

Article

Effects of Mandibular Advancement Device on Cardiovascular and Respiratory Parameters in OSA Patients

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Abstract

Background: Mandibular advancement devices (MADs) are considered an effective therapeutic option for managing obstructive sleep apnea syndrome (OSAS) in adults. Obstructive sleep apnea (OSA) is associated with a range of comorbidities, notably cardiovascular disease. The aim of the present retrospective study is to evaluate respiratory and cardiovascular parameters in OSA patients treated with a MAD. **Methods:** A total of 64 adults with OSA from moderate-to-severe OSAS underwent split-night polysomnography (SN-PSG) at baseline (T0) and after three months of treatment with a MAD (T1) and were subsequently analyzed using statistical methods for a comparative evaluation. **Results:** After 3 months of treatment, patients showed a significant decrease in mean heart rate ($p < 0.05$), maximum heart rate ($p < 0.01$) and in both the AHI and ODI ($p < 0.01$), along with a significant increase in minimum heart rate ($p < 0.05$). **Conclusions:** These findings indicate that MAD therapy may contribute to improvements in both respiratory efficiency and cardiovascular function in individuals with OSAS, offering a valuable integrated treatment strategy for patients with coexisting cardiovascular conditions.

Keywords: obstructive sleep apnea; OSA; cardiovascular function; mandibular advancement device (MAD)



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1. Introduction

Obstructive Sleep Apnea Syndrome is a sleep disorder characterized by repeated upper airway collapse that can lead to total obstruction (apnea) or partial obstruction (hypopnea) despite maintenance of inspiratory efforts. By definition, the duration of apnea is at least 10 s, usually in association with hypoxia and sleep fragmentation. Apnea events are categorized as either obstructive or central depending on whether respiratory effort is detected during the episode [1]. Based on the Chicago criteria, hypopnea is identified when at least one of the following conditions is met: a significant airflow reduction exceeding 50%, or a moderate reduction below 50% with desaturation ($>3\%$), or a moderate reduction in airflow ($<50\%$) with electroencephalographic evidence of arousal [2]. OSAS is one of the most prevalent sleep-related respiratory disorders, ranking second only to asthma in terms of overall frequency [3]. OSAS is estimated to impact between 2% and 4% of adults, with middle-aged men representing the demographic most frequently affected.

One in five adults have moderate OSAS, while one in fifteen have moderate-to-severe OSAS. OSAS is also highly underdiagnosed: 82% of men and 93% of women in the United States with OSA are undiagnosed [4]. According to Punjabi, risk factors are age, body weight, sex, craniofacial anatomy, familial predisposition and medical comorbidity [5]. Risk factors for obstructive sleep apnea can be divided in modifiable and unmodifiable factors. Unmodifiable factors are sex, age and race, while modifiable ones are obesity, medications like opiates, smoking, endocrine system disorders and nasal obstruction [4]. Age is a common risk factor. Older individuals have a reduction in tissue elasticity with reduced production of collagen, which lead to increased collapsibility [6]. Some studies report a significant gender difference in the occurrence of OSA between men and women, but this gender gap decreases with age, probably according to the hormonal changes that women have during menopausal age [7].

Multiple studies have consistently identified obesity as the most significant risk factor in the development of OSA [8]. In addition to excess body weight, craniofacial anomalies such as hypertrophy of the tongue base and tonsillar and uvular enlargement, as well as skeletal deficiencies of the maxilla and mandible, play a critical role in predisposing individuals to OSA by narrowing the upper airway lumen [1,9]. Regarding symptomatology, this can be classified as nocturnal and diurnal. Daytime symptoms include daytime sleepiness, tiredness and chronic morning headaches, while nocturnal symptoms are habitual snoring, nocturia, gasping or choking [6]. Obstructive sleep apnea is associated with many consequences: metabolic dysfunctions [10], impairment of neurocognitive function [11] and OSAS-associated daytime sleepiness, which increases the occurrence of driving accidents [12], but it is also linked to cardiovascular disease [13]. OSAS relates to hypertension, ischemic stroke, atrial fibrillation, coronary artery disease, cardiac arrhythmias and heart rate variability [14–16]. The mechanisms involved in the development of cardiovascular disorders associated with OSA are multifactorial and include numerous events. Recent advances have enhanced the understanding of the variability within obstructive sleep apnea (OSA), leading to the development of symptom-based subgroups and the identification of specific biomarkers linked to cardiovascular risk [17]. One such indicator is the heart rate response following an obstructive breathing event, known as the delta heart rate (Δ HR), which reflects both the intensity and length of the episode. Higher Δ HR values, especially when the event ends with cortical arousal, have been linked to a greater likelihood of adverse cardiovascular outcomes and mortality in OSA patients [18]. Additionally, in studies involving individuals diagnosed with both OSA and coronary artery disease, elevated Δ HR levels were correlated with more pronounced cardiovascular improvements following continuous positive airway pressure (CPAP) therapy [19].

One of the most established mechanisms is certainly the hyperactivity of the sympathetic system in individuals with sleep apnea with a relative increase in blood pressure during sleep; this is subsequently associated with endothelial dysfunction, inflammation and oxidative stress [20]. Heart rate variability (HRV) describes the oscillations in rate between consecutive cardiac cycles on an ECG recording; this is a noninvasive assessment and evaluation of selective cardiovascular autonomic function and its variation can be related to adverse cardiovascular events [21]. Respiratory sinus arrhythmia (RSA) is a normal physiological process representing the coordination between cardiac and pulmonary activity. It is marked by rhythmic changes in heart rate, which increases during inhalation and decreases during exhalation. As a result, heart rate variability (HRV) during normal breathing presents differently compared to patterns seen in deep breathing or apneic episodes due to changes in the respiratory cycle. Additionally, research indicates that treatments for obstructive sleep apnea (OSA) may restore autonomic system regulation not only during nocturnal sleep but also across waking hours. Specifically, Glos et al. [22] demonstrated that

both continuous positive airway pressure (CPAP) and mandibular advancement device (MAD) therapies enhance vagal output to the heart.

The gold standard in the treatment of sleep apnea is continuous positive airway pressure (CPAP), especially in severe cases when non-surgical techniques fail or are unacceptable to patients. Surgery is another treatment choice that can be considered depending on anatomical risks. The American Association of Sleep Medicine (AASM) has also proposed the use of oral appliances in snoring and sleep apnea treatment [3]. Mandibular advancement device (MAD) therapy is recommended by the AASM as a first-line treatment in mild-to-moderate OSA [23]. Therefore, a strong correlation between obstructive sleep apnea syndrome (OSAS) and cardiovascular disease has been demonstrated. Given this relationship, it is crucial to investigate the impact of mandibular advancement devices (MADs) not only on respiratory indices but also on cardiovascular parameters. Despite the widespread clinical use of MADs, their effects on cardiac function remain insufficiently characterized in the current literature. A deeper understanding of these interactions is essential to fully assess the therapeutic potential of MADs and to optimize their role in the multidisciplinary management of OSAS.

The aim of the present study was to evaluate cardiovascular and respiratory activity in OSA patients using a mandibular advancement device (MAD). The null hypothesis is that the mandibular advancement device (MAD) has no effect on cardiac parameters.

2. Materials and Methods

2.1. Study Population

This retrospective study included 64 patients diagnosed with obstructive sleep apnea syndrome (OSAS): 34 males and 30 females with a mean age of 30.5 ± 8.7 years. Participants were selected in chronological order from among those treated at the Department of Orthodontics, University of Foggia, Italy, between January 2016 and July 2022.

All patients had a confirmed diagnosis of obstructive sleep apnea (OSA) based on cardiorespiratory polysomnography (PSG) and underwent treatment with a mandibular advancement device (MAD). Prior to participation, all individuals provided written informed consent. The study protocol adhered to the ethical standards set forth in the Declaration of Helsinki and its later amendments. Ethical approval for all procedures was granted by the Ethics Committee of the University of Foggia.

The patients were recruited based on the following inclusion criteria: age over 25 years old, class II malocclusion, a diagnosis of moderate-to-severe OSA confirmed by PSG, a body mass index (BMI) lower than 34 kg/m^2 and the use of a MAD as therapy for OSA treatment. Patients with a smoking habit, medications for neurological disorders or a history of cervical head trauma, temporo-mandibular disease (TMD), comorbidities like arrhythmias, congenital heart disease, stroke and heart failure or pulmonary diseases at the time of diagnosis were excluded from the study.

2.2. Methods and Parameters

Prior to initiating therapy, each patient underwent drug-induced sleep endoscopy (DISE). In addition, a split-night polysomnographic study (SN-PSG) was conducted, involving a minimum of four hours of continuous monitoring using a type 2 portable system (Embletta X-100, Flaga, Reykjavik, Iceland) within a sleep laboratory setting, was conducted on every patient before MAD therapy (T0). The recordings comprised electroencephalograms, electrooculograms, electromyograms, pulse oximetry, abdominal respiratory effort belts, body position sensors, nasal cannulas and oral thermistors [24]. Manual scoring was performed on the initial three hours of data based on the 2007 AASM guidelines [23]. A follow-up sleep study using a mandibular advancement device was conducted three months

post-treatment (T1) (Protrusor[®] and nonrusso+[®], Dr. Giuseppe Burlon, Belluno, Italy). This fully customizable device consisted of two resin splints connected by two titanium bars, each secured with titanium screws, forming a protrusive mechanism (Figure 1). Mandibular advancement was individualized for each patient following an initial titration period. An initial advancement corresponding to 70% of the maximum protrusive capacity was set using an intraoral gauge (Occlusion[®] and nonrusso+[®], Dr. Giuseppe Burlon, Belluno, Italy). Two weeks into treatment, the mandibular position was fine-tuned in 1–2 mm steps to reach the most suitable and effective therapeutic alignment for each patient. The parameters evaluated included the apnea–hypopnea index (AHI); the oxygen desaturation index (ODI), defined as the number of events with oxygen drops exceeding 4% per hour of sleep; and heart rate (HR) values—mean, minimum and maximum. The device was worn 10 h per night. Therapy adherence was clinically assessed through monthly follow-up visits and confirmed through a polysomnographic evaluation conducted after three months of treatment.



Figure 1. Intraoral photos in frontal and lateral views of a patient treated with the Protrusor.

Polysomnography Quality Control

To ensure data accuracy and clinical reliability, comprehensive quality control procedures were applied throughout the polysomnographic assessment.

Prior to the examination, all sensors and recording channels were checked for proper functioning and calibration. Electrodes were placed in accordance with international standards, and signal stability was verified.

Following the examination, recorded data were reviewed to confirm signal integrity. This included the identification and exclusion of artifacts, detection of signal loss and correction of any recording errors to ensure the validity of the acquired physiological parameters.

2.3. Statistical Analysis

All statistical analyses were performed using GraphPad Prism software 6.0 (San Diego, CA, USA). Descriptive statistics were performed for all the variables. The Shapiro–Wilk test was applied to assess whether the data followed a normal distribution. Because the variables were not normally distributed, Wilcoxon’s signed-rank test was used to compare the variables analyzed (Table 1). To compare the differences in variables measured before and after treatment (T1 vs. T0), a Wilcoxon signed-rank test was conducted (Table 2). To account for the increased risk of Type I error associated with multiple comparisons, the Bonferroni correction was applied to adjust the significance threshold accordingly (Table 2). In addition, a “Power Analysis” test, introduced by Jacob Cohen, was performed to determine the correct sample size, which is necessary to detect the effects of desired size with a given power [25]. A power analysis performed using G*Power 3.1.9.2 (Franz Faul, University of Kiel, Kiel, Germany) determined that a sample size of 59 participants is required to detect a large effect size of 0.4 with a Wilcoxon signed-rank test, assuming an alpha level of 0.05 and a statistical power of 0.95.

3. Results

Descriptive statistics are reported in Table 1. Table 1 also presents the outcomes of the Wilcoxon signed-rank test comparing measurements at baseline (T0) and post-treatment (T1). All evaluated parameters showed statistically significant differences between the two time points. Table 2 and Figure 1 display the results for the T1–T0 variations across variables. The results showed a non-significant decrease in mean heart rate ($p > 0.05$), a significant reduction in maximum heart rate ($p < 0.01$) and a significant increase in minimum heart rate ($p < 0.01$). Additionally, both the apnea–hypopnea index (AHI) and oxygen desaturation index (ODI) demonstrated significant reductions ($p < 0.01$). Based on these findings, the null hypothesis was rejected. The application of the mandibular advancement device led to a marked improvement in respiratory indices, including significant reductions in both the apnea–hypopnea index (AHI) and oxygen desaturation index (ODI). Specifically, the AHI decreased by 21.48 events/hour, while the ODI declined by 15.05 events/hour after treatment. Improvements were also observed in cardiovascular metrics: the maximum heart rate dropped by 24 bpm, mean heart rate was reduced by 1.72 bpm and minimum heart rate increased by 4.16 bpm. Figure 2 summarizes the changes in polysomnographic variables before and after treatment, displayed as a column chart.

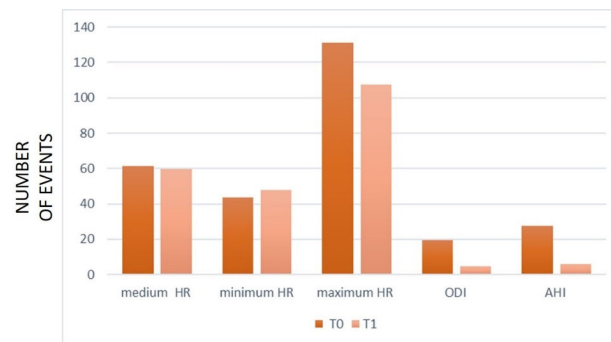


Figure 2. Column chart of the averages of polysomnographic variables before (T0) and after treatment (T1).

Table 1. Descriptive statistics for the variables analyzed and Wilcoxon signed-rank test for the variables measured at T0 and T1.

	Mean HR (T0)	Mean HR (T1)	Minimum HR (T0)	Minimum HR (T1)	Maximum HR (T0)	Maximum HR (T1)	ODI (T0)	ODI (T1)	AHI (T0)	AHI (T1)
Number of values	64	64	64	64	64	64	64	64	64	64
Mean	61.47	59.75	43.84	48.00	131.3	107.3	19.7	4.65	27.7	6.22
Std. Deviation	7.329	8.84	9.68	8.17	41.24	28.57	9.42	3.21	12.3	4.05
Std. Error of Mean	0.91	1.106	1.211	1.02	5.155	3.57	1.17	0.4	1.54	0.5
Lower 95% CI of mean	59.64	57.54	41.42	45.96	121.01	100.2	17.3	3.85	24.6	5.21
Upper 95% CI of mean	63.30	61.96	46.26	50.04	141.6	114.4	22.01	5.46	30.7	7.23
Passed normality test	No	No	No	Yes	No	No	No	No	No	No
<i>p</i> value		0.05		0.001		0.001		0.001		0.002

Table 2. Wilcoxon signed-rank test for the T1–T0 difference of each variable.

(N = 64)	Mean Difference	<i>p</i> Value *	Significance After Bonferroni Correction ($\alpha = 0.01$)
Mean HR	−1.72	0.047	Not significant
Minimum HR	4.16	0.001	significant
Maximum HR	−24	0.0001	significant
ODI	−15.05	0.0001	significant
AHI	−21.48	0.0001	significant

* $p < 0.05$.

4. Discussion

Numerous studies have confirmed the strong link between obstructive sleep apnea syndrome and various comorbidities, particularly an elevated risk of cardiovascular complications. OSA has been independently associated with a higher occurrence of conditions such as hypertension, stroke, heart failure, atrial fibrillation and coronary artery disease [26]. Several mechanisms are involved in the development of cardiovascular risk, but certainly the main ones are repetitive episodes of intermittent hypoxia, changes in intrathoracic pressure and sleep fragmentation that contributes to sympathetic system activation. Hypoxia, like hypercapnia, leads to the activation of chemoreceptors, resulting in increased sympathetic activity, and thus vasoconstriction and an increased heart rate. Apnea, as it occludes the airways, generates an increase in negative intra-thoracic pressure, which increases left ventricular transmural pressure and the venous return to the right ventricle, leaving consequences on the heart's anatomy. Apnea ends with awakening from sleep that increases sympathetic nerve discharge and blocks vagal tone, resulting in an increased heart rate and a peak of blood pressure that tend to rebalance again during sleep until a new apnea cycle occurs [27].

In assessing the clinical benefits of mandibular advancement devices (MADs), it is essential to evaluate not only the changes in respiratory parameters like the Apnea–Hypopnea Index (AHI) but also their potential impact on cardiovascular health. This comprehensive view is justified by the well-established link between OSA and heightened cardiovascular risk. Obstructive sleep apnea (OSA) is recognized as an independent contributor to both primary and treatment-resistant hypertension. It is estimated that nearly 30% of individuals with high blood pressure also suffer from OSA, while around half of those with OSA exhibit systemic hypertension. OSA can lead to the development or progression of heart failure, which may be associated not only with hypertension, but also with increased ischemic events, reduced contractility and recurrent negative intrathoracic pressure [28].

The study demonstrated an improvement in the heart rate parameter following the use of the mandibular advancement device due to the important change in all of the heart rate values considered before and after treatment. Evidence demonstrated the efficacy of using a MAD as treatment of apnea, significantly reducing obstructive phenomena [26]. Thus, the use of MADs has effects not only on improving obstructive sleep apnea but also on cardiac activity, limiting associated cardiovascular implications. In the current study, treatment with a MAD resulted in an increase in average minimum heart rate and a reduction in average maximum heart rate, aligning with outcomes reported in earlier research. Bratton et al. found important reductions in blood pressure using CPAP and MAD therapy as treatment in OSA patients [29]. Building on Bratton's findings, Dissanayake et al. [30] also reported notable enhancements in both quality of life and cardiovascular metrics with MAD treatment. A comprehensive review further revealed that the heart rate reduction achieved through MAD therapy is comparable to that seen with CPAP [31]. This aspect is particularly important, as the scientific literature has identified obstructive sleep apnea syndrome (OSAS) not only as an independent risk factor for heart failure, but also as a condition associated with reduced survival in patients with heart failure compared to those without sleep apnea [32].

Increased sympathetic nerve activity during both sleep and wakefulness leads to cardiac remodeling, ventricular hypertrophy and systolic and diastolic dysfunction, but this can also predispose to ventricular fibrosis. OSAS can be also a risk factor for developing arrhythmogenesis due to electrical and structural myocardial changes in sleep apnea patients. In general, scientific evidence has demonstrated that both higher and lower resting heart rates are associated with cardiovascular disease and increased mortality [33].

An elevated resting heart rate value appears to be an important predictor for CVDs such as coronary artery disease, myocardial infarction and chronic heart failure while a heart rate reduction could contribute to the reduction in CVD [34]. As Tjungen et al. say, heart rate is certainly a measurement that shows increased activity of the sympathetic nerve and can hold prognostic significance for the development of CVD and hypertension [34]. HR monitoring and analysis can be used also to predict cardiovascular risk in patients with obstructive sleep apnea [31].

Existing literature consistently shows that both CPAP and MAD treatments contribute to lowering blood pressure and enhancing cardiovascular performance. In a meta-analysis by Bratton et al. [29], meta-regression revealed that patients with higher initial blood pressures experienced greater reductions in both systolic and diastolic values when treated with CPAP compared to those using MAD. Nonetheless, a separate meta-analysis [35] found no significant differences in blood pressure outcomes between CPAP users (regardless of nightly usage duration) and MAD users. Despite these mixed results, it remains clear that both CPAP and MAD therapies can lead to meaningful improvements in cardiovascular health, potentially extending life expectancy and improving quality of life in patients with OSA.

The clinical relevance of this study is underscored by the high prevalence of cardiovascular comorbidities among patients with obstructive sleep apnea (OSA). The findings suggest that mandibular advancement devices (MADs) may confer therapeutic benefits beyond respiratory improvement by positively influencing cardiovascular parameters. This dual effect is particularly significant given the established association between OSA and increased cardiovascular morbidity and mortality. Therefore, incorporating MAD therapy in OSA management could provide a comprehensive approach that mitigates both respiratory dysfunction and cardiovascular risk.

Limitations of the Study

This study has several limitations. The retrospective design and short follow-up period limit the generalizability of the findings. Additionally, the limited duration of follow-up may affect the robustness of the observed outcomes. Further prospective research involving larger cohorts and longer follow-up durations is necessary to confirm and broaden the current findings.

5. Conclusions

The use of a mandibular advancement device (MAD) as therapy for obstructive sleep apnea syndrome (OSAS) is an excellent treatment option for adults with moderate-to-severe obstructive sleep apnea. MADs appear to be effective not only in reducing respiratory parameters such as AHI and ODI, but also in improving cardiac parameters by lowering the maximum HR and increasing the minimum HR. Therefore, the use of MADs not only improves respiratory function but also enhances cardiac function by reducing both tachycardic and bradycardic phenomena, which, according to the literature, are two distinct conditions that may predispose individuals to the development of cardiovascular disease.

In conclusion, mandibular advancement devices (MADs) represent an effective therapeutic option for patients with moderate-to-severe obstructive sleep apnea (OSA), particularly those presenting with associated cardiovascular comorbidities. The use of MADs not only alleviates respiratory parameters by reducing apnea–hypopnea indices but may also contribute to improved cardiovascular function, as evidenced by favorable modifications in heart rate parameters.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Conflicts of Interest: The authors declare that they have no conflicts of interest to disclose, except for Giuseppe Burlon, who is the owner of the patents and the registered trademarks for Occlusion[®], nonrusso+[®] and Protrusor[®].

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