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Role of craniofacial phenotypes in the response to oral appliance therapy for obstructive sleep apnea

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Abstract

Background: Mandibular advancement device (MAD) is a good alternative for patients with obstructive sleep apnea (OSA). However, the treatment response varies amongst individuals.

Objective: This study aimed to explore the role of craniofacial features in the response to MADs to improve prognostication and patient selection.

Methods: The retrospective trial contained 42 males aged 41.5 ± 9.0 years, and with an apnea-hypopnea index (AHI) of 21.5 ± 13.8 events/h. According to the mandibular plane angle, participants were divided into three groups: low angle (n = 13), average angle (n = 14) and high angle (n = 15). Under the monitoring of home sleep testing, adjustable MADs were used to titrate the mandible forward from 0 mm with an increment of 0.5 mm every day. The polysomnography outcomes, mandibular protrusion amounts, changes in upper airway MRI measurements and nasal resistance were compared amongst the three groups.

Results: The normalisation rate (AHI < 5 /h) was 92.3%, 57.1% and 46.7%, respectively, in the low-, average- and high-angle groups (p = .027). The effective protrusion where AHI was reduced by half was 20 (11.3 ~ 37.5) %, 31.3 (23.6 ~ 50) % and 50 (36.9 ~ 64.9) % of the maximal mandibular protrusion, in the low-, average- and high-angle groups (p = .004). Multivariate logistic regression revealed that increased gonion angle (OR = 0.878) and baseline AHI(OR = 0.868) can reduce the probability of normalisation.

Conclusion: The high mandibular plane angle might be an unfavourable factor to MAD treatment and more protrusion was needed to achieve a 50% reduction in AHI. Vertical craniofacial pattern (gonion angle) and baseline AHI constituted the model for predicting the effect of MADs.

KEYWORDS
Cephalometry, magnetic resonance imaging, mandibular advancement, orthodontic appliances, removable, sleep apnea, obstructive, treatment outcome

The work was conducted in the Department of Orthodontics, Peking University School and Hospital of Stomatology

Trial Registration Information: Chinese Clinical Trial Registry, registration number: ChiCTR-IND-17013232.

1 | BACKGROUND

Obstructive sleep apnea (OSA) is a heterogeneous disease, with complex symptoms and different treatment responses amongst different individuals.[1] Some scholars proposed to differentiate the phenotypes of OSA in combination with clinical practice, to carry out precision medicine, targeted to improve the curative effect, quality of life and patient compliance.[2–4] The craniofacial pattern has been proposed to phenotype OSA recently. The craniofacial factors such as hyperdivergent vertical patterns were proved to be the main contributing factors to AHI, equally important as obesity.[5] These findings can provide a basis for precise therapeutic decision-making including craniofacial skeletal intervention such as orthognathic surgery and oral appliance therapy.[6]

Mandibular advancement appliance (MAD) is the most widely used oral appliance as a good alternative option for patients with OSA, which can temporarily protrude the mandible forward and enlarge the upper airway.[7] Recent reviews suggested that an integrated basis to identify morphologic and biomechanical elements of phenotypic expressions of sleep-disordered breathing in the design and application of oral appliances is needed.[8] It is still unknown how the craniofacial pattern would influence the effect of mandibular advancement appliance.

A previous study showed that MAD was more successful amongst men with a more pervious airway, a larger interdental width, and milder OSA, however, no predictive factors of MAD success could be found.[9] A large sample study suggested that demographic, anthropometric and polysomnographic data only weakly inform about MAD efficacy.[10] Successful treatment with MAD can also be achieved in overweight patients and those with more severe diseases.[11]

Craniofacial morphology is regarded as an important anatomical feature, which not only affects the severity of OSA but also affects the curative effect, especially for the oral appliance. Craniometric parameters have been proposed to be predictors of the success or failure of appliance treatment.[12–16] Cephalometry studies showed that significant differences were found between responders and non-responders in the following variables: the minimal retroglossal airway, soft palate length, length of the anterior cranial base, mandibular position relative to the cranial base, anterior facial height, mandibular plane angle, upper-to-lower facial height ratio.[15,17–19] Most of the above craniometric parameters reflected the vertical facial pattern, which is usually classified into the low-angle (short facial types), average-angle (normal facial types) and high-angle (long facial types) groups in the practice of orthodontics. Meta-analysis showed that OSA patients tend to have clockwise rotated mandible and high mandibular plane angle,[20–23] which is an important risk factor in the development of OSA and may in return affect the upper airway dilation when the mandible moves forward. A recent study shows that craniofacial phenotypes influence the mandibular range of movement in the design of a mandibular advancement device.[24]

In our latest study, we systematically investigated the change of MAD treatment efficacy along with gradually increased mandibular protrusion[25] and noticed that the inter-individual response curve varies greatly. We hypothesize that the craniofacial features, especially the vertical facial pattern may play a role in the different reactions to mandibular protrusion. Therefore, this retrospective cohort study was designed based on the different congenital craniofacial phenotypes of patients with OSA and aimed to explore the role of craniofacial features in the response to MADs to improve prognostication and patient selection.

2 | MATERIALS AND METHODS

2.1 | Ethics statement

This study was consistent with the Declaration of Helsinki and approved by the Medical Ethics Committee of PKUSS (PKUSSIRB – 201418117). Informed consent was obtained from all participants. This article was in compliance with STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for observational studies.

2.2 | Study design

This retrospective study was conducted based on a cohort in the previous study about mandibular advancement degree titration.[25] The criteria of patient selection were the same: adult males (to avoid age and gender influence), diagnosed as OSA by qualified laboratory polysomnography, apnea-hypopnea index (AHI) > 5 events/h. Exclusion criteria were: insufficient number of teeth to anchor the appliance, history of uvulopalatopharyngoplasty or orthognathic surgery (to avoid unnatural morphological changes), severe nasal septal deviation, or acute temporomandibular joint pain whilst mouth opening. Patients were classified into three groups according to the vertical facial pattern. The sample size in each group was estimated as 13–15 with a power of 0.75–0.80 and a significance level of 0.05. The sample size of the cohort study met the requirements. Forty-four patients were included and baseline polysomnographic variables were obtained in all patients.

2.3 | Cephalometrics

Standard lateral cephalograms were taken before treatment by the same radiologist for all patients with the Frankfort plane parallel to the horizontal plane. Patients were asked to bite with their molars and restrained from swallowing. The digitised cephalograms were imported into the Dolphin software (Dolphin Imaging & Management Solutions) and analysed. The measurements were repeated by another researcher for validation to avoid potential bias. All cephalometric landmarks and measurements used in this study are illustrated in Figure 1. According to the normal value of mandibular plane angle (angle between anterior cranial base plane and

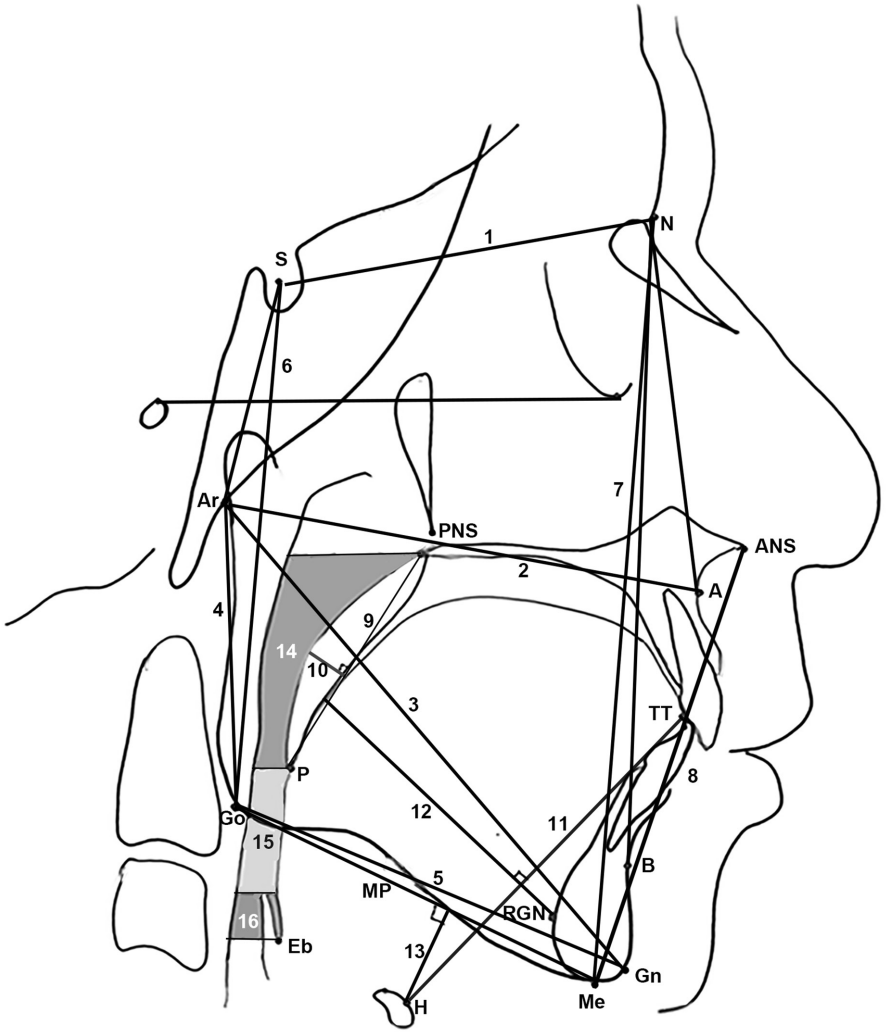

FIGURE 1 The cephalometric landmarks and measurements. Landmarks: *S*, sella; *N*, nasion; *ANS*, anterior nasal spine; *PNS*, posterior nasal spine; *A*, subspinale; *B*, supramentale; *Gn*, gnathion; *Me*, menton; *P*, soft palate tip; *TT*, tongue tip; *RGN*, retrognathion; *H*, hyoid bone; *Go*, gonion; *Ar*, articulare; *Eb*, the base of the epiglottis; *MP*, mandibular plane (Go-Me). Angle measurements: *SNA*, sagittal position of maxilla, angle of S, N, and A; *SNB*, sagittal position of mandible, angle of S, N, and B; *ANB*, anteroposterior maxilla/mandible discrepancy, angle of A, N, and B; *Sella angle*, angle of N, S, Ar; *Articulare angle*, angle of S, Ar, Go; *Gonion angle*, angle of Ar, Go, Me; *Mandibular plane angle*, angle between SN and MP. Linear measurements and segments: 1, *S-N*, length of anterior cranial base; 2, *MxL*, maxilla length, distance between Ar and A; 3, *MdL*, mandible length, distance between Ar and Gn; 4, *RH*, ramus height, distance between Ar and Go; 5, *MBL*, mandibular body length, distance between Go and Gn; 6, *PFH*, posterior facial height, distance between S and Go; 7, *AFH*, anterior facial height, distance between N and Me; 8, *ALFH*, anterior lower facial height, distance between ANS and Me; 9, *SPL*, soft palate length, distance between P and PNS; 10, *SPH*, soft palate height, the longest linear distance perpendicular to SPL; 11, *TL*, tongue length, distance between TT and H; 12, *TH*, tongue height, distance from RGN to the tongue surface perpendicular to TL; 13, *H-MP*, distance between H and MP; 14, *Velopharynx*, hard palate to the tip of uvula; 15, *Oropharynx*, the tip of the uvula to the tip of the epiglottis; 16, *Hypopharynx*, the tip of the epiglottis to the base of the epiglottis.

mandibular plane, SN/MP, 32.5 ± 5.2°) in the Chinese population,[26] patients were divided into three groups: low-angle group (SN/MP angle <27.3°), average-angle group (SN/MP angle 27.3–37.7°) and high-angle group (SN/MP angle >37.7°).

2.4 | Appliance titration and home sleep testing

The protocol of mandibular advancement appliance titration and home sleep testing was described in detail in our previous study.[25] The mandibular protrusion amounts were titrated from 0 mm (no protrusion) with a daily increment of 0.5 mm until AHI was reduced to the lowest. Home sleep testing was simultaneously conducted with a type III monitor (ApneaLink Air, ResMed). The symptoms in the masticatory muscles or TMJ were recorded by the patients on the chart during the titration process. They were instructed to stop the titration when they felt unbearable pain or severe discomfort.

The changing curves of AHI along with mandibular protrusion in the three groups were drawn. The following definitions were in line with the previous study[25]: The preliminary effective protrusion was

the point where AHI was reduced by half and the target protrusion was the point where AHI was reduced to the lowest. Normalisation was defined as the post-treatment AHI of less than 5 events/h, and effective treatment was defined as at least a 50% reduction in AHI. The AHI improvement rate was defined as the change ratio of post-treatment AHI compared with the baseline AHI.

2.5 | Change of morphology and respiratory function

Magnetic resonance imaging (MRI) of the upper airway and nasal respiratory function tests were both conducted with and without MAD.

The method of MRI scan was described in detail in the previously published article.[25] MRI images were analysed with Dolphin software (Dolphin Imaging & Management Solutions). The mean and minimum cross-sectional area, height, and volume of the nasopharynx, velopharynx, oropharynx, hypopharynx and total upper airway were obtained (see Figure 2).

Nasal respiratory capacity and resistance were both tested with and without MAD. Inspiratory capacity and expiratory capacity were measured with calm nasal breathing in 20 seconds using an NV1 rhinospirometer (GM Instruments Ltd). Inspiratory resistance and expiratory resistance were measured with the Broms method using a NR6 rhinomanometer (GM Instruments Ltd).

2.6 | Statistical analysis

Statistical analysis was conducted with the software package SPSS (version 24.0 for Mac, IBM). To identify the differences amongst the low-angle, average-angle and high-angle groups, homogeneity of variance was tested and one-way analysis of variance (ANOVA) was used for normally distributed variables and Kruskal-Wallis *H*-test was used for non-normally distributed variables. Fisher's exact test was used for categorical variables. The Bonferroni-Holm correction was used for multiple comparisons. *p* values were considered statistically significant when less than .05. The data of those who dropped out were excluded in the initial analysis, but sensitivity analysis would be conducted. Multivariate logistic regression analysis (using forward likelihood ratio selection) was conducted to identify potential confounding factors for the treatment outcome.

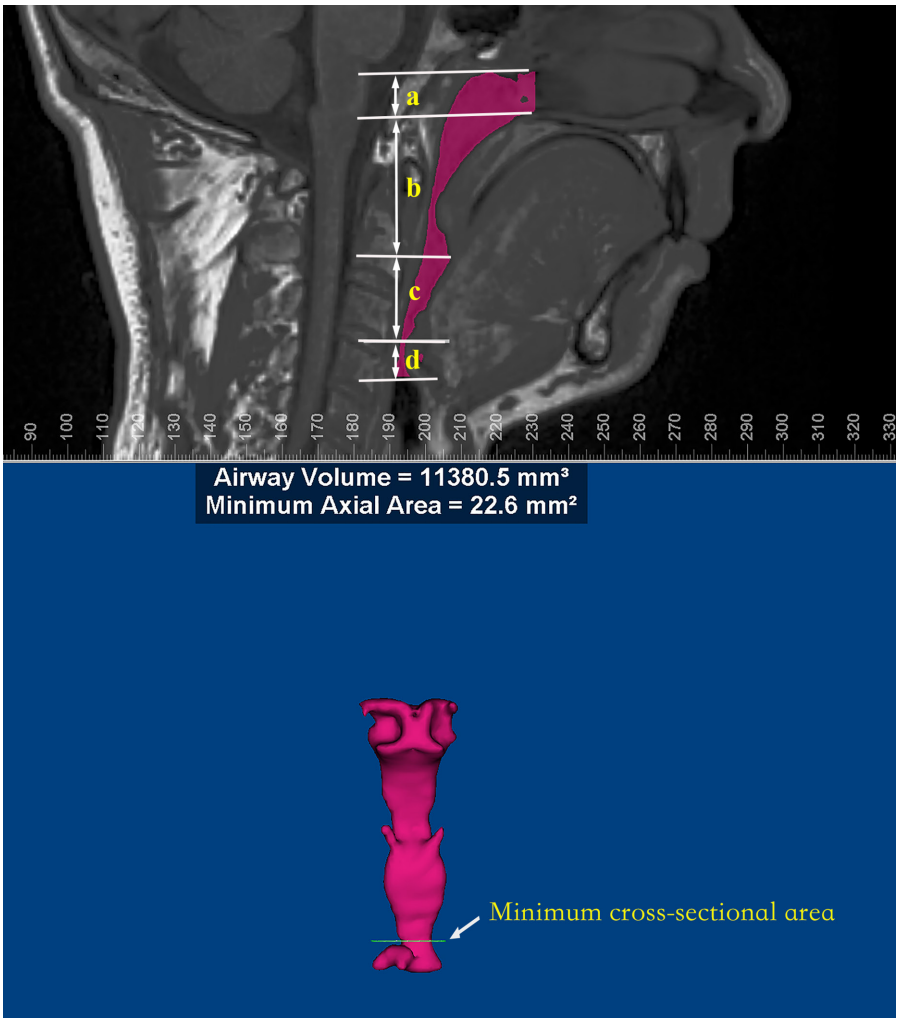

FIGURE 2 The segments of the upper airway and minimum cross-sectional area. A, nasopharynx, top of the nasopharynx to the hard palate; B, velopharynx, hard palate to the tip of uvula; C, oropharynx, tip of the uvula to tip of the epiglottis; D, hypopharynx, tip of the epiglottis to vocal cords.

3 | RESULTS

The cohort consisted of 44 patients initially and two dropped out. Finally, 13 in the low-angle group, 14 in the average-angle group and 15 in the high-angle group completed the follow-up. The average follow-up time was 21 ± 5 days. The baseline demographic characteristic and polysomnographic variables are shown in Table 1. There was no significant difference in age, BMI, and polysomnographic parameters amongst the three groups. A correlation analysis was conducted between the mandibular plane angle and the baseline AHI and the Pearson correlation coefficient was 0.110 ($p = .488$).

3.1 | Craniofacial features

Different vertical facial patterns are usually accompanied by some other craniofacial characteristics. Table 2 showed that the high-angle group had more retruded maxilla and mandible, open gonion angle, shorter posterior facial height, longer anterior lower facial height and more inferiorly positioned hyoid bone.

3.2 | Treatment outcome and mandibular protrusion

The comparison of treatment outcome and mandibular protrusion amongst low-, average- and high-angle groups was shown in Table 3. The residual AHI and ODI in the high-angle group were relatively higher but not statistically significant yet. Although there was no difference in the effective rate, the normalisation rate decreased significantly as the mandibular plane angle increased. The high-angle group needed more mandibular protrusion to achieve a 50% reduction of AHI, both in millimetre and a percentage value ($p = .012$ and .004). The change curves of the AHI improvement rate along with mandibular protrusion percentage in three groups were shown in Figure 3. The protrusion degrees where AHI reduced by 50% increased as the mandibular plane angle increased. Within small protrusion amounts, the AHI improvement rate in the low-angle group was higher. And at larger protrusion amounts, the AHI improvement rate in the high-angle group was relatively lower compared with the other two groups.

3.3 | Change of morphology and respiratory function

The differences in the change of upper airway dimensions and nasal respiratory function were tested amongst three groups (see Table 4). The difference in response to MAD lies in that the percentage change of the velopharynx was almost the same but the enlargement of the oropharynx in the high-angle group was more significant. Therefore, the differences between the cross-sectional area of the velopharynx and oropharynx decreased when the mandible protruded forward in the low- and average-angle groups but not in the high-angle group. No significant difference was found in the nasal respiratory function variables.

3.4 | Sensitivity analysis

A sensitivity analysis was conducted to consider the two patients lost to follow-up failed treatment. The normalisation rate became 92.3%, 53.3% and 43.8%, respectively, in the three groups. The differences between the three groups were still significant.

3.5 | Logistic regression analysis

The final treatment results may be influenced by many other factors. Therefore, multivariate logistic regression analysis was performed including age, BMI, cephalometric and MRI measurements, and nasal respiratory variables to identify potential confounders. The results are shown in Table 5. We found that the probability of normalisation decreased as the gonion angle and baseline AHI increased. An equation to predict the probability of normalisation was derived:

Probability of normalisation = exp (19.164–0.13 Gonion angle-0.142 Baseline AHI)/[1+ exp (19.164–0.13 Gonion angle-0.142 Baseline AHI)].

The sensitivity of the prediction model was 92.6% and the specificity was 80%. The area under the receiver operator characteristic curve of the regression model was 0.923, reflecting good model discrimination.

4 | DISCUSSION

Obstructive sleep apnea is a complex and heterogeneous disorder and improved phenotyping approaches are an important step towards the goal of personalised medicine for OSA patients.[1] Recent work focused on pathophysiologic risk factors for OSA (e.g. arousal threshold, craniofacial morphology, chemoreflex sensitivity) appears to capture heterogeneity in OSA.[1] The craniofacial deformity is an important etiological factor of OSA, especially in normal-weight patients.[27] And it is closely associated with oral appliance therapy. Based on the data of our previous mandibular advancement titration study, we hypothesized that the craniofacial features may affect the treatment response to MADs.

The logistic regression model in our study showed that increased baseline AHI and gonion angle can reduce the probability of normalisation. The negative effects of baseline severity of OSA have already been reported in many studies,[10,28,29] whilst the gonion angle emerged as another important factor influencing the treatment results. Skeletal class II and hyperdivergent patterns contribute to AHI and the effects of vertical facial patterns seem more important. The gonion angle indicates the vertical facial pattern, and the large gonion angle reflects the tendency of mandible clockwise rotation

TABLE 1 The baseline demographic characteristic and polysomnographic variables in low-, average- and high-angle groups.

	Low angle ($n = 13$)	Average angle ($n = 14$)	High angle ($n = 15$)	F/H value	*p* Value
Age (years)[a]	40.2 ± 9.7	40.9 ± 9.7	42.8 ± 7.8	0.306	.738
BMI (kg/m^2)	24.7 ± 1.9	24.7 ± 2.9	25.1 ± 2.8	0.161	.852
AHI(/h)	21.3(13.9 ~ 30.1)	17.8(12.5 ~ 31.7)	27.3(16.2 ~ 34.3)	1.557	.459
AI (/h)	11 (7.6 ~ 16.8)	13.3 (4.3 ~ 21.2)	21 (7.9 ~ 26.5)	2.984	0.225
HI (/h)	7.9 (4.9 ~ 12.9)	8 (2.3 ~ 16.7)	5.2 (3.9 ~ 7.6)	1.945	.378
Longest time of apnea(s)	51.2 (43.8 ~ 66.5)	50 (35.3 ~ 60.2)	68 (51.1 ~ 77)	4.171	.124
Longest time of hypopnea(s)	62.1 ± 17.6	50.6 ± 17.7	65.2 ± 17.5	5.081	.079
Supine AHI (/h)	31.3 (8.4 ~ 40.8)	28.3 (20.1 ~ 38)	34.8 (20.2 ~ 54)	1.394	.498
Non-supine AHI (/h)	13.2 (5.8 ~ 25.2)	12.7 (2.1 ~ 27.1)	17.7 (12.2 ~ 25.4)	1.152	.562
ODI (/h)	12.6 (8.2 ~ 17.5)	13.2 (4.8 ~ 28.7)	17.4 (10.3 ~ 26.3)	0.736	.692
Average SpO_2(%)	94.7 (93 ~ 96.1)	95 (92.6 ~ 97.2)	95.6 (94.5 ~ 96)	0.608	.738
Minimum SpO_2(%)	82.9 (77.8 ~ 84.9)	82.1 (78 ~ 86.4)	83 (82 ~ 86.1)	0.170	.919
Time spent $SpO_2 < 90\%$ (%)	1.62 (0.39 ~ 4.1)	0.81 (0.1 ~ 9.1)	1.07 (0.5 ~ 2.3)	0.073	.919

Abbreviations: AHI, apnea-hypopnea index; AI, apnea index; BMI, body mass index; HI, hypopnea index; ODI, oxygen desaturation index; SpO2, the pulse oxygen saturation.

[a]normally distributed data were expressed as mean ± standard deviation and skewed distributed data were expressed as median and interquartile range.

and high angle. There was some controversy about the influence of vertical facial patterns on the treatment response to MADs in previous studies. Mehta et al. found that collectively a larger mandibular plane angle, larger retropalatal airway space, smaller neck circumference, and lower baseline AHI favoured a lower final AHI with MAD.[30] Ng et al.[15] also found that a larger mandibular plane angle was associated with a lower final AHI. However, other authors found that a normal mandibular plane angle and a small anterior lower facial height were more likely to result in a good treatment response.[31] Our findings support the latter conclusion. There tended to be more clockwise rotation when the mandible protruded forward in high-angle patients, therefore having an adverse impact on treatment outcomes. According to our observation, when the mandible protruded from 70 to 80%, the vertical open distance tended to increase more in the high-angle patients and might bring some unfavourable effects.

The vertical facial pattern was also proved to be an important factor influencing the dose-dependent relationship between AHI reduction and mandibular protrusion. Individualised mandibular reposition is important to ensure good treatment outcomes and less side effects.[32] However, as for now, there was no consensus regarding the determination of effective protrusion position (50% reduction in AHI).[33,34] Some authors reported that only 1.7 ± 1.5 mm was needed to achieve a 50% reduction of AHI in 72% of the patients.[34] whilst others prefer more protrusion such as 50% or 75% of the maximal mandibular protrusion.[35–37] In our latest study, the mean lateral dimension of the oropharynx and the change of maximum lateral dimension were proved to be the main determinants of the effective protrusion.[25] Whilst in this study, MRI showed that the baseline dimension of the oropharynx was narrower and the cross-sectional area of the oropharynx enlarged more when the mandible protruded forward in the high-angle group. Therefore, more protrusion was needed to achieve a 50% reduction of AHI in the high-angle patients. The results in the two studies were consistent and the mandibular plane angle was easier to access on cephalograms. Therefore, the vertical facial pattern can be considered as a surrogate variable to predict effective protrusion. Cephalometry can be a convenient method to help clinicians to personalise the mandibular reposition for each patient and predict treatment outcomes.

There were some limitations to the study. First, the sample size was relatively small because the mandibular titration and home sleep testing were complex and time-consuming. Second, MRI was not dynamic or scanned during sleep, therefore it could not reflect the real sleep situation. Third, the population of this study was restricted to Asian males, with relatively lower BMI compared with Caucasians. And fourthly, the adverse effects in the masticatory muscles or TMJ were not objectively evaluated in the study.

In conclusion, our findings demonstrate that a high mandibular plane angle could be an unfavourable factor to MAD treatment

TABLE 2 The significant different cephalometric variables in low-, average- and high-angle groups.

	Low angle ($n = 13$)	Average angle ($n = 14$)	High angle ($n = 15$)	F/H value	p Value
SNA angle (°)	85 ± 3.7	82.1 ± 3.0	80.2 ± 3.5[c]	6.840	.003
SNB angle (°)	81 ± 2.6	78.0 ± 3.9[b]	74.3 ± 3.2[c]	15.054	.000
ANB angle (°)	4.1 ± 2.5	4 ± 2.1	6 ± 2.8	2.774	.075
Maxilla Length (cm)	8.5 ± 0.4	8.2 ± 0.3	8.1 ± 0.4[c]	4.117	.024
Mandibular plane angle (SN/MP) (°)	26.9 ± 3.7[a]	32.7 ± 2.5[b]	42.7 ± 4.5[c]	66.554	.000
Gonion Angle (°)	111.2 ± 4.3	116.1 ± 6.4	124.4 ± 6.2[c]	19.007	.000
Mandibular Body Length (cm)	7.6 ± 0.4	7.3 ± 0.5	7 ± 0.4[c]	5.628	.007
Posterior facial height (PFH) (cm)	9 ± 0.5	8.8 ± 0.6	8.3 ± 0.5[c]	5.991	.005
Anterior facial height (AFH) (cm)	12.2 ± 0.8	12.5 ± 0.7	12.9 ± 0.6[c]	6.747	.003
Anterior lower facial height (ALFH) (cm)	6.7 ± 0.6	7.0 ± 0.3	7.3 ± 0.4[c]	6.962	.003
ALFH/AFH	0.54 ± 0.02	0.56 ± 0.02	0.56 ± 0.01	3.433	.042
PFH/AFH	0.73 ± 0.03[a]	0.7 ± 0.03[b]	0.64 ± 0.02[c]	40.722	.000
H-MP (cm)	1.7 ± 0.5	1.8 ± 0.5	2.2 ± 0.4[c]	4.873	.013

Note: Data are presented as mean ± standard deviation; See Figure 1 for the definitions of the cephalometric variables.

[a]$p < .05$ after Bonferroni correction between low-angle group and average-angle group.

[b]$p < .05$ after Bonferroni correction between average-angle group and high-angle group.

[c]$p < .05$ after Bonferroni correction between low-angle group and high-angle group.

TABLE 3 Comparison of the treatment outcome and mandibular protrusion amongst low-, average- and high-angle groups.

	Low angle ($n = 13$)	Average angle ($n = 14$)	High angle ($n = 15$)	F/H/χ^2 value	p Value
Treatment outcome					
Post-treatment AHI (/h)[a]	3.3(2.3 ~ 4.4)	4.4(2.6 ~ 6.6)	5.7(2.5 ~ 10.5)	3.060	.216
Post-treatment ODI (/h)	3.1(1.9 ~ 4.0)	4.4(2.4 ~ 7.9)	5.9(2.5 ~ 9.7)	4.391	.111
Post-treatment SpO_2 (%)	88(83.5 ~ 90)	87.0(83.5 ~ 89.5)	86(78 ~ 89)	2.275	.321
AHI improvement rate	0.78(0.65 ~ 0.86)	0.73(0.63 ~ 0.86)	0.73(0.58 ~ 0.79)	2.241	.326
ODI improvement rate	0.67(0.32 ~ 0.82)	0.64(0.57 ~ 0.85)	0.67(0.4 ~ 0.75)	0.998	.607
Effective rate (%)	100.0	92.9	93.3	1.158	1.000
Normalisation rate (%)	92.3	57.1	46.7[c]	7.039	.027[b]
Mandibular protrusion					
Maximal mandibular protrusion (mm)	9.2 ± 1.3	8.8 ± 1.1	8.8 ± 1.8	0.300	.742
Effective protrusion where AHI reduced by 50% (mm)	2(1 ~ 3.8)	2.5(2 ~ 4)	4.3(3 ~ 5.6)[c]	8.795	.012[b]
Effective protrusion where AHI reduced by 50% (%)	20(11.3 ~ 37.5)	31.3(23.6 ~ 50)	50(36.9 ~ 64.9)[c]	6.535	.004[b]
Target protrusion (mm)	4.3 ± 2.6	5.1 ± 2.4	5.2 ± 2	0.680	.513
Target protrusion (%)	44.9 ± 24.8	57.7 ± 23.8	59.6 ± 19.5	1.694	.197

Abbreviations: AHI, apnea-hypopnea index; ODI, oxygen desaturation index; SpO_2, the pulse oxygen saturation.

[a]Normally distributed data were expressed as mean ± standard deviation (SD) and skewed distributed data were expressed as median and interquartile range.

[b]$p < .05$ amongst three groups.

[c]$p < .05$ after Bonferroni correction between low-angle group and high-angle group.

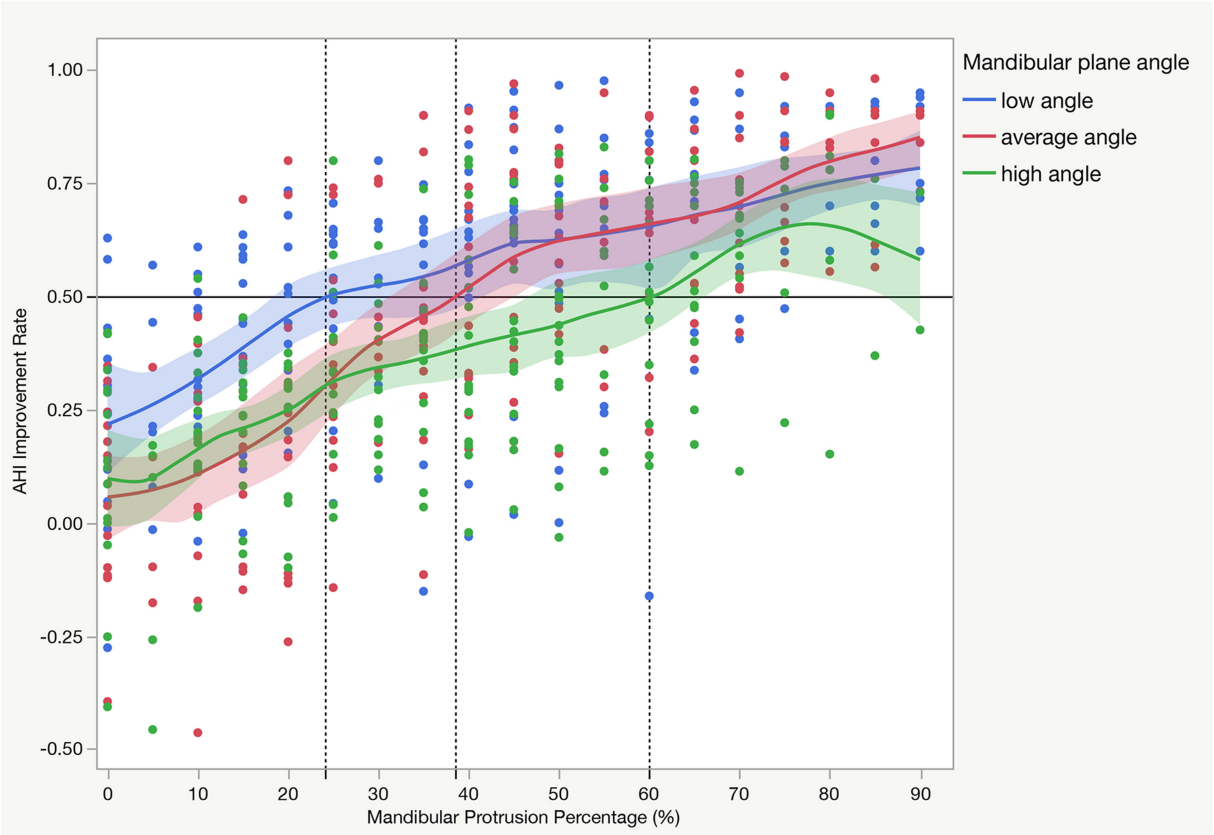

FIGURE 3 The change curves of apnea-hypopnea index (AHI) improvement rate along with mandibular protrusion (presented as the percentage of the maximal mandibular protrusion) in low- (blue), average- (red) and high- (green) angle groups. The line represents smoothing spline fitting and the shade represents the confidence interval. The vertical open distance tended to increase more in the high-angle patients and might bring some unfavourable effects when the mandible protruded from 70 to 80%.

TABLE 4 Comparison of the change of the upper airway dimensions and nasal respiratory function variables in low-, average- and high-angle groups.

	Low angle ($n = 13$)	Average angle ($n = 14$)	High angle ($n = 15$)	F/H value	p Value
MRI measurements					
Velopharynx mean CSA (mm^2)	120.2 ± 46.5	113.7 ± 43.8	136 ± 41.2	0.969	.389
Velopharynx height / Total upper airway height (%)	40.96 ± 3.71	41.58 ± 4.72	38.05 ± 3.86	2.962	.064
Oropharynx mean CSA (mm^2)	172.8 ± 50.7	179 ± 46.2	157.1 ± 39.7	0.875	.425
Oropharynx height (cm)	1.7 ± 0.6	2 ± 0.7	2.3 ± 0.6	2.967	.064
Oropharynx height / Total upper airway height (%)	20.37 ± 6.31	22.84 ± 6.71	25.69 ± 4.84	2.702	.08
Percentage change of velopharynx mean CSA (%)	28.42 ± 24.48	28.09 ± 38.13	31.05 ± 32.22	0.095	.954
Percentage change of velopharynx volume (%)	26.87 ± 25.17	31.46 ± 33.71	29.97 ± 32.97	0.044	.978
Percentage change of oropharynx mean CSA (%)	1.74 ± 25.42	−8.25 ± 21.39	24.98 ± 32.65	8.2	.017*
Percentage change of oropharynx volume (%)	−2.75 ± 22.39	−12.81 ± 35.11	14.25 ± 35.45	6.512	.039*
Nasal respiratory function measurements					
Percentage change of inspiratory capacity (%)	46.68 ± 72.75	−4.23 ± 44.79	60 ± 74.24	4.055	.132
Percentage change of expiratory capacity (%)	47.37 ± 138.95	13.65 ± 59.43	39.3 ± 103.54	0.099	.952
Percentage change of inspiratory resistance (%)	−2.5 ± 8.74	−1.71 ± 3.82	−3.59 ± 6.04	0.264	.876
Percentage change of expiratory resistance (%)	−1.96 ± 7.83	−0.32 ± 5.57	−3.18 ± 6.25	1.394	.498

Abbreviation: MRI, magnetic resonance imaging; CSA, cross-sectional area.

*$p < .05$ amongst three groups.

Variables	β†	Odds Ratio (95% confidence interval)	*p* Value
Gonion angle (Ar-Go-Me)	−0.13	0.878 (0.779–0.988)	.031
Baseline AHI	−0.142	0.868 (0.796–0.947)	.001
Constant	19.164	210 336 190	.011

TABLE 5 Multivariate logistic regression analysis for predictors of mandibular advancement device normalisation outcome.

†regression coefficient.

and more protrusion amount was needed to achieve a 50% AHI reduction in the high-angle patients. The vertical craniofacial pattern (gonion angle) and baseline AHI together constituted the model for predicting the curative effect of oral appliances.

AUTHOR CONTRIBUTIONS

Yanyan Ma had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis and manuscript preparation. Min Yu contributed substantially to the data analysis and the writing of the manuscript. Xuemei Gao designed the study and put forward suggestions for revising the article.

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CONFLICT OF INTEREST STATEMENT

No conflicts exist for Yanyan Ma, Min Yu and Xuemei Gao.

PEER REVIEW

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DATA AVAILABILITY STATEMENT

The data that support the findings of the study are available from the corresponding author upon reasonable request.

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