Research Article

FEV₁/FEV₆: A Reliable, Easy-to-Use, and Cheaper Alternative to FEV₁/FVC in Diagnosing Airway Obstruction in Indian Population

Anupam Kumar Singh¹,² and Amit Lohia²

¹ Department of Medicine, Rajendra Institute of Medical Sciences, Jharkhand, Ranchi 834009, India
² Department of Respiratory Medicine, L.R.S. Institute of Tuberculosis and Respiratory Diseases, New Delhi, India

Correspondence should be addressed to Anupam Kumar Singh, anupampom@gmail.com

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Background. FEV₁/FEV₆ has been proposed as a cheap, reproducible and valid alternative to FEV₁/FVC in spirometry. No Indian data exists on its utility to diagnose airway obstruction.

Aim. We sought to determine a fixed cut-off of FEV₁/FEV₆ to diagnose obstruction corresponding to FEV₁/FVC < 0.70 proposed by GOLD guidelines.

Method. Spirometry was done on patients referred to a tertiary centre in India. Age, sex, height weight were recorded in addition to spirometric variables like FEV₁, FVC, FEV₆. The sensitivity, specificity, positive and negative predictive values of FEV₁/FEV₆ were determined with respect to gold standard of FEV₁/FVC < 0.70.

Results. 467 spirometries were analysed after meeting the ATS acceptability criteria. Considering FEV₁/FVC < 0.7 as being the gold standard for obstruction, ROC curve was used to determine the best corresponding cut-off for FEV₁/FEV₆. The area under the curve was 99.3% (95% CI: 98.1–99.8%), and the FEV₁/FEV₆ cut-off, corresponding to the greatest sum of sensitivity and specificity, was 73%. For the total population, the FEV₁/FEV₆ sensitivity, specificity, PPV, NPV were 95.7%, 94.2%, 87.5% and 97.9% respectively. Agreement by Kappa value between two cut-offs was excellent 0.89 (0.87–0.91).

Conclusion. FEV₁/FEV₆ < 73% is a new reliable spirometry index to diagnose airway obstruction in Indian population.

1. Introduction

Undiagnosed airway obstruction is prevalent in smokers and occupational settings, leading to significant morbidity and adverse prognosis [1]. Many studies underline the importance of spirometry in primary care, as a screening tool for the early detection of COPD in all patients greater than forty years of age who are currently smoking as well as those with respiratory symptoms [2–5]. Forced expiratory volume in six seconds (FEV₆) [6] has been proposed as a convenient alternative for forced vital capacity (FVC) [7–10]. The advantages of FEV₆ described in the literature are easy execution (for patients and technicians) [11], reduction in the total duration of the spirometry test, and reduction in spirometry complications (such as syncope) [12, 13].

Studies show that the criteria adopted to define obstruction from the FEV₁/FEV₆ ratio are quite variable like LLN derived from reference equations [10–16] ROC curve analysis to find the best cutoff point [17, 18], and an empiric fixed FEV₁/FEV₆ ratio of 0.70 [19].

In developing countries due to lack of trained technicians in primary care who can effectively perform FVC with costly spirometers, FEV₆ promises to be a cheap, effective measure to use spirometry as a primary screening tool. However, its efficacy is limited by lack of universal reference equations [20–22]. Using a fixed cutoff of FEV₁/FEV₆ to simplify and increase its use like popular GOLD criteria as FEV₁/FVC < 0.70 [1], which were performed in different countries [11, 18], might not be suitable for use in a country like India with people of different age, race, height, and weight. Moreover, none of the studies has determined multilevel likelihood ratios of FEV₁/FEV₆ which can increase its utility. We aimed to determine a fixed cutoff for FEV₁/FEV₆ corresponding to FEV₁/FVC < 70% in Indian population and evaluate
the likelihood ratios and performance of FEV<sub>1</sub>/FEV<sub>6</sub> in diagnosing obstruction.

2. Materials and Methods

The spirometric data of adult patients referred to a tertiary respiratory referral centre in Delhi, India, between February 2008 and March 2009, were analysed. Spirometry measurements were performed with a mass-flow sensor (SensorMedics model 2200, VIASYS Healthcare, Yorba Linda, CA, USA), by 2 trained personnel, according to the guidelines of the ATS [23]. The spirometry tests thus obtained were analyzed by investigators for their quality and acceptability. Three acceptable manoeuvres were performed for each spirometric reading, and the spirometric measurement with the largest sum of FEV<sub>1</sub> and FVC was chosen for final analysis. FEV<sub>6</sub> was also taken from that manoeuvre itself. The consecutive acceptable spirometry results of middle-aged persons (18–60 years) were considered for analysis. The tests not reaching the 6-second expiration time were excluded from the study. The older patients were excluded from the analysis as it has been seen that fixed cutoff method used in GOLD guidelines tends to underestimate airway obstruction as seen by reference equations [1].

For the diagnosis of airway obstruction, FEV<sub>1</sub>/FVC < 70% was used as a fixed cutoff point, according to the GOLD guidelines [1]. From a receiver-operator characteristic (ROC) curve, the FEV<sub>1</sub>/FEV<sub>6</sub> ratio, that corresponded to the optimal combination of sensitivity and specificity (i.e., the greatest sum of both), was determined. We used two × two tables to calculate sensitivity and specificity for FEV<sub>1</sub>/FEV<sub>6</sub> below its cutoff as a predictor for airway obstruction. Similarly sensitivity and specificity were determined for FEV<sub>6</sub> as a predictor for a restrictive spirometric pattern. We also calculated the positive predictive value (PPV) and negative predictive value (NPV), positive likelihood ratio (PLR) and negative likelihood ratio (NLR). Furthermore, the discordant cases, that is, false positive and false negative, were analysed. Results are presented for the male, female, and total populations. Finally, agreement between the two categorisation schemes, based either on FVC or on FEV<sub>6</sub>, was assessed using kappa statistics: the number of obstructive patients was determined using FEV<sub>1</sub>/FVC < 70% as a fixed cutoff point. Kappa represents the agreement between the two categorisation schemes in excess of the amount of agreement that would be expected by chance. For statistical analysis, we used the statistical software (SPSS 15.0; SPSS; Chicago, IL, USA).

3. Results

3.1. Baseline Characteristics and Patient Flow. We had access to data of 500 consecutively done spirometric test results. We excluded 20 tests (2.5%) from analysis because an expiration time of 6 s had not been reached. Three subjects were excluded because the FEV<sub>6</sub> value was missing. Another eight subjects were excluded because of their age (<18 years of age). Two spirometries did not meet the acceptability criterion by ATS. This left us with spirometric data from 467 middle-aged subjects, of whom men were 60% and women were 40%. Subject characteristics and their stages of obstruction are shown in Table 1.

3.2. Spirometric Diagnosis of Obstruction. Before the analysis of accuracy, a scatter plot graph between FEV<sub>1</sub>/FEV<sub>6</sub> and FEV<sub>1</sub>/FVC ratios was constructed, and \( r^2 = 0.93 \) \((P < 0.001)\) was found (Figure 1).

Considering FEV<sub>1</sub>/FVC < 70% as being the gold standard for obstruction, an ROC curve was used to determine the best corresponding cutoff for FEV<sub>1</sub>/FEV<sub>6</sub> (Figure 2). The area under the ROC curve was 99.3% (95% confidence interval (CI): 98.1–99.8%), and the FEV<sub>1</sub>/FEV<sub>6</sub> cutoff, corresponding to the greatest sum of sensitivity and specificity, was 73%. For the total population, the FEV<sub>1</sub>/FEV<sub>6</sub> sensitivity was 95.7%, and specificity was 94.2%. The PPV of FEV<sub>1</sub>/FEV<sub>6</sub> was 87.5%, and the NPV was 97.9%. The prevalence of obstruction was 139 of 467 subjects (30.2%).

3.3. Sensitivity Analysis. When using an FEV<sub>1</sub>/FEV<sub>6</sub> cutoff of 73.6%, sensitivity reached 100%, but specificity dropped to 90% (PPV = 82.0%, NPV = 100.0%). Choosing a fixed cutoff of FEV<sub>1</sub>/FEV<sub>6</sub> < 70% resulted in a specificity of 99.29%, with a sensitivity of 84.4% (PPV = 99.1% NPV = 91.5%). Choosing a fixed cutoff of FEV<sub>1</sub>/FEV<sub>6</sub> < 63% resulted in a specificity of 100%, with a sensitivity of 24.8% (PPV = 100%, NPV = 75.5%). Multilevel likelihood ratios were constructed post hoc (Table 2).

The sensitivity of FEV<sub>1</sub>/FEV<sub>6</sub> in detecting obstruction in stage 1 and stage 2 COPD subgroup was 88.8% and 98%, respectively, while it was 100% in stages 3 and 4.

3.4. Discordant Cases Analysis. The spirometry test results for 25 workers (2.2%) were classified differently by the two techniques, and all of them had observed values close to the LLNs. Analysis of the 25 discordant cases (false positives and false negatives combined) showed that 98.8% of the discordant values of FEV<sub>1</sub>/FEV<sub>6</sub> are within a ±5% interval of...
Table 1: Subject demographics, presence, and severity of airway obstruction. Airway obstruction is defined as FEV₁/FVC < 0.7 and subclassified into stage 1 (FEV₁ > 80%), stage 2 (FEV₁ 50–80%), stage 3 (FEV₁ 30–50%), and stage 4 (FEV₁ < 30 percent or <50% with type 2 respiratory failure).

|    | Age   | Height   | Not obstructed | Stage 1 | Stage 2 | Stage 3 | Stage 4 |
|----|-------|----------|----------------|---------|---------|---------|---------|
| M  | 280   | 45.2 ± 10.2 | 166 ± 21       | 196     | 26      | 28      | 20      | 10      |
| F  | 187   | 48.6 ± 13.4 | 153 ± 15       | 132     | 19      | 22      | 10      | 4       |
| T  | 467   | 46.4 ± 12.6 | 160.2 ± 18     | 328     | 45      | 50      | 30      | 14      |

(32%) (35.3%) (22%) (10.7%)

Table 2: Multi-level likelihood ratios for FEV₁/FEV₆ as a marker for airway obstruction. PLR: positive likelihood ratio, NLR: negative likelihood ratio, PPV: positive predictive value, and NPV: negative predictive value.

| FEV₁/FEV₆ | Sensitivity | Specificity | PLR   | NLR   | PPV  | NPV  |
|-----------|-------------|-------------|-------|-------|------|------|
| (1) <63   | 24.82       | 99.69       | 80.92 | 0.75  | 97.2 | 75.4 |
| (2) <70   | 80.14       | 99.58       | 261.26| 0.2   | 99.1 | 92.1 |
| (3) <73   | 98.58       | 94.17       | 16.91 | 0.02  | 88.0 | 99.4 |
| (4) <73.6 | 100         | 90.49       | 10.52 | 0.0   | 82.0 | 100  |

4. Discussion

It has already been demonstrated that FEV₆ is a reliable alternative for FVC to identify obstructive and restrictive spirometric patterns [7–9]. The main purpose of the present study was to determine a fixed cutoff for the FEV₁/FEV₆ ratio and for the FEV₆ which are equivalent to the commonly used fixed cutoffs for the FEV₁/FVC ratio and for the FVC. This study demonstrates that FEV₁/FEV₆ < 73% can be used as a valid alternative for FEV₁/FVC < 70% as a fixed cutoff point for the detection of an obstructive or restrictive spirometric pattern in adults. The authors emphasise that the fixed cutoff terms should be used with caution, particularly outside the middle-aged population.

Other studies showed similar cutoff points (0.73) and (0.75) of the FEV₁/FEV₆ ratio for the detection of airway obstruction, both using the fixed FEV₁/FVC < 0.70 ratio for comparison. Melbye et al. [11] used a spirometry database of referenced patients from a medical facility, whereas Vandevoorde et al. [17] recruited subjects from a highly homogeneous population-based sample in a northern city of Norway. In PLATINO studies, fixed cutoff of 0.75 was obtained from healthy adults [14]. Despite the different population background between these two studies and the present one, a similar cutoff point for the FEV₁/FEV₆ ratio was found. The advantage of using a fixed cutoff value for the FEV₁/FEV₆ ratio instead of reference equation to diagnose airway obstruction is emphasized by the main COPD guidelines [1]. The use of the FEV₁/FEV₆ ratio being less time consuming, cheaper (available in $60–80 compared to $700–$1000 for other FVC-based portable spirometers), and easy to perform makes it ideal for objectively diagnosing and following up respiratory diseases in our busy primary care centers and medicine OPDs.

The findings of the present study apply to a population with similar demographic features and percentage of airway obstruction. Our study has an advantage that the spectrum of obstructed group has only 22% and 10.2% patients in severe
and very severe obstruction category, compared to other studies which had more severely obstructed patients, [8, 10, 12] so the sensitivity of FEV₁/FEV₆ in our study in detecting obstruction is less likely to be inflated. Furthermore, the prevalence of airway obstruction in our population group is similar to the prevalence of obstruction in the studies in which reference equations for FEV₁/FEV₆ were determined, so predictive values are likely to be similar. While fixed cutoff values are more widely used, in an attempt to simplify the diagnosis, there is potential for misclassification, for example, in elderly subjects, where the age-related decline in FEV₁/FVC and FEV₁/FEV₆ may cause a significant overdiagnosis of airway obstruction [25]. Finally, measured values that lie close to the threshold should be interpreted with caution, due to several sources of variability: diurnal variations of spirometric indices [14] and patients with obstruction having coefficients of variation for FEV₁ and FVC that are approximately twice those of normal subjects [26]. This is also demonstrated in our study where most of the discordant cases lie close to the prescribed cutoff.

Despite these limitations, FEV₁/FEV₆ is an effective, well-validated [27, 28] option that should be used in primary care to detect undiagnosed airway obstruction that is a rampant problem in India.

Disclosure

Presentation at a meeting: Chest 2008 Philadelphia.

Authors’ Contribution

One of the authors contributed in design, literature search, clinical studies, data acquisition, statistical analysis, paper preparation, paper editing, and paper review and was a guarantor; the author contributed in concepts, clinical studies, statistical analysis, paper editing, and paper review.

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