


## ORIGINAL RESEARCH

## Three-dimensional cone beam computed tomography analysis of craniofacial phenotype in nonobese apneic young adults

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## Abstract

**Objective:** The obstructive sleep apnea (OSA) syndrome with its various phenotypes, as assessed by the apnea-hypopnea index (AHI), has become a major public health issue. While physicians are regularly faced with a variety of patients with OSA complaints, they may not be aware that OSA in nonobese young adults remains a largely underinvestigated topic. It is hypothesized that, in these subjects, facial bone volumes are smaller than in healthy adults.**Methods:** This cross-sectional, nonrandomized, controlled study was designed to compare the 3D cephalometric analysis of bone and craniofacial soft tissues in a group of 23 nonobese apneic (AHI  $\geq 15$ ), young (18–35 years) adults and in a control group of 23 nonapneic (AHI  $< 15$ ) healthy subjects by using cone beam computed tomography (CBCT). All subjects were Caucasian and underwent a sleep examination in the Sleep Clinic of the University Hospital of Liege.**Results:** The two groups were comparable except for age and medications. The maxillary bone volume ( $23.2 \pm 4.6 \text{ cm}^3$  vs.  $24.8 \pm 2.9 \text{ cm}^3$ ) and the mandibular bone volume ( $44.0 \pm 6.4 \text{ cm}^3$  vs.  $46.9 \pm 5.2 \text{ cm}^3$ ) adjusted for demographic and biometric characteristics were significantly smaller in OSA subjects than in controls. OSA subjects had also a smaller angle of the maxillary diagonals ( $95.3 \pm 13.9^\circ$  vs.  $106 \pm 15.9^\circ$ ) and, at the mandible, a narrower width ( $90.8 \pm 8.0 \text{ mm}$  vs.  $95.1 \pm 5.3 \text{ mm}$ ), a wider gonial angle ( $119.9 \pm 5.5^\circ$  vs.  $116.5 \pm 4.4^\circ$ ), a longer ramus ( $51.2 \pm 6.6 \text{ mm}$  vs.  $47.3 \pm 5.0 \text{ mm}$ ), and a shorter corpus ( $74.1 \pm 10.3 \text{ mm}$  vs.  $78.9 \pm 5.8 \text{ mm}$ ) than controls.**Conclusion:** Craniofacial structures that most discerned apneic subjects from controls were the maxillary and mandible bone volumes. An overly narrow maxilla and a postero-rotating mandible were also associated with OSA.**Level of Evidence:** III.**Registration:** NCT06022679.

## KEYWORDS

obstructive sleep apnea, orthodontic treatment, three-dimensional cephalometry, young nonobese adult phenotype

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## 1 | INTRODUCTION

The obstructive sleep apnea (OSA) syndrome, commonly assessed by an apnea-hypopnea index (AHI) less than 15, is characterized by the occurrence of repeated episodes of airway obstruction during sleep.<sup>1</sup> Repetitive upper airway collapse alters gas exchanges, increases cardiac work up, triggers micro-awakening and sleep fragmentation leading to drowsiness. OSA concerns up to 20% of males and 10%–15% of females complaining of symptoms.<sup>1,2</sup> Six different apneic phenotypes were determined,<sup>3</sup> with varying risk factors, physio-pathological causes, clinical manifestations, and consequences.<sup>4</sup> However, clinicians and healthcare professionals should be aware that some phenotypes have been less investigated, as for instance nonobese adults in the age range 18–35 years. OSA is far from being a single pathology limited to obesity or soft tissue compliance. Its causes are multifactorial. In young adults, the pathophysiology may involve an abnormal growth pattern of the midface, progressively conducting to the anatomical disease. The craniofacial morphology of apneic adults is the result of slow processes of morphological adaptation to a particular functional environment during childhood and adolescence, causing bone deformities. Various etiologies of altered facial growth patterns have been identified, e.g., oral breathing and adenoid hypertrophy.<sup>5,6</sup> Bone factors predisposing young adults to OSA are influenced by childhood factors. While polysomnography (PSG) remains the gold standard to diagnose sleep-disordered breathing, it does not assess the site of upper airway collapse.<sup>7</sup> Alternative diagnostic modalities are needed to refine the obstruction sites, such as sleep endoscopy and medical imaging. In case of suspected bony factors, Cone Beam Computed Tomography (CBCT) is becoming increasingly used in daily clinical practice.<sup>8</sup> CBCT has many advantages, particularly by being less irradiant than conventional CT and having a short acquisition and reconstruction time, along with a good resolution to evaluate the areas of interest in 3D. This study hypothesized that maxilla-mandibular bone volumes are smaller in nonobese apneic young subjects than in normal young adults.

## 2 | MATERIALS AND METHODS

This cross-sectional, nonrandomized, controlled, comparative study was conducted between June and December 2022 on an OSA group of nonobese apneic young adults and a control group of presumably healthy subjects.<sup>9,10</sup> Sleep studies were scored based on the obstructive sleep apnea and hypopnea index (AHI) as recommended by the American Academy of Sleep Medicine (AASM), with a minimum threshold of 15 apneas per hour of sleep to be recognized as apneic. The study protocol was approved by the Ethics Medical Committee of the University of Liege (EudraCT B7072022000010). To be included in the study, subjects had to be (1) aged 18–35 years, (2) with a BMI < 30 kg/m<sup>2</sup>, (3) nonalcohol and/or tobacco consumers,<sup>11</sup> (4) non-illicit drug users, and (5) free of any chronic pathology other than OSA. They signed an informed consent form before taking part in the study. Subjects (1) with an acute illness, (2) treated with orthognathic

surgery after apnea screening, or (3) having undergone PSG under a sleep treatment device (Continuous Positive Airway Pressure or Mandibular Advancement Device) were excluded.

The study material consisted of 46 subjects, 23 OSA patients (9 women and 14 men) with AHI ≥ 15 as confirmed by PSG at the Sleep Clinic of the University Hospital for suspected sleep disorders, and 23 normal volunteers (14 women and 9 men) without OSA disorders as confirmed by a validated type 3 ventilatory polygraphy (Somnolter<sup>®</sup> measuring SaO<sub>2</sub>, mandibular movements, body position, heart rate, and nasal air flow and thoracic and abdominal breathing movements). Sleep analysis included the Epworth sleepiness scale (ESS), a polysomnography (AASM type 1 sleep recording) for the OSA group, and a validated ventilatory polygraphy (AASM type 3 sleep recording) for the control group. Sleep data recorded consisted of total sleep time, obstructive apnea, mixed apnea, obstructive hypopnea, apnea and hypopnea index (AHI), sleep fragmentation index, oxygen saturation (SpO<sub>2</sub>), oxygen saturation minimal (SpO<sub>2</sub> min), time spent with oxygen below 90%, and oxygen desaturation index (ODI). All subjects were invited to fill out a questionnaire regarding demographics, medication use, and orthodontic treatment.<sup>12</sup> They also underwent an ENT exam, including a modified Mallampati score, Friedman score and measure of neck circumference.<sup>13,14</sup> An ultralow dose (ULD) CBCT examination was conducted in each subject in a supine position at the end of expiration with the Frankfurt plane vertical to the ground. A computerized 3D analysis using Dolphin Imaging 12.0 software was performed and repeated three weeks later by the same operator according to a blind procedure, merely to avoid any gross error and get reliable measurements. The following parameters were measured: facial mandibular angle (FMA), ANB angle (maxillo-mandibular sagittal discrepancy), maxillary diagonals angle between the diagonals drawn inside the maxillary coronal section, gonial angle, mandibular length, mandibular height, mandibular width, hyoid bone-mandibular plan distance, sagittal median section of the tongue, sagittal median section of the soft palate, maxillary and mandibular volumes, upper airway (UA) volume, smallest UA section length, smallest UA section width, smallest transverse UA section, smallest transverse UA shape, and the smallest transverse UA localization. Segmentation of maxillary and mandibular volumes was performed using the dedicated Dolphin Imaging 12.0 software tool. Dental crowns were not included in the bone volume calculation.

### 2.1 | Statistical methods

The maxillary and mandibular bone volumes were taken as the primary outcome measure, while all other parameters were considered as secondary or descriptive outcomes. A power calculation showed that, with at least 22 subjects in each group, a mean difference of one standard deviation (SD) in bone volumes could be evidenced with a power of 90% and a significance level of 5%, using a two-sided *t*-test with equal standard deviations in both groups. The difference of one SD corresponds to an effect size (ES) of 1 and an odds ratio (OR) of 0.37 in favor of OSA.

**TABLE 1** Subject characteristics in control ( $N = 23$ ) and OSA ( $N = 23$ ) groups.

	Control $N = 23$	OSA $N = 23$	Comparison $p$ -value
Age (years)	$24.4 \pm 2.9$	$28.2 \pm 5.9$	.0076
Gender (female)	14 (60.9)	9 (39.1)	.14
Height (cm)	$174 \pm 6.4$	$174 \pm 10.1$	.94
BMI ( $\text{kg}/\text{m}^2$ )	$22.4 \pm 2.7$	$24.1 \pm 3.1$	.058
Neck circumference (cm)	$37.2 \pm 4.0$	$39.0 \pm 2.8$	.084
Mallampati score (mean $\pm$ SD)	$1.7 \pm 1.0$	$2.3 \pm 0.83$	.031
1	13 (56.5)	3 (13.0)	
2	5 (21.7)	11 (47.8)	
3	3 (13.0)	7 (30.4)	
4	2 (8.7)	2 (8.7)	
Friedman grade (mean $\pm$ SD)	$1.2 \pm 1.2$	$0.96 \pm 1.1$	.54
0	9 (39.1)	11 (47.8)	
1	6 (26.1)	5 (21.7)	
2	4 (17.4)	5 (21.7)	
3	3 (13.0)	1 (4.3)	
4	1 (4.3)	1 (4.3)	
Medication use	1 (4.3)	11 (47.8)	.0008
Previous orthodontic treatment	18 (78.3)	16 (69.6)	.50
Fixe appliance	18 (100.0)	14 (87.5)	.21
Removal appliance	7 (38.9)	5 (31.2)	.64
Premolar extractions	0 (0.0)	6 (37.5)	.0060

Note: Results are expressed as mean  $\pm$  SD or as number (%).

Results were expressed as mean  $\pm$  SD for quantitative data and as number (%) for categorical findings. Mean values of demographic, biometric, and sleep parameters in OSA and control groups were compared by the Kruskal-Wallis (KW) test, whereas the Fisher exact test was used for comparing proportions. Logistic regression analysis was used to compare cephalometric features in OSA and control groups and to adjust for subject characteristics. The association between OSA and maxilla-mandibular bone volumes was assessed by OR and its 95% confidence interval (95% CI). Results were considered significant at the 5% critical level ( $p < .05$ ). All calculations were performed with SAS (version 9.4).

### 3 | RESULTS

#### 3.1 | Baseline characteristics

Baseline characteristics of OSA and control subjects are given in Table 1. Compared to controls, OSA subjects were older ( $28.2 \pm 5.9$  vs.  $24.4 \pm 2.9$  years,  $p = .0076$ ) but did not differ for BMI ( $24.1 \pm 3.1$  vs.  $22.4 \pm 2.7$   $\text{kg}/\text{m}^2$ ,  $p = .058$ ) and neck circumference ( $39.0 \pm 2.8$  vs.  $37.2 \pm 4.0$  mm,  $p = .084$ ). Although the modified Mallampati grade was higher ( $2.3 \pm 0.83$  vs.  $1.7 \pm 1.0$ ,  $p = .031$ ) in the OSA group, the Friedman grade was comparable ( $0.96 \pm 1.1$  vs.  $1.2 \pm 1.2$ ,  $p = .54$ ). The proportion of subjects taking regular medication was higher in the OSA group than in controls (11% vs. 1%,  $p = .0008$ ). Regarding orthodontic treatment

history, 34 subjects (16 OSA patients and 18 controls) had been treated orthodontically before the beginning of the study. The two groups were comparable regarding the follow-up of the orthodontic treatment and the type of treatment, whether fixed or removable. Of note, however, they differed by the number of premolars extracted during orthodontic treatment, 6 in the OSA group and none in the control group ( $p = .006$ ).

#### 3.2 | Sleep analysis

The distributions of sleep analysis parameters, including the AHI used to define the two groups ( $\geq 15$  or  $< 15$ ) are displayed in Table 2. The Epworth sleepiness score was significantly higher in OSA subjects than in controls ( $11.1 \pm 5.8$  vs.  $4.8 \pm 2.4$ ,  $p < .0001$ ). While the total sleep time was comparable, most parameters recorded (obstructive apnea, mixed apnea, obstructive hypopnea, sleep fragmentation index, AHI, oxygen desaturation index) differed significantly between the two groups. By contrast, oxygen saturation ( $\text{SpO}_2$ ), oxygen saturation minimal ( $\text{SpO}_2$  min), and time spent with oxygen below 90% were similar in both groups.

#### 3.3 | Cephalometry

The cephalometric distances, surfaces, and volumes observed in the two groups were compared and adjusted for baseline characteristics

	Control N = 23	OSA N = 23	Comparison
	Ventilatory polygraphy	Polysomnography	p-value
Epworth scale	4.8 ± 2.4	11.1 ± 5.2	<.0001
Total sleep time (min)	418 ± 45	431 ± 82	.54
No. apnea hypopnea	34 ± 19	218 ± 118	<.0001
No. of obstructive apnea	2.0 ± 2.9	51.3 ± 103.2	<.0001
No. of mixed apnea	0.04 ± 0.21	1.0 ± 2.3	.035
No. of obstructive hypopnea	27.7 ± 17.0	160.9 ± 67.2	<.0001
Apnea-hypopnea index (AHI)	3.2 ± 2.1	31.5 ± 18.3	<.0001
CTEVE (%)	23.0 ± 20.2	NA	NA
Sleep fragmentation index	15.1 ± 4.1	31.2 ± 16.3	<.0001
Oxygen desaturation index	1.7 ± 1.3	9.5 ± 14.0	.0005
SpO <sub>2</sub> min	88.9 ± 5.3	87.0 ± 6.6	.28
SpO <sub>2</sub>	95.4 ± 1.0	95.3 ± 1.4	.99
Time SpO <sub>2</sub> < 90%	0.27 ± 0.56	1.6 ± 3.1	.26

Note: CTEVE Cumulative time of excessive ventilatory efforts (%).

**TABLE 2** Sleep analysis parameters recorded in control subjects (N = 23) and OSA patients (N = 23).

**TABLE 3** Cephalometric features derived by CBCT image analysis in control subjects (N = 23) and in OSA patients (N = 23).

	Control N = 23	OSA N = 23	p-value*
<i>Skeletal data</i>			
A. Morphological typology and growth potential			
FMA (degree)	20.8 ± 4.7	21.6 ± 4.4	.58
C. Maxilla			
Maxillary diagonals (degree)	106.0 ± 15.9	95.3 ± 13.9	.014
Maxillary volume (cm <sup>3</sup> )	24.8 ± 2.9	23.2 ± 4.6	.034
D. Mandible			
Gonial angle (AR-GO-GN) (degree)	116.5 ± 4.4	119.9 ± 5.5	.0090
Mandibular height (AR-GO) (mm)	47.3 ± 5.0	51.2 ± 6.6	.022
Mandibular length (GO-GN) (mm)	78.9 ± 5.8	74.1 ± 10.3	.013
Mandibular width (GO-GO) (mm)	95.1 ± 5.3	90.8 ± 8.0	.0053
Mandibular volume (cm <sup>3</sup> )	46.9 ± 5.2	44.0 ± 6.4	.0066
E. Intermaxillaries relationship			
ANB (degree)	3.7 ± 2.1	3.9 ± 1.8	.79
F. Pharynx			
Hyoid bone-mandibular plane (mm)	11.0 ± 4.2	11.3 ± 3.8	.86
Buccal floor (mm)	3.8 ± 0.46	3.5 ± 0.78	.048
<i>Soft tissues data</i>			
Smallest UA (cm <sup>2</sup> )	1.2 ± 0.62	1.2 ± 0.79	.72
Smallest UA section length (mm)	7.3 ± 2.2	6.2 ± 2.4	.52
Smallest UA section width (mm)	18.2 ± 5.5	18.8 ± 7.0	.38
Upper airway volume (cm <sup>3</sup> )	12.5 ± 4.5	13.0 ± 5.9	.52
Sagittal median section of the tongue (cm <sup>2</sup> )	23.9 ± 3.6	24.7 ± 3.5	.52
Sagittal median section of the soft palate (cm <sup>2</sup> )	2.52 ± 0.72	2.60 ± 0.71	.19
Smallest transverse upper airway shape (flattened), N (%)	19 (82.6%)	20 (87.0%)	.99
Smallest transverse upper airway localization (nasopharynx), N (%)	17 (73.9%)	14 (60.9%)	.34

\*p-values derived by logistic regression analysis adjusted for age, sex, height, and BMI.



(age, gender, height, and BMI) (Table 3). Maxillary bone volumes were lower in the OSA group ( $23.2 \pm 4.6 \text{ cm}^3$ ) than in the control group ( $24.8 \pm 2.9 \text{ cm}^3$ ); however, the difference was not significant ( $\text{OR} = 0.89$ , 95% CI  $0.76 - 1.49$ ,  $p = .17$ ). When adjusting for subject characteristics, though, a significant association was obtained between OSA and maxillary volumes ( $\text{OR} = 0.76$ , 95% CI  $0.59 - 0.98$ ,  $p = .034$ ). Similarly, mandibular bone volumes were lower in the OSA group ( $44.0 \pm 6.4 \text{ cm}^3$ ) compared to the control group ( $46.9 \pm 5.2 \text{ cm}^3$ ) but not significantly ( $\text{OR} = 0.92$ , 95% CI  $0.83 - 1.02$ ,  $p = .11$ ). When adjusting for subject characteristics, the association between mandibular volumes and OSA became significant ( $\text{OR} = 0.73$ , 95% CI  $0.58 - 0.92$ ,  $p = .0066$ ). In both multivariate logistic regression analyses, age and gender (two factors that were not matched in the selection of controls) were significant, while height was not. By contrast, BMI, which was markedly higher in OSA subjects ( $24.1 \pm 3.1$  vs.  $22.4 \pm 2.7 \text{ kg/m}^2$ ) was no longer significant when combined with the other variables (data not shown). Further, at the maxillary level, the angle of the maxillary diagonals was lower in the OSA subjects than in controls ( $95.3 \pm 13.9^\circ$  vs.  $106.0 \pm 15.9^\circ$ ,  $p = .014$ ). An association with OSA was also observed for the floor of the mouth (pterygoid muscles), represented by the distance between the hyoid bone and the right and left mandibular plane, which was smaller in the OSA group ( $3.5 \pm 0.78 \text{ mm}$  vs.  $3.8 \pm 0.46 \text{ mm}$ ,  $p = .048$ ). For the mandible, other significant correlations with OSA were highlighted; specifically, the mandibular body length ( $74.1 \pm 10.3 \text{ mm}$  vs.  $78.9 \pm 5.8 \text{ mm}$ ,  $p = .013$ ) and width ( $90.8 \pm 8.0 \text{ mm}$  vs.  $95.1 \pm 5.3 \text{ mm}$ ,  $p = .0053$ ) were significantly reduced, whereas the gonial angle ( $119.9 \pm 5.5^\circ$  vs.  $116.5 \pm 4.4^\circ$ ,  $p = .0090$ ) and ramus length ( $51.2 \pm 6.6 \text{ mm}$  vs.  $47.3 \pm 5.0 \text{ mm}$ ,  $p = .022$ ) were significantly increased. No relationship with OSA was noted for the FMA angle, ANB angle, base angle of the skull and skull length, and likewise for the volume of the upper airway, its dimensions, and the sagittal sections of the tongue and soft palate. The smallest section of the airway was mainly located at the level of the nasopharynx and had a flattened antero-posterior shape in both groups.

## 4 | DISCUSSION

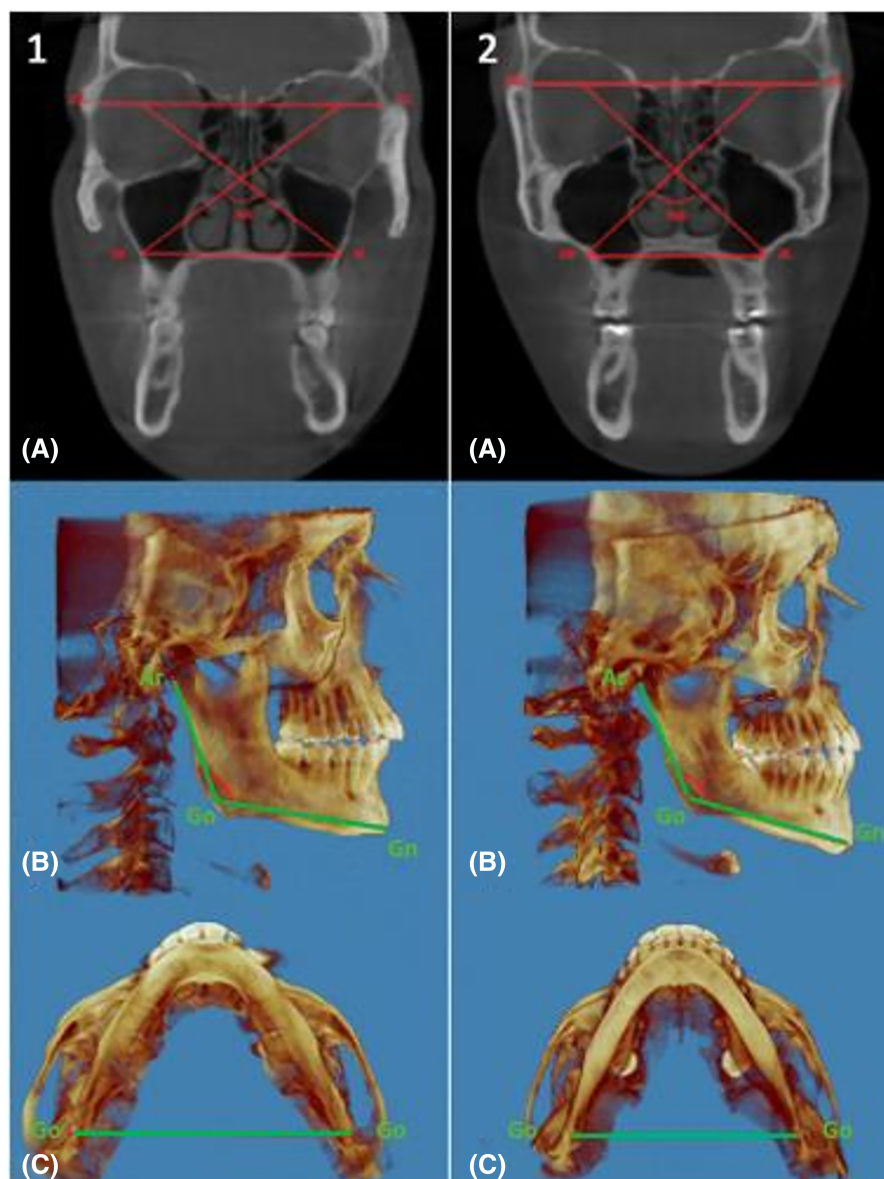
This study tends to evidence that nonobese young OSA subjects exhibit a particular phenotype of the maxilla and the mandible, with smaller volumes and narrower measures for several cephalometric features. These findings must be tempered by the fact that the difference between OSA and control subjects for maxillary and mandibular bone volumes only became significant after taking into account demographic (age, gender) and biometric (height, BMI) subject characteristics. The resulting effect sizes of maxilla-mandibular volumes, however, remained small, around 0.30, corresponding to an adjusted OR of 0.74 for OSA. Specifically, compared to a "normal" subject, all demographic and biometric characteristics being held fixed, any decrease of  $1 \text{ cm}^3$  in maxillary or mandibular volume augments the odds of OSA by 26% (approximate 95% CI 5%–40%). Thus, the assessment of maxilla-mandibular bone volumes needs to be

made with caution and in the light of demographic and biometric subject characteristics.

Young adults with sleep-related complaints are more likely to attend an ENT clinic than a sleep specialty clinic, although the severity of their OSA may be similar.<sup>15</sup> Some authors have advocated for an early detection of bone abnormal growth in childhood. The etiopathogenesis of OSA being complex, this study focused on bony anatomical factors as much as possible while excluding comorbidity factors such as alcohol, tobacco, and obesity.<sup>16</sup> Mallampati grade was significantly higher in the OSA group, hence emphasizing the involvement of soft tissues in the differentiation of the two groups. By contrast, the Friedman grade was not different, with a grade 0 present in 11 OSA subjects and in only 9 controls. The issue of tonsils in OSA is more relevant in children, due to a faster and more important growth of the lymphoid tissue compared to the airway growth, but not particularly in young adults,<sup>17,18</sup> where focus should be on the soft palate and tongue.<sup>19</sup> Surprisingly, no significant differences were found between OSA and control subjects regarding the sagittal surface of the tongue or the soft palate. This could be explained not by an increase in sagittal surface area but rather, in OSA patients, by a lower positioning of the less toned uvula, in some cases damaged by recurrent snoring.

In the present study, OSA patients took more medication than controls, presumably as a response to OSA symptoms already present before diagnosis of the syndrome. Regarding orthodontic treatment, the study found no influence of orthodontic treatment on OSA severity, nor on cephalometric variables. However, none of the subjects did undergo maxillary and/or mandibular distractions. According to several studies, premolar extractions are often claimed to be responsible for increasing the risk of OSA by altering the upper airway (UA) morphology,<sup>19–25</sup> in contrast to other studies that did not.<sup>26–28</sup> While the topic remains quite controversial, the present study confirmed the 2021 systematic review of the 3D measures of UA, which showed no differences in the UA volume and the smallest cross-sectional area of the UA when premolars were extracted<sup>29</sup>; there were also no changes in the 2D position of the hyoid bone<sup>30,31</sup> (Table 3). This research work should be part of a broader reflection and focus on the indications for premolar extractions in orthodontic treatment. The lack of space due to narrow jaws often leads orthodontists to prescribe extractions. It is unsure that extractions predispose to OSA. It would be more likely that the narrowness of the maxilla and the mandible and their small volume, prompting extractions, are predisposing factors to apnea and hypopnea syndrome. In addition, it may raise the question of lingual function in OSA. No study so far has studied the lingual function in the case of extractions. However, the position of the tongue at rest could be a determining factor in the genesis of sleep apnea, even if the airway volume remains unchanged. The space available for the tongue decreases in the presence of extractions. The study of lingual dynamics remains to be investigated.

A high and narrow maxilla with a smaller volume had an impact on AHI in young adults, as the angle of the maxillary diagonals and the maxillary volume were significantly smaller in apneic subjects of this study (Figure 1). The maxillary diagonal angle, when more closed,



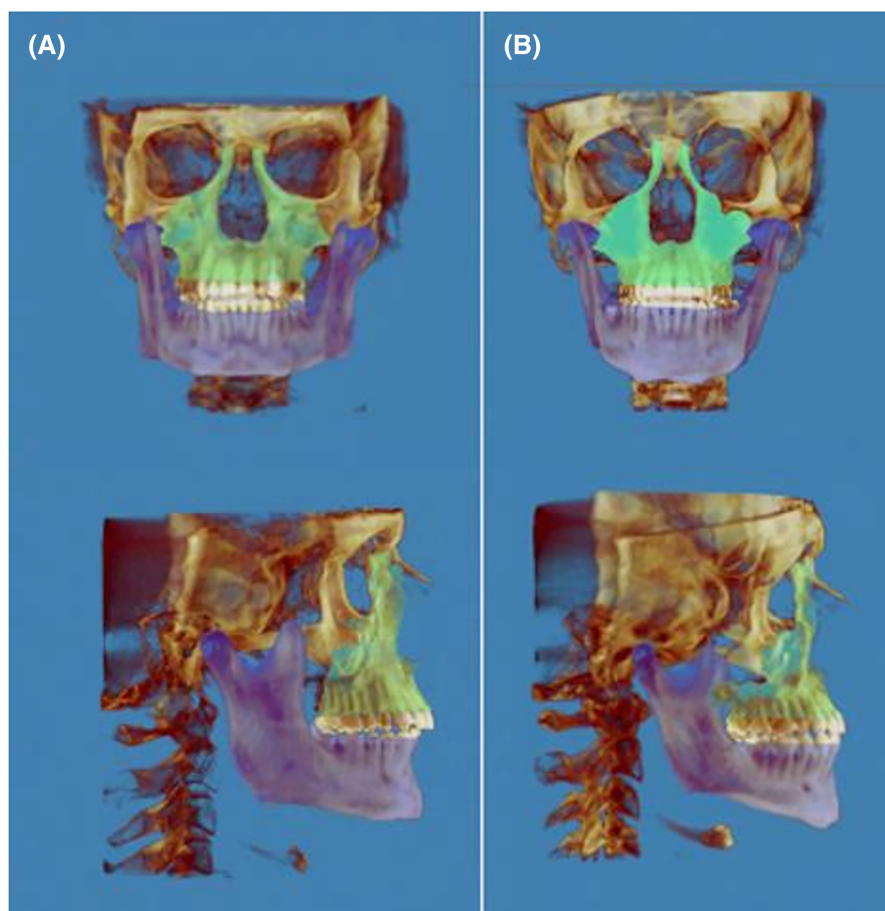
**FIGURE 1** Angles and distances measured on CBCT images discriminating control (1) and OSA subjects (2) (A) Maxillary diagonals, (B) Gonial angle, mandibular height, mandibular length, and (C) Mandibular width.

causes a vertical excess which increases the resistance of the UA and can provoke a collapse. This is in line with other studies on the transverse maxillary dimension.<sup>32–34</sup> An excessively narrow transverse distance as well as a thin face are characteristics of the apneic adult, reminiscent of the adenoid facies in children. The maxilla is a bone of the desmocranium, particularly sensitive to environmental behaviors during childhood. Similarly, rapid maxillary expansion is one of the first-line treatments in children with OSA.<sup>35</sup> It enlarges the UA, allowing nasal breathing and optimal facial growth. In the sagittal direction, mandibular data show that an open gonial angle and a longer mandibular ramus predispose to OSA. In contrast, mandibular body length, width, and volume are smaller in apneic young adults (Figure 2). The ANB angle was not significantly different between OSA subjects and controls. According to Andersson, Lowe<sup>36</sup> and Tangugsorn, the mandible is not displaced posteriorly, but shows postero-rotation related by Björk due to an opening of the gonial angle,<sup>4,11,37</sup> associated with a steeply tilted mandibular plane, a short corpus, and an excess of lower

face height, especially in subjects with a low BMI like in this study.<sup>4,11,35–37</sup>

Cephalometric characteristics of the mandible and the maxilla were narrower in OSA subjects, even after undergoing orthodontic treatment with slow expansion in childhood. Orthodontic treatments such as rapid jaw expansion, mandibular counterclockwise reorientation, and advancement could be more efficient to enlarge the upper airway. A long ramus increases the UA compliance due to an elongation of the oropharynx. In addition, the reduction in the size of the corpus decreases the sagittal length of the mandible and directly limits the diameter of the oropharynx. Indirectly, it moves backwards the insertion of the genioglossus muscle on the Geni apophysis backwards. A decrease of the mandibular width reduces the UA width and provokes the posterior recession of the tongue, which creates a collapse in the supine position during sleep. In general, the base of the skull and therefore the maxilla of Asian subjects is shorter than those of Caucasians. Caucasians, on the other hand, exhibit more often

**FIGURE 2** Maxillary volume (green) and mandibular volume (blue) discriminating control (A) and OSA subjects (B).



mandibular retrognathia. These two craniofacial morphology factors predispose to obstructive sleep apnea by reducing the space available for the tongue, which causes the upper airway to collapse in the supine position. Craniofacial phenotype variations across ethnic groups, here only Caucasians, can therefore limit the generalizability of the study conclusions.

The three-dimensional measure of the floor of the mouth, expressing the distance between the mandibular plane and the hyoid bone in 3D, was found significantly smaller in apneic subjects, whereas this distance in 2D was not. The 3D variable fluctuates with the distance between the hyoid bone and the mandibular plane, but also with the mandibular width. This reduction of the oral floor would then come from the mandibular narrowness rather than from the distance between the hyoid bone and the mandibular plane. Some 3D CBCT studies have demonstrated that the UA volume was significantly reduced in the apneic subject, with a reduced anteroposterior dimension and an oval shape of the lumen.<sup>8,33,34,38</sup> In contrast, the present work did not evidence any significant difference regarding the upper airway volume. In both groups, the airway was predominantly flattened, with the smallest section localized at the nasopharynx level. Finkelstein et al. also showed a narrowing of the velopharyngeal width in OSA subjects.<sup>39</sup>

Concerning sleep data recorded, a particularity of nonobese apneic young adults is that they do not desaturate their blood with

oxygen any more than healthy young people, unlike older adults who desaturate their blood with oxygen more in cases of obstructive sleep apnea than older adults without apnea.

This study has a number of limitations. At first, the use of CBCT cephalograms is still restrained by factors such as the lack of a standard protocol for airway imaging and the inherent nature of being a static image of a dynamic structure.<sup>40,41</sup> The image, highlighting the upper airway, the section of the soft palate, as well as the tongue, is taken at one given moment and will therefore not be identical to the next image. Moreover, even if the patient is in a supine position during the imaging (sleep position predisposing to OSA), the muscular tone during awakening is not identical to the one during sleep. A CBCT taken in induced sleep and during apnea would enable the study of the syndrome more closely and would be worth a future study. However, 2D imaging can still be useful, as 5 out of 8 significantly altered variables in OSA subjects could be studied in 2 dimensions. Despite the superimpositions and the inaccuracy of point location, the 2D imaging already gives a good indication regarding these 5 parameters. A second limitation of the study refers to computerized 3D analysis using Dolphin Imaging 12.0 software performed at inclusion and three weeks later by the same operator. Despite the fact that all measurements were supervised by an orthodontist accustomed to the technique, the implication of a second operator would have improved the accuracy of the measurements and the validity of



the study. As a third limitation of the study, home ventilation polygraphy for control subjects may have produced different results from polysomnography. These differences are small, however, as both types of examination use the same measurement technology, notably the Jaw Activity (Jawac) for analyzing mandibular movements. The type 3 monitor was validated in adult and pediatric populations with an excellent correlation with polysomnography.<sup>42,43</sup> Chakar demonstrated that these two diagnostic methods for studying obstructive sleep apnea, polygraphy and PSG, were similar in terms of distinguishing sleep states from wake states and in terms of efficiency in diagnosing OSA.<sup>44</sup> Besides oximetry, respiratory monitoring, cardiac monitoring, actigraphy, and body position, this portable monitor added mandible movement analysis to improve wake/sleep discrimination, micro-arousal detection, mouth opening measurement, and respiratory efforts quantification. The mandibular movement sensor used a resonant magnetic field transducer to quantify jaw movement. Lastly, regarding power calculation, the hypothesized effect size of 1 of maxilla-mandibular volumes on OSA was largely overestimated and did not account for potential confounders in the study design. The theoretical effect size of 1 corresponds to an odds ratio of 0.37 in favor of OSA. While the observed ORs were 0.89 for the maxillary and 0.92 for the mandible, when adjusting for demographic and biometric subject characteristics, they markedly decreased to 0.76 and 0.73, respectively, and became significant. These values correspond to an observed effect size of only 0.27 and 0.31, respectively. In conclusion, given the small sample size of this study and the large number of variables measured, study results should be interpreted with caution and be validated on larger subject populations.

## 5 | CONCLUSION

When phenotyping the nonobese OSA young adult, the craniofacial structures that most discriminate apneic and nonapneic adults were the jaws bone's volumes, maxilla, and mandible, even after undergoing orthodontic treatment with slow expansion in childhood. A narrow maxilla and a postero-rotating mandible with reduced volume were present in young apneic subjects. Moreover, the number of premolars extracted during orthodontic treatment was significantly higher in the OSA group than in the control group. Therefore, the recommendation of a double therapy in the case of risk factors for OSA in children may be put forward: rapid maxillary expansion followed by mandibular advancement in the case of mandibular retrognathia without premolar extraction if possible.

## CONFLICT OF INTEREST STATEMENT

None of the authors have a conflict of interest.

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