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Long-term oral-appliance therapy in obstructive sleep apnea: A cephalometric study of craniofacial changes☆

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ARTICLE INFO

Article history:
Received 10 June 2010
Received in revised form
26 August 2010
Accepted 30 August 2010

Keywords:
Obstructive sleep apnea syndrome
Oral-appliance
CPAP
Therapy
Craniofacial morphology
Cephalometry

ABSTRACT

Objectives: The aim of this randomized controlled study was to cephalometrically assess possible changes in craniofacial morphology associated with long-term use of an adjustable oral-appliance compared with continuous positive airway pressure (CPAP) in patients with the obstructive sleep apnea/hypopnea syndrome (OSAHS). In addition, we wanted to study the relationship between these possible changes and the degree of mandibular protrusion associated with oral-appliance therapy.

Methods: Fifty-one patients were randomized to oral-appliance therapy and 52 patients to CPAP therapy. At baseline and after follow-up (2.3 ± 0.2 years), a lateral cephalogram of all patients was made in maximum intercuspation to determine relevant cephalometric variables. Both baseline and follow-up cephalograms were traced digitally whereupon cephalometric variables were compared. Changes in craniofacial morphology between the oral-appliance- and CPAP group were evaluated with a linear regression analysis.

Results: Compared with CPAP, long-term use of an oral-appliance resulted in small but significant (dental) changes. Overbite and overjet decreased, 1.0 (±1.5) mm and 1.7 (±1.6) mm, respectively. Furthermore we found a retroclination (−2.0 (±2.8)°) of the upper incisors and a proclination (3.7 (±5.4)°) of the lower incisors. Moreover, the lower- and total anterior facial height increased significantly, 0.8 (±1.5) mm and 0.9 (±1.4) mm, respectively. No changes in skeletal variables were found. Linear regression analysis revealed that the decrease in overbite was associated with the mean mandibular protrusion during follow-up ($B = -0.029$, SE = 0.014, $p < 0.05$).

Conclusions: Oral-appliance therapy should be considered as a life long treatment, and there is a risk of craniofacial changes to occur. Therefore, patients treated with an oral-appliance, need a thorough follow-up by a dentist or dental-specialist experienced in the field of dental sleep medicine.

1. Introduction

The obstructive sleep apnea/hypopnea syndrome (OSAHS) is a sleep-related breathing disorder, characterized by disruptive snoring and repetitive partial or complete obstructions of the upper-airway (i.e. hypopneas and apneas, respectively).[1] The severity of the disorder is usually expressed by the apnea–hypopnea index (AHI), i.e. the mean number of apneas and

☆ *Financial disclosure statement*: The present paper was written in partial fulfilment of the requirements for a PhD degree.

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0300-5712/$ – see front matter.
doi:10.1016/j.jdent.2010.08.018

hypopneas per hour of sleep. OSAHS may be classified as mild (AHI 5–15), moderate (AHI 15–30), or severe (AHI >30).[25] As a result of the condition patients may suffer from excessive sleepiness, an increased risk of accidents, and an impaired quality of life. Furthermore, patients have an increased risk of ischemic heart disease, congestive heart failure, and stroke.[2,3]

For OSAHS patients, continuous positive airway pressure (CPAP) is generally considered the treatment of choice.[4] However, because of the obtrusive character of the device, patients may abandon therapy. An oral-appliance aims at relieving upper airway obstructions during sleep by repositioning the mandible in a forward and downward position.[5] Oral-appliance therapy has been demonstrated to be effective especially in mild and moderate OSAHS cases.[6,7] However, in severe OSAHS cases, CPAP is still the treatment of first choice.

When commencing oral-appliance therapy, side effects are commonly reported in the initial period of use. These usually transient and mild side effects include tooth pain, occlusal changes in the morning, dry mouth or excessive salivation, gum irritation, temporomandibular joint pain, temporomandibular joint sounds and myofascial pain.[8–15] Some authors report that some of these side effects can be more severe and continuous.[9,16–18]

Craniofacial changes related to long-term oral-appliance use have been studied with cephalometry.[15,19–23] Reported long-term changes (2–3 years) in craniofacial morphology were generally related to the patient's dentition. Most studies found a significant decrease in overjet and overbite.[8,13,15,21,23,24] Furthermore a retroclination of the maxillary incisors, a proclination of the lower incisors[8,13,15,23,24] and a more downward[19–21] and forward[21] position of the mandible have been reported. In the majority of these studies, however, a control group was absent. In addition, in most studies only patients with mild-to-moderate OSAHS or asymptomatic snorers were included. Furthermore, all studies except for one[23] evaluated the effects of an oral-appliance that was non-adjustable and fixed the mandible in a predefined position at 50–75% of the maximum mandibular protrusion. Therefore, the relationship between the amount of mandibular protrusion during follow-up and the extent of craniofacial changes is an aspect that needs further study.

The aim of the present study was to cephalometrically assess possible changes in craniofacial morphology associated with long-term use (2 years) of a titratable oral-appliance and compared with a CPAP control group, in patients with mild to severe OSAHS. Secondly, we studied the relationship between the occurrence of these changes and the degree of mandibular protrusion during oral-appliance therapy.

2. Materials and methods

2.1. Patient selection

The effectiveness of an oral-appliance compared with CPAP therapy for OSAHS was evaluated in a separate randomized controlled trial.[7] All patients in that study 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 OSAHS (AHI >5) based on polysomnography[25] were eligible, and if they obeyed predefined medical, psychological, and dental inclusion criteria, patients were randomized for either oral-appliance- ($n = 51$) or CPAP therapy ($n = 52$) (Table 1).

For the present study, we assessed changes in the craniofacial morphology as a result of long-term oral-appliance therapy in OSAHS patients. After 2 years, 37 patients (including those who had switched) in the CPAP group and 31 patients (including those who had switched) in the oral-appliance group completed the follow-up. Details of patient selection criteria for our study are provided in Fig. 1. Patients randomized for oral-appliance therapy who had switched to CPAP therapy were excluded if they had been using the appliance for more than 3 months. Patients who were *nonresponsive* or *nonadherent*[7] to treatment and patients who underwent upper airway surgery during the follow-up period were also excluded.

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

2.2. Study design

At baseline, patients had been subjected to a polysomnographic evaluation, based on which they were classified as having non-severe (AHI ≥5–30) or severe (AHI >30) OSAHS. In all patients a digital lateral cephalogram was obtained at

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/hour)	39 ± 31	40 ± 28
Neck circumference (cm)	44 ± 4	45 ± 4
minSaO_2 (%)	78 ± 9	78 ± 10
OSAHS severity	Non-severe: $n = 25$ (49%) Severe: $n = 26$ (51%)	Non-severe: $n = 25$ (48%) Severe: $n = 27$ (52%)

minSaO_2, lowest oxyhemoglobin saturation during sleep, NS, not significant.
[a] Plus–minus values are means ± standard deviations.

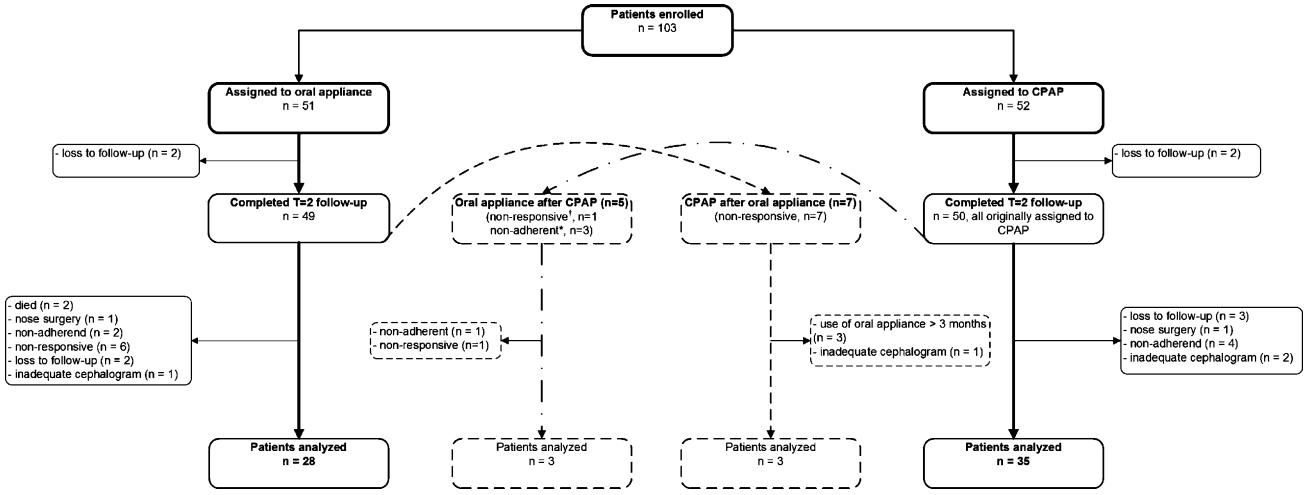

Fig. 1 – Flow diagram of the patient selection procedure. *Patients who discontinued treatment for any reason were considered *nonadherent* to treatment. †Treatment was considered effective when the apnea–hypopnea index was <5 or showed substantial reduction, defined as reduction in the index of at least 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*.

baseline to determine cephalometric variables related to the craniofacial morphology.[22,26–29] 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. By turning a propulsion screw that was incorporated anteriorly in the appliance, patients could gradually adjust the mandibular advancement with 0.2 mm increments. The maximal 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 adjust the oral-appliance during a 6-week period. When OSAHS symptomatology (snoring, excessive daytime sleepiness, apneas and/or hypopneas) appeared to persist, patients were instructed to advance the mandible each night with 1–2 increments (i.e. 0.2–0.4 mm). Adjustment of the oral-appliance was continued until symptoms had improved to the patient's satisfaction, or until further protrusion of the mandible resulted in discomfort.

CPAP-adjustment 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 adjustment of CPAP.[30]

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. 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,"[7] defined as 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 either treatment was not effective at any time during the follow-up period, patients were offered the alternative (CPAP or oral-appliance, respectively) therapy, which was thereupon titrated in the same way as with the initial therapy.

After a 2-year follow-up period all patients were subjected to a final polysomnographic evaluation and a second digital lateral cephalogram. 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) were measured with a digital sliding calliper with 0.01 mm accuracy. These measurements were carried out at baseline, after 2 months, 1 year and 2 years of treatment. At these intervals also other clinical measurements (weight, length, neck circumference and intoxications) were carried out.

The primary outcome measure was the change in craniofacial morphology, measured using cephalometric variables, between baseline and the final follow-up visit. Secondly the relationship between the mean mandibular protrusion during the follow-up and the magnitude of changes in the craniofacial morphology was studied.

2.3. *Cephalometric analysis*

All digital lateral cephalograms were recorded using a ProMax Cephalostat (Planmeca, Helsinki, Finland). The *mirror position*[31] was used in order to obtain a reproducible position of the head. Patients were instructed to swallow and close their mouth with the mandible in maximum intercuspation and the lips in

Table 2 – Cephalometric variables used in the study.

Variable	Oral-appliance[a] $n = 31$			CPAP[a] $n = 37$			Significance of the difference[b] (Cohen's d) [c]
	Baseline	Follow-up	Difference	Baseline	Follow-up	Difference	
Base of the skull							
Ba–S–N; the angle between the lines Ba–S and S–N (°)	48.8 ± 5.4	48.6 ± 5.3	−0.22 ± 0.7	47.7 ± 6.7	47.4 ± 6.7	−0.30 ± 1.1	NS
SN-length; distance between S and N (mm)	70.4 ± 3.4	70.5 ± 3.4	0.0 ± 0.2	69.8 ± 3.1	70.0 ± 3.2	0.3 ± 0.7	NS
Maxilla							
SNA (°)	79.2 ± 4.2	79.2 ± 4.3	−0.0 ± 0,5	80.3 ± 4.0	80.2 ± 4.1	−0.1 ± 0.6	NS
Ui–MxP; angle between the upper incisor line and the maxillary plane (°)	107.0 ± 8.1	105.0 ± 7.9	−2.0 ± 2.8[†]	114.1 ± 8.3	113.9 ± 8.3	−0.2 ± 3.1	$p < 0.05$ (0.6)
Maxillary length; distance between ans and pns (mm)	54.3 ± 4.3	54.4 ± 4.4	0.1 ± 1.1	53.9 ±3.7	53.8 ±3.5	−0.0 ± 1.7	NS
Mandible							
SNB (°)	75.2 ± 3.9	74.8 ± 4.2	−0.4 ± 0.9[†]	77.7 ± 3.9	77.5 ± 3.9	−0.2 ± 1.0	NS
Li–MnP; angle between the lower incisor line and the mandibular plane (°)	102.2 ± 7.4	105.9 ± 8.2	3.7 ± 5.4[†]	102.1 ± 9.3	102.6 ± 9.1	0.6 ± 3.0	$p < 0.05$ (0.7)
MnP–SN; angle between the mandibular plane and SN-line (°)	34.3 ± 7.1	34.7 ± 6.8	0.4 ± 1.1	31.7 ± 6.3	31.9 ± 6.1	0.2 ± 1.4	NS
Ramus length; distance between Arm and Go (mm)	51.6 ± 6.7	51.7 ± 7.0	0.1 ± 1.6	55.0 ± 5.8	54.5 ± 5.7	−0.5 ± 1.6	NS
Body length; distance between Go and Me (mm)	66.9 ± 5.2	66.8 ± 5.6	−0.1 ± 1.7	68.5 ± 5.4	68.4 ± 4.9	−0.1 ± 2.9	NS
Mandibular length; distance between Arm and Me (mm)	102.8 ± 7.3	102.9 ± 6.8	0.1 ± 1.4	107.0 ± 5.3	106.7 ± 5.3	−0.3 ± 2.0	NS
Me-hor; shortest linear distance from Me to line SN-perp (mm)	31.6 ± 9.6	30.9 ± 9.7	−0.7 ± 1.6[†]	37.6 ± 8.2	37.3 ± 8.3	0.3 ± 2.6	NS
Me-ver; shortest linear distance from Me to line SN (mm)	118.0 ± 6.9	118.7 ± 6.6	0.7 ± 1.4[†]	118.7 ± 6.3	118.7 ± 6.3	0.0 ± 1.5	NS
Arm-hor; shortest linear distance from Arm to line SN-perp (mm)	16.9 ± 3.0	17.0 ± 3.3	0.1 ± 1.4	15.6 ± 3.1	15.8 ± 3.4	0.2 ± 1.2	NS
Arm-ver; shortest linear distance from Arm to line SN (mm)	27.8 ± 3.3	28.0 ± 3.2	0.2 ± 0.8	26.1 ± 3.4	26.4 ± 3.6	0.3 ± 1.2	NS
Intermaxillary relationships							
ANB; angle between the lines NA and NB (°)	4.0 ± 1.9	4.3 ± 2.2	0.3 ± 0.9[†]	2.5 ± 3.1	2.6 ± 2.8	0.1 ± 0.9	NS
Ui–Li (interincisal angle); angle between the lines Ui and Li (°)	124.8 ± 10.8	122.5 ± 10.9	−2.3 ± 5.8[†]	120.4 ± 13.4	119.7 ± 13.0	−0.6 ± 0.7	NS
Overbite; linear dimension measured from the most mesial point of the upper central incisor edge to the perpendicular projection on the buccale surface of the lower central incisor (mm)	2.4 ± 2.4	1.4 ± 2.4	−1.0 ± 1.5[†]	1.8 ± 2.3	1.5 ± 2.1	−0.2 ± 1.2	$p < 0.05$ (0.6)
Overjet; linear distance measured from the buccal surface of the lower central incisor to the projected point of the incisal edge of the upper central incisor (mm)	4.4 ± 2.2	2.8 ± 2.6	−1.7 ± 1.6[†]	3.3 ± 2.9	3.5 ± 2.8	0.2 ± 1.3	$p < 0.05$ (1.3)
Facial height							
Upper anterior facial height; distance between N and MxP along line N–Me (mm)	53.4 ± 3.7	53.5 ± 3.5	0.0 ± 0.5	52.5 ± 3.0	52.6 ± 2.8	0.1 ± 0.6	NS
Lower anterior facial height; distance between MnP and MxP along line N–Me (mm)	71.2 ± 5.7	72.0 ± 5.7	0.8 ± 1.5[†]	70.7 ± 5.0	70.8 ± 4.9	0.1 ± 0.6	$p < 0.05$ (0.6)
Total anterior facial height; distance between N and Me (mm)	124.6 ± 7.6	125.4 ± 7.4	0.9 ± 1.4[†]	123.2 ± 6.7	123.4 ± 6.4	0.2 ± 1.4	$p < 0.05$ (0.5)
Anterior facial height ratio; ratio between the upper anterior facial height and the lower anterior facial height (percent)	75.5 ± 7.1	74.6 ± 6.8	−0.8 ± 1.9[†]	74.6 ± 5.6	74.6 ± 5.6	0.1 ±1.7	NS
Upper posterior facial height; distance between S and MxP along line S–Go (mm)	42.9 ± 4.4	43.2 ± 4.5	0.3 ± 1.0	42.3 ± 3.6	42.4 ± 3.7	0.1 ± 0.8	NS
Lower posterior facial height; distance between Go and MxP along line S–Go (mm)	39.2 ± 7.0	39.3 ± 7.3	0.1 ± 2.2	40.9 ± 5.6	40.7 ± 5.7	−0.2 ± 1.4	NS
Total posterior facial height; distance between S and Go (mm)	82.1 ± 8.0	82.5 ± 7.9	0.4 ± 1.6	83.3 ± 6.2	83.1 ± 6.4	−0.2 ± 1.3	NS

Table 2 (*Continued*)

Variable	Oral-appliance[a] $n = 31$			CPAP[a] $n = 37$			Significance of the difference[b] [c] (Cohen's d)
	Baseline	Follow-up	Difference	Baseline	Follow-up	Difference	
Posterior facial height ratio; ratio between the upper posterior facial height and the lower posterior facial height (%)	113.1 ± 23.7	114.2 ± 26.8	1.1 ± 10.2	105.4 ± 17.9	106.2 ± 18.2	0.8 ± 5.1	NS
Facial height ratio; ratio between the total posterior facial height and the total anterior facial height (%)	65.9 ± 5.4	65.8 ± 5.3	−0.1 ± 1.0	67.7 ± 5.0	67.4 ± 5.1	−0.2 ± 1.3	NS

[a] Plus–minus values are means ± standard deviations.
[b] After regression-to-the-mean analysis.
[c] Cohen's d is the standardized mean difference between the oral-appliance group and the CPAP group.
† $p < 0.05$.

a relaxed position. After a short period of relaxed tidal breathing the cephalogram was taken at end-expiration. Early morning visits were avoided because some patients were not able to close in maximum intercuspation at that time but were habituated to bite with the mandible in a more protrusive position.

A predefined trace-protocol (Table 2 and Fig. 2) was used to perform all tracings using Viewbox software® (version 3.1.1.6, Dhal Software, Kifissia, Greece). To minimize identification error, one blinded observer (MD) performed all tracings. Furthermore, for sagittal and vertical measurements, superimposition was performed on the anterior contour of the sella turcica and sella-nasion (SN).[32] In order to further reduce the error of measurements, the coordinates of sella and nasion were, after superimposition, transferred from the baseline to the follow-up cephalogram in order to obtain exactly the same coordinates on both cephalograms. All linear cephalometric measurements were corrected for a radiographic enlargement of 12%.

2.4. *Statistical analysis*

Statistical analyses were performed using the Statistical Package for the Social Sciences (version 16.0, SPSS Inc., Chicago, IL, USA). All variables were normally distributed and their means and standard deviations (s.d.) are reported. The AHI of the oral-appliance and CPAP patients at baseline was distributed normally after logarithmic transformation. To compare outcomes between cephalometric variables at baseline and follow-up, paired Student's t-tests were performed. Although proper randomisation is executed, a (small) difference in the average values of a determinant for the two treatment arms may occur. To correct for this regression-to-the-mean fenomenon statistically in our analysis, the baseline value was at all times included in the regression model.

For continuous cephalometric measures, 'between groups' effect sizes are reported as Cohen's d, the standardized mean difference, based on mean group change scores divided by the pooled standard deviation. The differences in craniofacial morphology between the oral-appliance and CPAP group d reflect the net side-effects associated with oral-appliance therapy, a measure that controls for spontaneous changes in the control group and pre-existing random group differences at baseline. Cohen's d effect sizes are interpreted as small (0.20), medium (0.50), or large (>0.80)[33].

For the oral-appliance group, linear regression analysis was used to determine the relationship between the changes in craniofacial morphology and the mean mandibular protrusion during the follow-up period. A significance level of 0.05 was predefined in all cases.

3. Results

For analysis, 31 and 37 patients were included in the oral-appliance group and the CPAP group, respectively (Fig. 1). The mean follow-up period was 2.3 (±0.2) years in the oral-appliance group (range 2.1–3.1 years) and 2.4 (±0.3) years in the CPAP group (range 2.1–3.2 years).

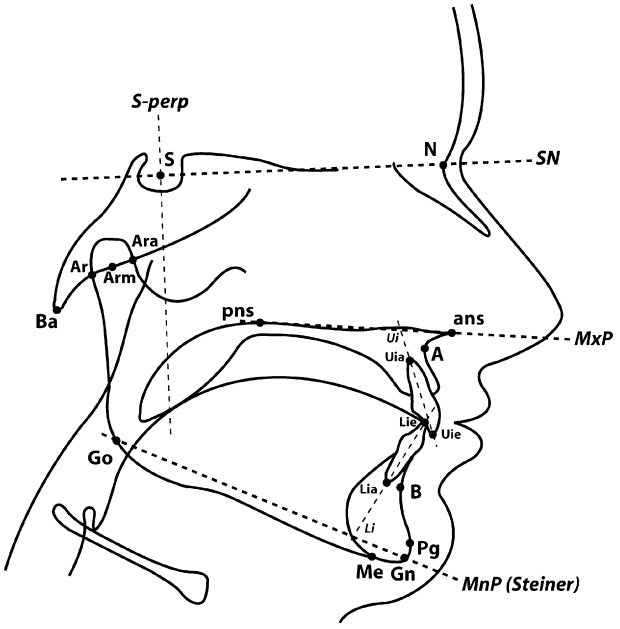

Fig. 2 – Cephalometric landmarks and reference lines traced on lateral cephalograms. The following 18 reference points were identified on lateral cephalograms: A (point A: the deepest midline concavity on the anterior maxilla), ans (anterior nasal spine: the tip of the median, sharp bony process of the maxilla at the lower margin of the anterior nasal opening), Ara (anterior articulare: the point of intersection of the inferior cranial base surface and the averaged anterior surfaces of the mandibular condyles), Arm (articulare midpoint; the midpoint of the line between Aa–Ar), Ar (articulare; the point of intersection of the inferior cranial base surface and the averaged posterior surfaces of the mandibular condyles), B (point B: the deepest midline concavity on the mandibular symphysis), Ba (Basion; the median point of the anterior margin of the foramen magnum), Gn (gnathion: the most anterior-inferior point on the contour on the bony chin symphysis. Determined by bisecting the angle formed by the mandibular plane and a line through pogonion and nasion), Go (gonion: the constructed point of the intersection of the ramus plane and the tangent to the body of the mandible), Lia (lower incisor apex), Lie (lower central incisor edge: the incisal tip of the mandibular central incisor), Me (menton: the intersection of the bony inferior symphysis with the inferior margin of the mandibular body), N (nasion: the most anterior point on the frontonasal suture), Pg (pogonion: the most anterior point on the contour of the bony chin determined by a tangent through nasion), pns (posterior nasal spine: the intersection of a continuation of the anterior wall of the pterygopalatine fossa and the floor of the nose, marking the dorsal limit of the maxilla), S (sella; the midpoint of the pituitary fossa), Uia (upper incisor apex), Uie (upper incisor incisal edge: the incisal tip of the maxillary central incisor). The following six reference lines were identified on lateral cephalograms: Li (lower incisor line: the line through the lower incisor apex and the lower incisor incisal edge), MnP (mandibular plane according to Steiner: the line through gonion and gnathion), MxP (maxillary plane: the line through the posterior nasal spine (pns) and the anterior nasal spine (ans)), SN (sella-nasion line: the line through sella and nasion), SN-perp (SN-perpendicular: the line through Sella (S) perpendicular on line SN), Ui (upper incisor line: the line through the upper incisor apex and the upper incisor incisal edge).

In the oral-appliance group, the mean mandibular protrusion during the follow-up period was 79 (±20)% of the maximal mandibular protrusion. The mean mouth opening (including overbite) while wearing the oral-appliance was 13 (±3) mm.

3.1. *Cephalometric analysis*

In the oral-appliance group, no significant changes were found in the variables pertaining to the base of the skull. Concerning maxillary measurements, the angle between the upper incisor line and the maxillary plane (Ui–MxP) decreased 2.0 (±2.8) degrees as a result of long-term oral-appliance therapy compared with CPAP therapy, indicating a retroclination of the maxillary incisors (Table 2).

Mandibular measurements showed that the position of the mandible in relation to the skull base, i.e. the SNB-angle, was reduced 0.4 (±0.9)° and the angle between the lower incisor line and the mandibular plane (Li–MnP) increased 3.7 (±5.4)°, indicating a proclination of the mandibular incisors. Furthermore, a downward and backward rotation of the mandible was observed, as the shortest linear distance from menton to line SN-perp (Me-hor) decreased 0.7 (±1.6) mm and the shortest linear distance between menton and line SN (Me-ver) increased 0.7 (±1.4) mm.

Regarding the intermaxillary relationships, the ANB-angle increased 0.3 (±0.9)° and the interincisal angle (Ui–Li) decreased 2.3 (±5.8)°. Furthermore, the overbite and overjet decreased 1.0 (±1.5) mm and 1.7 (±1.6) mm, respectively.

Concerning facial height there was an increase in the lower anterior facial height (0.8 ± 1.5 mm) and the total anterior facial height (0.9 ± 1.4 mm), resulting in a decrease of the anterior facial height ratio (0.8 ± 1.9%). No significant changes were observed in any of the variables regarding the posterior facial heights.

When adjusted for regression-to-the-mean effects, our data show significant, mainly dental changes in the craniofacial morphology in the oral-appliance group compared with the CPAP group following 2 years of treatment (Table 2 and Fig. 3). A retroclination of the upper incisors ($d = 0.6$) and a proclination of the lower incisors ($d = 0.7$) was found, the overjet ($d = 1.3$) and overbite ($d = 0.6$) had decreased, and the lower anterior facial height ($d = 0.6$) as well as the total anterior facial height ($d = 0.5$) had increased in the oral-appliance group compared with the CPAP group. Conversely, the anterior facial height ratio did not change significantly when comparing the oral-appliance and CPAP group.

Linear regression analysis revealed that the decrease in overbite was significantly associated with the mean mandibular protrusion during follow-up ($B = -0.029$, $SE = 0.014$, $p < 0.05$). The control (CPAP) group did not reveal any significant changes in the craniofacial morphology after 2 years of treatment.

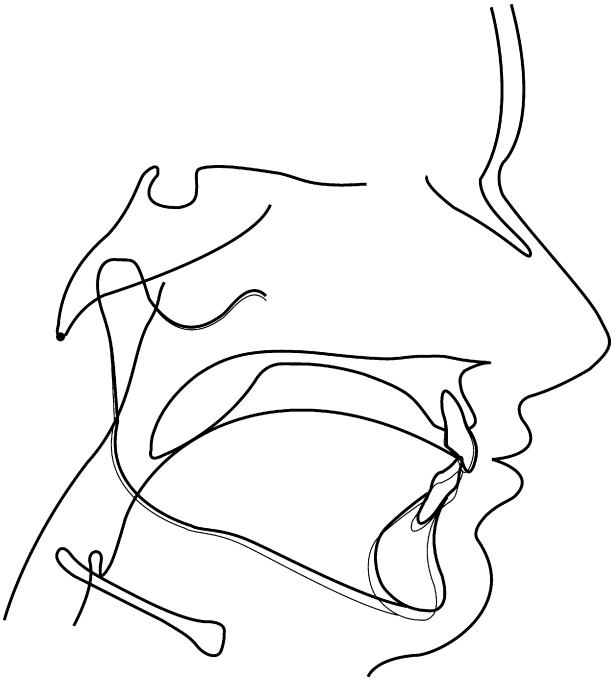

Fig. 3 – Craniofacial changes represented in an overall tracing, before (thick line) and after (thin line) oral-appliance therapy.

4. Discussion

To our knowledge, this is the first study in which changes in craniofacial morphology as a result of long-term oral-appliance therapy are evaluated in a controlled study concerning patients from the full OSAHS spectrum. The results of this study indicate that changes in craniofacial morphology should be anticipated in OSAHS patients using an oral-appliance for 2 years when compared with CPAP therapy. These changes, however, were predominantly dental in nature. Furthermore, by using linear regression analysis, an association was observed between the mean mandibular protrusion during the follow-up period and the decrease in overbite.

Changes in overbite and overjet, retroclination of the upper incisors and a proclination of the lower incisors have also been described in previous studies.[8,15,23,24] These changes have been attributed to a labially directed force to the mandibular incisors and a palatally directed force to the maxillary incisors while the appliance is in place and the mandible attempts to return to a less constrained position. Conversely, Ringqvist et al.[20] did not find significant changes in overbite, overjet, and inclination of the upper or lower incisors after 2 years of oral-appliance use. A first explanation for this erratic result could be the different design of the oral-appliance used in their study. The frontal parts of both tooth arches were not covered by acrylate. Therefore, the palatally and labially directed forces were not applied directly to the upper and lower incisors, respectively. Another explanation could be the degree of mandibular protrusion of 50% while wearing the oral-appliance. Both explanations seem viable but it is unclear to what extent each of these possibilities contributes to the observed differences.

Protrusive positions of the mandible over 75% of the patient's maximum were applied in some patients in the present study. This could be explained by the fact that patients with mild, moderate, and severe OSAHS were included. Severe OSAHS patients may need more pronounced protrusive positions of the mandible in order to experience sufficient benefit from the oral-appliance. Ringqvist et al.[20] only included patients with mild-to-moderate disease. As dose dependency of oral-appliance therapy has previously been described,[34] it is conceivable that the oral-appliance in this category is already effective in a less protrusive position, resulting in less severe dental side-effects.

In the oral-appliance group, we found a backward (decreased Me-hor) and downward (increased Me-ver) rotation of the mandible, resulting in small but significant increases in the lower and total anterior facial heights, but not in the anterior facial height ratio. These findings corroborate the results from previous studies.[19,22,23] It could be hypothesized that over-eruption of the molars, caused by possible inadequacies in the oral-appliance's fit during follow-up, results in an increase in anterior facial height. However, in the present study the quality and fit of the oral-appliances was checked annually and adjusted if required. Therefore, it seems unlikely that this mechanism explains the increase in the lower and total anterior facial heights in our study. The small increase in anterior facial height is most likely the result of oral-appliance-induced dental changes. The retroclination of the upper incisors and the proclination of the lower incisors result in a downward rotation of the mandible through incisal guidance, most likely resulting in a small but significant increase in the total and lower anterior facial height.[35]

Bondemark[21] found an increase in mandibular length after 2 years of oral-appliance use. We did not observe any significant changes in mandibular length (Arm–Me), ramus length (Arm–Go) or mandibular body length (Go–Me) in our patients. This discrepancy could be explained by the differences in mandibular landmarks used. Bondemark used the linear distance between condylion (Cd) and pogonion (Pg). We calculated mandibular length as the linear distance between articulare midpoint (Arm) and menton (Me). Pogonion could be an unreliable landmark if rotation of the mandible occurs, because the most anterior point of the mandibular symphysis will be displaced. However, menton is an anatomical landmark rather than a constructed landmark and, therefore, is more reliable when mandibular rotation is to be expected. Furthermore, it has been suggested that articulare is more reproducible than condylion on cephalograms exposed in habitual occlusion.[36] We constructed the landmark articulare midpoint (Arm) as we hypothesized that this point is less susceptible to displacement when rotation of the mandible occurs.[37]

It could be hypothesized that the long-term use of CPAP causes changes in the dental or skeletal morphology as a result of its tight-fitting (mouth-) nose mask. However, in the present study we did not find any changes in either dental- or skeletal variables in the CPAP group. Therefore, in retrospect the CPAP group appeared to be adequate as a control group.

In this study an adjustable oral-appliance was used. The regression analysis showed that there appears to be an association between the decrease in overbite and the extent of mandibular protrusion. Therefore, it appears to be of

importance to keep the mandibular protrusion associated with oral-appliance use to a minimum. This finding may become increasingly important, as with increasing age OSAHS symptomatology may worsen in patients who require a more extended protrusive mandibular position. It could be hypothesized that the extent of dental side effects might be more pronounced with adjustable appliances as there is a risk of advancing the mandible beyond an optimum position. As a result of including severe OSAHS patients in this study, the mean mandibular protrusion might be larger in the present sample when compared with other studies that only studied patients with mild-moderate OSAHS or snorers without OSAHS.

Martinez-Gomis et al.[38] found a significant reduction in the number of posterior occlusal contacts after 2 years use of oral-appliance. This tendency however, reversed during the period of 2–5 years of treatment. Therefore it seems viable that most dental changes occur during the first years of treatment with an oral-appliance but tend to stabilize over time.

Inter- and intraobserver reliability measurements were not carried out in this study. However, in a recent study,[26] interclass correlation coefficients (ICCs) were calculated for two experienced observers (MD and GP) after digital tracings using Viewbox 3.1.1.6 software®. Except for one, all ICCs were considered excellent (range 0.69–0.97).

Notwithstanding the fact that this study was prospective in design, the randomization and sample size calculation were performed based on the primary outcome measure for the randomized controlled trial by Hoekema et al.[7]. A post-analysis power calculation, using the change in overjet as clinical most important outcome variable, yielded a power of 88% ($n1 = 31$, $n2 = 37$, $\alpha = 0.05$).

In conclusion, our results show that the long-term use of an oral-appliance causes predominantly dental changes in the craniofacial morphology in OSAHS patients. All effect sizes of the observed significant changes, expressed as Cohen's *d*, were medium-to-large and should be considered as clinically important. Nevertheless, a disorder with serious cardiovascular consequences should be treated as effective as possible. This supersedes the maintenance of a patients' baseline craniofacial morphology. Discontinuation of oral-appliance therapy because of the development of craniofacial side-effects should only be considered in patients who are able to tolerate or accept another effective treatment modality for the OSAHS. However, in agreement with Almeida et al.,[23] we endorse the importance of collecting clinical data as cast-models and intra-oral photographs before and during treatment with an oral-appliance. Thus, patients treated with an oral-appliance need a thorough follow-up by a dentist or dental-specialist experienced in the field of dental sleep medicine.

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