Prediction of oral appliance treatment outcome in obstructive sleep apnea syndrome: a preliminary study

K. Suzuki¹, S. Nakata², M. Tagaya³, F. Yasuma⁴, S. Moral⁵, E. Miyao⁵, S. Tsuiki⁶ and T. Nakashima⁷

¹Department of Otorhinolaryngology, Graduate School of Medicine, Nagoya University, Nagoya, Japan and the department of Otorhinolaryngology, Japanese Red Cross Nagoya Daiichi Hospital, Nagoya, Japan; ²Department of Otorhinolaryngology, Second Hospital, Fujita Health University School of Medicine, Nagoya, Japan; ³Department of Otorhinolaryngology, Graduate School of Medicine, Nagoya University, Nagoya, Japan and the department of Otorhinolaryngology, Tosei General Hospital, Aichi, Japan; ⁴Department of Internal Medicine, National Hospital Organization Suzuka Hospital, Mie, Japan; ⁵Department of Otolaryngology-Head & Neck Surgery, The Medical City Hospital, Manila, Philippines and the department of Otorhinolaryngology, Second Hospital, Fujita Health University School of Medicine, Nagoya, Japan; ⁶Ars Orthodontics Clinic, Nagoya, Japan; ⁷Japan Somnology Center, Neuropsychiatric Research Institute, Tokyo, Japan; ⁸Department of Otorhinolaryngology, Graduate School of Medicine, Nagoya University, Nagoya, Japan.

Key-words. Sleep apnea; mandibular advancement; body mass index; pharynx

Abstract. Prediction of oral appliance treatment outcome in obstructive sleep apnea syndrome: a preliminary study. Objective: Predictors of treatment outcome of oral appliances (OAs) in patients with obstructive sleep apnea syndrome (OSAS) are not known. There is a pressing need for simple, clinically useful tools to predict treatment outcome. This study aimed to identify predictors of successful OA therapy for OSAS, including evaluation of pharyngeal morphology, which can be measured during routine examination by an otorhinolaryngologist.

Methodology: This was a prospective study of 26 OSAS patients treated with OAs. A favourable outcome was obtained in 14 patients (responders) but not in 12 patients (nonresponders). The baseline patient characteristics and polysomnography and rhinopharyngeal findings were analysed.

Results: Body mass index (BMI) was significantly lower in responders versus nonresponders (23.6±2.8 vs. 27.9±4.7 kg/m²; p<0.05). Pharyngeal morphology, age, sex and nasal resistance did not differ between the groups. Multiple regression analysis showed that BMI was a significant predictor of improvement in the apnea/hypopnea index after OA treatment (p<0.05).

Conclusion: Here we demonstrated that BMI is a favourable predictor of OA treatment outcome in OSAS patients. Among the OSAS patients, responders had wider retroglossal spaces than nonresponders.

Introduction

Sleep apnea/hypopnea occurs when the pharyngeal airway is occluded either completely (apnea) or partly (hypopnea) at the pharynx level during sleep. An epidemiological study showed that obstructive sleep apnea syndrome (OSAS) is a fairly common pathology that affects 4% of middle-aged men and 2% of middle-aged women in the US¹ and 4.5% of men and 3.2% of women in Korea.² Continuous positive airway pressure (CPAP), the most common form of treatment, maintains the patency of the upper airway using positive pressure. However, some OSAS patients cannot tolerate CPAP or refuse CPAP treatment.

Oral appliances (OAs) provide an alternative to CPAP and can be used as an initial treatment for mild OSAS. OAs are designed mainly to produce mandibular advancement by holding the lower jaw and tongue forward during sleep. However, the efficacy of OAs varies, and the outcome of using OAs as a treatment for OSAS is unpredictable. Specifically, the ability of cephalometry to predict the outcome of OA treatment for OSAS is controversial.³⁴ Because of the mechanism of action of OA treatment, the morphology of the upper airway, especially the velopharynx, might play an important role in determining the effectiveness of treatment.

The primary purpose of this study was to identify factors that predict the success of OA therapy in patients with OSAS. The assessed factors included the patient’s baseline characteristics, pharyngeal morphology and nasal patency, which are all measures that can be obtained easily by otorhinolaryngologists in clinical practice.
Materials and methods

Patients and treatment selection

This study was approved by the institutional review board of Nagoya University Hospital, Nagoya, Japan. Patients provided informed written consent about this study. In Japan, health insurance covers the cost of CPAP treatment for OSAS patients with apnea/hypopnea index (AHI) values ≥ 20/hour. From January 2004 to December 2008, 40 consecutive OSAS patients were treated with OAs at Nagoya University Hospital. Patients treated with OAs were offered various treatment options but chose to use OA treatment.

Of the 40 patients, 26 used the OA on a regular basis i.e. for the entire night and almost every day as reported at a 6-month follow-up exam. The OA compliance rate was thus 65%. These 26 patients were included in this analysis while the 14 patients who failed to continue using the OA were excluded. The study population included 20 patients with moderate or severe OSAS (AHI ≥ 20/hour) who could not tolerate CPAP treatment and 6 patients with mild OSAS (AHI < 20/hour). Polysomnography (PSG) was performed in these 26 patients to assess the effect of the OA after 6 months of use. The study population included 19 men and 7 women with a mean age of 52.2 ± 14.8 years (range, 21-76 years). The nasal cavity and pharynx morphology was examined by the designated otorhinolaryngologist (SN) who was blinded to the PSG results.

We used a custom-made hard OA that had two separate pieces. First, we estimated the distance of anterior mandibular advancement using a George Gauge® distance (SomnoMed, Denton, TX, USA). The anterior mandibular advancement distance was 3-8 mm in these Japanese patients. Most patients become accustomed to using this type of OA within two weeks.

Classification of the airway morphological features

Most of the morphological features of the upper airway were assessed by direct inspection of the oral cavity and pharyngeal space with the patient sitting upright and awake during the daytime. The retroglossal space was inspected at the end of expiration by nasopharyngeal endoscopy with the patient in the supine position. Simultaneously, the bilateral nasal resistance at DP = 100 Pa was measured with active anterior rhinomanometry (MPR-3100, Nihon Kohden, Tokyo, Japan). The otolaryngological features of the pharynx were graded as follows.

1. **Tonsil size (Figure 1)***
   - Grade 1: The tonsils are in the tonsillar fossa and barely seen behind the anterior fossa.
   - Grade 2: The tonsils are visible behind the anterior pillars.
   - Grade 3: The tonsils extend three-quarters of the way to the midline.
   - Grade 4: The tonsils obstruct the airway completely.

2. **Modified Mallampati score (MMS) (Figure 1)***
   - Grade 1: The tonsils, pillars and soft palate are clearly visible.
   - Grade 2: The uvula, pillars and upper pole are visible.
   - Grade 3: The soft palate is partly visible, but the tonsils, pillars and the base of the uvula are not visible.
   - Grade 4: Only the hard palate is visible.

3. **Narrowness in the fauces (Figure 1)***
   - Grade 1: The palatopharyngeal arch intersects at the edge of the tongue.
   - Grade 2: The palatopharyngeal arch intersects at 25% or more of the whole tongue diameter.
   - Grade 3: The palatopharyngeal arch intersects at 50% or more of the whole tongue diameter.
   - Grade 4: The palatopharyngeal arch intersects at 75% or more of the whole tongue diameter.

4. **Retroglossal space (Figure 2)***
   - Grade 1: The retroglossal space is widely patent, allowing visualization of the larynx. Normal.

---

*Figure 1 Tonsil size, narrowness of fauces and modified Mallampati score (MMS).*
Prediction of OA treatment outcome in OSAS

Chapter 1

Grades 2: The retroglossal space allows visualization of the vocal folds. The opposing walls are not in proximity. Small.

Grade 3: The retroglossal space only allows visualization of the posterior arytenoids. Very small.

Grade 4: The retroglossal space is in contact with the opposing walls. Obstructed.

The grades ranged from 1 to 4 and are shown relative to the oral cavity and retroglossal space (Figures 1 and 2).

Sleep study

The sleep study involved standard overnight PSG (Alice 3, Respironics Inc., Murrysville, PA, USA) with pulse oximetry. The C3-A2, C4-A1, O1-A2 and O2-A1 electroencephalograms, electro-oculograms, electromyograms (mentalis, legs and diaphragm), and electrocardiograms (bipolar CM5 and standard V5 lead positions) were recorded. Respiration was monitored with an oronasal thermistor and a thoracoabdominal piezo sensor.

All recordings were double-checked by designated polysomnographers who were blinded to the patients' information. An episode of apnea was defined as the cessation of airflow through the mouth and nose for 10 or more seconds, and an episode of hypopnea was defined as a 50% or more reduction in airflow accompanied by either an oxygen desaturation level of at least 3% or an arousal lasting for 10 or more seconds. Patients with AHI ≥ 5/hour were diagnosed as having OSAS. The AHI improvement ratio was calculated using this formula: (pre-treatment AHI – post-treatment AHI)/pre-treatment AHI) × 100.

Statistical analysis

The 26 subjects were classified as either responders or nonresponders to the OA treatment according to the degree of improvement in AHI after OA treatment (AHI improvement ratio) and according to the post-treatment AHI value. The responders had AHI improvement ratios ≥ 50% or post-treatment AHI < 10/hour. The nonresponders had AHI improvement ratios < 50%.

A t test was used to compare continuous variables. Morphology grades were treated as continuous variables. Pearson’s correlation coefficient was calculated using the AHI improvement ratio and OSAS factors. Possible predictors of the AHI improvement ratio were incorporated as independent variables in multivariate analysis using logistic regression models. A p value < 0.05 was regarded as significant. A receiver operating characteristic (ROC) curve was plotted, and the area under the curve was calculated. Analyses were performed using IBM SPSS for Windows version 19.0.

Results

The baseline characteristics of the patients are shown in Table 1. The success rate, defined as a reduction in AHI to < 10/hour with the OA treatment, was 42.3% (11/26). The response rate, defined as at least a 50% reduction in the initial AHI (despite the AHI still being > 10/hour), was 11.5% (3/26). Fourteen patients (9 men and 5 women) were classified as responders to the OA treatment; their mean age was 50.9 ± 17.0 years. Twelve patients were nonresponders (10 men and 2 women) with a mean age of 53.8 ± 12.2 years. Age, sex and nasal resistance did not differ between the two groups. However, the BMI was significantly lower in responders than in nonresponders (23.6 ± 2.8 vs. 27.9 ± 4.7 kg/m², respectively; p < 0.05). The morphological features did not differ between the two groups. The PSG results showed that AHI decreased from before OA
preferred by many patients, mainly because of the convenience and low cost. The velopharynx is important for securing the patency of the airway. In previous reports, the compliance rate with OAs ranged from 75% after a mean of 7 months to 50.9% after 6 months. The compliance rate in our study was 65%, which is similar to the rates reported by the other studies. A review of 3027 patients in 89 publications showed that the OA success rate, which was defined as the ability of the OA to reduce AHI to <10/hour, was 54% on average, and the response rate, defined as a 50% or greater reduction in the initial AHI (even if the AHI was still >10/hour), was 21% on average. In randomized, cross-over, placebo-controlled studies, the OA success and response rates were 50% and 14%, respectively.

In the present study, the success and response rates were similar to those in previous studies, i.e. 42.3% (11/26) and 11.5% (3/26), respectively.

BMI is a major contributor to OA treatment outcome in patients with OSAS. Our study also showed that BMI was the sole significant predictor of OA treatment outcome and that BMI was inversely related to the AHI improvement ratio. Patients with a BMI < 25 kg/m² had a good outcome. Obesity contributes to OSAS through fat deposition around the upper airway, which compromises its patency. Obesity might therefore limit the efficacy of OA treatment to after OA treatment from 25.8±11.9/hour to 5.9±4.6/hour in the responders but was unchanged (26.7±9.1/hour to 18.9±6.2/hour) in the nonresponders.

The results of the multiple regression analyses are summarized in Table 2. Only BMI (p<0.05) was a significant predictor of the AHI improvement ratio after treatment with OA. Scatter plots of the AHI improvement ratio and BMI, age and nasal resistance are shown in Figure 3. BMI and the AHI improvement ratio were inversely correlated (Pearson’s correlation efficient = -0.637, p<0.01). The AHI improvement ratio did not correlate significantly with age or nasal resistance.

Figure 4 shows the ROC curve for BMI as a predictor of response. Moderate differentiation was obtained between responders and nonresponders (area under the curve = 0.762). The cut-off BMI value was 24.7 kg/m², yielding a sensitivity of 71.4% and a specificity of 66.7%.

### Discussion

Here we investigated predictors of OA treatment outcome in OSAS patients using variables that can be measured easily during a routine examination by an otorhinolaryngologist. OAs are less effective than CPAP treatment for OSAS. However, OAs are preferred by many patients, mainly because of the convenience and low cost. The velopharynx is important for securing the patency of the airway. In previous reports, the compliance rate with OAs ranged from 75% after a mean of 7 months to 50.9% after 6 months. The compliance rate in our study was 65%, which is similar to the rates reported by the other studies. A review of 3027 patients in 89 publications showed that the OA success rate, which was defined as the ability of the OA to reduce AHI to <10/hour, was 54% on average, and the response rate, defined as a 50% or greater reduction in the initial AHI (even if the AHI was still >10/hour), was 21% on average. In randomized, cross-over, placebo-controlled studies, the OA success and response rates were 50% and 14%, respectively.

In the present study, the success and response rates were similar to those in previous studies, i.e. 42.3% (11/26) and 11.5% (3/26), respectively.

BMI is a major contributor to OA treatment outcome in patients with OSAS. Our study also showed that BMI was the sole significant predictor of OA treatment outcome and that BMI was inversely related to the AHI improvement ratio. Patients with a BMI < 25 kg/m² had a good outcome. Obesity contributes to OSAS through fat deposition around the upper airway, which compromises its patency. Obesity might therefore limit the efficacy

### Table 2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Responders Mean (SD)</th>
<th>Nonresponders Mean (SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>14 (54%)</td>
<td>12 (46%)</td>
<td></td>
</tr>
<tr>
<td>Male/Female</td>
<td>9/5</td>
<td>10/2</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>50.9 (17.0)</td>
<td>53.8 (12.2)</td>
<td>0.619</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23.6 (2.8)</td>
<td>27.9 (4.7)</td>
<td>0.008</td>
</tr>
<tr>
<td>Nasal resistance (Pa/cm³/sec)</td>
<td>0.22 (0.07)</td>
<td>0.27 (0.21)</td>
<td>0.343</td>
</tr>
<tr>
<td>Morphological features</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tonsil size</td>
<td>1.0 (0.0)</td>
<td>1.1 (0.3)</td>
<td>0.289</td>
</tr>
<tr>
<td>Modified Mallampati score</td>
<td>2.8 (1.3)</td>
<td>3.2 (0.9)</td>
<td>0.410</td>
</tr>
<tr>
<td>Narrowness of fauces</td>
<td>2.4 (0.9)</td>
<td>2.6 (0.9)</td>
<td>0.492</td>
</tr>
<tr>
<td>Retroglossal space</td>
<td>2.3 (1.2)</td>
<td>1.8 (0.8)</td>
<td>0.196</td>
</tr>
<tr>
<td>PSG results</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-treatment AHI (/hour)</td>
<td>25.8 (11.9)</td>
<td>26.7 (9.1)</td>
<td>0.840</td>
</tr>
<tr>
<td>Post-treatment AHI (/hour)</td>
<td>5.9 (4.6)</td>
<td>18.9 (6.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AHI improvement ratio (%)</td>
<td>75.2 (14.9)</td>
<td>26.1 (20.6)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

AHI: apnea/hypopnea index; OA: oral appliance; PSG: polysomnography; SD: standard deviation.

AHI improvement ratio: ([pre-treatment AHI – post-treatment AHI]/pre-treatment AHI) × 100.
which predisposes patients to desaturation during sleep; both result in breathing disorders during sleep. Thus, having a higher BMI predisposes a patient to have an increased chance of upper airway collapse and might compromise the efficacy of OAs or sleep surgery. Therefore, it is important to evaluate the morphological features of the upper airway to predict treatment outcome for both types of treatments.

Several studies have tried to identify predictors of OA treatment outcome using imaging with cephalometry or CT to evaluate the morphological features of the upper airway. The results suggested that a small oropharynx with no OA or a short soft palate length with an OA were predictors of a favourable outcome. Endoscopy is useful for dynamic evaluation of the upper airway of OSAS patients. A recent study described the use of a custom-made simulation bite with maximal comfortable protrusion during drug-induced sleep endoscopy (DISE) for predicting the outcome of OA treatment for OSAS. In one study, OA treatment did not improve the airway patency of the velopharynx (retropalatal space) in obese persons. Moreover, obesity is known to be a major predictor of sleep surgery, e.g. uvulopalatopharyngoplasty. Some reports have suggested that in patients who undergo surgery, nonresponders have significantly higher BMIs. Abdominal mass loading can influence breathing pattern by predisposing patients to hypoventilation or by reducing the oxygen store,
second limitation was that we evaluated rhinopharyngeal findings and nasal resistance in patients while they were in the sitting position (except for examination of the retroglossal space) rather than in the supine position. The third limitation was that we evaluated the rhinopharyngeal findings and nasal resistance in patients while they were awake rather than when they were asleep. Further experiments are needed to overcome these limitations.

**Conclusion**

We found that BMI was a significant predictor of OA treatment outcome in OSAS patients. In addition, OA treatment responders had wider retroglossal spaces than nonresponders.

**References**


Keisuke Suzuki
Department of Otorhinolaryngology
Japanese Red Cross Nagoya Daiichi Hospital
3-35 Michisita-Cho
Nakamura-ku, Nagoya 453-8511, Japan
Tel: 81-52-481-5111
Fax: 81-52-482-7733
E-mail: kekeke1974@yahoo.co.jp