

Title page

Title:

Is there a relationship between obstructive sleep apnea severity and dental arch form in adult patients? An observational retrospective study

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Abstract

Study objectives: The purpose of this study was to investigate the relationship between dental arch morphological characteristics and OSA severity, after controlling potential confounders such as gender, age and body mass index (BMI).

Methods: The dental casts of 91 OSA patients were scanned and reference points of the dental arches were identified. Inter-tooth distances were determined. Cartesian coordinates of the bracket slot points were used to generate the best fitting fourth degree polynomial equation and to compare the patient's arch form with three standard arch forms (square, ovoid, tapered). Hierarchical regressions were run to examine the amount of variability in apnea-hypopnea index (AHI) that dental arch linear parameters, coefficients of the polynomial curve that best fitted the arch and arch forms explained after controlling for patients' general characteristics (gender, age and BMI).

Results: The increase in AHI variance accounted for by dental parameters (either linear parameters or polynomial coefficients or arch forms) was not statistically significant ($p>0.05$).

Conclusions: No relationship was found between OSA severity and dental arch morphological characteristics after controlling potential confounders like gender, age and BMI.

Clinical implications: Until there is a better understanding of OSA anatomical and pathophysiological phenotypes, dentists should rely on parameters other than arch morphological characteristics to make assumptions about OSA severity.

Keywords: obstructive sleep apnea; apnea/hypopnea index; dental arch; dental casts.

Introduction

Obstructive sleep apnea (OSA) is a common disorder characterized by repetitive episodes of partial or complete obstruction of the upper airway during sleep, resulting in oxygen desaturation, sleep fragmentation and excessive daytime sleepiness.¹ Polysomnography (PSG) is the current gold standard test for the diagnosis of OSA. The severity of the disorder is defined as the number of partial or complete cessations of breathing per hour of sleep (apnea-hypopnea index, AHI), with $5 \leq \text{AHI} < 15$ being classified as mild, $15 \leq \text{AHI} < 30$ as moderate, and $\text{AHI} \geq 30$ as severe.^{2,3} The pathogenesis is multifactorial, with both anatomic and nonanatomic pathophysiological traits contributing, alone or in combination, to the development of the disorder.⁴ Nonanatomic pathophysiological traits include the ability of the upper airway dilator muscles to respond to respiratory challenge during sleep, the propensity to wake from increased respiratory drive during sleep (arousal threshold) and the stability of the respiratory control system (loop gain).^{4,5} Anatomically, an imbalance between the volume of the upper airway soft tissue and the bony enclosure size may result in pharyngeal airway obstruction during sleep.⁶ Obstruction may occur at multisegmental sections of the upper airway: nasopharynx, oropharynx and hypopharynx. Locating the level of upper airway obstruction is a key clinical feature for addressing OSA treatment, however the assessment of the disease does not require knowing at which point the obstruction is. Drug-induced sleep endoscopy (DISE) is currently the best technique for direct visualization of the site or sites of obstruction in sleeping patients.⁷ With regard to the anatomical aspect, several cephalometric studies have investigated the craniofacial characteristics in adult patients with OSA and, also, the relationship between cephalometric parameters and AHI.⁸⁻¹⁷ A recent systematic review concluded that there is a strong evidence for reduced pharyngeal airway space, inferiorly placed hyoid bone and increased vertical growth pattern in adult OSA patients

compared to healthy subjects.¹⁸ Conversely, limited data are available on dental arch morphology, with narrower dental arches being generally observed in patients with OSA.¹⁹⁻²³ This method can be considered more practical because it does not require radiographic examinations and several landmarks identification but, so far, no study has investigated the relationship between dental arch morphology and OSA severity taking into consideration the effect of potential confounders such as gender, age and body mass index (BMI). Generally, OSA severity increases with age and women are less severely affected than men, but this gender difference narrows with age due to the increased risk of OSA brought by menopause.²⁴ Moreover, obesity is recognized as an important risk factor for OSA and a significant positive correlation exists between BMI and AHI.^{25,26} Therefore, the aim of this study was to investigate the relationship between dental arch morphological characteristics and AHI on a sample of adult Caucasian OSA patients, controlling the effect of gender, age and BMI.

Methods

Study design and sample

The study was designed as an observational retrospective study. It was approved by the Ethical Committee of the [REDACTED]. Consent was obtained by the study participants prior to study commencement.

Participants were retrieved from patients who accessed the [REDACTED] [REDACTED] for consultation for treatment with mandibular advancement device between January 2008 and June 2016. Inclusion criteria were: white ancestry, age over 18 years, a diagnosis of OSA based on PSG (*i.e.* AHI ≥ 5 with symptoms/sequelae or AHI ≥ 15 regardless of

associated symptoms),²⁷ good quality dental casts, presence of at least 10 teeth (excluding third molars) in each dental arch. Exclusion criteria were: previous or ongoing orthodontic treatment, history of reconstructive/orthognathic surgery to the head and neck, history of pharyngeal surgery, craniofacial syndromes, severe crowding (8 mm or more).

Data collection

Demographic data, BMI and AHI were obtained from manual medical record review. Dental casts were digitized using an optical scanner (AGE Solutions SRL, Pisa, Italy) and scans were saved in stereolithography (STL) format. The digitized renderings were analysed using Rhinoceros software (Rhinoceros® Nurbs modeling for Windows, Robert McNeel & Associates, Seattle, Washington, USA).

One operator (DRI) identified on each cast of both dental arches the points shown in Figure 1a. A second point, "BS", was obtained using the method of Andrews²⁸ as shown in Figure 1b and used only to determine dental arch form. The projections of the points in Fig 1a were used to compute linear measurements (Figure 2). The X and Y coordinates for the BS points projections on the occlusal plane were inputted into the mathematical software MATLAB (MATLAB version 8.5.0.197613 (R2015a), Natick, MA, USA: The MathWorks Inc., 2015). These projections were used to generate the best fitting curve that represented the arch, by using the fourth degree polynomial equation ($f(x)=ax^4+bx^3+cx^2+dx+e$). Using a series of complex mathematical steps (available upon request), each subject's dental arch was classified into one of the three standard arch forms (square, ovoid, tapered; OrthoForm, 3M Unitek, Monrovia, California, USA) (Figure 3).

Statistical analysis

Method error and reliability

To assess the errors associated with the dental casts measurements, 15 casts were randomly selected and their measurements were repeated by the same operator three weeks apart. A second blinded, duly calibrated operator analysed the same 15 casts and inter-observer reliability was tested using the intraclass correlation coefficient (ICC)

Relationship between AHI and dental arch characteristics

Hierarchical regressions were run to examine the amount of variability in AHI that dental arch characteristics (expressed as linear parameters, polynomial coefficients and arch forms) explained after controlling patients' general characteristics (gender, age and BMI). Therefore, in the first step of the hierarchical regression procedure, patients' general characteristics (gender, age and BMI) were block entered providing the variance accounted for by this group of independent variables. In the second step dental arch linear parameters/coefficients of the polynomial curve that best fitted the arch/arch forms were entered into the step 1 model, providing their unique contribution to AHI. All statistical analyses were conducted using the Statistical Package for Social Sciences Software (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp). $P < 0.05$ was set as the level for statistical significance.

Results

Out of a total of 133 patients considered for inclusion, 42 were excluded (n=11: simple snorers, n=24: insufficient number of teeth in either maxillary or mandibular arch, n=7 damaged dental casts). Therefore the final sample consisted of 91 OSA patients. The gender distribution was 16 (17.6%) women and 75 (82.4%) men. The average age was 53.55 years (95% CI: range 19-77

years). The mean BMI was 27.56 Kg/m² (95% CI: 26.83 to 28.29 Kg/m²) with 24 (26.4%) obese patients (BMI \geq 30) (Table 1). Dental arch characteristics (expressed as linear parameters, polynomial coefficients and arch forms) according to OSA severity are reported in Table 2 for the upper arch and in Table 3 for the lower arch.

In the step one of hierarchical regression, the variance accounted for (R^2) by the patients' general characteristics equaled 0.10, which was significantly different from zero ($F(3,86) = 3.201$, $p=0.027$). Among the patients' general characteristics, only gender was statistically significant ($p=0.012$). Next, dental parameters (expressed either as linear parameters, polynomial coefficients or arch forms) were entered into the regression equation. The increase in variance accounted for (ΔR^2) by dental parameters was not significant (linear parameters: $\Delta R^2=0.306$, $\Delta F(14,17)=0.842$, $p=0.623$; polynomial coefficients: $\Delta R^2=0.073$, $\Delta F(8,78)=0.857$, $p=0.556$; arch forms: $\Delta R^2=0.027$, $\Delta F(2,84)=1.306$, $p=0.276$).

Method error and reliability

The random error, determined using Dahlberg's formula, ranged between 0.17 and 0.59 mm for linear measurements and between 0.08 and 0.24 mm for the BS points coordinates. No systematic error was detected by the paired t-test for any measurements ($p>0.05$).

Satisfactory values were found for inter-observer reliability, with the ICC ranging between 0.881 and 0.997 for linear measurements and between 0.727 and 0.997 for the BS points coordinates.

Discussion

Several data are available on the craniofacial characteristics of adult patients with OSA and, also, on the relationship between cephalometric parameters and AHI. The evaluation of dental arch

morphological characteristics in OSA patients has the advantage that does not require radiographic examination but limited and controversial data are available on this topic.

So far, narrow maxillary dental arches have been thought to diminish the oropharyngeal volume available for the tongue, thus being considered a predisposing factor for OSA.²⁹ Few studies have been carried out on the correlation between adult patients' arch parameters and the presence of OSA, with inconclusive results.^{19-21,30,31} Methodological limitations include the use of questionnaires for the screening of OSA for the selection of the control group, while the diagnosis of OSA absence should be based on PSG criteria.²³ Moreover, the measurements were often taken on bi-dimensional images and limited to the upper arch. The comparison between OSA and non-OSA patients was usually based on linear measurements (inter-tooth widths and arch depths) or at most on the polynomial coefficients. Regarding the upper arch, OSA patients showed significantly narrower inter-tooth widths and a shorter maxillary depth than non-snoring, non-apnoeic subjects.¹⁹ A study on three-dimensional maxillary dental casts found that OSA patients had significantly narrower maxilla with smaller intermolar and intercanine widths when compared with controls.²¹ Conversely, other Authors did not report significant differences in any inter-tooth distances.²⁰ Patients with Marfan's syndrome proved to have a significant reduction of intercanine, inter-first premolar and inter-first molar widths compared with control subjects.³⁰ However, it should be acknowledged that Marfan's syndrome is associated with a high prevalence of OSA. The mean upper arch width of the OSA group has also shown to be narrower in the canine region and wider in the premolar and molar regions when compared to the non-OSA group.³¹ Moreover, mandibular arches of the OSA group were narrower in the canine region and wider in the premolar and molar areas.³¹ Looking at width and depth independently is not adequate to evaluate arch form since these parameters are affected by arch size as well as by arch form. To

overcome this limitation arch form could be represented by a mathematical equation. However only one study compared the maxillary arch forms of OSA and non-OSA subjects based on the coefficients of the polynomial curve that best fitted the arch.¹⁹ Comparison of the polynomial coefficients indicated that the quadratic coefficient was significantly greater in OSA patients than in controls, indicative of greater tapering of the maxillary arch. In a study comparing dental arches of OSA and non-OSA subjects through finite-element morphometry it was found that OSA patients showed 7–11% narrower upper arches in the transverse plane in the incisor and canine regions and 10–11% narrower lower arches in the antero-posterior plane in the pre-molar and molar regions.²⁹ If several studies have investigated the association between adult patients' arch parameters and the presence of OSA, only a few of them analysed whether these parameters and disease severity were correlated. A significant correlation between indexes of maxillary constriction and AHI in patients with Marfan's syndrome has been found.³⁰ However, in addition to the limitations of the study highlighted above, this study did not take into account the effect of potential confounders as we did in the present study. A further study found that a significant yet weak correlation ($r=-0.158$, $p=0.044$) existed between the upper dental arch width (defined as the distance between the cusps of the right and left first premolars) and AHI.³² However only Japanese male subjects were included in the study, the correlation between lower dental arch width and AHI was not analysed and the arch width was evaluated only at the first premolar level. Moreover, potential confounders were not considered in the analysis.

Therefore, the present study aimed to overcome the limitations which burdened the studies currently available on this issue, providing a comprehensive analysis of the correlation between adult patients' arch morphological characteristics and OSA severity by using three-dimensional cast analysis and reliable mathematical methods and taking into account potential confounders like

gender, age and BMI. Age and BMI did not prove to be significant predictors of AHI in our sample of OSA patients. However, they were included in the final model, regardless of their statistical significance, since the correlation between AHI and both age and BMI has been widely described in the literature.²⁴⁻²⁶

No significant relationships were found between dental arch parameters and AHI after controlling gender, age and BMI neither in the upper arch nor in the lower arch. Therefore, in OSA patients the relationship between arch form characteristics and disease severity is not so evident. This finding is consistent with other studies on anatomical characteristics of OSA patients, which showed that various anatomical correlates were poor predictors of OSA prevalence or severity.³³⁻

³⁵ A possible explanation for this finding is that, although anatomical characteristics can help determine pharyngeal collapsibility, anatomical factors alone do not cause OSA. In the pathogenesis of OSA nonanatomic factors such as the ability of the upper airway dilator muscles to respond to respiratory challenge during sleep, the propensity to wake from increased respiratory drive during sleep (arousal threshold) and the stability of the respiratory control system (loop gain) must be taken into account too.⁴ Since several factors can contribute to upper airway collapse during sleep, the extent to which craniofacial skeletal restriction (which could result in narrower dental arches) contribute to the phenomenon of repetitive collapse of the upper airway during sleep probably varies from patient to patient.³⁶ Moreover, the onset and the duration of OSA must be considered as it can greatly affect the morphological features: as OSA occurring in adults does not affect growth and development, the effect of OSA on the morphology of the hard palate (and consequently on arch form) is not obvious.³⁷ Further studies are needed to properly evaluate this issue since a better characterization of OSA anatomical and pathophysiological phenotypes is an essential step towards tailored approaches to therapy to ensure treatment effectiveness.^{38,39}

Limitations of the study

Unavailability of information on confounders can potentially bias the results of retrospective studies. Given the retrospective nature of this study, certain confounding variables that have the potential to impact the outcome may not have been considered or recorded at all (*e.g.* lifestyle factors like dietary habits, alcohol consumption, cigarettes and physical activity or abnormalities in either function or position of the tongue). Especially tongue function, posture, and size, which could not be evaluated in this work, should be considered in future studies. It is generally assumed that the alveolar bone responds to external influences: the altered position of tongue may cause imbalance in the forces, which may result in alteration in the dental arch form. However conflicting reports exist in the pertinent literature about variations in tongue size or posture affecting the characteristics of the maxillary and mandibular dental arches, mainly assessed as transverse linear measurements.^{40,41}

Patients with previous or ongoing orthodontic treatment had to be excluded from the sample to avoid misleading results given by the change in morphology arch parameters determined by orthodontic treatment. However we cannot know what impact could have had the exclusion of subjects with very narrow or wide dental arch, who has undergone orthodontic treatment. Moreover, the study subjects may not be representative of the population and study results from larger sample size might be more generalizable to the whole population.

Conclusions

No significant relationship was found between dental arch morphological characteristics and AHI after controlling potential confounders like gender, age and BMI, suggesting that dental arch

parameters are poor predictors of OSA severity. Further prospective studies conducted on larger sample size could improve the generalization of the results.

Abbreviations

AHI: apnea-hypopnea index

BMI: body mass index

BS point: Bracket Slot point

CI: Confidence Interval

FA point: facial axis point

ICC: intraclass correlation coefficient

OSA: Obstructive sleep apnea

PSG: Polysomnography

STL: stereolithography

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Figure Titles and Captions

Figure 1 - Definition of the points.

1a, Reference points used to compute linear measurements: A, the midincisal point of the incisors; B1, B2, the canines' cusp tips; C1, C2, the buccal cusp tips of the first premolars; D1, D2, the buccal cusp tips of the first premolars; E1, E2, the distobuccal cusp tips of the first molars; F1, F2, the distobuccal cusp tips of the second molars; **1b**, Reference points used to determine dental arch form: bracket slot points (BS points).

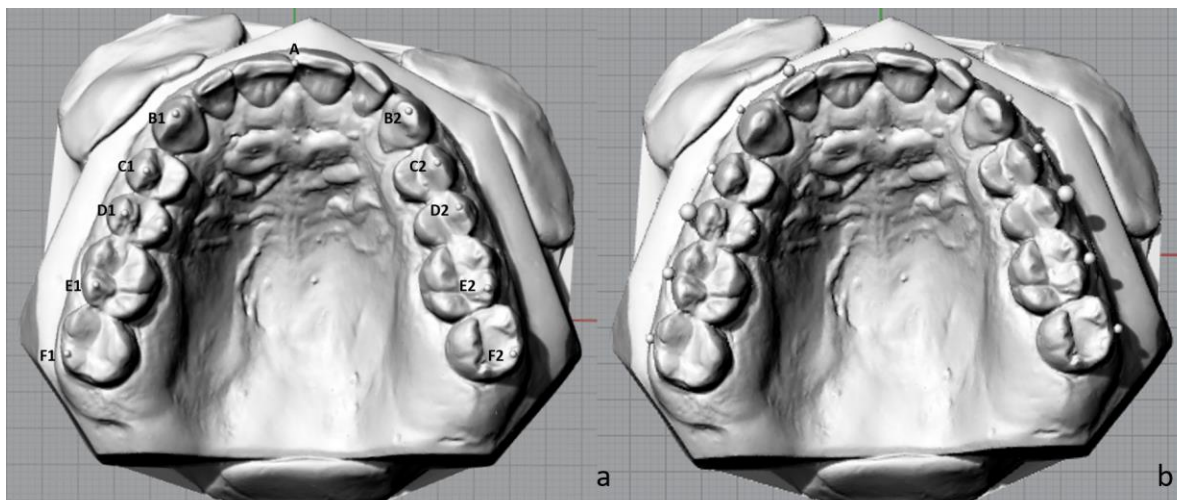


Figure 2 - Arch-dimension variables.

Wc, intercanine width: distance between the canine cusp tips; Wp1, interfirst premolar width: distance between the first premolar cusp tips; Wp2, intersecond premolar width: distance between the second premolar cusp tips; Wm1, interfirst molar width: distance between the distobuccal cusp tips of the first molars; Wm2, intersecond molar width: distance between the distobuccal cusp tips of the second molars; Dc: canine depth: distance between the contact of the central incisors and a line that connects the canine cusp tips; Dm: second molar depth: Distance between the contact of the central incisors and a line that connects the distobuccal cusp tips of the second molars.

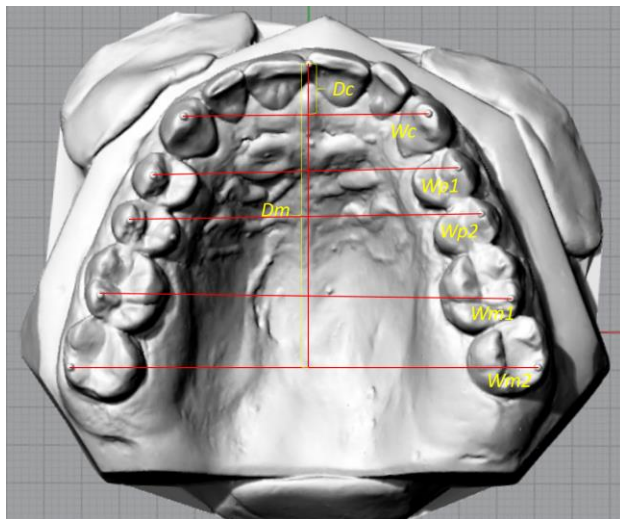
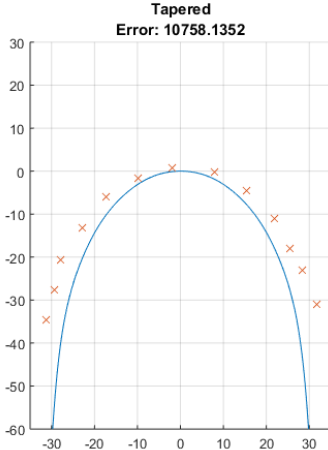
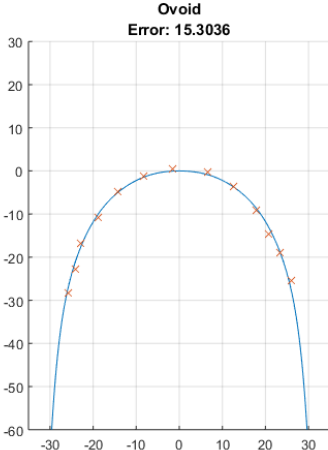
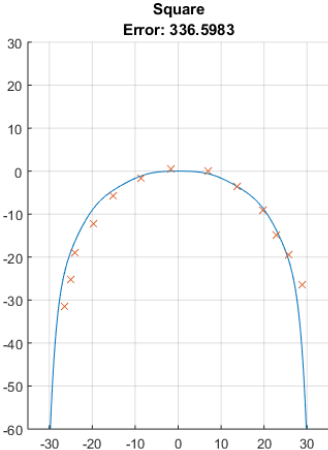


Figure 3 - Comparison between patient's arch form and standard arch forms by using the method of least squares.

The red crosses are the BS points; the blue lines are the standard arch forms (square, ovoid, tapered).



Tables

Table 1 - Subjects' demographic and clinical characteristics.

	Total (n=91)	OSA severity level		
		Mild ($5 \leq \text{AHI} < 15$) (n=28)	Moderate ($15 \leq \text{AHI} < 30$) (n=29)	Severe ($\text{AHI} \geq 30$) (n=34)
Males [n(%)]	75 (82.4%)	18 (64.3%)	26 (89.7%)	31 (91.2%)
Age (years) [mean (95% CI)]	53.55 (51.43 to 55.67)	54.21 (50.21 to 58.21)	52.76 (48.31 to 57.20)	53.68 (50.60 to 56.75)
BMI (kg/m ²) [mean (95% CI)]	27.56 (26.83 to 28.29)	27.65 (26.11 to 29.19)	26.60 (25.27 to 27.93)	28.28 (27.23 to 29.32)
AHI (events/h) [mean (95% CI)]	25.49 (22.34 to 28.65)	10.14 (9.06 to 11.22)	20.65 (19.13 to 22.16)	42.27 (38.85 to 45.69)

N: number; 95% CI: 95% confidence interval.

Table 2 - Upper arch characteristics (linear measurements, polynomial coefficients and arch forms) according to OSA severity.

		OSA severity level		
		Mild ($5 \leq \text{AHI} < 15$) (n=28)	Moderate ($15 \leq \text{AHI} < 30$) (n=29)	Severe ($\text{AHI} \geq 30$) (n=34)
Linear parameters (mm)				
	Inter canine width (Wc)	34.1 (32.9 to 35.3)	33.7 (33.2 to 34.3)	34.2 (33.4 to 35.0)
	Interfirst premolar width (Wp1)	41.4 (40.3 to 42.4)	41.3 (40.5 to 42.0)	42.2 (41.4 to 43.1)
	Intersecond premolar width (Wp2)	46.7 (45.4 to 48.0)	47.7 (46.5 to 48.8)	48.3 (47.4 to 49.3)
	Interfirst molar width (Wm1)	54.2 (53.0 to 55.5)	55.5 (54.2 to 56.9)	56.0 (54.7 to 57.2)
	Intersecond molar width (Wm2)	60.2 (59.0 to 61.4)	59.8 (58.5 to 61.1)	61.6 (60.1 to 63.1)
	Canine depth (Dc)	7.6 (6.9 to 8.3)	8.2 (7.4 to 9.0)	7.5 (7.0 to 8.1)
	Second molar depth (Dm)	39.2 (38.0 to 40.4)	41.2 (40.1 to 42.4)	39.3 (38.2 to 40.4)
Polynomial coefficients				
	1 st degree	-2.5E-03 (-2.8E-02 to 2.3E-02)	-1.1E-02 (-5.0E-02 to 2.8E-02)	2.4E-02 (-4.9E-03 to 5.2E-02)
	2 nd degree	-1.9E-02 (-2.2E-02 to -1.5E-02)	-1.8E-02 (-2.1E-02 to -1.5E-02)	-1.7E-02 (-2.0E-02 to -1.4E-02)
	3 rd degree	9.0E-06 (-5.3E-05 to 7.0E-05)	2.6E-05 (-7.0E-05 to 1.2E-04)	-5.9E-05 (-1.2E-04 to -2.8E-06)
	4 th degree	-2.3E-05 (-2.7E-05 to -1.8E-05)	-2.3E-05 (-2.7E-05 to -1.9E-05)	-2.1E-05 (-2.5E-05 to -1.7E-05)
Arch form				
	Square [n (%)]	5 (17.9%)	2 (6.9%)	10 (29.4%)
	Ovoid [n (%)]	19 (67.9%)	20 (69.0%)	21 (61.8%)
	Tapered [n (%)]	4 (14.3%)	7 (24.1%)	3 (8.8%)

Data are presented as mean (95% confidence interval) unless otherwise specified.

Table 3 - Lower arch characteristics (linear measurements, polynomial coefficients and arch forms) according to OSA severity.

		OSA severity level		
		Mild ($5 \leq \text{AHI} < 15$) (n=28)	Moderate ($15 \leq \text{AHI} < 30$) (n=29)	Severe ($\text{AHI} \geq 30$) (n=34)
Linear parameters (mm)				
	Inter canine width (Wc)	25.5 (24.7 to 26.3)	25.2 (24.3 to 26.1)	25.9 (25.3 to 26.6)
	Interfirst premolar width (Wp1)	34.4 (33.2 to 35.6)	33.6 (32.6 to 34.6)	35.0 (34.2 to 35.9)
	Intersecond premolar width (Wp2)	40.9 (39.4 to 42.3)	41.0 (39.8 to 42.1)	42.6 (41.6 to 43.6)
	Interfirst molar width (Wm1)	49.8 (48.3 to 51.4)	50.4 (48.9 to 52.0)	51.6 (49.9 to 53.3)
	Intersecond molar width (Wm2)	56.7 (55.5 to 58.0)	56.5 (54.7 to 58.2)	57.5 (56.1 to 58.9)
	Canine depth (Dc)	5.6 (5.0 to 6.3)	5.4 (4.7 to 6.0)	5.9 (5.2 to 6.6)
	Second molar depth (Dm)	35.3 (34.0 to 36.5)	36.0 (34.9 to 37.0)	36.0 (33.8 to 38.2)
Polynomial coefficients				
	1 st degree	-2.8E-03 (-3.9E-02 to 3.4E-02)	-1.3E-02 (-4.4E-02 to 1.8E-02)	9.8E-03 (-1.9E-02 to 3.9E-02)
	2 nd degree	-2.3E-02 (-2.5E-02 to -2.1E-02)	-2.2E-02 (-2.5E-02 to -1.9E-02)	-2.1E-023 (-2.3E-02 to -1.9E-02)
	3 rd degree	3.8E-05 (-4.9E-05 to 1.3E-04)	-3.5E-07 (-8.2E-05 to 8.2E-05)	-7.75E-05 (-1.6E-04 to 6.4E-06)
	4 th degree	-1.6E-05 (-1.9E-05 to -1.3E-05)	-1.8E-05 (-2.2E-05 to -1.4E-05)	-1.5E-05 (-1.8E-05 to -1.3E-05)
Arch form				
	Square [n (%)]	4 (14.3%)	4 (13.8%)	9 (26.5%)
	Ovoid [n (%)]	21 (75.0%)	20 (69.0%)	21 (61.8%)
	Tapered [n (%)]	3 (10.7%)	5 (17.2%)	4 (11.8%)

Data are presented as mean (95% confidence interval) unless otherwise specified.