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RESEARCH ARTICLE

Impulse Oscillometry Parameters in Childhood Asthma, Childhood Obesity and Childhood Obesity with Asthma

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ABSTRACT

Background: Monitoring of lung function is necessary to detect irreversible airway obstruction in both asthma and obesity. Impulse oscillometry (IOS), a novo non-invasive equipment, is increasing popularity to measure airway resistance in young children worldwide.
Aims: To compare IOS parameters among Thai asthmatic children and Thai obese children with and without asthma.
Methods: A cross-sectional study was conducted in 120 participants, aged 4-15 years old. Forty children were in each group (asthma, obesity, and obesity with asthma). All volunteers were consented to measure airway resistance by IOS technique (Jaeger, Germany).
Results: Seventy-three percent of patients were male with the mean age at 8.8 + 2.61 years old. Mean X5 was found normal in childhood obesity (-0.13) when compared to children with asthma (-0.23) and obesity with asthma (-0.19) ($p < 0.001$ and 0.013 respectively). The cut-off value of X5, according to ROC curve, for predicting asthma in obese patients was -0.16 kPa/L/s with 70% sensitivity, 70% specificity and 70% accuracy (AUC= 0.69). However, with the bronchodilator effect (adjusted by duration of asthma control), we found significant higher percentage change of IOS parameters, including resonant frequency, area of reactance and R5-R20, in asthma (Fres -24.57 $\pm$ 15.82, AX -58.28 $\pm$ 13.37, R5-R20 -51.32 $\pm$ 20.13) than in asthma with obesity (Fres -13.77 $\pm$ 16.42, AX -43.35 $\pm$ 21.4, R5-R20 -34.72 $\pm$ 18.21), ($p = 0.014, 0.004, 0.002$ respectively).
Conclusions: X5 and percentage changes after bronchodilator of Fres, AX, and R5-R20 are useful parameters to differentiate airway dysfunction in asthmatic children from obese children.

Keywords: Impulse oscillometry, asthma, obesity, lung function, respiratory impedance

Introduction

Asthma, a reversible airway inflammation disease, characterized by recurrent exacerbations as shown as persistent cough, dyspnea and expiratory wheezing.[1] These symptoms usually are stimulated by various triggers and associated with obesity, reflux, stress, allergic rhinitis and obstructive sleep apnea.[2] As indicated by Stern that asthma was an important global concerning respiratory illness effected more than 300 million people in all age group and the prevalence is increasing globally, especially in low-to-middle income country.[3] In addition, the severity of this disease likely relate to the obesity, as mentioned in many studies.[4] The correlation between these two diseases and the similarity of increasing prevalence urged researchers to study the relationship between these two illnesses. [5,6]

Obesity is found to be a risk factor for asthma in multiple demographic studies.[5,6] Additionally, obesity is suggested by GINA guideline to be an important comorbidity for asthma exacerbation.[2] Mohanan et.al. indicated that obese state does not only play a crucial role but also alter both inflammation and immune responses in this allergic airway disease.[7] As known, the inflammation in asthma is usually derived from various triggers, e.g., allergens, smokes, and climate. However, both asthma and overweight have exercise as a same cause to make respiratory deterioration. The fact that obesity has overlap respiratory symptoms and able to compromise lung function creates a challenge and likely to induce a misinterpret in asthma diagnosis.[8] For this reason, asthma can be underestimate for airflow obstruction and may lead to under treatment in obese population.[9] Therefore, appropriate lung function tests should be employed to differentiate these two diseases apart. According to GINA guideline, the diagnosis of asthma should be compatible with typical symptoms and evidence of variable airflow obstruction which measured by spirometry.[2] Nevertheless, this effort dependent measurement is hardly performed in children younger than 5 years of age. Thus, impulse oscillometry (IOS), new fast and effortless lung function test, which able to perform in children as young as 3 years old is increasing popularity and likely to use for lung function measurement in preschool children. Additionally, IOS is proved to be more sensitive than spirometry in detecting small airway obstruction in asthmatic patients.[10,11]

Children with asthma tend to have high resistance of small airways as shown in specific parameters (high R5, R5-R20 and low X5) compared with children without asthma. Therefore, changes of R5 and X5 after bronchodilator treatment are considered positive tests in pediatric asthma. However, the cut-off values of these parameters are still varied among studies.[12–14]

In obesity, the lung impairment from airway obstruction caused by a reduction of peripheral airway diameter is also presented with IOS measurement.[15] This similar information is supported by Assumpcao's study which demonstrated respiratory resistance in obese children who had normal spirometry by IOS.[16]

The advance techniques of IOS which make pulmonary function test easier to be done in children and produce higher chance to detect small airway obstruction in both obesity and asthma intrigue us to choose IOS over spirometry to study airway resistance in our children, both asthma and obesity. The aim of this study is to compare IOS parameters among Thai children with asthma and Thai obese children with and without asthma.

Methods

Study population and study design

A cross-sectional study was conducted in 120 participants, aged 4-15 years old. Forty children in each group (asthma, obesity, and obesity with asthma) were recruited in Queen Sirikit National Institute of Child Health from September 1st, 2019, to February 28th, 2020. Participants who were in asthma group required to have weight for height less than 120% and fulfilled clinical criteria of asthma as determined by pediatric allergist.

Obese children in our study had weight for height more than 140%, according to Thai Pediatric Nutrition Association Guideline for childhood obesity. The participants who had no history of recurrent wheezing nor atopy regarding the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire were enrolled as obesity without asthma.[17] Obese children who fulfilled criteria of asthma and continued treatment with inhaled corticosteroid were recruited into obesity with asthma group.

Participants were excluded from our study if they had chronic lung disease, cardiac problems, or previous history of preterm. Among patients who had respiratory tract infection, they were required to be completely cured at least 2 weeks before including into the study.

All participants were consented to measure lung function by IOS technique (Jaeger, Germany). Processes of our study were approved by the

Research Ethics Review Committee of Queen Sirikit National Institute of Child Health. The study was registered in the Thai clinical Trial Registry as TCTR20200527002.

IOS parameters

Vyntus IOS (JEAGER®, Germany) which applied in all volunteers were calibrated daily before collecting data. To get the acceptable test, patients had to repeat the same procedure at least 3 times. Initially, each participant was asked to sit in comfortably position and wear a nose clip. After that, underwent regular breathing for 20 seconds through a plastic mouthpiece with supported cheeks to reduce upper airway shunt effect. To increase the reliability, measurements were obliged to perform repeatedly until consistency was > 0.7 for frequency at 5 Hz and > 0.9 for frequency at 20 Hz.

The following important parameters for airway resistance including resistance to 5-20 Hz (R5, R10 and R20), reactance to 5-20 Hz (X5, X10 and X20), and frequency of resonance (Fres) were recorded. Parameters at high frequency, 20 Hz, were represented the pathology in large airway while resistance (R) at low frequencies (5 Hz) was demonstrated total airway pathology.[18] The difference between R5 and R20 (R5-R20), frequency of resonance (Fres), reactance at 5 Hz (X5) were used to indicate small airway obstruction whereas area of reactance (AX) and R5-R20 were suggested for asthma control.[19–21]

Statistical analysis

The cross-sectional data was analyzed by the Statistical Package for the Social Science version 20 (SPSS, Chicago, IL, USA). Mean and standard deviation used in normal distribution data while median and interquartile range applied in non-normal distribution data. Degree of homogeneity among study groups was verified by Chi-square and ANOVA test. To compare the oscillometry parameter results among 3 groups, one-way ANOVA test (*post hoc* Bonferroni) was applied. The independent t-test with variable adjusted by analysis of covariance (ANCOVA) used to assess bronchodilator response between asthma and asthma with obesity group. Pearson's correlation test was used to determine association between IOS parameters and variable data.

Sample size was calculated from the pilot study containing 44 asthmatic and 35 obese children, aged between 4-15 years. To receive 5% significance level and 80% of power, according to the X5 variable, an importance parameter to differentiate these two diseases, 25 volunteers were required in each group.

Results

One hundred and twenty children, age ranged 4-15 years old, were recruited in the study. They were divided into 3 groups: asthma, asthma with obesity, and obesity with 40 patients in each group. The mean age of each group was 9.01 ± 2.59, 8.48 ± 2.78 and 9.03 ± 2.5, respectively. Males were predominated in all groups (60, 75 and 85% respectively). Body weight, weight for height, and BMI were significantly higher in the obesity (BW 62.67 ± 21.13, %W/H 183.01 ± 29.34, BMI 29.89 ± 5.9) and obesity with asthma (BW 48.35 ± 18.17, %W/H 154.55 ± 14.79, BMI 24.68 ± 3.37) than in asthma group (BW 28.91 ± 9.2, %W/H 98.69 ± 10.9, BMI 15.79 ± 2.14), p <0.001. There was no difference regarding age and height among the 3 groups. Details of the general characteristics are shown in table 1.

Among asthmatic patients, there was no statistical difference between asthma and asthma with obesity concerning asthma severity and duration of asthmatic treatment. However, patients in asthma with obesity group had longer duration of asthma control than the asthma group (p = 0.006) as shown in table 2.

Table 1. The demographic characteristics of participants in each group

	Asthma (n=40)	Obesity (n=40)	Asthma with obesity (n=40)	p-value ANOVA
Age (year)	9.01 ± 2.59	9.03 ± 2.5	8.48 ± 2.78	0.566
Sex: male (n)	24 (60%)	34 (85%)	30 (75%)	0.039*
Body weight (kg)	28.91 ± 9.2	62.67 ± 21.13	48.35 ± 18.17	<0.001*
Height (cm)	133.82 ± 14.6	141.36 ± 15.69	136.78 ± 16.58	0.099
BMI (kg/m²)	15.79 ± 2.14	29.89 ± 5.9	24.68 ± 3.37	<0.001*
% W/H	98.69 ± 10.9	183.01 ± 29.34	154.55 ± 14.79	<0.001*

Table 2. The characteristics of the asthmatic children

	Asthma (n=40)	Asthma with obesity (n=40)	p-value
Asthma onset	6 (4,8)	5.5 (4,7)	0.456
Duration of asthma treatment (month)	14 (0,36)	18 (3,42)	0.426
Duration of asthma control (month)	0 (0,2)	2 (0,4.5)	0.006*
Asthma severity #	3.25 ± 0.63	2.98 ± 0.8	0.092

According to stepwise guideline following GINA recommendation

The baseline impulse oscillometry parameters among 3 groups were presented in table 3. In our study, the %R20 was an important parameter to detect large airway dysfunction in obese patients (113.2 + 25.54), when compared to asthmatic patients (93.15 + 25.03), p = 0.001. On asthmatic highlight, more negative on X5 reactant was found in the asthmatic group (-0.23 ± 0.09) and asthmatic with obese group (-0.19 ± 0.11) than in the obesity group (-0.13 ± 0.08) with p = 0.001 and 0.013, respectively. The Receiver Operating Characteristic (ROC) curve was applied to define an optimal value of X5 for predicting asthmatic tendency among our obese children. From the ROC curve as shown in figure 1, figure 2 and table 4, X5 at -0.16 kPa/L/s and %X5 at 74.5% were the best value to forecast obstructive airway in obesity with 70% sensitivity, 60-70% specificity and 65-70% accuracy (AUC= 0.69, 0.67, respectively). Intriguingly, apart from X5, other parameters related to small airway constriction, including R5-R20, Fres and AX were not different among 3 groups.

The percentage change of IOS parameters in table 5 used to compare post-bronchodilator effect between asthma and asthma with obesity. Asthmatic children had higher response to bronchodilator than young asthma with obesity as shown as the percentage change of Fres (-24.57 ± 15.82, -13.77 ± 16.42), AX (-58.28 ± 13.37, -43.35 ± 21.4), Z5 (-23.13 ± 9.53, -18.58 ± 9.92), and R5-R20 (-51.32 ± 20.13, -34.72 ± 18.21) (p = 0.004, 0.001, 0.04 and 0.001, respectively). Percentage changes of Fres, AX, R5-R20 were still significant higher in asthma than in asthma with obesity, after we adjusted the duration of asthma control, (p = 0.014, 0.004, 0.002 respectively). Interestingly, the percentage change of R5-R20 also had weakly negative correlation with BMI (r = - 0.354, p = 0.001).

Table 3. The baseline IOS parameters among 3 groups of participants

Variable kPa/L/s	G1: asthma (n=40)	G2: Obesity (n=40)	G3: obesity + asthma (n=40)	G1 VS G2		G1 VS G3		G2 VS G3	
				Mean difference (95%CI)	p-value	Mean difference (95%CI)	p-value	Mean difference (95%CI)	p-value
R5	0.81 ± 0.24	0.93 ± 0.32	0.92 ± 0.24	-0.12 (-0.27, 0.02)	0.137	-0.11 (-0.25, 0.04)	0.214	0.01 (-0.13, 0.16)	1
% R5	113.85 ± 28.42	119.62 ± 34.48	122.5 ± 24.01	-5.78 (-21.68, 10.13)	1	-8.65 (-24.55, 7.25)	0.567	-2.88 (-18.78, 13.03)	1
X5	-0.23 ± 0.09	-0.13 ± 0.08	-0.19 ± 0.11	-0.11 (-0.16, -0.06)	<0.001*	-0.05 (-0.1, 0)	0.083	0.06 (0.01, 0.11)	0.013*
% X5	104.17 ± 39.43	60.65 ± 38.42	87.45 ± 47.66	43.53 (20.69, 66.36)	<0.001*	16.73 (-6.11, 39.56)	0.233	-26.8 (-49.63, -3.97)	0.015*
Fres	23.06 ± 4.62	23.86 ± 6.38	23.58 ± 4.2	-0.81 (-3.61, 1.99)	1	-0.52 (-3.32, 2.28)	1	0.28 (-2.52, 3.08)	1
% Fres	140.25 ± 27.73	128.7 ± 36.39	133.38 ± 23.49	11.55 (-4.58, 27.68)	0.254	6.88 (-9.25, 23)	0.908	-4.68 (-20.8, 11.45)	1
AX	2.66 ± 1.74	2.76 ± 1.99	2.99 ± 1.42	-0.1 (-1.04, 0.84)	1	-0.33 (-1.27, 0.61)	1	-0.23 (-1.17, 0.71)	1
Z5	0.85 ± 0.24	0.95 ± 0.32	0.95 ± 0.24	-0.1 (-0.24, 0.05)	0.323	-0.1 (-0.24, 0.05)	0.337	0 (-0.14, 0.15)	1
% Z5	113.5 ± 27.05	116.42 ± 32.96	119.75 ± 23.33	-2.93 (-18.16, 12.31)	1	-6.25 (-21.49, 8.99)	0.964	-3.33 (-18.56, 11.91)	1
R20	0.5 ± 0.13	0.58 ± 0.16	0.53 ± 0.14	-0.08 (-0.16, 0)	0.058	-0.03 (-0.11, 0.05)	1	0.05 (-0.03, 0.13)	0.372
% R20	93.15 ± 25.03	113.2 ± 25.54	100.45 ± 24.49	-20.05 (-33.64, -6.46)	0.001*	-7.3 (-20.89, 6.29)	0.584	12.75 (-0.84, 26.34)	0.073
X20	-0.05 ± 0.08	-0.04 ± 0.14	-0.06 ± 0.06	-0.01 (-0.06, 0.05)	1	0.01 (-0.05, 0.06)	1	0.02 (-0.04, 0.07)	1
% X20	-84.5 ± 140.92	4.78 ± 668.04	-143.93 ± 194.12	-89.28 (-311.84, 133.29)	0.996	59.43 (-163.14, 281.99)	1	148.7 (-73.87, 371.27)	0.322
R5-R20	0.31 ± 0.17	0.35 ± 0.2	0.39 ± 0.17	-0.04 (-0.14, 0.06)	0.895	-0.08 (-0.18, 0.02)	0.146	-0.04 (-0.14, 0.06)	1

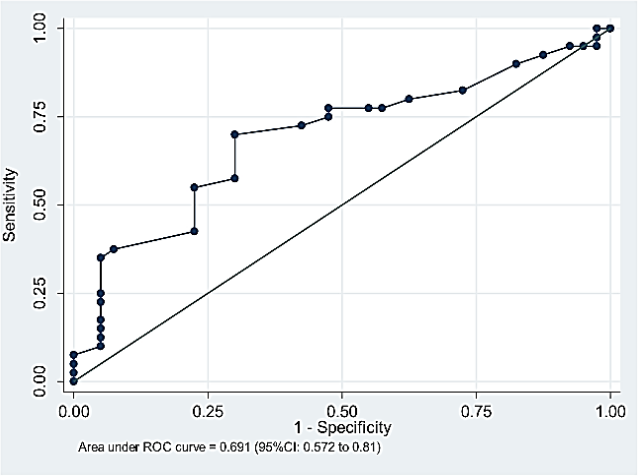

Figure 1. ROC analysis of X5 value for predicting asthma in obese children

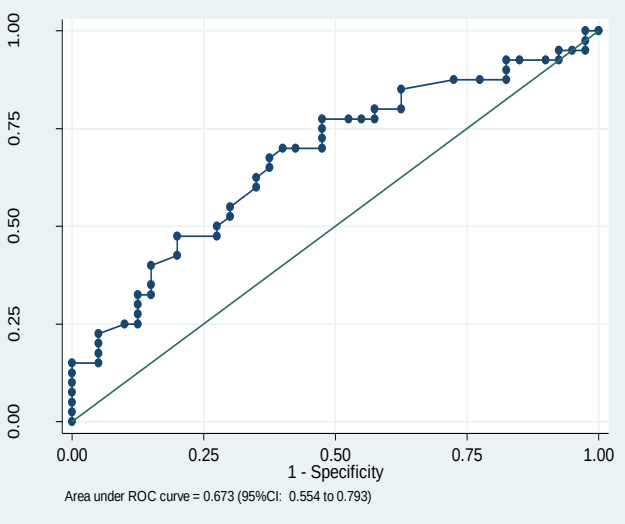

Figure 2. ROC analysis of %X5 value for predicting asthma in obese children

Table 4. Validity of X5 and %X5 values to identify asthma in obese patients

The cut point of IOS parameter	Sensitivity	Specificity	PPV	NPV	Accuracy	P-value
X5 = -0.16 kPa/L/s	70%	70%	70%	70%	70%	0.001
%X5 = 74.5%	70%	60%	63.6%	66.7%	65%	0.013

Table 5. The bronchodilator response (percentage change) of IOS parameters between asthma and asthma with obesity

	G1: asthma (n=40)	G3: obesity + asthma (n=40)	Mean difference (95%CI)	p-value	Adjusted by Duration control: Mean difference (95%CI)	p-value
%change of R5	-22.1 ± 10.27	-17.9 ± 10.11	-4.2 (-8.74, 0.34)	0.069	-3.38 (-8.06, 1.3)	0.155
%change of X5	-34.75 ± 28	-22.15 ± 84.42	-12.6 (-40.6, 15.4)	0.373	-7.03 (-35.85, 21.8)	0.629
%change of Fres	-24.57 ± 15.82	-13.77 ± 16.42	-10.8 (-17.98, -3.62)	0.004*	-9.32 (-16.71, -1.94)	0.014*
%change of AX	-58.28 ± 13.37	-43.35 ± 21.4	-14.93 (-22.87, -6.98)	<0.001*	-11.39 (-19.11, -3.68)	0.004*
%change of Z5	-23.13 ± 9.53	-18.58 ± 9.92	-4.55 (-8.88, -0.22)	0.040*	-3.55 (-7.98, 0.89)	0.116
%change of R20	-6.23 ± 15.56	-5.5 ± 11.56	-0.73 (-6.83, 5.38)	0.814	-1.43 (-7.77, 4.91)	0.654
%change of X20	-37.1 ± 823.94	102.93 ± 1042.23	-140.03 (-558.24, 278.19)	0.507	-159.94 (-596.12, 276.23)	0.467
%change of R5-R20	-51.32 ± 20.13	-34.72 ± 18.21	-16.6 (-8.06, -25.15)	<0.001*	-13.64 (-5.09, -22.18)	0.002*

Discussion

This is the first study to demonstrate IOS measurement in childhood obesity and childhood obesity with asthma in Thailand. Among children with asthma, both obesity and non-obesity, the baseline onset and severity of asthma were similar (p-value >0.05). When performed IOS, the standard respiratory reactance to 5 hertz (X5) revealed significantly more negative in childhood asthmatic group (-0.23 ± 0.09, p = 0.001) and obese children with asthma group (-0.19 ± 0.11, p = 0.001) than in the childhood obesity group (-0.13 ± 0.08). These results confirmed the benefit of small airway resistance in childhood asthma measured by X5[22] and concurred with the study by by Tirakitsoontorn et.al which demonstrated X5 as the most important parameter to confirm the peripheral airway impairment measured by IOS in well-controlled asthmatic children aged 4-18 years old.[14] Their study suggested that X5 highly correlated with peripheral airway impairment in children with asthma; AUC = 0.65 (0.58-0.73), particularly children aged 8-11 years old; AUC = 0.74 (0.64-0.83).[14] This evidence resembled to our study which suggested the X5 at -0.16 kPa/L/s (figure 1) and %X5 at 74.5% (figure 2) were the best value to predict airway obstruction in obesity with asthma.

Prior studies of peripheral airway obstruction in obesity[16,23], as well as our study, recommended X5 < - 0.16 kPa/L/s was associated with small airway obstruction regardless obesity. This tendency was supported by Assumpcao's study which demonstrated narrowing airway in obesity (X5= -0.17 ± 0.6, R5 = 0.68 ± 0.19, Fres = 19.68 ± 4.44, AX = 1.37 (0.61–2.09) and Z5 = 0.711± 0.19).[16] We suggested the higher resistance of patients' airway found in our study (R5 = 0.93 ± 0.32, Fres = 23.86 ± 6.38, AX = 2.76 ± 1.99 and Z5 = 0.95 ± 0.32) were from greater

BMI of our patients (29.89 ± 5.9) than patients in his study (24.41 ± 3.21).[16] Therefore, we proposed that high BMI children with asthma required X5 and other IOS parameters related to small airway resistance to classify asthma severity, similar to the recent study in school- age obese asthmatic children published in 2021.[23]

In comparison to childhood asthma who had total airway resistance (R5 = 0.81 ± 0.24), obese children in our study presented more airway resistance (R5 = 0.93 ± 0.32, %R5 = 119.62 ± 34.48). However, this parameter did not showed statistically significance between groups (p-value 0.137, 0.214, and 1). This information approved by the study in obese Finish children, aged 5-7 years, which suggested that obesity did not relate to bronchial hyper-reactivity.[24] For this reason, childhood obesity in our study had less response to bronchodilator as shown as less percentage change in some parameters; R5-R20 (-34.72 ± 18.21), AX (-43.35 ± 21.4), Fres (-13.77 ±16.42), than in asthma (R5-R20 -51.32 ± 20.13, AX -58.28 ± 13.37, Fres -24.57 ± 15.82). In addition, obese patients had both restrictive and obstructive respiratory diseases as mentioned in Zammit's study.[25] Jones and his colleague also suggested that restrictive ventilator pattern and decreases in lung volumes were from rising BMI.[26] However, these results may not be found in children with obesity by the spirometry as mentioned in the meta-analysis study by Forno and et.al that FEV1 and FVC in children were not changed when compared to adult.[27] The mild restrictive lung, (TLC ≥ 70 %predict) which detected by body plethysmography possibly not be found by IOS as indicated by Savushkina and colleagues.[28] In contradictory, the outcomes of moderate or severe restrictive disorders (TLC < 70 %predict.) in adult patients should be found by IOS examination as abnormal X5 with increasing Fres and without changing of R20.[28] Resembling the study by Albuquerque which reported higher total and peripheral airway resistance with more negative reactance value in severe 85 adults with obesity.[29] Unlike those, obese children in our study had no restrictive airway. This possibly due to less severity of obesity and younger age than adults in previous studies.

With the bronchodilator effect, the percentage changes of Fres (p-value = 0.014), AX (p-value = 0.004), R5-R20 (p-value = 0.002) were significantly correlated to the severity of the obstructive airway in obese children compared to asthmatic patients. These parameters also indicated in the adult study of asthma who presented with small airway obstruction by Cottini and et.al. published in 2019.[30] Their study demonstrated R5,X5, R5-R20,AX, Fres were all important parameters to evaluate small airway resistance among asthma either uncontrolled or partially controlled status.[30] In study of school-age children with asthma confirmed the value of R5 and R5-20 related to constrictive airway in obesity in their study.[23]

Therefore, we suggested small airway parameters including baseline X5, R5-R20, AX, Fres and percentage changes of R5-R20, AX, Fres after bronchodilator were helpful parameters among children with asthma both non-obesity and obesity.

Limitations in our study may be from no healthy control to compare the IOS parameters and less severity of asthma status in childhood asthma. These reasons may cause some non-statistically significance among important small airway obstruction IOS parameters in childhood asthma, and childhood obesity with asthma.

Conclusions

Our study demonstrated that either obesity or asthma independently promoted an airway resistance, detected by X5 and %X5. The IOS parameters including percentage changes of Fres, AX, R5-R20 after bronchodilator are crucial values to differentiate and monitor airway obstruction in children with asthma. A further study with larger sample size and healthy control may provide different data between these two diseases.

Conflicts of interest: We have no conflicts of interest to declare.

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References

1. Kudo M, Ishigatsubo Y, Aoki I. Pathology of asthma. *Front Microbiol*. 2013;4:263. Published 2013 Sep 10. doi:10.3389/fmicb.2013.00263
2. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2020. https://ginasthma.org/wp-content/uploads/2020/06/GINA-2020-report_20_06_04-1-wms.pdf. Accessed June 20, 2020.
3. Stern J, Pier J, Litonjua AA. Asthma epidemiology and risk factors. *Semin Immunopathol*. 2020;42(1):5-15. doi:10.1007/s00281-020-00785-1
4. Peters U, Dixon AE, Forno E. Obesity and asthma. *J Allergy Clin Immunol*. 2018;141(4):1169-1179. doi:10.1016/j.jaci.2018.02.004
5. Dixon AE, Holguin F, Sood A, et al. An official American thoracic society workshop report: Obesity and asthma. *Proc Am Thorac Soc*. 2010;7(5):325-335. doi:10.1513/pats.200903-013ST
6. Manion AB. Asthma and Obesity. The Dose Effect. *Nurs Clin North Am*. 2013;48(1):151-158. doi:10.1016/j.cnur.2012.12.002
7. Mohanan S, Tapp H, Mcwilliams A, Dulin M. Obesity and asthma: Pathophysiology and implications for diagnosis and management in primary care. *Exp Biol Med*. 2014;239:1531-1540. doi:10.1177/1535370214525302
8. Myers TR, Tomasio L. Asthma: 2015 and beyond. *Respir Care*. 2011;56(9):1389-1407. doi:10.4187/respcare.01334
9. Quinto KB, Zuraw BL, Poon KYT, Chen W, Schatz M, Christiansen SC. The association of obesity and asthma severity and control in children. *J Allergy Clin Immunol*. 2011;128(5):964-969. doi:10.1016/j.jaci.2011.06.031
10. Batmaz SB, Kuyucu S, Arikoglu T, Tezol O, Aydogdu A. Impulse oscillometry in acute and stable asthmatic children: A comparison with spirometry. *J Asthma*. 2016;53(2):179-186. doi:10.3109/02770903.2015.1081699
11. Nielsen KG, Bisgaard H. Discriminative capacity of bronchodilator response measured with three different lung function techniques in asthmatic and healthy children aged 2 to 5 years. *Am J Respir Crit Care Med*. 2001;164(4):554-559. doi:10.1164/ajrccm.164.4.2006119
12. McDowell KM. Recent Diagnosis Techniques in Pediatric Asthma: Impulse Oscillometry in Preschool Asthma and Use of Exhaled Nitric Oxide. *Immunol Allergy Clin North Am*. 2019;39(2):205-219. doi:10.1016/j.iac.2018.12.002
13. Zeng J, Chen Z, Hu Y, Hu Q, Zhong S, Liao W. Asthma control in preschool children with small airway function as measured by IOS and fractional exhaled nitric oxide. *Respir Med*. 2018;145(October):8-13. doi:10.1016/j.rmed.2018.10.009
14. Tirakitsoontorn P, Crookes M, Fregeau W, et al. Recognition of the peripheral airway impairment phenotype in children with well-controlled asthma. *Ann Allergy, Asthma Immunol*. 2018;121(6):692-698. doi:10.1016/j.anai.2018.08.023
15. Ekström S, Hallberg J, Kull I, et al. Body mass index status and peripheral airway obstruction in school-age children: a population-based cohort study. *Thorax*. 2018;73(6):538-545. doi:10.1136/thoraxjnl-2017-210716
16. Assumpção MS d., Ribeiro JD, Wamosy RMG, Figueiredo FCXS d., Parazzi PLF, Schivinski CIS. Impulse oscillometry and obesity in children. *J Pediatr (Rio J)*. 2018;94(4):419-424. doi:10.1016/j.jped.2017.06.007
17. Asher MI, Keil U, Anderson HR, et al. International study of asthma and allergies in childhood (ISAAC): Rationale and methods. *Eur Respir J*. 1995;8(3):483-491. doi:10.1183/09031936.95.08030483
18. Desiraju K, Agrawal A. Impulse oscillometry: The state-of-art for lung function testing. *Lung India*. 2016;33(4):410-416. doi:10.4103/0970-2113.184875
19. Desai U, Joshi JM. Impulse oscillometry. *Adv Respir Med*. 2019;87(4):235-238. doi:10.5603/ARM.a2019.0039
20. Komarow HD, Skinner J, Young M, et al. A Study of the Use of Impulse Oscillometry in the Evaluation of Children With Asthma: Analysis of Lung Parameters, Order Effect, and Utility Compared With Spirometry. *Pediatr Pulmonol*. 2012;47:18-26. doi:10.1002/ppul.21507
21. de Oliveira Jorge PP, de Lima JHP, Chong e Silva DC, Medeiros D, Solé D, Wandalsen GF.

Impulse oscillometry in the assessment of children's lung function. *Allergol Immunopathol (Madr)*. 2019;47(3):295-302. doi:10.1016/j.aller.2018.03.003

22. Cottini M, Licini A, Lombardi C, Bagnasco D, Comberiati P, Berti A. Small airway dysfunction and poor asthma control: a dangerous liaison. *Clin Mol Allergy*. 2021;19(1):1-10. doi:10.1186/s12948-021-00147-8
23. Uysal P, Anik A, Anik A. School-age obese asthmatic children have distinct lung function measures from lean asthmatics and obese children. *J Asthma*. 2021;0(0):1-12. doi:10.1080/02770903.2021.1959925
24. Lauhkonen E, Koponen P, Nuolivirta K, et al. Obesity and bronchial obstruction in impulse oscillometry at age 5-7 years in a prospective post-bronchiolitis cohort. *Pediatr Pulmonol*. 2015;50(9):908-914. doi:10.1002/ppul.23085
25. Zammit C, Liddicoat H, Moonsie I, Makker H. Obesity and respiratory diseases. *Am J Clin Hypn*. 2011;53(4):335-343. doi:10.2147/IJGM.S11926
26. Jones RL, Nzekwu MMU. The effects of body mass index on lung volumes. *Chest*. 2006;130(3):827-833. doi:10.1378/chest.130.3.827
27. Forno E, Weiner DJ, Mullen J, et al. Obesity and airway dysanapsis in children with and without asthma. *Am J Respir Crit Care Med*. 2017;195(3):314-323. doi:10.1164/rccm.201605-1039OC
28. Savushkina O, Cherniak A, Kameneva M, Kryukov E, Zaytsev A. Impulse oscillometry in restrictive respiratory diseases. *Eur Respir Journa*. Published online 2018:PA3394. doi:10.1183/13993003.congress-2018.pa3394
29. de Albuquerque CG, de Andrade FMD, Rocha MA de A, et al. Determining respiratory system resistance and reactance by impulse oscillometry in obese individuals. *J Bras Pneumol*. 2015;41(5):422-426. doi:10.1590/S1806-37132015000004517
30. Cottini M, Licini A, Lombardi C, Berti A. Clinical Characterization and Predictors of IOS-Defined Small-Airway Dysfunction in Asthma. *J Allergy Clin Immunol Pract*. 2020;8(3):997-1004.e2. doi:10.1016/j.jaip.2019.10.040