What is the difference between FEV\textsubscript{1} change in percentage predicted value and change over baseline in the assessment of bronchodilator responsiveness in patients with COPD?

Wenhua Jian\textsuperscript{1}, Jinping Zheng\textsuperscript{1}, Yi Hu\textsuperscript{2}, Yin Li\textsuperscript{2}, Yi Gao\textsuperscript{1}, Jiaying An\textsuperscript{1}

\textsuperscript{1}State Key Lab of Respiratory Disease, Guangzhou Institute of Respiratory Disease, First Affiliated Hospital of Guangzhou Medical University, Guangzhou 510120, China; \textsuperscript{2}Guangzhou Medical University, Guangzhou 510182, China

ABSTRACT

Background: Several criteria are clinically applied in the assessment of significant bronchodilator responsiveness in chronic obstructive pulmonary disease (COPD). The present study aimed to investigate the differences in various degree of severity of COPD among these criteria.

Methods: After 400 micrograms of salbutamol administered via spacer by metered dose inhaler (MDI), forced expiratory volume in one second (FEV\textsubscript{1}) and forced vital capacity (FVC) changes (including percentage change, absolute change and absolute change in percentage predicted value) were retrospectively analysed in 933 stable patients with mild-to-very-severe COPD. Significant bronchodilator responsiveness was assessed using American Thoracic Society and European Respiratory Society (ATS-ERS) criterion based on FEV\textsubscript{1} or/and FVC (both \geq 12\% increase over baseline and \geq 200 mL) and FEV\textsubscript{1} percentage predicted criterion (\geq 10\% absolute increase in percentage predicted FEV\textsubscript{1}) in different grades of COPD.

Results: Of the patients [age 66.8 years, baseline FEV\textsubscript{1} 974 mL (39.3\% predicted) and FVC 2,242 mL], mean improvements were 126 mL in FEV\textsubscript{1} and 265 mL in FVC; 21.4\% and 45.3\% met ATS-ERS criterion based on FEV\textsubscript{1} and FVC, respectively; and 13.5\% met FEV\textsubscript{1} percentage predicted criterion. The responsive ratios of ATS-ERS criterion based on FEV\textsubscript{1} to FEV\textsubscript{1} percentage predicted criterion in grade I, II, III and IV of COPD were 0.95:1.26:2.53:6.00, respectively (P<0.01 in grade II and P<0.001 in grade III). As the degree of severity increased, the mean improvement of FEV\textsubscript{1} was reduced; on the contrary, that of FVC was increased.

Conclusions: Compared with FEV\textsubscript{1} percentage predicted criterion, ATS-ERS criterion based on FEV\textsubscript{1} as well as FVC, the later in particular, detected a larger percentage of patients with significant responsiveness. The increasing difference was relevant as a function of the severity of airflow obstruction.

KEY WORDS

Airflow obstruction; bronchodilator responsiveness; chronic obstructive pulmonary disease (COPD); forced vital capacity (FVC); forced expiratory volume in one second (FEV\textsubscript{1})
The difference between FEV$_1$ change in percentage predicted value and change over baseline in the assessment of significant FEV$_1$ responsiveness in patients with COPD was reported by Tashkin (11), Hanania (12) and Anthonisen (13). However, the difference in various degree of severity among these criteria was not revealed in detail. Is the difference related to the degree of severity of COPD? Which criterion is better for clinical practice? Meanwhile, the use of FVC as an outcome of bronchodilator response in determining significant bronchodilator responsiveness was recommended by American Thoracic Society (ATS) and European Respiratory Society (ERS) in the statement of standardization (5) and interpretation (6) for lung function tests. This criterion based on FEV$_1$ was adopted by Global initiative for Chronic Obstructive Lung Disease (GOLD) (1) and Global Initiative for Asthma (GINA) (7) guidelines. However, the criterion of FEV$_1$ absolute change in percentage predicted value ($\Delta$FEV$_1$%pred) with a cut-off threshold also was widely applied in many studies (2-4,8,9) for assessing significant FEV$_1$ responsiveness. Some investigators even addressed FEV$_1$ percentage predicted criterion was more advanced in distinguishing COPD from asthma (8,10).

The protocol was approved by local ethic committee and written informed consent was obtained from all patients in the study. All information was kept confidentially.

### Subjects and methods

**Patients**

This study retrospectively analysed 933 stable patients with COPD diagnosed by chest physicians in our hospital from January 2004 to July 2009. They were aged ≥40 years, had dyspnoea, chronic cough, and/or sputum production, and/or a history of exposure to risk factors for the disease, and had a post-bronchodilator FEV$_1$/FVC of <0.70. Patients were excluded if they had a history of asthma or pulmonary resection, had an exacerbation of COPD or a respiratory infection within 4 weeks, used supplemental oxygen for >12 hours per day, or had significant diseases that might influence the results of the study or patient’s ability to perform spirometry. The demographics and baseline characteristics are shown in Table 1.

The protocol was approved by local ethic committee and written informed consent was obtained from all patients in the study. All information was kept confidentially.

**Methods**

Spirometers (Jaeger Masterscreen, Germany; Cosmed PFT Quark, Italy; Sensormedics, USA; Medisoft Body, Belgium) all met the instrument standardization of American Thoracic Society and European Respiratory Society (ATS-ERS) (5). Technicians who performed spirometry were trained and certified. Calibration check was undertaken daily prior to spirometry by a 3,000 mL syringe, and validated that the devices were within calibration limits, e.g., ±3% of true (90 mL). With correct sitting posture, patients attached nose clip or manual occlusion of the nares, placed mouthpiece in mouth and closed lips around the mouthpiece. Then they were encouraged to inhale completely and rapidly with a pause of <1 s at total lung capacity, and exhale maximally until no more air can be expelled while maintaining an upright posture. Acceptable manoeuvre: (I) free from artefacts (cough during the first second of exhalation; glottis closure that influenced the measurement; early termination or cut-off; effort that was not maximal throughout; leak or obstructed mouthpiece); (II) good starts (extrapolated volume less than 5% of FVC or 0.15 L, whichever is greater); (III) satisfactory exhalation (a plateau in the volume-time curve or forced expiratory time of >6 s or if the subject cannot or should not continue to exhale). Manoeuvres were repeated for 3 to 8 times in each test until three acceptable and repeatable spirograms were obtained. For both FVC and FEV$_1$, the acceptable
difference was within 0.15 L of the largest and second largest values. Then the largest FVC and FEV₁ were reported. Predicted values of FVC and FEV₁ were selected from the statement of European Committee of Steel and Coal (14) and adjusted for Chinese with the recommendation of Zheng and Zhong (15). Technique for performing spirometry that met quality criteria according to the standardisation (5) and interpretation (6) of ATS-ERS has been published elsewhere (16-18).

Prior to bronchodilation test, medication wash-out requirements included withholding short- and long-acting β-agonists (for ≥6 and ≥12 hours, respectively), short- and long-acting anticholinergic agent (for ≥6 and ≥24 hours, respectively), short- and long-acting theophylline (for ≥24 and ≥48 hours, respectively) and anti-leukotrienes (for ≥48 hours). Patients were not permitted to smoke, exercise or have a tea/coffee within 6 hours before spirometry. Spirometry was performed before and 20 to 30 minutes after 400 micrograms of salbutamol administered via spacer by metered dose inhaler (MDI). The change of FEV₁ was expressed as: (I) FEV₁ percentage change over baseline (ΔFEV₁%), (II) absolute change in percentage predicted value (ΔFEV₁%pred); (III) absolute change over baseline (ΔFEV₁). The change of FVC was expressed similarly as FEV₁. The significant bronchodilator responsiveness was assessed by the following criteria: (I) ATS-ERS criterion based on FEV₁: ΔFEV₁% ≥12% and ΔFEV₁ ≥200 mL, (II) FEV₁ percentage predicted criterion: ΔFEV₁%pred ≥10%, (III) ATS-ERS criterion based on FVC: FVC percentage change over baseline (ΔFVC%) ≥12% and FVC absolute change over baseline (ΔFVC) ≥200 mL. The grade (degree of severity) of COPD was defined by GOLD guideline (1).

These data were analysed by SPSS software 15.0 (Chicago, IL, USA). The demographics and baseline characteristics were presented as percentage of population or mean ± SD. After bronchodilator inhalation, the variation and distribution of FEV₁ and FVC changes were described. Significant FEV₁ responsiveness of COPD in different degree of severity was assessed using ATS-ERS criterion and FEV₁ percentage predicted criterion, and the differences between these criteria were examined with McNemar Test. Logistic regression with stepwise selection procedure for significant bronchodilator responsiveness was performed among these criteria. P<0.05 was considered as statistically significant.

Results

Pre- and post-bronchodilator spirometry in patients with COPD

Of the patients, pre-bronchodilator FEV₁ and FVC were 974±448 and 2,242±703 mL, respectively. Mean improvements after bronchodilator inhalation were 122 mL in FEV₁ and 264 mL in FVC (both versus baseline, P<0.001). The changes of FEV₁ and FVC in different grade of COPD are shown in Table 2. As the degree of severity increased, the mean improvement of FEV₁ was reduced; on the contrary, that of FVC was increased.

Variation and distribution of FEV₁ change after bronchodilator inhalation

Improvement of FEV₁ was found in 856 out of 933 patients (91.7%). Of all the patients, 13.5% met ΔFEV₁%pred ≥10%, 22.3% met ΔFEV₁ ≥200 mL and 49.8% met ΔFEV₁% ≥12%. When ATS-ERS criterion based on FEV₁ and FEV₁ percentage predicted criterion were evaluated independently, the percentage of patients considered to show significant responsiveness differed substantially (21.4% versus 13.5%, χ²=59.5, P<0.001). The variation and distribution of FEV₁ change (including ΔFEV₁, ΔFEV₁% and ΔFEV₁%pred) are shown in Figure 1.

Variation and distribution of FVC change after bronchodilator inhalation

Improvement of FVC was found in 819 out of 933 patients (87.8%). Of all the patients, 56.0% met ΔFVC ≥200 mL and 46.7% met ΔFVC% ≥12%. When ATS-ERS criterion based on FVC and ATS-ERS criterion based on FEV₁ were evaluated independently, the percentage of patients considered to show significant responsiveness differed substantially (45.3% versus

<table>
<thead>
<tr>
<th>GOLD grade</th>
<th>FVC (L)</th>
<th>Before BD</th>
<th>After BD</th>
<th>Δ</th>
<th>Δ %</th>
<th>Δ % pred</th>
<th>FEV₁ (L)</th>
<th>Before BD</th>
<th>After BD</th>
<th>Δ</th>
<th>Δ %</th>
<th>Δ % pred</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>3.10±0.87</td>
<td>3.28±0.81^i</td>
<td>0.18±0.29</td>
<td>7.7±13.2</td>
<td>7.2±11.9</td>
<td>1.87±0.56</td>
<td>2.06±0.54^i</td>
<td>0.19±0.17</td>
<td>12.3±13.0</td>
<td>9.1±8.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>2.54±0.66</td>
<td>2.79±0.70^i</td>
<td>0.25±0.26</td>
<td>10.5±11.3</td>
<td>8.1±8.5</td>
<td>1.29±0.35</td>
<td>1.45±0.35^i</td>
<td>0.16±0.14</td>
<td>13.8±13.3</td>
<td>6.7±5.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>2.15±0.57</td>
<td>2.43±0.60^i</td>
<td>0.28±0.26</td>
<td>14.5±14.4</td>
<td>9.0±8.0</td>
<td>0.83±0.19</td>
<td>0.95±0.19^i</td>
<td>0.11±0.10</td>
<td>15.2±13.5</td>
<td>4.8±3.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>1.72±0.48</td>
<td>2.00±0.53^i</td>
<td>0.28±0.26</td>
<td>18.1±17.7</td>
<td>8.5±7.5</td>
<td>0.54±0.12</td>
<td>0.60±0.13^i</td>
<td>0.07±0.07</td>
<td>13.2±13.1</td>
<td>2.5±2.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD. GOLD, Global Initiative for Chronic Obstructive Lung Disease; BD, bronchodilator inhalation. Δ, absolute change; Δ%, percentage change over baseline. Δ% pred, absolute change in percentage predicted value; †, compared with pre-bronchodilator value (t=4.6-24.6, P<0.001).
21.4%, $\chi^2 = 154.07, P < 0.001$). The variation and distribution of FVC change (including $\Delta$FVC and $\Delta$FVC\%) are shown in Figure 2. Of all the patients, 50.7% met ATS-ERS criterion based on FEV\(_1\) or/and FVC.

**Significant bronchodilator responsiveness in different grades of COPD**

The percentages of patients with COPD met ATS-ERS criterion based on FEV\(_1\) and FEV\(_1\)\% percentage predicted criterion were 36.8% and 38.6% in grade I ($P=1.00$), 31.3% and 24.8% in grade II ($P<0.01$), 20.8% and 8.2% in grade III ($P<0.001$), 3.24% and 0.54% in grade IV ($P=0.074$), respectively (Figure 3). The responsive ratios of ATS-ERS criterion based on FEV\(_1\) to FEV\(_1\)\% percentage predicted criterion were 0.95 in grade I, 1.26 in grade II, 2.53 in grade III and 6.00 in grade IV, respectively.

Using ATS-ERS criterion based on FVC, significant responsiveness were found in 26.3% of grade I, 36.7% of grade II, 48.8% of grade III and 56.5% of grade IV, respectively. Furthermore, 40.4% of grade I, 47.1% of grade II, 51.9% of grade III and 56.5% of grade IV met ATS-ERS criterion based on FEV\(_1\) or/and FVC, respectively.

**Figure 1.** Variation and distribution of $\Delta$FEV\(_1\), $\Delta$FEV\(_1\)% and $\Delta$FEV\(_1\)% pred after bronchodilator inhalation. A. Vertical solid line is the limit of 200 mL on the abscissa and shadow area represents $\Delta$FEV\(_1\) ≥ 200 mL in 22.3% of patients; B. Vertical solid line is the limit of 12% on the abscissa and shadow area represents $\Delta$FEV\(_1\)% ≥ 12% in 49.8% of patients; C. Vertical solid line is the limit of 10% on the abscissa and shadow area represents $\Delta$FEV\(_1\)% pred ≥ 10% in 13.5% of patients.

**Figure 2.** Variation and distribution of $\Delta$FVC and $\Delta$FVC\% after bronchodilator inhalation. A. Vertical solid line is the limit of 200 mL on the abscissa and shadow area represents $\Delta$FVC ≥ 200 mL in 56.0% of patients; B. Vertical solid line is the limit of 12% on the abscissa and shadow area represents $\Delta$FVC\% ≥ 12% in 46.7% of patients.

**Figure 3.** Significant FEV\(_1\) responsiveness in patients with different grade of COPD. Significant responsiveness was assessed using ATS-ERS criterion based on FEV\(_1\) and FEV\(_1\)\% percentage predicted criterion in patients with different grade of COPD. The connected slash represents the responsive ratios of the two criteria across all the grades of COPD. **, $P<0.01$, compared with ATS-ERS criterion based on FEV\(_1\); ***, $P<0.001$, compared with ATS-ERS criterion based on FEV\(_1\).
Logistic regression with stepwise selection procedure for significant bronchodilator responsiveness

The significant variables from the multivariate logistic regression model are demonstrated in Table 3. The odds of milder COPD patient tended to be higher for meeting the criterion based on FEV\textsubscript{I} (P<0.001), whereas lower odds for meeting ATS-ERS criterion based on FVC (P<0.001). The model also showed that higher odds of significant responsiveness were associated with shorter disease duration by ATS-ERS criterion based on FEV\textsubscript{I} (P=0.011) or FEV\textsubscript{I} percentage predicted criterion (P=0.008); on the contrary, lower odds of significant responsiveness were associated with shorter disease duration by ATS-ERS criterion based on FVC (P=0.02). Predicted value of FEV\textsubscript{I} was a significant factor only for ATS-ERS criterion based on FEV\textsubscript{I} and a patient with higher predicted value of FEV\textsubscript{I} tended to exhibit higher odds of being responsive under this criterion (P<0.001). However, age, gender, body mass index, smoking status, smoking history, predicted value of FVC did not show significance in the logistic regression in all cases.

Discussion

Up to 22.4% of patients met at least one criterion for significant FEV\textsubscript{I} responsiveness after bronchodilator inhalation in the present study. However, when ATS-ERS criterion based on FEV\textsubscript{I} and FEV\textsubscript{I} percentage predicted criterion were evaluated independently, the percentage of patients considered to show significant responsiveness differed substantially (21.4% versus 13.5%). This was consistent with the findings of Tashkin (11) and Hanania (12), although the percentages of patients with significant responsiveness were lower than that of their reports, probably due to more bronchodilator inhalation (80 micrograms of ipratropium followed by 400 micrograms of salbutamol) and less severe patients compared with the present study.

To our knowledge, bronchodilator responsiveness among different criteria in various degree of severity was not addressed at length in patients with COPD. In the present study, there was statistical significant difference between ATS-ERS criterion based on FEV\textsubscript{I} and FEV\textsubscript{I} percentage predicted criterion with significant responsiveness only in grade II and III of COPD. However, if we pay attention to the responsive ratios of these criteria, an obvious trend could be found across all the grades of COPD, indicating the more severity in airflow obstruction, the larger difference between the two criteria. None significant difference in grade I of COPD was probably due to the insufficient number of mild patients, while in grade IV, due to the very poor FEV\textsubscript{I} responsiveness. As reported by Zhong (16) in a large, population-based survey, the prevalence of COPD in China was 8.2% of people aged ≥40 years and the distributions of grade I, II, III, and IV of COPD were 25.3%, 48.1%, 21.5% and 5.1%, respectively. That indicated moderate-to-severe patients were accounted for over 2/3 of the large COPD population. Therefore, the significant differences between these criteria in grade II and III of COPD are very important and could impact on the diagnosis and treatment strategy of COPD.

Patients with milder grade or shorter disease duration of COPD appeared to more often meet both criteria based on FEV\textsubscript{I}. Probably due to the insufficient number of female, gender didn’t show significance in the logistic regression of significant bronchodilator responsiveness regardless of whichever criterion was applied, but a patient with higher predicted value of FEV\textsubscript{I} tended to exhibit higher odds for meeting ATS-ERS criterion based on FEV\textsubscript{I} (e.g., female has smaller lung volumes, comparing

<table>
<thead>
<tr>
<th>Varieties(^3)</th>
<th>OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST-ERS criterion based on FEV\textsubscript{I}</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predicted value of FEV\textsubscript{I}</td>
<td>1.639 (1.301-2.063)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Grade of COPD</td>
<td>0.454 (0.357-0.578)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>COPD duration</td>
<td>0.931 (0.908-0.963)</td>
<td>0.011</td>
</tr>
<tr>
<td>FEV\textsubscript{I} percentage predicted criterion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade of COPD</td>
<td>0.301 (0.221-0.391)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>COPD duration</td>
<td>0.957 (0.942-0.972)</td>
<td>0.008</td>
</tr>
<tr>
<td>AST-ERS criterion based on FVC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade of COPD</td>
<td>1.676 (1.381-2.034)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>COPD duration</td>
<td>1.063 (1.038-1.087)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

An event in the definition of the odds ratio (OR) is a significant responsive patient according to one of these criteria. The ORs for the variables (predicted value of FEV\textsubscript{I}, grade of COPD, and COPD duration) are calculated according to a one-unit increase in these variables. CI, confidence interval; \(^3\)selected from age, gender, body mass index, smoking status, smoking history, COPD duration (in years), grade of COPD, predicted value of FEV\textsubscript{I} and FVC. Variables with a P-value of <0.05 were kept in the model.
with male). However, self-reported cigarette use (pack-year) wasn't associated with significant bronchodilator responsiveness regardless of whichever criterion was applied, which differed from Tashkin's report (11). Therefore, the value of self-reported disease duration and smoking history should be viewed with caution.

The present study demonstrated that 422 of 931 patients had significant responsiveness with ATS-ERS criterion based on FVC, which was similar with Ben Saad H’s (77 of 168 patients) and Walker PP’s (125 of 266 patients) reports (19,20). However, their studies did not address the responsiveness after bronchodilator in various degree of severity. In our study, as the degree of severity of COPD increased, the improvement of FEV\textsubscript{1} was reduced; on the contrary, that of FVC was increased, and more patients met ATS-ERS criterion based on FVC. Interpretation strategies for lung function tests of ATS-ERS addressed that significant improvement in the FEV\textsubscript{1}, FVC or both would suggest the presence of reversible airflow obstruction (6), which is the ability to achieve a certain threshold of bronchodilator responsiveness.

As we know, FEV\textsubscript{1}, here represents flow response in particular, while FVC represents the volumetric response to bronchodilator. In fact, after bronchodilator treatment in the clinical practice, symptoms of dyspnoea (such as BD1/TD1) and exercise tolerance (such as 6-minutes’ walk distance) in some patients with COPD improved a lot, especially in more severity of airway obstruction. This phenomenon could not be explained by the airflow improvement due to no significant increase in FEV\textsubscript{1}. On the other hand, this can be explained by the improvement of FVC, representing airway opening, reduction of air trapping or reduction of residual volume. Of cause, the role of FVC change as an index of acute responsiveness of airway obstruction in COPD to be used for therapeutic purposes should be studied in the future. FVC might not be a good index to distinguish asthma from COPD, but further studies to confirm the hypothesis that FVC is a better index than FEV\textsubscript{1} in assessing the treatment response by the correlation between prognosis parameters (such as quality of life, exacerbation or 6 minutes’ walk distance, etc.) and change of FEV\textsubscript{1} as well as FVC is optimized. Unfortunately, only FEV\textsubscript{1} has been focused on in most studies of COPD.

In addition, some investigators used IC to assess bronchodilator responsiveness of COPD (21,22). The same meaning as FVC, increase of IC after bronchodilator inhalation suggests a reduction of dynamic hyperinflation. However, FVC could be obtained simultaneously when spirometry manoeuvre was performed; by comparison, IC has to be tested separately. Moreover, the reliability and quality control of IC are poor in some instance. Therefore, FVC have the advantage of easier obtainment in the clinical practice.

Compared with ATS-ERS criterion based on FEV\textsubscript{1}, FEV\textsubscript{1} percentage predicted criterion identified higher percentage of patients without significant responsiveness at every spirometry clinic visit in the Understanding Potential Long-term Impacts on Function with Tiotropium (UPLIFT) trial (12). Our finding showed that FEV\textsubscript{1} percentage predicted criterion (FEV\textsubscript{1} responsiveness only) underestimated the treatment response of patients with COPD, while better significant responsiveness was revealed by ATS-ERS criterion based on FEV\textsubscript{1} and FVC (the later in particular), which not only encouraged people to change pessimism into optimism in the treatment, but also better reflected the true bronchodilator responsiveness of COPD (including both FEV\textsubscript{1} responsiveness and FVC responsiveness), especially for more severity of airway obstruction. In fact, most patients who visited hospitals or clinics frequently were in severe condition. Consequently, we preferred ATS-ERS criterion based on FEV\textsubscript{1} and FVC to FEV\textsubscript{1} percentage predicted criterion in clinical practice.

There were some limitations in our study. The definition of airflow obstruction by the fixed FEV\textsubscript{1}/FVC of 0.70 could lead to over-diagnosis of COPD in elder population (23). Use of lower-limit-of-normal (LLN) of FEV\textsubscript{1}/FVC might be a better choice, but we selected 0.70 as the cut-off point due to the lack of LLN in Chinese population at the moment, and this cut-off point is more practical and recommended by many international guidelines to identify subjects with COPD (1). The present study didn’t record the data of daily medications used for COPD, which might influence the result of lung function test, but that was not a major factor to affect our conclusion because patients were required to withdraw bronchodilator or other drugs before spirometry and only a small proportion of Chinese patients took the treatment for COPD [e.g., 22.7% of total patients used any medicine for COPD in our previous study (3)]. In addition, mild patients and female patients were relatively insufficient, although it did reflect the real life of COPD management in China. Nevertheless, the present study still found the evidence of difference among these criteria and the different improvement between FEV\textsubscript{1} and FVC. Finally, the trend of bronchodilator responsiveness over time was not studied in the present research. These limitations will be concerned in future studies.

In conclusion, compared with FEV\textsubscript{1} percentage predicted criterion, ATS-ERS criterion based on FEV\textsubscript{1}, as well as FVC, the later in particular, detected a larger percentage of patients with significant responsiveness. The increasing difference was relevant as a function of the severity of airflow obstruction.

**Acknowledgements**

We thank Tian’en Jin*, Pingping Guo*, Mengjie Jiang* and Bo Yun* for collection of some data. (*Guangzhou Medical University, Guangzhou, China.)

**Disclosure**: Supported by Development Plan of Chang Jiang Scholars and Innovative Research Team (ITR0961), and The
Cite this article as: Jian W, Zheng J, Hu Y, Li Y, Gao Y, An J. What is the difference between FEV\textsubscript{1} change in percentage predicted value and change over baseline in the assessment of bronchodilator responsiveness in patients with COPD. J Thorac Dis 2013;5(4):393-399. doi: 10.3978/j.issn.2072-1439.2013.08.14