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RESEARCH ARTICLE

Comparison of Spirometry and Impulse Oscillometry in Thai Childhood Asthma

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ABSTRACT

Background: Impulse oscillometry (IOS), a new respiratory impedance measurement, is increasing in its popularity as a means to assess airway resistance in young children. Its great advantage lies in its effortless and fast performance, making the airway obstruction measurement easier for patients who are not able to perform spirometry tests. However, studies comparing spirometry with IOS in Thai children are rare.

Aims: To evaluate the correlation between IOS and spirometry parameters in Thai childhood asthma

Methods: Vyntus IOS (JEAGER®, Germany) and spirometry tests (Vyntus SPIRO) were performed in 48 children, aged 5-15 years old, who fulfilled the GINA asthma criteria. The study, approved by the hospital's ethics committee, was conducted between March 1, 2020 and March 31, 2021 at the Queen Sirikit National Institute of Child Health, Thailand. (TCTR20220527005)

Results: Forty-eight childhood asthma patients with a median age of 10.79 (IQR = 8.41, 11.87) years underwent both IOS and spirometry measurements. Male sex was predominant (64.58%), and 77% of patients had well-controlled asthma (C-ACT score ≥ 20). In our study population, the atopic comorbidities were allergic rhinitis (91.67%), atopic dermatitis (10.42%) and food allergy (10.42%). Moreover, parental asthma was found in 16.67% of the participants. In comparison with spirometry, the percentage change of FEF_{25-75%} was significantly negatively correlated with R5, R10, AX, and mean R5-R20 ($r = -0.608, -0.528, -0.500, -0.511$, respectively; $p < 0.001$). Likewise, FEV1 was significantly negatively correlated with R15 and R20 ($r = -0.520, -0.565$, respectively; $p < 0.001$). The linear regression prediction model demonstrated that a 30% increase in FEF_{25-75%} was related to a 22.7% reduction in R5 ($p = 0.007$).

Conclusion: The percentage change of FEF_{25-75%} was found to negatively correlate in statistically significant terms with R5 in Thai childhood asthma. Hence, IOS is an effective and feasible replacement for spirometry as a measurement modality of lung function, especially in young children.

Keywords: impulse oscillometry, spirometry, lung function, respiratory impedance, childhood asthma

Abbreviation: R = resistance, R5 = resistance at 5 Hz, R10 = resistance at 10 Hz, R15 = resistance at 15 Hz, R20 = resistance at 20 Hz, mean R5-R20 = mean resistance of peripheral airway, X = reactance, AX = the area of reactance

Introduction

Asthma, an important chronic respiratory illness of all ages, is indicated by the Global Initiative for Asthma to increase the prevalence in children worldwide.¹ The disease, during exacerbation, usually presents with shortness of breath, chest tightness, cough, and wheezing. These symptoms may reverse spontaneously or by treatment with bronchodilators +/- corticosteroids. To control the disease, patients are recommended to avoid asthma inducing aeroallergens, irritant exposure, smokes, and other forms of pollution.

In children younger than 5 years old, an associated atopic disease history and a history of asthma in a first-degree relative assist the confirmation of the diagnosis of asthma.¹ Moreover, in older children and adults, spirometry, which is capable of demonstrating both airway constriction or improvements in airway obstruction due to the use of bronchodilators, is required in order to confirm the asthma diagnosis.¹ When evaluating airway constriction via a spirometer, the patient is asked to perform various tasks related to the test, i.e., are forced expiratory volume in one second, forced expiratory flow between 25% and 75% of vital capacity (FEF_{25-75%}), ratio of forced expiratory volume in one second, and forced vital capacity (FEV₁/FVC).

The FEF_{25-75%} parameter, known to be related to small airway obstruction,² is being increasingly investigated and has been found to be of a significant importance among young patients with mild-to-moderate³ and severe asthma.⁴ Francisco and colleagues have reported that FEF_{75%}, the small airway test, is more sensitive than FEV₁, the large airway evaluation for severe bronchoconstriction.⁴ Similarly, the study by Lebecque et al., who was conducted among 100 children with ages ranging from 5 to 17 years and with wheezing symptoms, pointed out that an FEF_{25-75%} value below 2 standard deviations is more sensitive than FEV₁.⁵ Additionally, the measurement values yielded by spirometry in relation to small airway resistance have been shown to vary between 7.5% and 45.9%, and a consensus on a suitable cut-off value is yet to be reached.⁶ In the meantime, small airway disease is evaluated better by newer techniques of pulmonary function evaluation, namely the forced oscillation technique (FOT) and impulse oscillometry (IOS), which have been introduced as alternative modalities to assess lung function in patients who are not able to perform a full expiration on spirometry measurement.^{3,7}

FOT, first introduced by Dubois in 1956, is a machine that uses sound waves to evaluate airway resistance and reactance in patients while taking a normal breath.⁸ A similar technique, impulse oscillometer (Jaeger®, Germany), has been described in recent studies, particularly in children with asthma or other respiratory diseases, to be as useful as spirometry in the measurement of airway resistance.⁹ Bickel S. explained that the airway resistance at low frequency, 5 Hz, represents the total airway resistance, while the high frequency one, 20-25 Hz, indicates proximal airway resistance.¹⁰ Therefore, the difference between R₅ and R₂₀ (R₅-R₂₀) is applied in the evaluation of peripheral airway resistance.¹⁰ However, not only resistance parameters, but also the reactance ones, the values of which are obtained via the IOS machine, are helpful in evaluating pulmonary function in respiratory diseases. Reactance comprises both inertance and capacitance. Capacitance represents lung elasticity. Thus, the reactance at a low frequency, 5 Hz (X₅), reflects the elastic recoil of the distal airways.¹¹ However, this parameter at a low frequency could show a negative result as mentioned in many studies.¹¹ In addition, earlier published work has found that reactance becomes less negative with an increasing age and height.¹²

Resonance frequency (F_{res}), the frequency where lung tissue changes from passive distention to an active stretch by pressure wave signals, is another parameter, which is essential for the evaluation of the capacitance of the airway. As mentioned in previous studies, elevated F_{res} values have been found in both restrictive and obstructive disorders.¹³ However, as shown in many studies, F_{res} and resistance tend to reverse with age, i.e., they tend to be higher in younger children and lower in older children and adults.⁹⁻¹⁴ Meanwhile, the reactance area (AX), an integrated area between the low frequency of 5 Hz and F_{res}, also reflects the capacitance of the respiratory system and is required for the proper airway constriction examination.¹⁵

As mentioned earlier, children with asthma tend to have small airway defect. Thus, recent worldwide studies on asthma, especially those in young children, have increasingly used oscillometry as a tool to conduct asthma research as well as monitor patient pulmonary function.¹⁵⁻¹⁸ Therefore, in this investigation, we studied the impulse oscillometry (IOS) parameters in comparison with spirometry ones in Thai childhood asthma.

Materials and Methodology

Study population and study design

A cross-sectional study was conducted in 48 participants, aged 5-15 years old, at the Queen Sirikit National Institute of Child Health, Bangkok, Thailand from March 1, 2020 to March 31, 2021. We calculated the required sample size of patients ($n = 46$) based on the study of Batmaz¹⁹ and using the following formula:

$$n = \frac{(z_{1-\frac{\alpha}{2}} + z_{1-\beta})^2 \sigma^2}{\Delta^2}$$

where the standard deviation (SD) = 0.024, alpha (α) = 0.05, beta (β) = 0.2, and delta (Δ) = 0.01.

All of the enrolled participants fulfilled the GINA asthma criteria. Children with chronic lung disease, cardiac problems, recent respiratory tract infections (previous 2 weeks), and overweight (weight for height ratio ≥ 120) were excluded.

All participants consented to undergo lung function tests via both the IOS technique (Jaeger®, Germany) and spirometry (Vyntus SPIRO). They were instructed to avoid taking a short-acting beta₂ agonist for >4 hours and a long-lasting one for >15 hours prior to the performance of the tests. Our study was approved by the Research Ethics Review Committee of Queen Sirikit National Institute of Child Health and was registered in Thai clinical trials registry (TCTR20220527005).

Impulse oscillometry (IOS)

IOS (Jaeger®, Germany) testing was carried out after the calibration of the machine through a single volume of air (3 L) at different rates of flow and a specific resistance set at 0.2 kPa·L⁻¹·s⁻¹ as per the manufacture's protocol. An impulse generator produced frequencies between 5 and 20 Hz with brief pressure pulses at intervals of 0.2 seconds.

During IOS measurement, children sat upright with their heads rested against the back of a chair and wore nose clips on their noses. They were instructed to breathe normally and quietly with cheek support through the mouthpiece without pulling their tongue against it. The mean outcome of three correct measurements without any artefact caused by coughing, breath holding, swallowing or vocalization was considered acceptable and recorded.

The pulmonary impedance (resistance, reactance) and the area of reactance (AX) against those frequencies was measured and calculated at a minimal interval of 30 seconds, while the mean

resistance and reactance values were calculated over 60-second intervals. Reactance parameters—X, Fres, and AX—which reflect the elasticity properties of the respiratory system, were presented as negative values.

Spirometry

All participants were required to undergo spirometry testing after completing the IOS test. After calibration under the appropriate temperature and atmospheric pressure values, the children were asked to inhale and exhale forcefully over 6 seconds in order to achieve a true pulmonary function test. The best out of three acceptable blows was recorded and represented their FVC, FEV1 and FEF_{25-75%} values.

After the baseline IOS and spirometry measurements as mentioned above, each participant repeated the processes of the IOS and spirometry tests after receiving 400 mcg of salbutamol (4 puffs of 100 mcg/puff) via a spacer in order to confirm the asthma diagnosis.

Statistical analysis

The cross-sectional data were analyzed using the Statistical Package for Social Sciences, 20th version (SPSS, Chicago, IL, USA). Spearman's correlation test was used to determine correlations between IOS and spirometry parameters. Before running the test of correlation, the assumption of a potential correlation between the two was tested, and it showed a normal distribution. A p-value of <0.05 was considered to indicate statistical significance. The linear regression prediction model was also used to evaluate the relationship between FEF_{25-75%} and R5, R10, AX, and mean R5-R20.

Results

Forty-eight children with asthma agreed to participate in our study. The median age was 10.79 (8.41, 11.87) years, the median height was 137.25 (130, 154.25) cm, the median weight was 32.30 (26.05, 44) kg, and the median weight for height ratio (W/H) was 101 (95.3, 109.75). Male sex was predominant (64.58%), and 77% of the patients had well-controlled asthma (C-ACT score ≥ 20). Most participants (87.5%) were sensitized to aeroallergens. The most common aeroallergens among our patients were *Dermatophagoides farinae* (70.83%), *Dermatophagoides pteronyssinus* (64.58%), American cockroach (52.08%), and cat pelt (47.92%). The demographic characteristics data are presented in Table 1.

Table 1. The demographic characteristics of the asthmatic participants

Characteristics	N (%)	Median (IQR)
Sex: Male	31 (64.58)	
Age		10.79 (8.41, 11.87)
Body weight (kg)		32.30 (26.05, 44)
Height (cm)		137.25 (130, 154.25)
Body weight for height ratio		101 (95.3, 109.75)
Score of childhood asthma control test (C-ACT score)		23 (20, 23)
Well-controlled (CACT \geq 20)	37 (77)	
Comorbidities		
Allergic rhinitis	44 (91.67)	
Atopic dermatitis	5 (10.42)	
Food allergy	5 (10.42)	
Chronic spontaneous urticaria	2 (4.17)	
Allergic conjunctivitis	1 (2.08)	
Adeno-tonsillar hypertrophy	1 (2.08)	
Duration of ICS treatment (months)		24 (3.50, 78)
Family history	20 (41.67)	
Asthma	8 (16.67)	
Allergic rhinitis	13 (27.08)	
Skin prick test findings		
<i>Dermatophagoides farina</i>	34 (70.83)	
<i>Dermatophagoides pteronyssinus</i>	31 (64.58)	
American cockroach	25 (52.08)	
Cat pelt	23 (47.92)	

The baseline and post-bronchodilator administration spirometry values were shown in Table 2. The median FVC, FEF_{25-75%}, and FEV₁ was 95 (87, 106.50), 88 (58, 113), and 97.50 (81, 128.50), respectively. Meanwhile, the median predicted FEV₁/FVC was 86.13 (80.77, 89.79). After receiving the bronchodilator, the median increase in FEV₁ was 6 (3, 10.50), while the percent change of FEF_{25-75%} was 24 (13, 44.5).

The baseline impulse oscillometry values are also shown in Table 2. The median percent values for R5, R20, and X5 were 111 (90, 131), 103.5 (86.5, 114), and 98 (78.5, 112), respectively. Furthermore, the percent changes of R5 and X5 after the administration of the bronchodilator were -18 (-25.50, -9) and -26 (-46, -11), respectively.

Table 2. Baseline and post-bronchodilator response values of spirometry and IOS parameters

Baseline measurements	Median (IQR)	Bronchodilator response	Median (IQR)
Spirometry values			
FVC (% pre/pred)	95 (87, 106.50)	Δ FVC (%)	1.50 (-2, 3)
FEV ₁ (% pre/pred)	97.50 (81, 128.50)	Δ FEV ₁ (%)	6 (3, 10.50)
FEV ₁ /FVC (pre)	86.13 (80.77, 89.79)	Δ FEV ₁ /FVC (%)	6 (4.50, 9.50)
FEF _{25-75%} (% pre/pred)	88 (58, 113)	Δ FEF ₂₅₋₇₅ (%)	24 (13, 44.5)
IOS values			
R5 Hz (% pre)	111 (90, 131)	Δ R5 Hz (%)	-18 (-25.50, -9)
R10 Hz (% pre)	103 (90.5, 119)	Δ R10 Hz (%)	-15.50 (-23, -8)
R15 Hz (% pre)	104 (86, 114)	Δ R15 Hz (%)	-14 (-21, -5.50)
R20 Hz (% pre)	103.5 (86.5, 114)	Δ R20 Hz (%)	-11 (-20, -6.5)
X5 Hz (% pre)	98 (78.5, 112)	Δ X5 Hz (%)	-26 (-46, -11)
X10 Hz (% pre)	162.5 (93, 241)	Δ X10 Hz (%)	-37 (-65.5, -14)
X20 Hz (% pre)	-56 (-199, 22)	Δ X20 Hz (%)	-60 (-130, 26)
AX kPa/L	1.98 (0.88, 3.20)	Δ AX (%)	-43 (-61.50, -12)
Fres 1/s	137 (117.50, 156.5)	Δ Fres (%)	-17.50 (-31, -4.5)
Mean R5-R20 Hz kPa/(L/s)	0.59 (0.51, 0.70)	Δ R5-R20 (%)	-15 (-21.50, -8)

Table 3. Correlation between IOS and spirometry values

Parameter	R5	R10	R15	R20	X5	X10	X15	X20	Fres	AX	Mean R5-R20
Pre-bronchodilator											
FVC	-0.184	-0.291*	-0.378**	-0.410**	-0.311*	0.023	-0.128	-0.075	0.115	0.073	0.139
FEV1	-0.207	-0.418**	-0.520**	-0.565**	-0.387**	0.079	-0.035	-0.095	0.101	0.191	0.232
FEV1/FVC	-0.395**	-0.419**	-0.330*	-0.264	-0.330*	-0.296*	-0.088	0.276	-0.347*	-0.241	-0.278
FEF _{25-75%}	-0.307*	-0.463**	-0.486**	-0.486**	-0.394**	-0.056	-0.037	0.026	-0.068	0.058	0.108
Post-bronchodilator											
FVC	0.101	0.018	0.024	-0.002	0.007	0.031	-0.036	-0.154	0.066	0.062	0.121
FEV1	-0.354*	-0.357*	-0.190	-0.113	-0.192	-0.340*	-0.192	-0.329*	-0.231	-0.358*	-0.258
FEV1/FVC	-0.421**	-0.341*	-0.229	-0.154	-0.267	-0.353*	-0.174	-0.173	-0.334*	-0.396**	-0.349*
FEF _{25-75%}	-0.608**	-0.528**	-0.406**	-0.247	-0.162	-0.360*	-0.214	-0.308*	-0.395**	-0.500**	-0.511**

**p <0.01, *p <0.05

The results of the Spearman correlation coefficient analysis between spirometry and IOS measurements in our patients are demonstrated in Table 3. A significant negative correlation was observed between FEV1 and R15 and R20 ($r = -0.520, -0.565, p <0.001$). The percent change of FEF_{25-75%} after the bronchodilator administration

correlated negatively with R5, R10, AX, and mean R5-R20 at a statistically significant level ($r = -0.608, -0.528, -0.500, -0.511, p <0.001$). The linear regression prediction model demonstrated a 30% increase in FEF_{25-75%} was associated with a 22.7% reduction in R5 ($p = 0.007$); see Figure 1.

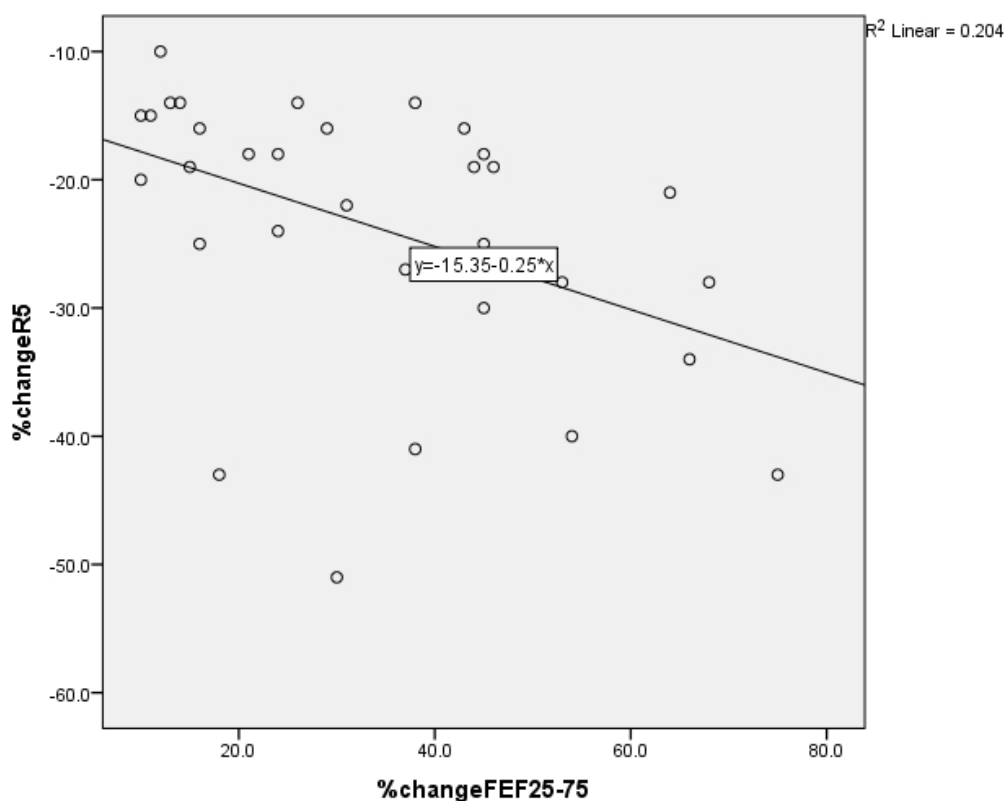


Figure 1. Linear regression prediction model between FEF_{25-75%} and R5

Discussion

This is the first study to compare spirometry and IOS parameters in Thai childhood asthma. An earlier study in Thai pediatric asthma used the force oscillation technique to predict the severity of the disease in comparison to spirometry and suggested that predicted percent change in R5 was related to lung impairment in Thai children with asthma.²⁰ In our children, without the bronchodilator effect, we found no significant decrease in FVC (95), FEV1 (97.5), FEV1/FVC (86.13) or FEF_{25-75%} (88) at baseline (% pre/pred). Our results go in the same direction as the data reported by Kreetapirom et al., who studied Thai asthmatic patients that had no impairment of lung function (FVC = 92.5 ± 10, FEV1 = 89.7 ± 13.3, FEV1/FVC = 88.5 ± 6.6, FEF_{25-75%} = 95 ± 29.3) in comparison to those with uncontrolled asthma (FVC = 98.7 ± 16.6, FEV1 = 96 ± 19.4, FEV1/FVC = 87.6 ± 5.5, FEF_{25-75%} = 92.3 ± 29.3).²⁰ However, after the bronchodilator effect, our patients experienced a 24% improvement in FEF_{25-75%}. This improvement confirmed the potency of small airway obstruction in children.²

The percent change of FEF_{25-75%} after bronchodilator administration in our study exhibited a statistically significant negative correlation with R5-R20, R5, R10, and AX ($r = -0.511, -0.608, -0.528, -0.500$, respectively; $p < 0.001$). The FEF_{25-75%} spirometry and the R5-R20, AX values of IOS parameters were grouped for small airway function evaluation of our asthmatic children.² Unsurprisingly, the results of our study confirmed the significance of small airway constriction in children as mentioned in previous studies.^{2,4,15,19-21} R5-R20 has been used in many studies to distinguish asthmatic from healthy children. In a bronchodilator response study, the receiver operating characteristic (ROC) analysis was employed to compare asthma control in children 6-17 years of age; it revealed that an R5-R20 value at 1.5 cm H₂O and an AX value at 9.5 cm H₂O were superior over R20 (large airway parameter) in correlation with asthma possibility.¹⁸ The benefit of the utilization of R5-R20 has not been pointed out only in young children where it was reported to demonstrate a significant change after a methacholine challenge test,²² but its usefulness has also been evidenced in a study on adults, which identified the advantage of combining the values of low FEF_{25-75%} and high resistance R5-R20 in order to increase the strength of their correlation with asthma severity (odds ratio = 2.77-3.07).²³ On the other hand, a previous study of 88 asthmatic children, which resembles our study, showed a statistically significant difference in the percentage change of R5, R10, X5 and AX after bronchodilator treatment; the R10 was the most valuable

parameter suggested by the ROC analysis.²⁴ Their ROC study seems to point out similar tendencies to those of our study except for R5-R20, which we found to associate with FEF_{25-75%} in children with asthma as well.²⁴ This discordance in findings may be due to differences in the backgrounds of the children under study.

Although, the baseline FEF_{25-75%} in our study correlated with R10 (-0.463**), R15 (-0.486**), R20 (-0.486**), and X5 (-0.394**) ($p < 0.01$), a better correlation of it with small airway function was demonstrated by the post-bronchodilator effect as mentioned earlier. The weak correlation between baseline FEF_{25-75%} and IOS parameters related to small airways found in this study may be elucidated by the explanation that even though FEF_{25-75%} has a good sensitivity, it possesses a decreased specificity for small airway obstruction; this has been mentioned in previous studies.^{2,25} Another explanation may be the fact that the majority of our patients (77 %) had well-controlled asthma (C-ACT ≥ 20) and had been on inhaled corticosteroid treatment with a median duration of 24 months. Nonetheless, the low-level correlation between FEF_{25-75%} and R5 ($r = -0.307, p < 0.05$), X5 ($r = -0.394, p < 0.01$) in our study ($r = -0.162$) was consistent with the findings of a study in Korean children, which found a weak correlation between FEF_{25-75%} and R5 ($r = 0.198, p = 0.084$) and X5 ($r = 0.327, p = 0.141$) as well as between FEV1 and R5 ($r = -0.366, p < 0.01$) and X5 ($r = 0.154, p = 0.102$).²⁶ These incongruencies in findings may be a result of differences in the ethnic backgrounds of the study populations involved.

To demonstrate the correlation between FEF_{25-75%} and R5 after bronchodilator administration, the strongest correlation (0.0608, $p < 0.01$) among the IOS parameters in our study, we used the linear regression prediction model. The results demonstrated a 30% increase in FEF_{25-75%} corresponded to a 22.7% reduction in R5 ($p = 0.007$), as shown in Table 1. This finding resembles those of Marotta and colleagues, which reported a 36% delta change in R5 and a 24.5% delta change in R10 among childhood asthma patients compared to healthy controls (13.4% and 10.5%, $p < 0.05$) to be good predictors for bronchodilator response. However, no statistically significant differences in the FEV1 and FEF_{25-75%} values of asthmatic children post-bronchodilator inhalation compared to those of healthy controls were observed in their study. Our post-bronchodilator response of the FEF_{25-75%} parameter exhibited a similar tendency to that of children from Turkey; that study reported a delta change of the maximum mid-expiratory flow percent (MMEF%) in stable asthma equal to 27.49 ± 26.89 compared to healthy children (24.69

± 31.35 , $p = 0.110$). However, these results were not consistent with the recommendations of the European Respiratory Society (ERS), which suggests that a positive bronchodilator response according to the IOS testing should be evidenced by changes of -40% in R5, $+50\%$ in X5 and -80% in AX.²⁷ We believe the reason that the bronchodilator response in our study was lower than the ERS recommendations owes to the fact that our patients had had their asthma under control for a long time (24 months). Therefore, we suggest that IOS testing be performed at the very beginning of the asthma diagnosis; alternatively, the patients could be tested repeatedly to see differences in outcome as mentioned in Burman's study.²⁸ A recent study by Burman and colleagues revealed significant differences in outcome in 42 children with mild asthma (median C-ACT score = 21) at the second visit (median C-ACT score = 24) and the third visit (median C-ACT score = 24) when compared to the baseline data (median C-ACT score = 21, $p < 0.01$).²⁸

We found that FEV1 correlated negatively with both R15 and R20 ($r = -0.520/-0.565$, $p < 0.001$). This finding is in concurrence with the data reported by Cottini et al., i.e., R20 had comparable values to those of FEV1 on examination of large airway function.² This tendency also found in Song's study, which reported that FEV1 correlated significantly with R5, R10, R20, R35 Hz ($r = -0.366$, -0.537 , -0.430 , -0.508 , respectively) in Korean children with asthma.²⁶ These results are strongly suggestive of the role FEV1, R15, and R20 could play in childhood asthma management.

Limitations

This study did not recruit children with asthma before the commencement of treatment with inhaled corticosteroids. In addition, our patients were not in the moderate-to-severe asthma group. Therefore, the results of our study were obtained from children with mild form of the disease; this may have confounded the IOS outcomes. In reference to future studies, we suggest the inclusion of patients earlier in the course of the disease, e.g., since the time of diagnosis, and the recruitment of more participants with a severe asthma status.

Conclusions

FEV1 was significantly associated with R15/R20 in relation to IOS parameters, and FEF_{25-75%} was significantly negatively correlated with R5. A 30% change in FEF_{25-75%} correlated with a 22.5% change in R5. Our study found evidence for small airway impairment in the Thai childhood asthma population. Spirometry may be safely replaced by IOS as an alternative modality for lung function measurement, especially in young children.

Conflicts of interest

The authors have no conflicts of interest to declare.

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