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ORIGINAL RESEARCH

Does tongue volume correlate with the upper airway and craniofacial structure of the skeletal Class III malocclusion pattern? A cross-sectional descriptive study in Vietnamese children

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Abstract

Background: This study aims to assess the impact of TV on craniofacial and maxillary airway morphology in Vietnamese children with skeletal Class III malocclusion using cone beam computed tomography (CBCT). **Methods**: A cross-sectional descriptive analysis was conducted on a total of 90 children (14–18 years old, 29 males and 61 females) from July 2023 to July 2024 with skeletal Class III malocclusion (angle formed by the A-nasion line and B-nasion line (ANB) ≤ 0, Wits appraisal ≤ 2), a body mass index of 18–25 kg/m^2, no history of orthodontic treatment or orthognathic surgery, and no history of cleft lip or palate treatment. Lateral cephalometric radiography and CBCT were performed for each participant to identify differences and analyze the correlation of airway dimensions and craniofacial structure with TV. **Results**: The study revealed significant gender variations in molar dimension, age, and craniofacial measures. Males had higher TV, OCV, and pharyngeal airway volume than females, but the TV/OCV ratio was not significant. Age raised most metrics, with TV, OCAV, and OCV positively correlated. Tongue volume may affect airway dimension, since TV demonstrated a significant positive correlation with different parts of. Some craniofacial measurements were significantly associated with TV, particularly those related to the line between ANS and PNS present for Palatal plane (ANS-PNS) and L7-7.Other measurements, such dental width, did not correlate with TV. **Conclusions**: The study found significant differences in TV and dental arch width among individuals with skeletal Class III malocclusion, a negative correlation between TV and interincisal angle, and a significant negative correlation between the TV/OCV ratio and pharyngeal and oral airway volumes, indicating that TV, OCV, and their ratio are important for preserving airway patency and early recognition of upper airway abnormalities.

Keywords

Airway volume; Cone beam computed tomography (CBCT); Malocclusion; Tongue volume (TV); Skeletal Class III; Vietnamese population

1. Introduction

The oral cavity connects the mouth and nose to the esophagus and larynx, consisting of the nasopharynx (NP), oropharynx (OP) and laryngopharynx [1, 2]. The oral cavity consists of two parts: the oral vestibule and the oral cavity proper, bounded by teeth and limited at the rear by surrounding folds. The maxilla and mandible serve as its bony boundaries, containing the anterior two-thirds of the tongue. The posterior one-third lies within the OP [2–4]. Tongue volume (TV) is a significant factor in biological mechanics, directly influencing occlusion, growth and facial morphology [5]. To maintain ideal occlusion and arch form, the TV and oral cavity should have a specific proportion. The equilibrium theory suggests that TV significantly influences tooth position and dental arch form, indicating its significant impact on alignment and occlusion [1, 6].

Previous studies on TV and oral cavity volume (OCV) have utilized various methods, including lateral cephalometric radiographs, alginate impressions, computed tomography (CT) and magnetic resonance imaging (MRI). However, these methods do not reveal complex three-dimensional (3D) variations in tongue and oral cavity shape. While cone beam computed tomography (CBCT) addresses this issue, it has other drawbacks, such as high radiation doses during scanning [7]. CT and MRI provide better insights into the 3D morphology of the tongue and oral cavity, but the shape and position of the tongue are significantly influenced by gravity. CBCT allows for scanning in an upright posture, which is an advantage that traditional CT devices cannot offer. CBCT is particularly useful for studying morphological structures within the oral cavity due to its relatively low cost and availability in dental clinics. It offers submillimeter resolution with high diagnostic image quality, short scan times (10–70 seconds), and reported radiation doses up to 15 times lower than in traditional scanning methods [8]. The upper airway structures can be delineated in CBCT through several techniques, such as cross-sectional imaging of the airway in the sagittal, axial and coronal planes [9, 10].

The relationship between TV and malocclusion has also been studied in adult patients, but reports on the existence of such a relationship remain inconsistent. A research in 2025 [11] found a correlation between tongue size and lower facial height in adult patients with obstructive sleep apnea syndrome (OSAS), suggesting that tongue size is closely associated with the position of the hyoid bone, craniofacial morphology, orthodontic treatment and OSAS. Gaffuri [12] (2021) found a significant correlation between TV and maxillary bone length, suggesting that TV may influence maxillary growth [1]. Hotwani [13] (2018) showed a significant difference in the tongue-to-mandible volume ratio (TV/MV) between children with obstructive sleep apnea (OSA) and controls. Changes in the size of the mandibular bone during certain orthognathic surgeries can lead to alterations in the airway dimensions. However, few studies have been conducted in the Mekong Delta region of Vietnam that provide an overview of the distribution and characteristics of malocclusion. Therefore, this study aimed to evaluate the impact of TV on craniofacial structure and maxilla airway morphology in skeletal Class III malocclusion using CBCT in Vietnamese children.

2. Materials and methods

2.1 Study participants

The inclusion criteria were as follows: participants aged 14 to 18 years, categorized into two age groups (14–16 and 17–18) based on physiological development, skeletal class III malocclusion (ANB angle of 0° or less, Wits appraisal of 2 mm or less), completely erupted initial permanent molars and upper permanent central incisors, a body mass index (BMI) of 18–25 kg/m^2, no history of orthodontic or orthognathic surgery, no cleft lip or palate treatment, dentition that shows mild crowding, a normal maxillary sagittal position, no apparent maxilla dental arch stenosis, no history of nasal cavity or sinus surgery, no subjective feelings of long-term nasal obstruction, and no acute maxilla respiratory tract infection in the previous 2 weeks.

2.2 Study methods

A cross-sectional descriptive analysis was conducted from July 2023 to July 2024 on a total of 90 children (14–18 years old, 29 boys and 61 girls) with skeletal Class III malocclusion (angle formed by the A-nasion line and B-nasion line ≤ 0, Wits appraisal ≤ 2), a BMI of 18–25 kg/m^2, no history of orthodontic treatment or orthognathic surgery and no history of cleft lip or palate treatment. Each participant was subjected to lateral cephalometric radiography and CBCT to identify differences and analyze the correlations of airway dimensions and craniofacial structure with TV. Analysis of variance (ANOVA) Test and Pearson's correlation coefficient were used for statistical analysis (Eqns. 1,2). The Can Tho University of Medicine and Pharmacy's Research Ethics Committee approved the present study (Approval Number 23.002/PCT-HDDD).

$$n = [(z_\alpha + z_\beta)/C]^2 + 3 \tag{1}$$

α: type 1 error probability ($\alpha = 0.05$).

z: value from the normal distribution; given 95% confidence, $z_\alpha = 1.96$; given 80% power ($\beta = 0.2$), $z_\beta = 0.84$.

$$C = 0.5 \times ln[(1 + r)/(1 - r)] \tag{2}$$

r: correlation coefficient.

In their article "Influence of TV, oral cavity volume and their ratio on upper airway: A cone beam computed tomography study", SS Rana (2020) found correlations between the NP and TV ($r = 0.29$, n = 90) [2].

2.3 Study procedures

2.3.1 CBCT scans

The imaging position was upright, with a predefined head position, where the reference horizontal plane was established by the Frankfort horizontal plane using a contour and digital gauge. Each participant was instructed to relax and place the tip of their tongue on the surface of the lower incisors, with the mandible in a natural interocclusal position. CBCT imaging was then performed. Patients were instructed not to swallow or breathe during imaging. The images were obtained using a Sirona Orthophos SL (Dentsply Sirona, Bensheim, HE, Germany), with a voxel base size of 0.08 mm, power lines and voltages of 3.0–16.0 mA and 60–90 kV, respectively, a scanning time of 14.9 seconds, and the capacity for cylindrical (field of view) measurements of 40–40 mm, 60–60 mm or 80–80 mm (according to the as low as reasonably achievable (ALARA) guidelines) [14].

2.3.2 Radiography measurements

The scanned CBCT images were processed using Mimics Research version 26.0 (Materialise NV, Leuven, Belgium) software on Samsung computer monitors (LF27T350FHEXXV, Samsung, Korea) to calculate the volume of the tongue and airway while scanning images were processed using GALILEOS software version 1.8 (Dentsply Sirona, Bensheim, HE, Germany) on the same type of Samsung monitor to measure the other distance parameters.

For volume analysis, the midsagittal plane was defined as the plane that passes through the anterior nasal spine (ANS), the posterior nasal spine (PNS), and the center of the chin tubercles. The palatal plane was defined as the plane passing through the ANS and PNS, which is perpendicular to the midsagittal plane. The plane passes through the two PNS points on either side, and the first cervical vertebra (C1) separates the NP above from the OP below (Fig. 1).

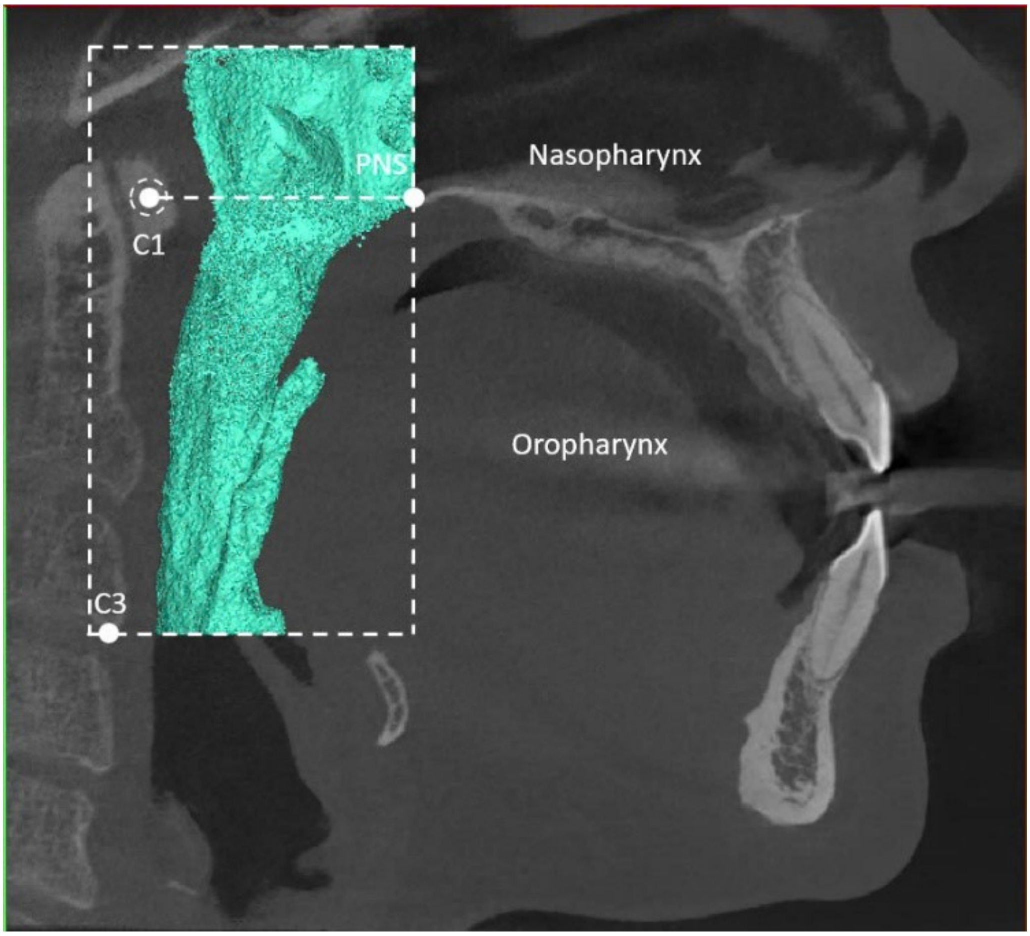

FIGURE 1. 3D image of the pharyngeal airway on CBCT. The region superior to the plane passes through the two points of the PNS on both sides and the first cervical vertebra (C1). The region inferior to the plane passes through the two points of the PNS on both sides and the first cervical vertebra (C1).

The volume of the oral cavity was found to be between −1000 and 200 Hounsfield units (HU). This included both the volume of the air and the volume of the soft tissues inside the cavity (Fig. 1). TV ranged from −200 to 200 HU. The top of the tongue was shaped by the dorsum of the tongue, and the bottom was shaped by lines connecting the frontmost point on the hyoid body (H) to the vallecula posterior and the frontmost point of the tongue, called the pogonion, which is the highest point on the lingual contour of the symphysis. Posteriorly, it follows the tongue's curvature in the OP. The tongue was manually separated with Hounsfield and gray values for the soft tissue scan tool. The inside of the tongue was smeared on each of the axial, coronal and sagittal planes, and the TV was calculated (Fig. 2).

To isolate the airway space, the threshold value was set to a range of −1024 to −100 HU. The pharyngeal airway volume was calculated by summing its maxillary and mandibular parts.

The contours of both the tongue and the oral cavity were manually traced on each tomographic slice. Specialized 3D image analysis software quantified both the TV and oral cavity airway volume (OCAV) after 3D image reconstruction. The oral cavity was defined as the region that encompasses both the oral cavity proper and the TV. The inter-molar distance was defined as the length from the lingual surface of one lateral lingual cusp to the corresponding cusp on the other molar. It was used to measure the distance between two opposing teeth in the dental arch. Similarly, the distance between premolars and canines was determined by measuring between the lingual surfaces of opposite teeth. The distances between the upper canine, second premolar, first molar and second molar were denoted as U3-3, U5-5, U6-6 and U7-7, respectively. Likewise, for the lower arch, the corresponding distances were L3-3, L5-5, L6-6 and L7-7. The interincisal angle measured the external angle formed by the long axes of the maxillary and mandibular central incisors. This angle reflects the degree of labial inclination or proclination of the incisors: the more proclined the incisors, the smaller the interincisal angle (Fig. 3) [13].

2.4 Measurement error

A single researcher performed all procedures to avoid errors in drawing and measuring operations on film. This researcher's consistency was tested as follows: after the previously estimated total samples were measured, 30 films were randomly selected to be plotted and measured again with the same method by the same person 30 days later (test-retest method). The data from the second measurement were compared with the first using Pearson's correlation coefficient.

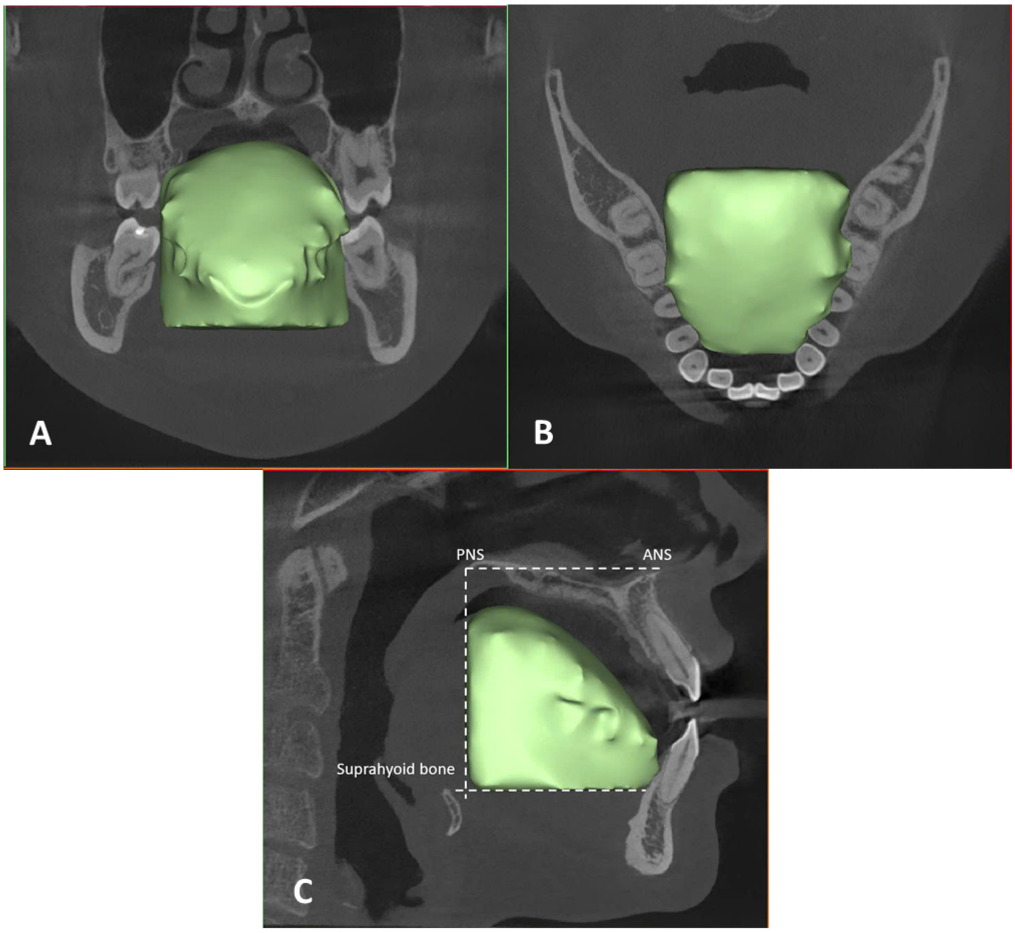

FIGURE 2. Assessment of TV on CBCT: (A) coronal plane, (B) axial plane and (C) sagittal plane. The plane that passes through the ANS and PNS was considered standard. The inferior border of the tongue was defined as the plane passing through the upper limit of the hyoid bone and parallel to the palatal plane. The posterior border of the tongue was determined by a line perpendicular to the PNS-ANS and a line parallel to the PNS-ANS and passing through the superior border of the hyoid bone. The front and upper parts followed the tongue's curvature in the OP. The tongue was manually separated with Hounsfield and gray values for the soft tissue scan tool. The inside of the tongue was smeared on each of the axial, coronal and sagittal planes, and the TV was calculated.

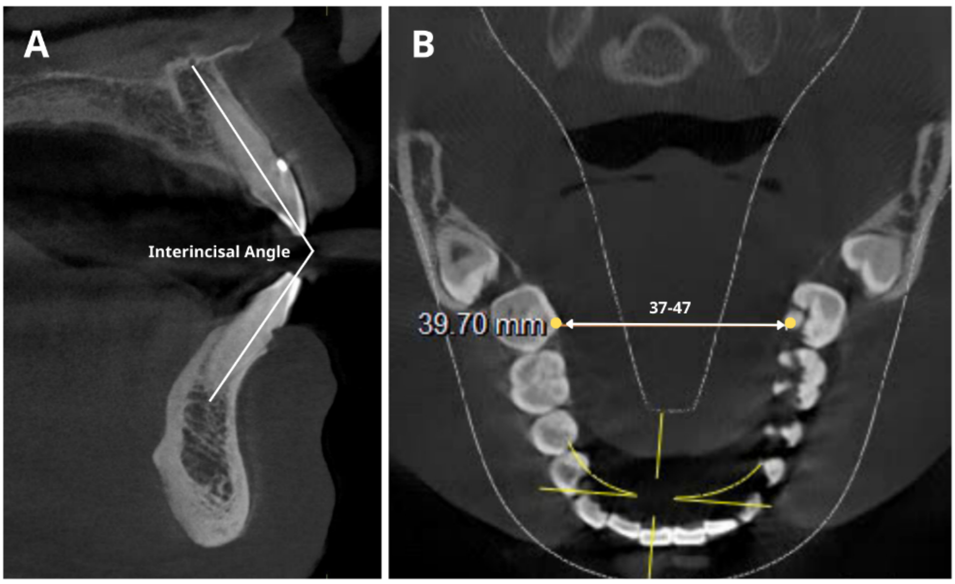

FIGURE 3. Anatomical measurements of the tongue on CBCT images: (A) cross-sectional plane and (B) axial plane.

2.5 Statistical analysis

The collected figures and data were imported into Microsoft Excel 2020 (Microsoft Corporation, Redmond, WA, USA) and Google Drive. A dental imaging technician obtained all radiographs. The results were evaluated by comparing and reformatting anatomical structural components with different planes in 3D space to obtain the most appropriate image, then evaluating and measuring the related parameters. Statistical analysis was performed using SPSS (version 20.0, IBM Corp., Chicago, IL, USA). The independent samples *t*-test, the Mann-Whitney U test, Pearson's correlation coefficient, Spearman's correlation coefficient, Two-way ANOVA and multiple linear regression were applied. For data to be deemed statistically significant, a threshold of $p \leq 0.05$ was defined.

3. Results

Differences between boys and girls: Most of the measured parameters showed statistically significant differences between male and female participants ($p < 0.05$), suggesting that there were differences in molar size between the two sexes. Age differences: Some parameters showed statistically significant differences between the 14–16 and 17–18 age groups, especially among girls. This suggests that molar size may change with age during this period (Table 1).

Gender and craniofacial measurements: There were statistically significant differences between the sexes ($p < 0.05$) in most measurements, except for the interincisal angle. Negative beta coefficients for sex variables showed that girls had smaller measurements than boys. Age and craniofacial measurements: There were no statistically significant differences between age groups ($p > 0.05$). Positive beta coefficients showed that most measurements, except for the interincisal angle, increase with age (Table 2).

Relationship between gender and volume measures: Boys had statistically a significantly larger TV, OCV and pharyngeal airway volume than girls ($p < 0.05$), suggesting that gender was a major factor influencing the size of these structures. There were no significant differences in the TV/OCV ratio between the genders. Relationship between age and volume measures: There were some differences in volume between the two age groups, but this was not consistent across all parameters. There were significant differences in the TV/OCV ratio between the two age groups, with the 17–18-year-old group having a higher ratio than the 14–16-year-old group ($p < 0.05$). Nasopharyngeal, oropharyngeal and total pharyngeal volume parameters also showed differences between the groups, although these were less clear than for the tongue and OCV parameters (Table 3).

A positive beta coefficient for TV and TV/OCV meant that the measure got better with age. On the other hand, negative beta coefficients for OCAV, OCV, NP, OP and total pharynx (TP) meant that the measure got worse with age (Table 4).

Variables with statistically significant differences between genders: L7-7, L6-6, L5-5, L3-3, U7-7, U6-6, U5-5, U3-3, OCV, NP, OP, TP. This suggests that there were differences in tooth and airway dimensions between genders. L6-6 showed statistically significant differences by age. This suggests that age may influence some tooth and airway dimensions (Table 5).

A link was found between the TV and the width of the dental arch. For most dental arch widths (ANS-PNS, L7-7, L6-6, L5-5, L3-3, U6-6, U5-5, U3-3), the link was positive and statistically significant, indicating that larger TVs were associated with wider dental arches. The strongest correlations were noted for ANS-PNS (0.467), L6-6 (0.442) and L5-5 (0.459). This suggests that the influence of the tongue was more pronounced in the molar and anterior regions of the maxilla. The correlation was weaker for U7-7 (0.203). A

TABLE 1. Cone beam computed tomography craniofacial measurements.

Measurements	Gender			Age (yr)		
	Male (Mean ± SD)	Female (Mean ± SD)	*p*	14–16 (Mean ± SD)	17–18 (Mean ± SD)	*p*
ANS-PNS (mm)	44.38 ± 2.77	40.99 ± 3.69	<0.001**	42.12 ± 3.06	42.06 ± 4.30	0.784**
L7-7 (mm)	42.43 ± 2.96	40.37 ± 2.83	0.002*	40.59 ± 3.10	41.45 ± 2.91	0.182*
L6-6 (mm)	36.25 ± 3.08	34.68 ± 3.22	0.031*	34.95 ± 3.19	35.41 ± 3.32	0.507*
L5-5 (mm)	31.83 ± 3.37	30.02 ± 3.58	0.025*	30.36 ± 3.19	30.83 ± 3.96	0.542*
L3-3 (mm)	29.17 ± 3.86	27.31 ± 3.62	0.008**	27.19 ± 3.98	28.58 ± 3.51	0.029**
U7-7 (mm)	46.94 ± 3.51	44.79 ± 3.67	0.010*	44.93 ± 4.10	46.00 ± 3.34	0.177*
U6-6 (mm)	41.42 ± 2.92	38.85 ± 3.37	0.001*	39.25 ± 3.71	40.09 ± 3.15	0.248*
U5-5 (mm)	36.54 ± 4.14	33.98 ± 4.47	0.008**	33.96 ± 4.27	35.60 ± 4.62	0.022**
U3-3 (mm)	35.80 ± 3.63	33.64 ± 4.35	0.006**	33.85 ± 4.02	34.79 ± 4.43	0.133**
Interincisal Angle (°)	133.26 ± 8.70	134.44 ± 8.19	0.535*	135.18 ± 8.29	133.04 ± 8.32	0.226*

**Independent samples t-test, **Mann-Whitney U test.*
SD: Standard deviation; ANS-PNS: Length of hard palate defined by shortest distance between ANS and PNS; Interincisal Angle: angle formed between the most prominent maxillary and mandibular incisors; U3-3: upper canine width; U5-5: upper second premolar width; U6-6: upper first molar width; U7-7: upper second molar width; L3-3: lower canine width; L5-5: lower second premolar width; L6-6: lower first molar width; L7-7: lower second molar width.

TABLE 2. Association of craniofacial measurements with gender and age.

Measurements	Unstandardized Coefficients Beta (B)	Standardized Coefficients Beta (B)	*p1*	R^2	Adjusted R^2	*F*	*p2*
ANS-PNS (mm)							
Gender	−3.421	−0.427	<0.001	0.181	0.163	9.636	<0.001
Age	−0.347	−0.046	0.635				
L7-7 (mm)							
Gender	−1.994	−0.311	0.003	0.116	0.095	5.698	0.050
Age	0.687	0.114	0.261				
L6-6 (mm)							
Gender	−1.543	−0.223	0.036	0.054	0.033	2.504	0.088
Age	0.331	0.677	0.636				
L5-5 (mm)							
Gender	−1.778	−0.232	0.029	0.058	0.036	2.662	0.075
Age	0.319	0.045	0.671				
L3-3 (mm)							
Gender	−1.745	−0.217	0.039	0.08	0.059	3.797	0.026
Age	1.240	0.165	0.115				
U7-7 (mm)							
Gender	−2.063	−0.259	0.014	0.087	0.066	4.159	0.019
Age	0.899	0.121	0.244				
U6-6 (mm)							
Gender	−2.504	−0.343	0.001	0.132	0.112	6.591	0.002
Age	0.635	0.093	0.357				
U5-5 (mm)							
Gender	−2.422	−0.252	0.016	0.097	0.076	4.659	0.012
Age	1.443	0.161	0.120				
U3-3 (mm)							
Gender	−2.087	−0.231	0.029	0.065	0.044	3.045	0.053
Age	0.763	0.090	0.387				
Interincisal Angle (°)							
Gender	0.981	0.055	0.605	0.020	−0.003	0.873	0.421
Age	−2.058	−0.124	0.248				

Multiple linear regression.
ANS-PNS: Length of hard palate defined by shortest distance between ANS and PNS; Interincisal Angle: angle formed between the most prominent maxillary and mandibular incisors; U3-3: upper canine width; U5-5: upper second premolar width; U6-6: upper first molar width; U7-7: upper second molar width; L3-3: lower canine width; L5-5: lower second premolar width; L6-6: lower first molar width; L7-7: lower second molar width. p1: T-test for significance of individual regression coefficients; p2: F-test for overall model significance.

positive, statistically significant correlation was found for the incisor angle (−0.172). Correlation between OP and dental arch width: The OP had a negative correlation with L7-7 (−0.45). This suggests that when the volume of the OP is large, the distance between the mandibular second molars tends to be smaller. Correlation between OCAV and dental arch width: Like TV, OCAV also had a positive, statistically significant correlation with most dental arch widths, which aligns with the fact that OCAV is closely related to the space occupied by the tongue. Strong correlations with ANS-PNS (0.463), L6-6 (0.464) and L5-5 (0.446) were observed. Correlation between TV/OCV and dental arch width: The TV/OCV ratio had a weaker correlation with dental arch width than either TV or OCAV alone. This suggests that the ratio itself is less directly reflective of dental arch development than absolute TV or OCV (Table 6).

TABLE 3. Tongue volume, oral cavity volume and pharyngeal airway volume on cone beam computed tomography.

Measurements	Gender			Age (yr)		
	Male	Female	*p*	14–16	17–18	*p*
TV (mm^3)	70,513.57 ± 15,502.42	50,011.04 ± 9426.77	<0.001**	54,689.45 ± 14,580.39	58,381.30 ± 15,525.92	0.198**
OCAV (mm^3)	13,216.06 ± 6568.55	11,013.88 ± 6121.26	0.141**	12,877.35 ± 6001.12	10,667.81 ± 6476.39	0.076**
OCV (mm^3)	83,729.64 ± 15,563.64	61,024.93 ± 10,715.63	<0.001**	67,566.80 ± 15,857.15	69,049.12 ± 16,936.03	0.695**
TV/OCV	0.84 ± 0.08	0.82 ± 0.09	0.346*	0.81 ± 0.09	0.85 ± 0.08	0.035*
NP (mm^3)	8835.36 ± 3417.13	8052.91 ± 3340.95	0.471**	8320.97 ± 3477.82	8290.46 ± 3299.15	0.831**
OP (mm^3)	19,357.30 ± 5077.77	15,714.02 ± 4741.75	0.001*	17,840.92 ± 4965.91	16,016.11 ± 5152.86	0.091*
TP (mm^3)	28,399.46 ± 7883.44	23,958.86 ± 7345.27	0.009**	26,435.6 ± 7662.64	24,432.85 ± 7814.13	0.104**

**Independent samples t-test, **Mann-Whitney U test.*
TV: tongue volume; OCAV: oral cavity airway volume; OCV: oral cavity volume; NP: nasopharynx; OP: oropharynx; TP: total pharynx.

TABLE 4. Association of tongue volume, oral cavity volume and pharyngeal airway volume with gender and age.

Measurements	Unstandardized Coefficients	Standardized Coefficients	*p1*	R^2	Adjusted R^2	*F*	*p2*
	Beta (B)	Beta (B)					
TV (mm^3)							
Gender	−20312.46	−0.632	<0.001	0.411	0.397	30.352	<0.001
Age	2013.38	0.067	0.420				
OCAV (mm^3)							
Gender	−2429.722	−0.181	0.086	0.063	0.042	2.939	0.058
Age	−2410.310	−0.192	0.069				
OCV (mm^3)							
Gender	−22742.18	−0.654	<0.001	0.426	0.413	32.258	<0.001
Age	−396.23	−0.012	0.882				
TV/OCV							
Gender	−0.015	−0.082	0.437	0.056	0.034	2.581	0.081
Age	0.036	0.215	0.043				
NP (mm^3)							
Gender	−791.51	−0.110	0.305	0.012	−0.011	0.534	0.588
Age	−95.91	−0.014	0.894				
OP (mm^3)							
Gender	−3845.55	−0.353	0.001	0.156	0.136	8.025	0.001
Age	−2142.58	−0.210	0.036				
TP (mm^3)							
Gender	−4666.07	−0.282	0.007	0.096	0.075	4.616	0.012
Age	−2388.32	−0.155	0.135				

Multiple linear regression.
TV: tongue volume; OCAV: oral cavity airway volume; OCV: oral cavity volume; NP: nasopharynx; OP: oropharynx; TP: total pharynx. p1: T-test for significance of individual regression coefficients; p2: F-test for overall model significance.

TABLE 5. Craniofacial measurements, tongue volume, oral cavity volume and pharyngeal airway volume with gender and age.

	Sum of square	*df*	Mean Squares	*F*	*p*
ANS-PNS					
Age	17.04	1	17.04	1.454	0.231
Gender	240.89	1	240.89	20.55	<0.001
Age × Gender	1.492	1	1.492	0.13	0.772
L7-7					
Age	0.16	1	0.16	0.02	0.889
Gender	81.65	1	81.65	10.02	0.002
Age × Gender	23.58	1	23.58	2.89	0.093
L6-6					
Age	48.59	1	48.59	5.02	0.028
Gender	65.27	1	65.27	6.75	0.011
Age × Gender	29.82	1	29.82	29.82	0.083
L5-5					
Age	36.68	1	36.68	3.00	0.087
Gender	80.08	1	80.08	6.55	0.012
Age × Gender	12.87	1	12.87	1.05	0.308
L3-3					
Age	44.23	1	44.23	3.30	0.073
Gender	86.58	1	86.58	6.46	0.013
Age × Gender	0.59	1	0.59	0.04	0.835
U7-7					
Age	5.79	1	5.79	0.44	0.507
Gender	79.86	1	79.86	6.11	0.015
Age × Gender	14.05	1	14.05	1.07	0.303
U6-6					
Age	4.12	1	4.12	0.40	0.529
Gender	132.85	1	132.85	12.92	0.001
Age × Gender	36.95	1	36.95	3.59	0.061
U5-5					
Age	66.65	1	66.65	3.58	0.062
Gender	158.30	1	158.30	8.50	0.005
Age × Gender	39.35	1	39.35	2.11	0.150
U3-3					
Age	0.07	1	0.07	0.004	0.948
Gender	89.72	1	89.72	5.12	0.026
Age × Gender	0.004	1	0.004	<0.001	0.987
Interincisal Angle (°)					
Age	76.29	1	76.29	1.08	0.301
Gender	44.23	1	44.23	0.63	0.431
Age × Gender	27.88	1	27.88	0.395	0.531
OCAV (mm^3)					
Age	11,707,279.36	1	11,707,279.36	0.299	0.586
Gender	103,609,431	1	103,609,431	2.65	0.107
Age × Gender	88,353,509.04	1	88,353,509.04	2.26	0.137

TABLE 5. Continued.

	Sum of square	*df*	Mean Squares	*F*	*p*
OCV (mm^3)					
Age	22,899,419.3	1	22,899,419.3	1.48	0.227
Gender	10,344,783,367	1	10,344,783,367	66.93	<0.001
Age × Gender	282,819,295	1	282,819,295	1.83	0.180
NP (mm^3)					
Age	454,447.31	1	454,447.31	0.039	0.843
Gender	10,934,664.4	1	10,934,664.4	0.95	0.332
Age × Gender	6,672,357.06	1	6,672,357.06	0.58	0.449
OP (mm^3)					
Age	1,093,447.29	1	1,093,447.29	0.046	0.831
Gender	247,473,783.6	1	247,473,783.6	10.33	0.002
Age × Gender	10,236,984.9	1	10,236,984.9	0.43	0.515
TP (mm^3)					
Age	3,135,434.57	1	3,135,434.57	0.55	0.816
Gender	364,804,713.5	1	364,804,713.5	6.372	0.013
Age × Gender	52,875,413.86	1	52,875,413.86	0.924	0.339

Two-way ANOVA.
df: Degrees of freedom; ANS-PNS: Length of hard palate defined by shortest distance between ANS and PNS; Interincisal Angle: angle formed between the most prominent maxillary and mandibular incisors; U3-3: upper canine width; U5-5: upper second premolar width; U6-6: upper first molar width; U7-7: upper second molar width; L3-3: lower canine width; L5-5: lower second premolar width; L6-6: lower first molar width; L7-7: lower second molar width; TV: tongue volume; OCAV: oral cavity airway volume; OCV: oral cavity volume; NP: nasopharynx; OP: oropharynx; TP: total pharynx.

TABLE 6. Correlation of tongue volume and oral cavity volume with dental arch width on cone beam computed tomography radiographs.

	ANS-PNS	L7-7	L6-6	L5-5	L3-3	U7-7	U6-6	U5-5	U3-3	Interincisal Angle
TV	0.467**	0.429*	0.442*	0.459*	0.318**	0.203*	0.340*	0.330**	0.300**	−0.172*
OP	0.047**	−0.450*	−0.105*	−0.094*	−0.063**	−0.107*	−0.028*	−0.093**	0.011**	−0.019*
OCAV	0.463**	0.415*	0.464*	0.446*	0.293**	0.231*	0.330*	0.258**	0.310**	−0.129*
TV/OCV	0.150**	0.135*	0.058*	0.128*	0.181**	0.014*	0.149*	0.235**	0.099**	−0.149*

**Pearson's correlation coefficient, **Spearman's correlation coefficient.*
ANS-PNS: Length of hard palate defined by shortest distance between ANS and PNS; Interincisal Angle: angle formed between the most prominent maxillary and mandibular incisors; U3-3: upper canine width; U5-5: upper second premolar width; U6-6: upper first molar width; U7-7: upper second molar width; L3-3: lower canine width; L5-5: lower second premolar width; L6-6: lower first molar width; L7-7: lower second molar width; TV: tongue volume; OP: oropharynx; OCAV: oral cavity airway volume; OCV: oral cavity volume.

TV had a significant positive correlation with the OCAV and the total OCV. Thus, as TV increases, the volumes of the associated structures in the oral cavity also tend to increase. TV also had a significant positive correlation with different parts of the pharyngeal airway (NP, OP and TP). This suggests a relationship between tongue size and the total size of the airway. The TV/OCV ratio had a significant negative correlation with different parts of the pharyngeal airway. This suggests that as the ratio of TV to OCV increases (*i.e.*, the tongue is larger than the oral cavity), the airway tends to narrow (Table 7).

Relationship between craniofacial measurements and TV: Some craniofacial measurements were significantly associated with TV, especially those related to ANS-PNS and L7-7. On the other hand, other measurements, such as dental width at different positions, did not have a clear relationship with TV. Relationship between craniofacial measurements and OCV: Some craniofacial measurements were significantly associated with OCV, especially those related to ANS-PNS, L7-7 and L6-6. Other measurements, such as dental width at different positions, did not have a clear relationship with OCV. Every *p*-value for the relationship between TV/OCV and measurements of the head and face (ANS-PNS, L7-7, L6-6, L5-5, L3-3, U7-7,

TABLE 7. Correlation between tongue volume, oral cavity volume and pharyngeal airway volume.

	NP	OP	TP
TV	0.113**	0.270**	0.235**
OCAV	0.302**	0.444**	0.478**
OCV	0.258**	0.446**	0.437**
TV/OCV	−0.264**	−0.328*	−0.355**

**Pearson's correlation coefficient, **Spearman's correlation coefficient.*
TV: tongue volume; OCAV: oral cavity airway volume; OCV: oral cavity volume; NP: nasopharynx; OP: oropharynx; TP: total pharynx.

U6-6, U5-5, U3-3 and the interincisal angle) was greater than 0.05. Thus, statistical evidence was insufficient to conclude a significant linear relationship between TV/OCV and each craniofacial measurement. The *p*-values for the relationship between TV/OCV and pharyngeal airway volume (NP, OP and TP) were also higher than 0.05, which means there was no statistically significant link. Beta values: The beta values were all quite small, indicating that the effect of TV/OCV on the dependent variables was not large, even when statistically significant overall (Table 8).

The figure illustrated the relationship between tongue volume (TV) and total pharyngeal volume (TP). The linear regression line showed an increasing trend: as tongue volume increases, pharyngeal volume also increases. This suggested a positive relationship between these two variables (Fig. 4).

The figure illustrated the relationship between tongue volume to oral cavity volume ratio (TV/OCV) and total pharyngeal volume (TP). The linear regression line shows a decreasing trend as the TV/OCV ratio increases; pharyngeal volume tends to decrease. This suggested that as the tongue occupies a larger proportion of the oral cavity, it may reduce the space for the airway (Fig. 5).

4. Discussion

Patients are increasingly focusing on aesthetic concerns and striving for a flawless appearance. As a result, the number of patients seeking consultations and desiring orthodontic and facial skeletal corrections has risen. Moreover, epidemiological studies on a variety of populations and ethnic groups show that both the number of people who have problems with their teeth fitting together properly and the number of people who want to get orthodontic treatment are growing. S.S. Rana's 2020 study highlighted a correlation between TV and craniofacial structural shape and the patency of the airway [2].

The study found that CBCT, a 3-dimensional method, is a reliable and reproducible alternative for evaluating tongue and oral cavity volumes. It can accurately measure the tongue space, including volume, oral cavity and air capacity. This method can also help identify soft tissue boundaries. Most authors established a standardized protocol to reduce variability, as small changes in the patient's head or tongue position could affect measurement accuracy. CBCT exhibits a favorable intraclass correlation coefficient, making it accurate, reliable and reproducible in evaluating tongue and oral cavity volumes. This makes CBCT a promising alternative for assessing tongue and oral cavity volumes [7].

The evaluation of pharyngeal airways has evolved from traditional two-dimensional lateral cephalograms to advanced three-dimensional analyses thanks to technological advancements. CBCT is now widely used because of its favorable risk-benefit profile, especially regarding its cost-effectiveness and low radiation exposure [15]. CBCT is very helpful for getting three-dimensional pictures of the head and face, including clear pictures of the airways, it is important to be aware of and talk about the ethical issues that come up with ionizing radiation exposure, especially in children. This increased sensitivity increases the risk of long-term effects from radiation exposure, such as the development of cancer. The ALARA (As Low as Reasonably Achievable) principle is fundamental. This principle requires that the potential diagnostic and therapeutic benefits be sufficient to justify the use of ionizing radiation in children. To ensure compliance with the ALARA (As Low as Reasonably Achievable) principles, it is essential to implement several strategies. First, there should be a strong clinical justification for using CBCT, as the data obtained from this imaging is vital for accurate diagnosis and effective treatment planning. It is essential to optimize radiation dose reduction while maintaining high-quality diagnostic images. Optimizing the Field of View (FOV): This process involves strictly limiting the FOV to the relevant areas, which should only include the skull and facial structures pertinent to the clinical study. And, implementing low-dose protocols: These techniques involve optimizing exposure parameters, which include reducing tube current and shortening exposure times while still ensuring diagnostic image quality scans.

Although CBCT has several advantages, such as providing three-dimensional visualization of cranial structures and enhancing physicians' assessment of airways. Alternative imaging modalities should be considered whenever possible. Even though lateral cephalograms can only show images in two dimensions, they are a low-radiation option for checking the bones and soft tissues for the first time. Panoramic radiographs provide a general overview of the dentition but have limited utility in assessing airway dimensions. Magnetic Resonance Imaging (MRI) is better at showing soft tissues and giving three-dimensional information without using ionizing radiation. However, it is expensive, hard to get to, and people who are afraid of being squished or who have metal implants may not be able to get an MRI. Therefore, the judicious selection of imaging modality should be based on a careful risk-benefit assessment, considering the patient's age, clinical indication, and the specific information required for diagnosis and treatment planning.

The significant relationship between tongue volume and airway dimensions, especially in skeletal Class III malocclusion, underscores the need to evaluate tongue size and function during the initial diagnostic assessment and treatment planning [15, 16]. This information may assist in treatment planning and influence the selection of treatment methods. Consider myofunctional therapy or surgical surgery in conjunction with orthodontic treatment in cases of significant tongue hypertrophy. Comprehending the relationship among tongue size, air-

TABLE 8. Association of tongue volume, oral cavity airway volume, oral cavity volume and TV/OCV with craniofacial measurements and pharyngeal airway.

Measurements	Unstandardized Coefficients	Standardized Coefficients	p	R^2	Adjusted R^2	F
	Beta (B)	Beta (B)				
TV (mm^3)						
ANS-PNS (mm)	1275.92	0.318	0.002	0.482	0.393	5.44 $p < 0.001$
L7-7 (mm)	1338.83	0.267	0.050			
L6-6 (mm)	574.18	0.123	0.430			
L5-5 (mm)	−185.16	−0.044	0.776			
L3-3 (mm)	573.49	0.144	0.158			
U7-7 (mm)	66.797	0.017	0.897			
U6-6 (mm)	−219.19	−0.05	0.757			
U5-5 (mm)	616.41	0.184	0.100			
U3-3 (mm)	−217.86	−0.061	0.543			
Interincisal Angle (°)	−50.95	−0.028	0.779			
NP (mm^3)	0.246	0.055	0.812			
OP (mm^3)	1.663	0.563	0.187			
TP (mm^3)	−0.655	−0.336	0.546			
OCAV (mm^3)						
ANS-PNS (mm)	215.05	0.128	0.256	0.304	0.185	2.555 $p = 0.006$
L7-7 (mm)	−393.11	−0.188	0.231			
L6-6 (mm)	567.69	0.292	0.110			
L5-5 (mm)	−99.56	−0.057	0.752			
L3-3 (mm)	−295.64	−0.177	0.134			
U7-7 (mm)	298.55	0.177	0.235			
U6-6 (mm)	−52.42	−0.029	0.879			
U5-5 (mm)	−122.87	−0.088	0.495			
U3-3 (mm)	68.69	0.046	0.692			
Interincisal Angle (°)	74.196	0.098	0.400			
NP (mm^3)	0.860	0.458	0.089			
OP (mm^3)	0.968	0.784	0.114			
TP (mm^3)	−0.558	0.523	0.289			
OCV (mm^3)						
ANS-PNS (mm)	1490.97	0.343	<0.001	0.558	0.483	7.392 $p < 0.001$
L7-7 (mm)	945.72	0.174	0.163			
L6-6 (mm)	1141.87	0.227	0.119			
L5-5 (mm)	−284.72	−0.063	0.661			
L3-3 (mm)	277.85	0.064	0.492			
U7-7 (mm)	365.34	0.084	0.48			
U6-6 (mm)	−271.62	−0.057	0.701			
U5-5 (mm)	493.54	0.136	0.186			
U3-3 (mm)	−149.17	−0.039	0.677			
Interincisal Angle (°)	23.251	0.012	0.898			
NP (mm^3)	1.106	0.228	0.286			
OP (mm^3)	2.631	0.823	0.038			
TP (mm^3)	−1.213	−0.576	0.264			

TABLE 8. Continued.

Measurements	Unstandardized Coefficients	Standardized Coefficients	p	R^2	Adjusted R^2	F
	Beta (B)	Beta (B)				
TV/OCV						
ANS-PNS (mm)	0.001	0.061	0.601			
L7-7 (mm)	0.007	0.255	0.117			
L6-6 (mm)	−0.005	−0.191	0.309			
L5-5 (mm)	0.001	−0.012	0.946			
L3-3 (mm)	0.004	0.187	0.125			
U7-7 (mm)	−0.004	−0.173	0.259			
U6-6 (mm)	0.001	0.057	0.766	0.258	0.131	2.036 $p = 0.029$
U5-5 (mm)	0.003	0.172	0.197			
U3-3 (mm)	−0.001	−0.064	0.597			
Interincisal Angle (°)	−0.001	−0.078	0.513			
NP (mm^3)	−6.313	−0.251	0.365			
OP (mm^3)	−4.511	−0.272	0.592			
TP (mm^3)	1.212	0.111	0.868			

Multiple linear regression.

ANS-PNS: Length of hard palate defined by shortest distance between ANS and PNS; Interincisal Angle: angle formed between the most prominent maxillary and mandibular incisors; U3-3: upper canine width; U5-5: upper second premolar width; U6-6: upper first molar width; U7-7: upper second molar width; L3-3: lower canine width; L5-5: lower second premolar width; L6-6: lower first molar width; L7-7: lower second molar width; TV: tongue volume; OCAV: oral cavity airway volume; OCV: oral cavity volume; NP: nasopharynx; OP: oropharynx; TP: total pharynx.

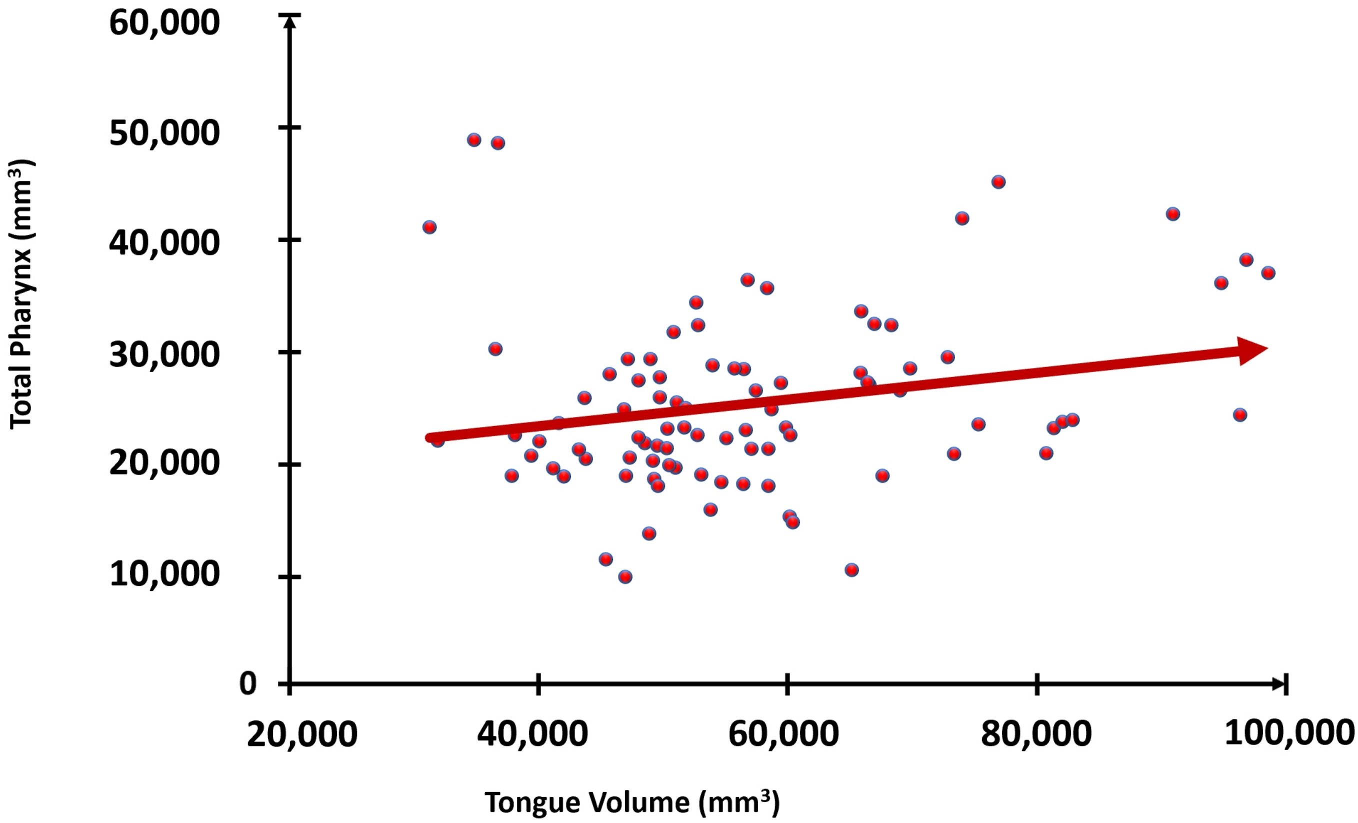

FIGURE 4. Scatter plot denoting the correlation between TV and total pharynx.

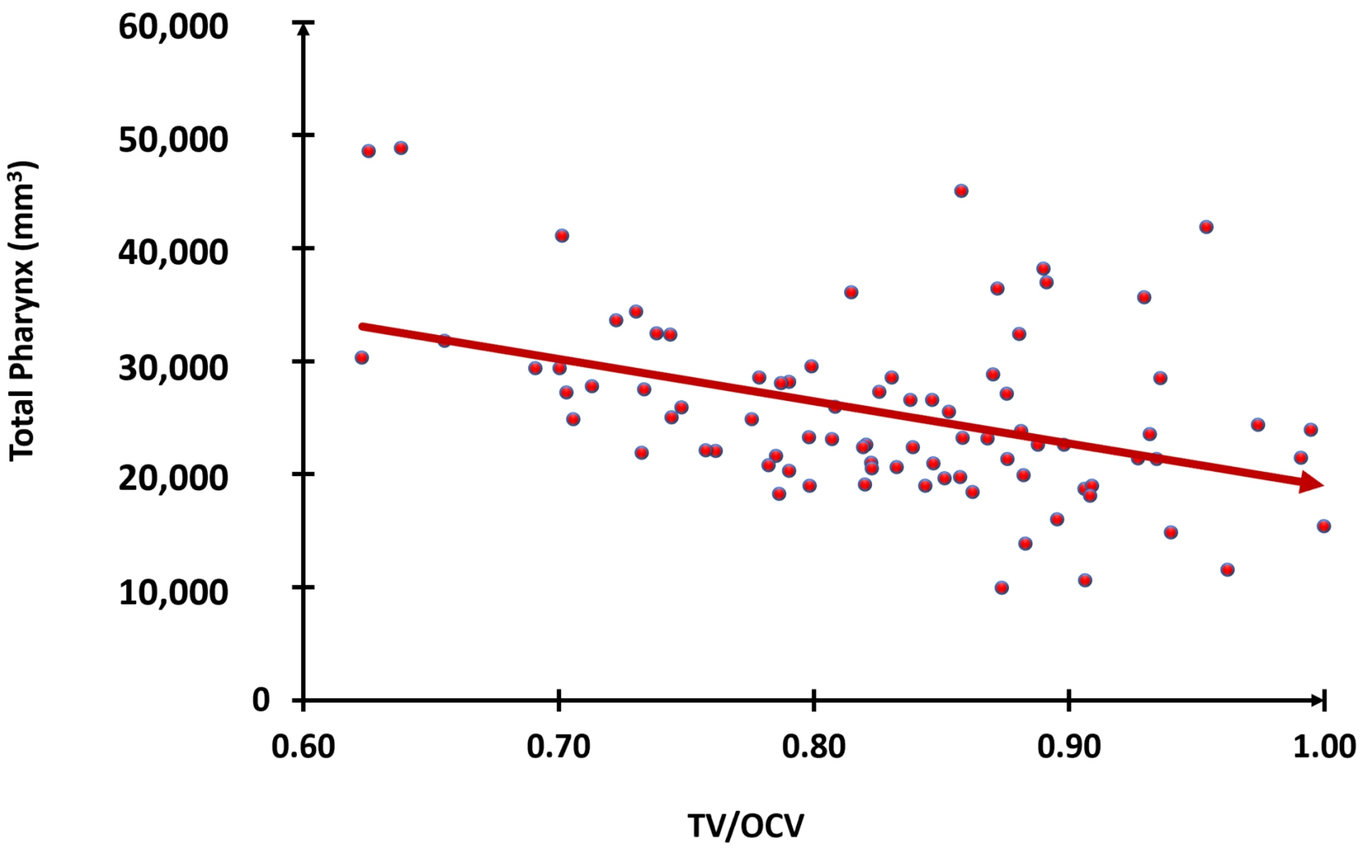

FIGURE 5. Scatter plot denoting the correlation between TV/OCV and total pharynx. TV/OCV: tongue volume/oral cavity volume.

way dimensions and skeletal malocclusion might facilitate the prediction of treatment results. Patients with enlarged tongues may need more comprehensive therapy or face an increased chance of recurrence post-treatment. This knowledge may facilitate the establishment of pragmatic treatment objectives and the management of patient anticipations [14, 17].

The strong correlation among tongue size, airway dimensions, and craniofacial morphology highlights the need for an integrative treatment strategy. Cooperation among orthodontists, sleep specialists, speech-language pathologists and other experts may guarantee thorough and successful treatment of patients with skeletal Class III malocclusion and possible airway complications [18, 19]. It is important to keep track of the tongue size and airway measurements, especially in people with skeletal Class III malocclusion and a history of airway obstruction, in order to see how well treatment is working and find any potential long-term problems [20].

The tongue plays a critical role in upper airway patency and consequently, in the development of OSA [21]. The tongue's size, position and interaction with surrounding structures significantly influence the severity and location of airway obstruction. An enlarged tongue, for instance, can encroach on the pharyngeal airway, leading to increased resistance to airflow and ultimately, episodes of apnea. Furthermore, the tongue's volume and position exert a profound influence on dental occlusion and facial skeletal development. Several structures in the mouth hold the tongue in place. These include the mandibular arch, the palate and the oropharyngeal muscles.

Tongue surgery in patients with OSA aims to reduce excessive TV due to genetic conditions like Beckwith-Wiedemann syndrome [22]. CBCT scans assess the tongue's position and volume, allowing for the selection of patients for retroglossal area surgery. Most scanners are designed for standing or seated patients but can also be used in prone, supine or lateral recumbent positions. Positional factors can change the shape of soft tissues in the upper airway. This is why scanners made for horizontal image acquisition may help people with sleep deprivation disorder. Mandibular advancement devices have been developed to target the anatomical structure of the tongue, as it is susceptible to collapse in supine positions [23, 24].

Assessment of subjective criteria, such as tongue shape and protrusion, speech impediments, swallowing issues and respiratory challenges, often establishes the diagnosis [25]. The protrusion of the tongue through the lips is the primary indicator of macroglossia. When the enlarged tongue is palpated, it appears clinically normal, and tongue pressure causes the alveolar bone to thin. Protrusion of the tongue may result in diastemas, forward inclination of the upper and lower incisors, and anterior open bite [26]. Additional clinical findings in patients with macroglossia may include Temporomandibular joint dysfunction (TMJ) disorders and maxillofacial issues. Macroglossia can lead to several health problems, such as noisy breathing, breathing problems like upper airway obstruction, trouble feeding that leads to malnutrition and infections on the tongue from its prolonged exposure to air. Skeletal Class III disharmony, an enlarged gonial angle, and an anterior open bite can all be caused by sticking out the tongue. All these problems can affect bone growth. Tulley defined tongue thrust as the position of the tongue between the dental arches that occurs when the tongue tip slides forward between the teeth to touch the lower lip during speech or tooth development. This condition leads to an open bite and the forward positioning of the front teeth segment [26].

Other research has shown that pharyngeal structures experience rapid growth up until the age of 13, followed by a period of stability from ages 14 to 18, during which there is minimal variation in airway size within this age group [27]. In the present study, participants aged 14 to 18 were sampled to standardize the age variable and reduce the influence of growth-related changes.

In this study, all the indices mentioned above showed a positive correlation with TV, except for the interincisal angle. Statistical analysis confirmed that these differences were significant. Tancan Uysal (2011) also found a significant inverse correlation between lower incisor abnormalities and TV. This suggests that deviations in the alignment or position of the lower incisors may be associated with reduced or altered TV [28]. Analyzing by gender, the average value of this index was higher in boys than in girls. However, the difference in the interincisal angle index was not statistically significant. In contrast to these findings, a study by Tancan Uysal (2011) concluded that TV has minimal impact on the width and length of the mandible, as well as less influence on the relationship between the incisors and the incisor angle relative to the mandibular plane. Additionally, the study identified a significant inverse correlation between lower incisor abnormalities and TV in male subjects. However, TV was comparable between male and female subjects [28]. Variations in the study population, specifically focusing on individuals with skeletal Class III malocclusion who present distinct craniofacial characteristics compared to other populations, can account for this difference. Their unique anatomical features may influence the outcomes, generating different results from studies that include other malocclusion types or more general populations [29].

The current study revealed a significant gender difference in tongue volumes, which aligns with most similar research, except for the study conducted by Uysal T. *et al*. [28] The male groups from Skeletal Class III and the control group exhibited significantly larger tongue volumes compared to the female groups. The tongue volumes measured in our control group are consistent with findings from other studies. Using MRI, Liégeois *et al*. [30] found that the tongue volumes of male and female groups were similar. N Ihan Hren [31] specifically measured tongue volumes using MRI for male adults with normal occlusion. Do *et al*. [32] reported significantly larger tongue volumes in a group of patients without sleep-disordered breathing, which contrasts with the current study. This discrepancy is likely due to the artificial determination of the posterior border of the tongue using CBCT images, which only measured the anterior portion of the mobile tongue.

In a study on arch width changes from 6 weeks to 45 years of age by Samir, a reduction in the L3-3 distance was observed during the period from 13 to 26 years [33]. However, our study found that the L3-3 distance increased in the 14–18-year age range. The lack of clarity regarding the developmental phase in the aforementioned study prevents direct comparison with our findings. Nevertheless, despite the closure of spaces between teeth during the permanent dentition phase, a width expansion of the dental arch occurs.

TV showed a stronger correlation with the lowest saturation during sleep. The proposed method allows for the generation of high-quality CBCT images, facilitating accurate measurement of TV and OCV. This was a simple and effective method with significant potential for widespread application in diagnosing abnormalities in tongue size [21]. Xuefang Ding [7] (2018) reported a mean TV of 47.07 $\pm$ 7.08 cm^3, with the mean OCAV and OCV being 4.40 $\pm$ 2.78 cm^3 and 51.47 $\pm$ 6.46 cm^3, respectively. Similarly, Balaji Rajkumar [6] (2021) reported a mean OCAV of 3.0 $\pm$ 1.1 cm^3 and a mean TV of 34.3 $\pm$ 6.6 cm^3. These results were lower than the values obtained in the present study. However, the mean TV/OCV ratio was 91 $\pm$ 5%, which was higher than the ratio reported in this study. On the other hand, when analyzing the influence of craniofacial measurements and airway volume on OCV, it is evident that the strongest influence is on OCV. This analysis demonstrates that the impact of craniofacial measurements on the overall OCV is more pronounced than the influence of individual components such as the tongue or airway. Evaluation of TV also revealed a positive influence, with ANS-PNS and L7-7 showing a statistically significant positive correlation with TV.

SS Rana *et al*. [2] (2020) found a significant negative correlation between TV/OCV and the OP ($r = -0.51$; $p = 0.04$), as well as between TV/OCV and OCAV ($r = -0.74$; $p = 0.002$). Additionally, the present study revealed a significant positive correlation ($r = 0.65$; $p = 0.009$) between TV/OCV and TV. This suggests that TV, OCV and their ratio influence the patency of the OP. In clinical practice, abnormal tongue size may serve as an early diagnostic indicator for upper airway abnormalities [5].

Nasim Shams [1] (2022) looked at old CBCT scans of 202 patients over 17 years old who had never been hurt or had any problems with their nose or throat and had never had any orthodontic or orthodontic treatments. The group included 129 women and 73 men with a mean age of 36.24 $\pm$ 14.61 years. The mean nasal pharyngeal volumes were 4.88 $\pm$ 1.49, 4.80 $\pm$ 1.43 and 5.04 $\pm$ 1.60 mm^3 for the total sample, women and men, respectively. Racial differences were suggested as a reason for the difference in results compared to our study. However, both studies found no significant gender differences in the nasopharyngeal volume.

Shoaleh Shahidi [34] (2016) found that in healthy adults, the pharyngeal airway had an average volume of 23.4 $\pm$ 8.7 cm^3. The superior component had an average volume of 9.7 $\pm$ 2.3 cm^3, and the inferior component had an average volume of 13.7 $\pm$ 7.2 cm^3. Similarly, Sirwan Fernandez Gurani [35] (2016) reported an oropharyngeal volume in the natural head position of 7221 $\pm$ 3494 mm^3. These results are consistent with our findings.

This study shows that the upper airway is affected by the tongue's volume, the oral cavity's volume and their ratio. TV/OCV has the potential to diagnose OSA and facilitate tongue removal in cases of macroglossia. This study is limited by its small sample size, the wide age range of evaluated subjects, and its failure to measure the tongue or OCV based on the patient's skeletal relationships and growth pattern, which can also affect upper airway size. To learn more about the connection between these body measurements and OSA, future studies should include a bigger and more evenly distributed sample. Longitudinal studies could also show how changes in tongue and mouth size over time affect how airways move and how well treatments work. Thus, a more comprehensive approach that considers individual anatomical variations and their implications for airway management is warranted.

5. Conclusions

The upper airway, craniofacial structure and TV of the skeletal Class III pattern were all directly linked in this study. The analysis of gender's and age's influence on the airway showed significant differences in airway parameters between boys and girls, as well as some changes with age. Boys had larger airways than girls, which may be related to differences in body size and anatomical structure between the sexes. Skeletal and tongue growth during adolescence may contribute to the changes in the TV/OCV ratio with age. The results show the importance of these parameters for detecting upper airway problems early on. These problems are linked to TV and landmarks on the skull and face that are part of the Class III malocclusion pattern, stressing how important it is for the mandible, tongue and pharyngeal airway volume to be compensated for in orthodontic treatment outcomes. Knowledge of these parameters and their links will help with orthodontic diagnosis and treatment planning and avoid recurrence after orthodontic treatment, especially when dentofacial orthopedic interventions and a referral to an Ear, Nose, and Throat (ENT) specialist are needed.

AVAILABILITY OF DATA AND MATERIALS

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

AUTHOR CONTRIBUTIONS

LNL and TTNN—collected and analyzed the data. LNL, TTNN, LTT, DTT, KVPL, TTD and KNT—designed the research study and wrote the manuscript. LNL, DTT, KNT and KVPL—reviewed and edited the manuscript. All authors read and approved the final version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This retrospective study was conducted according to the guidelines of the Declaration of Helsinki and all procedures performed were following the Ethics Committee of the University of Medicine and Pharmacy of Can Tho University in Biomedical Research No: 23.002/PCT-HDDD. Consent was obtained from the parents or guardians for the use of all images of children in the manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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