

# Acceptable alternatives for forced vital capacity in the spirometric diagnosis of bronchial asthma

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## ABSTRACT

**Background:** In patients with advanced obstructive ventilatory disorders, expiration may last for a relatively long time until the end-of-test standards for forced vital capacity (FVC) are satisfied. This may be difficult for both the patient and the technician. The Forced expiratory volume in 3 seconds (FEV3) and Forced expiratory volume in 6 seconds (FEV6) maneuvers are simple, undemanding and easier to perform when compared with FVC; however, their reliability to be used as alternatives for FVC is controversial. **Aim:** To judge whether FEV3 and FEV6 can be used instead of FVC in detecting airway obstruction in asthmatic patients. **Settings and Design:** This study was a cross-sectional case-control laboratory-based study. **Materials and Methods:** The study involved 40 known asthmatic patients and 40 apparently healthy, gender- and age-matched controls. Spirometry was used for assessing pulmonary function according to the American Thoracic Society and European Respiratory Society criteria. **Statistical Analysis:** A significant difference in the means between the groups was performed using Student's t-test. The receiver operating characteristic (ROC) curves were used to compare efficiency of the studied spirometric measurements on asthma diagnosis. **Results:** The mean of FEV3 was not significantly different when compared with the mean of FVC ( $P = 0.352$  for asthmatic patients and  $P = 0.957$  for control group). This was also true when the mean of FEV6 was compared with the mean of FVC ( $P = 0.805$  for asthmatic patients and  $P = 0.957$  for control group). The area under the ROC curves of FEV1/FVC%, FEV1/FEV3% and FEV1/FEV6% were also comparable. **Conclusion:** FEV3 and FEV6 are accurate and reliable alternatives for FVC in assessing airway obstruction of asthmatic patients.

**Key words:** Asthma, end-of-test, FVC, FEV3, FEV6, lung function tests

## INTRODUCTION

The forced vital capacity (FVC) maneuver is necessary for evaluating patients with obstructive airway disease.<sup>[1,2]</sup> The American Thoracic Society and the European Respiratory Society (ATS/ERS) had standardized the FVC maneuver.<sup>[3]</sup> For each subject, the maximum FVC of three acceptable and reproducible maneuvers is used to derive spirometric indices.

The FVC maneuver is usually performed in conjunction with

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the assessment of the timed forced expiratory volumes (FEV<sub>x</sub>). The FEV<sub>x</sub> is the volume exhaled during the first x seconds of a forced expiratory maneuver started from the level of total lung capacity. The commonly used forced expiratory volumes are FEV1, FEV3 and FEV6. FEV/FVC percentage is by far the most frequently used index for assessing airway obstruction, bronchoconstriction or bronchodilatation.<sup>[1,3]</sup>

In patients with advanced obstructive lung disease, expiration may last for a relatively long time, until the end-of-test standards for FVC are satisfied.<sup>[3,4]</sup> This may be difficult for both the patient and the technician.<sup>[5,6]</sup> Previous data showed that FEV3 and FEV6 behave like FVC in assessing ventilatory functions of the lungs.<sup>[7-9]</sup> However, other studies concluded that complete expirations are essential for accurate measurement of the FVC-dependent spirometric indices.<sup>[10-13]</sup>

The National Lung Health Education Program recommended FEV6 as a surrogate for FVC<sup>[14]</sup>; however, few years later, some studies were against the use of FEV6 in place of

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FVC.<sup>[11-13]</sup> This controversy could partly be explained by the fact that previous studies examined patients with different pathologies.<sup>[7-12]</sup> Studies on FEV3 and FEV6 were usually on patients with chronic obstructive lung diseases, smokers or obstructive lung diseases in general without special concern to bronchial asthma. This is important because inflammation and, hence, narrowing of smaller airways is more evident in asthmatic patients as compared with other obstructive lung diseases.<sup>[15-17]</sup> The aim of this study was to judge whether FEV3 and FEV6 could be used instead of FVC in detecting airways obstruction in asthmatic patients.

## MATERIALS AND METHODS

The study involved two groups: a group of 40 known non-smoking asthmatic patients (18 males and 22 females) selected from chest clinics of the teaching hospitals and a gender- and age-matched control group of 40 apparently healthy subjects (21 males and 19 females) recruited mainly from non-smoking university students and employees. Patients with past medical history suggestive of other chronic respiratory diseases (apart from asthma), diabetes mellitus, hypertension and heart diseases were excluded from the study.

The GIMA scale (Professional Medical Products, Italy) was used for measuring weight and height simultaneously. IQ-TQ Spirometer (Version 5.18, Clement Clarke International Limited, Edinburgh Way, Harlow, Essex, UK) was used for assessing pulmonary functions according to the ATS/ERS standards.<sup>[3]</sup> To minimize diurnal variations in lung function, spirometry was conducted between 09.00 and 12.00 am in all studied subjects.

Statistical evaluation was performed using the Microsoft Office Excel 2003 and SPSS 17. To compare the efficiency of the studied spirometric measurements on asthma diagnosis, the Receiver Operating Characteristic (ROC) curves were used. Screening studied variables for significant differences in the means between the groups was performed using Student's two-tailed, unpaired t-test. In all these statistical tests, only  $P < 0.05$  was considered significant.

## RESULTS

The ages of both the test and the control groups ranged between 20 and 40 years. The mean age was  $24.78 \pm 4.77$  years in non-asthmatic subjects and  $28.85 \pm 5.69$  years in asthmatic patients.

All spirometric measurements were significantly lower in the asthmatic patients as compared with the control group [Table 1]. The mean of FEV3 was not significantly different

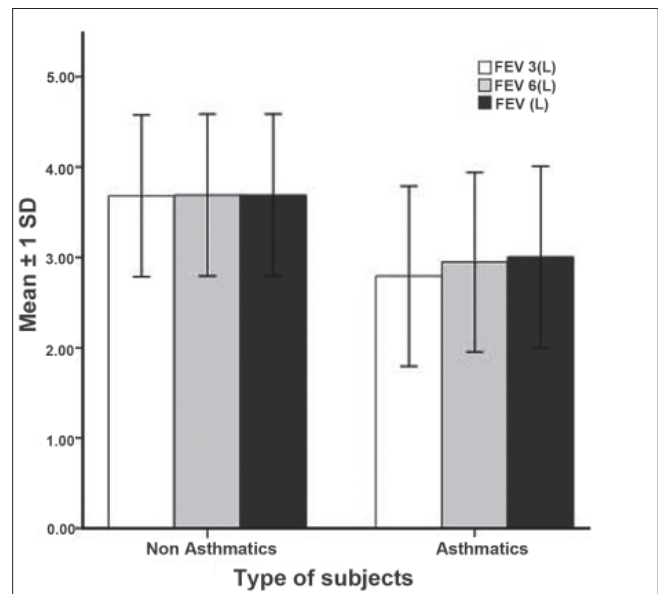
when compared with the mean of FVC ( $P = 0.352$  for asthmatic patients and  $P = 0.957$  for control group, for absolute values of means and standard deviations see Table 1). This was also true when the mean of FEV6 was compared with the mean of FVC ( $P = 0.805$  for asthmatic patients and  $P = 0.957$  for control group). However, all timed forced expiratory volumes (FEV1, FEV3, FEV6 and FVC) were significantly higher in the control group when compared with the asthmatic patients ( $P \leq 0.002$  for all) [Figure 1].

For further verification, accuracy of FEV1/FVC% was compared with both FEV1/FEV3% and FEV1/FEV6% using the ROC curve analysis. Area under the curve for FEV1/FVC%, FEV1/FEV3% and FEV1/FEV6% was  $0.849 \pm 0.045$  (95% confidence interval [CI] 0.761–0.936),  $0.843 \pm 0.045$  (CI 0.755–0.931) and 0.848

**Table 1: Comparison of spirometry between the asthmatic patients and the control group**

Parameter	Non-asthmatic patients	Asthmatic patients	P
FEV1 (L)	$3.32 \pm 0.80$	$2.19 \pm 0.88$	0.000
FEV3 (L)	$3.68 \pm 0.90$	$2.79 \pm 0.99$	0.000
FEV6 (L)	$3.69 \pm 0.90$	$2.95 \pm 0.99$	0.001
FVC (L)	$3.69 \pm 0.90$	$3.00 \pm 1.01$	0.002
FEV1/FVC%	$90.43 \pm 6.09$	$72.35 \pm 15.92$	0.000
FEV1/FEV3%	$90.70 \pm 5.88$	$77.39 \pm 11.32$	0.000
FEV1/FEV6%	$91 \pm 0.08$	$73 \pm 0.15$	0.000
PEFR (L/sec)	$7.49 \pm 1.81$	$4.75 \pm 2.10$	0.000
FEF25% (L/sec)	$6.85 \pm 1.63$	$3.98 \pm 2.30$	0.000
FEF50% (L/sec)	$4.86 \pm 1.54$	$2.50 \pm 1.91$	0.000
FEF75% (L/sec)	$2.29 \pm 0.83$	$1.06 \pm 0.92$	0.000
FEF25%–75% (L/sec)	$4.31 \pm 1.31$	$2.18 \pm 1.66$	0.000
FEF75%–85% (L/sec)	$1.77 \pm 0.70$	$0.80 \pm 0.73$	0.000

All values are in mean  $\pm$  standard deviation



**Figure 1:** Means and standard deviations of Forced expiratory volume 3 seconds (FEV3), Forced expiratory volume 6 seconds (FEV6) and forced vital capacity (FVC)

**Table-2: Statistical analysis of areas under ROC curves of FEV1/FEV3%, FEV1/FEV6% and FEV1/ FVC%**

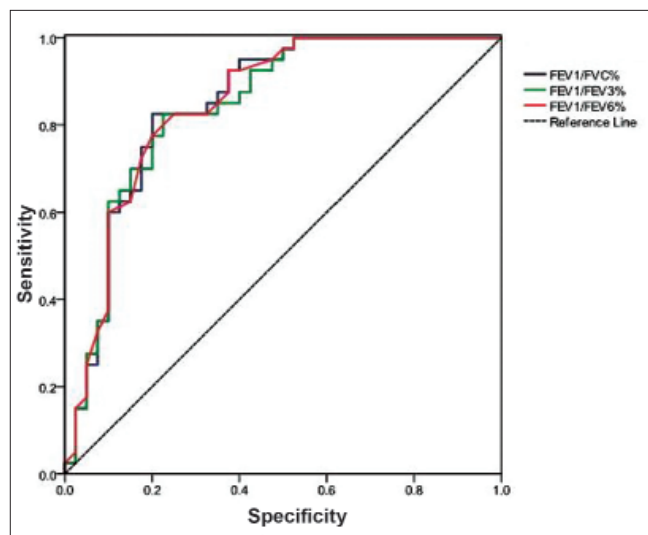
Variable (s)	Area Under the Curve	Standard Error	Significance	95% Confidence Interval	
				Lower Bound	Upper Bound
FEV1/FEV3	0.843	0.045	0.000	0.755	0.931
FEV1/FEV6	0.848	0.044	0.000	0.762	0.935
FEV1/FVC	0.849	0.045	0.000	0.761	0.936

$\pm 0.044$  (CI 0.762–0.935), respectively (mean  $\pm$  standard error of mean) [Figure 2]. Absolute values of the areas under the curves, standard errors, statistical significances and 95% confidence intervals are summarized in Table 2.

## DISCUSSION

In this study, all studied spirometric measurements were significantly lower in the asthmatic patients as compared with the control group, indicating that the patients have significant airway obstruction. The means of FEV3 and FEV6 were not significantly different when compared with the mean of FVC in both asthmatic patients and control group. Moreover, the areas under the ROC curves of FEV1/FVC%, FEV1/FEV3% and FEV1/FEV6% were comparable. These results demonstrate that FEV3 and FEV6 are accurate and reliable alternatives for FVC in assessing airway obstruction of asthmatic patients. Most of the previous studies in FEV6 were in favor of the current results<sup>[7,8,18,19]</sup>; however, the data regarding FEV3 are scarce.<sup>[5,6]</sup>

The area under the ROC curve of FEV1/FEV3% is slightly less compared with that of FEV1/FEV6%, but is still comparable with the area under the ROC curve of FEV1/FVC%. Allen *et al.* conducted a study in patients with mild cognitive impairment to know the proportion of subjects who could carry out FEV3 but were not able to satisfy end-of-test criteria of FVC maneuver and to observe whether FEV1/FEV3% concord with FEV1/FVC% in patients with airflow obstruction.<sup>[5]</sup> Results revealed that 51% of the patients were able to achieve FVC maneuver. Twenty-five percent of the patients were able to reach FEV3 but not FVC. Data also proved that the value of FEV1/FEV3% of <80% matched a FEV1/FVC% of <70% (sensitivity 96%, specificity 97%), concluding that FEV1/FEV3% <80% can be used to identify patients with airflow obstruction if they were unable to perform FVC maneuver.<sup>[5]</sup> Similar results were obtained by another study in which only 43% of the patients were able to achieve FVC maneuver.<sup>[20]</sup> In addition, FEV3 can be used to predict FVC using a model based on logarithmic values of the spirometric measurements.<sup>[6]</sup> This model had a good diagnostic performance and behaved reasonably accurate in situations of short exhalation time and/or when no expiratory plateau is achieved.



**Figure 2:** Receiver Operating Characteristic curves of Forced expiratory volume FEV1/FEV3%, FEV1/FEV6% and FEV1/forced vital capacity (FVC)%

Regarding FEV6, Swanney *et al.* analyzed the FEV1/FEV6 and FEV1/FVC results of 502 consecutive patients in the spirometric diagnosis of airway obstruction. The sensitivity of FEV1/FEV6 for diagnosing airway obstruction as defined by FEV1/FVC was 95.0%; the specificity was 97.4%.<sup>[7]</sup> Five years later, Vandevoorde *et al.* declared that the FEV1/FEV6% could be used as a valid alternative for FEV1/FVC% in the diagnosis of airway obstruction, especially for screening purposes in high-risk populations for chronic obstructive pulmonary disease in primary care. They also added that FEV6 is an acceptable surrogate for FVC in the detection of a spirometric restrictive pattern.<sup>[9]</sup> This conclusion was further supported by the outcome of Akpınar-Elci *et al.* in workers, although with some misclassification when compared with obtaining American Thoracic Society-acceptable maneuvers of longer duration.<sup>[21]</sup>

It is worth mentioning that in contrast to previous researches, which were largely based on measuring conditional ratios (i.e., sensitivity, specificity) and other measures of accuracy, the current study considered comparing the absolute values of FEV3 and FEV6 with FVC in asthmatic patients. However, some drawbacks against FEV6 were reported<sup>[11-13]</sup> and should be kept in mind when FEV6 is used as a screening test for airway obstruction. In patients with obstructive ventilatory diseases, spirometry may not reliably diagnose a concomitant restrictive defect, but it can rule out restriction for patients with FVC or FEV6 >85% predicted in males or >70% predicted in females.<sup>[22]</sup> These findings were easy to interpret in conjunction with the data obtained by Gleeson *et al.*, which showed moderate specificity of FEV6 for the detection of spirometric abnormalities.<sup>[23]</sup> Similarly, the relatively low sensitivity of FEV6 obtained by Demir *et al.* may lead to underestimation of airway obstruction if used alone.<sup>[24]</sup>

An important shortcoming of this study is that asthma severity was not considered. Although the present findings support FEV3 and FEV6 as satisfactory alternatives for FVC in the spirometric diagnosis of bronchial asthma, this may not be the case in advanced forms of the disease. Further studies are desirable to evaluate the capability of these parameters to differentiate classes of patients with different severities of ventilatory disorders.

In conclusion, the present study found that FEV3 and FEV6 are acceptable alternatives for FVC in the spirometric diagnosis of bronchial asthma. The conclusion was based on the absence of significant differences in the means when the absolute values of FEV3 and FEV6 were compared with FVC in asthmatic patients. In addition, ROC curves of these volumes were comparable. This important conclusion offers all advantages of FEV3 and FEV6 over FVC in asthmatic patients.

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