

Utility of Cephalometry and Acoustic Pharyngometry for the Assessment of Moderate to Severe Obstructive Sleep Apnea Before Treatment in Childhood

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Purpose: The ERS Statement dealing with childhood obstructive sleep apnea (OSA) declared that cephalometry and acoustic pharyngometry may be useful exams for the management of OSA. The objective of our cross-sectional study was to evaluate the correlations between the severity of OSA, namely obstructive apnea-hypopnea index (OAH), and indices obtained from both acoustic pharyngometry and cephalometry in children referred for OSA treatment.

Methods: Children referred for treatment of their moderate to severe OSA ($AHI \geq 5/\text{hour}$) underwent acoustic pharyngometry in sitting and supine positions (measurement of pharyngeal volume and calculation of estimated pharyngeal compliance) and cephalometry (measurement of Frankfort Mandibular plane Angle: FMA and Frankfort Mandibular Incisal Angle: FMIA, hyoid bone distance to mandibular plane).

Results: Two hundred and five consecutive children were enrolled (mean age $\pm$ SD: 11.2 ± 3.7 years, 73 females, type 1 OSA “enlarged tonsils”: 55 children, type 2 “obese”: 80, type 3 “syndromes”: 70). In a multiple regression analysis, only FMA and hyoid bone distance remained independently linked to OAH (adjusted r^2 of the model: 0.12, $p < 0.001$, weak explanatory power). The FMA angle allowed differentiating normodivergence ($21^\circ < \text{FMA} < 29^\circ$: 41% of the children), hyperdivergence ($\text{FMA} \geq 29^\circ$: 32%), and hypodivergence ($\leq 21^\circ$: 27%). The participants with hyperdivergence were younger, less obese, and had a longer lower face (adenoid facies). In a multiple regression analysis, only height and FMIA remained independently linked to pharyngeal volume (adjusted r^2 of the model: 0.32, $p < 0.001$, moderate explanatory power).

Conclusion: Childhood OSA can be associated with hypodivergence. Its severity is linked to craniofacial morphology, and cephalometry provides additional endotypic information in selected children.

Keywords: obstructive sleep apnea, cephalometry, acoustic pharyngometry, childhood

Introduction

The European Respiratory Society (ERS) Statement dealing with obstructive sleep apnea (OSA) in 2- to 18-year-old children recommended a stepwise approach to the diagnosis and management of OSA.¹ The techniques that can be used for the objective evaluation of abnormalities predisposing to OSA are debated. The ERS Statement declared that among these techniques, cephalometry and acoustic pharyngometry are useful for the evaluation of pharyngeal airway size in selected cases,¹ which remains debated. A meta-analysis of craniofacial features in children with OSA, mainly assessed through lateral cephalometrics, concluded that due to the very low to moderate level of certainty, neither an association nor a lack thereof between craniofacial morphology and pediatric OSA can be supported by the data.² The utility of noninvasive pharyngometry in childhood OSA has been suggested for a long time; the minimum pharyngeal cross-sectional area has

been proposed as a useful measure for evaluating OSA risk factors in preadolescent children,³ and the measurement of upper airway dynamics using acoustic pharyngometry also provided a useful clinical adjunct in another study.⁴

The appropriate sequence of treatment interventions for children with OSA has not been studied extensively.¹ One may hypothesize that among the available therapeutic options, the primary choice should be the one mostly linked to the obstructive apnea-hypopnea index (OAHI), particularly in children who are candidates for treatment, to ensure greater treatment efficacy: the identified endotype must therefore be modifiable and impactful.⁵ For instance, retrognathia on cephalometry with reduced pharyngeal volume on acoustic pharyngometry would lead to mandibular advancement device use,⁶ while increased pharyngeal compliance on acoustic pharyngometry with normal cephalometry would lead to orofacial myofunctional therapy.⁷

Our cross-sectional study aimed to evaluate the correlations between the severity of OSA, namely OAHI, and indices obtained from both acoustic pharyngometry and cephalometry in children referred for OSA treatment. Only children with moderate-to-severe OSA were included since an apnea-hypopnea index (AHI) ≥ 5 episodes·h⁻¹ has been used as an indication for treatment irrespective of the presence of morbidity.¹

A secondary objective was to evaluate whether treatment allocation patterns were based on the results of pharyngometry and cephalometry.

Materials and Methods

Design

The design was a prospective observational cross-sectional study of consecutive children referred for treatment of their moderate to severe OSA according to ERS recommendations.¹ We conducted the study at a university care center (Robert Debré pediatric hospital, Paris, France) over a five-year period. This study meets the criteria set by the latest revision of the Declaration of Helsinki and was approved by our local Ethics Committee (Comité d'Evaluation de l'Ethique des Projets de Recherche de Robert Debré) (PHENOSAS: N° 2018–416); the database of collected data (anonymized) was declared to the French regulatory agency: CNIL). The subjects and their parents were informed of the collection of their anonymous prospective data for research purposes, and they could request to be exempted from this study (informed consent was waived by the Ethics Committee) in accordance with French law (non-interventional observational research, not included in Jardé law: LOI n° 2012–300 du 5 mars 2012 relative aux recherches impliquant la personne humaine), as previously explained.⁸ Our study complies with STROBE Checklist of cross-sectional studies (<https://www.strobe-statement.org/checklists/>).

The children (3 to 18 years old) having a moderate to severe OSA (obstructive AHI determined by night-polysomnography ≥ 5 / hour of sleep during a previous hospitalization, as previously described^{9–11}), whatever their OSA class (OSA type 1 [enlarged tonsils and adenoids], type 2 [obesity] and type 3 [craniofacial abnormalities, syndromal, storage diseases and neuromuscular conditions]¹²), underwent a systematic evaluation on the same day in a multidisciplinary clinic (involving an orthodontist, an otolaryngologist, and a pediatrician specializing in sleep medicine) devoted to the multistep therapeutic approach of childhood OSA. The data collected included demographics, ethnicity, and z-score of body mass index (BMI, a nurse measured height, weight, and neck circumference).

Overnight Polysomnography

In-laboratory (children under 8 years old) or ambulatory (≥ 8 years) polysomnography studies were performed overnight using an Alice 6 LDx or PDX polysomnography system (Philips, Murrysville, PA) or Somté PSG system (Compumedics, Australia) as previously described^{9,10} and pediatric sleep physicians scored patients using standard pediatric sleep scoring criteria.¹³

Upper Airway Assessment

As part of the protocol of the multidisciplinary evaluation, a complete orthodontic assessment was performed, including a lateral cephalogram, as previously described.¹⁰ From the cephalogram, SNA, SNB, ANB, FMA, IMPA, FMIA angles, and ANS'-Me, N-ANS', Hyoid bone MP distances were calculated (see Figure 1 for the definitions). The participants were divided into three groups on the basis of FMA (hypodivergent: $FMA \leq 21^\circ$; normodivergent: $21^\circ < FMA < 29^\circ$; hyperdivergent: FMA

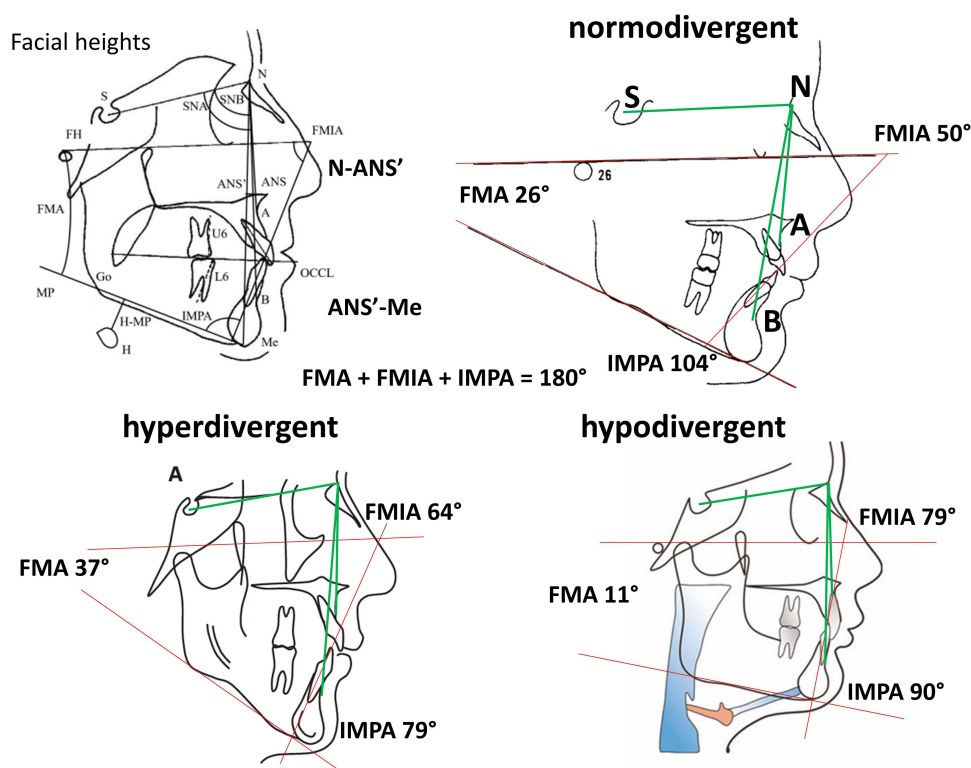


Figure 1 Cephalometry analysis and kinds of divergence. Anatomical landmarks: Anterior nasal spine (ANS), tip of the median sharp bony process of the palatine bone in the hard palate; A point, deepest midline point on the maxillary alveolus between ANS and the maxillary alveolar crest. B point, deepest midline point between the mandibular alveolar crest and most antero-inferior point on the bony mandibular symphysis. H, hyoid bone. N (nasion), most anterior point of the fronto-nasal suture. S (sella), the center of the sella turcica. Me (mentum), lowest point on the bony outline of the mandibular symphysis. ANS' is the orthogonal projection of ANS on the N-Me line. Bony dimensions: H-MP perpendicular distance from most antero-superior point on the body of the hyoid bone to the MP. The upper left panel gives facial heights with N-Me (nasion to mental), N-ANS' (nasion to anterior nasal spine) and ANS'-Me (anterior nasal spine to mental) distances, and increase in ANS'-Me is an increase in lower face height (expressed as mm and % of N-Me). The upper right panel shows the SNA (normal value, $82^{\circ} \pm 2^{\circ}$): angle formed by the intersection of sella (S)-nasion (N) and nasion- A (maxilla) green lines. SNB ($80^{\circ} \pm 2^{\circ}$): angle formed by the intersection of sella-nasion and nasion- B (mandible) green lines. ANB ($2^{\circ} \pm 2^{\circ}$): Angle formed by the intersection of nasion- A and nasion- B green lines. Thus, SNA is the sagittal position of the maxilla and SNB the sagittal position of the mandible. This upper right panel also shows the Frankfort horizontal plane: red line joining from external auditory meatus to orbitale, the Mandibular plane: red line passing tangent to the lower border of mandible, and the long axis of lower incisor (red line). The following three angles formed in Tweed's triangle were measured (normodivergent subject): Frankfort Mandibular plane Angle (FMA $25^{\circ} \pm 3^{\circ}$), Frankfort Mandibular Incisal Angle (FMIA $68^{\circ} \pm 5^{\circ}$), and Incisor Mandibular Plane Angle (IMPA $87^{\circ} \pm 5^{\circ}$). The lower left panel shows hyperdivergence with class II malocclusion, while the lower right panel shows hypodivergence (SNA $\sim 84^{\circ}$, SNB $\sim 80^{\circ}$).

$\geq 29^{\circ}$) and into three skeletal classes on the basis of ANB (class I: $0^{\circ} \leq \text{ANB} \leq 4^{\circ}$; class II: $\text{ANB} > 4^{\circ}$; class III: $\text{ANB} < 0^{\circ}$), as previously done.^{14,15}

Patients underwent acoustic pharyngometry testing using an Eccovision 4.50 acoustic pharyngometer (Sleep Group Solutions), as previously described.¹¹ Variables of pharyngometry were the minimal cross-sectional area corresponding to the junction between the oral cavity and oropharynx, the volume of the pharynx (between the oropharyngeal junction and glottis), and the mean pharyngeal area in both sitting and supine positions. An estimated pharyngeal compliance (cm^3/kPa) was then calculated, as described previously.¹¹ The operator was blinded to the polysomnography/cephalometry results.

Pulmonary Function Test

Functional respiratory capacity (FRC) was measured using body plethysmography (Master Scope Body, Carefusion Technologies, Yorba Linda, California, USA).

Statistical Analyses

Sample size calculation: The main aim of our cross-sectional observational study was to evaluate correlations; the total sample size required to determine whether a correlation coefficient differs from zero was 194 subjects with a type I error rate (two-tailed) of 0.05 and a type II error rate of 0.80 with an expected correlation coefficient (R) of 0.20 (weak correlation). Thus, we planned to enroll at least 200 subjects.

Results were expressed as mean $\pm$ standard deviation (SD) or median [25th–75th percentiles] according to the distribution of the variable. Two-group comparisons of continuous variables were performed using the unpaired *T*-test or Mann–Whitney *U*-test, as appropriate. Categorical variables were compared using the chi-squared test. Linear correlations were evaluated using Pearson's correlation coefficient. Multiple linear correlations are described in the text. The linearity of the data was checked by looking at the residual versus fitted plot. Some predictor variables were not included in the models due to multicollinearity, for instance, between age and height, or between SNA and SNB angles, and between FMIA and FMA angles. Binomial “exact” calculation was used for the calculation of confidence interval (CI) for proportions. A *p* value < 0.05 was deemed significant. Statistical analyses were performed with StatView 5.0 (SAS Institute) software.

Results

The characteristics of the 205 participants are described in Table 1 according to the severity of OSA (moderate versus severe). The participants with severe OSA, as compared with those with moderate OSA, were older, more obese, had more associated diseases (type 3 OSA), and had an increased distance from the hyoid bone to the mandibular plane.

Table 1 Characteristics of the Children/Adolescents with Moderate-to-Severe OSA

Characteristics	Moderate OSA N=77	Severe OSA N=128	P value
Age, years	10.7 $\pm$ 3.4	11.6 $\pm$ 3.9	0.090
Sex: female/male, n	25 / 52	48 / 80	0.466
Ethnicity: Af/As/C/M, n	26 / 7 / 39 / 5	49 / 5 / 64 / 10	0.458
z-score of BMI	1.11 [0.11; 2.28]	2.13 [0.66; 2.60]	<0.001
Neck circumference, cm	30.5 [27.9; 36.0]	35.0 [29.1; 40.3]	0.001
OSA type*: 1 / 2 / 3, n	32 / 23 / 22	23 / 57 / 48	0.001
FRC, L	1.57 $\pm$ 0.69	1.62 $\pm$ 0.66	0.662
Polysomnography			
AHI/hour of sleep	7.4 [6.3; 8.3]	19.8 [14.0; 33.9]	ND
Obstructive AHI/hour	6.4 [5.0; 7.5]	18.8 [13.2; 33.1]	ND
ODI _{3%} /hour	5.0 [3.1; 6.6]	15.9 [9.6; 26.8]	<0.001
SpO ₂ minimum, %	90 [88; 92]	84 [77; 88]	<0.001
Acoustic pharyngometry			
Sitting pharyngeal junction, cm ²	1.30 $\pm$ 0.47	1.32 $\pm$ 0.39	0.664
Sitting pharyngeal volume, cm ³	18.8 [13.9; 24.0]	18.3 [14.5; 24.4]	0.849
Pharyngeal compliance, cm ³ /kPa	11.7 $\pm$ 11.9	10.2 $\pm$ 9.6	0.329
Cephalometry			
SNA, °	82 $\pm$ 5	84 $\pm$ 5	0.064
SNB, °	78 $\pm$ 5	80 $\pm$ 5	0.075
ANB, °	4 $\pm$ 3	4 $\pm$ 3	0.692
Skeletal classes, I / II / III, n	40 / 34 / 3	66 / 57 / 5	0.998
N-Me, mm	104.9 $\pm$ 11.0	106.2 $\pm$ 11.2	0.406
N-ANS', mm	44.0 $\pm$ 5.6	44.7 $\pm$ 5.4	0.395
ANS'-Me, mm	60.9 $\pm$ 7.1	61.5 $\pm$ 7.3	0.524
ANS'-Me, %	58 $\pm$ 3	58 $\pm$ 3	0.763
FMA, °	27 $\pm$ 8	25 $\pm$ 6	0.148
Divergence, hypo/ normo/hyper, n	24 / 25 / 28	32 / 59 / 37	0.158
IMPA, °	91 $\pm$ 9	90 $\pm$ 9	0.791
FMIA, °	64 $\pm$ 12	65 $\pm$ 10	0.367
Hyoid bone MP distance, mm	11.9 $\pm$ 5.9	15.7 $\pm$ 6.7	<0.001

Notes: °degree. *OSA type 1 [enlarged tonsils and adenoids], type 2 [obesity] and type 3 [craniofacial abnormalities, syndromal (as Down syndrome, n=25), storage diseases and neuromuscular conditions]¹²). Ethnicities are African-Caribbean / Asian / Caucasian / Mixed; ODI_{3%} is oxygenation desaturation index $\geq 3\%$; MP is mandibular plane.

Correlates of OAHl

OAHl correlated with age ($R = 0.15$, $p = 0.031$), z-score of BMI ($R = 0.24$, $p < 0.001$), neck circumference ($R = 0.33$, $p < 0.001$), SNA ($R = 0.16$, $p = 0.021$), SNB ($R = 0.19$, $p = 0.009$), FMA ($R = -0.23$, $p = 0.001$), FMIA ($R = 0.15$, $p = 0.038$), and hyoid bone distance to mandibular plane ($R = 0.23$, $p = 0.001$). Neck circumference was related to both age and z-score of BMI (data not shown). In a multiple regression analysis with age, z-score of BMI, SNB, FMA, and hyoid bone distance as independent variables, only FMA and hyoid bone distance remained independently linked to OAHl (adjusted r^2 of the model: 0.12, $p < 0.001$). The detailed results of this multivariate analysis are provided in Table 2. Specifically, we found a $\sim 0.5/\text{hr}$ increase in OAHl for every 1° decrease in FMA and for every 1 mm increase in hyoid bone to mandibular plane distance. This multiple regression analysis was almost unchanged when excluding participants with type 3 OSA since FMA (estimated effect: -0.459 , $p = 0.049$), and hyoid bone distance (estimated effect: 0.592, $p = 0.010$) remained independently linked to OAHl (adjusted r^2 of the model: 0.11, $p = 0.001$).

Correlations of Cephalometric Indices

Since this hyoid bone position was one of two independent factors associated with OSA severity, we determined the correlates of this position.

Hyoid bone distance to mandibular plane correlated with age ($R = 0.36$, $p < 0.001$), height ($R = 0.36$, $p < 0.001$), z-score of BMI ($R = 0.25$, $p < 0.001$), neck circumference ($R = 0.38$, $p < 0.001$), FRC ($R = 0.36$, $p < 0.001$), SNB ($R = 0.15$, $p = 0.038$), N-ANS' ($R = 0.19$, $p = 0.008$), ANS'-Me ($R = 0.14$, $p = 0.044$), IMPA ($R = -0.14$, $p = 0.049$), and FMIA ($R = 0.16$, $p = 0.025$). In a multiple regression analysis with height, z-score of BMI, FRC, SNB, N-ANS', and FMIA as independent variables, only FRC (estimated effect: 2.41, $p = 0.049$) and FMIA (estimated effect: 0.140, $p = 0.002$) remained independently linked to hyoid bone position (adjusted r^2 of the model: 0.18, $p < 0.001$).

The other independent factor of OSA severity was FMA (divergence) that correlated with age ($R = -0.25$, $p < 0.001$), height ($R = -0.21$, $p = 0.002$), z-score of BMI ($R = -0.23$, $p < 0.001$), FRC ($R = -0.18$, $p = 0.012$), SNA ($R = -0.23$, $p < 0.001$), SNB ($R = -0.42$, $p < 0.001$), ANB ($R = 0.32$, $p < 0.001$), ANS'-Me ($R = 0.15$, $p = 0.035$), IMPA ($R = -0.36$, $p < 0.001$), and FMIA ($R = -0.34$, $p < 0.001$). In a multiple regression analysis with height, z-score of BMI, FRC, SNB, ANS'-Me, and FMIA as independent variables, only SNB (estimated effect: -0.339 , $p < 0.001$), ANS'-Me (estimated effect: 0.334, $p < 0.001$), and FMIA (estimated effect: -0.223 , $p < 0.001$) remained independently linked to FMA (adjusted r^2 of the model: 0.18, $p < 0.001$). It means that for every $\sim 3^\circ$ decrease in SNB, every ~ 3 mm increase in ANS'-Me, and every $\sim 2^\circ$ decrease in FMIA, the FMA angle increases by 10° . This model explained 36% of FMA variance (adjusted $r^2 = 0.36$, $p < 0.001$).

Table 3 and Figure 2 provide the comparison of children/adolescents according to their divergence status: normodivergence, 41% (95% confidence interval [CI]: 34–48); hyperdivergence, 32% (95% CI: 25–39); and hypodivergence, 27% (95% CI: 21–34). The participants with hyperdivergence were younger, less obese, and had a longer lower face (adenoid facies).

Table 2 Multiple Regression Analysis of OAHl

Characteristic	Estimated Effect	Standard Error of the Estimate	95% Confidence Interval	P value
Age	- 0.123	0.366	[-0.712; 0.722]	0.738
z-score of BMI	1.65	0.936	[-0.188; 3.544]	0.080
SNB	0.176	0.256	[-0.298; 0.724]	0.492
FMA	- 0.458	0.197	[-0.824; -0.043]	0.021
Hyoid position	0.567	0.182	[0.199; 0.919]	0.002

Notes: SNB: angle formed by the intersection of sella-nasion and nasion-B (mandible) green lines. FMA: Frankfort Mandibular plane Angle. See Figure 1 for the detailed description of these angles.

Table 3 Comparison of the Children/Adolescents According to the Divergent Type Based on FMA Angle

Characteristics	1: Hypodivergent (FMA $\leq 21^\circ$) N=56 27% 95% CI: 21-34	2: Normodivergent ($21^\circ < \text{FMA} < 29^\circ$) N=84 41% 95% CI: 34-48	3: Hyperdivergent (FMA $\geq 29^\circ$) N=65 32% 95% CI: 25-39	P value	Intergroup Comparisons
Age, years	12.4 $\pm$ 3.8	11.3 $\pm$ 3.6	10.4 $\pm$ 3.6	0.014	1 > 3
Sex: female/male, n	19 / 37	30 / 54	24 / 41	0.945	
Ethnicity: Af/As/ C/M, n	17 / 3 / 33 / 3	30 / 5 / 40 / 9	28 / 4 / 30 / 3	0.565	
z-score of BMI	2.19 [0.31; 2.61]	2.02 [0.85; 2.55]	1.11 [0.12; 2.16]	0.008	1 = 2 > 3
OSA class: 1/2/3, n	11 / 25 / 20	24 / 38 / 22	20 / 17 / 28	0.069	
Polysomnography					
Obstructive AHI/hour	10.4 [6.9; 18.8]	14.1 [7.5; 27.1]	8.5 [5.9; 15.2]	0.086	
Acoustic pharyngometry					
Pharyngeal junction, cm ²	1.20 $\pm$ 0.42	1.44 $\pm$ 0.40	1.28 $\pm$ 0.41	0.002	1 = 3 < 2
Pharyngeal volume, cm ³	16.9 [11.9; 23.0]	20.9 [16.2; 26.2]	17.8 [13.9; 22.3]	0.012	1 < 2
Pharyngeal cp, cm ³ /kPa	9.2 $\pm$ 12.2	12.3 $\pm$ 11.1	10.8 $\pm$ 8.4	0.254	
Cephalometry					
SNA, $^\circ$	84 $\pm$ 5	84 $\pm$ 5	82 $\pm$ 5	0.048	2 > 3
SNB, $^\circ$	81 $\pm$ 4	80 $\pm$ 5	77 $\pm$ 4	<0.001	1 = 2 > 3
ANB, $^\circ$	3 $\pm$ 3	4 $\pm$ 3	5 $\pm$ 3	<0.001	1 < 2 = 3
Skeletal class I/II/III, n	36 / 15 / 5	41 / 41 / 2	29 / 35 / 1	0.011	
N-Me, mm	104.8 $\pm$ 11.5	104.9 $\pm$ 11.7	107.6 $\pm$ 9.6	0.277	
N-ANS', mm	45 $\pm$ 6	44 $\pm$ 5	44 $\pm$ 5	0.785	
ANS'-Me, mm	60 $\pm$ 7	61 $\pm$ 8	64 $\pm$ 7	0.010	1 = 2 < 3
ANS'-Me, %	57 $\pm$ 3	58 $\pm$ 3	59 $\pm$ 3	0.002	1 = 2 < 3
FMA, $^\circ$	18 $\pm$ 3	25 $\pm$ 2	33 $\pm$ 3	ND	
IMPA, $^\circ$	95 $\pm$ 10	91 $\pm$ 8	86 $\pm$ 8	<0.001	1 > 2 > 3
FMIA, $^\circ$	68 $\pm$ 9	65 $\pm$ 8	61 $\pm$ 8	0.004	1 = 2 > 3
Hyoid bone to MP, mm	14 $\pm$ 7	15 $\pm$ 7	14 $\pm$ 7	0.639	

Correlations of Pharyngeal Volume Measured with Acoustic Pharyngometry

A comprehensive understanding of the interconnections between the pharyngeal volume and skeletal patterns is lacking.¹⁶ The pharyngeal volume measured in the sitting position correlated with age ($R = 0.48$, $p < 0.001$), height ($R = 0.56$, $p < 0.001$), z-score of BMI ($R = 0.36$, $p < 0.001$), FRC ($R = 0.47$, $p < 0.001$), SNA ($R = 0.19$, $p = 0.007$), SNB ($R = 0.24$, $p < 0.001$), N-ANS' ($R = 0.36$, $p < 0.001$), ANS'-Me ($R = 0.37$, $p < 0.001$), IMPA ($R = 0.25$, $p < 0.001$), and FMIA ($R = -0.18$, $p = 0.012$), and pharyngeal compliance ($R = 0.58$, $p < 0.001$). In a multiple regression analysis with height, z-score of BMI, FRC, SNB, ANS'-Me, and IMPA as independent variables, only height (estimated effect: 0.168, $p = 0.001$) and FMIA (estimated effect: -0.129 , $p = 0.014$) remained independently linked to pharyngeal volume (adjusted r^2 of the model: 0.32, $p < 0.001$).

Therapeutic Approaches in the Participants

Six kinds of therapeutic approaches were proposed to the participants: medical nasal obstruction treatment ($n = 91$, 44%), ENT surgery (mainly adenotonsillectomy, $n = 108$, 53%), orthodontic treatment ($n = 66$, 32%), myofunctional therapy ($n = 54$, 26%), maxilla-facial surgery ($n = 8$, 4%), and continuous positive airway pressure treatment ($n = 78$, 38%). Consequently, the children/adolescents often had several treatments at the same time (405 treatments across 205 participants, a mean of two treatments per patient).

The children/adolescents in whom orthodontic treatment was planned ($n = 139$), as compared to those without orthodontic treatment ($n = 66$), were characterized by non-different age (11.3 ± 3.5 years vs 11.2 ± 4.2 , $p = 0.931$), non-different BMI z-score (1.37 ± 1.28 vs 1.37 ± 1.48 , $p = 0.998$), non-different FMA ($25^\circ \pm 6^\circ$ vs $26^\circ \pm 7^\circ$, $p = 0.138$), lower

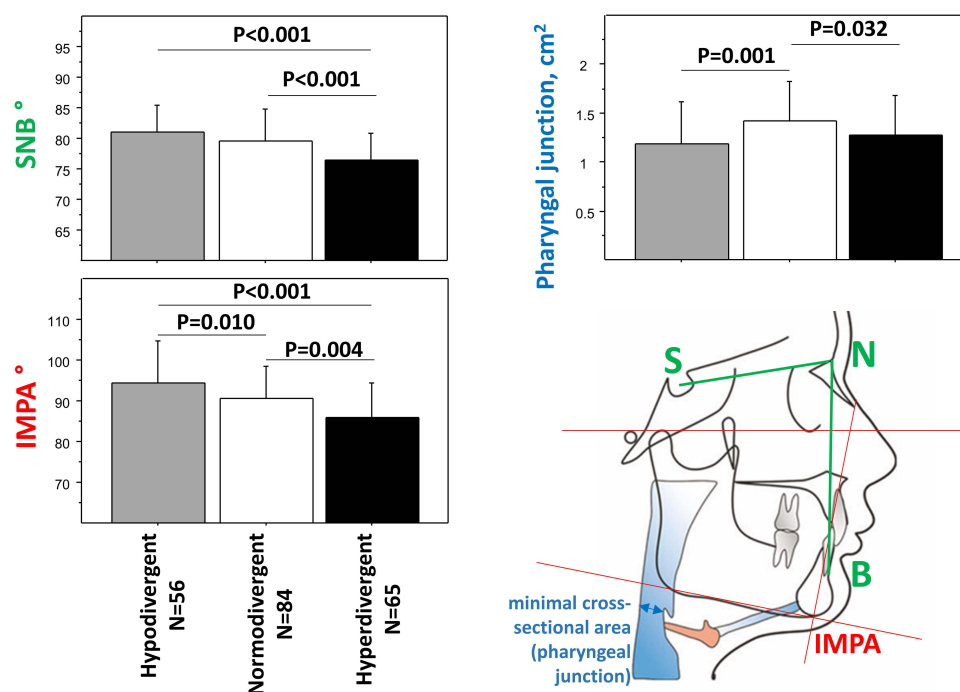


Figure 2 SNB, IMPA and pharyngeal junction area according to the kind of divergence. Upper left panel: SNB angle (described in the lower right panel). Lower left panel: IMPA angle (described in the lower right panel). Upper right panel: minimal cross-sectional area corresponding to the junction between the oral cavity and oropharynx: pharyngeal junction measured in sitting position. Results of the three groups (hypodivergence, normodivergence and hyperdivergence) are given as bars with their standard deviations. The results of the three group comparisons are given in Table 3 and the panels give the two group comparisons.

SNA ($82^\circ \pm 5^\circ$ vs $85^\circ \pm 5^\circ$, $p=0.003$), lower SNB ($78^\circ \pm 5^\circ$ vs $80^\circ \pm 5^\circ$, $p=0.017$), and lower OAH (16.4/hour $\pm$ 15.1 vs 22.4 $\pm$ 24.4, $p=0.034$).

The participants referred to myofunctional therapy had increased pharyngeal compliance as compared to those not referred for that treatment: 13.2 cm³.kPa⁻¹ $\pm$ 8.4 versus 9.9 $\pm$ 11.1, $p=0.049$ while their FMA angle was higher: $27^\circ \pm 7^\circ$ vs $25^\circ \pm 6^\circ$, $p=0.018$.

Participants in whom continuous positive airway pressure treatment was instituted, as compared to those who had not assisted ventilation, were older (12.8 ± 3.1 years vs 10.3 ± 3.8 , $p<0.001$), more obese (z-score BMI: 1.82 ± 1.13 vs 1.09 ± 1.39 , $p<0.001$), more severe (OAH: 25.6/hour $\pm$ 24.4 vs 13.8 ± 12.1 , $p<0.001$), and had non-different FMA angles ($25^\circ \pm 6^\circ$ vs $26^\circ \pm 7^\circ$, $p=0.221$).

Discussion

Our study shows that hyoid bone position and the Frankfort-mandibular plane angle (FMA) were independent determinants of OSA severity in children/adolescents suffering from moderate to severe OSA, although they accounted for a low level of OAH variance. This hyoid bone position was independently related to both lung volume (FRC) and Frankfort-Mandibular Incisor Angle (FMIA); this latter angle was also independently related to both the pharyngeal volume and FMA.

A high FMA is characterized by open-bite skeletal patterns (hyperdivergent) and a low FMA by closed-bite skeletal patterns (hypodivergent).¹⁷ Features commonly observed in hypodivergence are reduced or normal anterior lower face height, square facial type, hypertrophic masseter muscles, and increased overbite. The z-score of BMI and FMA negatively correlated to some extent in our study (result not shown, $r^2=0.05$), which is consistent with the fact that adult patients with OSA and with an early obesity onset showed a tendency for a more hypodivergent growth pattern.¹⁸ Thus, the well-known obesity effect on apnea risk may partly be related to its effect on facial growth. A retracted tongue position has been related to the low FMA,¹⁹ which may explain the decreased pharyngeal volume (see Table 3) and increased OAH. Nevertheless, adenoid facies, which is supposed to be commonly associated with OSA in children, is

associated with increased FMA (hyperdivergence) with increased lower face heights, steeper mandibular planes, and larger gonial angles. Accordingly, a dolichocephaly facial pattern has often been suggested to be present in children with OSA as compared to subjects without OSA.² It is often determined by bad habits, such as atypical swallowing,⁹ prolonged sucking of the finger or thumb, and oral breathing.¹⁰ Our results show that both hypo- and hyperdivergent children can be affected by OSA. These findings are consistent with a recent large multicenter cohort study, which reported no differences in the prevalence of these variables between children with and without OSA,²⁰ and with a systematic review and meta-analysis.² Our results are consistent with those of Villa et al since in their Sleep clinical record, both adenoid phenotype (hyperdivergent) and adult type (hypodivergent) increased the risk of OSA.²¹ Interestingly, Cakirer et al concluded that brachycephaly (ie, hypodivergence since decreased facial index is associated with reduced FMA) is associated with an increased AHI in adult White Americans.²²

Pharyngeal airway size is determined by an interaction between neural regulation of upper airway muscle activity and structural properties of the pharyngeal airway.²³ This pharyngeal airway size is the target of mandibular advancement devices that reduce pharyngeal collapsibility by enlarging the airway.²⁴ The only cephalometric index that negatively and independently correlated with pharyngeal volume was FMIA, which was unexpected. This angle is an important endpoint for orthodontic treatment as an edgewise appliance, and it has been shown that these appliances are able to improve this angle, regardless of the kind of divergence.¹⁵

Among the many characteristic craniofacial features of people with OSA, the caudal displacement of the hyoid bone has been repeatedly and consistently documented,^{25,26} suggesting the importance of the hyoid bone in the OSA pathogenesis.²⁷ The position of the hyoid bone is suggested to be neurally determined by the muscle force vector between supra- and infra-hyoid muscles that attach to the hyoid bone.²⁸ In addition to this neurally mediated traction, floating hyoid bone within soft tissue could also be displaced by non-muscular passive forces derived from surrounding soft tissue.²⁹ Relatively excessive soft tissue within the maxilla-mandible bony structure could shift the hyoid bone caudally, as well as narrow the pharyngeal airway in people with OSA; accordingly, in univariate analyses, hyoid bone distance was related to the z-score of BMI. Furthermore, lung volume increase could displace the hyoid bone, as well as the trachea, caudally, which consequently could decrease the extra-luminal tissue pressure.²⁹ Interestingly, we found that an increase in FRC was independently associated with increased hyoid bone distance to the mandibular plane. The results obtained by Kohno et al suggested that the hyoid bone position is a marker for changes in upper airway muscle activation and longitudinal pharyngeal wall tension due to lung volume change, as well as the balance between soft tissue volume and craniofacial size.²⁸ Our results show that the independent effects of both FRC and FMIA are in line with these experimental data.

Our study has clinical consequences. First, the cephalometry shows that, contrary to a common belief, OSA in children can be associated with a shorter face (27% with hypodivergence). Second, cephalometric analysis, especially facial divergence, is a key factor in diagnosis and in guiding orthodontic treatment decisions.³⁰ In bilateral Class II malocclusion, a frequent orthodontic problem, the Herbst appliance seems particularly favorable for patients with severe OSA, who were more often hypodivergent in our cohort. In these patients, the Herbst appliance promotes true forward mandibular rotation and anterior chin advancement, unlike the backward rotation seen in hyperdivergent patients. Such a biomechanical effect may improve mandibular profile and help prevent unfavorable skeletal changes as evidenced in non-OSA orthodontic literature,³¹ which could be especially beneficial in the context of OSA. Nevertheless, the estimated effect of FMA in our multivariate analysis shows that a reduction of OAH1 of 5 / h would be obtained with an increase in FMA of 10°, which is higher than that usually evidenced with class III correction appliances ($2.32 \pm 0.97^\circ$)³² suggesting the potential effect of these appliance in moderate OSA only. Computational fluid dynamics has been increasingly applied to simulate airflow behavior in the upper airway, enabling the assessment of airflow-related changes following orthodontic and orthognathic treatments that modify airway dimensions and shape, and therefore could be used to evaluate the effects of therapeutic approaches.³³ Third, acoustic pharyngometry allows for the calculation of pharyngeal compliance,¹¹ which may help to select candidates for passive myofunctional therapy¹⁰ that seems beneficial in childhood.³⁴

Overall, the treatment allocation was based on the results of pharyngeal compliance and craniofacial morphology modifications. Whether these multiple, simultaneous therapeutic approaches are effective was beyond the scope of our observational cross-sectional study.

Our study has limitations related to its cross-sectional design with no follow-up evaluation of treatment effect. Only moderate-to-severe children/adolescents with OSA were enrolled; we believe that the sole inclusion of a large sample of patients referred for OSA treatment is a strength of our study since the relationships evidenced could have been biased by the inclusion of patients without OSA and since the study was designed to assess the usefulness of acoustic pharyngometry and cephalometry for treatment planning. Consecutive children were enrolled without a specific selection of type 1 OSA (otherwise healthy), since the different therapeutic approaches in our practice are often proposed in the presence of obesity or syndromic diseases. Due to the restricted number of patients for each type of OSA, the multiple regression analyses were not evaluated for each type. It has to be emphasized that the angles and their cut-off values defining hypo- and hyperdivergence are not consensual,^{19,35} but there is a strong tendency to maintain the original facial type with age.³⁵ Finally, the variance of OAHl explained by craniofacial morphology is quite modest, in agreement with a recent multicenter study²⁰ and the degree of correlations of cephalometric indices are overall weak (R values ~ 0.20), which was expected but has to be emphasized.

In conclusion, our cross-sectional study in children/adolescents with moderate-to-severe OSA shows that OSA severity is linked to craniofacial morphology and that therapeutic approaches in our hands are guided accordingly by the results of both acoustic pharyngometry and cephalometry, which provide additional endotypic information for the evaluation of pharyngeal airway size in selected cases, as suggested by international recommendations.

Abbreviations

BMI, body mass index; SD, standard deviation; OSA, obstructive sleep apnea; OAHl, obstructive apnea-hypopnea index; FMA, Frankfort Mandibular plane Angle; FMIA, Frankfort Mandibular Incisal Angle; SNA, angle formed by the intersection of sella-nasion and nasion-maxilla; SNB, angle formed by the intersection of sella-nasion and nasion-mandible; ANB, angle formed by the intersection of nasion- A and nasion- B lines; IMPA, incisor Mandibular Plane Angle.

Data Sharing Statement

The data are available from the corresponding author on reasonable request.

Author Contributions

PB; Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing

CD₂ Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing

ALB; Data curation, Supervision, Writing – review & editing

AB; Formal analysis, Project administration, Resources, Validation, Visualization, Writing – review & editing

PA; Formal analysis, Investigation, Validation, Visualization, Writing – review & editing

BD Project administration, Validation, Writing – review & editing

JD; Resources, Validation, Visualization, Writing – review & editing

FS; Resources, Validation, Visualization, Writing – review & editing

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All authors took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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