Factors Associated With Hypertrophy of the Lingual Tonsils in Adults With Sleep-Disordered Breathing

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Importance: This study shows factors affecting lingual tonsil hypertrophy (LTH) in sleep-disordered breathing.

Objective: To identify the factors associated with LTH in adults with sleep-disordered breathing.

Design: Retrospective analysis.

Setting: Academic tertiary referral center.

Participants: Ninety-seven adult patients with obstructive sleep apnea, who visited the Department of Otorhinolaryngology sleep clinic, were included from February 2009 through August 2011.

Interventions: All patients underwent WatchPAT (peripheral arterial tone) examination, endoscopic examination of the upper airway, simple skull lateral radiography, and cine magnetic resonance imaging (MRI) sleep study of the upper airway tract.

Main Outcomes and Measures: Prognostic factors indicating LTH in adults with sleep-disordered breathing.

Results: A total of 97 subjects were included in this study. The median (interquartile range) apnea hypopnea index was 16.5/h (7.6/h-27.5/h). The median (interquartile range) thickness of the lingual tonsils as measured by MRI was 3.6 mm (1.9-5.2 mm) and 4.9 mm (2.9-6.7 mm) in the midline and paramidline of the tongue base, respectively ($P < .001$). Laryngopharyngeal reflux (reflux finding score $\geq 7$) was present in 32 patients. The endoscopic grade of LTH agreed with the radiographic grade ($k = 0.731$; $P < .001$). Lingual tonsil thickness as measured by MRI was correlated with the endoscopic grade of LTH ($P < .001$). Multivariate analysis revealed that laryngopharyngeal reflux ($P < .001$) and body mass index ($P = .046$) were independently significant factors associated with LTH as measured by MRI.

Conclusions and Relevance: Reflux finding score and body mass index were significantly associated with LTH in adults with sleep-disordered breathing, whereas the respiratory parameters were not associated with LTH.

The lingual tonsils constitute the Waldeyer ring along with the palatine tonsils, adenoids, tubal tonsils, and lateral pharyngeal bands. Hypertrophy of the lingual tonsils has several clinical implications such as dysphagia, upper airway obstruction, difficult intubation, and difficult gastrointestinal endoscopy because the lingual tonsils are located in the tongue base. In particular, lingual tonsil hypertrophy (LTH) has been thought to be an important factor for the development of sleep-disordered breathing including simple snoring and obstructive sleep apnea (OSA). Several causes might be contributing to LTH such as reactive lymphoid hyperplasia due to previous adenotonsillectomy, laryngopharyngeal reflux, obesity, and use of medications such as phenytoin. The evaluation of LTH can be performed by endoscopic examination, magnetic resonance imaging (MRI), computed tomography, or simple skull lateral radiography. There have been a few studies performing systematic analyses of multiple factors that might be associated with LTH in adults. This study was aimed to identify the factors associated with LTH in adults with sleep-disordered breathing.

Methods

Subjects

Subjects who underwent sleep apnea screening examinations at Gangnam Healthcare Center of Seoul National University Hospital from February 2009 through August 2011 were included in this study. All the subjects com-
plained of habitual snoring or sleep apnea. The exclusion criteria were as follows: younger than 19 years, the presence of cardiac arrhythmia, use of α-adrenergic receptor blockers (a washout period of >24 hours was required), history of bilateral cervical or thoracic sympathectomy, and peripheral vasculopathy or neuropathy. This study was approved by the institutional review board of Seoul National University Bundang Hospital.

STUDY PROTOCOL

The sleep apnea screening examinations included WatchPAT (peripheral arterial tone) (Itamar Medical Ltd) performed at home and endoscopic examination of the upper airway tract (including the nasal cavity, oral cavity, oropharynx, larynx, and hypopharynx), simple skull lateral radiography, and a cine MRI sleep study of the upper airway tract (Intera Achieva 1.5T; Philips Medical Systems) performed at the Gangnam center. The parameters obtained from the WatchPAT device concerned respiratory events, sleep position, oxygen desaturation, and snoring.

EVALUATION OF LTH

The lingual tonsils were endoscopically graded on scale from 0 to 4 based on their distribution and visibility of the vallecula and epiglottis by a blinded examiner using the endoscopic photographs taken with the tongue protruded: grade 0, no tonsils; grade 1, spotted tonsil tissues with the tongue base vasculature visible; grade 2, diffuse tonsil tissues with the tongue base vasculature invisible; grade 3, diffuse tonsil tissues with the vallecula invisible; and grade 4, diffuse tonsil tissues with the epiglottis invisible (Figure 1).

The lingual tonsils were also radiographically graded on a scale from 1 to 4 based on their size and visibility of the vallecula by a blinded radiologist using the simple skull lateral radiograph: grade 1, minimal irregularity of the tongue base by the lingual tonsil opacity with the vallecula fully visible; grade 2, lingual tonsil opacity with the vallecula partially obscured; grade 3, lingual tonsil opacity with the vallecula totally obscured; and grade 4, lingual tonsil opacity extending over the epiglottis (Figure 1).

All patients underwent a cine MRI sleep study of the upper airway as described elsewhere. For a dynamic airway examination, presedation and postsedation MRI images were obtained, but only presedation axial views were used in the present study. Subjects were placed in the supine position with their head and neck fixed in the neutral position. They were instructed to breathe in and out naturally. The MRI images were evaluated by a sleep specialist (J.-W.K.) and a radiologist (E.K.), who were blinded to the results of WatchPAT testing, endoscopy, and simple radiography. The lingual tonsils showed high signal intensity at the posterior aspect of the tongue base in the T2-weighted imaging. The thickness of the lingual tonsils including tongue base mucosa was measured in the anterior-posterior dimension, where the high signal intensity was greatest in the whole tongue base. The thickness of the tongue base mucosa per se was also measured (Figure 2). The net thickness of the lingual tonsils was obtained by subtracting mucosal thickness in the midline and paramidline of the tongue base.

EVALUATION OF LARYNGOPHARYNGEAL REFLUX

All patients underwent endoscopic laryngeal examination. The endoscopic findings were evaluated based on the reflux finding score system, which consists of 8-item endoscopic find-
ings. A patient with a reflux finding score greater than 7 was diagnosed as having laryngopharyngeal reflux.

**STATISTICAL ANALYSIS**

All parameters were evaluated for normality using a Kolmogorov-Smirnov test. When the normality is unmet, the data are presented as median (interquartile range [IQR]). Comparisons among the 4 groups were performed using a Kruskal-Wallis test for continuous variables and a $\chi^2$ test for discrete variables. A nonparametric paired test was performed using a Wilcoxon signed rank test. Multiple stepwise regression analyses were performed to determine any significant predictors among demographic, respiratory, endoscopic, and radiologic parameters associated with LTH. Statistical analyses were performed using SPSS 18.0 software (SPSS Inc). $P \leq .05$ was considered statistically significant.

**RESULTS**

**CHARACTERISTICS OF STUDY SAMPLES**

A total of 97 subjects (13 women) were included in this study. Their median age was 52 years (IQR, 47-57 years); body mass index (calculated as weight in kilograms divided by height in meters squared) 25.8 (IQR, 23.9-26.8); apnea hypopnea index (AHI), 16.5/h (IQR, 7.6/h-27.5/h); supine AHI, 26.4/h (IQR, 12.5/h-45.0/h); oxygen desaturation index, 11.1 (3.6-20.2); minimal oxygen saturation, 85% (81%-88%); loudness of snoring, 46 dB (IQR, 44-50 dB); and the percentage of sleep time with snoring louder than 45 dB, 38.5% (21.1%-63.8%). Thirty-two subjects had laryngopharyngeal reflux (reflux finding score $>7$). All patients were divided into 4 groups according to the severity of sleep-disordered breathing: 12 simple snorers (AHI $<5$/h), 30 patients with mild OSA (AHI $\geq 5$/h to $<15$/h), 35 with moderate OSA (AHI $\geq 15$/h to $<30$/h), and 20 with severe OSA (AHI $\geq 30$/h). The demographic, respiratory, and radiologic characteristics are given in Table 1. The presence of laryngopharyngeal reflux was not significantly different among the 4 OSA severity groups ($P = .10$).

**THICKNESS OF THE LINGUAL TONSILS**

The median (IQR) thickness of the lingual tonsils as measured by MRI was 3.6 mm (1.9-5.2 mm) and 4.9 mm (2.9-6.7 mm) in the midline and paramidline of the tongue base, respectively ($P < .001$). The mean of midline and paramidline lingual tonsil thickness was not significantly different among the 4 OSA severity groups ($P = .74$) (Table 1).

Endoscopically, 36 subjects had grade 1 LTH; 40, grade 2; and 21, grade 3. The radiographic examination of skull lateral view showed that 43 subjects had grade 1 LTH; 31, grade 2; and 23, grade 3. The endoscopic grade of LTH agreed with the radiographic grade (Cohen $\kappa$ coefficient $= 0.731$; $P < .001$) (Table 2).

The mean of the midline and paramidline lingual tonsil thickness measured by MRI was 2.5 mm (1.6-3.0 mm), 4.9 mm (3.0-5.5 mm), and 8.1 mm (6.5-9.1) in endoscopic grade 1, 2, and 3 LTH, respectively ($P < .001$) (Figure 3).
MULTIVARIATE ANALYSES PREDICTING LTH

Through multiple stepwise regression analyses, significant predictor parameters affecting the thickness of the lingual tonsils measured by MRI were identified (Table 3). Among demographic characteristics, age and sex did not have significant effects on LTH, but BMI significantly affected lingual tonsil thickness (standardized β coefficient = 0.189; P = .046). All respiratory variables, such as AHI, AHI in supine position, minimal oxygen saturation, and loudness and proportion of snoring, did not appear to have any significant effects on LTH. Another significant variable affecting the lingual tonsil thickness as measured by MRI was a reflux finding score of 7 or greater (standardized β coefficient = 0.381; P < .001).

### DISCUSSION

The lingual tonsils are known to be one of the anatomical structures involved in the pathogenesis of OSA.\(^{12,13}\) So far, most of the studies about the lingual tonsils have been done in children.\(^{6,8,14-16}\) The enlarged lingual tonsils are not uncommon and are sometimes a treatable cause of OSA, particularly in children with Down syndrome who already underwent adenotonsillectomy.\(^{6}\) In a study comparing children with persistent OSA after adenotonsillectomy and children without OSA after the same surgery, the prevalence of measurable lingual tonsils was significantly higher in children with OSA than in those without OSA.\(^{15}\) A case series of 26 children with polysomnography-proven persistent OSA after adenotonsillectomy...
The lingual tonsils may get hypertrophied in a compensatory manner after palatine tonsillectomy. A study showed that children without the palatine tonsils (due to previous tonsillectomy) had a higher prevalence of the measurable lingual tonsils than those with the palatine tonsils (78% vs 22%). Other causes have also been presented as possible causes of LTH such as laryngopharyngeal reflux, obesity, and use of medications such as phenytoin. To our knowledge, there have been a few studies systematically demonstrating important factors affecting LTH in adults with sleep-disordered breathing. The hypertrophied lingual tonsils obstructing the hypopharyngeal airway is also one of the factors leading to the treatment failure of pharyngeal surgery in adults with OSA.

Our multivariate analyses showed that the thickness of the lingual tonsils was significantly associated with reflux finding score. A 3-sensor pH study also showed that nasopharyngeal reflux events were more prevalent in patients with severe LTH than in those with mild or moderate LTH. To our knowledge, the first article that analyzed the relationship of LTH with OSA in a large population of adult patients was recently published. Lingual tonsil hypertrophy was not found in adults without laryngopharyngeal reflux or OSA, and LTH was larger in patients with laryngopharyngeal reflux and/or OSA than in those without either disease. The mechanism of the association between laryngopharyngeal reflux and LTH is not known. Given that the laryngeal mucosa is damaged by gastric acid and pepsin, the lymphoid tissues of the lingual tonsils might also be damaged and inflamed by gastric acid and pepsin. The relationship between laryngopharyngeal reflux and LTH was also present in children. In contrast, our multiple regression analyses did not show any significant association of lingual tonsil thickness with respiratory events such as AH1, oxygen desaturation, and snoring parameters. Although the palatine tonsils are important factors in causing OSA, their size is not necessarily associated with OSA severity, and also the thickness of the lingual tonsils is not likely to be associated with OSA severity. Our study also showed that body mass index was independently associated with lingual tonsil thickness.

Our study showed that the endoscopic grading of the lingual tonsils significantly agreed with the radiographic grading on the skull lateral view. In addition, the quantitative measurement of the lingual tonsil thickness on MRI results was also correlated with their endoscopic grading. Therefore, in real clinical settings, because MRI is very expensive and not feasible for patients with OSA, endoscopic evaluation may provide information enough to diagnose LTH.

To validate the results of our multivariate analyses showing that LTH is associated with laryngopharyngeal reflux and BMI, further studies should be pursued to show the effects treatment of reflux and BMI has on the hypertrophy of the lingual tonsils.

Our study has several limitations. First, instead of volumetric analyses, simple 2-dimensional thickness of the lingual tonsils was measured using MRI. In the future, volumetric analyses may reveal an association of LTH with OSA severity. Second, laryngopharyngeal reflux was not diagnosed through the use of 24-hour esophageal pH monitoring. However, our study also showed significant associations similar to studies that had performed 24-hour pH monitoring. In conclusion, this study showed that reflux finding score and BMI were significantly associated with LTH in adults with sleep-disordered breathing, whereas the respiratory parameters were not associated with LTH. Though the measurement of the lingual tonsils was not volumetric and laryngopharyngeal reflux was not diagnosed by a more objective method, our multiple regression analyses of demographic, respiratory, radiologic, and endoscopic findings demonstrate the association of the important factors with LTH after adjusting for confounders. Further systematic studies are required to identify the clinical significances of LTH in adults by showing surgical improvement after lingual tonsillectomy in OSA. In addition, more studies are also required to obtain epidemiologic data of LTH in general population and to more clearly identify the relationship of LTH with OSA severity.

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Author Contributions: All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Drs Sung and W. H. Lee contributed equally to this article. Study concept and design: Sung, C. H. Lee, and J.-W. Kim. Acquisition of data: W. H. Lee. Analysis and interpretation of data: W. H. Lee, Wee, E. Kim, and J.-W. Kim. Drafting of the manuscript: Sung, W. H. Lee, Wee, E. Kim, and J.-W. Kim. Critical revision of the manuscript for important intellectual content: C. H. Lee and J.-W. Kim. Statistical analysis: W. H. Lee. Administrative, technical, and

Table 3. Multiple Linear Regression Analysis Predicting the Thickness of the Lingual Tonsils

<table>
<thead>
<tr>
<th>Variable</th>
<th>Standardized β Coefficient</th>
<th>t</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.172</td>
<td>-1.864</td>
<td>0.07</td>
</tr>
<tr>
<td>Sex</td>
<td>0.098</td>
<td>0.970</td>
<td>0.33</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.189</td>
<td>2.021</td>
<td>0.046</td>
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<tr>
<td>AHI</td>
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<td>0.750</td>
<td>0.46</td>
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<tr>
<td>Supine AHI</td>
<td>0.030</td>
<td>0.305</td>
<td>0.76</td>
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<tr>
<td>SaO2 nadir</td>
<td>0.020</td>
<td>0.201</td>
<td>0.84</td>
</tr>
<tr>
<td>Loudness of snoring</td>
<td>0.053</td>
<td>0.555</td>
<td>0.58</td>
</tr>
<tr>
<td>% Snoring ≤45 dB</td>
<td>0.043</td>
<td>0.453</td>
<td>0.65</td>
</tr>
<tr>
<td>Reflux finding score ≥7</td>
<td>0.381</td>
<td>4.072</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: AHI, apnea hypopnea index; SaO2, oxygen saturation.

a F = 4.084 (P = .046); df1 = 1, df2 = 94; R = 0.423, R2 = 0.179, adjusted R2 = 0.161.

b Calculated from t distribution.
Conflict of Interest Disclosures: None reported.