



Forced oscillometry track sites of airway obstruction in bronchial asthma

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ARTICLE INFO

Article history:

Received for publication February 4, 2015.

Received in revised form April 14, 2015.

Accepted for publication April 20, 2015.

ABSTRACT

Background: Spirometry is the most commonly used method for assessment of airway function in bronchial asthma but has several limitations. Forced oscillometry was developed as a patient-friendly test that requires passive cooperation of the patient breathing normally through the mouth.

Objective: To compare spirometry with forced oscillometry to assess the role of forced oscillometry in the detection of the site of airway obstruction.

Methods: This case-and-control study included 50 patients with known stable asthma and 50 age- and sex-matched healthy subjects. All participants underwent spirometry (ratio of force expiration volume in 1 second to forced vital capacity, percentage predicted for forced expiration volume in 1 second, percentage predicted for forced vital capacity, percentage predicted for vital capacity, and forced expiratory flow at 25–75%) and forced oscillometry (resistance at 5, 20, and 5–20 Hz).

Results: By spirometry, all patients with asthma had airway obstruction, 8% had isolated small airway obstruction, 10% had isolated large airway obstruction, and 82% had large and small airway obstruction. By forced oscillometry, 12% had normal airway resistance, 50% had isolated small airway obstruction with frequency-dependent resistance, and 38% had large and small airway obstruction with frequency-independent resistance. There was significant difference between techniques for the detection of the site of airway obstruction ($P = .012$). Forced oscillometry indices were negatively correlated with spirometric indices ($P < .01$).

Conclusion: Forced oscillometry as an effortless test, conducted during quiet tidal breathing, and does not alter airway caliber; thus, it can detect normal airway function better than spirometry in patients with asthma. Forced oscillometry detects isolated small airway obstruction better than spirometry in bronchial asthma.

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Introduction

Asthma is a chronic inflammatory disorder of the airways associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, with variable and often reversible airflow limitation.¹

Assessment of respiratory function is important in the diagnosis and monitoring of asthma and other respiratory diseases.² Theoretically, obstructive lung diseases can be evaluated in 2 ways: (1) airway resistance measures the power required by the obstructed lung and (2) expiratory flow volume measures the time required for breathing by the obstructed lung. Of these evaluations, the most frequently used measurement of asthma is forced expiration volume in 1 second (FEV₁).³

Spirometry is the preferred method of measuring airflow limitation and bronchodilator reversibility to establish a diagnosis of

asthma and an assessment of its severity.⁴ It measures the volume of air that can be moved in or out of the lungs as a function of time with rapid and maximal inspiratory and expiratory efforts. This makes the diagnosis of asthma difficult owing to the lack of objective measurements.⁵ It has several limitations. First, the clinical usefulness of spirometry depends on the quality of the results. The first step in interpreting the results is ensuring that the test is performed correctly and meets the currently recommended acceptability and reproducibility criteria. Second, the forced vital capacity (FVC) maneuver is an effort-dependent process; thus, suboptimal performance will result in erroneous results. Third, the operator plays an important role in coaching the subject to perform the maneuver as best as possible. Fourth, failure to take a rapid full inspiration and/or hesitation before starting exhalation will result in lower FEV₁ values. Moreover, a variable inspiratory effort between repeated maneuvers is a common cause of poor reproducibility.⁶

In contrast to spirometry, forced oscillometry superimposes small air pressure perturbations on the natural breathing of a subject to measure lung mechanics. It was developed as a

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Disclosure: Authors have nothing to disclose.

<http://dx.doi.org/10.1016/j.anai.2015.04.017>

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patient-friendly lung function test that minimizes demands on the patient and requires only passive cooperation of the patient breathing normally through the mouth.⁷ Because forced oscillometry is performed without closure of a valve connected to the mouthpiece and without maximal or forced respiratory maneuvers, it is unlikely that forced oscillometry itself will alter smooth muscle tone in the airway.⁸ The forced oscillometry apparatus generates small pressure oscillations that are applied at the mouth and transmitted into the lungs to help determine the impedance (Z) of the respiratory system. Pulmonary resistance (R) and reactance (X) are the key components of impedance that are measured and graphically displayed.⁹ The resistive component of respiratory impedance includes proximal and distal airways (central and peripheral), lung tissue, and chest wall resistance. Normally, central resistance dominates, depending on airway caliber and the surface of the airway walls, whereas lung tissue and chest wall resistances are usually negligible.¹⁰

Forced oscillometry measures impedance over a range of frequencies (5–20 Hz). Resistance and reactance when measured at 5 Hz, for example, are designated R_5 and X_5 , respectively. Lower-frequency oscillations, such as 5 Hz, generally travel farther to the lung periphery and provide indices of the entire pulmonary system. Therefore, when proximal or distal airway obstruction occurs, R_5 might be increased. Higher-frequency oscillations, such as 20 Hz, transmit signals more proximally and provide information primarily concerning the central airways. Thus, central airway obstruction will be reflected by an increased R_{20} .⁹ A frequency of 5 Hz provides values for total airway resistance (R_5) and a frequency of 20 Hz provides a value for central or large airway resistance (R_{20}); if the value of central airway resistance is subtracted from that for total airway resistance (ie, $R_5 - R_{20}$ difference), then this provides a measurement of peripheral or small airway resistance.¹¹

Proximal airway obstruction elevates resistance evenly and independently of oscillation frequency. In distal airway obstruction, resistance is highest at low oscillation frequencies and decreases with increasing frequency. This negative frequency dependence of resistance has been explained in terms of intrapulmonary gas flow redistribution owing to peripheral pulmonary non-homogeneities or to changes in peripheral elastic reactive properties. As peripheral resistance increases, resistance becomes more frequency dependent. The frequency dependence of resistance can be a normal finding in small children and might be greater than in adults in the presence of peripheral airflow obstruction.¹² The main advantages of forced oscillometry are the simplicity in the performance of tests, which require little cooperation by patients, the production of parameters complementary to traditional methods for pulmonary assessment, and a shorter time to perform the tests.¹³

Therefore, the present study was carried out to compare the commonly used spirometric indices with the relatively new forced oscillometric parameters to assess the role of forced oscillometry in the detection of the site of airway obstruction in stable asthma.

Methods

This case-and-control study was conducted at the Chest Department of Al-Alzahraa University Hospital (Cairo, Egypt). The study was approved by the institutional ethical review board of the Faculty of Medicine for Girls at Al-Azhar University. Written informed consent was obtained from each subject before enrollment into the study. The study included 100 subjects divided into 2 groups.

Bronchial Asthma Group

Fifty patients with known asthma were selected from patients attending the chest outpatient clinic for regular follow-up. They

were diagnosed several years previously based on typical symptoms, and positive bronchodilator reversibility testing results at time of diagnosis showed an increase in FEV_1 greater than 200 mL, or greater than 12% of the baseline value 15 minutes after 4 puffs of inhaled salbutamol (400 μ g) given through a metered-dose inhaler. All had been treated with low-to moderate-dose inhaled corticosteroids plus long-acting β_2 -agonists. All were asymptomatic and had well-controlled asthma. Stable asthma was defined as a minimal need for rescue medications, no exacerbation, the medication had been not changed in the past year, and there was no use of systemic steroids during this period.

Control Group

Fifty age- and sex-matched healthy individuals were in the control group. These participants had no symptoms suggestive any chest diseases and their spirometric indices were in the normal range.

Exclusion Criteria

The following subjects were excluded from the study:

1. Those with irreversible or partially reversible airflow obstruction (ie, FEV_1 improvement) after a bronchodilator reversibility test showing less than 12% or 200 mL of the baseline value.
2. Patients with other clinically significant diseases, such as fibrothorax, bronchiectasis, tuberculosis, or neuromuscular diseases.
3. Children were excluded from the study because of extensive research evaluating the role of forced oscillometry in this group, especially those younger than 5 years.
4. Some patients were excluded for lack of compliance during the forced expiratory test.

All subjects underwent the taking of a full history and complete clinical examination. Body mass index was calculated as weight (kilograms) divided by height (meters) squared. Spirometry and forced oscillometry were carried out on a HypAir compact plus flowmeter pulmonary function testing station (Medisoft, Sorinnes, Belgium).

Preparations for Spirometry and Forced Oscillometry

1. Inhaled short-acting agonists, long-acting β -agonists, and sustained-release theophylline were withheld for 6, 12, and 24 hours, respectively, before the test.
2. Heavy meals, exercise, and smoking were avoided 2 hours before the test.
3. Patients wore light clothes.
4. The test procedure was explained in full detail.
5. The patient sat in an upright position with the head slightly elevated.
6. The patient wore a nose clip and kept the lips closely fitted around a mouthpiece.
7. Spirometry was performed in 1 day and forced oscillometry was performed the next day to avoid the effects of a forced expiratory maneuver and of inhaled salbutamol used for reversibility testing of airways.

Performance of Spirometry

The subjects perform a rapid and deep inspiration followed by a forced expiration (for approximately 6 seconds) through the mouthpiece sealed by the mouth until no air is expelled and the curve reaches a plateau while maintaining an upright posture. Patients are continuously encouraged to do their best throughout the procedure. The following measurements were recorded from

Table 1
Comparison of all studied variables between groups

Item	Bronchial asthma (n = 50)	Control (n = 50)	t Test	
	Mean ± SD	Mean ± SD	t	P value
Age (y)	32.34 ± 8.4	31.9 ± 6.9	0.26	.79
BMI (kg/m ²)	28.7 ± 5.4	28.16 ± 3.5	0.6	.5
FEV ₁ /FVC	63.48 ± 8.3	89.3 ± 7.8	15.9 ^a	.000
FEV ₁ (%)	61.74 ± 12.4	89.0 ± 10.6	11.7 ^a	.000
FVC (%)	71.8 ± 21.2	97.46 ± 17.1	6.6 ^a	.000
VC (%)	71.48 ± 17.7	94.7 ± 18.0	6.48 ^a	.000
FEF _{25–75%}	44.1 ± 14.8	79.8 ± 13.9	12.4 ^a	.000
R5 (%)	185.12 ± 36.3	87.84 ± 37.3	13.2 ^a	.000
R20 (%)	153.4 ± 30.5	51.12 ± 31.2	16.5 ^a	.000
R5–R20 (%)	243.5 ± 56.0	105.34 ± 29	15.4 ^a	.000

Abbreviations: BMI, body mass index; FEF_{25–75%}, forced expiratory flow rate at 25% to 75%; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; R20, central or large airway resistance; R5, total airway resistance; R5–R20, peripheral or small airway resistance; VC, vital capacity.

^aSignificant at $P \leq .01$.

the spirometric maneuver: vital capacity (VC; percentage predicted), FVC (percentage predicted), FEV₁ (percentage predicted), FEV₁/FVC ratio, and forced expiratory flow rate at 25% to 75% (FEF_{25–75%}). Spirometric evidence used for the diagnosis of bronchial asthma are an FEV₁/FVC ratio lower than 80%, an FEV₁ no higher than 80% (large airway obstruction),⁴ and an FEF_{25–75} lower than 65% (small airway obstruction). Spirometric indices were calculated using the best of 3 technically satisfactory performances.¹⁴

Performance of Forced Oscillometry

The patient approaches quite normal breathing through the mouth. The patient must manually support the cheeks and floor of the mouth to decrease upper airway shunting and loss of impulses through the cheeks while the test is performed. Three to 5 maneuvers are performed for each subject to ensure reproducible test results without artifacts caused by air leaks, swallowing, breath holding, or vocalization.¹⁵ The following oscillometric indices were recorded: R5, R20, and R5–R20 difference. The following criteria were used to diagnose increased airway resistance by forced oscillometry in this study:

- Normal test result: R5 and R20 are less than 150% predicted. Resistance is independent of frequency (resistance does not decrease with increased frequency, ie, R20 is approximately similar to R5).¹⁶
- Proximal obstruction: R5 and R20 are greater than 150% predicted. Resistance is independent of frequency (ie, R20 is approximately similar to R5).¹⁶
- Peripheral obstruction: R5 is greater than 150% predicted and R20 is considerably less than R5. Resistance is frequency dependent (ie, R20 is markedly <R5).¹⁶

Data were collected, coded, input to the computer, and analyzed using SPSS 17 (SPSS, Inc, Chicago, Illinois). Quantitative data were represented as mean ± SD. Comparison was performed by the Student *t* test. A linear correlation coefficient was used for the detection of a correlation between 2 quantitative variables in 1 group. A *P* value higher than .05 was considered nonsignificant, a value less than or equal to .05 was considered significant, and a value less than or equal to .01 was considered highly significant.

Results

There was a female predominance in the 2 groups (74% in the asthma group and 70% in the control group). A comparison of all studied variables between the 2 groups is presented in Table 1.

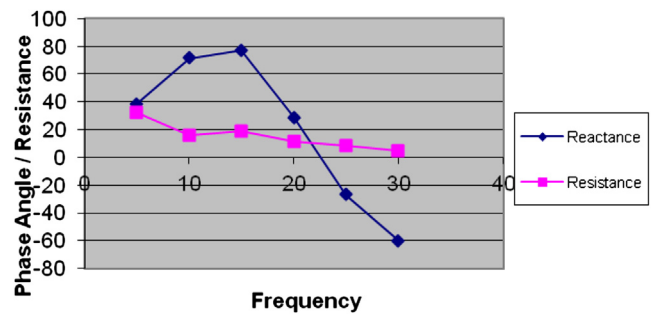


Figure 1. Forced oscillometry graph of a patient with small airway obstruction and frequency-dependent resistance.

By spirometry, all patients with asthma showed airway obstruction (FEV₁/FVC <80), 8% presented with isolated small airway obstruction (FEF_{25–75%} <65% with normal FEV₁ percentage predicted), 10% presented with isolated large airway obstruction (FEV₁ <80% predicted with normal FEF_{25–75%}), and 82% presented with large and small airway obstruction (FEV₁ <80% predicted and FEF_{25–75%} <65%). By oscillometry, 12% presented with normal airway resistance (R5 <150%), 50% presented with isolated small airway obstruction with frequency-dependent resistance (R5 >150% and R20 <150%; Fig 1), and 38% presented with large and small airway obstruction with frequency-independent resistance (R5 and R20 >150%). There was a significant difference between the 2 techniques for the detection of the site of airway obstruction ($P = .01$; Table 2).

Percentage of R5 correlated negatively with FEV₁/FVC and FEV₁ percentage predicted ($P = .000$). Percentage of R20 correlated negatively with predicted percentages of FEV₁, FVC, and VC and FEF_{25–75%} ($P = .000$, .008, .004, and .000 respectively). Percentage of R5–R20 correlated negatively with FEV₁/FVC, predicted percentages of FEV₁, FVC, and VC, and FEF_{25–75%} ($P = .000$, .000, .001, .005, and .000, respectively; Table 3 and Figs 2–4).

Discussion

In this study, all forced oscillometry indices (R5, R20, and R5–R20 difference) were significantly increased in the asthma group compared with the control group ($P < .01$; Table 1). Similar results were found by Nikkhah et al¹⁷ who reported that R5 and R20 were significantly increased in patients with asthma compared with controls.

The term *small airways* refers to approximately 7 to 19 generations of airways with an inner diameter of approximately 2 to 0.5 mm. These airways are considered an important site of inflammation in asthma and chronic obstructive pulmonary disease.¹⁵ FEF_{25–75%} is considered an early marker for the diagnosis of obstructive lung disease and more specific for obstruction in the small airways than FEV₁.¹⁸ In the present study, all patients with asthma showed a decreased FEV₁/FVC ratio (<80); 8% presented

Table 2
Comparison between spirometry and oscillometry for detection of site of airway obstruction in asthma group

Site of obstruction	Pulmonary function tests		χ^2 Test	
	Spirometry (n = 50)	Oscillometry (n = 50)	t	P value
Normal test result	0 (0%)	6 (12%)	6.38 ^a	.012
Small airway obstruction	4 (8.0%)	25 (50%)		
Large airway obstruction	5 (10.0%)	0 (0.0%)	28.0	.01 ^a
Large and small airway obstruction	41 (82.0%)	19 (38%)		

^aSignificant at $P \leq .05$.

Table 3
Correlations between forced oscillometry and spirometry in asthma group

Spirometric indices	Forced oscillometric indices					
	R5 (%)		R20 (%)		R5–R20 (%)	
	r	P value	r	P value	R	P value
FEV ₁ /FVC	–0.79 ^b	.000	–0.23 ^a	.096	–0.55 ^b	.000
FEV ₁ (%)	–0.36 ^b	.000	–0.70 ^b	.000	–0.63 ^b	.000
FVC (%)	0.030	.836	–0.37 ^b	.008	–0.46 ^b	.001
VC (%)	0.024	.871	–0.39 ^b	.004	–0.39 ^b	.005
FEF _{25–75%}	–0.44 ^b	.001	–0.50 ^b	.000	–0.96 ^b	.000

Abbreviations: FEF_{25–75%}, forced expiratory flow rate at 25% to 75%; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; R20, central or large airway resistance; R5, total airway resistance; R5–R20, peripheral or small airway resistance; VC, vital capacity.

^aCorrelation significant at .05 level.

^bCorrelation significant at .01 level.

with isolated small airway obstruction. By forced oscillometry, 12% presented with normal airway resistance and 50% presented with isolated small airway obstruction with frequency-dependent resistance. Therefore, forced oscillometry yields different values for the detection of small airway obstruction (Table 2). These findings could be explained by 2 facts: (1) spirometry is effort-dependent test and requires good cooperation from patients and (2) dynamic lung volume is measured during a forced expiratory maneuver that could alter the diameter of the airways and, hence, the spirometric indices. This explains the result reported by Cirillo et al¹⁹ who concluded that spirometry has a limited capacity to distinguish small from large airways. Peak expiratory flow and FEV₁ mainly reflect large airway function, whereas FEF_{25–75%} is believed to represent small airway function but has poor reproducibility.

Spirometry is the most common pulmonary function test; it is a measurement of maximal airflow after deep inspiration to fill up the lungs. It can provide information about the size of the airways (mainly large airways) and about the presence of limitations to airflow.²⁰ Forced oscillometry is indicated as a reliable diagnostic tool to perform tidal breathing analysis. One of the great advantages of forced oscillometry over spirometry is that the results measured are independent of the subject's respiratory pattern; therefore, it is independent of effort; it requires only passive cooperation from the subject breathing normally.²¹ Different results have been reported by Hira and Singh²² who found that

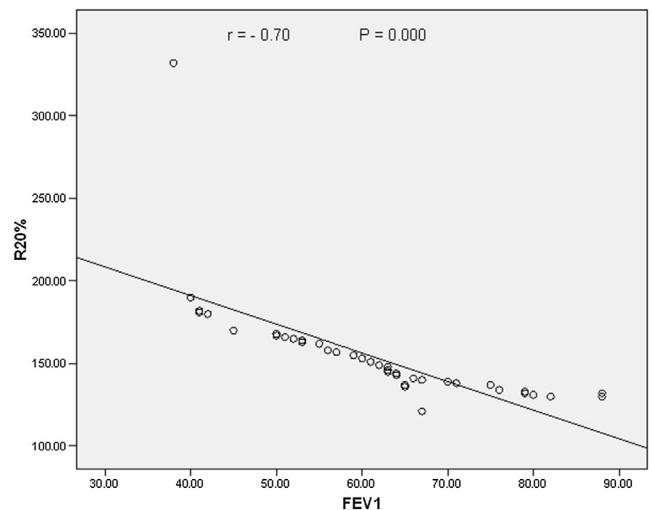


Figure 3. Correlation between percentage of resistance at 20 Hz (R20%) and predicted percentage of forced expiration volume in 1 second (FEV₁%) in the asthma group.

impulse oscillometry could detect obstruction in all patients, whereas flow volume loop showed obstruction in 78.2% ($P < .05$), localized obstruction (central and peripheral) in 52.2%, and peripheral obstruction in 26.1% of patients. In contrast, impulse oscillometry showed predominant central obstruction in 65.5% and predominant peripheral obstruction in 34.5%. This difference could be explained by the fact that all patients in the present study had stable asthma and all were asymptomatic.

This study showed a good correlation between spirometry and forced oscillometry; percentage of R5 was negatively correlated with FEV₁/FVC and FEV₁ percentage predicted ($P = .000$). Percentage of R20 was negatively correlated with FEV₁ percentage predicted and FEF_{25–75%} ($P < .01$). Percentage of R5–R20 difference was negatively correlated with FEV₁/FVC, FEV₁ percentage predicted, and FEF_{25–75%} ($P < .01$; Table 3). These results are in accord with those reported by Song et al³ who found that FEV₁ percentage predicted was significantly correlated with R5, R10, R20, and R35. FEF_{25–75%} did not show a correlation at any resistance (R5, R10, R20, or R35).

Similar results were reported by Pisi et al²³ who found that R5–R20 difference was significantly correlated with spirometry and

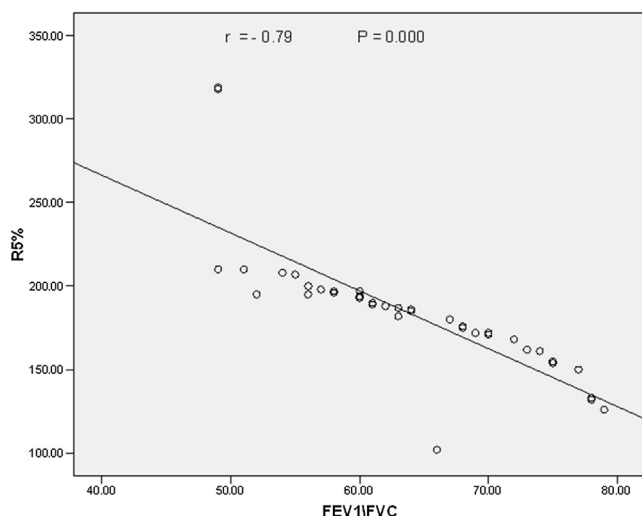


Figure 2. Correlation between percentage of resistance at 5 Hz (R5%) and the ratio of forced expiration volume in 1 second to forced vital capacity (FEV₁/FVC) in the asthma group.

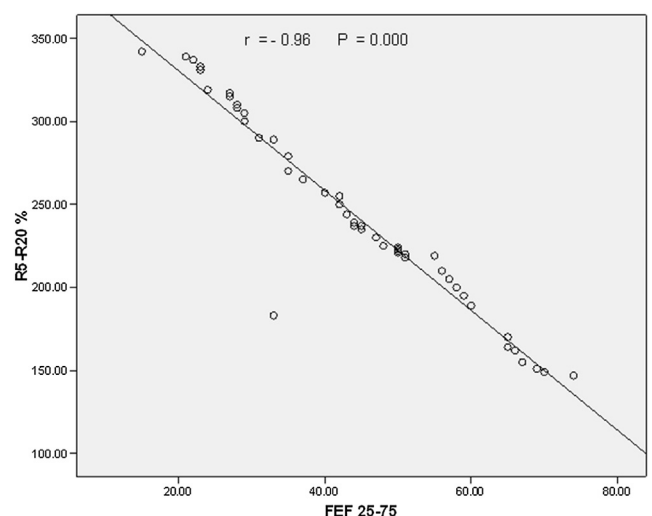


Figure 4. Correlation between percentage of difference between resistance at 5 and 20 Hz (R5–R20%) and forced expiratory flow rate at 25% to 75% (FEF_{25–75%}) in the asthma group.

FEF_{25–75%} was the parameter strongly correlated in patients with asthma. Similar results were reported by Tsuburai et al.²⁴ Oostveen et al.²⁵ and Qi et al.²⁶ who found that each of the oscillometry parameters (R5, R20, and R5–R20 difference) was significantly correlated with FEV₁ percentage predicted ($P < .001$). Nikkhah et al.¹⁷ reported that R20 was significantly correlated with FEV₁ percentage predicted and FEV₁/FVC in patients with asthma. Tanaka et al.²⁷ reported that R5–R20 difference was correlated with traditional lung function tests of small airway obstruction and FEV₁ percentage predicted and FEF_{25–75%} in elderly patients with asthma. Therefore, they concluded that R5–R20 difference might be a new index for small airway disease, with little effort by patients. Yamaguchi et al.²⁸ reported that R5–R20 difference had a good correlation with FEF_{25–75%}; therefore, R5–R20 difference seems to be a good maker for the detection of small airway disease. In contrast, Tsuburai et al.²⁴ concluded that R5–R20 difference seems to indicate heterogeneity of narrowing of the small airways and, hence, uneven ventilation of the lung and that R5 might indicate total airway narrowing.

Al-Mutairi et al.²⁹ documented that specificity was comparable for forced oscillometry (80.5%) and conventional pulmonary function testing (86.2%) in relation to asthma and that forced oscillometry had better sensitivity (45.8%) in detecting normal lung function than conventional pulmonary function testing (28.8%).

This study has limitations that need to be mentioned. The authors could not calculate the sensitivity, specificity, positive predictive value, and negative predictive value of forced oscillometry for the detection of the site of airway obstruction owing to the unavailability of gold standard tests (eg, body plethysmography) in their institution.

Forced oscillometry as an effortless test, conducted during quite tidal breathing, and does not alter airway caliber; therefore, it can detect normal airway function better than spirometry in patients with asthma. Forced oscillometry detects isolated small airway obstruction better than spirometry in bronchial asthma.

Forced oscillometry provides a rapid, noninvasive measurement of airway resistance, and it can be used easily in the diagnosis and management of airway diseases. Future work is required to assess the role of this specific and effective test in the diagnosis and monitoring of different respiratory diseases. Further research is required to measure whether oscillometry and spirometry are equally predictive of impaired asthma control as measured by oral steroid or short-acting β -agonist use. More research should be conducted in adult patients with asthma and normal FEV₁ to assess the role of oscillometry in the detection of small airway disease and to evaluate whether treatment based on this finding improves outcomes. Further studies to examine the performance of forced oscillometry and spirometry in patients with asthma during an episode of asthma exacerbation are warranted.

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