Oral-appliance therapy obstructive sleep apnea-hypopnea syndrome

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Publication date:
2007

Chapter 5

Predictors of treatment outcome

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Predictors of obstructive sleep apnea-hypopnea treatment outcome

This chapter is based on the following publication:
* Hoekema A, Doff MHJ, de Bont LGM, van der Hoeven JH, Wijkstra PJ, Pasma HR, Stegenga B. Predictors of obstructive sleep apnea-hypopnea treatment outcome (submitted for publication).

Summary

Background Oral-appliance therapy is an alternative to continuous positive airway pressure (CPAP) for treating the obstructive sleep apnea-hypopnea syndrome (OSAHS). Although oral-appliance therapy is generally less effective, many patients prefer it over CPAP therapy. The ability to preselect suitable candidates for either treatment is, however, limited. The aim of this study was to assess the value of relevant variables that can predict the outcome of oral-appliance and CPAP therapy.

Methods Fifty-one patients treated with oral-appliance therapy and 52 patients treated with CPAP were included. Relevant clinical, polysomnographic and cephalometric variables were determined at baseline. The predictive value of variables for the outcomes in both treatments was evaluated in univariate and multivariate analyses.

Results Univariate analyses demonstrated that the outcome of oral-appliance therapy was favorable especially in less obese patients with milder OSAHS, more extended maximum mandibular advancement and with certain craniofacial characteristics (mandibular retrognatism in particular). The multivariate analyses yielded two models providing a 80% correct classification of responders and non-responders to oral-appliance therapy. Variables included in the models were the apnea-hypopnea index, the maximum mandibular advancement, and the degree of mandibular and intermaxillary discrepancy. Neither univariate nor multivariate analyses yielded variables that reliably predicted the outcome of CPAP therapy.

Conclusions Variables with most predictive value for the outcome of oral-appliance therapy include the apnea-hypopnea index, maximum mandibular advancement and the degree of intermaxillary and mandibular deficiency. Contrary to oral-appliance therapy, the outcome of CPAP therapy could not be predicted reliably. The variables found in this study may be valuable for preselecting suitable candidates for oral-appliance therapy.

Introduction

The obstructive sleep apnea-hypopnea syndrome (OSAHS) is a common sleep-related breathing disorder characterized by disruptive snoring and repetitive upper airway collapse.[1] Continuous positive airway pressure (CPAP) is the preferred treatment for OSAHS.[2] As maintaining CPAP requires that patients wear an obtrusive device, patients may abandon therapy. Oral-appliance therapy is an alternative to CPAP that relieves upper-airway collapse during sleep by modifying the position of the mandible, tongue, and pharyngeal structures.[3] Although there is evidence that oral-appliance therapy is effective for OSAHS, it is generally less effective than CPAP.[4-6] Nevertheless, many patients prefer an oral-appliance to CPAP therapy.[4] Therefore, predictors of treatment outcome are of importance for selecting suitable candidates that may benefit from either treatment.

Numerous clinical and polysomnographic variables have been reported to correlate with increased effectiveness of oral-appliance therapy. For example, the outcome of treatment is generally more favorable in patients who are less obese[7,8] and have a lower apnea-hypopnea index (AHI).[9] Moreover, a variety of cephalometric variables have been implicated in the outcome of oral-appliance therapy.[10] Predictors of treatment outcome, however, are not uniformly reported.[11,12] The majority of these studies incorporate bias because patients with severe OSAHS or patients who have not been adherent to therapy have been excluded.[12] In addition, predictors have not been systematically validated to evaluate their accuracy in a separate population of patients.[5] Therefore, the ability to predict treatment outcome and preselect suitable candidates for a specific treatment modality is still limited.

The aim of this study was to assess the value of relevant clinical, polysomnographic and cephalometric variables to separately and jointly predict the outcome of oral-appliance and CPAP therapy.

Methods

Patient selection

Patients were recruited through the Department of Home Mechanical Ventilation of the University Medical Center Groningen (The Netherlands) for a randomized parallel trial comparing the effects of oral-appliance and CPAP therapy.[13] Patients over age 20 who underwent polysomnography and were diagnosed as having OSAHS were eligible.[14] Patients were selected based on medical, psychological, and dental criteria. Details of the trial are provided in Chapter 4.1 and Appendix 1.

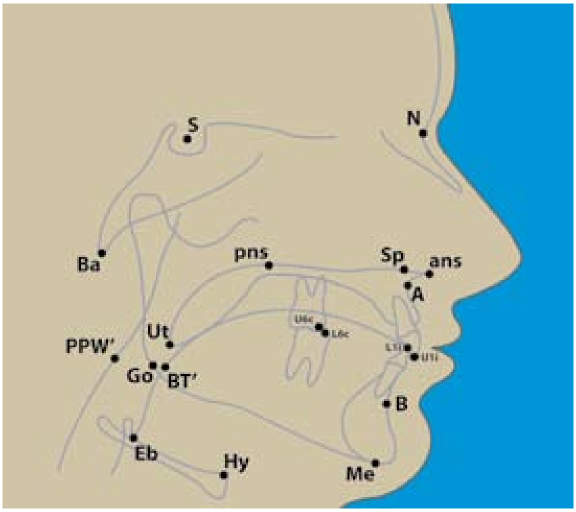

FIGURE 1. Reference points traced on lateral cephalograms.

The following 19 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 bony anterior nasal spine), B (point B: the deepest midline concavity on the mandibular symphysis), Ba (basion: the median point of the anterior margin of the foramen magnum), BT' (base of tongue intersection: intersection point of the line connecting B–Go with the base of tongue), Eb (epiglottis base: the point located at the intersection of the epiglottis and the base of tongue), Go (gonion: point on the bony contour of the gonial angle determined by bisecting the angle of the tangents to the body and ramus of the mandible, respectively), Hy (hyoid: the most anterior-superior point on the body of the hyoid bone), L1i (first lower incisor edge), L6c (first lower molar mesial cusp tip), Me (menthon: the most inferior point on the mandibular symphysis), N (nasion: the most anterior point on the frontonasal suture), pns (posterior nasal spine: the tip of the bony posterior nasal spine), PPW' (posterior pharyngeal wall intersection: intersection point of the line connecting B–Go with the posterior pharyngeal wall), S (sella: the midpoint of the pituitary fossa), Sp (spina prim: intersection point of the line connecting ans–pns and the line connecting Me–N), Ut (uvular tip: tip of the velum of the soft palate), U1i (first upper incisor edge), U6c (first upper molar mesial cusp tip).

Study design

Between September 2002 and May 2005, 103 eligible OSAHS patients were enrolled. Fifty-one patients had been randomly allocated to oral-appliance therapy and 52 to CPAP therapy. At baseline relevant clinical[7,8,12,15-17] and polysomnographic variables[8,9,10-12,15,18] were determined in all patients. A lateral cephalogram was also obtained in the oral-appliance group to determine relevant cephalometric variables.[7,10,19-25] All variables were considered relevant because they had been implicated in the outcome of oral-appliance therapy in one or more previous studies.

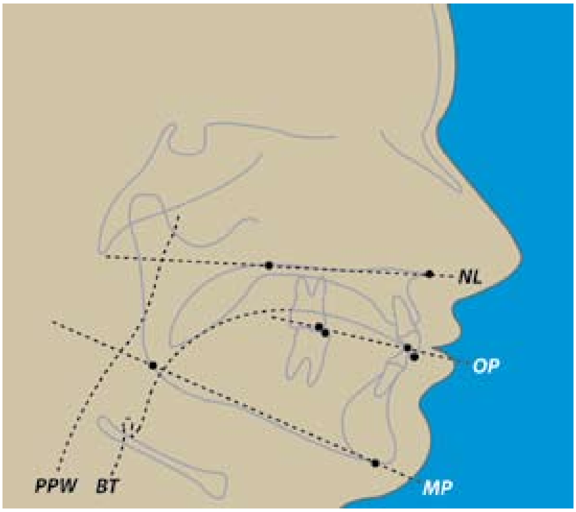

FIGURE 2. Reference lines traced on lateral cephalograms.

The following five reference lines were identified on lateral cephalograms: *BT* (base of tongue: the posterior outline of the tongue base extending from the base of the epiglottis to first maxillary molar), *MP* (mandibular plane: line connecting Me and Go), *NL* (nasal line: line connecting the ans and pns), *OP* (occlusal plane: line connecting the midpoint between U1i and L1i with the midpoint between U6c and L6c. The distance between the horizontal and vertical projections of U1i and L1i on the occlusal plane were used to calculate the overjet and overbite, respectively), *PPW* (posterior pharyngeal wall: the anterior outline of the posterior pharyngeal wall).

After patients had used an oral appliance or CPAP for approximately a two- to three-month period, the treatment effect was assessed with polysomnography. At the final follow-up review treatment was considered effective when the AHI either 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 who had no symptoms while using therapy.[4] Patients not meeting these criteria at their final review were considered "nonresponsive" to treatment. Patients who discontinued treatment for any reason were considered "nonadherent" to treatment.

Clinical predictors

The following clinical variables were determined at baseline: sex, age, body-mass index, neck circumference, and the Epworth sleepiness scale.[26] Furthermore in the oral-appliance group the maximum mandibular advancement was determined at baseline with a George-Gauge™ (H-Orthodontics, Michigan City, IN, USA).

Polysomnographic predictors

Polysomnography (Embla® A10 digital recorder, Medcare, Reykjavik, Iceland) for baseline and follow-up evaluations was conducted ambulatory in the patient's home situation. Each study started 11 AM and stopped 9 AM the next morning. Outcomes were limited to the time in bed part of the study. Standardized criteria were used to score apneas and hypopneas,[14] arousals,[27] sleep stages[28] and periodic limb movements.[29] All polysomnographic studies were evaluated and scored by one neurophysiologist (J.H. van der Hoeven) who was unaware of the patient's treatment assignment.

The following polysomnographic variables were determined at baseline: AHI, lowest oxyhemoglobin saturation during sleep (minSaO_2), the percentage of non-rapid-eye-movement sleep during sleep stages 3 & 4, and the ratio supine-AHI to lateral-AHI. Patients were also classified as having non-severe (AHI 5–30) or severe (AHI >30) OSAHS, and supine-dependent (defined by an AHI <10 in the lateral position) or nonsupine-dependent OSAHS.[12]

Cephalometric predictors

All lateral cephalograms were taken using a ProMax Cephalostat (Planmeca, Helsinki, Finland). In order to obtain an unrestrained reproducible position of the head, each cephalogram was taken in the "mirror position".[30] 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, each cephalogram was taken at end-expiration.

The lateral cephalograms were traced using Viewbox software® (version 3.1.1.6, Dhal Software, Kifissia, Greece). To minimize identification error all tracings were performed by one observer (M.H.J. Doff) and repeated after a two-week period. The mean values of the two tracings were used for further analysis. All linear cephalometric measurements were converted to values of life size. In each lateral cephalogram 19 reference points and five reference lines were identified (Figure 1 & 2). The cephalometric analysis yielded 20 variables.

Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (version 12.0, SPSS Inc, Chicago, IL, USA). Means and standard deviations, or medians and interquartile ranges in skewed distributions, are reported. Patients that were lost to follow-up review were excluded from analysis. First, in each treatment group variables were submitted for univariate analysis. Categorical variables (*i.e.*, sex, OSAHS-severity and supine-dependence of OSAHS) were only submitted for multivariate analysis. The univariate analysis consisted of calculation of receiver-operating characteristics curves of each variable with treatment effectiveness and an AHI <5 following treatment being the dependent variables, respectively. In order to obtain a summary measure for the predictive ability of each variable, the area under the curve (AUC) of each receiver-operating characteristics curve was calculated. In calculating the AUC, the predictive ability of a variable was considered excellent with an AUC of 0.9–1, good with an AUC of 0.8–0.9, fair with an AUC of 0.7–0.8, poor with an AUC of 0.6–0.7, and non-discriminative with an AUC of 0.5–0.6.[31] All variables with an AUC ≥0.7 were admitted for logistic regression analyses. By excluding variables stepwise backward, predictive models were constructed in both the oral-appliance and CPAP groups with treatment effectiveness and an AHI <5 following treatment being the dependent variables, respectively. A discriminant analysis was used to select the predictive model that classified the highest percentage of patients correctly. Subsequently, the selected model was cross-validated in another discriminant analysis by applying a "leave-one-out classification".

Results

Two patients in both the oral-appliance and CPAP group did not return for the follow-up review. The median period to final review was 68 (interquartile range 60–96) days in the oral-appliance group and 63 (interquartile range 60–88) days in the CPAP group ($p>0.05$). At final follow-up review, mean advancement of the mandible with the oral appliance was 81 ± 19% of maximum advancement. Mean CPAP pressure was 8.1 ± 1.9 cm H_2O at final review. Oral-appliance therapy was effective for 39 patients (79.6%); of the other ten patients, eight were "nonresponsive," and two were "nonadherent" to treatment. In the CPAP group, treatment was effective for 43 patients (86.0%); of the other seven patients, two were "nonresponsive," and five were "nonadherent" to treatment. Oral-appliance therapy yielded an AHI <5 in 29 of the 49 patients (59.2%). CPAP therapy yielded an AHI <5 in 40 of the 50 patients (80.0%).

Clinical and polysomnographic predictors

In predicting the effectiveness of oral-appliance therapy, a lower body-mass index had fair predictive ability (Table 1). In predicting an AHI <5 following oral-appliance therapy a lower body-mass index, more extended maximum mandibular advancement and a lower AHI had fair predictive ability. In predicting effectiveness of or an AHI <5 with CPAP therapy, all variables had a poor predictive ability or were non-discriminative.

Cephalometric predictors

In predicting effectiveness of oral-appliance therapy, a larger intermaxillary discrepancy (*i.e.*, larger ANB-angle) had good predictive ability, and a greater

TABLE 1. Univariate analysis of clinical and polysomnographic variables for predicting effectiveness of or an AHI <5 with oral-appliance and CPAP therapy.

Variable	Oral appliance			CPAP		
	Baseline* (n = 49)	AUC: effectiveness†	AUC: AHI <5	Baseline* (n = 50)	AUC: effectiveness†	AUC: AHI <5
Age (years)	49 ± 10	0.57‖	0.52¶	49 ± 10	0.61‖	0.64‖
Body-mass index (kg/m²)	32 ± 6	0.72¶	0.71¶	33 ± 6	0.59‖	0.56‖
Neck circumference (cm)	44 ± 4	0.58¶	0.65¶	45 ± 4	0.50¶	0.56¶
Epworth sleepiness scale	13 ± 6	0.53‖	0.59¶	15 ± 5	0.67‖	0.61‖
Maximum mandibular advancement (mm)	13 ± 2	0.65‖	0.75‖	-	-	-
AHI (no/hour)	38 ± 30	0.63¶	0.78¶	41 ± 28	0.59‖	0.59¶
$minSaO_2$ (%)	78 ± 9	0.69‖	0.69‖	78 ± 10	0.62¶	0.56‖
Non-REM sleep stage 3 & 4 (%)‡	14 ± 9	0.66‖	0.65‖	13 ± 12	0.59¶	0.51¶
Ratio supine-AHI / lateral-AHI§	2.0 (1.2–5.2)	0.61‖	0.64‖	2.1 (1.1–6.8)	0.63¶	0.54‖

* Plus-minus values are means ± standard deviations, values with additives in parentheses are medians with interquartile ranges.
† 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 who had no symptoms while using therapy.
‡ Sleep stages are expressed as a percentage of total sleep time.
§ This item could be determined in 39 patients in both the oral-appliance and CPAP group.
‖ Larger value of variable associated with a more positive response to treatment.
¶ Smaller value of variable associated with a more positive response to treatment.
Abbreviations: AHI = apnea-hypopnea index, AUC = area under the curve, CPAP = continuous positive airway pressure, $minSaO_2$ = lowest oxyhemoglobin saturation during sleep, REM = rapid-eye-movement.

TABLE 2. Univariate analysis of cephalometric variables for predicting effectiveness of or an AHI <5 with oral-appliance therapy.

Variable		Oral appliance	
	Baseline* (n = 48)	AUC: effective-ness†	AUC: AHI <5
Cranial base			
- S–N (mm)	72 ± 8	0.52‡	0.52‡
- Ba–S–N (mm)	179 ± 20	0.61‡	0.58‡
Sagittal jaw relationships			
- SNA (degrees)	79 ± 5	0.51§	0.56‡
- SNB (degrees)	77 ± 5	0.74§	0.57§
- ANB (degrees)	2.5 ± 2.7	0.80‡	0.64‡
- Overjet (mm)	4.0 ± 3.0	0.79‡	0.66‡
- Overbite (mm)	4.4 ± 3.0	0.79‡	0.64‡
Vertical craniofacial dimensions			
- N–Me; anterior face height (mm)	127 ± 15	0.62‡	0.54§
- S–Go; posterior face height (mm)	84 ± 11	0.52‡	0.53‡
- Me–Sp; lower anterior face height (mm)	73 ± 10	0.53‡	0.59§
- N–Sp; upper anterior face height (mm)	54 ± 7	0.72‡	0.59‡
- Posterior face height : anterior face height (ratio)	0.66 ± 0.06	0.55§	0.58‡
- Upper anterior face height : lower anterior face height (ratio)	0.74 ± 0.08	0.63‡	0.64‡
- *MP*–SN; mandibular plane angle (degrees)	35 ± 8	0.56‡	0.59§
Pharyngeal dimensions/hyoid bone position			
- pns–Ut; uvular length (mm)	43 ± 8	0.51‡	0.58§
- Ut–*PPW*; retropalatal airway space (mm)	8.2 ± 2.9	0.50‡	0.57‡
- PPW'–BT'; posterior airway space (mm)	10 ± 4	0.50§	0.58‡
- pns–Eb; vertical airway length (mm)	82 ± 10	0.56‡	0.55‡
-Hy–*MP* (mm)	26 ± 6	0.55‡	0.52‡
- Hy–Me (mm)	49 ± 8	0.60§	0.53§

* Plus-minus values are means ± standard deviations. Cephalometric radiographs were available for 48 of the 49 patients completing the follow-up review for oral-appliance therapy.
† 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 who had no symptoms while using therapy.
‡ Larger value of variable associated with a more positive response to treatment.
§ Smaller value of variable associated with a more positive response to treatment.
Abbreviations: AHI = apnea-hypopnea index, AUC = area under the curve.

mandibular deficiency (*i.e.*, smaller SNB-angle), a larger overjet and overbite, and a greater upper anterior face height had fair predictive ability (Table 2). In predicting an AHI <5 following oral-appliance therapy all cephalometric variables had poor predictive ability or were non-discriminative.

Multivariate Analysis

The logistic regression analysis for predicting effectiveness of oral-appliance therapy yielded a model providing a 84% correct classification of responders and non-responders. Variables included in the model were the AHI, SNB-angle and ANB-angle (Table 3). When cross-validating the selected model, 80% of the patients was classified correctly. The logistic regression analysis for predicting an AHI <5 with oral-appliance therapy yielded a model providing a 80% correct classification of responders and non-responders. Variables included in the model were the AHI and the maximum mandibular advancement (Table 3). When cross-validating the selected model, 80% of patients was classified correctly.

The logistic regression analysis for predicting effectiveness of CPAP therapy yielded a model providing a 65% correct classification of responders and non-responders. Variables included in the model were the body-mass index, AHI, OSAHS-severity and supine-dependence of OSAHS (Table 3). When cross-validating the selected model, 54% of patients was classified correctly. The logistic regression analysis for predicting an AHI <5 with CPAP therapy yielded a model providing a 65% correct classification of responders and non-responders. Variables included in the model were the body-mass index and AHI (Table 3). When cross-validating the selected model, 65% of patients was classified correctly.

Discussion

This study demonstrates that the AHI, maximum mandibular advancement and the degree of intermaxillary discrepancy and mandibular deficiency are variables with most predictive value for the outcome of oral-appliance therapy. Contrary to oral-appliance therapy, neither univariate nor multivariate analysis yielded clinical or polysomnographic variables that could reliably predict the outcome of CPAP therapy.

Univariate analysis demonstrated that a lower body-mass index, larger ANB-angle, smaller SNB-angle, and more pronounced overjet, overbite and upper anterior face height were the best predictors for effectiveness of oral-appliance therapy. In predicting an AHI <5 following oral-appliance therapy a lower body-mass index, more extended maximum mandibular advancement and a lower AHI were the best predictors. Our results concur with previous studies that demonstrated that these clinical,[7,8,16] polysomnnographic[8,11,15] and cephalometric[7,19,22] variables

TABLE 3. Logistic regression model for predicting effectiveness of or an AHI <5 with oral-appliance and CPAP therapy.

Variable	Logistic Regression Analysis*		
	Coefficient	Standard error	Odds ratio (95% CI)
Effectiveness of oral-appliance therapy†			
- AHI (no/hour)	-0.014	0.014	0.99 (0.96 to 1.01)
- SNB (degrees)	-0.162	0.120	0.85 (0.67 to 1.08)
- ANB (degrees)	0.507	0.220	1.66 (1.08 to 2.56)
- Constant	13.580	9.476	
- -2 Log Likelihood = 31,646			
AHI <5 with oral-appliance therapy			
- AHI (no/hour)	-0.038	0.015	0.96 (0.94 to 0.99)
- Maximum mandibular advancement (mm)	0.544	0.217	1.72 (1.13 to 2.64)
- Constant	-5.137	2.711	
- -2 Log Likelihood = 43,567			
Effectiveness of CPAP therapy†			
- Body-mass index (kg/m^2)	0.118	0.127	1.13 (0.88 to 1.44)
- AHI (no/hour)	0.059	0.050	1.06 (0.96 to 1.17)
- OSAHS-severity‡	-2.342	2.283	0.10 (0.00 to 8.44)
- Supine-dependence OSAHS§	-1.396	1.364	0.25 (0.02 to 3.59)
- Constant	-2.089	3.835	
- -2 Log Likelihood = 32,159			
AHI <5 with CPAP therapy			
- Body-mass index (kg/m^2)	0.100	0.095	1.11 (0.92 to 1.33)
- AHI (no/hour)	-0.027	0.016	0.97 (0.94 to 1.01)
- Constant	-0.763	2.777	
- -2 Log Likelihood = 41,068			

* Due to missing variables the multivariate analysis included 45 patients from the oral-appliance group and 43 patients from the CPAP group.
† 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 who had no symptoms while using therapy.
‡ (severe = 1, non-severe = 0)
§ (non-supine dependent = 1, supine-dependent = 0)
Abbreviations: AHI = apnea-hypopnea index, CI = confidence interval, CPAP = continuous positive airway pressure.

correlate with increased effectiveness of oral-appliance therapy. Except for upper anterior face height, the cephalometric predictors found in the present study primarily relate to mandibular retrognatism. Contrary to other studies, variables including supine dependence of OSAHS[12,18] or pharyngeal dimensions and hyoid bone position[7,10,15,19,20-22] could not be implicated in the outcome of oral-appliance therapy. These results indicate that patients, who are less obese, have milder OSAHS and have certain craniofacial characteristics (mandibular retrognatism in particular) respond more favorable to oral-appliance therapy.

Multivariate analysis yielded predictive models that, following the cross-validation, classified the outcome of oral-appliance therapy in 80% of patients correctly. Variables included in the predictive models were the maximum mandibular advancement, AHI, and the SNB- and ANB-angle. Recent studies suggest an important role for more sophisticated techniques to predict the outcome of oral-appliance therapy. It has for instance been shown that a remotely controlled mandibular positioner[32] or upper airway imaging techniques including sleep nasendoscopy[33] or magnetic resonance imaging[34] are highly predictive for the patient's response to oral-appliance therapy. Although these techniques may be of additional value in selecting suitable candidates, they are generally costly, laborious or sensitive to a specific operator. The present study aimed at constructing a predictive model convenient for the clinical situation. By using variables that are relevant and that can be easily determined, two predictive models were obtained that allow for a reliable prediction of the effectiveness or an AHI <5 with oral-appliance therapy.

Contrary to oral-appliance therapy, clinical and polysomnographic variables had poor predictive value for the outcome of CPAP therapy. Moreover, multivariate analysis yielded predictive models for an effective treatment and AHI <5 with CPAP therapy that, following the cross-validation, classified only 54% and 65% of patients correctly. These results indicate that patients in whom CPAP therapy does not have a favorable outcome cannot be easily preselected. Unfortunately in clinical practice these patients are usually deemed the best candidates for oral-appliance therapy.[5] The limited predictive ability of the predictive models is possibly best explained by the fact that CPAP therapy was effective and yielded an AHI <5 in the majority of patients.

It may be questioned to what extent the results found in this study can be extrapolated to other types of oral appliances. Although different aspects in the design of oral appliances may affect the patient's preference, clinical effects of different oral appliances that reposition the mandible are usually remarkably consistent.[4] Moreover, the present study only evaluated variables that had been implicated in the outcome of oral-appliance therapy in previous studies. We therefore believe that the results from this study can also be used when predicting the outcome of most other types of oral appliances that reposition the mandible. A second aspect that requires consideration is the fact that cephalograms were obtained in the upright position. The use of supine rather than upright cephalograms has been reported to account for the influence of posture on upper airway dimensions.[35] This may explain why pharyngeal dimensions and hyoid bone position could not be implicated in the outcome of oral-appliance therapy. However, the added value of supine cephalometry should also be considered in the light of its more laborious character.

In conclusion, the outcome of CPAP therapy could not be predicted reliably with the clinical and polysomnographic variables evaluated in this study. The outcome of oral-appliance therapy, however, appears favorable especially in patients who are less obese, have milder OSAHS and have certain craniofacial characteristics (mandibular retrognatism in particular). While only requiring information on the patient's maximum mandibular advancement, AHI, and intermaxillary and mandibular relationship (*i.e.*, ANB- and SNB-angle), the predictive models validated in the present study classified the outcome of oral appliance therapy correctly in 80% of cases. Predictive variables obtained from the univariate and multivariate analysis are therefore valuable for preselecting suitable candidates for oral-appliance therapy.

Acknowledgement The authors wish to thank Dr. G.J. Pruim (Department of Orthodontics of the University Medical Center Groningen) for his assistance in the cephalometric analysis.

REFERENCES

1. Malhotra A, White DP. Obstructive sleep apnoea. *Lancet* 2005;360:237-245.
2. Giles T, Lasserson T, Smith B, White J, Wright J, Cates C. Continuous positive airways pressure for obstructive sleep apnoea in adults. *Cochrane Database Syst Rev* 2006;1: CD001106.
3. Cistulli PA, Gotsopoulos H, Marklund M, Lowe AA. Treatment of snoring and obstructive sleep apnea with mandibular repositioning appliances. *Sleep Med Rev* 2004;8:443-457.
4. Hoekema A, Stegenga B, de Bont LGM. Efficacy and co-morbidity of oral appliances in the treatment of obstructive sleep apnea-hypopnea: a systematic review. *Crit Rev Oral Biol Med* 2004;15:137-155.
5. Lim J, Lasserson T, Fleetham J, Wright J. Oral appliances for obstructive sleep apnoea. *Cochrane Database Syst Rev* 2006;1:CD004435.
6. Barnes M, McEvoy RD, Banks S, Tarquinio N, Murray CG, Vowles N, et al. Efficacy of positive airway pressure and oral appliance in mild to moderate obstructive sleep apnea. *Am J Respir Crit Care Med* 2004;170:656-664.
7. Liu Y, Lowe AA, Fleetham JA, Park YC. Cephalometric and physiologic predictors of the efficacy of an adjustable oral appliance for treating obstructive sleep apnea. *Am J Orthod Dentofacial Orthop* 2001;120:639-647.
8. Pancer J, Al Faifi S, Al Faifi M, Hoffstein V. Evaluation of variable mandibular advancement appliance for treatment of snoring and sleep apnea. *Chest* 1999;116:1511-1518.
9. Rose E, Staats R, Schulte-Mönting J, Jonas IE. Treatment of obstructive sleep apnea with the Karwetzky oral appliance. *Eur J Oral Sci* 2002;110:99-105.
10. Horiuchi A, Suzuki M, Ookubo M, Ikeda K, Mitani H, Sugawara J. Measurement techniques predicting the effectiveness of an oral appliance for obstructive sleep apnea hypopnea syndrome. *Angle Orthod* 2005;75:1003-1011.
11. Henke KG, Frantz DE, Kuna ST. An oral elastic mandibular advancement device for obstructive sleep apnea. *Am J Respir Crit Care Med* 2000;161:420-425.
12. Marklund M, Stenlund H, Franklin KA. Mandibular advancement devices in 630 men and women with obstructive sleep apnea and snoring: tolerability and predictors of treatment success. *Chest* 2004;125:1270-1278.
13. Hoekema A, Stegenga B, Wijkstra PJ, van der Hoeven JH, Meinesz AF, de Bont LGM. Effectiveness of obstructive sleep apnea therapy: a randomized parallel trial of oral-appliance versus continuous positive airway pressure therapy. (submitted for publication).
14. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The report of an American Academy of Sleep Medicine task force. *Sleep* 1999;22:667-689.
15. Mehta A, Qian J, Petocz P, Darendeliler MA, Cistulli PA. A randomized, controlled study of a mandibular advancement splint for obstructive sleep apnea. *Am J Respir Crit Care Med* 2001;163:1457-1461.
16. Marklund M, Franklin KA, Sahlin C, Lundgren R. The effect of a mandibular advancement device on apneas and sleep in patients with obstructive sleep apnea. *Chest* 1998;113:707-713.
17. Walker-Engstrom ML, Ringqvist I, Vestling O, Wilhelmsson B, Tegelberg A. A prospective randomized study comparing two different degrees of mandibular advancement with a dental appliance in treatment of severe obstructive sleep apnea. *Sleep Breath* 2003;7:119-130.
18. Yoshida K. Influence of sleep posture on response to oral appliance therapy for sleep

apnea syndrome. *Sleep* 2001;24:538-544.
19. Yoshida K. Prosthetic therapy for sleep apnea syndrome. *J Prosthet Dent* 1994;72:296-302.
20. Rose E, Lehner M, Staats R, Jonas IE. Cephalometric analysis in patients with obstructive sleep apnea. Part II: Prognostic value in treatment with a mandibular advancement device. *J Orofac Orthop* 2002;63:315-324.
21. Skinner MA, Robertson CJ, Kingshott RN, Jones DR, Taylor DR. The efficacy of a mandibular advancement splint in relation to cephalometric variables. *Sleep Breath* 2002;6:115-124.
22. Mayer G, Meier-Ewert K. Cephalometric predictors for orthopaedic mandibular advancement in obstructive sleep apnoea. *Eur J Orthod* 1995;17:35-43.
23. Marklund M, Persson M, Franklin KA. Treatment success with a mandibular advancement device is related to supine-dependent sleep apnea. *Chest* 1998;114:1630-1635.
24. Bonham PE, Currier GF, Orr WC, Othman J, Nanda RS. The effect of a modified functional appliance on obstructive sleep apnea. *Am J Orthod Dentofacial Orthop* 1988;94:384-392.
25. Eveloff SE, Rosenberg CL, Carlisle CC, Millman RP. Efficacy of a Herbst mandibular advancement device in obstrructive sleep apnea. *Am J Respir Crit Care Med* 1994;149:905-909.
26. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 1991;14:540-545.
27. EEG arousals: scoring rules and examples: a preliminary report from the Sleep Disorders Atlas task force of the American Sleep Disorders Association. *Sleep* 1992;15:173-184.
28. Rechtschaffen A, Kales AA. Manual of standardized terminology, techniques and scoring system for the sleep stages of human subjects. U.S. Government Printing Office, Washington DC. *NIH Publication* 1968;204:1-1-0068.
29. Recording and scoring leg movements. The Atlas Task Force. *Sleep* 1993;16:748-759.
30. Solow B, Tallgren A. Natural head position in standing subjects. *Acta Odontol Scand* 1971;29:591-607.
31. Swets JA. Measuring the accuracy of diagnostic systems. *Science* 1988;240:1285-1293.
32. Tsai WH, Vazquez JC, Oshima T, Dort L, Roycroft B, Lowe AA, et al. Remotely controlled mandibular positioner predicts efficacy of oral appliances in sleep apnea. *Am J Respir Crit Care Med* 2004;170:366-370.
33. Battagel JM, Johal A, Kotecha BT. Sleep nasendoscopy as a predictor of treatment success in snorers using mandibular advancement splints. *J Laryngol Otol* 2005;119:106-112.
34. Sanner BM, Heise M, Knoben B, Machnick M, Laufer U, Kikuth R, et al. MRI of the pharynx and treatment efficacy of a mandibular advancement device in obstructive sleep apnoea syndrome. *Eur Respir J* 2002;20:143-150.
35. Johal A, Battagel JM. An investigation into the changes in airway dimension and the efficacy of mandibular advancement appliances in subjects with obstructive sleep apnoea. *Br J Orthod* 1999;26:205-210.