Effects of a mandibular advancement device on the upper airway morphology: a cephalometric analysis

M. H. J. DOFF*, A. HOEKEMA*, G. J. PRUIM†, J. H. VAN DER HOEVEN‡, L. G. M. DE BONT* & B. STEGENGA*

Departments of *Oral and Maxillofacial Surgery, †Orthodontics and ‡Clinical Neurophysiology, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands

SUMMARY The aims of this study were to assess changes in the upper airway morphology associated with an oral appliance in situ in patients suffering from the obstructive sleep apnoea-hypopnoea syndrome and to relate these changes to treatment response. Changes in upper airway morphology as a result of an oral appliance were assessed in 52 patients with obstructive sleep apnoea-hypopnoea syndrome by means of cephalometric analysis. Lateral cephalograms were taken at baseline and after 2–3 months of treatment. Baseline and follow-up cephalograms were traced twice and cephalometric variables were compared. The predictive value of changes in upper airway morphology for the treatment response was evaluated in univariate and multivariate regression analyses. Oral appliance therapy resulted in an increased posterior airway space at the level of the second vertebra, the uvular tip and the base of the tongue. The increase of the posterior airway space at the level of the second vertebra and the uvular tip were the best predictors for relative improvement of the apnoea-hypopnoea index. However, the predictive value for treatment response of these cephalometric upper airway changes should be interpreted with caution.

KEYWORDS: obstructive sleep apnoea syndromes, oral appliance, cephalometry

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Introduction

The obstructive sleep apnoea–hypopnoea syndrome (OSAHS) is a sleep-related breathing disorder, characterized by repetitive partial (hypopnoea) or complete (apnoea) airway obstructions and disruptive snoring during sleep (1). These airway obstructions can cause recurrent arousals from sleep, ultimately resulting in excessive daytime sleepiness, neurocognitive impairment, a higher risk of motor vehicle accidents and cardiovascular disease events (2–5).

Severity of the disorder is usually expressed by the apnoea–hypopnoea index (AHI), i.e. the mean number of apnoeas and hypopnoeas per hour sleep. Obstructive sleep apnoea–hypopnoea syndrome may be classified as mild (AHI: 5–15), moderate (AHI: 15–30) or severe (AHI>30) (6). Obstructive sleep apnoea–hypopnoea syndrome of at least mild severity is diagnosed in 2% of women and 4% of middle-aged men in the North American population (7).

To improve upper airway patency during sleep, a variety of treatment options, ranging from non-invasive to surgical, is available. Continuous positive airway pressure (CPAP) is generally considered the treatment of first choice in severe OSAHS cases (8). However, compliance with this relatively obtrusive therapy may be poor (9, 10). Oral appliance therapy is an effective alternative, and is especially effective in mild/moderate OSAHS cases (2). Most oral appliances used in a clinical setting are mandibular advancement devices which keep the mandible and its attached musculature in a protruded position.

Upper airway imaging provides insight into the complex pathophysiology of OSAHS. There are several ways of imaging the upper airway in OSAHS patients, including computed tomography, magnetic resonance imaging and ultrasonography.
imaging and videoendoscopy. Most of these imaging techniques are expensive, invasive or not readily available in clinical practice. Cephalometry is a widely available, less expensive and easy to perform technique to examine upper airway craniofacial and soft tissue structures (11). It has also been used to visualize changes in upper airway morphology with an oral appliance in situ (12, 13). However, to our knowledge, it is unclear whether there is a relationship between changes in the upper airway morphology with an oral appliance and the treatment response to oral appliance therapy. To answer this question, we determined changes in upper airway morphology in OSAHS patients by means of cephalometric analysis.

Materials and methods

Patient selection

The effectiveness of an oral appliance in the treatment of OSAHS, as compared with CPAP, has been determined in a separate randomized controlled trial (14). In that trial, patients with OSAHS (AHI>5) (6) were recruited from the Department of Home Mechanical Ventilation of the University Medical Center Groningen, the Netherlands. Based on dental, medical and psychological criteria (Table 1), patients were selected for that trial and consequently randomized for either CPAP- or oral appliance therapy (14). In the course of that study, several patients switched from CPAP to oral appliance therapy. For this study, the patients who had been randomized to the oral appliance group (n = 51) as well as patients who had switched from CPAP to oral appliance therapy before follow-up (n = 6) were included. Of the latter patients, five were considered non-compliant to CPAP and CPAP was ‘not effective’ in one patient. Of the fifty-one patients, randomized to oral appliance therapy, two were lost to follow-up. Furthermore, three patients were excluded because of an inadequate quality of the cephalograms, resulting in 52 patients for analysis. This study was approved by the Groningen University Medical Center’s Ethics Committee (METc2002/032). Written informed consent was obtained from patients before enrolment.

Study design

To determine whether there is a relationship between changes in upper airway morphology with an oral appliance in situ and treatment response to oral appliance therapy, patients had been subjected to a polysomnographic evaluation at baseline. In addition, a lateral cephalogram of all patients was taken. The oral appliance used in this study (Thornton Adjustable Positioner)* consisted of two separate parts, fixing the patient’s mandible in a protruded and downward position (Fig. 1). The mandibular protrusion could be adjusted with 0Æ2 mm increments with a propulsion screw, which was incorporated anteriorly in the oral appliance. Before starting oral appliance therapy, the maximal range of mandibular protrusion of each patient was determined with a George-Gauge/C212.† When initiating oral appliance therapy, the mandible was set at approximately 50% of the patient’s maximal protrusion. After having adapted to this position during a 2-week period, patients were allowed to further adjust the oral appliance during a 6-week period. After this ‘titration’ period, the treatment effect was assessed with a second polysomnogram. This period was, if necessary,

Table 1. Criteria for exclusion

<table>
<thead>
<tr>
<th>Medical and psychological criteria</th>
<th>Dental criteria</th>
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</thead>
<tbody>
<tr>
<td>Previous treatment of OSAHS (continuous positive airway pressure, oral appliance therapy, or uvulopalatopharyngoplasty)</td>
<td>Extensive periodontal disease or tooth decay</td>
</tr>
<tr>
<td>Morphological airway abnormalities requiring treatment</td>
<td>Active temporo-mandibular joint disease (including severe bruxism)</td>
</tr>
<tr>
<td>Endocrine dysfunction</td>
<td>Restrictions in mouth opening (&lt;25 mm) or advancement of the mandible (&lt;5 mm)</td>
</tr>
<tr>
<td>A reported or documented history of severe cardiac or pulmonary disease</td>
<td>Partial or complete edentulism (&lt;8 teeth in upper or lower jaw)</td>
</tr>
</tbody>
</table>

OSAHS, obstructive sleep apnoea–hypopnoea syndrome.

*Airway Management Inc., Dallas, TX, USA.
†H-Orthodontics, Michigan City, IN, USA.
continued until the AHI was <5 or until the adjustments became uncomfortable for the patient. Follow-up review ended with a final polysomnographic evaluation or when the patient discontinued treatment (e.g. because of poor tolerance). Furthermore, a second lateral cephalogram was taken with the oral appliance intra-orally. The degree of protrusion and the vertical dimension of the oral appliance were kept constant during the follow-up measurements (e.g. second cephalogram and polysomnographic evaluation). Mandibular protrusion and the mouth opening (including the vertical overbite) were measured with a digital sliding calliper with a 0.01 mm accuracy.

The primary outcome measure was the relative improvement of the AHI. Secondary outcome measures were an AHI<5 and the criterion of ‘effectiveness of treatment’ as suggested by Hoekema et al. (2), defined as an AHI<5 or a reduction in the AHI of at least 50% from the baseline value to a value of <20 in a patient who had no symptoms while using therapy.

Polysomnography

Polysomnography (Embla® A10 digital recorder) for baseline and follow-up evaluations was conducted ambulatory in the patient’s home. Based on the AHI, patients were classified as having non-severe (AHI: 5–30) or severe (AHI>30) OSAHS. All polysomnograms were evaluated and scored by the same neurophysiologist (J. H. V.) who was unaware of the patient’s treatment assignment.

Cephalometric analysis

All lateral cephalograms were recorded using a ProMax Cephalostat. The ‘mirror position’ (15) was used to get a reproducible position of the head. Patients were instructed to swallow and to close their mouths with the mandible in maximal intercuspation and the lips in a relaxed position. After a short period of relaxed tidal breathing, the cephalogram was taken at end expiration. A trace protocol (Table 2, Fig. 2) was designed and all tracings were performed using Viewbox 3.1.6 software. As a first step, to determine interobserver reliability, 10 baseline cephalograms were randomly chosen and traced by two experienced clinicians (GP, MD). Next, to minimize identification error, all 52 cephalograms were traced blindly with respect to treatment outcome by one observer (MD) and repeated after a 1-week period. Mean outcomes of both tracings were used for further statistical analysis. All linear cephalometric measurements were converted to values of life size.

Statistical analyses

All statistical analyses were performed using the Statistical Package for the Social Sciences version 14.0. To assess interobserver reliability of the tracings, the interclass correlation coefficient (ICC) was calculated for each variable. Interclass correlation coefficients <0.4 were considered poor, ICCs of 0.4 to 0.75 were considered fair to good and those >0.75 were considered excellent (16).

All variables were normally distributed (AHI at baseline and follow-up after log transformation) and their means ± s.d. are reported. To compare outcomes between demographic and cephalometric variables at baseline and follow-up, paired Student’s t-tests were performed. α was set at 5%.

The differences in upper airway morphology between baseline and follow-up variables were selected for regression analysis. For matters of broad inclusion of possible determinants, α was set at 0.2 for the univariate analyses. The dependent variable was the relative improvement of the AHI following treatment for the linear regression analysis, and the presence or absence

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Fig. 1. Oral appliance in situ.

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8Planmeca, Helsinki, Finland.
9Viewbox, Athens, Greece.
**SPSS Inc., Chicago, IL, USA.
of ‘effectiveness of treatment’ and an AHI<5 following treatment for the logistic regression analysis. All significant variables concerning pharyngeal dimensions resulting from univariate linear and logistic regression analyses were then submitted for multivariate linear regression analysis.

Results

Treatment response

Demographic variables of all patients and variables regarding treatment response at baseline and follow-up are shown in Table 3. According to Hoekema’s (14) definition of success, treatment was ‘effective’ in 42 patients (81%). An AHI<5 was found in 31 patients (60%). The average mandibular protrusion for patients with effective treatment according to Hoekema (responders) at the follow-up review was 79·9 ± 18·1% (mean ± s.d.) and 76·2 ± 18·1% for the patients in which treatment was not effective (non-responders). The difference in mandibular protrusion between the responders and non-responders was not significant (t-test, P > 0·05). The average mouth opening at follow-up, when the patient was wearing the oral appliance, was 13·2 ± 2·8 mm in the responders group and 12·2 ± 2·4 mm in the non-responders group. The latter difference between these two groups was not significant (t-test, P > 0·05).

Reliability

An ‘excellent’ agreement between both examiners was found for all cephalometric variables (Table 4), except

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline (n = 52)</th>
<th>Follow-up with oral appliance (n = 52)</th>
<th>95% CI of the difference</th>
<th>Significance paired t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sagittal jaw relationship</td>
<td></td>
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<tr>
<td>SNA (degrees)</td>
<td>80·3 4·6</td>
<td>80·1 4·5</td>
<td>[−0·1–0·7]</td>
<td>NS</td>
</tr>
<tr>
<td>SNB (degrees)</td>
<td>76·5 4·4</td>
<td>78·0 4·5</td>
<td>[−2·0–1·0]</td>
<td>P &lt; 0·05</td>
</tr>
<tr>
<td>ANB (degrees)</td>
<td>3·8 2·6</td>
<td>2·0 3·1</td>
<td>[1·2–2·3]</td>
<td>P &lt; 0·05</td>
</tr>
<tr>
<td>Pharyngeal dimensions</td>
<td></td>
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<tr>
<td>C2a-P2a: perpendicular distance from point C2a to the anterior pharyngeal wall (mm)</td>
<td>13·1 3·3</td>
<td>14·5 3·9</td>
<td>[−2·3–0·5]</td>
<td>P &lt; 0·05</td>
</tr>
<tr>
<td>C2a-P2p: perpendicular distance from point C2a and P2p (mm)</td>
<td>4·6 2·3</td>
<td>4·4 1·5</td>
<td>[−2·8–0·7]</td>
<td>NS</td>
</tr>
<tr>
<td>Pas-C2: posterior airway space at the level of the second vertebra; linear distance between P2a and P2p (mm)</td>
<td>8·5 3·5</td>
<td>10·1 3·7</td>
<td>[−2·6–0·6]</td>
<td>P &lt; 0·05</td>
</tr>
<tr>
<td>Pas-BT: linear distance between point BT and PPW (mm)</td>
<td>8·7 3·4</td>
<td>9·9 3·3</td>
<td>[−2·2–0·1]</td>
<td>P &lt; 0·05</td>
</tr>
<tr>
<td>Pas-Ut: linear distance between point PT and PPW (mm)</td>
<td>7·5 2·6</td>
<td>9·4 3·1</td>
<td>[−2·6–1·1]</td>
<td>P &lt; 0·05</td>
</tr>
<tr>
<td>pns-Ut: uvular length; linear distance between the posterior nasal spine and the tip of the velum (mm)</td>
<td>41·7 5·4</td>
<td>41·8 5·5</td>
<td>[−1·3–1·0]</td>
<td>NS</td>
</tr>
<tr>
<td>Hyoid bone position</td>
<td></td>
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<tr>
<td>Hy-C3a: linear distance from Hy to C3a (mm)</td>
<td>39·6 4·0</td>
<td>39·4 4·2</td>
<td>[0·6–1·0]</td>
<td>NS</td>
</tr>
<tr>
<td>Hy-MP: linear distance from Hy to the mandibular plane (mm)</td>
<td>28·6 5·2</td>
<td>19·5 5·5</td>
<td>[8·1–10·2]</td>
<td>P &lt; 0·05</td>
</tr>
<tr>
<td>Hy-SN: perpendicular distance from Hy to line SN (mm)</td>
<td>121·0 8·2</td>
<td>117·6 7·9</td>
<td>[2·2–4·5]</td>
<td>P &lt; 0·05</td>
</tr>
</tbody>
</table>

CI, confidence interval; NS, not significant; BT, base of tongue; Hy, hyoid; pns, posterior nasal spine; PPW, posterior pharyngeal wall; S, sella; Ut, uvular tip; MP, mandibular plane; SN, sella-nasion; Pas, posterior airway space.

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for the posterior airway space at the level of the base of the tongue (Pas-BT) which demonstrated ‘fair to good’ agreement (16).

Cephalometric analysis

Regarding the sagittal jaw relationship the SNB-angle increased 1.5° (±1.9°) and the ANB-angle decreased 1.8° (±2.0°) as a result of wearing an oral appliance (Table 2). Concerning pharyngeal dimensions, increases were found in the posterior airway space at the level of the BT (Pas-BT) (1.2 ± 3.6 mm), at the level of the second vertebra (Pas-C2) (1.6 ± 3.7 mm), and at the level of the uvular tip (Pas-Ut) (1.8 ± 2.6 mm) with the oral appliance intra-orally. Moreover, both the distance from the Hy to the mandibular plane (Hy-MP) and the distance between Hy and the sella-nasion line (Hy-SN) had decreased (~9.2 ± 3.8 mm and ~3.4 ± 4.1 mm respectively), indicating a more cranial position of the hyoid bone.

Regression analyses

Univariate linear regression analysis demonstrated that an increased posterior airway space at the level of the second vertebra (Pas-C2) and at the level of the Ut (Pas-Ut) was significantly associated with a relative improvement of the AHI (Table 5). Logistic regression analysis for predicting an AHI<5 or ‘effectiveness of treatment’ did not yield any significant predictive cephalometric variables.

Multivariate linear regression analysis for predicting the extent of the relative improvement of the AHI yielded a model with the increase in posterior airway space at the level of the Ut (ΔPas-Ut) as the strongest predictor (β = -5.40, 95% CI: [-9.16, -1.56], P<0.05).

Discussion

The results of this study show that an oral appliance in situ improves the antero-posterior dimensions of the posterior airway space at the level of the second vertebra (Pas-C2), the Ut (Pas-Ut) and the BT (Pas-BT). At the former two sites, the increased posterior airway space was associated with a relative improvement of the AHI.

No significant changes could be demonstrated in the linear distance between point C2a and P2p, suggesting that the increase of the posterior airway space at the level of C2 is caused by a more ventral position of the anterior pharyngeal wall. The increase in the posterior airway space can be attributed to the oral appliance, which holds the mandible in an anterior position. Isono et al. (20) proposed possible mechanical interactions in the pharyngeal region. As the tongue is directly connected to the mandible, a more anterior position of the mandible most likely displaces the tongue anteriorly, thus increasing the retroglossal airway space. Considering the working mechanism of an oral appliance (i.e. protruding the mandible and its attached soft tissue structures) one would expect the largest
Pharyngeal dimensions

- C2a-P2a: 0.96, [0.30–0.99]
- C2a-P2p: 0.83, [0.49–0.96]
- Pas-BT: 0.69, [0.38–0.91]
- Pas-C2: 0.95, [0.78–0.99]
- Pas-Ut: 0.90, [0.60–0.97]
- pns-Ut: 0.94, [0.78–0.99]

Hyoid bone position

- Hy-C3a: 0.93, [0.22–0.99]
- Hy-MP: 0.92, [0.70–0.98]
- Hy-SNL: 0.95, [0.81–0.99]

CI, confidence interval; ICC, interclass correlation coefficient; BT, base of tongue; Hy, hyoid; pns, posterior nasal spine; Ut, uvular tip; MP, mandibular plane; SNL, sella-nasion line; Pas, posterior airway space.

The increase in posterior airway space to be located at the level of the BT. However, we found the largest increase at the level of the Ut. The first explanation for this finding is that in most OSAHS patients the BT opposes the anterior wall of the soft palate because of macroglossia and/or a longer uvula associated with the disorder (21). By forcing the tongue in a more anterior position, the gravitational effect on the soft palate may be decreased. The resulting increase of the velopharyngeal airway space (Pas-Ut) with oral appliance therapy might be explained by this theory. A second explanation may be the decrease in snoring levels accompanied with oral appliance therapy, which might result in a decrease in edematous tissue of the velum. Both explanations seem viable but it is unknown to what extent each of both mechanisms contributes to this increase in velopharyngeal airway space.

In several studies, a more inferiorly positioned hyoid bone has been described in OSAHS patients when compared with healthy subjects (22–24). In this study, we demonstrated a more cranial position of the hyoid bone as a result of an oral appliance, as indicated by a decrease in the linear distance between Hy and SN and that between Hy and MP. Although the decrease in Hy and SN indicates a more cranial position of the hyoid bone, the decrease in distance between Hy and MP most likely results from the mouth opening associated with wearing an oral appliance. The more cranial position of the hyoid bone might also be the result of the more protruded position of the mandible and tongue with the oral appliance intra-orally. Consequently, the tongue musculature might pull the hyoid bone to a more anterior-superior position. However, contrary to other results, (19) we could not demonstrate a more anterior position of the hyoid bone with an oral appliance as indicated by a non-significant change in the linear distance between point Hy and the most antero-inferior point on the third vertebra (C3a). This difference in Hy position could be explained by the fact that Tsuiki et al. (18) recorded their cephalograms in the supine position. The gravitational effect on the antero-posterior position of the hyoid bone is probably larger in supine position than in the upright position. This gravitational
Sophisticated techniques like sleep nasendoscopy and a remotely controlled mandibular positioner have been suggested to predict the response to oral appliance therapy (17, 26). These techniques may be of additional value in selecting suitable candidates for oral appliance therapy. However, unlike cephalometry, most of these techniques are expensive and complex or not available in a dental or orthodontic practice. Cephalometry provides two-dimensional information. Imaging techniques providing three-dimensional information could be of additional value in assessing the complex pathophysiology of OSAHS and the working mechanism of an oral appliance during sleep. On the other hand, these imaging techniques would be impractical and expensive in large groups of patients. Therefore, this study aimed at providing predictive upper airway variables convenient for the clinical situation.

Multivariate linear regression analyses yielded a single-variate predictive model, with a positive change in posterior airway space at the level of the Ut (ΔPas-Ut) being the best predictor for a relative improvement of the apnoea–hypopnoea. However, logistic regression analysis for predicting an AHI < 5 or ‘effective treatment’ did not yield any predictive variables. Therefore, it could be hypothesized that the actual positive changes in upper airway dimensions with an oral appliance during sleep are not the main contributors to treatment response. In Table 2, it is shown that these actual changes are rather small (i.e. 0.1–2.2 mm). Therefore, it seems a plausible explanation that the effectiveness of an oral appliance is largely based on protecting the posterior airway space from collapsing during sleep rather than on increasing it. Another possible explanation is that obstructive sleep apnoea patients experience a greater degree of lateral than antero-posterior increase in airway size with an oral appliance (27). Thus we conclude that, considering these possible mechanisms and some methodological limitations of this study (i.e. awake, upright position, two-dimensional), the predictive value for treatment response of these cephalometric upper airway changes should be interpreted with caution.

Table 5. Univariate analysis of cephalometric variables predicting a relative improvement of the AHI with oral appliance therapy and logistic regression analysis for predicting an AHI < 5 or ’effectiveness of treatment’ with oral appliance therapy

<table>
<thead>
<tr>
<th>Variable</th>
<th>ΔAHI%† (β)</th>
<th>95% CI</th>
<th>AHI &lt; 5 (OR)</th>
<th>95% CI</th>
<th>Effectiveness of treatment‡ (OR)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sagittal jaw relationship</td>
<td></td>
<td></td>
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<tr>
<td>ΔSNB (degrees)</td>
<td>−0.07</td>
<td>[−5.60−5.47]</td>
<td>1.36</td>
<td>[1.0−1.86]</td>
<td>0.98</td>
<td>[0.68–1.41]</td>
</tr>
<tr>
<td>ΔANB (degrees)</td>
<td>0.74</td>
<td>[−4.70−6.18]</td>
<td>0.76</td>
<td>[0.55–1.03]</td>
<td>1.08</td>
<td>[0.75–1.55]</td>
</tr>
<tr>
<td>Pharyngeal dimensions</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Δ C2a-P2a (mm)</td>
<td>−0.23</td>
<td>[−3.57−3.12]</td>
<td>0.93</td>
<td>[0.78–1.11]</td>
<td>1.00</td>
<td>[0.80–1.24]</td>
</tr>
<tr>
<td>Δ PAS-C2 (mm)</td>
<td>−3.37</td>
<td>[−6.11→0.63]</td>
<td>0.85</td>
<td>[0.70–1.02]</td>
<td>0.91</td>
<td>[0.77–1.07]</td>
</tr>
<tr>
<td>Δ PAS-BT (mm)</td>
<td>−2.70</td>
<td>[−5.53−0.13]</td>
<td>0.89</td>
<td>[0.75–1.06]</td>
<td>0.90</td>
<td>[0.76–1.07]</td>
</tr>
<tr>
<td>Δ PAS-Ut (mm)</td>
<td>−5.36</td>
<td>[−9.16→1.56]</td>
<td>0.99</td>
<td>[0.80–1.23]</td>
<td>0.77</td>
<td>[0.58–1.01]</td>
</tr>
<tr>
<td>Hyoid bone position</td>
<td></td>
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<tr>
<td>ΔHy-MP (mm)</td>
<td>−0.54</td>
<td>[−3.34−2.27]</td>
<td>0.94</td>
<td>[0.81–1.10]</td>
<td>0.95</td>
<td>[0.78–1.14]</td>
</tr>
<tr>
<td>Δ Hy-SN (mm)</td>
<td>−0.86</td>
<td>[−3.45−1.74]</td>
<td>0.92</td>
<td>[0.79–1.07]</td>
<td>0.97</td>
<td>[0.80–1.16]</td>
</tr>
</tbody>
</table>

BT, base of tongue; Hy, hyoid; Ut, uvular tip; MP, mandibular plane; SNL, sella-nasion line; AHI, apnoea–hypopnoea index; CI, confidence interval; OR, odds ratio; Pas, posterior airway space.

†≥0.05.

‡ Treatment was considered effective when the AHI either was <5 or showed substantial reduction, defined as reduction in the AHI of at least 50% from the baseline value to a value of <20 in a patient without symptoms while using therapy.
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References


Correspondence: M. H. J. Doff, Department of Oral and Maxillofacial Surgery, University Medical Center Groningen, University of Groningen, Hanzeplein 1, PO Box 30001, 9700 RB, Groningen, the Netherlands. E-mail: m.h.j.doff@kchir.umcg.nl