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Clinical Prediction Models for Upper Airway Volume Based on Soft Palate and Airway Lumen Dimensions in Adults With Varying Vertical Skeletal Patterns

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ABSTRACT

Objectives: To determine the intricate associations between soft palate dimensions, pharyngeal airway lumen area, the minimal constricted area of the airway (MinAx), and pharyngeal airway volume in subjects with diverse vertical skeletal patterns, and to develop prediction models that could help clinicians predict upper airway volume using soft palate dimensions, airway lumen dimensions, and MinAx.

Materials and Methods: Pre-treatment lateral cephalometric radiographs and magnetic resonance imaging (MRI) scans of 80 women were classified into three vertical skeletal groups based on Frankfort-mandibular plane angle (FMA angle): hypodivergent (FMA < 26.9°, n = 26), normodivergent (26.9°≤ FMA ≤ 34.1°, n = 29), and hyperdivergent (FMA > 34.1°, n = 25). Soft palate dimensions, pharyngeal airway lumen data, MinAx, retropalatal airway volume (RPV), and retroglossal airway volume (RGV) data were measured using MRI. Forward multiple linear regression was used to predict pharyngeal airway volumes.

Results: Among the eight predictive models developed, six exhibited strong performance, explaining 50%-77% of the variability in airway volumes. MinAx, RPV, and total pharyngeal airway volume (TPV) were considerably higher in hypodivergent subjects than in hyperdivergent subjects. Hyperdivergent subjects had a longer soft palate length (SPL) than normodivergent and hypodivergent subjects.

Conclusions: The present study highlights the necessity of considering soft palate dimensions and airway characteristics in orthodontic treatment planning, especially for patients with varying vertical skeletal patterns. Understanding these relationships can help in predicting potential airway issues and customising treatment plans accordingly.

Introduction

The intricate configuration of the human pharyngeal airway lumen helps in determining airflow and ventilation, particularly in obstructive sleep apnea (OSA) patients.[1,2] Critical factors like contour and size influence these functions; however, existing methodologies cannot fully delineate the intricate details of the pharyngeal airway lumen. Descriptions often compress complex characteristics into singular points corresponding to the nasopharynx, oropharynx, and hypopharynx.[2] A comprehensive understanding of the interconnections between the airway lumen areas and volumetric size in distinct pharyngeal compartments is lacking, particularly in individuals with varying vertical skeletal patterns. In addition, the predictive role of the airway lumen at the second cervical vertebra (C2), epiglottis,

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and soft palate regions in the retroglossal and retropalatal airway volumes remains uncertain.

The soft palate, as a landmark for the airway collapse region, significantly impacts oral functions like swallowing, respiration, and phonation.[3,4] Few studies have investigated the relationship between soft palate and three-dimensional (3-D) airway dimensions. Existing literature predominantly focuses on patients with OSA, with conflicting findings. For instance, Shigeta et al. noted increased soft palate length in OSA patients,[5] whereas Battagel et al. reported longer soft palates in control subjects.[6] Moreover, in non-OSA subjects, Akcam et al.[4] in a previous cephalometric-based study found that the linear increase of the soft palate was related to a vertical rotation pattern. However, the relationship with the nasopharyngeal airway dimensions was not significantly different among the vertical rotation groups. According to Jayaprakash, the curved shape of the soft palate in a vertical growth pattern is more likely to predispose individuals to velopharyngeal insufficiency, resulting in misarticulation and sleep apnea,[7] However, the two dimensional (2-D) nature of the lateral cephalograms used in these studies limits their ability to evaluate 3-D airway structures.[8] This underscores the need to conduct a detailed 3-D investigation, particularly in non-OSA individuals with diverse vertical skeletal patterns.

Magnetic resonance imaging (MRI) offers superior soft tissue visualization without radiation exposure, allowing detailed assessment of airway morphology and soft palate dimensions.[9-11] This study aimed to investigate the predictive role of the soft palate and pharyngeal airway lumen dimensions in determining airway volume in subjects with different vertical skeletal patterns.

Materials and methods

This retrospective cross-sectional study was approved by the Institutional Ethics Committee of Okayama University, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, and Okayama University Hospital. All patients' records in the Department of Orthodontics from September 25, 2017 to February 14, 2020, were included in this study.

The sample size was determined through power calculation using the formula by Pandis[12] to detect a significant difference of 1584.09 mm^3 in airway volume in subjects with different vertical skeletal patterns, based on the average standard deviation of 1323.92 mm^3 from a prior study by Wang et al.[13] The calculations indicated that a minimum of 15 individuals were required to detect this difference, with 90% power and significance of 0.05. We used MRI scans of 80 women who met the inclusion criteria. The subjects were further categorised into three distinct vertical skeletal groups based on the Frankfort-Mandibular Plane Angle (FMA angle)[14,15]: hypodivergent (FMA < 26.9°, $n = 26$), normodivergent (26.9° ≤ FMA ≤ 34.1°, $n = 29$), and hyperdivergent (FMA > 34.1°, $n = 25$).

Inclusion criteria were: (1) nongrowing subjects with a mean age of 31.40 ± 11.17 years and (2) subjects with normal body mass index (BMI) of 18.5-23.5 kg/m^2 with available initial radiographic records, particularly MRI scans with clear landmarks, and lateral cephalometric scans. We excluded patients with a history of orthodontic treatment, developmental disorders, or craniofacial malformations such as cleft lip and palate. In addition, subjects with OSA were excluded.

MRI was conducted using open-configuration equipment, specifically the Magnetom Aera 1.5 T, Siemens Healthineers, Erlangen, Bavaria, Germany. The patients underwent MRI while awake and in supine position. A 3D-volumetric interpolated breath-hold examination sequence was employed for each participant with following imaging parameters: repetition time, 3.87 ms, echo time, 1.35 ms, flip angle, 12°; field of view, 300 mm; slice thickness, 1.0 mm, matrix dimensions, 288 × 230; bandwidth, 480 Hz/px; and an acceleration factor of 2. Cephalometric analysis and conversion of Digital Imaging and Communications in Medicine (DICOM) data into 3-D images for airway analysis were conducted using the Dolphin Imaging software version 11.95 (Dolphin Imaging & Management Solutions, Chatsworth, CA, USA).

Figure 1 shows the measurements of the soft palate dimensions[5] and pharyngeal lumen measurements.[9] Pharyngeal airway volume was measured using landmarks outlined in a previous study[16] (Figure 2). The airway sensitivity was set at 73 during the measurement of the airway volume.[10,17] The images were reoriented by aligning the palatal plane parallel to the horizontal plane in the midsagittal section.[10] The definitions of all landmarks used in this study are provided in Supplementary Table 1.

Statistical analysis

All statistical analyses were performed using the SPSS software version 25 (IBM Corp., Armonk, NY, USA). To assess operator reliability, measurements of radiographic records of 10 randomly selected patients were repeated after a 3-week interval. Intra-rater reliability was evaluated using the intraclass correlation coefficient (ICC). The method error was determined using Dahlberg's formula.[18]

The normality of the variables was assessed using the Shapiro–Wilk test and normality Q-Q plots. Given the non-normal distribution of the parameters, intergroup comparisons were conducted using the Kruskal–Wallis test, followed by the Bonferroni-corrected Mann–Whitney U-test for pairwise comparisons if significant interactions were observed.

Bivariate analysis was performed using Spearman's correlation coefficient. To develop model equations predicting airway volume parameters, specifically retropalatal airway volume (RPV), retroglossal airway volume (RGV), and total pharyngeal airway volume (TPV), all included measurements were used in a forward multiple linear regression. The data for RPV, RGV and TPV (dependent variables) displayed positive skewness and a non-normal distribution. To address this, a logarithmic transformation was applied to normalize the distributions and enhance their suitability for the linear regression model (Supplementary Figure 1).

To evaluate the model's predictive performance, we split the dataset into training and test sets using a 60-40 split. The training set was used to develop the model, and the test set was employed to assess the model's accuracy. We evaluated the model's performance using multiple metrics, including adjusted R-squared, Mean Square, F-statistics, and *P*-values. These metrics were computed for each subgroup (Hypodivergent, Normodivergent, Hyperdivergent and Total Sample) across the RPV, RGV and TPV measurements.

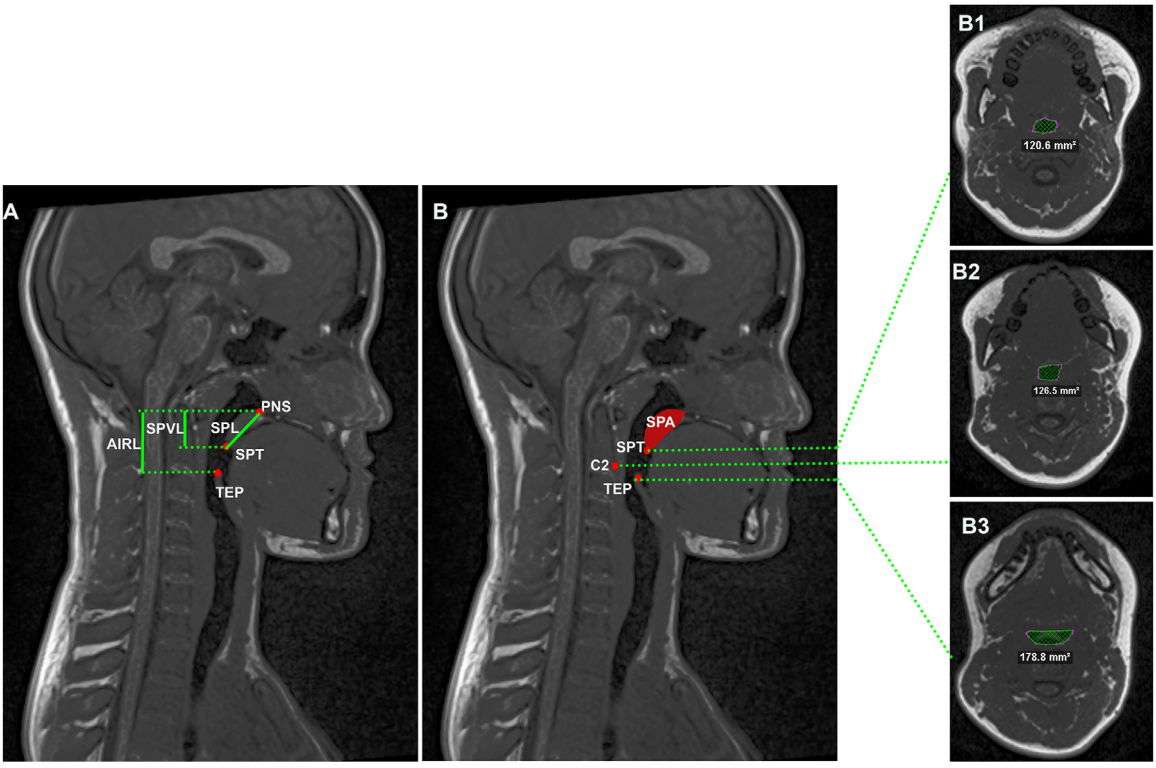

Fig. 1 – Dimensions of the soft palate and pharyngeal airway lumen area at different anatomical locations. (A) displays measurements for SPL, SPVL and AIRL. (B1) PALA-SPT, (B2) PALA-C2 and (B3) PALA-TEP.

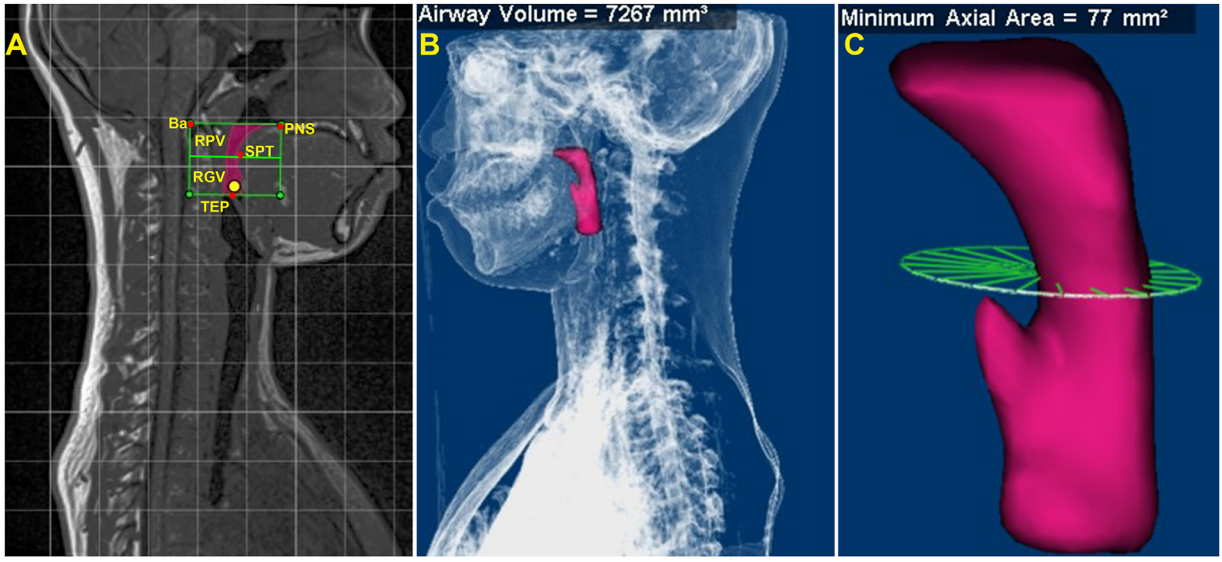

Fig. 2 – Measurement of pharyngeal airway (PA) volume: (A) PA landmarks, (B) PA volume and (C) MinAx.

The statistical significance for tests incorporating Bonferroni correction was set at $P < .017$ and at $P < .05$ for all other tests.

Results

The ICC for all parameters ranged from 0.89-0.99, indicating strong agreement between the initial and second measurements. Dahlberg's formula yielded values of 0.82°-1.46° for angular measurements, 0.21-0.66 mm for linear measurements, 4.07-7.01 mm^2 for area measurements, and 67.01-107.35 mm^3 for volumetric measurements.

Supplementary Table 2 shows the demographic characteristics of the study subjects.

Table 1 shows correlation results, MinAx, pharyngeal airway lumen area at the tip of the soft palate (PALA-SPT),

Table 1 – Spearman correlation coefficient between airway volumes and parameters used in this study.

ρ	MinAx (mm^2)	AIRL (mm)	PALA-SPT (mm^2)	PALA-C2 (mm^2)	PALA-TEP (mm^2)	SPL (mm)	SPVL (mm)	SPVL/AIRL (%)
RPV (mm^3)	0.715***	0.009	0.420***	0.273*	0.231*	-0.303**	-0.279*	-0.207
RGV (mm^3)	0.340**	0.106	0.243*	0.367**	0.347**	-0.165	-0.292**	-0.285*
TPV (mm^3)	0.681***	-0.016	0.457***	0.399***	0.344**	-0.315**	-0.301**	-0.218

* $P < .05$,
** $P < .01$,
*** $P < .001$,ρ: Spearman rho, see Supplementary Table 1 for additional abbreviations.

Table 2 – Forward linear regression model for RPV and TPV (after logarithmic transformation) of the groups and the total sample.

		Dependent variables: Log RPV and Log TPV	Unstandardised coefficients		Standardised coefficients			ANOVA		
			Beta	SE	Beta	t	P	F	P	Adjusted R^2
RPV	Hypodivergent	**Constant**	3.52	0.07		53.95	.000***	40.49	.000***	0.61
		MinAx (mm^2)	0.002	0.0002	0.79	6.36	.000***			
	Normodivergent	**Constant**	3.05	0.20		15.47	.000***	31.34	.000***	0.68
		MinAx (mm^2)	0.002	0.0002	0.92	7.83	.000***			
		SPL (mm)	0.014	0.006	0.28	2.39	.024*			
	Hyperdivergent	**Constant**	3.65	0.06		58.50	.000***	5.50	.028*	0.15
		MinAx (mm^2)	0.001	0.0003	0.44	2.35	.028*			
	Total sample	**Constant**	3.54	0.03		106.97	.000***	104.29	.000***	0.57
		MinAx (mm^2)	0.002	0.0001	0.76	10.21	.000***			
TPV	Hypodivergent	**Constant**	3.83	0.07		54.59	.000***	24.24	.000***	0.50
		MinAx (mm^2)	0.001	0.0002	0.71	4.92	.000***			
	Normodivergent	**Constant**	3.45	0.15		23.28	.000***	23.72	.000***	0.77
		MinAx (mm^2)	0.001	0.0002	0.59	4.22	.000***			
		SPL (mm)	0.02	0.005	0.50	4.27	.000***			
		SPVL/AIRL (%)	-0.005	0.0010	-0.41	-3.66	.001*			
		PALA-SPT (mm^2)	0.001	0.0002	0.36	2.83	.009**			
	Hyperdivergent	**Constant**	3.89	0.050		78.28	.000***	7.98	.010*	0.23
		MinAx (mm^2)	0.001	0.0001	0.50	2.82	.009**			
	Total sample	**Constant**	3.78	0.04		105.08	.000***	46.46	.000***	0.54
		MinAx (mm^2)	0.001	0.0001	0.66	7.94	.000***			
		PALA-C2 (mm^2)	0.0003	0.0001	0.17	2.04	.040*			

* $P < .05$,
** $P < .01$,
*** $P < .001$,see Supplementary Table 1 for additional abbreviation.

pharyngeal airway lumen area at the second cervical vertebra (C2) level (PALA-C2), and pharyngeal airway lumen area at the epiglottis tip level (PALA-TEP) significantly showed positive correlation with RPV, RGV and TPV. Soft palate vertical length (SPVL) showed significant and negative correlation with both RPV, RGV and TPV. Soft palate length (SPL) was significantly negatively correlated with RPV and TPV. The percentage of airways occupied by the soft palate (SPVL/AIRL) showed a significant negative correlation with RGV.

Our analysis revealed that an accurate model for RGV could not be developed, as the performance metrics did not meet the accuracy criteria. Consequently, RGV was excluded from further analysis. In contrast, the RPV and TPV models showed more reliable performance, with detailed metrics provided in Supplementary Table 3. Results from the test set indicated consistency and, in some cases, improvement over the training set results, demonstrating the models' reliability in predicting pharyngeal airway volume.

Table 2, Figure 3, Supplementary Figure 2 show the multiple linear regression models for RPV and TPV, respectively. The models were used for individual groups separately and for the entire sample. All models for the various groups and the total sample exhibited moderate-to-great potential for explaining the RPV (Table 2 and Figure 3). The models for normodivergence (adjusted $R^2 = 0.68$), hypodivergence (adjusted $R^2 = 0.61$), and total sample (adjusted $R^2 = 0.57$) can be regarded as the most robust, as they account for over 50% of the variance in RPV. In contrast, the hyperdivergent model (adjusted $R^2 = 0.15$) was considered less effective. MinAx was incorporated into all models (hypodivergent, beta = 0.79, $P < .001$; hyperdivergent, beta = 0.44, $P < .05$). For the total sample, MinAx was the only parameter entered into the equation (beta = 0.76, $P < .001$). In contrast, for normodivergent group, MinAx was included along with SPL (beta = 0.92, $P < .001$ for MinAx and beta = 0.28, $P < .05$ for SPL).

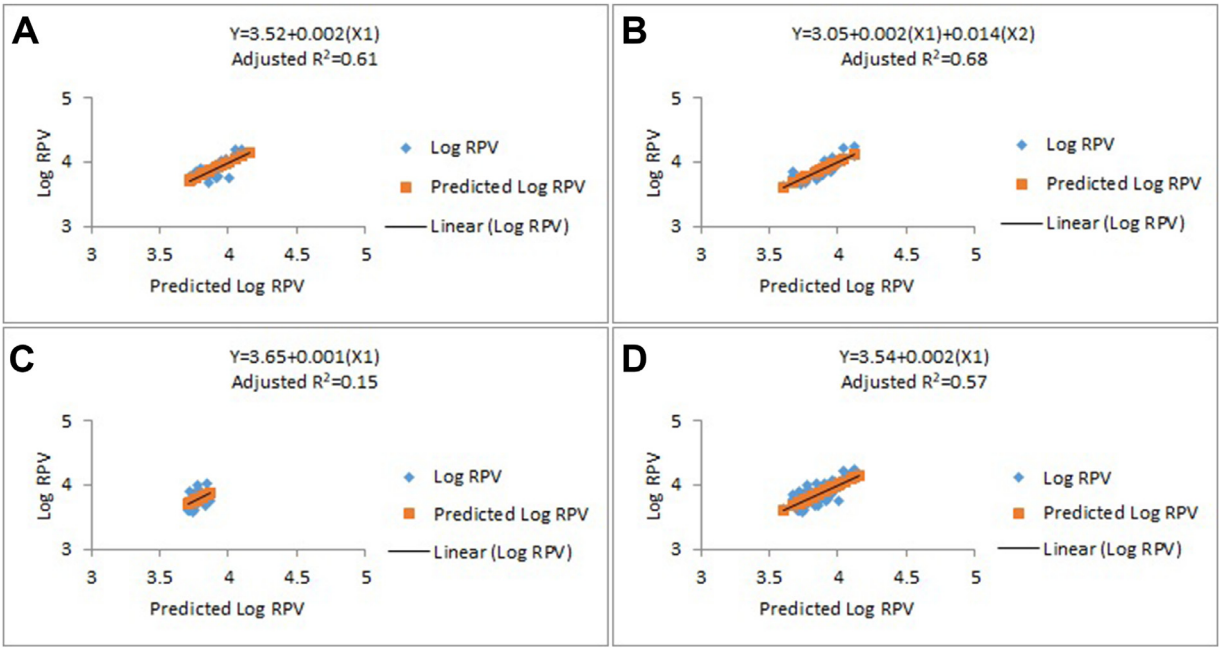

Fig. 3 – Multiple linear regression analyses between Log RPV and predicted Log RPV: (A) Hypodivergent group, (B) Normodivergent group, (C) Hyperdivergent group and (D) Total sample. RPV = Retropalatal airway volume, Y = {Log RPV}, X1 = {MinAx}, X2 = {SPL}.

All models for the various groups and the total sample exhibited moderate-to-great potential in explaining the TPV (Table 2 and Supplementary Figure 2); the normodivergence model was the strongest (adjusted R^2 = 0.77), followed by the models for the total sample (adjusted R^2 = 0.54), hypodivergence (adjusted R^2 = 0.50), and hyperdivergence (adjusted R^2 = 0.23). MinAx was incorporated into all the models. For the hypodivergent group, MinAx was the only parameter entered (beta = 0.71, $P < .001$); for the normodivergent group, MinAx, SPL, SPVL/AIRL and PALA-SPT were entered into the equation (beta = 0.59, $P < .001$ for MinAx, beta = 0.50, $P < .001$ for SPL, beta = -0.41, $P < .01$ for SPVL/AIRL and beta = 0.36, $P < .01$ for PALA-SPT). In the hyperdivergent group, MinAx was entered into the model (beta = 0.50, $P < .01$), whereas in the total sample, MinAx was entered into the model along with PALA-C2 (beta = 0.66, $P < .001$ for MinAx and beta = 0.17, $P < .05$ for PALA-C2).

Table 3 shows the intergroup analyses of the assessed parameters. MinAx ($P < .01$), RPV ($P < .017$) and TPV ($P < .01$) were considerably higher in hypodivergent subjects than in hyperdivergent subjects. However, hyperdivergent subjects had longer airway length (AIRL) ($P < .01$) than hypodivergent subjects. Regarding the pharyngeal airway lumen area, hyperdivergent subjects had narrower PALA-SPT than hypodivergent ($P < .01$) and normodivergent subjects ($P < .017$), and narrower PALA-C2 ($P < .017$) were observed in the hyperdivergent group compared with the hypodivergent group. Hyperdivergent subjects had a longer SPL than normodivergent ($P < .001$) and hypodivergent ($P < .01$) subjects. PALA-TEP, SPVL, SPV/AIRL and RGV were similar across the studied groups.

Discussion

In this study, all participants underwent supine MRI scans, in the supine position, anatomical changes occur in the pharyngeal airway, tongue and soft palate owing to gravitational forces and upper airway reflexes.[8,19] These conditions approximate those observed during sleep, making supine assessments diagnostically relevant for individuals at risk for airway-related sleep disorders.[8]

We mainly aimed to determine the predictive factors influencing upper airway volume parameters using forward multiple linear regression analyses conducted at both the group and overall sample levels for each dependent variable. No previous studies have investigated the use of soft palate and pharyngeal airway lumen dimensions as predictors of these parameters in subjects with different vertical skeletal patterns.

In all groups and the total sample, MinAx predicted RPV, TPV. Its significance in influencing the airway volume was underscored by its positive correlation with all airway volume parameters in our study. This was supported by El and Palomo's previous study,[20] where MinAx was a crucial variable for oropharyngeal airway volume variability. Moreover, previous study on OSA patients have identified minimal cross-sectional area of the airway as essential predictive parameters for OSA.[21]

Another parameter, PALA-C2, emerged as a predictor of TPV in the total sample. PALA-SPT was a predictor of TPV in the normodivergent group. Airway lumen area parameters were positively correlated with all airway volume parameters. In a previous 2-D cephalometric study, Joseph et al. indicated

Table 3 – Results of intergroup comparisons with the Kruskal–Wallis and pair-wise comparisons with Mann–Whitney U tests with the Bonferroni adjustment.

Measurements	Hypodivergent Mean (SD)	Normodivergent Mean (SD)	Hyperdivergent Mean (SD)	KW test (*P* value)	Pairwise Mann–Whitney U-test (with Bonferonni adjustment)		
					Hypodivergent vs. normodivergent	Hypodivergent vs. hyperdivergent	Normodivergent vs. hyperdivergent
RPV (mm^3)	8903.11 ±3366.79	8051.79 ± 3217.31	6293.12 ± 1730.49	.012*	NS	S†	NS
RGV (mm^3)	6239.69 ± 3375.80	5075.00 ± 1858.53	4488.48 ± 1384.57	.167	NS	NS	NS
TPV (mm^3)	15142.80 ± 5428.36	13126.79 ± 4549.52	10781.60 ± 2418.62	.006**	NS	S**	NS
MinAx (mm^2)	231.80 ± 73.79	214.03 ± 72.15	158.96 ± 61.49	.002**	NS	S**	NS
AIRL (mm)	37.55 ± 5.95	41.18 ± 5.38	44.23 ± 6.47	.003**	NS	S**	NS
PALA-SPT (mm^2)	188.95 ± 59.97	185.66 ± 80.45	128.04 ± 59.35	.002**	NS	S**	S†
PALA-C2 (mm^2)	234.00 ± 72.24	217.09 ± 75.47	171.31 ± 71.61	.012*	NS	S†	NS
PALA-TEP (mm^2)	237.06 ± 71.11	231.35 ± 76.92	202.39 ± 76.49	.281	NS	NS	NS
SPL (mm)	28.97 ± 2.66	28.48 ± 3.15	31.99 ± 2.25	.000***	NS	S**	S***
SPVL (mm)	23.68 ± 2.69	24.55 ± 4.05	27.34 ± 5.26	.040*	NS	NS	NS
SPVL/AIRL (%)	64.98 ± 14.68	60.30 ± 11.01	63.05 ± 15.05	.657	NS	NS	NS

KW test: Kruskal–Wallis test followed by pairwise Mann–Whitney U-test with a Bonferroni correction.

* $P < .05$,
† $P < .017$,
** $P < .01$,
*** $P < .001$,NS = Not significant, see Supplementary Table 1 for additional abbreviation.

that the hyperdivergent group presented with a narrower pharyngeal dimension than the normodivergent control group at the tip of the soft palate.[22] This underscores the significant role of anatomical landmarks in determining airway size in subjects with different vertical skeletal patterns.

The soft palate, which plays a crucial role in velopharyngeal closure, has been investigated in many studies involving OSA patients, and examination of this parameter suggests its potential utility as an OSA predictor.[5,23] However, in a prior study on non-OSA patients undergoing mandibular setback surgery, the treatment affected soft palate dimensions and the pharyngeal airway space.[24] The interaction between the soft palate and airway space highlights their interconnected nature, emphasising the importance of assessing both aspects in orthodontists' treatment planning. Our study revealed close associations between several soft palate dimensions and airway size, indicated by the negative correlations of the SPVL and SPL with airway volume parameters. Notably, SPL predicted RPV in the normodivergent group. In normodivergent individuals, SPL and SPVL/AIRL predicted TPV. Previous studies showed that reduction in airway area during sleep results from the posterior movement of the soft palate and thickening of the lateral pharyngeal walls, indicating that the soft palate significantly influences airway size.[25] Shigeta et al. reported that the length of the soft palate, as a percentage of the oropharyngeal airway length, was significantly larger in OSA patients than in controls.[5] These findings may explain why soft palate dimensions served as predictors of airway size in our study.

Intergroup analysis across all vertical skeletal groups revealed that hyperdivergent group showed smaller RPV, TPV and MinAx measurements compared to hypodivergent group, consistent with previous findings.[13,26] Al-Somairi et al.[26] found that hyperdivergent patients exhibited the lowest total pharyngeal airway volume and MinAx, potentially linked to mandibular deficiency and downward and backward mandibular rotations. While our subjects showed no statistically significant difference in the ANB angle between the groups, the SNB angle was lower in the hyperdivergent group (Supplementary Table 2), indicating a tendency toward a more skeletal class II relationship. Therefore, the observed differences among the groups may be related to mandibular retropositioning, suggesting the need for future studies on these parameters and sagittal jaw positions.

It is crucial to ascertain the anatomical risk factors contributing to airway constriction to understand the specific airway sites susceptible to narrowing. Our findings revealed that hyperdivergent individuals exhibited narrower PALA-SPT than hypodivergent and normodivergent individuals. In addition, a narrow PALA-C2 was observed in the hyperdivergent group as opposed to the hypodivergent group, consistent with previous 2-D cephalometric study.[22] However, hyperdivergent subjects had a longer airway length (AIRL) than hypodivergent subjects, consistent with a previous study showing an increase in airway length in hyperdivergent individuals compared with their counterparts.[27]

Several studies proposed that the soft palate is an indicator of OSA.[5,23] However, its essential role in velopharyngeal closure[3,4] suggests the need to expand investigation beyond OSA patients. In our study, hyperdivergent subjects showed

longer SPL than normodivergent and hypodivergent individuals. A cephalometric study on the soft palate and nasopharyngeal airway relationships in different rotation types revealed that the SPL experienced the most significant increase within the posterior rotation group.[4] These findings might support our results of a longer SPL in hyperdivergent subjects.

The lack of an accurate model for RGV, unlike the RPV and TPV models, may be attributed to the limited variability in the RGV data. Additionally, RGV measurements did not reveal significant differences among the hypodivergent, hyperdivergent and normodivergent groups. These findings suggest that future research should consider longitudinal designs with larger sample sizes to gain a more comprehensive understanding of airway dimensions and associated factors.

This study had some limitations. Female subjects were exclusively used because of the absence of adequate male data for meaningful analysis. This underscores the need for future longitudinal studies with large sample sizes incorporating both sexes. Additionally, while our study focused on vertical skeletal patterns, we recommend that future research with larger and more diverse samples also examine the relationships among soft palate dimensions, airway volume and sagittal skeletal patterns.

Conclusion

- Hypodivergent subjects had significantly higher MinAx, RPV and TPV compared to hyperdivergent subjects. Conversely, hyperdivergent individuals displayed longer SPL than both normodivergent and hypodivergent subjects.
- Among the eight predictive models developed, six exhibited strong performance, explaining 50%-77% of the variability in airway volumes. This underscores the models' robustness in predicting airway volumes based on soft palate dimensions and related parameters.
- The present study highlights the necessity of considering soft palate dimensions and airway characteristics in orthodontic treatment planning, especially for patients with varying vertical skeletal patterns. Understanding these relationships can help in predicting potential airway issues and customising treatment plans accordingly.

Conflict of interest

The authors have no conflict of interests to report.

Author contributions

Author contribution statement: JH contributed to conceptualization, methodology, software and the original draft preparation. SI, MN and KK contributed methodology, manuscript review and editing. KU, TM, MK, SH and TI contributed to conceptualization, software and methodology. HK contributed to conceptualization, methodology, review, editing and supervision. All authors have read and approved the final manuscript.

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Ethical information

The institutional ethics committee of Okayama University, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences and Okayama University Hospital approved this study (Rin1701-009). Informed consent for study participation and the use of patients' records for research purposes was obtained during the initial history assessment stage.

Data availability statement

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

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.identj.2024.09.023.

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