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Original Article

The utility of acoustic pharyngometry and rhinometry in pediatric obstructive sleep apnea syndrome☆

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ABSTRACT

Objective: Our objective was to evaluate the usefulness of acoustic pharyngometry and rhinometry in assessing obstructive sleep apnea (OSA) syndrome in children.
Patients/Methods: Patients who were hospitalized for polysomnography underwent acoustic pharyngometry and rhinometry in sitting and supine positions to measure anatomical (pharyngeal and nasopharyngeal) volumes and collapsibility characteristics (reduction of pharyngeal volume, estimated pharyngeal compliance, and reduction of nasopharyngeal volume).
Results: In this study, we prospectively enrolled 103 children (median age, 10.4 years; 47 girls). Measures obtained from rhinometry correlated with height and were further height-normalized whereas measures obtained from pharyngometry did not correlate with height. Sleep apnea was ruled out in 51 subjects, while 52 children fulfilled OSA criteria (35 with obstructive apnea-hypopnea index ≥ 2 and $< 5.h^{-1}$ [mild] and 17 with an index ≥ 5). The three groups differed on the z-score of BMI, the reduction of pharyngeal volume when supine, the estimated pharyngeal compliance and the supine normalized nasopharyngeal volume. These four factors linearly correlated with the apnea index even though children without OSA and mild OSA were found to be similar overall. A multivariate analysis with apnea index as the dependent variable and BMI z-score, neck circumference, mean pharyngeal area in supine position, estimated pharyngeal compliance and normalized nasopharyngeal volume as independent variables, showed that only BMI z-score and estimated compliance remained independent predictors of obstructive apnea (r^2 value $= 0.25$, $p < 0.0001$).
Conclusion: An increase in pharyngeal compliance is an independent risk factor of OSA syndrome in children; it can be measured using acoustic pharyngometry while awake.

1. Introduction

Obstructive sleep apnea (OSA) syndrome is a breathing disorder characterized by recurrent, partial or complete episodes of upper airway obstruction and is commonly associated with intermittent hypoxemia and sleep fragmentation. Although multiple pathophysiological mechanisms are involved in the development of OSA, anatomical factors that restrict the upper airway and neuronal factors that increase the collapsibility of the upper airway are considered important contributors [1]. Even though adenotonsillar hypertrophy is a major risk factor for OSA syndrome in children, the association between subjective tonsil size and objective OSA syndrome severity is found to be weak at best with high-quality studies suggesting no association [2]. Thus, objective measures of airway size for identifying OSA patients are warranted. Indeed, almost all studies that have compared the size of the upper airway lumen between OSA patients and normal control individuals in a state of wakefulness have reported smaller airways in OSA patients [3]. This observation is consistent among various imaging approaches. The difference in lumen size is generally greater in the retropalatal region than other regions of the airway; however, it has

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been noted that the retroglossal area tends to be smaller in OSA patients as well [3].

Ideally, an imaging method for identifying OSA patients would allow the assessment of both anatomical factors that restrict the upper airway and the neuronal factors that increase the collapsibility of the upper airway. Acoustic reflection technology provides a non-invasive method for evaluating the airway's cross-sectional area as a function of the distance from the mouth (pharyngometry) or nostril (rhinometry) and its measurements are accurate and reproducible in both adults and children [4–7]. Acoustic rhinometry was shown to be able to detect adenoid hypertrophy [7,8], while acoustic pharyngometry has been used to detect tonsil hypertrophy [9]. By using acoustic reflection technology, airway anatomy can be easily determined, and indices of airway collapsibility can be calculated by comparing measurements in sitting and supine positions or before and after topical anesthesia [5,10]. This non-invasive approach might also help in characterizing the pathophysiological contributors to OSA syndrome that have yet to be evaluated, such as the anatomical and neuromuscular factors that increase airway collapsibility. Thus, the objective of our prospective study was to assess the usefulness of acoustic rhinometry and pharyngometry in describing the mechanistic predictors of OSA syndrome in children.

2. Material and methods

2.1. Patients

Subjects who were 4 to 16 years of age and were referred to the Pediatric Sleep Center at the Robert Debré University Hospital for suspicion of OSA, but were otherwise healthy, were enrolled for this study. These subjects were suspected of experiencing OSA based on certain characteristics, including snoring, witnessed apneas, restless sleep, excessive daytime sleepiness or inattention/hyperactivity symptoms, and mouth breathing. None of the participants suffered from any known craniofacial abnormality nor had undergone previous upper airway surgical procedure. These inclusion criteria were similar to those of previous studies that evaluated the role of anatomical factors in OSA pathophysiology [5]. Acoustic rhinometry and pharyngometry were conducted on the children as part of the usual assessment for OSA at the Pediatric Sleep Centre. This study was approved by our local Ethics Committee (CEER-0012-2017), and the database of collected data was declared to the French regulatory agency (CNIL). The subjects and their parents were informed of the collection of their prospective data for research purposes, and they could request to be exempted from this study per French law (non-interventional research).

2.2. Acoustic pharyngometry

Pharyngometry data was collected on the day of the sleep study using the EccoVision Acoustic Pharyngometer (E. Benson Hood Laboratories, Pembroke, MA). Each measurement consisted of a plot of cross-sectional area (square centimeters: Y-axis) as a function of distance (centimeters: X-axis) from the incisors. For each subject, measurements were obtained using oral breathing with a pediatric mouthpiece at functional residual capacity. At least four curves were obtained, and the data was considered valid if the cross-sectional area differed by 10% or less from one another. X- and Y-values were recorded for the oropharyngeal junction and glottis. The volumes of the oral cavity (between the incisors and oropharyngeal junction) and the pharynx (between the oropharyngeal junction and glottis) were calculated with the mean pharyngeal area. These measurements were made on patients in sitting and supine positions. Measurements were made on patients in the supine position after they were in this position for 5 min. The percentage of change in the oropharyngeal junction, mean pharyngeal area, and pharyngeal volume [100 × (sitting−supine)/sitting] between the two positions were calculated. Estimated pharyngeal compliance (cm^3/kPa) was calculated using the following formula:

$$10^4 * (\text{sitting} - \text{supine pharyngeal volume}) \Big/ \left[\rho * g * \left(\frac{NC}{2*\pi} - \sqrt{\frac{SPA}{\pi}} \right) \right] \quad (1)$$

where $\rho = 1$ g/cm^3, $g = 981$ cm·s^{-2}, and NC and SPA denote neck circumference and the mean sitting pharyngeal area, respectively.

This formula reflects the modification of the pharyngeal volume under the effect of hydrostatic pressure applied by the neck on the pharynx. Our approach is justified by the fact that the peripharyngeal pressure appears to be the principal determinant of pharyngeal collapsibility [11].

Since the critical pressure at which the pharynx collapses (Pcrit) corresponds to the pressure that yields zero flow through the pharynx, an estimate of that pressure ($Pcrit_{calc}$) can be obtained by:

$$\Delta V \Big/ C = \left(0 - V_{ph}\right) \Big/ C = -V_{ph} \Big/ C \quad (2)$$

where V_{ph} is the volume of the pharynx in the supine position and C is the compliance of the pharynx.

2.3. Acoustic rhinometry

The measurements were conducted with the EccoVision Acoustic Rhinometer (E. Benson Hood Laboratories, Pembroke, MA). Minimal cross-sectional areas (MCAs) were measured as described in Ref. [12]. Three distances were determined that correspond to the distance from the nostrils to the isthmus notch and conchal notch (MCA1 and MCA2), and the distance that separated the mid-cavity from the nasopharynx (CA3). We subsequently recorded MCA1, the volume of the mid-cavity (from MCA2 to CA3) and the volume of the nasopharynx (from CA3 to the end of the nasopharynx). The length of the nasopharynx was set to a distance of CA3 plus the distance from the nostril to CA3 to take account of the potential lengthening of the nasopharynx with age or height. The maximal length of the X-axis was set at 12 cm from the nostril. This approach was different compared to the approach in which predefined lengths of the segments were set (volume from 0 to 4 cm, 0–5, 1–4 and 2–5 cm) [13]. The mean values (measurements from the two nostrils) of the MCAs and volumes were recorded. These measurements were made on patients in sitting and supine positions during a breathing pause. Measurements were made on patients in the supine position after they were in this position for 5 min. The percentage of change between the two positions was calculated for MCA1, the volume of mid-cavity and the volume of nasopharynx as follows: [100 × (sitting−supine)/sitting].

2.4. In-laboratory polysomnography

Polysomnography studies were performed overnight. An Alice 6 LDx polysomnography system (Philips, Murrysville, PA) recorded the following parameters: chest and abdominal wall motion using respiratory inductance plethysmography, heart rate by electrocardiogram, arterial oxygen saturation (SpO2) by pulse oximetry, airflow using a 3-pronged thermistor, nasal pressure by a pressure transducer, electroencephalographic leads (C3/A2, C4/A1, F3A2,

F4A1, O1/A2, O2/A1), left and right electrooculograms, submental electromyogram, and tibial electromyogram. Study participants were also recorded with an infrared video camera. Patients were scored using standard pediatric sleep scoring criteria by experienced pediatric sleep physicians [14]. Obstructive apnea index (OAI) $\geq$ 1 or obstructive apnea-hypopnea index (OAHI) $\geq$2 were used for the diagnosis of OSA in patients. Based on the OAHI, patients were further classified as having mild (2 $\leq$ OAHI < 5) or moderate to severe (OAHI $\geq$ 5) OSA.

2.5. Questionnaires

We used standard sleep questionnaires for the clinical evaluation of the study population. The modified Epworth Sleepiness Scale was used for the evaluation of excessive daytime sleepiness [15]. Hyperactivity/inattention related symptoms were evaluated by the Conners' abbreviated teacher rating scale (CATRS-10) that was completed by a parent [16]. Sleep-related breathing symptoms were assessed by the Brouilette questionnaire [17] and the Spruyt-Gozal questionnaire [18] in its validated French-translation version [19].

2.6. Statistical analyses

Our objective was to determine independent contributors to OSA. We decided to conduct a multivariate analysis with at least four factors. These factors include two anthropometric factors, namely body mass index (BMI) z-score and neck circumference, a factor from pharyngometry measurements, and another factor from rhinometry measurements. To perform a multivariate analysis with at least four factors, the sample size of OSA cases would have to be ~40 subjects (10 subjects per factor). In our pediatric sleep center, the prevalence of OSA is around 50%. Thus, we enrolled ~100 children.

Results were expressed as medians [25th − 75th percentiles]. Comparisons of continuous variables between children without OSA and children with mild and moderate to severe OSA were performed using the Kruskal–Wallis test. Subsequent intergroup comparisons were performed using the Mann–Whitney *U*-test. Categorical variables were compared using the chi-square test. Correlations were evaluated using Pearson's correlation coefficient. Additional statistical analyses are described in the text. A P value < 0.05 was deemed significant. No correction for multiple testing was done due to the pathophysiological design of the study [20]. All statistical analyses were performed with Statview 5.0 software (SAS Institute, Cary, North Carolina, USA).

3. Results

We enrolled 103 consecutive children for this study and evaluated which parameters obtained from acoustic measurements correlated with height or age to determine which parameters needed to be corrected for body growth. We observed a 100% (103/103) success rate for sitting/supine pharyngometry and a 91% (94/103) success rate for sitting/supine rhinometry measurements. The correlation between the height of the children and airway parameters are described in Table 1. Based on the correlation coefficients between height and airway parameters, the volume of the nasopharynx was found to be the most correlated parameter (r~0.20) and was corrected for height to obtain a normalized parameter.

The prevalence (%) of OSA syndrome in our population was 52/103 children (50%; 95% CI: 41–60%). The characteristics of the 103 children are described in Table 2 according to the presence of moderate to severe (n = 17) OSA, mild (n = 35) OSA or the absence of OSA (n = 51). The BMI z-score was found to correlate weakly with the mean supine pharyngeal area (r = −0.20; p = 0.038). Intergroup comparisons of the three groups of children are also provided in Table 2. The BMI z-score, reduction (%) of pharyngeal volume, estimated pharyngeal compliance, and normalized nasopharynx volume were significantly different between the three groups. However, children without OSA did not differ from children with mild OSA overall.

Table 1
Correlates of acoustic measurements with height.

Acoustic parameters	r^2 value (Pearson test)	P value
Pharyngometry		
Sitting position		
Oral cavity volume, cm^3	0.06	0.017
Oropharyngeal junction distance, cm	0.38	<0.001
Oropharyngeal junction area, cm^2	0.01	0.313
Mean pharyngeal area, cm^2	0.02	0.113
Pharyngeal volume, cm^3	0.05	0.053
Glottis distance, cm	0.30	<0.001
Supine position		
Oropharyngeal junction area, cm^2	<0.01	0.938
Mean pharyngeal area, cm^2	0.01	0.248
Pharyngeal volume, cm^3	0.02	0.176
Rhinometry		
Sitting position		
MCA1 distance, cm	0.06	0.011
MCA1 area, cm^2	0.15	<0.001
MCA2 distance, cm	0.08	0.035
CA3 distance, cm	0.05	0.005
Volume of mid-cavity, cm^3	0.17	<0.001
Volume of nasopharynx, cm^3	0.19	<0.001
Supine position		
MCA1 area, cm^2	0.12	<0.001
Volume of mid-cavity, cm^3	0.08	0.005
Volume of nasopharynx, cm^3	0.24	<0.001

To determine the independent contributors to OSA, univariate and multivariate analyses with OAHI were conducted. Univariate analyses demonstrated that OAHI correlated with the BMI z-score (r = 0.38, p < 0.001), reduction (%) of pharyngeal volume (r = 0.19, p = 0.049), estimated pharyngeal compliance (r = 0.26, p = 0.007) and normalized nasopharynx volume (r = −0.26, p = 0.012). A multivariate analysis was subsequently conducted with OAHI as the dependent variable and BMI z-score, neck circumference, mean pharyngeal area in the supine position, estimated pharyngeal compliance, and normalized nasopharyngeal volume as the independent variables (P values < 0.10 in univariate analyses). The multivariate analysis showed that only the BMI z-score (p < 0.0001) and estimated compliance (p = 0.0460) remained as independent predictors of OSA (r^2 value of the model = 0.25, p < 0.0001) in our population.

We further evaluated if our results could be reproduced in patients with more severe OSA (OAHI $\geq$ 5). Thus, we conducted a logistic regression analysis with OAHI $\geq$5 or <5 hr^{-1} as the dependent variable and BMI z-score and estimated compliance as the independent variables. We observed that both the BMI z-score (p = 0.0003) and estimated pharyngeal compliance (p = 0.0029) remained as independent predictors (r^2 value of the model = 0.33) of moderate to severe OSA.

4. Discussion

Our study demonstrates that acoustic measurements can provide useful parameters that can predict OSA pathophysiology. In particular, the multivariate analysis suggests that acoustic pharyngometry provides the most useful measurements because they are used to calculate estimated pharyngeal compliance, which we demonstrate is an independent risk factor of OSA.

Table 2
Characteristics of the children according to the presence of OSAS.

Characteristics n or median [25th − 75th percentiles]	OAHI ≥5/hour N = 17 (group 1)	5 < OAHI ≥2 N = 35 (group 2)	OAHI <2/hour N = 51 (group 3)	P value	Intergroup comparisons
Sex, female/male	8/9	18/17	21/30	0.639	
Age, years	9.6 [6.1; 13.7]	11.7 [7.9; 13.7]	9.9 [6.8; 12.9]	0.453	
Ethnicity				0.075	
Caucasian	9	30	40		
African	6	5	9		
Other	2	0	2		
Height, cm	138 [122; 160]	146 [129; 157]	135 [121; 155]	0.435	
Weight, kg	50.5 [34.1; 82.4]	45.0 [29.1; 57.1]	35.0 [22.2; 59.2]	0.098	
Z-score of BMI	+2.46 [+1.32; +2.96]	+0.49 [-0.13; +1.26]	+0.97 [+0.01; 1.72]	**<0.001**	1>2 = 3
Neck circumference, cm	32.0 [30.7; 37.4]	31.5 [28.0; 34.9]	29.5 [27.1; 33.0]	0.054	
Questionnaires					
Brouilette [17]	−0.99 [−2.76; −+2.37]	−1.70 [−3.12; −0.28]	−1.70 [−3.12; −0.28]	0.483	[b]
Brouilette >3.5/filled questionnaires	3/13	1/26	1/36	**0.033**	
Spruyt-Gozal [18]	1.23 [0.37; 2.25]	1.06 [0.23; 2.44]	1.12 [0.16; 2.00]	0.855	[b]
Spruyt-Gozal >2.75/filled quest.	2/12	3/27	4/36	0.863	
Epworth [15]	9 [2; 14]	11 [7; 16]	7 [5; 12]	0.163	[b]
Epworth >10/filled quest.	5/13	14/25	10/36	0.085	
CATRS-10 [16]	13 [9; 21]	15 [6; 25]	12 [5; 21]	0.719	[b]
CATRS-10 > 15/filled quest.	4/12	12/27	15/36	0.808	
Polysomnography					
OAI. h^{-1}	4.1 [1.9; 6.3]	1.3 [0.8; 2.0]	0.1 [0.0; 0.3]	Not tested	
OAHI. h^{-1}	6.7 [5.3; 13.9]	2.7 [2.1; 3.3]	0.5 [0.1; 0.8]	Not tested	
AHI. h^{-1}	8.6 [5.6; 14.7]	3.6 [2.9; 4.9]	1.5 [0.6; 2.4]	<0.001	1>2 > 3
Arousal index. h^{-1}	2.3 [0.9; 7.5]	0.8 [0.3; 1.7]	0.3 [0.1; 0.5]	<0.001	1>2 > 3
Desaturation index. h^{-1}	2.7 [1.6; 10.1]	1.5 [0.8; 3.4]	1.0 [0.5; 2.2]	0.003	1 > 2 = 3
Arterial oxygen saturation nadir, %	86 [79; 92]	91 [87; 94]	92 [88; 93]	0.111	
Pharyngometry, n = 103					
Sitting position					
Oral cavity volume, cm^3	27.3 [23.3; 33.1]	29.9 [24.4; 33.6]	27.9 [25.2; 32.9]	0.844	
Oropharyngeal junction distance, cm	8.0 [7.6; 8.6]	7.6 [7.2; 8.4]	7.6 [7.6; 8.4]	0.652	
Oropharyngeal junction area, cm^2	0.67 [0.47; 1.48]	0.85 [0.58; 1.36]	0.59 [0.52; 1.43]	0.652	
Mean pharyngeal area, cm^2	1.12 [0.83; 2.02]	1.38 [0.93; 2.04]	0.96 [0.81; 1.88]	0.252	
Pharyngeal volume, cm^3	14.8 [6.9; 21.7]	12.0 [7.3; 16.7]	7.7 [6.3; 15.4]	0.423	
Glottis distance, cm	16.2 [15.7; 17.4]	16.2 [15.7; 16.8]	15.7 [15.3; 16.6]	0.685	
Supine position					
Oropharyngeal junction area, cm^2	0.51 [0.47; 0.74]	0.70 [0.49; 1.00]	0.53 [0.44; 1.04]	0.252	
Mean pharyngeal area, cm^2	0.81 [0.76; 1.17]	1.17 [0.77; 1.87]	0.83 [0.72; 1.54]	0.071	
Pharyngeal volume, cm^3	6.6 [5.8; 9.8]	9.0 [6.2; 15.7]	6.5 [5.6; 12.8]	0.079	
Collapsibility indices					
% reduction of junction area	+14 [−5; +48]	+19 [+7; +28]	+13 [−2; +32]	0.883	
% reduction of pharyngeal volume	+22 [+10; +52]	+13 [0; +23]	+10 [+2; +19]	**0.046**	1 = 2 = 3[a]
% reduction of mean pharyngeal area	+14 [+5; +53]	+12 [+3; +20]	+11 [+3; +19]	0.488	
Pharyngeal compliance, cm^3/kPa	13.81 [2.79; 22.80]	2.75 [0.12; 8.05]	1.90 [0.31; 5.05]	**0.006**	1 > 2 = 3
$Pcrit_{calc}$, cmH_2O	−6.7 [−21.4; +3.4]	−12.3 [−27.9; +2.9]	−20.3 [−51.2; −3.4]	0.259	
Rhinometry, n = 94					
Sitting position					
MCA1 distance, cm	1.7 [1.2; 2.0]	1.9 [1.3; 2.1]	1.9 [1.5; 2.0]	0.778	
MCA1 area, cm^2	0.42 [0.35; 0.57]	0.40 [0.33; 0.50]	0.39 [0.35; 0.48]	0.794	
MCA2 distance, cm	3.3 [2.7; 3.9]	3.6 [3.2; 3.9]	3.5 [3.1; 3.9]	0.496	
CA3 distance, cm	5.1 [4.6; 6.0]	5.6 [4.7; 6.0]	5.3 [5.1; 5.7]	0.579	
Volume of mid-cavity, cm^3	1.8 [1.2; 2.8]	2.0 [1.5; 2.7]	1.8 [1.4; 2.6]	0.483	
Volume of nasopharynx, cm^3	11.4 [7.1; 17.1]	12.1 [10.2; 18.9]	13.1 [10.1; 19.0]	0.355	
Supine position					
MCA1 area, cm^2	0.34 [0.27; 0.47]	0.36 [0.29; 0.45]	0.32 [0.27; 0.43]	0.814	
Volume of mid-cavity, cm^3	1.2 [0.9; 2.1]	1.6 [1.3; 2.1]	1.5 [1.0; 2.3]	0.321	
Volume of nasopharynx, cm^3	9.4 [6.3; 14.0]	11.4 [8.0; 14.4]	10.1 [7.8; 14.8]	0.400	
Normalized nasopharynx volume, cm^2	0.41 [0.38; 0.61]	0.64 [0.51; 0.76]	0.58 [0.45; 0.73]	**0.027**	1 < 2 = 3
Collapsibility indices					
% reduction of MCA1	+21 [+5; +34]	+9 [+1; +25]	+18 [+3; +32]	0.368	
% reduction of mid-cavity volume	+9 [−3; +35]	+16 [−7; +30]	+16 [−3; +31]	0.890	
% reduction of nasopharynx volume	+13 [−12; +37]	+13 [+1; +29]	+19 [+8; +33]	0.619	

Bold represents p value < 0.05.
[a] Group 1 > group 3 (Mann Whitney test).
[b] No significant differences for the four questionnaires were evidenced when comparing OSA children and children without OSAS (Mann Whitney tests).

Before we address the potential significance of our findings, some technical issues deserve comment.

To the best of our knowledge, our study is the only one that has performed both acoustic pharyngometry and rhinometry to identify independent risk factors of OSA and questioned the methodological need to normalize recorded parameters for child growth. Prior to this study, there have only been two studies that performed pharyngometry [5,6] and two other studies that performed rhinometry [4,7] in children suspected of having OSA syndrome. The reproducibility of acoustic diagnostic methods have already been demonstrated [4–7]. However, the idea of normalizing data of acoustic measurements for height, age or even gender for children and adolescents have not been addressed. We showed that pharyngeal distances were related to the height of the children, which was

expected. Surprisingly, measured cross-sectional areas and pharyngeal volume were found to be unrelated to the height of the children. Instead, 30–40% of the total variance in the minimum cross-section area measurements of the pharynx can be explained by shared familial factors [21], which might explain the heritability of OSA.

The measurements obtained from acoustic rhinometry were more closely linked to child growth. The MCA1 area was related to height as previously shown [13]. We further demonstrated that the other acoustic rhinometry measurements were also related to the height of the children. This observation argues against the selection of pre-determined areas based on centimeters away from the nostril as they would correspond to different anatomical regions according to the height of the subject. Due to adenoidal hypertrophy causing indents in the nasopharyngeal space, the volume displacement caused by hypertrophy can be easily measured using acoustic rhinometry. Nevertheless, it is still challenging to determine the location of the nasopharynx using acoustic rhinometry. Okun and colleagues reported that the nasopharyngeal airway is between 6 and 8 cm posterior to the nostril [7]. In our study, the volume of the nasopharynx was selected from ~5.5 to 11 cm from the nostrils, and the normalized nasopharyngeal volume was found to be reduced in moderate to severe OSA patients (OAHI $\geq$ 5). This reduction of the normalized nasopharyngeal volume is probably linked to adenoid hypertrophy as previously shown [22].

Many studies have reported smaller airways in OSA patients [3]. In contrast to previous acoustic pharyngometry results of children [5,6], we did not observe a reduced pharyngeal minimal cross-section area in the sitting position for OSA patients. The absence of this observation might be related to the more restricted sample size or the inclusion of mainly snoring children in this study. Consistent with our observations, Brown, and colleagues found that snoring apneic and snoring non-apneic adults have a similar pharyngeal cross-sectional area [23]. When we assessed the sitting pharyngeal volume, it appeared to increase with OAHI. This observation could be related to pharyngeal muscle activation because the more collapsible upper airway in OSA patients increases dilator muscle activity through negative-pressure reflex during wakeful periods [24].

As early as 1987, acoustic pharyngometry has been used to show that pharyngeal distensibility is higher in snoring apneic patients versus snoring non-apneic patients [23]. Furthermore, Jung and colleagues have shown that the oropharyngeal junction and mean pharyngeal area are significantly reduced in OSA patients in the supine position only [10]. These latter results are consistent with the enhanced pharyngeal collapsibility in OSA patients in the recumbent position. In this study, we showed that pharyngeal collapsibility is elevated in OSA children. Consistent with our findings, Gozal and Burnside demonstrated enhanced pharyngeal collapsibility in OSA children after topical anesthesia using acoustic pharyngometry [5]. In this study, the authors suggested that the anatomical effects imposed by the hypertrophy of lymphatic tissues in the airway were the major determinants of increased upper airway collapsibility in a majority of pediatric patients with OSA [5]. This idea is in line with the overall anticipated outcomes of tonsillectomy and adenoidectomy [25], and it also concurs with the overall proposed mechanisms that underlie upper airway collapsibility in children [26]. We have included an Appendix section that further describes the mechanical meaning of the measured pharyngeal compliance with respect to OSA pathophysiology [27].

The gold-standard measurement for pharyngeal collapsibility is the pharyngeal critical pressure (Pcrit). Thus, we performed measurements of airway collapsibility during wakefulness that allowed us to calculate active Pcrit values and compared our calculated Pcrit values to those reported in the literature. Previous studies demonstrated that active Pcrit explained only 5% of the OAHI variance in adult OSA patients [28] and 12% of the OAHI variance in obese adolescents [29]. These findings are consistent with our observation that only 7% of the OAHI variance in children can be explained by Pcrit. Our Pcrit estimates are also consistent with the Pcrit values of -11.6 ± 9.4 cm H_2O in obese adolescents with OSA versus -18.0 ± 9.0 cm H_2O in age and BMI matched controls that were measured by Marcus and colleagues [29]. Although our calculated Pcrit values are similar to those reported in the literature, a validation of our simpler method of Pcrit evaluation against the gold-standard method still needs to be conducted.

Nasal obstruction is a well-known risk factor for the OSA syndrome [30]. In this study, normalized supine nasopharyngeal volume was reduced in patients with moderate to severe OSA. This observation was consistent with the results of Schwab and colleagues who demonstrated that obese OSA adolescents had a smaller nasopharyngeal airway than obese control subjects [31]. However, normalized supine nasopharyngeal volume was found to be only associated with OSA in univariate analyses (see Table 2), suggesting that nasal obstruction treatment would be insufficient in treating OSA as suggested by randomized trials [32].

Our study has several limitations. Our acoustic measurements can only explain a small part of the variance of OAHI as previously noted in the use of acoustic pharyngometry and rhinometry on adult patients [30]. It is necessary to gain a full understanding of the pathophysiological traits of OSA patients, including upper airway anatomical collapsibility, loop gain, arousal threshold, and upper airway gain, for customized OSA treatment to be a reality [33]. As stated by Eckert, the anatomical contribution to OSA varies substantially. Indeed, impairment in pharyngeal anatomy can be modest, and in many patients (~20%), pharyngeal collapsibility asleep is not different from people without OSA. Thus, non-anatomical factors that modulate pharyngeal patency are crucial determinants of OSA for many people [34]. Nonetheless, our work contributes to our understanding of the characteristics of children with OSA. Furthermore, we did not try to determine the sensitivity and specificity of our measurements because our results could not be generalized due to the monocenter design of our study. Although our study could have recruitment biases, moderate to severe OSA syndrome prevalence was not significantly different than in a recent French study (17% 95% CI: 9–24 versus 29% 95% CI: 20–38) [19] and our OSA prevalence was also similar to that observed by Kang and colleagues (52.3%) in Taiwan who recruited children aged 2–18 years old with symptoms suggestive of OSA [35]. On the other hand, a strength of our study is the fact that it is the only one that performed both acoustic measurements (pharyngometry and rhinometry) and that questioned the methodological need of normalization of recorded parameters for growth. Finally, the median age of our population (>8 years old) may have selected children without lymphoid tissue hypertrophy. Nevertheless, it has been demonstrated that in children with snoring, appreciable pharyngeal lymphoid tissue enlargement persists beyond the eighth birthday [36].

Our study also has clinical implications. An OAHI >5 h^{-1} has been used as a threshold for delivering treatment irrespective of the presence of morbidity [37]. In these children, their increased pharyngeal compliance suggests that myofunctional therapy alone or in addition to tonsillectomy may be effective modalities of treatment. Depending on the presence or absence of tonsillar hypertrophy, myofunctional therapy would involve certain sets of isotonic and isometric exercises that target oral and oropharyngeal structures [38]. Our study, by demonstrating the utility of estimated pharyngeal compliance in the assessment of OSA, may also be of utility for investigating the effects of OSA treatments. However, studies would have to be conducted to confirm if this is the case.

In conclusion, an increase in pharyngeal compliance is an independent risk factor of OSA syndrome in children, and it can be measured using acoustic pharyngometry during wakefulness.

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Appendix

To gain greater insight into the mechanical meaning of measured compliance, one should consider the mechanics of the upper airways. The compliance of a thin elastic tube is described in Ref. [39], and it may be expressed as (per unit tube length):

$$C = \frac{4\pi R^3(1+\sigma)\sigma}{Eh} \quad \text{Eq. (1)}$$

In this equation, R is the inner radius of the tube, E is its Young's modulus, h is the thickness and σ is Poisson's ratio for the elastic material of the tube. Muscle fibers can be considered incompressible, ie, $\sigma = 0.5$.

Equation (1) shows that the compliance of the pharynx is proportional to the third power of the radius; therefore, it explains why the upper airways in children are more stable than those of adults. With regards to the effective Young's modulus, measurements for compliance were made after the patients were in a supine position for several minutes thereby allowing the muscles to adapt their strength. Hill's functional model of muscle contraction addresses the modification of Young's modulus in muscles in an active state [40]. The simplified Hill's model is reduced to the two-element model with only a contractile element and a series elastic element. By using this model, it is shown that stiffness (per unit length) of the muscle is linearly related to tension T, ie, $E'h = \alpha(T+\beta)$. Hence, the effective Young's modulus can be written as $E' = E+\alpha T/h$. Thus,

$$C = \frac{3\pi R^3}{Eh + \alpha T} \quad \text{Eq. (2)}$$

in which the tension (T) is developed by the pharyngeal dilator muscles and α is a coefficient close to 0.5.

There were no differences in the mean pharyngeal sections (~R values) in the sitting position between the different groups, and a decrease in the thickness of the pharyngeal dilator muscle sheet (h values) seemed unlikely. In contrast, hypertrophy of the pharyngeal dilator muscles is expected because of the repeated effort of dilating the pharynx during apneas. Thus, the most plausible explanation for the increase in pharyngeal compliance is a decrease in Young's modulus (E), a neuromuscular deficit of the pharyngeal dilators (decrease in T) in the group of patients with moderate to severe OSA syndrome (see Equation (2)) or both. A decrease in the elasticity of the pharynx can occur as a result of lymphoid tissue hypertrophy, fat deposition, or both. Consistent with the plausible explanation for increased pharyngeal compliance, Marcus and colleagues showed that Pcrit significantly declined in three OSA children re-evaluated after tonsillectomy and adenoidectomy [26]. Furthermore, BMI z-score is associated with an increase in neck parapharyngeal fat [41]; weight loss has been observed to be associated with a decrease in Pcrit in OSA patients [42]. Finally, a decrease in muscle tension is supported by experiments that showed that Pcrit decreased during electrical stimulation of the genioglossus [43].

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2019.03.003.

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