Correlation between impulse oscillometry with bronchodilator reversibility in asthmatic population in a tertiary referral centre

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ABSTRACT

Introduction: Spirometry is considered as a 'gold standard' for diagnosis of asthma. Impulse oscillometry (IOS) is an alternative diagnostic tool which requires less cooperation by the participants. We performed a study to determine the correlation of IOS with bronchodilator reversibility from spirometry in asthmatic participants. We studied the correlation between forced expiratory flow ($FEF_{25\%–75\%}$) and differences between the resistance at 5Hz and 20Hz ($R_5–R_{20}$) in small airway disease (SAD) and the proportion of SAD diagnosed using IOS.

Materials and Methods: This was a cross-sectional study involving 82 asthmatic participants in Hospital Canselor Tuanku Muhriz (HCTM), Universiti Kebangsaan Malaysia (UKM) conducted between December 2020 till January 2022. Participants performed pre- and post-bronchodilator IOS and spirometry within the same day. Correlation between spirometry and IOS parameters and $FEF_{25\%–75\%}$ with IOS were determined and analysed.

Results: The change of forced expiratory volume in 1 second (FEV_1) was statistically correlated with a change of R5 in IOS. A decrement of 14.5% in R5 can be correlated with positive bronchodilator response (BDR) with a sensitivity of 63.9% and specificity of 60.9%, p=0.007. Pre-bronchodilator $FEF_{25\%–75\%}$ correlated with all parameters of SAD in IOS, e.g., R_5-R_{20}, reactance at 5Hz (X_5) and area of reactance (AX), p < 0.05. IOS detection for SAD is higher compared to $FEF_{25\%–75\%}$ in the BDR negative group (91.3% vs 58.7%).

Conclusion: IOS detected both bronchodilator reversibility and SAD hence can be considered as an alternative tool to spirometry for diagnosis of asthma in adults. IOS detected SAD more than $FEF_{25\%–75\%}$, especially in BDR-negative group.

KEYWORDS:
asthma; impulse oscillometry; bronchodilator reversibility; small airway disease; spirometry

INTRODUCTION

Asthma is a chronic inflammatory airway disease affecting large and small airways.[1,2] Asthma affects approximately 339 million people worldwide, and the prevalence of asthma among the Malaysian adult population was reported as high as 6.4% based on National Health and Morbidity Survey 2011.[3,4]

Typical asthma symptoms include wheezing, shortness of breath, chest tightness and coughing.[1,5] Spirometry is an important tool used to demonstrate variable expiratory airflow limitation to confirm the diagnosis of asthma.[1] It measures the amount of air that is expelled from a patient. A good spirometry manoeuvre requires a good expiratory effort, cooperation from the patient and trained personnel to coach the patient.[6] Although spirometry is reproducible, non-invasive and sensitive to changes in airflow obstruction, the actual manoeuvre can have many errors which may affect the results.

When performing spirometry, it is necessary to achieve acceptable quality. The patient must perform the test with maximal inspiration and expiration without hesitation with a back-extrapolation volume of <0.15 L. There must be strictly no cough or cessation of airflow during the manoeuvre. The manoeuvres should meet the end of test criteria defined by exhalation of more than 6 seconds with less than 0.025 L being exhaled in the last 2 seconds or a plateau of at least 1 second.6 Spirometry typically shows an obstructive pattern in participants with asthma, defined by an FEV_1/FVC ratio of less than 0.7.

Impulse oscillometry (IOS) is a useful tool as an alternative to spirometry.[7,8] It is a non-invasive test requiring minimal cooperation from the patient. It is effort independent and is especially useful in both young children and elderly participants.

It is relatively easy to perform. Participants are seated during the procedure. A nasal clip is attached, and tight seal is applied between the mouthpiece and lips to prevent air leak. Participants perform normal tidal breathing during the procedure for about 30 seconds. Around 120–150 sound impulses are transmitted into the lungs, resulting in informative parameters for the interpretation.[9]

IOS indicates the respiratory system impedance (Zrs). Impedance is based on resistance (Rrs) and reactance (Xrs) of the respiratory system. Rrs is the energy required to pass through the whole airway, including large and small airways, to distend the lung. Resistance at 5Hz (R_5) is an index affected by large and small airways. Resistance at 20Hz

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(R_{20}) indicates an index of resistance of large airways. Differences between R_{20} and R_5 show the resistance of small peripheral airways. Resistance is independent of oscillation frequency in a healthy person. R_5 is increased whenever central or peripheral airways obstruction occurs. Central airway obstruction increases Rrs evenly independent of oscillation frequency; however, in peripheral airway obstruction, Rrs is elevated at low frequency; thus, it becomes frequency-dependent. Xrs is composed of forces of the moving air column named as inertance (I) and the elastic properties of the lung called capacitance (C).

Both Rrs and Xrs are measured in cmH2O L^{-1} s^{-1} or kPa L^{-1} s^{-1}. At lower frequencies, the elastic properties of the lung (C) are dominant, but at the higher frequency, the inertive pressure of the large airway takes place. The reactance at 5Hz (X_5) indicates the combined effect of inertance and capacitance of the lung; however, the elastic properties of the lung are dominant. In other words, X_5 indicates the elastic recoil of the peripheral airways. The reactance (AX) area is the area under the curve between the reactance values for 5Hz and resonance frequency. AX reflects the changes in the degree of peripheral airway obstruction.[9]

Early detection of small airway disease (SAD) is crucial, especially for individuals with preserved pulmonary function. In a observational cohort study performed, 91% of asthmatic patients have SAD after undergoing various test; and SAD is associated with future risk of exacerbations.[10] Another study showed that SAD is associated with poor asthma control despite FEV_1 within normal range.[11] It is proven that early treatment for this category of participants can improve the long-term outcome and reduce exacerbation in the future.[9,12]

In spirometry, forced expiratory flow between 25% and 75% of vital capacity ($FEF_{25\%–75\%}$) is used to detect the SAD, but this value is highly dependent on forced vital capacity (FVC).[13]

$FEF_{25\%–75\%}$ is routinely obtained during spirometry. It is used as a measurement of distal airways calibre. It is reported to be more sensitive in reflecting airway hyperresponsiveness than FEV_1 in asthmatic participants. Therefore, the impairment of $FEF_{25\%–75\%}$, which is defined by < 65%, especially in those participants with normal FEV_1 may indicate the presence of SAD in asthma.[9]

IOS can be an alternative tool for the detection of SAD. Studies also show that IOS can detect small airway problems better than spirometry.[9-10,13] It is particularly important as bronchial asthma affects the small airway.[9,10]

However, IOS faces limited global and Malaysian adoption as a spirometry substitute due to several factors. Firstly, spirometry is well-established, cost-effective, and universally accepted, making a shift challenging. Additionally, standardisation issues and lack of extensive normative data for IOS hinder its widespread use. Training requirements for technicians and physicians may contribute to the reluctance in adopting IOS, as it demands specialised knowledge. Economic constraints in some regions, including Malaysia, may also impede the integration of IOS into routine respiratory assessments.

Overall, a combination of historical prevalence, standardisation concerns and economic considerations collectively limits the global and Malaysian embrace of IOS over spirometry.

A study done mainly on children showed accuracy in diagnosing bronchial asthma.[14] IOS parameters have also been found to be a better tool for evaluating asthma control compared to the usage of spirometry.[15] Palacios et al. did a study on 142 adult asthmatic participants and showed that IOS values had a good association with spirometry values. Thus, IOS could be considered an alternative tool to spirometry. However, IOS could not classify the participants based on the degree of asthma control.[12] Another study was done by Park et al. also showed that IOS may play a role in diagnosing airway obstruction and bronchodilation in adult asthmatic participants. This study, however, demonstrated the discrepancies between spirometry values and respiratory resistance from IOS.[16]

The correlation between IOS and spirometry in asthma has not yet become a standard method for assessing lung function, especially in adults. IOS should be considered another useful tool for detecting SAD. More studies and data are required to interpret IOS parameters to be implanted in clinical practice in the future for better asthma control in the population.

Hence, our study's primary objective was to determine the correlation between IOS and bronchodilator reversibility in the asthmatic population. Our secondary objective was to study the correlation of $FEF_{25\%–75\%}$ and differences between R_5 and R_{20} (R_5-R_{20}) in peripheral airway disease and the proportion of SAD in asthmatic participants using IOS.

MATERIALS AND METHODS

Study Design:

A cross-sectional study of outpatient asthmatic participants was done in HCTM, UKM between December 2020 and January 2022. This study was approved by the Research Ethics Committee, UKM, FF-2020-291. Participants attending the outpatient clinic were screened.

We included the following participants: age 18 years and above with physician diagnosis of asthma, non-smokers, or ex-smokers who had smoked < 5 pack-years but had not smoked for > 1 year.

Participants were excluded if they were current smokers, had a recent exacerbation of asthma requiring oral steroids and/or hospitalisation within the last 1 month, diagnosed with other respiratory diseases, and pregnancy. Participants who tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with reverse-transcriptase-polymerase chain reaction (RT-PCR) within 48 hours before recruitment were also excluded. Participants were included in the study after informed consent was provided.

Sample size was calculated based on the intended primary objective of determining the correlation between IOS with bronchodilator reversibility in the asthmatic population in HCTM, UKM. With 95% confidence level and 80% power for

different area under curve (AUC = 0.76)[17] and effects (δ = 0.1), the sample required was 156.

Procedure

The demographic data, including age and gender were recorded. Participants completed the self-administered survey, Asthma Control Test (ACT) in either English or Malay language depending on the subject's preference.

Participants were required to answer 5 five questions based on day-night time symptoms, rescue bronchodilators, and daily activities.[4] An ACT score of 19 or less was defined as not well-controlled asthma, while a score of 20 or more was defined as controlled asthma.[4]

All participants were required to perform a COVID-19 RT-PCR test 48 hours before performing the lung function tests. Long-acting bronchodilators were withheld at least 12 hours before the test, and short-acting bronchodilators 4 hours before the test. Participants who tested positive for COVID-19 were excluded from the study and were referred to the nearest healthcare clinic for further assessment.

Participants with negative results were allowed to continue in the study. They were asked to perform pre- and post-bronchodilator IOS and spirometry.

IOS was conducted first, followed by spirometry to avoid the influence of forced expiration on IOS parameters. Following that, participants were given bronchodilator via nebulisation with 400mcg Salbutamol, and both spirometry and IOS tests were repeated. Positive bronchodilator response (BDR) was 12% and greater than 200ml increased in FEV_1.[6]

IOS (Carefusion Germany 23X) was performed following a standardiszed protocol based on the manufacturer's instructions. Participants sat in a neutral position with a nose clip in place. An impulse generated by the loudspeaker was connected to the subject's mouth. The frequency ranges from 5 to -30 Hz were delivered. Resistance at 5Hz (R_5) and 20 Hz (R_{20}) were measured.

Spirometry was performed using SpiroUSB (CareFusion Germany 23X). Participants were asked to blow out for at least 6 seconds according to the American Thoracic Society (ATS) criteria.[6] This was performed at least three[3] times and a maximum of 8 tests depending on the quality of the test. A minimum of three[3] acceptable measurements were recorded for each participants, and the test was only be considered if fulfilled acceptability and repeatability criteria for FEV_1 and FVC.

Statistical Analysis

Statistical Package for Social Sciences (SPSS) software version 26 was used for data analysis. Variables were expressed as mean ± SD. Independent -t test, one-way ANOVA, Kruskal–-Wallis test, and Pearson correlations were used for comparisons. Correlation coefficient (r) was used to examine the relationship between measures. A P- value of ˂ 0.05 was considered statistically significant. Numerical analysis was used for the ROC curve, including the AUC, sensitivity, specificity, and optimal cut-off values for the IOS parameter.

RESULTS

A total of 82 participants were recruited. The mean age of all participants was 45.8 years + 15.0 years. Majority 48 (58.5%) were females, and 34 (41.5%) were males. Majority of the participants, 68 (82.9%) had good asthma control (ACT score > 20) and 14 (17.1%) had poorly controlled asthma (ACT score < 19). Table I describes the demographics of the study population.

Participants were further divided into four groups based on the BDR and airflow obstruction ($FEV_1/FVC < 0.7$). The four groups were obstructive +/- BDR and non-obstructive +/- BDR. 28 participants were categorised in the obstructive group, of which 19 were BDR positive, and 9 were BDR negative. 54 participants were classified under the non-obstructive group which 17 of them were BDR positive and 37 BDR negative.

A one-way between-group analysis of variance (ANOVA) was used to investigate the association of demographic characteristics with the bronchodilator response (BDR) group for normally distributed data. Inspection of skewness, kurtosis and Shapiro–Wilk statistics indicated that the assumption of normality was supported (Age, FEV, FEV_1, FEF and FVC) in each of the conditions. Levene's statistics were not significant for Age, FEV, FEV_1, FEF and FVC, R_5, R_{20}, X_5 and AX.

Post-hoc analyses with Tukey's Honest Significant Difference (HSD) test (using an α of .05) for age revealed the group of obstructive, BDR negative (M = 60.00, SD + 13.49) has significantly higher age compared to the non-obstructive, BDR negative group (M = 42.51, SD + 14.09).

Post-hoc analyses with Tukey's HSD (using an α of .05) revealed that obstructive group, BDR positive had lower pre-bronchodilator FEV_1 (L) (M=1.71, SD+0.51), and FEV_1, % predicted (M= 59.95%, SD+15.00) compared to non-obstructive, BDR negative group with pre-bronchodilator FEV_1(L) (M=2.21, SD+0.63) and FEV_1, % predicted (M = 81.19, SD + 14.78)

Post-hoc analyses with Tukey's HSD (using an α of .05) for $FEF_{25\%–75\%}$ revealed the group of obstructive, BDR positive (M=31.79, SD + 16.06) has significantly lower values compared to non-obstructive, BDR negative group (M = 70.92, SD + 21.91)

The between-group analysis of participants in BDR positive and negative without airflow limitation is presented in Table II.

An independent-samples t-test was used to compare two groups: positive (n=36) and negative (n=46), with a bronchodilator reversibility test.

For FEV_1 (L), the t-test was statistically significant, in which BDR negative group (M = 2.12, SD + 0.72) reporting 0.32L higher FEV_1 (L) value, compared to BDR positive group (M = 1.80, SD + 0.57), t (80) = 2.185 p = 0.032, two-tailed.

For FEV_1,(% predicted) the t-test was statistically significant, in which BDR negative group (M = 78.46, SD + 17.94) reported a 12.24% higher FEV_1 value compared to BDR

Table I: Participants' demographic, ACT score, spirometry and IOS characteristics between obstructive and non-obstructive group

Parameter	Obstructive group FEV1/FVC <0.7		Non-obstructive group FEV1/FVC >0.7		p-value
	BDR positive	BDR negative	BDR positive	BDR negative	
Characteristics					
N	19	9	17	37	
Age	44.7 +14.66	60.00 + 13.49	46.6 + 14.77	42.5 + 14.09	0.016
Male, n (%)	12 (63.2)	6 (66.7)	6 (35.3)	10 (27)	0.022
Female, n (%)	7 (36.8)	3 (33.3)	11 (64.7)	27 (73)	0.022
ACT score	22.16 + 3.01	23.33 + 1.23	21.94 + 2.90	22.00 + 2.94	0.622
Spirometry					
FEV_1 (L)	1.7 + 0.6	1.7 + 0.9	1.9 + 0.5	2.2 + 0.6	0.024
FEV_1 (% predicted)	60 + 15.0	67.2 + 25.5	72.5 + 12.2	81.2 + 14.8	<0.01
FVC (L)	2.8 + 1.0	2.8 + 1.1	2.5 + 0.8	2.7 + 0.8	0.571
FVC (% predicted)	76.5+16.1	80.2+21.9	72.7+ 13.4	77.8+ 3.3	0.075
FEV_1/FVC	0.6 + 0.1	0.6 + 0.1	0.8 + 0.1	0.8 + 0.1	<0.01
$FEF_{25\%–75\%}$,% predicted	31.8 + 16.1	32.8 + 16.5	57.9 + 19.2	70.9 + 21.9	<0.01
$FEF_{25\%–75\%}$<65% predicted n(%)	18 (94.7)	9 (100)	14 (82.4)	18 (48.6)	<0.01
IOS					
R_5 (cmH_20/L/s)	6.4 + 2.0	6.3 + 2.9	5.9 + 2.4	5.5 + 2.3	0.464
R_{20} (cmH_20/L/s)	3.60 + 0.8	3.4 + 0.8	3.5 + 0.9	3.3 + 1.0	0.564
R_{5-R20} (cmH_20/L/s)	2.9 + 1.4	2.9 + 2.3	2.4 + 1.7	2.2 + 1.5	0.46
X_5 (cmH_20/L/s)	–3.2 + 1.7	–2.6 + 1.9	–2.1 + 1.5	–2.2 + 1.3	0.071
AX (cmH_20/L)	25.9 + 15.5	25.9 + 21.6	20.3 + 16.70	17.3 + 13.5	0.2

The data are described using mean + SD or n (%). p-value is for one-way ANOVA for four groups.

Table II: Analysis between the group of BDR positive and negative in total population

Parameter	BDR positive	BDR negative	p-value
Characteristics			
N	36	46	
Age, mean + SD	45.6 + 14.5	45.9 + 15.5	0.92
Male, n (%)	18 (50.0)	16 (34.8)	0.169
Female, n (%)	18 (50.0)	30 (65.2)	0.169
Spirometry			
FEV_1 (L)	1.80 + 0.6	2.1 + 0.	0.032
FEV_1, % predicted	65.9 + 15.0	78.5 + 17.9	0.001
FVC (L)	2.7 + 0.9	2.8 + 0.8	0.595
FEV_1/FVC	0.7 + 0.1	0.8 + 0.1	0.006
$FEF_{25\%–75\%}$, % predicted	44.1 + 21.8	63.5 + 25.8	0.001
$FEF_{25\%–75\%}$ < 65% predicted, n (%)	32 (88.9)	27 (58.7)	0.002
IOS			
R_5 (cmH_20/L/s))	6.2 + 2.2	5.6 + 2.4	0.279
R_{20} (cmH_20/L/s))	3.6 + 0.8	3.30 + 0.9	0.195
$R_5–R_{20}$ (cmH_20/L/s))	2.6 + 1.5	2.33+ 1.7	0.391
X_5 (cmH_20/L/s))	–2.7 + 1.7	-2.3 + 1.4	0.213
AX (cmH_20/L)	23.2 + 16.1	19.0 + 15.5	0.234

The data are described using mean + SD or n (%).

Table III: Correlation of change of FEV_1 and $FEF_{25\%–75\%}$ <65% predicted to IOS parameters

Change of FEV_1	r	p-value
IOS parameters		
Change of R_5	–0.25[a]	0.023
Change of R_{20}	–0.18	0.11
Change of AX	–0.104	0.351
$FEF_{25\%–75\%}$ <65% predicted	R	p-value
IOS parameters		
$R_5–R_{20}$	–0.34[a]	0.008
X_5	0.46[a]	<0.001
AX	–0.41[a]	0.001

[a]Correlation is significant at the level 0.05 level (two-tailed)
Based on Cohen,1988 classification strength

Table IV: Incidence of SAD defined by $FEF_{25\%–75\%}$ and IOS parameters

Small airway parameters	BDR positive	BDR negative
$FEF_{25\%–75\%}$ < 65% predicted, n(%);	32 (88.9)	27 (58.7)
R_5-R_{20} > 0.07, n(%)	35 (97.2)	42 (91.3)
X_5 < –0.10, n(%)	30 (83.3)	38 (82.6)
AX > 0.38, n(%)	35 (97.2)	42 (91.3)

[a]Pre-bronchodilator values (FEF 25-75)

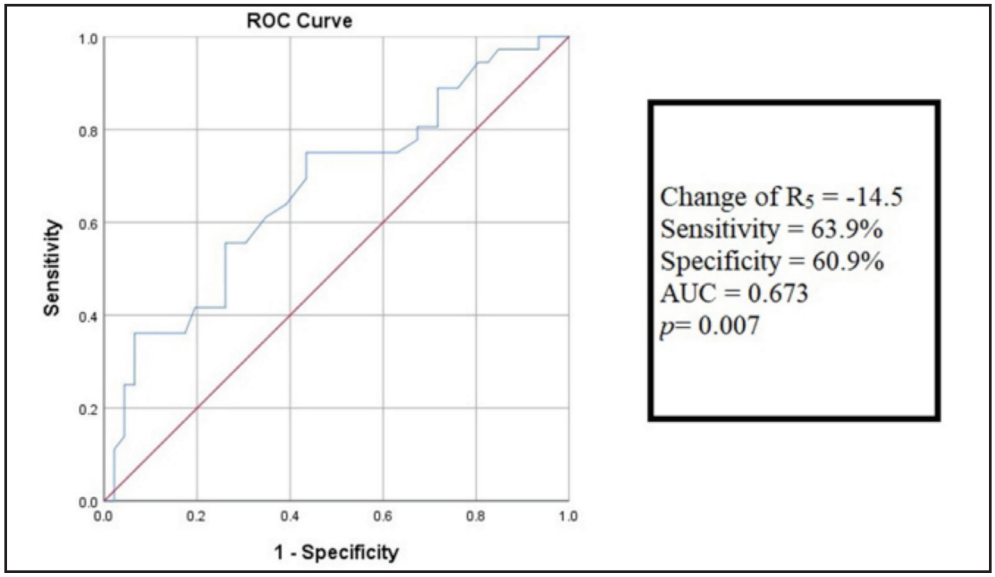

Fig. 1: Receiver operating characteristic (ROC) curve showing the accuracy of spirometry and IOS.

positive group (M = 65.86, SD + 14.98), t (79.1) = 3.304, p = 0.001, two-tailed.

For FEV_1/FVC ratio, the t-test was statistically significant, in which BDR negative group (M = 0.76, SD + 0.12) reported 0.07 higher ratio FEV_1/FVC value compared to BDR positive group (M = 0.69, SD + 0.12), t (80) =2.841, p=0.006, two-tailed.

For FEF 25%–75% the t-test was statistically significant, in which BDR negative group (M = 63.46, SD + 25.82) reported 19.35% higher FEF 25%–75% value compared to BDR positive group (M = 44.11, SD + 21.81), t (80) = 4.055, p < 0.001, two-tailed.

Table III described the correlation between IOS and spirometric parameters of the study population with $FEF_{25\%–75\%}$ <65% predicted. Change of $FEF_{25\%–75\%}$ was correlated with the R_5-R_{20}, X_5 and AX from IOS (Table IV).

Table IV describes the incidence of SAD between BDR positive and negative group. Detection of SAD in BDR positive using IOS was 97.2% compared to spirometry was 88.9%. Especially in the BDR negative group, detection of SAD by IOS was as high as 91.3% compared to spirometry, accounting for 58.7% only (Table IV).

Our study showed that the decrement of 14.5% in R5 can be correlated with positive BDR with the sensitivity of 63.9% and specificity of 60.9% (Figure 1).

DISCUSSION

Our study showed a correlation between IOS with bronchodilator reversibility in asthmatic participants. We found a correlation between the change of FEV_1 and the change of R_5. Although the correlation was weak, it was statistically significant. The weak correlation between IOS and spirometry parameters could be due to sample size limitation and the fact that spirometry is an effort-dependent procedure while IOS is relatively easier to perform. The other parameters from the IOS (e.g., change of R_{20} and change of AX) did not show any significant correlation to the change of FEV_1 from the spirometry.

There is no direct comparison study to compare cost-effectiveness of using spirometry and IOS in diagnosing asthma. However, in general, spirometry is generally considered more cost-effective due to its widespread use, established protocols and lower equipment costs. The training required for technicians and healthcare professionals is widely available and less specialised. Spirometers are relatively affordable and have become a standard diagnostic tool.

On the other hand, IOS tends to be more expensive, both in terms of equipment and training. The devices used in IOS are more sophisticated and can incur higher initial costs. Additionally, specialised training is often required for accurate interpretation, adding to the overall expenses.

While spirometry remains a cost-effective and widely accepted method, the growing recognition of IOS's unique capabilities may impact its cost-effectiveness in the future as technology advances and becomes more commonplace.

Several studies reported that positive BDR as expressed by IOS could be ranged from 8.6% to more than 40%, depending on the population or differentiating the participants' asthma control.[5] However, most of the data showed that a positive BDR was strongly suggested when there was a 40% decrease in R_5.[17] It signified significant airway reversibility in children and adults; however, this cut-off value may not be applicable in differentiating participants with asthma from those without asthma.

The advantage of using IOS is that it requires less effort from the participants. Our study showed that the readings produced from the IOS were able to achieve a satisfactory result compared to the spirometry. It should be considered a preferred tool for detecting BDR, especially for participants with physical and cognitive limitations participants. Even though several studies have proved that parameters from IOS were correlated with spirometry, clinical implications of using the IOS index in adult participants remain under discussion and observation until now.

Apart from the good markers for the diagnosis of bronchial asthma by the IOS indices, it can be used to evaluate disease control, especially in elderly participants.[16] In our study, we could not perform the comparison between different asthma control groups due to sample size limitations.

Our study proved a correlation between $FEF_{25\%–75\%}$ from spirometry to IOS parameters, including R_5-R_{20}, area of reactant (AX) and X_5. From the ECLIPSE trial, the predictive value of SAD was defined as R_5-R_{20} greater than 0.07 kPa/L/s, Ax more than 0.38 kPa/L/s and X_5 lesser than –0.10 kPa/L/s respectively.[18] Our IOS parameters were measured in cmH_20/L/s. During the data analysis, we converted the measurement to the unit, kPa/L/s, with the standard value of $1cmH_20$ equal to 0.098 kPa. Our study showed that IOS parameters could detect SAD better than spirometry. Especially in the BDR negative group, detection of SAD by IOS was as high as 91.3% compared to spirometry, accounting for 58.7% only.

Earlier detection of SAD by using spirometry or IOS is essential. The presence of SAD is associated with increased disease severity, risk of frequent exacerbation of asthma attacks and poorer symptom control. It is generally accepted that $FEF_{25\%–75\%}$ in the spirometry with a value of less than 65% predicted the SAD. We need to consider that usage of $FEF_{25\%–75\%}$ is limited when not adjusted by lung volume. While performing spirometry, lung volume is largely influenced by inadequate effort, especially in the elderly and children.

The limitation of the study was the small sample size. Due to the COVID-19 pandemic in Malaysia since March 2020, clinic appointments have been delayed. We also found fewer asthma participants attending the outpatient clinic for fear of contracting COVID-19 infection. To perform the spirometry and IOS, the participants were required to perform the COVID-19 PCR at least 48 hours before the procedure. Unfortunately, although they initially agreed to the study, some participants were not keen/did not turn up for the scheduled COVID-19 PCR test.

In conclusion, our study showed promising results in the correlation of spirometry and IOS. There was a correlation between IOS with bronchodilator reversibility. However, we need to consider the use of bronchodilator may alter the results. Additionally, our study showed a correlation of $FEF_{25\%–75\%}$ and differences between R20 and R5 (R_5–R_{20}) in SAD. The detection of SAD in the asthmatic patient by using IOS was better than $FEF_{25\%–75\%}$, especially in the BDR negative group. IOS can be be considered as an alternative tool to spirometry for the diagnosis of asthma in adults.

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