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ORIGINAL ARTICLE

Long-term oral appliance therapy in obstructive sleep apnea syndrome: a controlled study on temporomandibular side effects

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Abstract The objective of this study was to assess variations in the occurrence of temporomandibular disorders (TMDs) and the risk of developing pain and function impairment of the temporomandibular complex in obstructive sleep apnea syndrome (OSAS) patients treated with either an oral appliance (mandibular advancement device) or continuous positive airway pressure (CPAP) in a 2-year follow-up study. In addition, we assessed the relationship between the mean mandibular protrusion and the frequency of wearing the appliance during follow-up with the occurrence of pain and function impairment of the temporomandibular complex. Fifty-one patients were randomized to oral appliance therapy and 52 patients to CPAP therapy. TMDs (diagnosed according to the Axis I Research Diagnostic Criteria for TMD), pain intensity and disability and mandibular function impairment were recorded at baseline, after 2 months, 1 year and 2 years of therapy. Only in the initial period of treatment the occurrence of pain-related TMDs was considerably higher (24%) in the oral appliance group compared to CPAP (6%). Oral appliance therapy furthermore resulted in more temporomandibular pain compared to CPAP (odds ratio 2.33, 95% confidence interval (1.22–4.43)). However, there were no limitations in mandibular function in both groups during the (entire) follow-up period. Although generally not serious and of transient nature, oral appliance therapy results in more pain-related TMDs in the initial period of use compared with CPAP therapy. Oral appliance therapy is associated with increased pain in the temporomandibular complex in the initial period of use. Because of the transient nature, this pain is not a reason to contra-indicate an oral appliance in OSAS patients. Moreover, TMDs and the risk of developing pain and function impairment of the temporomandibular complex appear limited with long-term oral appliance use.

Keywords Obstructive sleep apnea syndrome · Oral appliance · CPAP · Side effects · Temporomandibular dysfunction · Research diagnostic criteria

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Introduction

Obstructive sleep apnea syndrome (OSAS) is a highly prevalent sleep-related breathing disorder affecting approximately 4% of the male and 2% of the female adults in the North American population [1]. The disorder is characterized by disruptive snoring and repetitive partial or complete obstructions of the upper airway (i.e. hypopneas and apneas, respectively) during sleep [2]. This disrupted sleep may result in various (serious) neurobehavioral and cardiovascular sequelae, ultimately depriving the patient's quality of life and life expectancy [3, 4]. Standard treatment with continuous positive airway pressure (CPAP) is very effective in reducing symptoms [5, 6]; however, because of the obtrusive nature of CPAP, patients may abandon or adhere poorly to this therapy [7]. Oral appliance therapy has been demonstrated an effective alternative in treating

OSAS, especially in the mild and moderate spectrum of the disorder and in patients unwilling or unable to tolerate CPAP [8]. Oral appliances generally aim at relieving the upper airway obstructions by positioning the mandible in a forward and downward position [9].

Mild and 'transient' side effects are commonly reported in the initial period of oral appliance use [10–13]. Known side effects, associated with long-term use of an oral appliance, are predominantly dental in nature and include a decreased overjet and overbite [14–16]. Furthermore, a change in inclination of the mandibular and maxillary incisors has been reported [14–16]. Moreover, some authors have reported a downward and forward displacement of the mandible as a result of oral appliance therapy [15, 17, 18].

Temporomandibular disorders (TMDs) is a collective term that embraces a number of clinical problems that involve the masticatory muscles, the temporomandibular joint and the associated structures [19]. When using an oral appliance during sleep, the mandible is positioned in an unnatural forward and downward position, which could ultimately result in TMDs. Studies regarding TMDs associated with oral appliance therapy for the management of OSAS are still limited in number and quality [20–25]. Most studies to date have been retrospective, comprised small study samples or did not include a (matched) control group. Furthermore, in most studies the oral appliance was not adjustable but fixated the patients' mandible in a predefined protrusive position (50–75% of the maximal mandibular protrusion). Therefore, a clear association between the mandibular protrusion and the occurrence of TMDs is still unknown. It could be hypothesized that more serious TMD-related complaints will occur in patients with the mandible positioned in a more forward position or in patients using the oral appliance more frequently.

The objectives of this parallel randomized controlled study were to assess:

1. Variations in the occurrence of TMDs and the risk of developing pain and function impairment of the temporomandibular complex in OSAS patients treated with an oral appliance compared to CPAP during a 2-year follow-up
2. The relationship between the mean mandibular protrusion and the frequency of wearing the appliance during follow-up with the occurrence of pain and function impairment of the temporomandibular complex

Materials and methods

Patient selection

The effectiveness of an oral appliance in the treatment of OSAS, compared with CPAP, has been evaluated in a previous executed randomized controlled trial [26]. The materials and methods of this specific study are briefly summarized below. All patients were recruited through the Department of Home Mechanical Ventilation of the University Medical Center Groningen, The Netherlands. Subjects over 20 years of age and diagnosed with OSAS (apnea hypopnea index (AHI)≥5) based on polysomnography [27] were eligible. If patients fulfilled predefined medical, psychological and dental inclusion criteria, they were selected for the study [26] and subsequently randomized for either oral appliance (n=51) or CPAP therapy (n=52).

For the present study, we assessed the occurrence of disorders of the temporomandibular complex as a result of long-term use of an oral appliance compared to CPAP in OSAS patients (Table 1). Patients considered *nonresponsive* or *nonadherent* [26] were offered to switch to the alternative therapy at any time during the follow-up. Details of patient selection criteria for our study are provided in Fig. 1.

The present study was approved by the Groningen University Medical Center's Ethics Committee. Written informed consent was obtained from each patient before enrolment.

Variables

At baseline, clinical variables were determined [26]. Prior to (T0), after 2 months (T2), 1 year (T15) and 2 years (T27)

Table 1 Baseline characteristics of 103 patients treated with an oral appliance or CPAP

Variable	Oral appliance[a] (n=51)	CPAP[a] (n=52)
Male/female ratio	43:8	49:3
Age (years)	49±10	49±10
Body mass index (kg/m^2)	32±6	33±6
Apnea–hypopnea index (no/h)	39±31	40±28
Neck circumference (cm)	44±4	45±4
minSaO$_2$ (%)	78±9	78±10
OSAS severity	Non-severe: n=25 (49%)	Non-severe: n=25 (48%)
	Severe: n=26 (51%)	Severe: n=27 (52%)

minSaO$_2$ lowest oxyhemoglobin saturation during sleep

[a] Values are means ± standard deviations

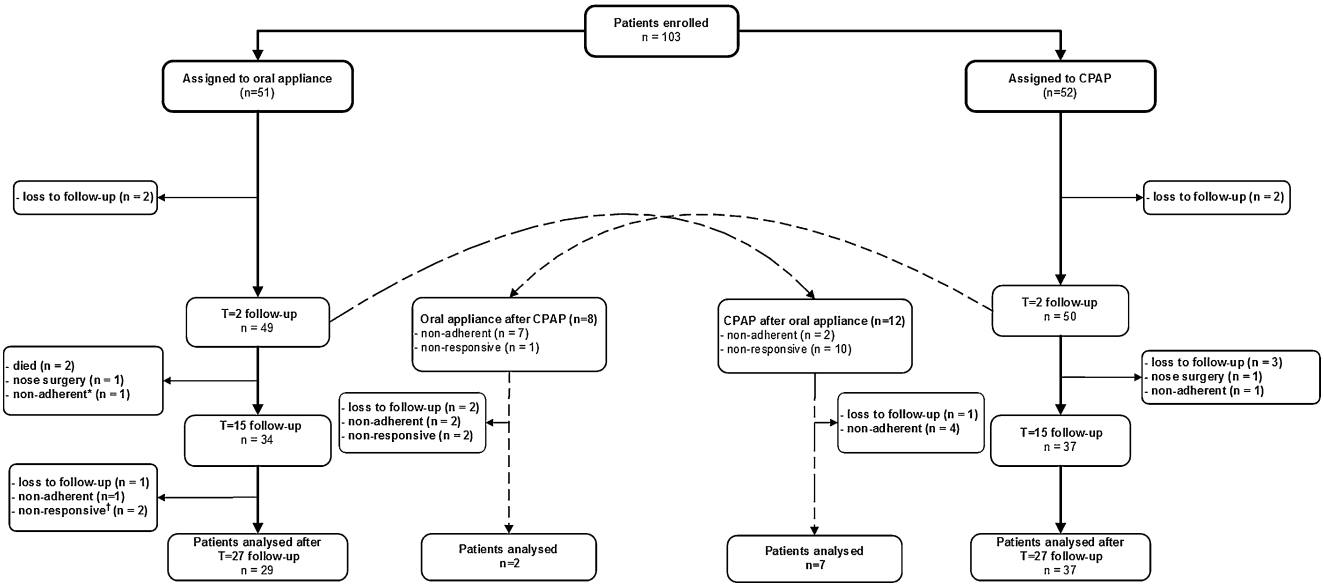

Fig. 1 Flow diagram of the patient selection procedure. *Patients who discontinued treatment for any reason were considered *nonadherent* to treatment. †Treatment was considered effective when the apnea–hypopnea index was <5 or showed substantial reduction, defined as reduction in the index of at least 50% from the baseline value to a value of <20 in a patient without symptoms while using therapy. Patients not meeting these criteria were considered *nonresponsive*

of therapy, the occurrence of TMDs was assessed based on Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) Axis I (Table 3) [28]. The RDC/TMD is developed for research purposes and constitutes a reliable system for the assessment of TMDs [28, 29]. Axis I from the RDC/TMD is based on clinical signs and symptoms. The RDC/TMD Axis II was designed to grade chronic pain severity (Graded Chronic Pain Scale). Examinations were standardized and one experienced observer (MD) was responsible for all examinations throughout the study. The observer reviewed the RDC/TMD procedure after being thoroughly instructed by an orofacial pain specialist (BS). According to the RDC/TMD guidelines, clinical diagnoses were made (Table 3). For this study, the patient rather than the joint was the entity of research. In theory, each patient can have multiple RDC diagnoses (maximum of 5). In practice, patients with more than three RDC diagnoses are very rare [28].

To assess pain of the temporomandibular complex, the RDC/TMD Axis II was used. This scale has been specifically designed to grade chronic pain severity (Graded Chronic Pain Scale) ranging from grade 0 to grade IV (Table 2) [28]. At all time points (T0, T2, T15 and T27), patients filled out the seven-item Graded Chronic Pain Scale. Two clinical cutoff points were defined, i.e. grade > 0 represents 'pain' and grade > II represents 'pain-induced limitation'.

At all time points (T0, T2, T15 and T27), the Mandibular Function and Impairment Questionnaire (MFIQ) was filled out by all patients to subjectively assess function impairment of the temporomandibular complex during therapy. The MFIQ is a validated questionnaire to assess the impact of TMDs on mandibular function and movements in patients' daily life circumstances [30]. This questionnaire scores perceived difficulty of 17 representative mandibular functions in relation to joint or muscle complaints. The possible answers are scored on a five-point Likert scale from 0 to 4, representing 'no difficulty (0)' to 'very great difficulty or impossible without help (4)'. The sum item score for function impairment ranges from 0 to 68. Then the raw component score was calculated (range 0–1). From this raw component score, the Function Impairment Rating Scale (FIRS; range 0–5) was determined, and thereupon, to enhance interpretation, the FIRS was converted to a more qualitative indication of the level of function impairment (low (FIRS 0 or 1)/moderate (FIRS 2 or 3)/severe (FIRS 4 or 5)) [30]. Finally, at each time point, patients filled out a questionnaire about therapy use. In this questionnaire,

Table 2 Classification of the outcome of the seven-item questionnaire for graded chronic pain; Research Diagnostic Criteria for Temporomandibular Disorders: Axis II

Grade	Description
Grade 0	No temporomandibular pain in the prior 6 months
Grade I	Low disability—low intensity pain
Grade II	Low disability—high intensity pain
Grade III	High disability—moderately limiting
Grade IV	High disability—severely limiting

[a] Dworkin and LeResche [27]

patients were asked how many nights per week and how many hours per night the therapy was used.

Interventions

The oral appliance used in this study (Thornton Adjustable Positioner, Airway Management Inc., Dallas, TX, USA) consisted of two separate parts: fixing the patient's mandible in a forward and downward position. This type of oral appliance is often referred to as a mandibular advancement device. By turning a propulsion screw that was incorporated anteriorly in the appliance, patients could adjust the mandibular advancement with 0.2 mm increments with each turn. The maximum range of mandibular protrusion was first determined with a George-Gauge™ (H-Orthodontics, Michigan City, IN, USA). When initiating oral appliance therapy, the mandible was set at approximately 50% of the patient's maximum protrusion. After having accustomed to this protrusive position during a 2-week period, patients were allowed to further adjust the oral appliance during a 6-week period. When OSAS symptomatology (e.g. snoring, excessive daytime sleepiness, apneas and/or hypopneas) appeared to persist, patients were instructed to advance the mandible each night with 1 to 2 increments (i.e. 0.2–0.4 mm). This 'titration' of the oral appliance was continued until symptoms were adequately improved (e.g. no signs of apneas, hypopneas and snoring) or until further protrusion of the mandible resulted in discomfort. The mean mandibular protrusion during the follow-up period (expressed as percentage of the maximum mandibular protrusion) was used for further analysis. The vertical dimension of the oral appliance was kept constant during the entire follow-up period. Both mandibular protrusion and mouth opening (including the vertical overbite) imposed by the oral appliance were measured with a digital sliding calliper. These measurements were carried out at baseline, after 2 months, 1 year and 2 years of treatment. At these time points, also other clinical measurements (weight, length, neck circumference and intoxications) were carried out.

CPAP titration was performed during an afternoon nap. This technique, aimed at abolishing all signs of apneas, hypopneas and snoring, has been shown to be an appropriate procedure for the effective titration of CPAP [31].

Following CPAP and oral appliance adjustment, an 8-week follow-up period was arranged that allowed for habituation and, if necessary, adjustment of CPAP or the oral appliance. After this period, a second polysomnographic study was performed. If polysomnography indicated an apnea–hypopnea index$\geq$5, CPAP or the oral appliance was further adjusted by the physician (not during polysomnography). A third polysomnographic study was performed 4 weeks after that adjustment.

Treatment was considered effective when the apnea–hypopnea index either was <5 or showed 'substantial reduction' [26], defined as a reduction in the index of at least 50% from the baseline value to a value of <20 in a patient who had no symptoms while using therapy. Patients for whom oral appliance or CPAP therapy was effective continued this treatment. If one of both treatments was not effective at any time during the follow-up period, patients were offered the alternative therapy (CPAP or oral appliance, respectively), which was titrated as described above. After a 2-year follow-up period, all patients were subjected to a final polysomnographic evaluation. Patients were always encouraged to contact our clinic between regular follow-up appointments when problems were faced concerning the oral appliance, CPAP device or treatment effect.

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (version 16.0, SPSS Inc., Chicago, IL, USA). All continuous demographic variables at baseline were normally distributed and their means and SD are reported. The AHI of the oral appliance and CPAP patients at baseline was normally distributed after logarithmic transformation.

An 'intention-to-treat' analysis was carried out for all measurements (i.e. all patients were analysed in the group to which they were randomized, regardless of whether they complied with the assigned treatment). Statistical analysis for longitudinally, repeated measurements were performed using Stata (version 10.1, StataCorp, College Station, TX, USA) by means of generalized estimating equations (GEE). With GEE, the joint relationship of different variables (e.g. difference in pain, pain-induced limitations and the MFIQ score) at different time points is analysed.

For oral appliance therapy, the mean mandibular protrusion during the follow-up, therapy use or possible switching of therapy was related to the MFIQ scores or pain in the temporomandibular complex with GEE models. Odds ratios (OR) for dichotomous variables and regression coefficients (β) for continuous variables and their 95% confidence intervals (CIs) are reported. The significance level α of all analyses was set at 5%. The occurrence of TMDs at different time points is reported in a descriptive way.

Results

After 2 years, 36 out of 51 patients randomized to an oral appliance (71%) and 39 out of 52 patients randomized to CPAP (75%) completed the follow-up. In the oral appliance

group, 29 patients (57%) completed the 2-year follow-up still using their oral appliance, while in the CPAP group, 37 patients (71%) completed the 2-year follow-up using CPAP. Twenty patients switched to the alternative therapy during the follow-up, all within 2 or 3 months after commencing the initial therapy (T2). Twelve patients switched from oral appliance therapy (ten were considered nonresponsive and two nonadherent) to CPAP therapy, of whom seven completed the 2-year follow-up. Eight patients (15%) switched from CPAP therapy (one was considered nonresponsive and seven nonadherent) to oral appliance, of whom two completed the 2-year follow-up.

In the oral appliance group (n=36), the mean (±SD) mandibular protrusion during the follow-up period was 76% (±25%) of the maximum mandibular protrusion. The mean mouth opening (including overbite) while wearing the oral appliance was 12.8 (±2.7)mm. Patients in the oral appliance group used their device on average 6.7 (±0.6) nights per week and 7.2 (±0.8)h per night. In the CPAP group (n=39), patients used their device on average 6.9 (±0.4) nights per week and 6.9 (±1.3)h per night. No patient withdrew from the study during the follow-up period because of signs or symptoms of TMDs.

Clinical measurements

The outcomes of the RDC/TMD indicate that most of the patients in both the oral appliance and CPAP group could be classified as 'no-TMD' at all time points (Table 3). At baseline, 12 out of 52 patients (23%) in the CPAP group and 18 out of 51 patients (35%) in the oral appliance group were diagnosed with TMDs, of which a disc displacement with reduction (2a) was the most prevalent in both groups. In the oral appliance group, however, this diagnosis was twice as prevalent when compared with the CPAP group. Two patients in the CPAP group were diagnosed with osteoarthrosis (3c) at baseline, whereas this condition was not observed in the oral appliance group. After 2 months of therapy (T2), there was an increase in occurrence of 5% and 10% of total TMDs compared to baseline in the CPAP and oral appliance group, respectively. At the 1-year follow-up (T15), a decrease in the occurrence of TMDs was observed in both CPAP (7%) and oral appliance group (12%) when compared with the 2-month follow-up. Compared to the 1-year follow-up, only small changes in the occurrence of TMDs occurred after 2 years (T27) of treatment in both groups (1%).

At baseline (T0), two out of 52 patients (4%) in the CPAP group and four out of 51 patients (8%) in the oral appliance group were diagnosed with either one or a combination of pain-related diagnoses (i.e. tendomyalgia (1a), arthralgia (3a) and osteoarthritis (3b)). After 2 months, an increase in occurrence of 2% and 16% of one or a combination of pain-related TMDs was observed in the CPAP and oral appliance group, respectively. At the 1-year follow-up, there was an

Table 3 Number of patients diagnosed with TMDs according to the RDC/TMD: Axis I at each check-up

Clinical diagnosis[a] (RDC/TMD)	T0			T2			T15			T27		
	CPAP (n=52)	OA (n=51)	Total (n=103)	CPAP (n=50)	OA (n=49)	Total (n=99)	CPAP (n=41)	OA (n=40)	Total (n=81)	CPAP (n=39)	OA (n=36)	Total (n=75)
No TMD	40	33	73	36	27	63	32	27	59	31	24	55
1a:myofascial pain[b]	*0*	*1*	*1*	*1*	*2*	*3*	*0*	*1*	*1*	*0*	*1*	*1*
2a: disc displacement with reduction	7	14	21	9	10	19	3	10	13	3	10	13
2b: disc displacement without reduction with limited opening	0	0	0	0	0	0	0	0	0	0	1	1
3a: Arthralgia	*1*	*1*	*2*	*1*	*4*	*5*	*2*	*1*	*3*	*1*	*0*	*1*
3c: Osteoarthrosis of the temporomandibular joint	2	0	2	2	0	2	2	0	2	2	0	2
1a+2a	*0*	*1*	*1*	*0*	*2*	*2*	*0*	*0*	*0*	*0*	*0*	*0*
1a+3a	*1*	*1*	*2*	*1*	*2*	*3*	*1*	*1*	*2*	*2*	*0*	*2*
2a+3a	*0*	*0*	*0*	*0*	*2*	*2*	*1*	*0*	*1*	*0*	*0*	*0*
2a+3c	1	0	1	0	0	0	0	0	0	0	0	0
Total TMD (%)	23	35	29	28(↑5)[c]	45 (↑10)	36 (↑7)	22 (↓7)	32 (↓12)	27 (↓9)	21 (↓1)	33 (↑1)	27
Pain-related TMD (%)	4	8	6	6 (↑2)	24 (↑16)	15 (↑9)	10(↑4)	8 (↓16)	9 (↓6)	8 (↓2)	3 (↓5)	5 (↓4)

[a] Only those clinical diagnoses or combinations of diagnoses which were prevalent during the study

[b] Diagnoses or combinations of diagnoses in *italic* represent pain-related diagnoses

[c] Within parenthesis, the percentage increase (↑) or decrease (↓) in the occurrence of TMD compared to the preceding check-up is described

increase in the occurrence of pain-related TMDs in the CPAP group (4%), while in the oral appliance group a decrease (16%) was observed when compared with the 2-month follow-up. Compared to the 1-year follow-up, only small changes in the occurrence of pain-related TMDs occurred after 2 years (T27) of treatment in both groups.

Questionnaires

A significant difference was found in pain intensity between oral appliance and CPAP therapy at different time points. Patients receiving oral appliance therapy have a higher risk of developing pain than patients using CPAP therapy during a 2-year follow-up (OR=2.33, 95% CI (1.22–4.43)). No associations were found between pain intensity and mandibular protrusion (OR=1.02 (0.84–1.24)), therapy use (OR=1.13(0.90–1.44)) or switching of therapy (OR=0.87 (0.33–2.28)) during the follow-up. No significant differences were found in pain-induced limitations between CPAP and oral appliance therapy. Pre-therapeutically, one patient in the CPAP group was classified as suffering from pain-induced limitation. However, this patient was also familiar with orofacial pain complaints. These complaints did not increase during the follow-up period and were no reason for the patient to cease the CPAP therapy. In the oral appliance group, also one patient was pre-therapeutically classified as suffering from pain-induced limitation. During the follow-up period, these complaints disappeared.

Regarding mandibular function impairment, no significant differences between oral appliance therapy and CPAP therapy were observed at the different time points (β=0.56, 95% CI (−1.77–2.88)). For the oral appliance group, no association was found between the mean mandibular protrusion during the follow-up (β=−0.23 (−2.83–13.90)), therapy use (β=0.96 (−0.29–2.21)), possible switching of therapy (β=0.02 (−1.24–1.28)) and the MFIQ scores at different time points. Regarding the function impairment score, at baseline, all patients could be classified as ‘low’ impairment (FIRS 0 or 1). After 2 months of treatment (T2), one patient using an oral appliance and one patient using CPAP was classified with ‘moderate’ impairment. At the 1-year follow-up (T15), the same patient in the oral appliance group remained being classified with ‘moderate’ impairment. In the CPAP group, two patients suffered from ‘severe’ impairment at the 1-year follow-up (T15). At the last follow-up visit (T27), one patient in the oral appliance group still suffered from ‘moderate’ impairment, and one of the patients who was ‘severely’ impaired in the CPAP group was now classified as being ‘moderately’ impaired. The other patient remained ‘severely’ impaired.

Discussion

To our knowledge, this is the first study in which the occurrence of different TMDs as a result of long-term oral appliance therapy at different time points has been evaluated in a controlled study concerning patients from the full OSAS spectrum. This study shows that in the initial period after initiating oral appliance or CPAP therapy, the occurrence of (particularly pain-related) TMDs increases, being substantially higher (24%) in the oral appliance group than in the CPAP group (6%). Furthermore, we found that oral appliance therapy results in significantly more pain during a 2-year follow-up compared with CPAP therapy. This pain did not induce limitations of the temporomandibular complex, neither in the oral appliance nor in the CPAP group. No differences were found in mandibular function impairment during the 2-year follow-up between oral appliance and CPAP therapy. No relationship could be found between the mean mandibular protrusion and the frequency of wearing the appliance during follow-up with the occurrence of pain and function impairment of the temporomandibular complex.

The occurrence of TMDs as a result of long-term oral appliance therapy has been described previously by Martinez-Gomis and co-workers [23]. They found that the occurrence of TMDs at different time points was not affected by long-term oral appliance therapy in OSAS patients. In the present study, the occurrence of pain-related TMDs after 2 to 3 months of using an oral appliance (T2) was considerably higher as compared to baseline, in contrast to the CPAP group. This could be the result of the strain in the muscles of the temporomandibular complex or the capsular ligament of the temporomandibular joint (TMJ) when protruding the mandible during sleep. The condyle of the mandible is positioned out of its natural resting position into a more forward and downward position, resulting in possible strain of the retrodiscal tissue. Another possible explanation is the increase in occlusal vertical dimension while wearing an oral appliance. A study by Le Belle and co-workers shows that after applying artificial occlusal interferences, the occurrence of temporomandibular pain symptoms increased but decreased after a few days [32]. Therefore, the authors suggest that patients can adapt to a new vertical occlusal situation. In a study by Giannasi and co-workers, the intensity of TMDs symptoms decreased significantly after oral appliance therapy [25]. Particularly the occurrence of jaw fatigue decreased during the follow-up period. These authors hypothesized that protruding the mandible results in less compression of the TMJ and related structures. Unfortunately, a matched control group was absent in this study, so it remains unclear to what extent oral appliance therapy contributes to these phenomena. Furthermore, in the latter

study, the Helkimo Anamnestic Dysfunction Index was used. This index has been developed for epidemiological purposes and not, like the RDC/TMD Axis I used in this study, for clinical purposes. The Helkimo Anamnestic Dysfunction Index furthermore classifies patients into three 'dysfunction' groups rather than clinical diagnoses. In the present study, we did not find a clinical relevant change during the follow-up of different TMDs occurrences in the oral appliance group compared with the CPAP group. After the initial increase of different (pain-related) TMDs and combinations thereof in the oral appliance group, the occurrence decreased to values similar to baseline during the follow-up. This finding suggests that the temporomandibular complex has adaptive capacities to the unnatural protrusive position during sleep while wearing an oral appliance. After 2 to 3 months of therapy, all pain-related TMDs had decreased in the oral appliance group in the remaining period of the follow-up. From that perspective, it appears that an oral appliance could have a therapeutic effect in patients with TMDs. It has been described that treatment with an anterior repositioning splint reduces reciprocal clicking of the TMJ [33]. Because the oral appliance used in this study also positions the mandible in a forward position, it could be hypothesized that patients with a TMD experience a favourable effect. However, scientific evidence for this possible phenomenon is weak [34]. Furthermore, the number of patients in our study may be too low to draw conclusions with respect to this possible effect. Moreover, it has been described that in some patients with disc displacement without reduction, symptoms did resolve spontaneously over time without treatment [35].

The results of this study show that patients with OSAS, treated with an oral appliance, have a higher risk of developing pain in the temporomandibular complex (OR 2.33) as compared to CPAP therapy. However, this pain is most pronounced in the initial period of oral appliance treatment and tends to decrease afterwards. These findings correspond with the results of other studies [10, 20, 22, 25]. It has been described that OSAS patients with TMDs could benefit from mandibular exercises during oral appliance therapy [36]. This might suggest that support therapy could reduce TMD-related pain, probably resulting in higher compliance rates in the initial phase of oral appliance therapy. However, in a research setting, the risk of nonadherence in patients suffering from oromandibular pain may be little as patients are frequently monitored. Conversely, in a regular clinical setting, nonadherence due to TMD problems might hamper the outcome of the results.

No significant differences were found in mandibular function impairment between the oral appliance and CPAP group. Since a dose dependency of oral appliance therapy on the AHI has previously been described [13, 37], it is conceivable that in severe OSAS patients, oral appliance therapy might result in more mandibular function impairment. However, we did not find an association between the mandibular protrusion during the follow-up and the MFIQ scores at different time points. This finding corresponds with the results of another study [13] that also did not show a difference in adverse effects on the stomatognathic system between patients with 50% and 75% mandibular protrusion during a 6-month follow-up. We also did not find an association between therapy use or switch of therapy and MFIQ scores or pain intensity. This could partially be explained by the fact that there were only minor differences in therapy use, making it more difficult to discriminate between these patients. Moreover, only few patients switched to the alternative therapy during the follow-up period.

In the present study, patients with active TMDs (e.g. osteoarthritis) and restrictions in mouth opening (<25 mm) or advancement of the mandible (<5 mm) were excluded. This resulted in a total occurrence of single TMD or combinations of TMDs in 29% of our total study group assessed with the RDC/TMD. In another study [24], the occurrence of TMDs at baseline was 52%. These findings suggest that standardized criteria for TMDs diagnosis, such as the RDC/TMD, should be part of a standard examination in order to discriminate between active and inactive TMDs, prior to oral appliance therapy, as it should be considered a life-long treatment unless alternative therapies can bring help.

After randomisation, a difference in TMDs between both groups at baseline (23% for CPAP and 35% for oral appliance) was observed and more women (16%) were allocated to the oral appliance group compared to the CPAP group (6%). As it is known that TMDs occur more frequently in women than man [38], this could be a possible confounding factor. However, we believe that the total amount of women in our study was too low to distort our results. Nevertheless, we did not study these possible effects in detail.

Considering the fact that OSAS is a disorder with serious cardiovascular consequences, it should be treated as effective as possible. Discontinuation of oral appliance therapy because of the development of TMDs should only be considered in patients who are able to tolerate or accept another effective treatment modality for their OSAS.

In conclusion, our results show that the occurrence of (pain-related) TMDs increases in the initial period of oral appliance therapy but tends to return to baseline values during a 2-year follow-up. In OSAS patients, oral appliance therapy results in more pain of the temporomandibular complex compared to CPAP therapy but does not cause pain-induced limitations in these patients. Mandibular function was not impaired in OSAS patients using an oral appliance or CPAP therapy for 2 years. These findings

suggest that the possible development of TMDs or temporary pain of the temporomandibular complex is not a contra-indication for oral appliance therapy in OSAS patients.

Conflict of interest The authors declare that they have no conflict of interest.

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