

Original Article

Airflow limitation in brazilian caucasians: FEV₁/FEV₆ vs. FEV₁/FVC*

Limitação ao fluxo aéreo em brasileiros da raça branca: VEF₁/VEF₆ vs. VEF₁/CVF

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Abstract

Objective: To evaluate the use of the forced expiratory volume in one second/forced expiratory volume in six seconds (FEV₁/FEV₆) ratio as an alternative to the FEV₁/forced vital capacity (FVC) ratio in the detection of mild airway obstruction. **Methods:** Reference equations for the Brazilian population in 2006 were used in order to determine the lower limits of normality for the FEV₁/FEV₆ and FEV₁/FVC ratios. The spirometry findings of 155 patients from 20 to 84 years of age were analyzed. All of the patients presented the following: a < 15% difference between predicted and observed FEV₁/FVC ratio; an FEV₁ ≥ 60% of predicted; and an exhalation time of at least 6 s. The Brazilian Thoracic Society criteria for acceptability and reproducibility in spirometry were met. **Results:** Mean values (± SD) for FEV₁/FEV₆ and FEV₁/FVC were 73 ± 4% and 75 ± 3%, respectively. Using the FEV₁/FVC ratio, we identified airflow obstruction in 61 patients, compared with only 46 patients when we used the FEV₁/FEV₆ ratio, showing a sensitivity of 75% (p < 0.001). **Conclusions:** The FEV₁/FEV₆ ratio has poor sensitivity and should not be used to replace the FEV₁/FVC ratio in the diagnosis of mild airway obstruction.

Keywords: Forced expiratory volume; Vital capacity; Airway obstruction; Spirometry; Respiratory function tests.

Resumo

Objetivo: Avaliar a utilidade da relação volume expiratório forçado no primeiro segundo/volume expiratório forçado nos primeiros seis segundos (VEF₁/VEF₆) na detecção de obstrução leve ao fluxo aéreo como alternativa à relação VEF₁/capacidade vital forçada (CVF). **Métodos:** As equações sugeridas para a população brasileira em 2006 foram utilizadas para determinar os limites inferiores normais para as relações entre VEF₁/VEF₆ e VEF₁/CVF. Foram avaliadas as espirometrias de 155 pacientes com diferença entre a relação VEF₁/CVF prevista-observada abaixo de 15% e VEF₁ ≥ 60% do previsto, com idades entre 20 e 84 anos e com tempo expiratório de 6 s no mínimo. Os critérios de aceitabilidade e reprodutibilidade para a espirometria sugeridos pela Sociedade Brasileira de Pneumologia e Tisiologia foram preenchidos. **Resultados:** Os valores médios (± dp) para VEF₁/CVF e VEF₁/VEF₆ foram, respectivamente, 73 ± 4% e 75 ± 3%. A obstrução ao fluxo aéreo foi detectada pela relação VEF₁/CVF em 61 pacientes, mas foi detectada pela relação VEF₁/VEF₆ em apenas 46 deles, mostrando uma sensibilidade de 75% (p < 0,001). **Conclusões:** A relação VEF₁/VEF₆ tem sensibilidade insuficiente para substituir a relação VEF₁/CVF no diagnóstico de obstrução leve ao fluxo aéreo.

Descritores: Volume expiratório forçado; Capacidade vital; Obstrução das vias respiratórias; Espirometria; Testes de função pulmonar.

Introduction

Spirometry is a noninvasive affordable test with many clinical applications and allows the diagnosis of numerous lung diseases.⁽¹⁾

Obstructive lung disease (OLD), principally observed in individuals with asthma and chronic obstructive pulmonary disease (COPD), is characterized by reduced expiratory flow in relation to expiratory lung volume. The classical parameter used to characterize lung diseases as obstructive is the

reduction in the ratio between forced expiratory volume in one second and forced vital capacity (FEV₁/FVC ratio). The FVC maneuver is a test that requires effort and collaboration from the patient. For the test to meet the acceptability and reproducibility criteria, patients must empty their lungs completely in at least three maneuvers. Each of these maneuvers can last up to 20 s and are exhausting for debilitated patients, older patients and patients with advanced

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lung disease. In normal individuals, the duration of the FVC maneuver increases with age.^(1,2)

In recent years, the FEV₁/FEV₆ in six seconds (FEV₁/FEV₆) ratio was proposed as a parameter for use in the diagnosis of OLD. Using this ratio would have the following advantages: greater convenience for the patient during the performance of the test, since it would last only 6 s; reduced risk of syncope (albeit rare); greater ease in meeting acceptability and reproducibility criteria; and, finally, the ability to perform tests rapidly using portable spirometers, allowing the early en masse diagnosis of OLD.⁽³⁻¹⁰⁾ Predicted values for this ratio have been recently derived for the Brazilian population.⁽¹¹⁾

The positive impact of early diagnosis in patients with OLD would principally affect patients who present subtle symptoms and minimal alterations on pulmonary function tests. Many studies have assessed the sensitivity of the FEV₁/FEV₆ ratio in the diagnosis of airway obstruction. However, young patients and patients with moderate or pronounced obstruction have been included in such studies, inflating the sensitivity of the test.^(5,7,9,10) Reduced end-expiratory flows and prolonged expiratory time, which can exceed 6 s, occur in the initial stage of airway obstruction. The FEV₁/FEV₆ ratio can therefore lose sensitivity in early diagnosis, especially in aging patients, in whom the time required to complete the FVC maneuver increases progressively.

The objective of the present study was to assess the sensitivity of the FEV₁/FEV₆ ratio in the diagnosis of mild airflow limitation.

Methods

We evaluated 155 consecutive Caucasian patients who underwent spirometry at the pulmonary function laboratories of the São Paulo Hospital for State Civil Servants and Brazil Diagnostic Center. Technicians certified in pulmonary function by the Brazilian Thoracic Society (BTS) carried out the tests using two spirometers (SensorMedics, Yorba Linda, CA, USA). The following inclusion criteria were applied: presenting < 15% difference between the predicted and observed FEV₁/FVC ratio; having an FEV₁ ≥ 60% of predicted; and meeting the BTS criteria for acceptability and reproducibility (including exhalation time of at least 6 s). The reference values used were predicted values recently

proposed for the Brazilian population.⁽¹¹⁾ For all of the cases included, age and height were within the range of observed values for each gender in the sample from which reference equations were derived. Ratio values derived from this study are shown in Chart 1.

The sensitivity of the FEV₁/FEV₆ ratio was calculated based on data published in four studies, considering only patients with mild airway obstruction.^(5,7,8,10) The mean sensitivity in those studies was 76% (24% false-negative results). Considering this value for the number of false-negatives using the FEV₁/FEV₆ ratio and a 15% lower limit of 95% CI (a value considered high and unacceptable), it would be necessary to analyze at least 90 spirometry tests in order to confirm these data.⁽¹²⁾

This was a retrospective study using routine functional tests requested by attending physicians or periodic health tests, performed under the doctor-patient privilege. The study was approved with no restrictions by the Ethics Committee of the Institute for the Medical Treatment of Civil Servants, protocol no. 031/07.

Airway obstruction was characterized by FEV₁/FVC ratio values below the 5th percentile of predicted. Values for FEV₁/FVC and FEV₁/FEV₆ ratios classified as normal or reduced were compared using the chi-square test. In the statistical analysis, we used was the Statistical Package for Social Sciences, version 10 (SPSS, Chicago, IL, USA).⁽¹³⁾

Chart 1 - Predicted reference values for the Brazilian population.

	Formulas; percentiles
Males	
FEV ₁ /FVC (%)	120.3 – height × 0.175 – age × 0.197; 5th percentile = 7.6
FEV ₁ /FEV ₆ (%)	117.1 – height × 0.165 – age × –0.151; 5th percentile = 6.9
Females	
FEV ₁ /FVC (%)	111.5 – height × 0.14 – age × 0.158; 5th percentile = 8.5
FEV ₁ /FEV ₆ (%)	105.9 – height × 0.107 – age × 0.141; 5th percentile = 7.9

FEV₁: forced expiratory volume in one second; FVC: forced vital capacity; and FEV₆: forced expiratory volume in six seconds. Source: Pereira et al.⁽¹¹⁾

Results

The general characteristics of the sample are described in Table 1.

The FEV₁/FVC ratio identified airway obstruction in 61 patients, compared with only 46 patients for the FEV₁/FEV₆ ratio ($p < 0.001$). There was one false-positive result. Sensitivity of the FEV₁/FEV₆ ratio for the detection of mild airway obstruction was therefore 75% ($p < 0.0001$) and specificity was 99%, as can be seen in Table 2. The 95% CI calculated for this sample was 19 to 31%.

Discussion

In the present study, using the FEV₁/FEV₆ ratio in the diagnosis of mild airway obstruction resulted in a great number of false-negatives.

The lower limit of the FEV₁/FVC ratio is established by subtracting 7.6 and 8.5 from predicted values in males and females, respectively, in the Brazilian population.⁽¹¹⁾ In the present study, sample selection was restricted to cases with a $< 15\%$ difference between predicted and observed FEV₁/FVC ratio and with a FEV₁ $\geq 60\%$. This was done in order to include only patients presenting normal spirometry findings or spirometry findings of mild airway obstruction.

One study assessed 337 spirometry findings of normal individuals and patients with OLD or restrictive lung disease.⁽⁷⁾ In that study, the sensitivity of the FEV₁/FEV₆ ratio was found to be 95%. Only 41 patients (12.1%) presented mild OLD. All cases with discordant FEV₁/FEV₆ and FEV₁/FVC ratios presented FEV₁/FVC ratio values near the lower limit of normality, with a maximum difference of four percentage points. When the group of patients with

mild obstruction was analyzed independently, the sensitivity of the FEV₁/FEV₆ ratio in the diagnosis of mild OLD dropped to 73%.

Another study⁽⁵⁾ assessed the spirometry findings for 11,676 patients aged 20-80 years. The authors observed that the sensitivity of the FEV₁/FEV₆ ratio, in comparison with the FEV₁/FVC ratio, was 94%. In that sample, 13.3% of the patients had mild OLD. Similarly to the findings of the previously cited study, 100% of discordant patients were near the lower limit of normality. When the group of patients with mild obstruction was analyzed independently, the sensitivity of the FEV₁/FEV₆ ratio for the diagnosis of mild OLD was 82%.

Another study⁽⁹⁾ assessed the spirometry findings for 1,139 workers aged 18-71 years. The study showed 92% sensitivity for the FEV₁/FEV₆ ratio. This sample was principally composed of patients with normal spirometry results: only 14.4% presented obstruction (the severity of the obstruction was not classified). In addition, the mean age of the patients studied was 37 years, which inflates the sensitivity of the FEV₁/FEV₆ ratio.

One group of authors⁽¹⁰⁾ studied 1,926 spirometry tests, evaluating the sensitivity of the FEV₁/FEV₆ ratio in different ethnic groups and with varying degrees of airway obstruction. The overall sensitivity was 85.6%. The sensitivity of the ratio ranged from 74% (among patients with mild obstruction) to 100% (among patients with pronounced obstruction).

The results obtained in the present study are in agreement with the data found by the above-mentioned authors^(5,7,9,10) and clearly show that the FEV₁/FEV₆ ratio has poor sensitivity for the detection of mild airway obstruction.

Other authors,⁽¹⁴⁾ based on a study of individuals over the age of 60, suggested that the 73% value for the FEV₁/FEV₆ ratio could be used in place of the fixed value of 70% for the FEV₁/FVC ratio proposed by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) consensus⁽¹⁵⁾ for characterizing airway obstruction. The limitations of the use of a fixed FEV₁/FVC ratio value to characterize obstruction are widely recognized.⁽¹⁶⁻¹⁸⁾ The FEV₁/FVC ratio drops with age.⁽¹¹⁾ In the Brazilian population, the lower limit of 70% is reached at the mean age of 65 years for males and 70 years for females.⁽¹¹⁾ Smokers who are sensitive to the effects of tobacco will present reduced values for the FEV₁/FVC ratio

Table 1 – Characteristics of the 155-patient sample.^a

Variable	
Males/females	60/95
Age, years	56 ± 15
FVC, % of predicted	96 ± 15
FEV ₁ , % of predicted	87 ± 14
FEV ₁ /FVC, %	73 ± 4
FEV ₁ /FEV ₆ , %	75 ± 3

FVC: forced vital capacity; FEV₁: forced expiratory volume in one second; and FEV₆: forced expiratory volume in six seconds.

^aContinuous data are presented as mean ± standard deviation.

Table 2 - Comparison between normal and reduced spirometry values.^a

	FEV ₁ /FVC		Total
	Reduced	Normal	
FEV ₁ /FEV ₆			
Reduced, n	46	1	47
Normal, n	15	93	108
Total, n	61	94	155

FEV₁: forced expiratory volume in one second; FVC: forced vital capacity; and FEV₆: forced expiratory volume in six seconds.
^aSensitivity = 75%; and specificity = 99%.

at approximately 45 years of age. At this age, the lower limit of the predicted value is approximately 75%. Based on these data, the frequency of airway obstruction detection will be insufficient in the age bracket in which COPD is incipient, whereas it will be exacerbated in older individuals.⁽¹⁸⁾ Although all smokers should be encouraged to stop smoking, the detection of airway obstruction can result in greater cessation, as has been demonstrated in some studies.⁽¹⁹⁾

After the present study had been concluded, a national field study compared the sensitivity of the FEV₁/FEV₆ ratio with that of the FEV₁/FVC ratio.⁽²⁰⁾ In that study, only two curves were considered acceptable, and no reference was made to the race of the individuals tested. Obstruction was considered present when the FEV₁/FVC ratio was <70%. Regarding the FEV₁/FEV₆ ratio, the individual lower limits suggested by Hankinson were used, regardless of race (there are values for Caucasians, Mexican-Americans and for blacks, derived from the North-American population). These data might represent an underestimation of the sensitivity of the FEV₁/FVC ratio and an overestimation of the sensitivity of the FEV₁/FEV₆ ratio.

In a Brazilian sample of individuals without cardiorespiratory disease,⁽¹¹⁾ the mean expiratory time was 7.07 ± 1.56 s in 270 males aged 26-86 years, compared with 6.13 ± 1.35 s among 373 females aged 20-85 years. Expiratory time was typically below 6 s in males under the age of 45 years and in females under 50 years. However, expiratory times longer than 6 s are often observed in lower age brackets.⁽¹¹⁾

In the online version of the GOLD consensus, it was recently stated that the use of a fixed cut-off point of 70% can result in false-positive results in

older individuals. However, in the same document, it is clear that the fixed FEV₁/FVC ratio < 70% continues to be the recommended cut-off point for characterizing airway obstruction.⁽²¹⁾ In addition, the GOLD consensus recommends that this value be obtained after the use of a bronchodilator, a parameter for which reference values are unavailable.

Incipient obstruction in diffuse distal obstructive diseases such as COPD and asthma is a result of slow end-expiratory flows with prolonged expiratory time. From a pathophysiological standpoint, it is difficult to understand how the FEV₁/FEV₆ ratio can be below the lower limit of predicted in a certain number of cases in which the FEV₁/FVC ratio remains normal.^(5,7) In our study, there was only one case in which there was an isolated reduction in the FEV₁/FEV₆ ratio.

All of the previously mentioned studies used the Hankinson equation as a reference value of normality.⁽³⁾ The reference values used in the present study were those recently proposed for the Brazilian population.⁽¹¹⁾ They differ significantly from the values proposed by Hankinson.⁽³⁾ The predicted values for FEV₁/FVC and FEV₁/FEV₆ ratios are lower in individuals of shorter stature, due to the effect of greater dynamic compression resulting from greater muscle strength.⁽¹¹⁾ Not correcting values for height results in overestimated frequency of airway obstruction in taller individuals.⁽¹¹⁾ In the equations proposed by Hankinson, the regressions are adjusted only for age.

From the epidemiological point of view and considering the evolution of the disease, early detection of COPD is important. However, it is made difficult by the use of the FEV₁/FEV₆ ratio.

In conclusion, the FEV₁/FEV₆ ratio has poor sensitivity and should not be used as a substitute for the FEV₁/FVC ratio in the diagnosis of mild airway obstruction in Brazilian Caucasians.

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