Prevalence of Temporomandibular Disorders in Obstructive Sleep Apnea Patients Referred for Oral Appliance Therapy

Paulo A. Cunali, DDS, PhD Professor Department of Dentistry Universidade Federal do Parana Parana, Brazil, and Sleep Medicine and Biology Discipline Psychobiology Department Universidade Federal de São Paulo São Paulo, Brazil

Fernanda R. Almeida, DDS, PhD Professor Department of Oral Health Sciences The University of British Columbia Vancouver, Canada

Camila D. Santos, DDS Postgraduate Student Sleep Medicine and Biology Discipline

Natália Y. Valdrighi, MD Graduate Student Sleep Medicine and Biology Discipline

Liliane S. Nascimento, MD Graduate Student Sleep Medicine and Biology Discipline

Cibele Dal'Fabbro, DDS, MSc Postgraduate Student Sleep Medicine and Biology Discipline

Sérgio Tufik, MD, PhD Professor Sleep Medicine and Biology Discipline

Lia Rita A. Bittencourt, MD, PhD Professor Sleep Medicine and Biology Discipline

Psychobiology Department Universidade Federal de São Paulo São Paulo, Brazil

Correspondence to:

Dr Paulo Afonso Cunali Rua Cel. Napoleao Marcondes Franca, 360 Hugo Lange – 80.040-270 Curitiba, PR, Brazil Fax: 55-11-3322-1234 Email: pacunali@onda.com.br

Aims: To evaluate the prevalence of pain associated with temporomandibular disorders (TMD) in obstructive sleep apnea syndrome (OSAS) patients referred for oral appliance therapy. Methods: Eighty-seven patients (46 men and 41 women), between 18 and 65 years of age, with an apnea-hypopnea index (AHI) of > 5 and < 30(events by sleep hour), and body mass index (BMI) of $\leq 30 \text{ Kg/m}^2$ were evaluated according to the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) to determine the presence of signs and symptoms of TMD. Statistical analyses included correlations assessed by Pearson's test. Results: Fifty-two percent of patients presented symptoms of TMD. Thirty-two patients (average age 47 ± 11 years, AHI 17.3 ± 8.7, BMI 25.9 ± 3.8 kg/m^2) completed the study. According to the Scoring Protocol for Graded Chronic Pain (Axis II-RDC/TMD), 75% of the patients presented chronic pain related to TMD, categorized as low disability grade I (< 50 points for pain intensity, and < 3 disability points). The most common TMD diagnosis was myofascial pain with and without limited mouth opening and arthralgia (50%). Conclusion: The high prevalence of TMD in the current study indicates that patients with OSAS referred for oral appliance therapy require specific evaluation related to TMD. J OROFAC PAIN 2009;23:339-344

Key words: oral appliance, prevalence, side effects, sleep apnea, temporomandibular disorders

bstructive sleep apnea syndrome (OSAS) is considered to be a serious problem,¹ triggering multiple physiological processes that detrimentally affect normal body function. OSAS is a rather frequent respiratory sleep disturbance² that affects 4% to 9% of the middle-aged population.¹

The use of a mandibular repositioning oral appliance has demonstrated effectiveness in the treatment of mild to moderate OSAS.^{3–5} The device normalizes the apnea-hypopnea index (AHI), ie, the number of obstructive events per sleep hour, and also improves daytime symptoms, cardiovascular and neurocognitive function, and the quality of life.⁵

An oral appliance is an alternative treatment for those patients with severe OSAS who cannot tolerate nasal continuous positive airway pressure therapy (CPAP).⁶ Similar to CPAP, some adverse effects can be observed during the use of an oral appliance. Excessive salivation, dry mouth, and pain or discomfort in the supporting teeth, oral mucosa, masticatory muscle, and temporomandibular joint (TMJ) have been reported as temporary side effects during short and medium periods of oral appliance wear.⁷⁻¹¹ Long-term side effects are characterized by occlusal changes without the presence of pain.¹²⁻¹⁴

Temporomandibular disorders (TMD) have a complex and multifactorial etiology.¹⁵ The primary signs and symptoms of TMD are pain in the facial region and TMJ, limited asymmetric mandibular movement, TMJ sounds, headache, and sleep disturbances.¹⁶⁻²¹ The prevalence of TMD is high in the general population^{18,19,21}; 3% to 7% of the population seeks treatment for pain and dysfunction of the TMJ or related structures.^{18,21,22} The distribution of patients with TMD shows that women are more affected by these dysfunctions than men, with patients generally between the ages of 20 to 50 years.^{18,19,21,22} This high prevalence creates the likelihood that patients with OSAS could also present TMD. A diagnosis of TMD is determined by TMJ sounds, palpation of the masticatory muscles and TMD which triggers or increases pain, and also by pain resulting from mandibular movement.²³ TMJ noise without pain can characterize an anatomical disorder without acute inflammation.²² The Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) are commonly used to diagnose most common TMD (Axis I) and assess the impact of TMD pain in patients (Axis II).²³

The relationship between quality of sleep and TMD is not fully understood. Some studies have shown a significant correlation between loss of sleep quality and a higher perception of TMD pain.^{24–27} Since the main complaints of patients who suffer from OSAS are snoring, excessive day-time sleepiness, and poor quality of sleep,² the signs and symptoms of TMD might go unnoticed by both patients and professionals, indicating that patients with OSAS as well as those with TMD must be evaluated more effectively.

As the prevalences of TMD and OSAS are high in the general population, many patients might complain of TMD pain during oral appliance treatment. The aim of this study was to evaluate the prevalence of pain associated with TMD in OSAS patients referred for oral appliance therapy.

Materials and Methods

Subjects

Patients diagnosed with mild to moderate OSAS referred for oral appliance therapy were evaluated at the Sleep Clinic at the Psychobiology

Department of the Universidade Federal de São Paulo (UNIFESP)-Brazil. The clinical and polysomnographic criteria for mild to moderate OSAS followed the International Classification of Sleep Disorders (ICSD-2) proposed by the American Academy of Sleep Medicine.² Subjects were considered to have OSAS if they had an AHI between 5 and 14.9 (obstructive events by sleep hour) and presented at least one of the following complaints: loud snoring, daytime sleepiness, fatigue, and breathing interruptions observed during sleep. Subjects with an AHI \geq 15 to 30, were also considered to have moderate OSAS, regardless of whether they had any of the aforementioned complaints. The inclusion criteria for the present study were: age between 18 and 65 years old, body mass index (BMI) of $\leq 30 \text{ kg/m}^2$ assessed through medical examination, and complete odontological health examinations (clinical and x-ray examinations) that did not contraindicate the use of an oral appliance. Patients who reported alcohol abuse, use of drugs that interfere with sleep, the presence of any sleep disturbances other than OSAS, or previous OSAS treatment were excluded. During polysomnography, breathing was measured by air flow with a nasal canula, thoracic and abdominal movements with plestismography, and oxygen saturation with an oxymetry device.

Ethical approval for this study was obtained from the Hospital São Paulo Ethical Committee (n°. 0162/06), and informed consent was obtained from all patients.

Epworth Sleepiness Scale (ESS)

Changes in self-reported sleepiness were measured using the ESS.²⁸ The patients were instructed to imagine their sleepiness in eight everyday situations that require different attention levels, and to score sleepiness as 1, 2, or 3 corresponding to a mild, moderate, or high chance of falling asleep, respectively. The total score was determined and an outcome > 10 was considered to reflect excessive daytime sleepiness.

TMD Evaluation

For the TMD evaluation, a version of the RDC/TMD was used that was culturally adapted and translated into Portuguese,^{29,30} with the objective of diagnosing, classifying, qualifying, and quantifying the chronic pain associated with TMD through signs, symptoms, and physical examination. The examination was standardized and only one experienced observer (PC) was responsible for

all the examinations throughout the study. Axis I (RDC/TMD): Clinical Physical Examination was used to diagnose TMD. The diagnostic algorithms for muscle pain were used. Myofascial pain was diagnosed when more than three tender muscle sites were observed by palpation on the same side as ongoing pain, and the pain-free opening was \geq 40 mm, or when this opening was \leq 40 mm and passive stretch produced a difference < 5 mm. When the pain-free opening was < 40 mm and passive stretch produced a difference of > 5 mm, a diagnosis of myofascial pain with limited opening was made. Other situations were not considered muscle TMD. Diagnosis of joint pain associated with TMD was established by the RDC/TMD algorithms for left and right joint pain. Thus, arthralgia was diagnosed when pain was present upon joint palpation on the same side as the palpation, during opening movement or upon mandibular excursion, and no coarse crepitus was observed during any mandibular movement. The presence of coarse crepitus justified a diagnosis of osteoarthritis. The diagnosis of osteoarthrosis was made when neither pain nor palpation pain was reported, but coarse crepitus was present in the joint during any movement. Other situations were not considered joint dysfunction associated with TMD. Axis II (RDC/TMD): Biobehavioral Questionnaires, from the Scoring Protocol for Graded Chronic Pain index, were used to classify pain according to its intensity and the pursuant limitation. Patients who reported < 50 points for pain intensity on a visual analog scale (VAS) (0-100, where 0 indicated absence of pain and 100 unbearable pain) and < 3disability points were categorized as low disability grade I (low disability and low pain intensity). Patients were classified as low disability grade II (low disability and high pain intensity) when the reported results were ≥ 50 points for pain intensity and < 3 disability points. High disability grade III (high disability and moderately limiting) refers to patients who report 3 to 4 disability points regardless of pain intensity. High disability grade IV (high disability and severely limiting) refers to patients who report 5 to 6 disability points, regardless of pain intensity.²³ All patients filled out the Axis II: Biobehavioral Questionnaires from the RDC³⁰ in order to evaluate the presence during the past month of pain in the face, jaw, temple, and ear area. The clinical examination used for confirmation and classification of TMD was carried out according to the Axis I: Clinical Physical Examination Forms and specifications of the RDC/TMD.29

Table 1Subject Characteristics and Clinical and Polysomnographic Data (n = 32)				
	Mean	SD	Minimum	Maximum
Age (y)	47	11	27	65
Gender (male/female)	11/21			
BMI (kg/m²)	25.9	3.8	19.9	32.9
AHI (events/h)	17.3	8.7	5.1	19.2
Mean oxygen saturation, %	94.7	1.9	90	99.8
Minimum oxygen saturation, %	6 86.2	3.8	79	93
ESS	13	6	0	24

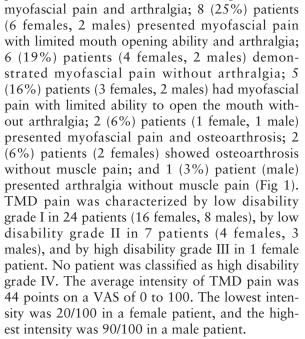
Statistical Analyses

Most of the data are descriptive. Demographic and polysomnographic data are presented as mean and standard deviation, and minimum and maximum values are also shown. Correlations between pain, age, BMI, and AHI were assessed by Pearson's test. A significance level of < .05 was considered to reflect statistical significance.

Results

Among the 87 patients with mild to moderate OSAS (46 male, 41 female; mean 46 ± 2.19 years old), 45 (52%) presented some type of sign and/or symptom of TMD. Of those 45 patients with TMD, 13 were excluded due to the following conditions: one female patient suffered from congenital muscle disease, one male patient had a different sleep disturbance (delayed sleep syndrome), and 11 patients did not return for the clinical physical examination.

As a result, the population in the current study consisted of 32 patients diagnosed with TMD by the RDC who also had an indication for oral appliance therapy. Patient characteristics and results of their baseline polysomnography are shown in Table 1. The patient population comprised 21 females and 11 males with a mean age of 47 years. Most of the patients were not obese and had an average BMI of 25.9 Kg/m². The average ESS and AHI scores were 13 and 17.3/hour, respectively. None of the studied patients presented comorbidities, restless leg syndrome, or periodic limb movement syndrome complaints, or polysomnographic findings indicating sleep disturbances other than OSAS. Eight (25%) of these



patients (5 females, 3 males) were diagnosed with

There were no correlations between pain intensity and age (r = -0.06, P = .5), BMI (r = -0.13, P = .72), or AHI (r = -0.05, P = .65).

Discussion

The results of the present study showed that the presence of TMD and the impact of this dysfunctional pain were high among OSAS patients referred for oral appliance therapy. There is controversy surrounding oral appliance contraindications and adverse effects of its use to treat OSAS patients with TMD. Regarding the side effects of oral appliance usage, the literature shows that between 10% to 77%⁷⁻¹¹ of patients reported pain or discomfort from TMD related to oral appliance wear, but often cited these symptoms as not clinically significant.³¹

In the present study, 52% of the OSAS patients presented TMD. Other studies observed TMD in only 2% of their sample³¹ or did not report any patients with contraindications for use of an oral appliance to treat OSAS. Our findings concerning the TMD grade scale in OSAS patients are also consistent with some TMD studies examining the general population.^{32–34}

Pain in the masticatory muscles and/or TMJs is commonly identified as a contraindication for oral appliance therapy, and can lead to the noncompliance of patients provided with an oral appliance as an OSAS treatment.^{6,31,35,36} Some studies have reported that TMD pain may be a side effect of oral appliance therapy which may have been the reason for the contraindication.7-11 These studies did not classify TMD or evaluate the intensity and disability grade of the TMD pain. The gender, age, and complaints of preexisting TMD pain in patients who interrupted the use of an oral appliance were also not mentioned.7-11 Since these studies were based on different models with various methodologies,⁷⁻¹¹ there is a lack of consistency in the literature regarding the contraindication of oral appliance usage to treat OSAS patients with TMD.

In a prospective study,³⁵ TMJ anatomical integrity following treatment with an oral appliance was evaluated using magnetic resonance imaging. In this study, the authors did not find any significant change in the morphology of the TMJ caused by oral appliance therapy. Additionally, patients with TMD symptoms were excluded without standardized criteria. In another prospective study,³¹ the contraindication for oral appliance usage was evaluated according to preestablished criteria⁷ in 100 consecutive patients with OSAS. The signs and symptoms of TMD were evaluated using a yes or no questionnaire completed by the patients or answered during clinical examination. Lateral x-rays of the TMJ were taken to determine whether joint morphology and function were normal or

342 Volume 23, Number 4, 2009

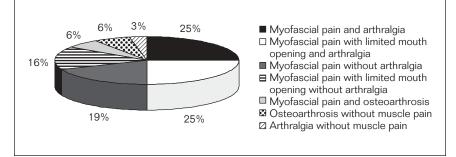


Fig 1 Prevalence of patients with different types of TMD (n = 32).

^{© 2009} BY QUINTESSENCE PUBLISHING CO, INC. PRINTING OF THIS DOCUMENT IS RESTRICTED TO PERSONAL USE ONLY. NO PART OF THIS ARTICLE MAY BE REPRODUCED OR TRANSMITTED IN ANY FORM WITHOUT WRITTEN PERMISSION FROM THE PUBLISHER.

altered. Although that study is more detailed than other studies, it did not classify and establish a grade scale of TMD pain. Another prospective study³⁶ evaluated the tolerance and predictors of success for oral appliance treatment. In that study, patients with TMJ pain and/or myofascial pain were excluded from the treatment instead of being followed-up, and the methodology used for TMD evaluation was unclear.

There have been several studies of the prevalence of TMD in the OSAS population, but the present study is the first that followed a standardized methodology with criteria to classify and establish the grade and impact of TMD chronic pain by the RDC/TMD. This lack of criteria used in previous studies might explain why TMD is still undervalued or overvalued by both professionals and patients. As the prevalence of TMD is high in the general population,^{18,19,21} it was expected that a significant number of individuals with OSAS evaluated in this study would also exhibit TMD.

The lower prevalence (seven out of 32 patients) of low disability grade II (low disability and high intensity pain) and a single patient with high disability grade III (high disability and moderate limiting) in the present sample might explain those patients who report pain when using an oral appliance. It is possible that out of the 32 patients with TMD evaluated in this study, these eight patients may not have complied with oral appliance treatment.

TMD pain is characterized by fluctuations in pain levels. The present study observed that low disability grade I (low disability and low-intensity pain) was the more frequent classification. The effects of OSAS are more likely to affect the quality of life of individuals who have both OSAS and TMD pain; however, many patients with TMD are unaware that they suffer from TMD. Thus, TMD pain as a side effect during oral appliance treatment might be manifested in patients with severe TMD who have not been diagnosed before oral appliance treatment.

The present study has several limitations. The first limitation is the small sample size (n = 87) with a higher number of females (21 females/11 males) and relatively young age (mean age 47). The second limitation was that the diagnosis of TMD was performed by only one dental professional; independent confirmation of TMD diagnosis by two professionals would be an important improvement to study design. The lack of a control sample population matched for age and gender without OSAS would also improve the reliability of the results.

Conclusion

The prevalence of pain associated with TMD and the impact of this dysfunctional pain were high in OSAS patients referred for oral appliance therapy. The findings suggest that standardized criteria for TMD diagnosis, such as the RDC/TMD, should be part of the examination procedure for OSAS patients referred for oral appliance treatment. They also suggest that support therapy for TMD should be used by OSAS patients undergoing oral appliance therapy, and by patients with preexisting TMD symptoms. Support therapy could prevent or reduce pain associated with TMD. Further studies are necessary to evaluate the effect of oral appliance therapy on patients with different grades of TMD.

Although not the objective of the present study, it is important to note that patients with TMD pain report a poor quality of sleep, while patients who do not sleep well are more susceptible to TMD.^{20,24-27} The quality of life is also reduced in OSAS patients,³⁷ and this condition can be worsened if they suffer simultaneously from TMD. Further studies are necessary to understand the connection between sleep quality and the incidence of TMD.

Acknowledgments

The authors are grateful for support from Fundacao de Amparo a Pesquisa do Estado de Sao Paulo (FAPESP number: 2006/04488-4), FAPESP-CEPID, and Associacao Fundo de Incentivo a Psicofarmacologia (AFIP). Sergio Tufik and Lia Rita Azeredo Bittencourt are FAPESP principal investigators and CNPq researchers.

References

- 1. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: A population health perspective. Am J Respir Crit Care Med 2002;165:1217–1239.
- 2. The International Classification of Sleep Disorders, ed 2. Diagnostic and Coding Manual. Westchester, IL: American Academy of Sleep Medicine, 2005.
- Hoekema A, Stegenga B, de Bont LGM. Efficacy and comorbidity of oral appliances in the treatment of obstructive sleep apnea-hypopnea: A systematic review. Crit Rev Oral Biol Med 2004;15:137–155.
- Ferguson KA, Cartwrigt R, Rogers R, Schimidt-Nowara W. Oral appliance for snoring and obstructive sleep apnea: A review. Sleep 2006;29:244–262.
- Hoffstein V. Review of oral appliances for treatment of sleep-disordered breathing. Sleep Breath 2007;11:1–22.
- 6. Kushida CA, Morgenthaler TI, Littner MR, et al. Practice parameters for the treatment of snoring and obstructive sleep apnea with oral appliances: An update for 2005. Sleep 2006;29:240–243.

- 7. Clark GT. Mandibular advancement devices and sleep disordered breathing. Sleep Med Rev 1998;2:163–174.
- Bloch KE, Iseli A, Zhang JN, et al. A randomized controlled crossover trial of two appliances for sleep apnea treatment. Am J Respir Crit Care Med 2000;162: 246–251.
- Fritsch KM, Iseli A, Russi EW, Block KE. Side effects of mandibular advancement devices for sleep apnea treatment. J Respir Crit Care Med 2001;164:813–818.
- McGown AD, Makker HK, Battagel JM, L'Estrange PR, Grant HR, Spiro SG. Long-term use of mandibular advancement splints of snoring and obstructive sleep apnea. A questionnaire survey. Eur Respir J 2001; 17:462–466.
- Johnston CD, Gleadhill IC, Cinnamond MJ, Gabbey J, Burden DJ. Mandibular advancement appliances and obstructive sleep apnoea: A randomized clinical trial. Eur J Orthod 2002;24:251–262.
- 12. Almeida FR, Lowe AA, Tsuiki S, Otsuka R, Wong M, Fastlicht S, Ryan F. Long-term compliance and side effects of oral appliances used for the treatment of snoring and obsrtructive sleep apnea syndrome. J Clin Sleep Med 2005;1:143–152.
- Almeida FR, Lowe AA, Sung JO, Tsuiki S, Otsuka R. Long-term sequellae of oral appliance therapy in obstructive sleep apnea patients: Part 1. Cephalometric analysis. Am J Orthod Dentofacial Orthop 2006;129:195–204.
- Almeida FR, Lowe AA, Otsuka R, Fastlicht S, Farbood M, Tsuiki S. Long-term sequelle of oral appliance therapy in obstructive sleep apnea patients: Part 2. Study-model analysis. Am J Orthod Dentofacial Orthop 2006;129:205–213.
- Okeson JP. Etiology of functional disturbances in the masticatory system. In: Management of Temporomandibular Disorders and Occlusion, ed 6. St. Louis: Mosby, 2008:140–163.
- Okeson JP (ed). Orofacial Pain: Guidelines for Assessment, Diagnosis, and Management. Chicago: Quintessence, 1996:116.
- 17. McNeill C. Management of temporomandibular disorders: Concepts and controversies. J Prosthet Dent 1997;77:510-522.
- Solberg WK, Woo MW, Houston JB. Prevalence of mandibular dysfunction in young adults. Am Dent Assoc 1979;98:25-34.
- 19. Cooper BC, Kleinberg I. Examination of a large patient population for the presence of symptoms and sings of temporomandibular disorders. Cranio 2007;25:114–126.
- Selaimen CM, Jeronymo JC, Brilhante DP, Grossi ML. Sleep and depression as risk indicators for temporomandibular disorders in a cross-cultural perspective: A case-control study. Int J Prosthodont 2006;19:154–161.
- Oliveira AS, Dias EM, Contato RG, Berzin F. Prevalence study of signs and symptoms of temporomandibular disorders in Brazilian college students. Braz Oral Res 2006; 20:3–7.
- 22. Poveda Roda R, Bagan JV, Diaz Fernandez JM, Hernandez Bazan S, Jimenez Soriano Y. Review of temporomandibular joint pathology. Part I: Classification, epidemiology and risk factors. Med Oral Patol Oral Cir Bucal 2007;12:E292–E298.

- 23. Dworkin SF, LeResche L. Research diagnostic criteria for temporomandibular disorers: Review, criteria, examinations and specifications, critique. J Craniomandib Disord Facial Oral Pain 1992;6:301–355.
- 24. Yatani H, Studts J, Cordova M, Carlson CR, Okeson JP. Comparison of sleep quality and clinical psychologist characteristics in patients with temporomandibular disorders. J Orofac Pain 2002;16:221–228.
- 25. Vasquez-Delgado E, Schmidt JE, Carlson CR, DeLeeuw R, Okeson JP. Psychological and sleep quality differences between chronic daily headache and temporomandibular disorders patients. Cephalalgia 2004;24:446–454.
- Collesano V, Segu M, Masseroli C, Manni R. Temporomandibular disorders and sleep disorders: Which relationship? Minerva Stomatol 2004;53:661–668.
- Schütz TC, Andersen ML, Tufik S. Sleep alterations in an experimental orofacial pain model in rats. Brain Res 2003;993:164–171.
- Johns MW. A new method for measuring daytime sleepiness: The Epworth sleepiness scale. Sleep 1991;14:540–545.
- Pereira FJ Jr, Favilla EE, Dworkin SF, Huggings K. Research diagnostic criteria for temporomandibular disorders (RDC/TMD); Formal translation to Portuguese. J Brasileiro de Clin Odontol Integrada 2004;8:384–395.
- 30. Kosminsky M, de Lucena LB, Siqueira JTT, Pereira JF Jr, Góes PSA. Cultutal adaptation of the "Researche Diagnostic Criteria dor Tempodomandibular Disorders: Axix II" questionnaire. J Brasileiro de Clin Odontol Integrada 2004;8:51–61.
- 31. Petit FX, Pepin JL, Bettega G, Sadek H, Raphael B, Levy P. Mandibular advancement devices: Rate of contraindications in 100 consecutive obstructive apnea patients. Am J Respir Crit Care Med 2002;166:274–278.
- 32. Von Korff MR, Ormel J, Keefe FJ, Dworking SF. Grading the severity of chronic pain. Pain 1992;50:133–149.
- Yap AU, Tan KB, Chua EK, Tan HH. Depression and somatization in patients with temporomandibular disorder. J Prosthet Dent 2002;88:479–484.
- 34. Yap AU, Dworkin SF, Chua EK, List L, Tan KB, Tan HH. Prevalence of temporomandibular disorder subtypes, psychologic distress, and psychosocial dysfunction in Asian patients. J Orofac Pain 2003;17:21–28.
- 35. de Almeida FR, Bittencourt LR, de Almeida CI, Tsuiki S, Lowe AA, Tufik S. Effects of mandibular posture on obstructive sleep apnea severity and the temporomandibular joint in patients fitted with an oral appliance. Sleep 2002;25:507–513.
- 36 Marklund M, Stenlund H, Franklin KA. Mandibular advancement devices in 630 men and women with obstructive sleep apnea and snoring: Tolerability and predictors of treatment success. Chest 2004;125:1207–1278.
- 37. Young T, Finn L, Peppard PE, et al. Sleep disordered breathing and mortality: Eighteen-year follow-up of the Wisconsin sleep cohort. Sleep 2008;31:1071–1078.