FEV_1/FEV_6 in Primary Care Is a Reliable and Easy Method for the Diagnosis of COPD

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BACKGROUND: FEV_6 can be used as a convenient alternative to FVC. The aim of this study was to determine an alternative to the fixed cutoff points of FEV_1/FVC <0.70 suitable for FEV_1/FEV_6 in primary care. METHODS: Pulmonary function testing was conducted on volunteers recruited from 4 community centers in Xi'an, China, between July and August 2012. Participants underwent 3 FVC maneuvers. The maneuver with the best FEV_1 was retained. FVC, FEV_1, and FEV_6 were measured by portable spirometer. The receiver operating characteristic curves that corresponded to the optimal combination of sensitivity and specificity for FEV_1/FEV_6 were determined. A kappa test was used to compare the agreement between FEV_1/FVC and FEV_1/FEV_6. The positive predictive value and negative predictive value were also calculated. RESULTS: A total of 767 volunteers participated in this study, of whom 297 were male and 470 were female. Considering FEV_1/FVC <0.70 as the accepted standard for COPD, the area under the curve was 98% (P < .001), and the FEV_1/FEV_6 cutoff, corresponding to the greatest sum of sensitivity and specificity, was 0.72. For the total population, the FEV_1/FEV_6 sensitivity, specificity, positive predictive value, and negative predictive value were 96.9, 98.8, 95.8, and 99.2%, respectively. The agreement between the 2 cutoff points was excellent, and the kappa value was 0.954. CONCLUSIONS: FEV_1/FEV_6 <0.72 can be used in primary care as a valid alternative to FEV_1/FVC <0.70 as a fixed cutoff point for the detection of COPD in adults. This study suggests that FEV_1/FEV_6 is an effective and well validated option that should be used in primary care to detect COPD, which is a rampant problem. *Key words: COPD; forced expiratory volume in six seconds; pulmonary function testing; spirometry.* [Respir Care 2016;61(3):349–353. © 2016 Daedalus Enterprises]

Introduction

COPD is characterized by a decrease in air flow and shortness of breath. It has been shown that about 15% of United States adults age 40–79 have some form of COPD.[1] Common types of obstructive lung diseases include COPD, chronic bronchitis, and asthma. The cause of about 90% of air flow limitation is COPD for adults without a diagnosis of asthma.[2] It is estimated that COPD will be the third leading cause of death by 2020.[3-6] Its prevalence and consequent burden is rising rapidly with high smoking rates in developing countries. Moreover, an aging population with these factors accounts for the actual and forecasted rapid growth in COPD.

Spirometry is the most frequently used pulmonary function test and is the fundamental tool for the screening, diagnosis, and follow-up of COPD in primary care, but the diagnostic standard for COPD is still debated. The use of reference equations, derived from a representative sample of healthy subjects, to determine lower limits of normal is recommended by the American Thoracic Society and the European Respiratory Society guidelines.[7,8] Presently, spirometers, and in particular handheld spirometers, still do not provide reference equation-based lower limits of normal. Thus, it is

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difficult for the primary care practitioner to diagnose COPD.

To date, it is common practice to determine COPD by use of a fixed cutoff point, FEV$_1$/FVC <0.70, according to the guidelines from the Global Initiative for Chronic Obstructive Lung Disease (GOLD).[9] This definition is widely accepted, mainly because of its practicability.

In developing countries, due to a lack of trained technicians who can effectively assess FVC with costly spirometers in primary care, any less expensive alternative method would be highly desirable. Increasing evidence shows that FEV$_6$ can be used as a convenient alternative to FVC.[10-14] The use of 6-s expiratory maneuvers makes handheld spirometry faster and easier, provides a more explicit end-of-test definition, and reduces spirometry complications (such as syncope).[15] However, reference equations for FEV$_6$ and FEV$_1$/FEV$_6$ have been developed from the third National Health and Nutrition Examination Survey database and are only available for the United States population.[16] As a developing country, China has a population of different age, race, height, and weight. It is necessary to develop the value of FEV$_1$/FEV$_6$ suitable for the Chinese population. The aim of this study is to determine an alternative to the fixed cutoff point of FEV$_1$/FVC <0.70 suitable for FEV$_1$/FEV$_6$ in primary care.

Methods

Subjects

Xi'an is divided into 4 districts according to administrative region: North, East, South, and West. Two communities in each district were selected to be analyzed. The participants were between 18 and 80 y old and were residing in their current community for at least 2 years. Participants provided informed consent and pulmonary function test evaluation between July and August 2012. This study was approved by the ethics committee of the First Affiliated Hospital of Xi'an Medical University.

Definition of COPD

COPD is defined as: FEV$_1$ <80% predicted; FVC normal or reduced, usually to a lesser degree than FEV$_1$; and FEV$_1$/FVC <0.70.[9] All predicted values were based on the Knutson prediction model.

Pulmonary Function Test

FVC, FEV$_1$, and FEV$_6$ were measured by portable spirometer (Spirobank, GTM, Medical International Research, Rome Italy). Participants underwent 3 FVC maneuvers, and the maneuver with the best FEV$_1$ was retained. Efforts that were incomplete or in which the participant coughed

QUICK LOOK

Current knowledge

COPD is commonly defined using a fixed cutoff point, FEV$_1$/FVC <0.70, based on the guidelines from the Global Initiative for Chronic Obstructive Lung Disease. These measurements are typically made in the pulmonary function laboratory adhering to American Thoracic Society standards.

What this paper contributes to our knowledge

In a group of nearly 800 subjects, FEV$_1$/FEV$_6$ <0.72 was capable of being used in primary care as a valid alternative to FEV$_1$/FVC <0.70 for the detection of COPD in adults. This study suggests that FEV$_1$/FEV$_6$ is an effective option that could be used in primary care to detect COPD.

were excluded. Pulmonary function tests were performed by highly trained and experienced pulmonary function respiratory therapists, according to the guidelines of the European Respiratory Society.[8]

Statistics

The data were analyzed using JMPTM 10 (SAS, Cary, North Carolina) and GraphPad Prism 5.0 (GraphPad Software, San Diego, California). The chi-square test or Fisher exact test was used for the analysis of categorical variables. Analysis of variance was utilized to compare measurement variables. The receiver operating characteristic curves that corresponded to the optimal combination of sensitivity and specificity for FEV$_1$/FEV$_6$ were determined. The kappa test was used to compare the agreement between FEV$_1$/FVC and FEV$_1$/FEV$_6$. We also calculated the positive predictive value and negative predictive value. Results are reported as mean ± SD, and P <.05 was considered statistically significant.

Results

Spirometric data from 767 subjects were studied, of whom 297 were male and 470 were female. Subjects' characteristics are shown in Table 1. In this table, FEV$_1$/FVC <0.70 was used for the diagnosis of COPD. For the analyzed cohort, the average age was 58.2 ± 15.6 y. Of these participants, 164 subjects (21.4%) were diagnosed by the GOLD standard. The prevalence of cigarette smoking was 49.8% among men and 4.0% among women.

Considering FEV$_1$/FVC <0.70 as the accepted standard for COPD diagnosis, a receiver operating characteristic curve

Table 1. Summary Statistics and Comparison of Characteristics Between Sexes

| Characteristic	Total ($N = 767$)	Male ($n = 297$)	Female ($n = 470$)	P
Age, mean $\pm$ SD y	58.2 $\pm$ 15.6	57.9 $\pm$ 16.4	58.3 $\pm$ 15.2	.77
Height, mean $\pm$ SD cm	163.1 $\pm$ 5.5	170.1 $\pm$ 6.0	158.6 $\pm$ 5.2	<.001
Weight, mean $\pm$ SD kg	62.0 $\pm$ 9.8	67.4 $\pm$ 10.4	58.6 $\pm$ 9.3	<.001
BMI, mean $\pm$ SD kg/m^2	23.3 $\pm$ 3.3	23.3 $\pm$ 3.1	23.3 $\pm$ 3.5	.84
Smoking status, n (%)				
Non-smoker	526 (68.6)	80 (26.9)	446 (94.9)	
Smoker	167 (21.8)	148 (49.8)	19 (4.0)	<.001
Ex-smoker	74 (9.6)	69 (23.2)	5 (1.1)	
FVC, mean $\pm$ SD L	3.0 $\pm$ 0.8	3.7 $\pm$ 0.9	2.5 $\pm$ 0.6	<.001
FEV$_1$, mean $\pm$ SD L	2.2 $\pm$ 0.6	2.7 $\pm$ 0.8	1.9 $\pm$ 0.6	<.001
FEV$_6$, mean $\pm$ SD L	2.9 $\pm$ 0.8	3.6 $\pm$ 1.0	2.5 $\pm$ 0.7	<.001
FEV$_1$/FVC, mean $\pm$ SD	0.76 $\pm$ 0.10	0.74 $\pm$ 0.10	0.77 $\pm$ 0.10	<.001
FEV$_1$/FEV$_6$, mean $\pm$ SD	0.75 $\pm$ 0.13	0.72 $\pm$ 0.15	0.76 $\pm$ 0.11	<.001
COPD, n (%)	164 (21.4)	87 (29.3)	77 (16.4)	<.001

BMI = body mass index
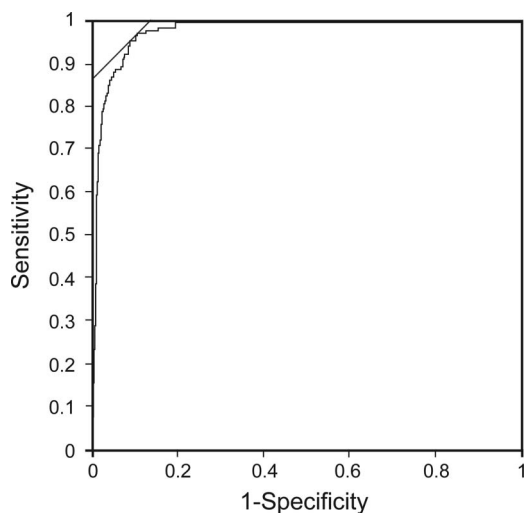
Fig. 1. Receiver operator characteristic curve for FEV$_1$/FEV$_6$ using FEV$_1$/FVC <0.70 as the preferred standard for COPD. The diagonal line represents the optimal combination of sensitivity and specificity.

Table 2. Multilevel Likelihood Ratios for FEV$_1$/FEV$_6$ as a Marker for COPD

FEV$_1$/FEV$_6$	Sensitivity, %	Specificity, %	Positive Predictive Value, %	Negative Predictive Value, %
<0.70	84.0	100	100	75.2
<0.72	96.9	98.8	95.8	99.2
<0.74	100	90	82.2	100

Table 3. Comparison of FEV$_1$/FEV$_6$ With FEV$_1$/FVC for the Diagnosis of COPD

FEV$_1$/FEV$_6$	FEV$_1$/FVC		
	Normal	Reduced	Total
Normal	596	5	601
Reduced	7	159	166
Total	603	164	767

Using FEV$_1$/FVC <0.70 as a fixed cut-off, using FEV$_1$/FEV$_6$ <0.72 as a fixed cut-off. Kappa = 0.954.

was utilized to determine the best corresponding cutoff for FEV$_1$/FEV$_6$ (Fig. 1). The area under the receiver operating characteristic curve was 98% ($P < .001$). The 0.72 of FEV$_1$/FEV$_6$ cutoff represented the greatest combination of sensitivity and specificity. For the total population in this study, the FEV$_1$/FEV$_6$ sensitivity was 96.9%, and specificity was 98.8%. The positive predictive value of FEV$_1$/FEV$_6$ was 95.8%, and the negative predictive value was 99.2%.

When using an FEV$_1$/FEV$_6$ cutoff of 0.74, sensitivity reached 100%, but specificity dropped to 90% (positive predictive value = 82.2%, negative predictive value = 100%). Choosing a fixed cutoff of FEV$_1$/FEV$_6$ of 0.70 resulted in a specificity of 100% with a sensitivity of

84.0% (positive predictive value = 100%, negative predictive value = 75.2%). Multilevel likelihood ratios were constructed in Table 2.

The spirometry test results for 12 participants were classified differently by the 2 methods, and all of them had observed values close to the lower limits of normal (Table 3). Analysis of the 12 discordant cases showed that 98.5% of the discordant values of FEV$_1$/FEV$_6$ were within a $\pm5\%$ interval of the chosen fixed cutoff of 0.72. Overall agreement between the 2 criterion was excellent, and the kappa value was 0.954.

Discussion

Obtaining 99% of the FVC in 6.64 s is sufficient and FEV$_6$ is obtained in >80% of tests. Moreover, the spirometric maneuver for FEV$_6$ is performed easily, and it satisfies the standard for repeatability and diagnostic accuracy.[17] Thus, FEV$_6$ could be a valid alternative to FVC for the diagnosis of COPD in primary care. The main purpose of the present study is to determine a fixed cutoff for the FEV$_1$/FEV$_6$ ratio that is equivalent to the commonly used fixed cutoff of FEV$_1$/FVC <0.70. Our study demonstrates that FEV$_1$/FEV$_6$ <0.72 can be considered as a valid alternative to FEV$_1$/FVC <0.70, and it is possible to detect COPD as a fixed cutoff point for primary care in adults.

The use of FEV$_1$ and FEV$_1$/FVC ratio seems to have become the predominant, if not the unique, factor for determining the presence of COPD. Reduced FEV$_1$/FVC provides a powerful and reliable judgment for COPD, but clinicians have recognized its limitations for quite a while. The most obvious one is that diagnosis of COPD in elderly people will be falsely elevated.[18,19] This is the main reason driving the interest in FEV$_6$ and the FEV$_1$/FEV$_6$ ratio. Additionally, the use of FEV$_1$/FVC is more time-consuming and more expensive than the use of FEV$_1$/FEV$_6$, FVC-based portable spirometers generally costing $700 to $1,000, compared with only $60 to $80 for FEV$_1$/FEV$_6$ instruments. Therefore, it is an ideal method for objectively diagnosing and following up respiratory diseases in busy primary care centers. Indeed, with a receiver operating characteristic (area under the curve) value of 0.98, excellent overall performance was obtained for FEV$_1$/FEV$_6$ <0.72 as a fixed cutoff for the detection of COPD. The following as standards are used to classify the accuracy of a diagnostic test: 0.9–1 = excellent, 0.8–0.9 = good, 0.7–0.8 = fair, 0.6–0.7 = poor, 0.5–0.6 = fail.

Other studies showed similar cutoff points (0.73 and 0.75) of the FEV$_1$/FEV$_6$ ratio to detect COPD, both using the fixed FEV$_1$/FVC <0.70 for comparison. Melbye et al[20] used a spirometry database of referenced subjects from a medical facility, whereas subjects from a highly homogeneous population-based sample in a northern city of Norway were recruited in the study by Vandevoorde et al.[21] A fixed cutoff of 0.75 was obtained from healthy adults in PLATINO studies.[22] In our study, the volunteers are from local communities, and this can reflect actual lung function. Despite the different population backgrounds among these studies, a similar cutoff point for the FEV$_1$/FEV$_6$ ratio was obtained.

A fixed cutoff point for FEV$_1$/FEV$_6$ is an effective method for the diagnosis of COPD, but certain disadvantages have to be taken into account. One, for example, is that FEV$_6$, like FVC, was easily affected by sex and by education level.[17] In addition, there is potential misclassification for elderly subjects, where the age-related decline in FEV$_1$/FVC and FEV$_1$/FEV$_6$ may cause a significant overdiagnosis of COPD.[18] FEV$_1$ is also vulnerable to the impact of smoking and ambient air pollution.[23,24] Therefore, the fixed ration of FEV$_1$/FEV$_6$ for diagnosis of COPD also should be interpreted in the context of the patient's risk factors, age, and symptoms. However, the merit of using a fixed cutoff value for the FEV$_1$/FEV$_6$ instead of a reference equation to diagnose COPD is still highlighted by the COPD guidelines.[9]

This study has some limitations due to its cross-sectional design. Our results are more suitable for this region of China. In addition, the sample size is small for a survey of lung function. A study with a larger sample size would provide more data and enhance the generalizability of the findings.

Conclusion

Our results demonstrate that FEV$_1$/FEV$_6$ <0.72 can be used in primary care as a valid alternative to FEV$_1$/FVC <0.70 as a fixed cutoff point for the detection of COPD in adults. This study suggests that FEV$_1$/FEV$_6$ is an effective and well validated option that should be used in primary care to detect COPD, which is a rampant problem.

REFERENCES

1. Tilert T, Paulose-Ram R, Brody DJ. Lung obstruction among adults aged 40-79: United States, 2007-2012. NCHS Data Brief 2015;(180):1-8.
2. Enright PL, Kaminsky DA. Strategies for screening for chronic obstructive pulmonary disease. Respir Care 48(12):1194-1201, 2003; discussion 1201-1193.
3. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. Lancet 1997;349(9064):1498-1504.
4. Lopez AD, Shibuya K, Rao C, Mathers CD, Hansell AL, Held LS, et al. Chronic obstructive pulmonary disease: current burden and future projections. Eur Respir J 2006;27(2):397-412.
5. Murray CJ, Lopez AD, Black R, Mathers CD, Shibuya K, Ezzati M, et al. Global burden of disease 2005: call for collaborators. Lancet 2007;370(9582):109-110.
6. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 2006;3(11):e442.
7. American Thoracic Society. Lung function testing: selection of reference values and interpretative strategies. Am Rev Respir Dis 1991;144(5):1202-1218.
8. Standardized lung function testing: official statement of the European Respiratory Society. Eur Respir J Suppl 1993;16:1-100.
9. Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: NHLBI/WHO Global Initiative for

Chronic Obstructive Lung Disease (GOLD) Workshop summary. Am J Respir Crit Care Med 2001;163(5):1256-1276.

10. Enright RL, Connett JE, Bailey WC. The FEV$_1$/FEV$_6$ predicts lung function decline in adult smokers. Respir Med 2002;96(6):444-449.

11. Swanney MP, Jensen RL, Crichton DA, Beckert LE, Cardno LA, Crapo RO. FEV$_6$ is an acceptable surrogate for FVC in the spirometric diagnosis of airway obstruction and restriction. Am J Respir Crit Care Med 2000;162(3 Pt 1):917-919.

12. Swanney MP, Beckert LE, Frampton CM, Wallace LA, Jensen RL, Crapo RO. Validity of the American Thoracic Society and other spirometric algorithms using FVC and forced expiratory volume at 6 s for predicting a reduced total lung capacity. Chest 2004;126(6):1861-1866.

13. Vandevoorde J, Verbanck S, Schuermans D, Kartounian J, Vincken W. FEV$_1$/FEV$_6$ and FEV$_6$ as an alternative for FEV$_1$/FVC and FVC in the spirometric detection of airway obstruction and restriction. Chest 2005;127(5):1560-1564.

14. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. Eur Respir J 2005;26(2):319-338.

15. Ferguson GT, Enright PL, Buist AS, Higgins MW. Office spirometry for lung health assessment in adults: a consensus statement from the National Lung Health Education Program. Chest 2000;117(4):1146-1161.

16. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. Am J Respir Crit Care Med 1999;159(1):179-187.

17. Bellia V, Sorino C, Catalano F, Augugliaro G, Scichilone N, Pistelli R, et al. Validation of FEV$_6$ in the elderly: correlates of performance and repeatability. Thorax 2008;63(1):60-66.

18. Hardie JA, Buist AS, Vollmer WM, Ellingsen I, Bakke PS, Mørkve O. Risk of over-diagnosis of COPD in asymptomatic elderly never-smokers. Eur Respir J 2002;20(5):1117-1122.

19. Celli BR, Halbert RJ, Isonaka S, Schau B. Population impact of different definitions of airway obstruction. Eur Respir J 2003;22(2):268-273.

20. Melbye H, Medbø A, Crockett A. The FEV$_1$/FEV$_6$ ratio is a good substitute for the FEV$_1$/FVC ratio in the elderly. Prim Care Respir J 2006;15(5):294-298.

21. Vandevoorde J, Verbanck S, Schuermans D, Vincken W. The role of FEV$_6$ in the detection of airway obstruction. Respir Med 2005;99(11):1465-1466.

22. Rosa FW, Perez-Padilla R, Camelier A, Nascimento OA, Menezes AM, Jardim JR, Latin American Project for Investigation of Obstructive Lung Disease (PLATINO) Group. Efficacy of the FEV$_1$/FEV$_6$ ratio compared to the FEV$_1$/FVC ratio for the diagnosis of airway obstruction in subjects aged 40 years or over. Braz J Med Biol Res 2007;40(12):1615-1621.

23. Götschi T, Heinrich J, Sunyer J, Künzli N. Long-term effects of ambient air pollution on lung function: a review. Epidemiology 2008;19(5):690-701.

24. Scanlon PD, Connett JE, Waller LA, Altose MD, Bailey WC, Buist AS, et al. Smoking cessation and lung function in mild-to-moderate chronic obstructive pulmonary disease: the Lung Health Study. Am J Respir Crit Care Med 2000;161(2 Pt 1):381-390.