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Research Article

FEV_1/FEV_6: A Reliable, Easy-to-Use, and Cheaper Alternative to FEV_1/FVC in Diagnosing Airway Obstruction in Indian Population

Anupam Kumar Singh[1,2] and Amit Lohia[2]

[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. FEV_1/FEV_6 has been proposed as a cheap, reproducible and valid alternative to FEV_1/FVC in spirometry. No Indian data exists on its utility to diagnose airway obstruction. *Aim*. we sought to determine a fixed cut off of FEV_1/FEV_6 to diagnose obstruction corresponding to $FEV_1/FVC < 0.70$ proposed by GOLD guidelines. *Method*. Spirometry was done on patient referred to a tertiary centre in India. Age, sex, height weight were recorded in addition to spirometric variables like FEV_1, FVC, FEV_6. The sensitivity, specificity, positive and negative predictive values of FEV_1/FEV_6 were determined with respect to gold standard of $FEV_1/FVC < 0.70$. *Results*. 467 spirometries were analysed after meeting the ATS acceptability criteria. Considering $FEV_1/FVC < 0.7$ as being the gold standard for obstruction, ROC curve was used to determine the best corresponding cut-off for FEV_1/FEV_6. The area under the curve was 99.3% (95% CI: 98.1–99.8%), and the FEV_1/FEV_6 cut-off, corresponding to the greatest sum of sensitivity and specificity, was 73%. For the total population, the FEV_1/FEV_6 sensitivity, specificity, PPV, NPV were was 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*. $FEV_1/FEV_6 < 73\%$ 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 (FEV_6) [6] has been proposed as a convenient alternative for forced vital capacity (FVC) [7–10]. The advantages of FEV_6 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 FEV_1/FEV_6 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 FEV_1/FEV_6 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, FEV_6 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 FEV_1/FEV_6 to simplify and increase its use like popular GOLD criteria as $FEV_1/FVC < 0.70$ [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 FEV_1/FEV_6 which can increase its utility. We aimed to determine a fixed cutoff for FEV_1/FEV_6 corresponding to $FEV_1/FVC < 70\%$ in Indian population and evaluate

the likelihood ratios and performance of FEV_1/FEV_6 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_1 and FVC was chosen for final analysis. FEV_6 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, $FEV_1/FVC < 70\%$ was used as a fixed cutoff point, according to the GOLD guidelines [1]. From a receiver-operator characteristic (ROC) curve, the FEV_1/FEV_6 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_1/FEV_6 below its cutoff as a predictor for airway obstruction. Similarly sensitivity and specificity were determined for FEV_6 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_6, was assessed using kappa statistics: the number of obstructive patients was determined using $FEV_1/FVC < 70\%$ 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_6 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.

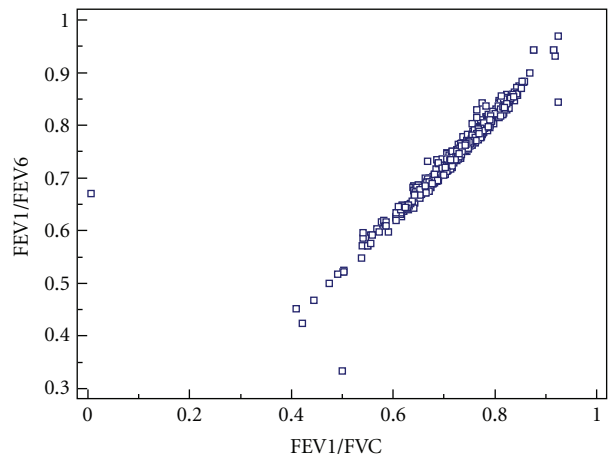

Figure 1: Correlation between FEV_1/FEV_6 and FEV_1/FVC.

3.2. Spirometric Diagnosis of Obstruction. Before the analysis of accuracy, a scatter plot graph between FEV_1/FEV_6 and FEV_1/FVC ratios was constructed, and $r^2 = 0.93$ ($P < 0.001$) was found (Figure 1).

Considering $FEV_1/FVC < 70\%$ as being the gold standard for obstruction, an ROC curve was used to determine the best corresponding cutoff for FEV_1/FEV_6 (Figure 2). The area under the ROC curve was 99.3% (95% confidence interval (CI): 98.1–99.8%), and the FEV_1/FEV_6 cutoff, corresponding to the greatest sum of sensitivity and specificity, was 73%. For the total population, the FEV_1/FEV_6 sensitivity was 95.7%, and specificity was 94.2%. The PPV of FEV_1/FEV_6 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_1/FEV_6 cutoff of 73.6%, sensitivity reached 100%, but specificity dropped to 90% (PPV = 82.0%, NPV = 100.0%). Choosing a fixed cutoff of $FEV_1/FEV_6 < 70\%$ resulted in a specificity of 99.29%, with a sensitivity of 84.4% (PPV = 99.1% NPV = 91.5%). Choosing a fixed cutoff of $FEV_1/FEV_6 < 63\%$ 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_1/FEV_6 in detecting obstruction in stage 1 and stage 2 COPD subgroup was 88.88% 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_1/FEV_6 are within a ±5% interval of

Table 1: Subject demographics, presence, and severity of airway obstruction. Airway obstruction is defined as $FEV_1/FVC < 0.7$ and subclassified into stage 1 ($FEV_1 > 80\%$), stage 2 (FEV_1 50–80%), stage 3 (FEV_1 30–50%), and stage 4 ($FEV_1 < 30$ percent or <50% with type 2 respiratory failure).

		Age	Height	Not obstructed	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 FEV_1/FEV_6 as a marker for airway obstruction. PLR: positive likelihood ratio, NLR: negative likelihood ratio, PPV: positive predictive value, and NPV: negative predictive value.

FEV_1/FEV_6	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

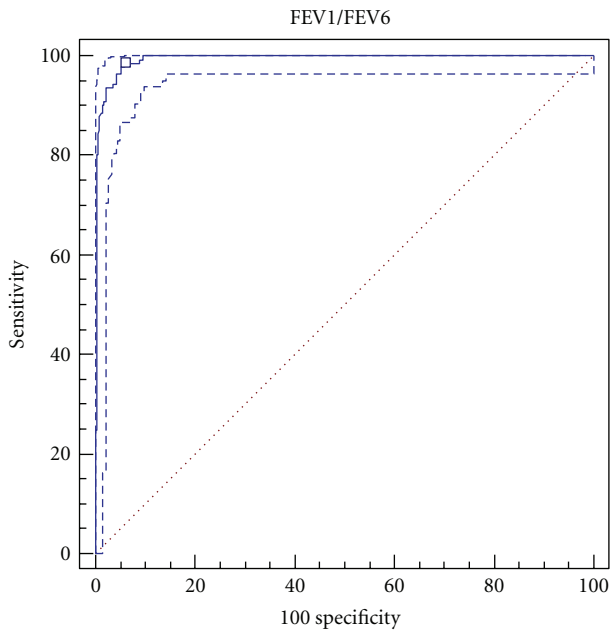

Figure 2: Receiver-operator characteristic curve for forced expiratory volume in one second (FEV_1)/FEV_6 using FEV_1/forced vital capacity <70% as a "gold standard" for obstruction.

the chosen fixed cutoff of 73%. In the 19 false-positive cases, the mean difference of FEV_1/FVC and FEV_1/FEV_6 −1.8% (SD = 1.3%). In the 6 false-negative cases, the mean difference of FEV_1/FVC and FEV_1/FEV_6 was −2.93%.

3.5. Overall Agreement Using Kappa Statistics. Overall agreement between the two categorisation schemes was assessed using kappa statistics. In this study, a kappa value of 0.89 and concordance correlation coefficient of 0.892 (95% CI = 0.87−0.91) were obtained, indicating a very good agreement between FEV_6- and FVC-derived indices.

4. Discussion

It has already been demonstrated that FEV_6 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 FEV_1/FEV_6 ratio and for the FEV_6 which are equivalent to the commonly used fixed cutoffs for the FEV_1/FVC ratio and for the FVC. This study demonstrates that $FEV_1/FEV_6 < 73\%$ can be used as a valid alternative for $FEV_1/FVC < 70\%$ 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 FEV_1/FEV_6 ratio for the detection of airway obstruction, both using the fixed $FEV_1/FVC < 0.70$ 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 [24]. Despite the different population background between these two studies and the present one, a similar cutoff point for the FEV_1/FEV_6 ratio was found. The advantage of using a fixed cutoff value for the FEV_1/FEV_6 ratio instead of reference equation to diagnose airway obstruction is emphasized by the main COPD guidelines [1]. The use of the FEV_1/FEV_6 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 FEV_1/FEV_6 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 FEV_1/FEV_6 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 FEV_1/FVC and FEV_1/FEV_6 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 FEV_1 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, FEV_1/FEV_6 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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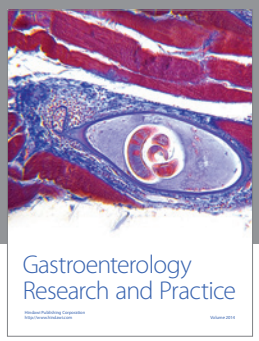

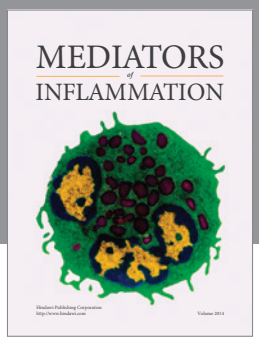

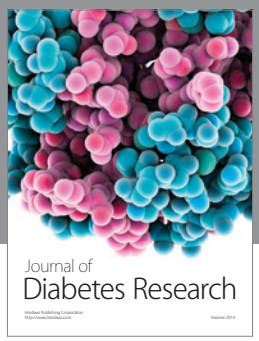

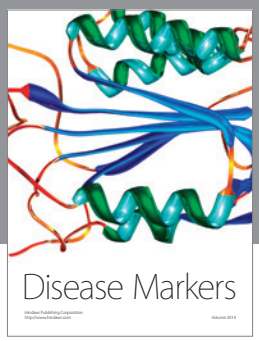

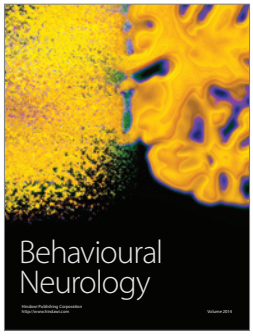

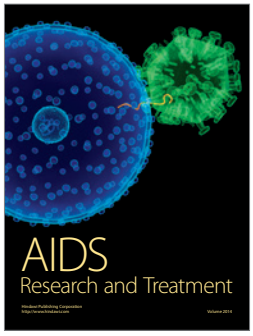

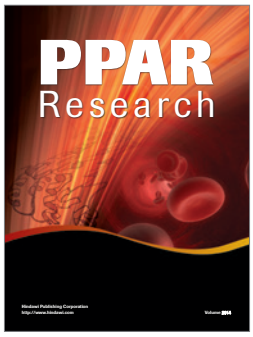

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