Effectiveness of Mandibular Advancement Devices in Positional OSA Patients: A Retrospective Analysis of Predictive Variables in a Sample of Adult Patients

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Abstract

Objectives To evaluate the efficacy of mandibular advancement devices (MADs) in improving apnea-hypopnea index (AHI) in positional obstructive sleep apnea (POSA), compared with a control group of nonpositional OSA (NPOSA) patients, from mild to very severe degree, in order to to find the main variables characterizing the examined group as potential predictors of treatment success.

Materials and Methods In the present observational study, we retrospectively collected polysomnographic records of 39 positional adult patients, divided into 30 supine isolated OSA (siOSA) and 9 supine predominant OSA (spOSA) undergoing MADs from 2003 to 2019, and compared with those of a control group of 47 NPOSA patients. Demographics and anthropometrical data, home sleep apnea test (HSAT) records, drug-induced sleep endoscopy (DISE) results, and dental casts evaluation were analyzed pre- and post-treatment with MADs.

Results A prevalence of the male sex (86%), mean age of $49{,}4 \pm 14.98$ years, and mean body mass index (BMI) of $26.74 \pm 4.29\,kg/m^2$ were found among the OSA patients with significant differences between the three groups for sex and BMI. After MADs, the HSAT revealed significant reduction of AHI in all of the groups, with greater reduction of the supine AHI in POSA and significant reduction of the snore index for NPOSA. The hypopharynx section (H) of the NOHL Index, a fourth degree of hypopharyngeal collapse and an anteroposterior pattern was the most frequent to occur (19.9%) from DISE exam. No significant correlation between the initial total AHI and the dental variables was found, except for a reduced maxillary intermolar distance.

Conclusion MADs are effective in reducing AHI in POSA and NPOSA patients from mild to very severe degree. Supine AHI decreased after treatment with MADs mainly in siOSA and spOSA patients compared with the NPOSA group. The snore index decreased

Keywords
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- mandibular advancement
- supine position

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significantly after treatment with MADs in all groups, showing the greater reduction in the NPOSA group. The tongue base (H) represented the most frequent anatomic area of collapse and there was a high prevalence of upper maxillary constriction.

Introduction

The treatment for obstructive sleep apnea (OSA) is individualized, depending on the severity and epidemiology. Continuous positive airway pressure (CPAP) is considered the gold standard therapy for OSA.[1] Despite its benefits, a significant proportion of patients is unable to tolerate this approach, considering the device uncomfortable. Accordingly, a major problem with CPAP is the long-term adherence for which the literature reported a 50% of wear time reduction.[2]

Indeed, mandibular advancement devices (MADs) are increasingly prescribed as a noninvasive treatment option for patients diagnosed with mild to moderate OSA (apnea-hypopnea index [AHI] $\leq$ 30),[3] mechanically increasing airway patency by protruding mandible during sleep. Compared with CPAP, MADs are less efficacious in reducing respiratory obstruction but are more accepted and tolerated by patients, which, in turn, may lead to an increased compliance and a comparable level of therapeutic effectiveness.[4]

For that reason, it is fundamental to define which patients may benefit from MADs. As a matter of fact, there is currently no consensus on predictors of treatment outcome.

Several clinical and polysomnographic variables have been reported in the literature to be strictly correlated with greater efficacy of MADs therapy as lower baseline age, body mass index (BMI), and AHI.[5] On the other hand, the causal relationship between cephalometric variable and OSA is not sufficiently supported by the literature.[6–9] Most published studies have bias in that they exclude patients with severe OSA or patients who have not adhered to CPAP therapy.[10] In addition, predictors have not been systematically validated to assess their accuracy in a separate patient population.[3] Thus, the ability to preselect suitable candidates for a specific treatment modality is still limited.

There are different clinical phenotypes of OSA, although the most common is positional apnea, in which the obstructive events occur more in supine position than in lateral position. The latest definition of positional apnea released by Joosten et al. differentiates two categories of positional apnea depending on the phenotype with which positionality presents: supine predominant OSA (spOSA) was defined as having an overall AHI $\geq$ 5 with supine AHI $>$ 2 times the non-supine AHI; supine isolated OSA (siOSA) when non-supine AHI was negligible ($<$ 5).[11]

Numerous studies highlighted the drop-off of the lung volume in the supine position and the resulting increase in the critical pressure, thus an increased collapsibility of the upper airways compared with the lateral position. To explain this phenomenon, we must refer to Laplace law, according to which the transmural pressure gradient required for the tube collapse is inversely proportional to the curvature tube radius.[12] According to literature, the upper airway has an elliptical shape with the long axis oriented laterally in the supine position. Positional OSA (POSA) patients also show a significant reduction in lung volume when they move from the lateral to the supine position, resulting in a significant decrease in residual functional capacity.[13] Mandibular advancement devices act mainly at the velopharynx and oropharynx levels by increasing the lateral airway dimension, which explains their efficacy in this type of patients. The OSA treatment must act at the level of the pharynx lateral wall which is the critical structure of the upper airway.[14] In severe non-positional OSA (NPOSA) patients, a collapse in the final segment of the long axis has been observed and this could explain why MADs are less effective, as demonstrated in the literature.[15]

Despite what has been said so far, there are no scientific studies that investigated the efficacy of MADs in POSA patients, comparing those data to the ones obtained by treating NPOSA patients with MADs.

Therefore, the primary objective of the present retrospective study was to evaluate the efficacy of MADs in improving the AHI in POSA patients, with mild ($5 \leq$ AHI$<$ 1 5), moderate ($15 \leq$ AHI < 30), severe ($30 \leq$ AHI < 60) to very severe (AHI $\geq$ 60) degrees of the disease, and the secondary objective was to analyze the demographics and anthropometrical variables, the polysomnographic results, the data obtained by DISE and the measurement of the dental casts, in order to find any predictive factors of treatment success.

Materials and Methods

The present observational retrospective study design was performed in accordance with the 1975 Declaration of Helsinki ethical standards and its later amendments and comparable ethical standards. It was approved by the Ethics Committee of the Ferrara University Postgraduate School of Orthodontics (approval Number 2/2019).

Medical records of 415 Caucasian adult patients affected by a diagnosed OSA and treated with 2-pieces MADs from 2003 to 2019 were retrospectively selected and analyzed by the same operator (FP) 5 times to reduce the intraoperator risk of bias. All patients were treated at the Otorhinolaryngology Unit of the 'G.B. Morgagni-Pierantoni Hospital' (Forlì, Italy).

All patients enrolled in the study underwent a level-III home sleep apnea test (HSAT; NOX-T3, MedicAir Group, Athens, Greece) which is a portable polysomnography (PSG) with integrated 3-D sensor for cardio-respiratory home monitoring at night and detecting the position of the patient. The tracks obtained from the recording were interpreted by a qualified sleep medical doctor (CV) and analyzed at T0 (baseline time at diagnosis) and T1 (4 to

6 months or > 6 months from the start of MADs, which is the necessary time to verify significant and reliable changes due to the therapy).

Only patients who underwent pretreatment and post-treatment HSAT with MADs in situ and successfully completed the test for two consecutive nights were included in the present retrospective analysis, with a record time of at least 4 hours of valid registration per night. The study excluded patients for whom MADs therapy was contraindicated (presence of periodontal disease, insufficient number of teeth, or temporomandibular joint dysfunction), with psychiatric or pulmonary diseases, presence of predominant central sleep apnea, CPAP users during the observational period and without HSAT with MADs in situ or post-treatment HSAT performed after a period < 4 months from the pretreatment PSG.

All patients were treated exclusively with a customized two-piece MADs (SomnoDent, SomnoMed Ltd., Sidney, Australia), in association with elastics to minimize mouth opening during sleep (►**Figure 1**). Vertical elastics were carefully selected not to interfere with device retention and to avoid the possibility of dislodging one of the two pieces of the appliance at the maximal mouth opening. Patients were asked to incrementally titrate the appliance as far forward as comfortably possible, over a 4- to 8-week period.[16]

The DISE investigation with propofol was performed only on demand of the ENT specialist in order to simulate the effect of MADs by advancing the mandible identifying any improvement in upper airway patency or snoring and to find, according to the NOHL classification, the upper airway sites involved in apneic obstruction specifying the degree and the pattern of pharyngeal collapse. The NOHL classification system, proposed by Vicini et al.[17] in 2012, assesses the degree and pattern of obstruction of four anatomical sites: N (nasopharyngeal cavity and wall), O (oropharyngeal and retropalatal space), H (hypopharynx and tongue base) and L (larynx-epiglottis). The degree of nasopharyngeal cavity and pharyngeal wall obstruction observed during the Muller maneuver is classified as follows:

- Grade 1: 0-25% collapse;
- Grade 2: 25-50% collapse;
- Grade 3: 50-75% collapse; and
- Grade 4: 100% total collapse.

The NOHL classification also enables the description of the pattern of the pharyngeal collapse (for O and H) as transverse (t), anteroposterior (ap) or concentric (c).

Furthermore, for selected hospital patients, dental records were available, and the measurements were performed manually on the dental casts using a digital millimeter caliper with an accuracy of 0,001 mm (Prodigital). Manual measurements that use a calibrated gauge produce the most accurate, reliable, and reproducible results.[18]

Finally, for each patient, the following measurements were analyzed: demographic and anthropometrical data (date of birth, date of realization of pre- and post-treatment PSG with MADs, sex, BMI, score on the Epworth Sleepiness Scale, ESS), polysomnographic records from the HSAT (total, supine, and nonsupine AHI), nadir (minimum oxygen saturation), the oxygen disturbance index (ODI), mean oxygen saturation (SaO2), the snore index, the DISE results (are, degree of obstruction and collapse pattern), and the evaluation of dental casts (molar and canine relationship, overjet, overbite, intermolar and intercanine distance, curve of Spee, crossbite, openbite, midline, and bolton index).

Fig. 1 Custom-made two-piece mandibular advancement device (Somnodent) associated with vertical elastics to prevent mouth opening.

Statistical Analysis

Statistical analysis was conducted with the following objectives: to evaluate if any differences existed in the initial sample between the experimental and the control group and to evaluate if there were any differences in the final results between the analyzed groups. Statistical analyses were conducted with R Statistical Software (R Foundation for Statistical Computing, Vienna, Austria) using the Fixed Effects in the Linear Mixed Model[19] and the corresponding post hoc analysis. The analysis of the PSG data acquisition was enriched by the application of the analysis of variance (ANOVA). Statistical analysis for the evaluation of the DISE parameters aimed to define the association between the scores on the N, O H, L scores and the initial AHI. Therefore, the nonparametric correlation (Spearman rank correlation) was used, with the NOHL scores expressed as noncontinuous values. In order to define which anatomical site was potentially responsible for collapse, the parameters (N, O, H and L) were analyzed individually. The classical bivariate inferential analysis was used to analyze the measurements obtained by the dental casts. The significance was set with a *p*-value of 5%. No power analysis was performed in the present observational retrospective study.[20]

Results

In total, 86 out of the initial 415 analyzed medical records matched the inclusion criteria. The experimental group

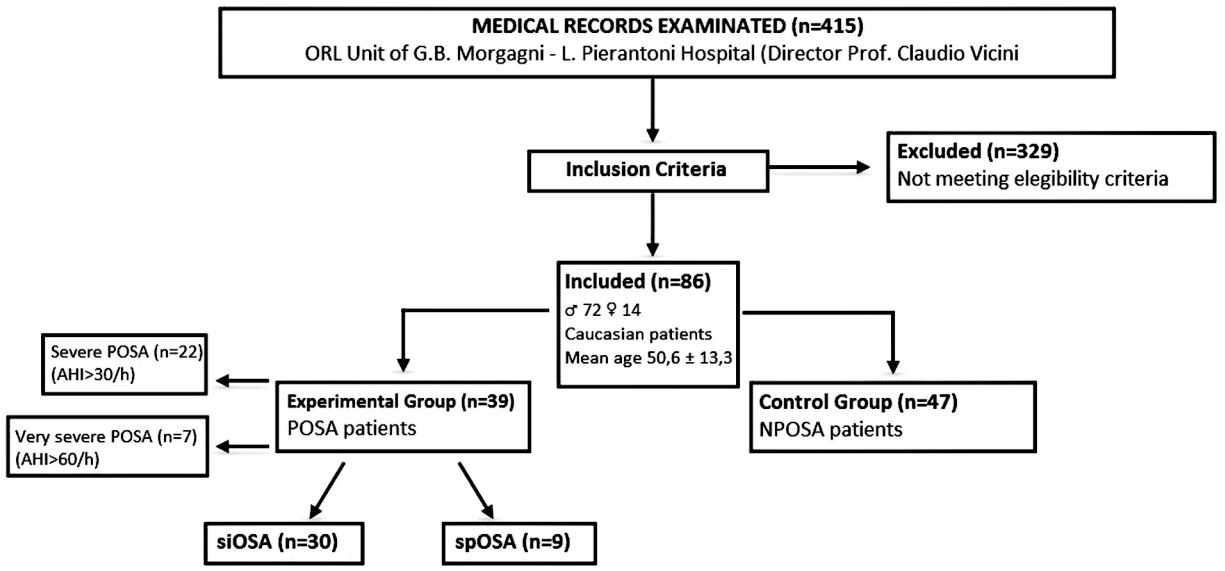

Fig. 2 Flow chart of the included medical records.
Abbreviations: OSA, obstructive sleep apnea; POSA, Positional OSA; siOSA, supine isolated OSA; spOSA, supine predominant OSA; NPOSA, non-positional OSA; AHI, apnea-hypopnea index.

consisted of 39 patients affected by POSA, divided in two subgroups: siOSA and spOSA. On the other hand, the control group consisted of 47 patients affected by NPOSA (►**Figure 2**).

In total, 46 out of the 86 patients included in the present study underwent DISE with MADs in place.

Demographics and Anthropometrical Analysis

The 86 Caucasian patients showed a prevalence of male sex and a mean age of 49.4 ± 14.98 years. ►**Table 1** shows the mean values and *p*-values for each group of each variable examined. The initial BMI differed significantly in the three groups examined: BMI in spOSA was lower than in the other groups and showed a statistically significant difference (p-value $= 0.038$).

Polysomnographic Analysis

Comparison analysis was performed between T0 and T1 in the three groups. For each outcome, we reported: the descriptive statistics, the repeated measures ANOVA, which shows if at T1 there were statistically significant differences between the analyzed groups and post hoc analysis, performed when the "time:group" interaction.

The descriptive analysis of all parameters recorded during the PSG at T0 and T1 are reported in ►**Table 2**.

The ANOVA test (►**Table 3**) highlights statistically significant changes after the observational period for all variables, as the corresponding plots shows (►**Figure 3**). The snore index is the only parameter analyzed that shows significant changes for the three conditions examined in the three interactions.

A total of 22 out of 39 POSA patients were diagnosed with a severe obstructive syndrome (AHI > 30) and 7 with very severe (AHI > 60). Most of these patients was supposed to be treated with CPAP therapy but refused it. Nevertheless, 9 out of 22 of the patients affected by severe POSA experimented a therapeutic response with MAD therapy (AHI reduced by 50%), 5 had a therapeutic success (post-treatment AHI < 10) and 8 healed completely (post-treatment AHI < 5). Of the 7 patients affected from very severe POSA, 5 had a therapeutic response, 1 had a therapeutic success and 1 healed completely. Specifically, a decrease in total AHI of 73.5% in the NPOSA

Table 1 Mean values of the demographics and anthropometrical measurements for each group and the respective p-value.

Variables		siOSA	spOSA	NPOSA	*p*-value
Body mass index		27 kg/m 2	23 kg/m 2	27 kg/m 2	0.038
Sex	Male	28	5	39	0.02
	Female	2	4	8	
Mean age (years old)		49	54	49	> 0.05
Epworth Sleepiness Scale		10.6	9.1	10.8	> 0.05

Table 2 Descriptive statistics (mean/standard deviation) of all variables recorded during the PSG at T0 and T1.

	NPOSA T0	NPOSA T1	spOSA T0	spOSA T1	siOSA T0	siOSA T1
Total AHI: mean ± SD	31.6 ± 19.9	8.4 ± 7.2	30.5 ± 16.8	4.9 ± 4.3	27.7 ± 20.1	7.7 ± 5.8
Supine AHI: mean ± SD	24.1 ± 18.0	4.8 ± 4.2	72.6 ± 85.8	10.3 ± 12.4	40.5 ± 17.5	16.4 ± 12.7
Non-supine AHI: mean ± SD	19.0 ± 10.6	10.4 ± 4.1	16.8 ± 14.5	3.8 ± 4.3	10.3 ± 16.2	2.7 ± 3.2
ODI: mean ± SD	24.6 ± 17.2	8.7 ± 10.8	28.4 ± 22.0	5.0 ± 4.8	26.2 ± 20.3	11.1 ± 13.8
SaO2: mean ± SD	90 ± 5.94	94 ± 2.60	94 ± 1.70	96 ± 0.84	93 ± 2.83	94 ± 1.90
Nadir: mean ± SD	76 ± 12.8	87 ± 5.0	80 ± 7.8	86 ± 4.0	82 ± 7.9	77 ± 29.7
Snore index: mean ± SD	52 ± 27.0	28 ± 25.4	15 ± 14.3	13 ± 8.4	21 ± 22.4	17 ± 18.6

Abbreviations: AHI, apnea-hypopnea index; ODI, oxygen disturbance index; NPOSA, non-positional obstructive sleep apnea; PSG, polysomnography; SaO2, oxygen saturation; SD, standard deviation; siOSA, supine isolated obstructive sleep apnea; spOSA, supine predominant obstructive sleep apnea OSA; T0, baseline; T1, 4 to 6 months or > 6 months since the beginning of the MADs treatment.

Table 3 ANOVA analysis results: *p*-value and F. ratio.

	Group	Time	Group:Time
Total AHI	0.64 (0.46)	**0.00 (92.00)**	0.62 (0.48)
Supine AHI	0.134 (2.1)	**0.009 (7.3)**	0.204 (1.7)
Non-supine AHI	0.193 (1.71)	**0.016 (6.20)**	0.774 (0.26)
ODI	0.84 (0.18)	**0.00 (52.69)**	0.47 (0.76)
SaO2	0.068 (2.8)	**0.001 (14.1)**	0.118 (2.3)
Nadir	0.722 (0.33)	**0.012 (7.57)**	0.204 (1.72)
Snore index	**0.00 (7.8)**	**0.02 (5.7)**	**0.05 (3.1)**

group, 84% in the siOSA group, and 72.2% in the spOSA group (mean reduction of −29.64 events/hour in the 3 groups) was observed between T0 and T1. Thus, the mean difference expressed as a percentage in total AHI after treatment with MADs (T1) was greater in siOSA rather than in NPOSA. Supine AHI demonstrated a statistically significant decrease (p-value = 0.009) at T1 in all 3 groups examined (mean reduction equal to - 27.06 events/hour in the 3 groups). The supine AHI post-hoc analysis found a statistically significant difference between T0 and T1 only for the siOSA and spOSA groups (p-value = 0.00). Post-hoc analysis of snore index values (►**Table 4**) shows a statistically significant difference between T0 and T1 only for the NPOSA group (p-value = 0.00).

DISE Analysis

The N, O, H and L variables, expressed as numerical values, were associated with the initial AHI. The nonparametric Spearman rank correlation coefficient, identified with the "ρ (rho)" symbol, was calculated. Even though all the analyzed variables showed a maximum correlation, only one statistical significantly correlation was found, between the variable H and the values of total AHI at T0. ►**Table 5** shows the mean values of AHI at T0 and T1 by the grade of H collapse. N (p-value = 0.7), O (p-value = 0.1) and L (p-value = 1) did not show any statistical significantly correlation relative to total AHI values at T0.

Dental Casts Measurement

Data obtained by the measurement of the dental casts were analyzed using a Welch two-sample *t*-test, in order to show any correlation with the pretreatment total AHI value. ►**Table 6** reports the p-value obtained by the correlation between the initial total AHI and the intraoral variables. The Pearson product moment correlation between the initial total AHI value and each variable was not statistically significantly relevant, as it showed a p-value > 0.05. The only variable that showed a statistically significant correlation was the maxillary intermolar distance (p-value = 0.05).

Discussion

In the present retrospective analysis, OSA patients were treated with a two-piece MAD in association with vertical elastics in order to prevent mouth opening. A study performed by Milano et al.[21] demonstrated a significant decrease in AHI, supine AHI, and nonsupine AHI in patients treated with the same appliance used in our study. These results highlight the potential importance of MADs design characteristics in relation to specific phenotypes as part of a personalized approach to treatment. Among the various mechanisms that may contribute to airway collapse during supine sleep position, gravity plays a key role which promotes tongue collapse and mandibular opening resulting in a downward rotation of the mandible which further facilitates

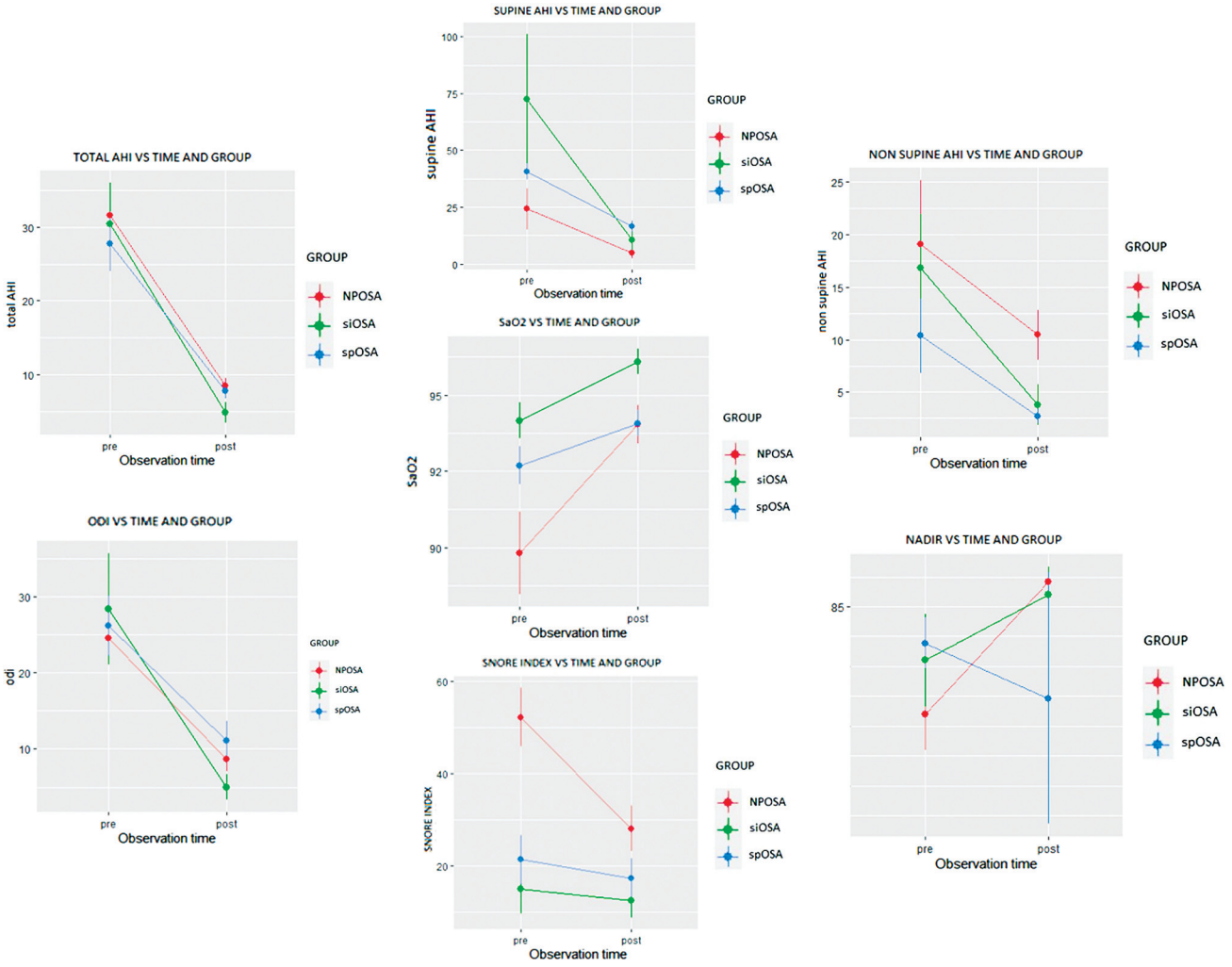

Fig. 3 Descriptive analysis of different variables in all study groups: plot of variations by time.
Abbreviations: OSA, obstructive sleep apnea; POSA, Positional OSA; siOSA, supine isolated OSA; spOSA, supine predominant OSA; NPOSA, non-positional OSA; AHI, apnea-hypopnea index.

Table 4 Post-hoc analysis of the supine AHI and snore index: statistical significant differences between pre- and post MAD therapy for the siOSA, spOSA, and NPOSA groups.

Contrast	Group	Variable	Estimate	Standart Error	df	Lower Confidence Level	Upper CL	T ratio	*p*-value
Pre/post	NPOSA	Supine AHI; snore Index	19; 24.5	29.4; 5.6	44 42	−40; 13.2	79; 36	0.66; 4.38	0,51; **0.00**
Pre/post	spOSA	Supine AHI; snore index	41; 2.1	8.6; 10.9	24 45	23; −19.9	58; 24	4.75; 0.19	**0.00**; 0.85
Pre/post	siOSA	Supine AHI; snore index	23; 6.2	4.3; 6.2	24 47	15; −6.2	32; 19	5.47; 1.00	**0.00;** 0.32

tongue collapse. Mandibular advancement devices are expected to improve the cross-sectional area of the upper airway in the supine position, due to their mandibular protrusion effect and also to their ability to stabilize the mandible and counteract the gravitation effect.[22] Some authors, using a one-piece device, concluded that POSA is a good predictor for the treatment of OSA.[23] In contrast, other authors observed that POSA patients presented a poorer response to MADs treatment, but they were treated with an appliance that allowed full mouth opening. Thus, differences in appliance design appear to be important in the context of POSA.

The diagnosis of POSA may be difficult or underestimated as patients may avoid supine position during nocturnal PSG.[24,25] Studies have observed that only 33% of patients achieve adequate supine sleep time during nocturnal PSG,

Table 5 Mean apnea-hypopnea index (AHI) at T0 and T1 by grade of hypopharyngeal (H) collapse (1-4).

	1c	2ap	1t	2t	2c	3ap	3t	3c	4ap	4t	4c
Mean AHI: T0	25.0	39.0	17	24.2	22.4	52.3	31	36.0	**37**	35	37
Mean AHI: T1	0.8	5.0	2.03	6.0	3.3	5.4	4.7	7.0	**6.0**	5.8	9.0
Number of patients	2	4	3	6	2	3	4	5	**9**	4	4
Percentage	4.3%	8.6%	6.6%	13.1%	4.3%	6.6%	8.6%	10.8%	**19.9%**	8.6%	8.6%

defined as > 15 minutes in the supine position.[24] Sunnergren et al.,[25] in a study of 265 subjects with hypertension, found that 5 out of 81 patients would have been diagnosed with OSA while 16 out of 53 patients diagnosed with mild OSA would have been reclassified as moderate or severe if they had slept supine.[26] In the present study, only those patients who successfully completed PSG for two nights, spending at least 10% of the pre- and post-treatment PSG recording time with MADs in the supine position during at least 4 hours of sleep, were considered as positional patients.

Approximately 60% of OSA patients present with supine-predominant apnea while 32% of OSA patients present with supine-isolated apnea.[11] In the present study, 55% of patients observed were NPOSA while 45% were POSA, of which 11% were spOSA and 34% were siOSA.

Compared with NPOSA patients, POSA patients are more likely to be younger, less obese, have less severe OSA, are more likely to snore and have less objective daytime sleepiness. They are also less likely to adhere well to CPAP treatment.[27] According to Sutherland et al., factors which negatively influence the effectiveness of MADs therapy include a age > 58 years, basal AHI > 30 events per hour, and BMI > 30 kg/m^2, while there is no consensus on gender.[28] In the present study, 415 patient records of patients undergoing treatment with MADs were examined, of which only 86 formed the sample of the study because they had pre- and post-treatment PSGs with MADs and fulfilled the inclusion criteria. The reason for this probably lies in the fact that healthy patients are unlikely to undergo a post-treatment PSG. The 86 patients examined had POSA and NPOSA of varying degrees of severity. In particular, 47 patients were classified as NPOSA and 39 patients as POSA. Of the 39 POSA patients, 22 had a severe obstructive syndrome (AHI > 30) and 7 had a very severe one (AHI > 60). Most of these patients had been candidates for CPAP therapy but refused therapy. Despite this, of the 22 patients with severe POSA, 9 patients experienced a therapeutic response with MADs (50% reduction in AHI), in 5 of whom therapeutic success was observed (post-treatment AHI < 10) and in 8 of whom recovery occurred (posttreatment AHI < 5). Of the 7 patients with very severe POSA, therapeutic response occurred in 5 patients, therapeutic success in 1 patient, and recovery in 1 patient. In our study, the 86 patients examined were aged between 34.42 and 64.38 years (49.4 ± 4.98 years), with a statistically non-significant difference in age between the 3 groups examined, and had a BMI between 22.45 and 31.03 (26.74 ± 4.29) kg/m^2, that is, between normal weight and first degree obesity. In particular, in the present study, siOSA had a mean BMI of 26.9 kg/m^2, spOSA of 23,15 and NPOSA of 27,34, with a statistically relevant difference between them (p-value = 0.038). These findings are consistent with the observations by Joosten et al.[27], by which positional patients show a higher BMI than nonpositional patients, even though that study, in opposition to what we found, reported lower BMI values in siOSA than in spOSA patients. This difference can be explained by the numerical difference in the sample selected.

Table 6 Correlation (p-value) between intraoral variables and initial total apnea-hypopnea index.

Variable	p-value
Molar relationship	0.5
Canine relationship	0.3
Overbite	0.9
Overjet	0.4
Maxillary intermolar distance	**0.06**
Maxillary intercanine distance	0.5
Curve of Spee	0.7

According to the literature, OSA is more prevalent in men than in women,[12] which is confirmed by our sample, since 86% of patients were males and 14% were females. These results are comparable to those observed by Kim et al.[15]

Patients with predominant OSA often present to a sleep doctor due to bed partner complaints of snoring. Therefore, any treatment which improves AHI should also improve the snoring index in the long term. Published studies do not often consider this aspect. However, given the importance of the symptom for the patients and the bed partner, it is important to analyze the snore index in different body positions.[29]

A statistically significant reduction in the snore index was observed between T0 and T1 (p-value = 0.02) in all three groups examined (p-value = 0.00). In accordance with Chung et al.,[26] we found a higher decrease of total AHI and supine AHI in POSA patients rather than in NPOSA patients.

From a descriptive standpoint, it is interesting to observe that the fourth degree hypopharyngeal collapse (H) with anteroposterior pattern was the most frequent. On the other hand, the N, O, and L scores showed a nonstatistically significant correlation compared with the total pretreatment AHI value. Therefore, according to these statements, the tongue base H was the most represented anatomic area of collapse in patients affected by OSA, confirming the results of a previous study by Vicini et al.[30] On the other hand, Vroegop et al., in 2014, concluded that 81% of obstructions occur at the

retropalatal level. The differences in outcomes are probably caused by the different classification system used; the velum, oropharynx, tongue, and/or epiglottis (VOTE) classification used by Vroegop et al.[31] involved a difference in the description of the anatomical sites.

From an orthodontic standpoint, malocclusion can influence the occurrence of sleep apnea, but the pathology of malocclusion in OSA has not yet been fully investigated. In the present study, we did not observe any statistically significant correlation (Pearson product moment correlation) between the initial total AHI and overjet, overbite, or molar relationship at T0 (p-value > 0.05), although 64% of the dental casts showed a Class II molar relationship, 36% showed an increased overjet ($\geq$ 6.5 mm), and 52% deepbite ($\leq$ 7 mm). All the examined patients showed an increased Curve of Spee (p-value $= 0.7$), while 52% of the examined dental casts showed crossbite (p-value $= 0.6$). We found a correlation between the upper intermolar distance and the pretreatment AHI (correlation index = - 0.39 and p-value $= 0.06$). The decrease of the transversal diameters is associated with an increased nasal resistance and posterior tongue displacement. Liu et al. reported a 10.9-fold increase in the odds of OSA with this phenotype.[32] According to Marino et al., no correlation between lower intermolar and intercanine distance and the severity of the OSA exists.[33]

The main strength of the present study is represented by the comparability between the three categories of patients (NPOSA, siOSA, and spOSA), all treated in the same center, with the same appliance design and following the same clinical protocol of titration. Few studies published up to now have investigated the efficacy of MADs in a defined category of OSA, such as POSA[21,34–37]; none of them distinguished this category of patients into siOSA and spOSA and compared this category of patients to a control group of NPOSA patients. The use of a home PSG represented the main limitation of the present study due to the impossibility to evaluate respiratory effort related arousal (RERA), and therefore the respiratory disturbance index (RDI).

Conclusions

Within the limitations of the present study, the following conclusions are drawn:

- Mandibular advancement device therapy appears to be effective in reducing the total AHI, supine AHI, and non-supine AHI in patients affected by NPOSA, siOSA, and spOSA from a mild to a very severe degree.
- Positional OSA affects predominantly the male sex in a mean age of 49.4 ± 14.98 years and a BMI of 26.74 ± 4.29 kg/m^2 with greater prevalence in the siOSA group than spOSA.
- Supine AHI decreases at T1 with MADs mainly in patients siOSA and spOSA compared with the NPOSA group. It is likely that POSA may be considered a potential predictor for MAD success.
- Snore index decreased significantly at T1 with MADs in all groups. Nonpositional OSA may be considered good responders for this kind of treatment in case of snoring, because the snore index reduction appeared to be greater than in other groups.
- The tongue base H was the most represented respiratory collapse area at T0 in OSA patients, suggesting that patients with this obstruction localization are likely to be good responders to MADs therapy.
- At T0, OSA patients showed more often superior maxillary constriction at the intermolar level with a rho correlation index of -0.39.

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Conflict of Interests
The authors have no conflict of interests to declare.

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