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Spirometric Detection of Airway Obstruction and Restriction**
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A M E R I C A N C O L L E G E O F
 **C H E S T**
P H Y S I C I A N S

FEV₁/FEV₆ and FEV₆ as an Alternative for FEV₁/FVC and FVC in the Spirometric Detection of Airway Obstruction and Restriction*

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Study objectives: To evaluate the use of the FEV₁/forced expiratory volume at 6 s of exhalation (FEV₆) ratio and FEV₆ as an alternative for FEV₁/FVC and FVC in the detection of airway obstruction and lung restriction, respectively.

Setting: Pulmonary function laboratory of the Academic Hospital of the Free University of Brussels.

Participants: A total of 11,676 spirometric examinations were analyzed on subjects with the following characteristics: white race; 20 to 80 years of age; 7,010 men and 4,666 women; and able to exhale for at least 6 s.

Methods: Published reference equations were used to determine lower limits of normal (LLN) for FEV₆, FVC, FEV₁/FEV₆, and FEV₁/FVC. We considered a subject to have obstruction if FEV₁/FVC was below its LLN. A restrictive spirometric pattern was defined as FVC below its LLN, in the absence of obstruction. From these data, sensitivity and specificity of FEV₁/FEV₆ and FEV₆ were calculated.

Results: For the spirometric diagnosis of airway obstruction, FEV₁/FEV₆ sensitivity was 94.0% and specificity was 93.1%; the positive predictive value (PPV) and negative predictive value (NPV) were 89.8% and 96.0%, respectively. The prevalence of obstruction in the entire study population was 39.5%. For the spirometric detection of a restrictive pattern, FEV₆ sensitivity was 83.2% and specificity was 99.6%; the PPVs and NPVs were 97.4% and 96.9%, respectively. The prevalence of a restrictive pattern was 15.7%. Similar results were obtained for male and female subjects. When diagnostic interpretation differed between the two indexes, measured values were close to the LLN.

Conclusions: The FEV₁/FEV₆ ratio can be used as a valid alternative for FEV₁/FVC in the diagnosis of airway obstruction, especially for screening purposes in high-risk populations for COPD in primary care. In addition, FEV₆ is an acceptable surrogate for FVC in the detection of a spirometric restrictive pattern. Using FEV₆ instead of FVC has the advantage that the end of a spirometric examination is more explicitly defined and is easier to achieve.

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Key words: COPD; forced expiratory volume; forced expiratory volume at 6 s of exhalation; pulmonary function testing; spirometry

Abbreviations: FEV₆ = forced expiratory volume at 6 s of exhalation; FET = forced expiratory time; LLN = lower limits of normal; NHANES III = third National Health and Nutrition Examination Survey; NPV = negative predictive value; PPV = positive predictive value

Spirometry is the most widely used pulmonary function test. It is a relatively simple, noninvasive test that measures the volume of air expelled from fully inflated lungs as a function of time.^{1,2} Spirometric examination is an essential tool in the diagnosis of

airway obstruction, and to some extent in the detection of restriction. However, variability of spirometric measurements is greater than in most other clinical laboratory tests because the result is highly dependent on the consistency of the efforts made by

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patients and technicians.¹ The effort to empty the lungs completely, in order to reach FVC, can be particularly difficult for some patients.

Spirometry ought to be used in primary care as a screening tool for the early detection of COPD in all patients > 45 years of age who are currently smoking, as well as those with respiratory symptoms.² This requires that spirometry should be easy to perform. Recently, increasing attention has been given to the use of the forced expiratory volume at 6 s of exhalation (FEV₆) as an alternative for FVC.² From the third National Health and Nutrition Examination Survey (NHANES III), reference values have become available³ including lower limits of normal (LLN) for FEV₆ and the FEV₁/FEV₆ ratio, and more recently for related indexes such as the forced expiratory flow between 25% and 75% of the largest observed volume during the first 6 s of a FVC maneuver (FEF 25-75% 6).⁴

Data from the Lung Health Study showed that the FEV₁/FEV₆ ratio is as good as the FEV₁/FVC ratio in predicting the decline in lung function in adult smokers during 5 years of follow-up.⁵ A study by Swanney and coworkers⁶ already demonstrated some evidence that FEV₆ is an acceptable surrogate for FVC in the detection of airway obstruction and restriction. However, as pointed out by these authors, their findings still needed confirmation, particularly with respect to the detection of restrictive lung disease. In the present study, we examined an almost 40-fold larger population than in the previous study, and data for the male and female populations were studied separately.

MATERIALS AND METHODS

We analyzed data of consecutive adult patients referred to the lung function laboratory of the Academic Hospital of the University of Brussels (Vrije Universiteit Brussel), between February 1992 and December 2000. Spirometry was performed with a mass flow sensor (model 2200; SensorMedics; Yorba Linda, CA) by highly trained and experienced pulmonary function technicians, according to the guidelines of the European Respiratory Society.⁷

For the diagnosis of airway obstruction or a restrictive spirometric

pattern, we used the NHANES III reference equations³ to calculate the LLN for FEV₁, FEV₆, FVC, FEV₁/FEV₆, and FEV₁/FVC. In that study, LLN was computed as predicted - 1.645 × SE of the estimate, which corresponds to the fifth percentile, and separate equations were developed for whites, African-Americans, and Mexican-Americans from 8 to 80 years of age. This study also provided separate regression equations for white men aged 20 to 80 years and white women aged 18 to 80 years. Our study was limited to white adults in the 20- to 80-year age range. We considered a subject as having airway obstruction if FEV₁/FVC was below its LLN, and to have a restrictive spirometric pattern if FVC was below its LLN in the presence of a normal FEV₁/FVC. We used two × two tables to calculate sensitivity and specificity for FEV₁/FEV₆ below its LLN as a predictor for obstruction. Similarly sensitivity and specificity were determined for FEV₆ as a predictor for a restrictive spirometric pattern. For both indexes, we also calculated the positive predictive value (PPV) and negative predictive value (NPV). The PPV represents the proportion of patients with abnormal test results who have the disease, and the NPV represents the proportion of patients with normal test results who do not have the disease. Furthermore, in each analysis the discordant cases, *ie*, false-positive and false-negative, were scrutinized. Results are presented for the male, female, and total populations. For statistical analysis we used the statistical software (SPSS 11.0; SPSS; Chicago IL).

RESULTS

We had access to data of 50,172 spirometric test results. We excluded 2,726 tests (5.4%) from analysis because an expiration time of 6 s had not been reached. Of the remaining 47,446 test results, we decided to consider only 1 test per patient. If a subject had undergone multiple spirometric examinations over this 9-year period, we used only the measurements from their last visit. In this way, we obtained results on 12,548 consecutive different patients for further evaluation. Three subjects were excluded because the FEV₁ value was missing. Another 796 subjects were excluded because of their age (82 subjects because they were < 20 years of age, 714 subjects because they were > 80 years of age). Finally, 73 subjects were excluded because they were not white. This left us with spirometric data from 11,676 white subjects, of whom 7,010 were men (60%) and 4,666 were women (40%). Subject characteristics are shown in Table 1; the LLN on

Table 1—Subject Demographics, Presence and Severity of Airway Obstruction*

Subjects	No.	Age Median, yr (Range)	Height Median, cm (Range)	Not Obstructed, No. (%)†			Obstructed, No. (%)‡		
				Normal	Restricted	Normal Variant	Mild	Moderate	Severe
Male	7010	60 (20–80)	173 (142–203)	3,275 (46.7)	697 (9.9)	72 (1.0)	943 (13.5)	957 (13.7)	1,066 (15.2)
Female	4666	56 (20–80)	163 (135–185)	2,677 (57.4)	414 (8.9)	69 (1.5)	610 (13.1)	461 (9.9)	435 (9.3)
Total	11676	59 (20–80)	170 (135–203)	5,952 (51.0)	1,111 (9.5)	141 (1.2)	1,553 (13.3)	1,418 (12.1)	1,501 (12.9)

*Using the LLN on FEV₁, FVC, and FEV₁/FVC, based on the NHANES III reference equations.³

†Total not obstructed, 7,063 (60.5%).

‡Total obstructed, 4,613 (39.5%).

FEV₁, FVC, and FEV₁/FVC as defined by the NHANES III reference equations were used for the diagnosis of obstruction and a restrictive pattern.³ The obstructive group was further classified into subgroups according to the severity of airway obstruction, in accordance with the European Respiratory Society definition⁸: possible normal variant (FEV₁ ≥ 100% predicted), mild (FEV₁ ≥ 70% to < 100% predicted), moderate (FEV₁ ≥ 50% to < 70% predicted), and severe (FEV₁ < 50% predicted).

Spirometric Diagnosis of Obstruction

These results are shown in Table 2. For the total population, the FEV₁/FEV₆ sensitivity was 94.0% and specificity was 93.1%. The PPV of FEV₁/FEV₆ was 89.8%, and the NPV was 96.0%. The prevalence of obstruction was 4,613 of 11,676 subjects (39.5%) [Table 2]. Similar results were obtained when considering male and female subjects separately (Table 2). In the male subgroup, the nonobstructed subjects and the obstructed subjects had mean forced expiratory times (FETs) of 8.8 ± 2.6 s and 10.9 ± 3.7 s [± SD], respectively. In the female subgroup, the nonobstructed subjects and the obstructed subjects had mean FETs of 8.1 ± 2.1 s and 9.8 ± 3.1 s, respectively.

Analysis of the 767 discordant cases (false-positive and false-negative combined) showed that the majority of the discordant cases were very close to their LLN (Table 3). In the 490 false-positive cases, the mean difference of FEV₁/FVC and FEV₁/FEV₆ with

Table 3—Findings in the 767 Discordant Cases in the Detection of Obstruction

Results	No.	Mean Difference		
		With LLN, %	SD, %	
False-positive	490	FEV ₁ × 100/FVC	0.9	1.1
		FEV ₁ × 100/FEV ₆	-1.8	1.1
False-negative	277	FEV ₁ × 100/FVC	-2.3	1.6
		FEV ₁ × 100/FEV ₆	0.9	1.3

their respective LLN was 0.9% (SD, 1.1%) and -1.8% (SD, 1.1%). In the 277 false-negative cases, the mean difference of FEV₁/FVC and FEV₁/FEV₆ with their respective LLN was -2.3% (SD, 1.6%) and 0.9% (SD, 1.3%). Results were similar for both sexes (data not shown).

Spirometric Detection of Restriction

In all subjects with normal FEV₁/FVC, we assessed the usefulness of FEV₆ as a surrogate for FVC in the detection of a restrictive spirometric pattern. For the total population, FEV₆ sensitivity was 83.2% and specificity was 99.6%. The PPV was 97.4%, and the NPV was 96.9%. In this subgroup, the prevalence of a restrictive pattern was 1,111 of 7,063 subjects (15.7%) [Table 4]. Similar results were obtained for male and female subjects separately (Table 4). In the male subgroup, the nonrestricted subjects and the restricted subjects had mean FETs of 8.9 ± 2.7 s and 8.0 ± 1.9 s, respectively. In the

Table 2—Diagnosis of Airway Obstruction*

Variables	FEV ₁ /FVC		Total
	Obstruction	No Obstruction	
Total population†			
FEV ₁ /FEV ₆ , obstruction	4,336	490	4,826
FEV ₁ /FEV ₆ , no obstruction	277	6,573	6,850
Total	4,613	7,063	11,676
Male population‡			
FEV ₁ /FEV ₆ , obstruction	2,861	268	3,129
FEV ₁ /FEV ₆ , no obstruction	177	3,704	3,881
Total	3,038	3,972	7,010
Female population§			
FEV ₁ /FEV ₆ , obstruction	1,475	222	1,697
FEV ₁ /FEV ₆ , no obstruction	100	2,869	2,969
Total	1,575	3,091	4,666

*Using LLN on FEV₁, FVC, and FEV₁/FVC based on NHANES III reference equations.³

†Sensitivity, 94.0%; specificity, 93.1%; prevalence of obstruction, 39.5%; PPV, 89.8%; NPV, 96.0%.

‡Sensitivity, 94.2%; specificity, 93.3%; prevalence of obstruction, 43.3%; PPV, 91.4%; NPV, 95.4%.

§Sensitivity, 93.7%; specificity, 92.8%; prevalence of obstruction, 33.8%; PPV, 86.9%; NPV, 96.6%.

Table 4—Diagnosis of a Spirometric Restrictive Pattern*

	FVC		Total
	Reduced	Normal	
Total population†			
FEV ₆ , reduced	924	25	949
FEV ₆ , normal	187	5,927	6,114
Total	1,111	5,952	7,063
Male population‡			
FEV ₆ , reduced	573	18	591
FEV ₆ , normal	124	3,257	3,381
Total	697	3,275	3,972
Female population§			
FEV ₆ , reduced	351	7	358
FEV ₆ , normal	63	2,670	2,733
Total	414	2,677	3,091

*Using the LLN on FEV₁, FVC, and FEV₁/FVC, based on the NHANES III reference equations.³

†Sensitivity, 83.2%; specificity, 99.6%; prevalence of a restrictive pattern, 15.7%; PPV, 97.4%; NPV, 96.9%.

‡Sensitivity, 82.2%; specificity, 99.5%; prevalence of a restrictive pattern, 17.5%; PPV, 97.0%; NPV, 96.3%.

§Sensitivity, 84.8%; specificity, 99.7%; prevalence of a restrictive pattern, 13.4%; PPV, 98.0%; NPV, 97.7%.

female subgroup, the nonrestricted subjects and the restricted subjects had mean FETs of 8.2 ± 2.1 s and 7.6 ± 1.8 s, respectively.

Analysis of the 212 discordant cases (false-positive and false-negative combined) showed that most discordant values were close to their LLN (Table 5). In the 25 false-positive cases, the mean difference of FVC and FEV₆ with their respective LLN was 0.2% (SD, 1.7%) and -2.9% (SD, 1.9%). In the 187 false-negative cases, the mean difference of FVC and FEV₆ with their respective LLN was -3.7% (SD, 1.6%) and 0.4% (SD, 1.6%). Results were similar for both sexes (data not shown).

DISCUSSION

Spirometric Diagnosis of Obstruction

The main purpose of this study was to determine whether the same diagnosis can be made using the FEV₁/FEV₆ ratio instead of the FEV₁/FVC ratio. Our results show very satisfactory figures for FEV₁/FEV₆ sensitivity, specificity, and PPVs and NPVs for both sexes (Table 2). In addition, almost all of the discordant cases were close to the LLN (Table 3). American Thoracic Society guidelines state that LLN are variable and, therefore, should not be considered as arbitrary limits that correctly classify all patients into normal and abnormal groups. Patient values that lie close to lower limits should be interpreted with caution.⁹ It should also be considered that diurnal and day-to-day variations of spirometric indexes could shift results across the LLN, depending on time of testing. Moreover, patients with obstruction have coefficients of variation for FEV₁ and FVC that are about twice those of normal subjects.¹⁰

When comparing our results to those of Swanney and coworkers,⁶ we obtained slightly lower values of sensitivity and specificity (94.0% and 93.1% in our study, respectively, vs 95.0% and 97.4% in theirs). The PPV in our study is lower (89.8% vs 98.6%), whereas our NPV is higher (96.0% vs 91.1%). However, in Swanney et al,⁶ the population under study (n = 337) showed a much higher proportion of

subjects with obstruction (65.6%) than in our study (n = 11,676; 39.5% obstruction). Hence, the lower PPV and the higher NPV were to be expected in the present study.¹¹

We should indeed emphasize that the findings of our study apply to a population with an overall prevalence of airway obstruction of 39.5% (43.3% in men, 33.8% in women). Studies¹²⁻¹⁴ have reported a prevalence of COPD in smokers of 30 to 50%, if diagnosed by spirometry. Hence, using FEV₁/FEV₆ instead of FEV₁/FVC could be very useful in the context of primary care, where spirometry can be used as a screening tool for the early detection of COPD in a high-risk population, *ie*, smokers > 45 years of age and subjects with respiratory symptoms. Using FEV₆ instead of FVC, both in obstructive and restrictive patients, has several advantages: (1) it is easier for the patient and the technician, especially for older patients and those with severe respiratory diseases²; (2) there is a more precise end-of-test definition²; (3) there is some evidence that FEV₆ is more reproducible than FVC⁶; (4) shorter maneuvers reduce the risk of syncope²; and (5) it reduces the overall time to perform a test.²

Spirometric Detection of Restriction

The diagnosis of restriction is usually based on the presence of a reduced total lung capacity. As stated by the American Thoracic Society guidelines, a reduced FVC in the presence of a normal FEV₁/FVC may be used to suggest but not to diagnose the presence of a restrictive abnormality.⁹ In fact, a study by Aaron and coworkers¹⁵ showed that for patients with a typical spirometric restrictive pattern, < 60% of patients were found to have true restriction when total lung capacity was measured (the PPV of FVC was 58%). However, in that report,¹⁵ the NPV was 95.4%, which means that spirometry is very useful at excluding a restrictive defect. In our study, we found high NPVs when comparing FEV₆ and FVC as a predictor of a restrictive pattern. This makes the use of FEV₆ suitable for the exclusion of restriction.

CONCLUSION

This study demonstrates that the FEV₁/FEV₆ ratio can be used as a valid alternative for FEV₁/FVC in the diagnosis of airway obstruction in adults. In addition, FEV₆ is an acceptable surrogate for FVC in the exclusion of a restrictive abnormality.

We should emphasize that our findings derive from an adult population able to exhale for at least 6 s, with a prevalence of airway obstruction of about 40% and a prevalence of a spirometric restrictive pattern of about 16% in the group without obstructive

Table 5—Findings in the 212 Discordant Cases in the Detection of a Restrictive Pattern

Results	No.		Mean Difference With LLN, %	SD, %
False-positive	25	FVC	0.2	1.7
		FEV ₆	-2.9	1.9
False-negative	187	FVC	-3.7	1.6
		FEV ₆	0.4	1.6

tion. Since FEV₆ seems to have a greater reproducibility than FVC and the end-of-test criteria are more easily met, it is possible that FEV₁/FEV₆ is not only as good, but could even be more accurate than FEV₁/FVC in the detection of airway obstruction, especially when screening high-risk populations for COPD in primary care.

REFERENCES

- 1 Crapo RO. Pulmonary-function testing. *N Engl J Med* 1994; 331:25–30
- 2 Ferguson GT, Enright PL, Buist AS, et al. Office spirometry for lung health assessment in adults: a consensus statement from the National Lung Health Education Program. *Chest* 2000; 117:1146–1161
- 3 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; 159:179–187
- 4 Hankinson JL, Crapo RO, Jensen RL. Spirometric reference values for the 6-s FVC maneuver. *Chest* 2003; 124:1805–1811
- 5 Enright PL, Connett JE, Bailey WC. The FEV₁/FEV₆ predicts lung function decline in adult smokers. *Respir Med* 2002; 96:444–449
- 6 Swanney MP, Jensen RL, Crichton DA, et al. FEV₆ is an acceptable surrogate for FVC in the spirometric diagnosis of airway obstruction and restriction. *Am J Respir Crit Care Med* 2000; 162:917–919
- 7 Quanjer PhH, Tammeling GJ, Cotes JE, et al. Standardized lung function testing: lung volumes and forced ventilatory flows. *Eur Respir J* 1993; 6(suppl):5s–40s
- 8 Siafakas NM, Vermeire P, Pride NB, et al. Optimal assessment and management of chronic obstructive pulmonary disease (COPD). *Eur Respir J* 1995; 8:1398–1420
- 9 Medical Section of the American Lung Association. Lung function testing: selection of reference values and interpretative strategies. *Am Rev Respir Dis* 1991; 144:1202–1218
- 10 Pennock BE, Rogers RM, McCaffree DR. Changes in measured spirometric indices: what is significant? *Chest* 1981; 80:97–99
- 11 Sackett DL, Haynes RB, Guyatt GH, et al. *Clinical epidemiology: a basic science for clinical medicine*. 2nd ed. Boston, MA: Little, Brown and Company, 1991; 85–91
- 12 Lundbäck B, Lindberg A, Lindström M, et al. Not 15 but 50% of smokers develop COPD? Report from the Obstructive Lung Disease in Northern Sweden Studies. *Respir Med* 2003; 97:115–122
- 13 Stratelis G, Jakobsson P, Molstad S, et al. Early detection of COPD in primary care: screening by invitation of smokers aged 40 to 55 years. *Br J Gen Pract* 2004; 54:201–206
- 14 Zieliński J, Bednarek M. Early detection of COPD in a high-risk population using spirometric screening. *Chest* 2001; 119:731–736
- 15 Aaron SD, Dales RE, Cardinal P. How accurate is spirometry at predicting restrictive pulmonary impairment? *Chest* 1999; 115:869–873

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