSI) to identify the distribution of the RSI score, and the results were compared with 62 patients with OME by BMI and PG concentration in the MEEs.

Results. The RSI-positive (score >13) rate was 7.1% in the health checkup examinees. The highest rate was observed in men in their 40s, who had the highest average BMI. None of the men in their 80s were RSI positive. The RSI-positive rate in patients with OME was 21.0%. None of the male patients ≥70 years of age were RSI positive, whereas the average PG concentration was significantly higher in this group.

Conclusion. The prevalence of LPR symptoms evaluated by the RSI was significantly higher in OME patients than in the health checkup examinees; however, a similar pattern in which LPR symptoms were prominent in middle-aged men with a high BMI and much less in elderly men was observed. Middle-aged men with a high BMI might be diagnosed as having LPR disease based on the relevant symptoms. LPR findings would be more sensitive than symptoms in elderly men.

Keywords
laryngopharyngeal reflux, health checkup, otitis media with effusion, body mass index, pepsinogen

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Supraesophageal reflux of gastric contents, known as laryngopharyngeal reflux (LPR), induces several manifestations in the otorhinolaryngologic region, such as laryngopharyngeal reflux disease (LPRD), including laryngitis, pharyngitis, sinusitis, obstructive sleep apnea syndrome, and otitis media. Gastroesophageal reflux disease (GERD) is defined as a condition that develops when the reflux of stomach contents causes troublesome symptoms and/or complications,1 and a relationship between GERD and LPRD has been suggested.2,3 Reflux laryngitis is defined as an established part of the extraesophageal syndrome of GERD, but no confirmed data indicate that GERD is a clinically significant contributor to pharyngitis or otitis media.1

Quality of life (QOL) has been reported to decrease in patients with LPRD,4,5 and adequate diagnosis and treatment are necessary to improve QOL in patients with reflux-related disease. It is difficult to apply a gold-standard examination to detect the presence of reflux, such as endoscopy of the upper gastrointestinal tract or 24-hour pH monitoring, for all subjects in whom reflux is suspected. For the assessment of symptoms in patients with LPR, use of the reflux symptom
index (RSI) proposed by Belafsky et al\textsuperscript{6} has been widely reported.\textsuperscript{2,3,7-10} The exact sensitivity and specificity of RSI were not described in the original study, but the mean pretreatment RSI was reported to be significantly higher in patients with LPR than in controls, and the mean RSI of patients with LPR after 6 months of PPI therapy approached that of asymptomatic controls.\textsuperscript{6} The RSI has been reported to have a highly significant correlation with the severity of GERD\textsuperscript{5} or LPR findings.\textsuperscript{10}

Previous studies have shown that GERD symptoms were prevalent in adult patients with otitis media with effusion (OME) of undetermined etiology.\textsuperscript{11,12} However, sensitivity to gastric reflux in the supragesophageal portion is different from that in the esophagus, and symptoms in patients with LPRD would not be the same as in those with GERD.\textsuperscript{5} It is necessary to conduct a survey using LPR-specific tools, such as the RSI, to search for a relationship between reflux and OME.

This study was planned to investigate the prevalence of LPR symptoms among health checkup examinees using the RSI, to identify the distribution of symptoms, and to compare the results with those in patients with OME of undetermined etiology.

**Subjects and Methods**

**Health Checkup Examinees**

The subjects were derived from the participants of the Yakumo Study,\textsuperscript{13} where an annual health checkup for research purposes has been provided to the inhabitants of Yakumotown, Hokkaido, Japan, since 1982. Yakumo is a rural town with a population of 20,000, where roughly equal numbers of inhabitants work in fishing, dairy farming, or commerce. Of the 593 apparently healthy inhabitants who attended the health checkup, 410 subjects (153 men and 257 women, aged 40-89 years, mean age 64.0 years) responded to a questionnaire including 9 items, and their RSI scores were evaluated. The RSI items were translated into Japanese. Each item was scaled from 0 (no problem) to 5 (severe problem) according to the original study,\textsuperscript{6} and an RSI score of greater than 13 was considered to indicate LPR (RSI positive). Questionnaire data were evaluated by the subjects’ sex, age, and body mass index (BMI).

**Patients with OME**

A total of 62 patients with OME of undetermined etiology (31 men and 31 women; age range 26-91 years; mean age 63.6 years), who consulted the authors’ private clinics, were recruited into this study. Otitis media with effusion was diagnosed by otoscopic examination and tympanometry. Those with identified etiologies for OME, such as acute otitis media, acute or chronic sinusitis, common cold, or air travel, and those with other otorhinolaryngological conditions were excluded. These conditions also included episodes of recent infection in the upper respiratory tract within months, irradiation to the head and neck, and allergic or immunological reactions.

Patients were asked to complete the RSI questionnaire. A middle ear effusion (MEE) sample was obtained from each subject by fine-needle aspiration, and the concentration of pepsinogen (PG) in the supernatants of these samples was measured using a chemiluminescence enzyme immunoassay kit, with a modified technique described in detail elsewhere.\textsuperscript{12} Briefly, samples were incubated with a pretreatment solution at 37°C. After incubation, the mixture was placed in an automated analyzer that facilitated the antigen-antibody reaction. Reactions were detected by enhanced chemiluminescence and quantified by the analyzer. The measurement was performed by an outside contractor (SRL, Tokyo, Japan). The questionnaire data were analyzed by the patients’ sex, age, BMI, and MEE PG concentration.

Data were analyzed statistically using the Fisher exact probability test and the unpaired Student $t$ test. The comparison of the prevalence of RSI positivity between health checkup examinees and the OME group was performed using logistic regression with age and BMI as covariates. $P$ values $<.05$ were considered significant.

The research protocol was reviewed and approved by the Institutional Review Board at Nagoya University Hospital, and informed consent was obtained from all participants.

**Results**

**Health Checkup Examinees**

Overall, the average RSI score in the health checkup examinees was 4.0, and the highest average score was found among women in their 80s, although their number was few. The overall RSI-positive rate was 7.1% (men, 9.2%; women, 5.8%). The RSI-positive rates by BMI are shown in Figure 1. Men with BMIs from 26 to 28 kg/m$^2$ had significantly higher RSI-positive rates (30.8%) than other men. There was no difference in the RSI-positive rates by BMI among women. Results of the average BMI and RSI-positive rates by age are shown in Table 1. The highest RSI-positive rate was observed in men in their 40s, who had the highest average...
BMI. None of the men in their 80s was RSI positive, whereas women in their 80s had the highest RSI-positive rate.

Patients with OME

Overall, the average RSI score in patients with OME was 7.4, and the highest average score was found among men younger than age 50 years. The RSI-positive rate in subjects with OME of undetermined etiology was 21.0% overall (men, 15.6%; women, 25.8%), which was significantly higher than in those in the health checkup examinees on logistic regression analysis. The RSI-positive rates by BMI are shown in Figure 2. Men with a BMI higher than 24 kg/m² had higher RSI-positive rates (33.3%), whereas no man with a BMI lower than 21 kg/m² was RSI positive. There was no significant difference in the RSI-positive rates by BMI among women.

Results of average BMIs, PGs in MEEs, and RSI-positive rates by age in patients with OME are shown in Table 2. Among men, the RSI-positive rate was the highest in those younger than age 50 years, who had the highest average BMI. This group also showed a higher average PG concentration, which was just below that of the group ≥70 years of age, although there was no correlation between PG concentration and RSI score in this group. None of the men ≥70 years of age was RSI positive, but the average PG concentration was significantly higher in this group than in others. In women, the average BMI showed no significant difference by age. Each group demonstrated a variable RSI-positive rate but a stable average PG concentration.

Discussion

Similar to patients with GERD, QOL in patients with LPRD is significantly impaired in many aspects, including social functioning and vitality. Therefore, adequate diagnosis and effective treatment are necessary before progression of LPRD. The RSI, a means to assess the symptoms in subjects with LPR proposed by Belafsky et al, has been used to evaluate LPR in certain populations. In the present study, the RSI was used to survey the prevalence of LPR in health checkup examinees and in patients with OME of undetermined etiology, and the results were compared. The average RSI score was higher in patients with OME than in health checkup examinees. Moreover, patients with OME had a significantly higher RSI-positive rate than the health checkup examinees; however, the study showed that the distribution pattern of RSI-positive rates was similar between the health checkup examinees and patients with OME, and the RSI-positive rate was lower in elderly men than in men of other ages.

A positive association between increasing BMI and the presence of GERD has been proposed by a systematic review and meta-analysis. An increase in BMI is associated with an increase in esophageal acid exposure. The highest RSI-positive rate in the health checkup examinees was observed in men in their 40s, who had the highest BMI. The RSI-positive rate was less in elderly men, especially those older than age 80 years. These findings appear to agree with those of another study, which reported that the RSI score decreased as subjects with laryngeal symptoms grew older. Asymptomatic esophagitis has been reported to be associated with male sex, lower BMI, and older age. Aging decreases visceral pain, but no decline in the RSI-positive rate with age was observed in women. This might be due to mechanisms similar to esophageal hypersensitivity reported in women.

Detection of pepsin in throat sputum has been introduced as a sensitive, noninvasive method to detect LPR. Higher sputum levels of pepsin have been reported to be associated with higher RSI scores in patients with laryngitis, although the subjects in that study were relatively young. The presence of pepsin/PG in MEE in children represents an association between LPR and OME. Activated pepsin with acid is a direct

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**Table 1.** Average BMI and RSI-Positive Rate by Age in Health Checkup Examinees

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Number</th>
<th>Average BMI</th>
<th>RSI-positive rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>~49</td>
<td>M 10</td>
<td>25.2</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>F 28</td>
<td>21.6</td>
<td>7.1</td>
</tr>
<tr>
<td>50-59</td>
<td>M 23</td>
<td>23.1</td>
<td>8.7</td>
</tr>
<tr>
<td></td>
<td>F 65</td>
<td>22.4</td>
<td>4.6</td>
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<tr>
<td>60-69</td>
<td>M 59</td>
<td>23.8</td>
<td>10.2</td>
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<tr>
<td></td>
<td>F 101</td>
<td>23.4</td>
<td>5.9</td>
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<tr>
<td>70-79</td>
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<td>9.1</td>
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<td>M 17</td>
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<tr>
<td></td>
<td>F 8</td>
<td>23.5</td>
<td>12.5</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; F, female; M, male; RSI, reflux symptom index.
factor causing injury in the supraesophageal region, but pepsin is not stable under normal middle ear conditions.25 A high PG concentration in MEE in children25,26 or adults11,12 has been proposed as a marker of LPR-induced OME. In general, OME in children may be multifactorial, and rates of gastroesophageal reflux decrease as they grow; however, reflux in adults persists for long periods without adequate care. In this sense, accurate diagnoses are more necessary for adult patients with reflux-related OME than for children.

The average serum PG concentration is about 60 ng/mL based on the present measuring method (data not shown), which was similar to that previously reported.26 The average PG concentration in MEE in men ≥70 years of age was much higher than the serum level. Older age and male sex were reported to be significant contributing factors for high acid exposure to the esophagus.16 Refluxed contents might easily reach the middle ear cavity in elderly men, and this phenomenon could cause dysfunction of ventilation in the middle ear through the eustachian tube.

This study had some limitations, including the absence of endoscopic evaluation, especially in the health checkup examinees. Most patients with reflux disease in Asian countries would be of the mild type,27 and the present findings may be applicable to a limited number of countries. Therefore, further investigations in other regions would be desirable.

Conclusions

The prevalence of LPR symptoms evaluated by the RSI was significantly higher in OME patients than in health checkup examinees; however, a similar pattern in which LPR symptoms were prominent in middle-aged men with a high BMI and much less frequent in elderly men was observed. Men with a high BMI might be diagnosed as having LPRD based on the relevant symptoms, whereas LPR findings would be more sensitive than symptoms in aged men. Comprehensive diagnoses based on LPR symptoms and findings are necessary in women.

Author Contributions

Michihiko Sone, conception and design, analysis and interpretation of data, drafting the article, final approval of the version to be published; Naomi Katayama, acquisition of data, final approval of the version to be published; Toshinari Kato, acquisition of data, final approval of the version to be published; Kazuhiro Izawa, acquisition of data, final approval of the version to be published; Masaki Wada, acquisition of data, final approval of the version to be published; Nobuyuki Hamajima, conception and design, final approval of the version to be published; Tsutomu Nakashima, conception and design, final approval of the version to be published.

Disclosures

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References


