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Editorial

EDITORIAL

Prediction of mandibular advancement splint treatment response: moving toward individualized therapy for obstructive sleep apnea

Toru Ogawa*

Division of Advanced Prosthetic Dentistry, Tohoku University Graduate School of Dentistry, Sendai, Japan

*Corresponding author. Toru Ogawa, Division of Advanced Prosthetic Dentistry, Tohoku University Graduate School of Dentistry, 4-1, Seiryo-machi, Aoba-ku, Sendai, Miyagi 980-8575, Japan. Email: toru.ogawa.d7@tohoku.ac.jp

Obstructive sleep apnea (OSA) syndrome is a common respiratory sleep disorder that is characterized by repetitive upper airway collapse and is associated with snoring and excessive daytime sleepiness [1]. OSA is associated with significant health problems and increased risks of high blood pressure, stroke, heart attack, motor vehicle accidents, and occupational accidents. The first-line treatment for OSA is continuous positive airway pressure (CPAP), which can be limited by suboptimal tolerance and compliance [2]. One alternative to CPAP for OSA is treatment with an oral appliance (OA), specifically a mandibular advancement splint (MAS) device, which is less efficacious but more acceptable to patients [1, 3]. The American Academy of Sleep Medicine and American Academy of Dental Sleep Medicine clinical practice guidelines recommend OA treatment for adults with OSA who prefer OA therapy or are intolerant of CPAP therapy [1].

Although many studies have attempted to understand the mechanism of action of the MAS and predict the treatment outcome, it is still unclear why some patients do not respond to MAS therapy. Therefore, the prediction of the MAS treatment outcome is unreliable and leads to treatment delays for nonresponders. These delays can be particularly detrimental to patients with moderate to severe OSA [4]. Thus, there is an ongoing need to develop reliable prediction methods to select appropriate patients for MAS treatment. This information may also be useful to determine the baseline protrusion position of the MAS before titration.

The factors associated with MAS therapy outcomes include baseline characteristics such as the baseline apnea/hypopnea index (AHI), age, sex, neck circumference, and body mass index (BMI). The proposed indicators of OSA treatment success are younger age, female sex, and less obesity (lower BMI and smaller neck circumference) [3]. However, these variables are poor predictors of MAS treatment outcome [5].

Studies have found associations between the MAS treatment response and the craniofacial features on lateral cephalometry. The craniofacial features associated with a favorable MAS treatment outcome include a shorter soft palate length, lower hyoid bone position, greater angle between the cranial base and mandibular plane, and a retrognathic mandible [4, 6–9]. However, these findings are not consistent between studies, suggesting that cephalometric variables alone may be inadequate to select patients for MAS treatment [10].

Multiple studies have investigated the relationship between MAS treatment response and the morphology of hard and soft tissue in the orofacial and pharyngeal regions on MRI. In terms of tongue morphology, although the total tongue volume does not differ between responders and nonresponders to MAS treatment [11], MAS does induce changes in tongue shape. MAS treatment responders show a greater decrease in tongue length (from the tongue tip to the hyoid bone) [12]. MRI-based computational fluid dynamic data have the strongest relationship with the AHI change after OA treatment [13].

The main issue with the abovementioned studies investigating predictors of the MAS treatment response is that they are derivation studies rather than validation studies, which are lacking in the existing literature. Although these studies show statistically significant differences between responders and nonresponders, they do not present cutoff values or outcomes including sensitivity, specificity, and positive and negative predictive values. Therefore, the results are unsuitable for inclusion in a systematic review assessing their aptness as predictors, which makes comparisons difficult [14].

Several recent studies have investigated methods of predicting the outcome of MAS therapy for OSA. Okuno et al. [15] used nasendoscopic evaluation of awake subjects to measure the airway morphology and found that responders had a greater cross-sectional area expansion ratio of the velopharynx after mandibular advancement than nonresponders, with a high level of predictive accuracy at a cutoff value of 2.0 (sensitivity 85.7%, specificity 80.8%, positive predictive value 85.7%, negative predictive value 80.8% for criterion 2).

Wellman et al. [16] developed a simplified method to determine multiple physiological traits causing OSA. Edwards et al. [17] reported an excellent level of classification accuracy using an analysis with multiple phenotypic parameters, although their study had a small sample size. Because OSA is a multifactorial disorder caused not just by compromised pharyngeal anatomy but also by a confluence of abnormalities in several nonanatomic traits, including inadequate upper airway muscle function, a large ventilatory response to a respiratory disturbance (high loop gain), and a low arousal threshold, these phenotypic traits (i.e. upper airway anatomy/collapsibility and muscle function, loop gain, and arousal threshold) were included as variables. Multivariate analysis showed that baseline passive upper airway collapsibility and loop gain were independent predictors of the reduction in AHI (r^2 = 0.70; p = 0.001), and 7 (50%) and 6 (43%) of 14 patients were correctly classified as responders and nonresponders (total prediction accuracy: 93%). Recently, Vena et al. [18] further developed the analysis method by combining routine polysomnography (airflow features), age, and BMI, and achieved a prediction accuracy of 74% in a larger sample (n = 81).

Good predictive accuracy for OA treatment outcome has also been achieved using a remotely controlled mandibular device (RCMP) [19, 20]. Sutherland et al. [20] reported that a commercially available RCMP device had a sensitivity of 81.8%, specificity of 92.9%, positive predictive value of 90%, and negative predictive value of 86.7% (n = 3 misclassified), although there was a high rate of inconclusive tests (8 of 33).

Recently, Jugé et al. [21] used dynamic magnetic resonance imaging measurements during sleep with and without a MAS to classify participants as responders, partial responders, or nonresponders. They confirmed that responders had the greatest amount of tongue advancement and oropharyngeal enlargement with mandibular advancement, which may help improve MAS response prediction. Furthermore, a multivariate model and k-fold cross-validation procedure showed that when the variables included tongue movement and percentage of airway enlargement per millimeter of mandibular advancement along with baseline AHI, 69.2% of participants (fivefold cross-validated 62.5%, n = 39) were correctly classified in the three response categories when the jaw was advanced by >4 mm. In comparison, a model using only the baseline AHI correctly classified 50.0% of patients (fivefold cross-validated 52.5%, n = 40). These results imply that baseline characteristics alone are limited for predicting MAS treatment outcomes. More complex measurements are needed to develop better prediction models.

It is important to accurately predict the MAS treatment outcome for patients with OSA. However, although sufficiently accurate prediction methods have been reported, there is also a need to consider the clinical feasibility and practicality. For example, while MRI is currently capable of measuring upper airway cross-sectional area changes and dynamic tongue movement with mandibular advancement, this approach may be impractical in terms of the equipment, expense, and analysis complexity. Furthermore, although nasendoscopy and RCMP showed accurate prediction results, these methods also require technical expertise or special devices and settings. Therefore, developments that make these methods or modalities simpler and more practical will enable the prediction of MAS treatment outcome.

Physiological traits such as passive upper airway anatomy/collapsibility, loop gain, and arousal threshold, which can be obtained from routine clinical information including baseline polysomnography or CPAP data, might provide key insights into the physiologic characteristics that distinguish OA treatment responders from nonresponders [16–18]. Recent techniques developed to measure the underlying physiology causing an individual's OSA using routine clinical information may bring clinicians one step closer to individualizing precise OSA therapies by considering the mechanism and benefits of each treatment option.

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