

Treatment outcomes of mandibular advancement devices in positional and nonpositional OSA patients

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Objective. The aim of the study was to investigate treatment outcome of mandibular advancement devices (MADs) for positional and nonpositional obstructive sleep apnea (OSA).

Study design. Forty-two positional (supine apnea-hypopnea index [AHI] ≥ 2 times lateral AHI) and 30 nonpositional (supine AHI < 2 times lateral AHI) OSA patients performed 2-nights of sleep study before and after insertion of MADs.

Results. The decreases in apnea severity based on a reduction in the overall and supine AHI values after MADs therapy were significantly greater for the positional OSA than nonpositional OSA group. A multiple linear regression analysis showed that decrease in overall AHI was significantly associated with being in the positional group (standardized coefficient = 0.505). Age, body mass index, gender, and time in supine position during sleep did not show significant associations with decrease in overall AHI after MAD therapy.

Conclusion. Our data suggest that MADs are more effective in positional OSA than nonpositional OSA patients. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;xx:xxx)

Obstructive sleep apnea (OSA) is a common disorder characterized by recurrent episodes of obstruction in the upper airway during sleep. OSA has been identified as a major public health concern and has serious consequences such as daytime somnolence, systemic hypertension, and cardiovascular diseases.¹⁻⁴ A number of risk factors including aging, gender, obesity, and craniofacial development have been found to be associated with OSA.⁵⁻⁷

Mandibular advancement devices (MADs) have become a common treatment for OSA and are used as a

treatment alternative to positive airway pressure (PAP) devices.^{8,9} MADs are designed to protrude the mandible and increase the caliber of the airway during sleep. Many clinical studies have reported that MADs are less effective than PAP in reducing sleep apnea but that oral devices are preferred by more patients and are more readily accepted than PAP.⁸ MADs have been most commonly prescribed for patients with mild to moderate, but not severe OSA.¹⁰⁻¹² Previous reports have suggested that the effectiveness of MADs may be influenced by sleep position and that outcomes are improved in what they described as “supine-dependent” sleep apnea.¹³⁻¹⁵ In contrast, higher body mass index (BMI) and neck circumference negatively predict outcomes for MADs, but without consideration of sleep position.¹⁶ These findings raise the questions: “How does sleep position affect MAD outcome, independent of other factors?” and “Can we obtain efficacious outcomes in positional OSA patients even though they have moderate to severe OSA?”

Patients with OSA usually have more obstructive events in the supine position than in the lateral position, and when this is the case, forcing a change to the nonsupine position during sleep may be an effective treatment.¹⁷⁻²⁰ Positional OSA patients have been defined as those who have a supine apnea-hypopnea index (AHI) that is at least 2 times higher than their lateral AHI, and nonpositional patients are those in whom the supine AHI is less than 2 times higher than the lateral AHI.¹⁸ Obviously, position restriction therapy is less

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logical for patients with nonpositional OSA. The anthropomorphic studies that have been reported regarding patient differences between and risk factors for positional and nonpositional OSA are few and conflicting. There are a limited number of studies describing positional apnea as a distinct risk factor for severity of disease or related comorbidities. Some investigators have reported positional OSA patients to be younger and less obese with less severe respiratory disturbance than nonpositional patients.^{18,21} Others have found no differences in BMI between these groups, suggesting a cause other than weight gain.²² Although studies have consistently shown less severe respiratory disturbance in positional OSA patients, the anatomical and physiological mechanisms for this phenomenon have not been well explained.

We hypothesized that there may be factors other than age and BMI that influence the differences in sleep-disordered breathing between positional and nonpositional patients with OSA and, if so, the treatment outcomes with MADs would likely be different between these 2 groups of patients with OSA. We further speculate that identifying patients with OSA as either positional or nonpositional might have important therapeutic implications. The aim of the study was to investigate the treatment outcome of MADs for positional and nonpositional OSA using multnight in-home recordings.

METHODS

Subjects

Seventy-two consecutive patients with OSA (51 men and 21 women) were recruited from 3 dental practices. The study was approved by an institutional review board (BioMed IRB, San Diego, CA). After obtaining an informed consent, patients completed a 2-night pretreatment in-home sleep study (described later in this article). The inclusion criteria of the subjects were the patients who successfully completed a sleep study over 2 nights with a minimum of 4 hours of valid recording time each night, and had an AHI of 5 or greater.

Patient information including age, gender, height, weight, and neck size were obtained and Epworth Sleepiness Scale (ESS) for daytime sleepiness was acquired at the time of both sleep studies.

Mandibular advancement devices

All appliances that were used advanced the mandible and were custom made. The 3 types of MADs used in this study were the TAP II and III (Airway Management, Dallas, TX), and a Modified Herbst appliance (Great Lakes Orthodontics, Ltd., Tonawanda, NY). For the positional patients, 12 were fitted with the TAP II, 16 with TAP III, and 14 with the Modified Herbst

appliance. For the nonpositional patients, 8 were fitted with the TAP II, 12 with TAP III, and 10 with the Herbst appliance. The appliances were made by the respective laboratories and the degree of mandibular advancement was set to 60% of the patient's maximum protrusion using George Gauge measures taken at the time the impressions were made. After a titration period during which incremental anterior adjustments of the mandible were made until the maximum comfortable limit was reached, an additional sleep study was performed with the MAD to determine treatment efficacy.

Sleep study data

Two-night in-home recordings were performed for each pre- and posttreatment study with the Apnea Risk Evaluation System (ARES) Unicorder (Advanced Brain Monitoring, Carlsbad, CA). The ARES Unicorder measures oxygen saturation, pulse rate, airflow, respiratory effort, snoring levels, head movement, and head position from a wireless recorder self-applied with a single strap to the forehead. Reflectance oximetry is used to obtain the oxygen saturation (SpO₂) and pulse rate signals. Respiratory effort is derived from the measurement of changes in forehead venous pressure acquired using a combination of photoplethysmography and changes in surface pressure of the reflectance oximetry sensor, and head movement. Airflow is obtained via a nasal cannula and a pressure transducer. A calibrated acoustic microphone is used to acquire quantified snoring levels (dB). Accelerometers are used to measure head movement and derive head position. The recorder was designed to be easily affixed by the patient, and provide alerts during the study if poor-quality airflow or SpO₂ is detected so the device could be adjusted.

The description and validation of this device has been reported in 2 studies. The first had 284 valid comparisons of the in-laboratory simultaneous PSG and ARES and 187 valid comparisons of the in-laboratory PSG with a separate 2 nights of unattended self-applied ARES Unicorder.²³ The second study with 102 participants had 92 simultaneous in-laboratory comparisons and 86 in-home to in-laboratory comparisons. Both studies showed that the ARES had high sensitivity and specificity.²⁴

Automated scoring algorithms were applied off-line to detect sleep-disordered breathing. The AHI was computed using a time-in-bed measure based on recording time with acceptable signal quality minus periods when the patient was upright or presumed to be awake based on actigraphy. Automated algorithms were used to detect apnea (based on a 10-second cessation of airflow) and hypopnea events (based on a 50% reduction and recovery in airflow, a minimum 3.5% reduction in SpO₂ and at least a 1.0% recovery) for

Table I. Characteristics of study population at baseline

Variables	Positional OSA (n = 42)	Nonpositional OSA (n = 30)	P value
Age, y	53.9 ± 10.4	50.0 ± 9.0	.095*
Gender, % male	83.3	53.3	.008†
BMI	27.6 ± 3.4	30.9 ± 5.9	.004*
Neck circumference, inch	16.3 ± 1.1	16.4 ± 1.5	.758*
Overall AHI	21.79 ± 12.83	18.47 ± 16.24	.378*
Supine AHI	39.62 ± 20.21	24.74 ± 22.78	.006*
Nonsupine AHI	6.15 ± 6.18	16.03 ± 16.47	.001‡
% time snoring	22.30 ± 17.12	26.53 ± 19.03	.328*
% of time supine	49.14 ± 23.56	46.10 ± 26.63	.662*
ESS	10.93 ± 4.33	11.10 ± 4.90	.876*

AHI, apnea-hypopnea index; BMI, body mass index; ESS, Epworth Sleepiness Scale; OSA, obstructive sleep apnea.

*P values were obtained from independent *t* test.

†P values were obtained from chi-square test.

‡P values were obtained from Mann-Whitney test.

calculation of the AHI. After the automated scoring was applied, the full disclosure recordings were visually inspected by a sleep medicine physician to confirm the accuracy of the automated scoring, and to reclassify as central and/or exclude auto-detected events if necessary. The physiological data including percentage of time in supine position, total AHI, supine AHI, nonsupine AHI values, and percentage of time snoring greater than 40 dB were then calculated.

Data stratification

The patients were divided into 2 groups as having positional or nonpositional OSA following the criteria suggested by Cartwright.¹⁸ Specifically, Cartwright's criteria state that positional OSA patients have a supine AHI at least 2 times higher than their lateral AHI, and nonpositional patients have their supine AHI less than 2 times higher than their lateral AHI. Additionally, we revised these criteria to include 2 additional rules to improve sampling: (1) all the patients should have at least 30 minutes of supine- and 30 minutes of nonsupine-positioned sleep, and (2) should have a supine AHI more than 5. Forty-two positional OSA patients and 30 nonpositional OSA patients were evaluated. Demographic data of the subjects are shown in Table I.

Statistical analysis

The comparison of all measures of apnea severity and the effect of MAD between positional and nonpositional OSA groups was performed by *t* test for normal variables and Mann-Whitney test for nonparametric variables. Normality of the variables was evaluated with the formal Kolmogorov-Smirnov test. The effect of MAD on AHIs was calculated from the percent changes of AHIs after MAD therapy compared with the

pretreatment AHI. A second measure of treatment efficacy assessed the percentage of positional and nonpositional patients with posttreatment AHI less than 5. The comparison of the second measure of treatment efficacy was performed by chi-square test.

The percent changes in supine AHI and in nonsupine AHI were compared in each OSA group using the paired *t* test, and the relationships between percent change of overall AHI and the percentage of time in the supine position were evaluated in each group using Pearson's correlation test.

To evaluate the relative influence of each independent variable (age, BMI, gender, positional OSA, and percentage of time in supine position) on overall AHI values, multiple linear regression analyses were performed. The linear regression assumptions of linearity, homoscedasticity, and normality of the residuals were successfully evaluated.

The associations between treatment outcome (post-treatment AHI < 5) and each independent variable (age, BMI, gender, positional OSA, and percentage of time in supine position) were estimated by odds ratios (ORs) using the multiple logistic regression analysis. Each predictive value was stratified into 2 groups based on gender (men versus women), group (positional versus nonpositional OSA), the median values for age (53 years), BMI (30 kg/m²), and percentage of time supine (50%).

RESULTS

Pretreatment sleep study data

Pretreatment anthropomorphic and sleep study data for the subjects are shown in Table I. There were no statistically significant differences in overall AHI, percentage of time in supine position, percentage of time with snoring above 40 dB, and ESS between the 2 groups. Supine AHI was higher in positional OSA patients and nonsupine AHI was higher in nonpositional OSA patients.

After the titration period, the degree of mandibular advancement was close to 80% of the maximum protrusive distance in most cases and the advancement ranged from 5.6 mm to 9.6 mm. The amounts of the mandibular advancement were not significantly different between the 2 groups.

Comparison of the effects of MADs between positional and nonpositional OSA patients

We performed statistical analyses to investigate the differences in the effects (decreases and percent changes in overall, supine, and nonsupine AHIs after MAD therapy) among 3 types of MADs used in this study, and confirmed that there were no significant differences in all treatment outcomes among 3 types of devices

Table II. Changes in AHIs, percent time snoring, and ESS values after MAD therapy in positional and nonpositional OSA patients

Variables	Positional OSA				Nonpositional OSA				P value†	
	Pre	Post	Difference*	% change*	Pre	Post	Difference*	% change*	Difference	% change
Overall AHI	21.79 ± 12.83	5.17 ± 4.04	16.62 ± 11.55	74.69 ± 16.92	18.47 ± 16.23	7.93 ± 6.77	10.53 ± 12.95	46.03 ± 36.44	.040‡	<.001‡
Supine AHI	39.62 ± 20.21	8.95 ± 7.55	30.67 ± 17.46	77.99 ± 14.89	24.74 ± 22.78	9.67 ± 8.38	15.07 ± 17.65	50.00 ± 39.14	.001‡	<.001‡
Non-supine AHI	6.15 ± 6.18	2.17 ± 2.46	3.98 ± 5.79	44.72 ± 81.48	16.03 ± 16.47	5.83 ± 6.47	10.20 ± 12.83	51.52 ± 41.46	.058§	.336§
% time snoring	22.30 ± 17.12	9.20 ± 12.16	13.10 ± 13.95	52.43 ± 64.42	26.53 ± 19.03	14.67 ± 16.88	11.86 ± 17.11	40.03 ± 63.60	.736‡	.522§
ESS	10.93 ± 4.33	4.78 ± 4.29	5.67 ± 5.72	55.60 ± 36.82	11.10 ± 4.90	5.42 ± 4.26	5.55 ± 5.53	47.46 ± 36.30	.774§	.355‡

AHI, apnea-hypopnea index; ESS, Epworth Sleepiness Scale; MAD, mandibular advancement devices; OSA, obstructive sleep apnea.

*Means and standard deviations calculated from each subject's score.

†Comparison between positional and nonpositional OSA patients.

‡P values were obtained from independent *t* test.

§P values were obtained from Mann-Whitney test.

(all *P* values > .410 from 1-way analysis of variance [ANOVA]).

Mean and standard deviation of percent change of overall AHI after MADs therapy in total subjects was 62.75% ± 30.17%. Table II shows the descriptive data of the effects of MADs in each positional and nonpositional OSA group. Mean difference and percent change of overall AHI (*P* = .040, *P* < .001), and mean difference and percent change of supine AHI (*P* = .001, *P* < .001) after MADs therapy were significantly higher in positional OSA patients than nonpositional OSA patients. However, mean difference and percent change of nonsupine AHI, percent time of snoring greater than 40dB, and ESS after MADs therapy did not show any statistically significant difference between the 2 groups.

Marklund et al.¹⁴ suggested other criteria for positional dependency of OSA patients. They reported that supine-dependent OSA was defined by a supine AHI of 10 or greater, together with a lateral AHI less than 10 and nonsupine-dependent OSA was considered in patients with a lateral AHI of 10 or greater. When we used Marklund et al's criteria in our subjects, the results were very similar, and percent changes of overall AHI and supine AHI were also significantly higher in supine-dependent OSA than nonsupine-dependent OSA patients.

In the positional OSA group, percent change in supine AHI (77.32% ± 15.27%) was significantly higher than percent change in nonsupine AHI (44.72% ± 81.48%, *P* = .014); conversely, there were no significant differences in the nonpositional group. Percent change of overall AHI showed significant correlation with the percentage of time in the supine position in the positional OSA patients (*r* = 0.327, *P* = .034) but not in the nonpositional group.

Fig. 1 shows pre- and posttreatment changes of overall AHI, supine AHI, and nonsupine AHI in each patient of the 2 groups. Percentages of the patients in whom the effect of MAD on overall AHI were above

50% were 92.9% (39/42) in the positional OSA group and 53.3% (16/30) in the nonpositional OSA group (*P* < .001).

Fig. 2 shows the second measure of treatment efficacy. For overall patients, 69.0% (29/42) of positional patients were successfully treated with residual AHI less than 5 whereas 43.3% (13/30) of nonpositional patients showed the same results (*P* = .029). For the patients with pretreatment clinical cut-offs of overall AHI of 10 or greater, 64.9% (24/37) of positional patients were successfully treated such that residual AHIs were less than 5, whereas only 31.3% (5/16) of nonpositional patients were treated with same level (*P* = .024). For the patients with pretreatment overall AHI of 20 or more, 65.2% (15/23) of positional patients and 22.2% (2/9) of nonpositional patients were treated with residual AHIs less than 5 (*P* = .028). When we analyzed the severe OSA patients who had AHI of 30 or more at baseline, 77.8% (7/9) of positional patients and 42.9% (3/7) of nonpositional patients were treated with residual AHIs less than 10.

Impacts of risk factors on the effect of MADs on overall AHI

In Table III we present the results of the multiple linear regression analysis. After adjusting for the explanatory variables in the model (age, BMI, gender, percent of time in supine position), the percent change of overall AHI was significantly associated only with being in the positional OSA group (standardized coefficient = 0.505, coefficient = 30.700, 95% confidence interval [CI] = 16.104, 45.296). Age, BMI, gender, and percent of time supine did not show any significant associations with the percent change of overall AHI after MADs therapy.

Table IV shows the adjusted ORs of the risk factors on the treatment outcome with posttreatment AHI less than 5. Positional OSA patients were 4.1 times more likely to have successful treatment outcome with AHI

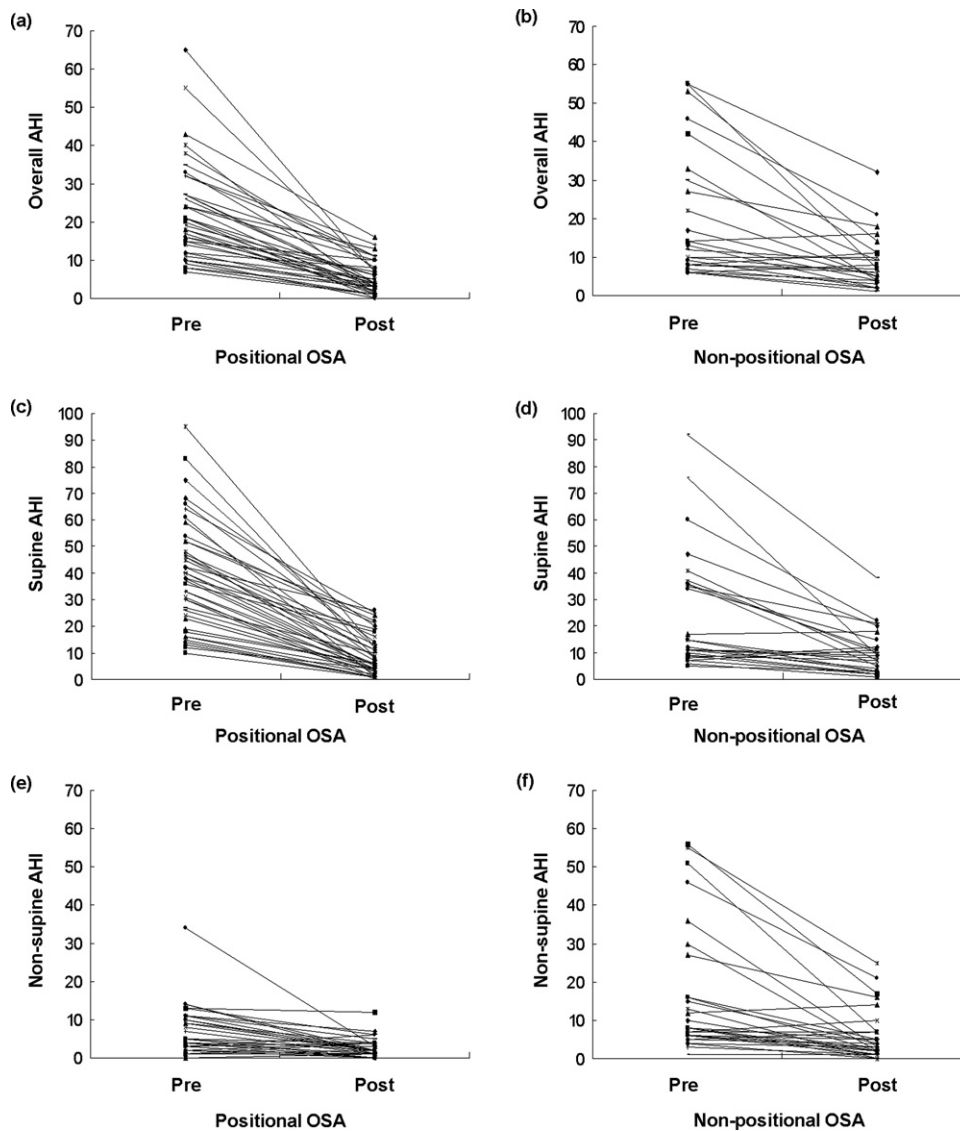


Fig. 1. These 6 graphs show the pre-post MAD changes for positional subjects (left-side figures) and nonpositional subjects (right-side figures). The 2 top figures (a and b) show the overall AHI data, the middle 2 figures (c and d) show the supine-only AHI data, and the bottom 2 figures (e and f) show the nonsupine AHI data.

less than 5 after MAD therapy than nonpositional OSA patients (95% CI = 1.126-15.158). The ORs of other variables (age, gender, BMI, and percent of time supine) were not statistically significant.

DISCUSSION

Most of the previous studies assessing treatment outcomes with MADs focused on changes in the overall severity of obstructive sleep apnea and have not examined defined subgroups of OSA patients (e.g., positional versus nonpositional OSA patients). To date, MAD therapy has been recommended only as first-line therapy in mild and moderate OSA patients. In our

clinical experience, it is not uncommon for some patients with more severe OSA to have efficacious outcomes, but to date we are unable to predict when this might occur. This is one of the first studies to investigate the contribution of positional versus nonpositional OSA in predicting successful MAD outcomes, independent of OSA severity level.

In this study we found that patients with positional OSA had substantially better treatment outcomes than patients with nonpositional OSA. When we used Marklund et al's criteria,¹⁴ the results were very similar and supine-dependent OSA patients also showed better treatment efficacy than nonsupine-dependent OSA pa-

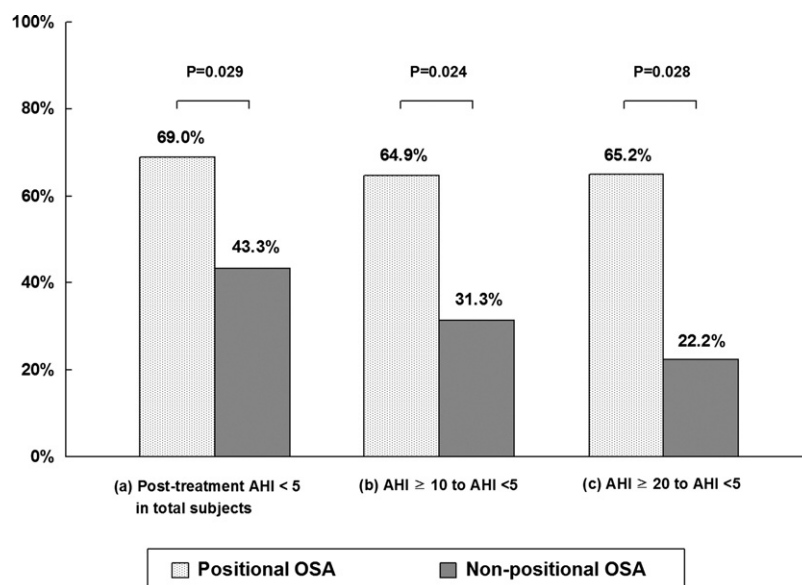


Fig. 2. Treatment efficacy of MAD in positional and nonpositional OSA patients.

Percentages of the patients (a) with posttreatment AHI less than 5 in total patients, (b) with pretreatment clinical cut-offs of overall AHI 15 or more and posttreatment AHI less than 5, (c) with pretreatment clinical cut-offs of overall AHI of 20 or more and posttreatment AHI less than 5. *P* values were obtained from chi-square test.

Table III. Multiple linear regression analysis of the risk factors on the effect of MAD on AHI (percent change of overall AHI)

Explanatory variables	Standardized coefficient	Coefficient	95% CI	<i>P</i> value
Age	-0.152	-0.459	-1.158, 0.239	.194
BMI	-0.152	-0.780	-2.215, 0.656	.282
Gender (Male)	0.139	9.191	-6.332, 24.713	.241
Positional OSA	0.505	30.700	16.104, 45.296	<.001
% of time in supine*	0.007	0.009	-0.258, 0.277	.946

AHI, apnea-hypopnea index; BMI, body mass index; CI, confidence interval; MAD, mandibular advancement devices; OSA, obstructive sleep apnea.

Multivariate ANOVA F-test *P* = .001, R^2 = 0.259.

*Average value in pre- and posttreatment sleep study.

tients. Moreover, this effect cannot be explained by differences in OSA severity, as there were no significant differences in the overall AHI in the 2 groups at baseline. Because the BMI and percentage of females were significantly different between the 2 groups, we elected to perform the multiple linear regression analyses to evaluate the relative influence of each independent variable (age, BMI, gender, positional OSA, and percentage of time supine) on the effect of MAD therapy, and the percent change of overall AHI after MAD therapy was significantly associated only with being in

Table IV. Adjusted ORs of the risk factors on the effect of MAD on AHI (posttreatment AHI <5)

Explanatory variables	Adjusted OR	95% CI	<i>P</i> value
Age (≥53 y)	0.337	0.093, 1.220	.098
BMI (≥30)	0.434	0.128, 1.465	.179
Gender (Male)	2.758	0.678, 11.216	.156
Positional OSA	4.132	1.126, 15.158	.032
% of time in supine* (≥50%)	1.041	0.373, 2.908	.939

AHI, apnea-hypopnea index; BMI, body mass index; CI, confidence interval; MAD, mandibular advancement devices; OSA, obstructive sleep apnea.

Model χ^2 = 9.54, df = 5, *P* = .089, adjusted R^2 = 0.167.

*Average value in pre- and posttreatment sleep study.

the positional OSA group. These findings begin to make sense if we hypothesize the nonpositional OSA group has a substantially more collapsible airway than our positional OSA group. We found that positional patients had significantly greater percentage changes in the supine AHI as a result of MAD therapy as compared with the nonpositional group. Interestingly, in our positional OSA patients, MAD efficacy increased as the percentage of time in the supine position increased, and the percent reduction in supine AHI was significantly greater than the percentage change in nonsupine AHI. The lack of change in the lateral AHI may be because of a “floor effect,” as the pretreatment lateral AHI in

our positional group was low to begin with so less subject to change. A previous cephalometric study reported that positional OSA patients were found to have a larger posterior airway space, less elongated soft palate, and somewhat more prominent retrognathia.^{25,26} More recently, pharyngeal magnetic resonance imaging and cephalometric radiography obtained during wakefulness found that positional OSA patients have wider airways in the lateral parts, lower facial height, and more backward position of the lower jaw, which may explain differences in the maintenance of pharyngeal airway patency in the lateral sleep position.²⁷ Regardless of these putative anatomic changes, the ultimate determinant of the effectiveness of MADs therapy may be the degree of upper airway collapsibility during sleep. Because MADs are designed to protrude the mandible and thus the tongue and epiglottis during sleep, we were surprised to find the effects of gravity on the pharyngeal airway were not equally resolved by MAD therapy in our positional and nonpositional OSA patients. Previously, Levendowski et al.¹⁶ found that BMI and neck circumference were predictors of patients who had less efficacious outcomes with MADs. Oksenberg et al.²¹ found that the positional OSA patients were younger and less obese than nonpositional OSA patients. They speculated that age and BMI might explain the difference between the 2 groups and they also suggested that the 2 conditions (positional and nonpositional OSA) are part of the same disorder with the difference being a progression in severity. However, in our subjects, there was no significant difference in age, neck circumference, and overall AHI severity between positional and nonpositional OSA groups. And multiple linear regression analysis showed that the effect of MADs was significantly associated with being in the positional OSA group, whereas age, BMI, gender, and percent of time supine did not show any significant associations.

MAD therapy has been recommended and considered for the patient who has mild to moderate, but not severe OSA.¹⁰⁻¹² However, our study showed that the positional OSA subjects who had severe degrees of AHIs also showed efficacious outcomes after MAD therapy.

Three limitations should be mentioned. First, the patients were treated at a limited number of dental sleep medicine practices so there were several dental therapists involved. Our perspective is that this makes our study more, not less generalized to private practice treatment of OSA patients. Of course a larger, multisite study might be required to confirm these results. Second, we used 3 types of MADs in this study because we would suggest that using 3 different appliances adds to the value of the article in that it gives the results more

generalizability to the community of practitioners who might want to apply our results to their practices. Even though the mechanism of action of these devices is similar, i.e., advancement of the mandible, we should consider that having 3 different appliance designs can be a possible confounder. However, we performed the statistical analyses to investigate the differences in the effects among the 3 devices, and confirmed that there were no significant differences in all treatment outcomes among the 3 types of devices. Moreover, the distribution of the 3 types of MADs was almost the same between positional and nonpositional groups in this study. Third, we did not set the same amount of the mandibular advancement for each patient and the differences in the amounts of advancement can have an effect on the treatment outcome of MADs. However, we can state that the amounts of the mandibular advancement were not significantly different between positional and nonpositional groups and did not influence the final results of our study.

In summary, positional OSA is based on a ratio of the supine AHI divided by nonsupine AHI greater than 2.0, and it is important to know if the patient was classified to the positional or nonpositional group in order to predict the treatment outcome of MADs. We have shown that MADs are more effective in positional OSA patients than nonpositional OSA patients. We speculate that the nonpositional group may have an altered or more inherent pharyngeal airway collapsibility, which distinctly worsens with obesity. Possibly, other factors beyond age and BMI are contributory to OSA in these subjects. Additional studies, such as evaluation of dynamic pharyngeal airway collapsibility, will be required to identify factors contributing to the differences in positional and nonpositional OSA patients.

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