FEV1/FEV6 versus FEV1/FVC in the Spirometric Detection of Airway Obstruction among Asians

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Background --- Forced expiratory volume in six seconds (FEV6) is an acceptable alternative to forced vital capacity (FVC) for diagnosing airway obstruction in adults. The use of FEV6 simplifies testing procedures, reduces test variability, and may improve accuracy in diagnosing airway obstruction. The study was conducted to determine the relationship of FEV1/FEV6 with FEV1/FVC in the spirometric detection of severity of airway obstruction among Asians at Philippine Heart Center.

Methods --- This is a one year cross sectional study comparing the FEV1/FEV6 versus FEV1/FVC in the spirometric diagnosis of airway obstruction among Asians at the Philippine Heart Center. Patients who underwent spirometric studies at Philippine Heart Center Pulmonary Laboratory from May 2005 to April 30, 2006 were evaluated. Baseline demographic data, smoking history and spirometric results were evaluated. The highest post-bronchodilator FEV1 , FEV6 and FEV1/FEV6 % from tests of acceptable quality were used for analysis. Each subject was categorized as having "airway obstruction " by comparing both FEV1/FVC and FEV1/FEV6 with the respective lower limits of normal defined by Hankinson and coworkers. We used FEV1/FVC as the "gold standard" for diagnosing airway obstruction. The severity of airway obstruction was graded into one of four categories; possible normal variant (FEV1>100% predicted), mild (FEV1 70-100% predicted), moderate (FEV1 50-70% predicted), and severe (FEV1 <50% predicted).The sensitivity, specificity, positive predictive value (PPV) and negative predictive values (NPV) of FEV1/FEV6 % in predicting airway obstruction as defined by FEV1/FVC were calculated. The agreement between test result classification based on FVC and FEV6 was calculated using the Kappa test.

Results --- Of 597 spirometric tests analyzed, 352 were males and 245 were females. 78% of males were smokers. FEV1/FEV6 has 97.6% sensitivity and has 83.6% specificity in detecting mild airway obstruction, with a positive and negative predictive values of 93.1% and 93.3% respectively. Indeed, with a kappa value of 0.837, a very good overall performance was obtained for FEV1/FEV6 % in detecting mild airway obstruction. In addition , a kappa value of 0.694 was a substantial agreement for FEV1/FEV6 in detecting moderate airway obstruction.

Conclusion --- FEV6 is an acceptable surrogate for FVC in detecting airway obstruction in Asian adults. Using FEV6 instead of FVC has the advantage that the end of a spirometric examination is more explicitly defined and is easier to achieve. ***Phil Heart Center J 2008; 14(1):34-38.***

Key Words: Spirometry ■ FEV1 ■ FVC ■ Obstructive Lung Disease ■ Validity Study

Spirometry is the most widely used pulmonary function test. It is relatively simple and noninvasive test that measures the volume of air expelled from fully inflated lungs as a function of time. Spirometric examination is an essential tool in the diagnosis of airway obstruction, and to some extent in the detection of restriction.[1]

The acceptability criteria for forced vital capacity (FVC) maneuver during pulmonary function tests (PFT) have been previously described by American Thoracic Society (ATS). Duration of exhalation should be at least 6 seconds, during which a minimum 1 second plateau could be reached. This total duration may be as long as 15-20 seconds in cases with airway obstruction.

However, patients frequently experience problems during expiration, finding it difficult to fulfill the end-of-test criteria for the FVC maneuver. Because of this observation, utilization of forced expiratory volume in 6s (FEV6) in place of FVC has been proposed in order to make the spirometry a simpler and more widely used diagnostic modality in primary health care.

Spirometry is an effort-dependent test. It takes effort by the patient to fill the lungs completely and a complete uninterrupted effort to empty the lungs. It is now known that the forced expiratory volume in six seconds (FEV6), is an excellent surrogate for FVC. Thus, doing a six second expiratory maneuver is more pleasant for the patient and more convenient for the tester.

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Forced expiratory volume in six seconds (FEV6) is an acceptable alternative to forced vital capacity (FVC) for diagnosing airway obstruction in adults. The use of FEV6 simplifies testing procedures, reduces test variability, and may improve accuracy in diagnosing airway obstruction.

FEV6 has many advantages over FVC since spirometry may be easier in older and impaired patients because they would not have to exhale as long and the end of the test is more clearly defined, permitting more reliable correspondence between measured and referenced values.

A study done by Vandevoorde et al[1] demonstrated that forced expiratory volume in one second/forced expiratory volume in six seconds <73% and forced expiratory volume in six seconds <82% predicted can be used as a valid alternative for forced expiratory volume in one second/forced vital capacity <70% and forced vital capacity 80% predicted as a fixed cut-off points for the detection of an obstructive or restrictive spirometric pattern in adults.[1]

At 95% confidence intervals, 21.3% of 3,515 smokers and 41.3% of smokers aged >51 yrs had airway obstruction; when comparing FEV1/FEV6 with FEV1/FVC, 13.5% were concurrently abnormal, 1.5% were false positives and 4.1% were false negatives; and when comparing FEV3/FEV6 with FEV3/FVC, 11.6% were concurrently abnormal, 3.3% were false positives and 5.7% were false negatives. Substituting forced expiratory volume in six seconds for forced vital capacity to determine the fractional rates of exhaled volumes reduces the sensitivity of spirometry to detect airflow obstruction, especially in older individuals and those with lesser obstruction.[2]

Akpinar et. al [3] confirms that the forced expiratory volume in six seconds can be used as a surrogate for forced vital capacity in detecting airways obstruction and restriction in workers, although with some misclassification when compared with obtaining American Thoracic-Society-acceptable maneuvers of longer duration.

Swanney et. al.[4] provided an evidence that the spirometry-based algorithms can accurately predict when TLC is either normal or increased, and can also increase the a priori probability that TLC is reduced to approximately 50%. FEV6 is equivalent to FVC in these predictions. However, although it is easier to use FEV6 in place of FVC, Demir et al[5] said that relatively low sensitivity in the setting may result in the underestimation of airway obstruction . This drawback should be kept in mind when FEV6 is utilized to detect airway obstruction.

Vandervoorde [6] et. al. proved that 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. The FEV1/FEV6 sensitivity was 94.5% and was 93.1% specific. The positive predictive value of FEV1/ FV6 was 89.9% and the negative predictive value was 96.0%. When the values of FEV1/ FEV6 % were used , the sensitivity for detecting airways obstruction was 92% and specificity was 98%.[3] 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. This study was done to determine the relationship of FEV1/FEV6 with FEV1/ FVC in the spirometric detection of severity of airway obstruction among Asians at Philippine Heart Center. Specifically, the validity measures of FEV1/FEV6 in detecting severity of airway obstruction will be determined.

Methods

This was cross-sectional study done at the Pulmonary Laboratory, Division of Pulmonary and Critical Care Medicine of the Philippine Heart Center, a tertiary hospital in Quezon City, Philippines. Included subjects were adult Asian patients ages 18-90 years old referred to Philippine Heart Center Pulmonary Laboratory for spirometric studies from May 2005 to April 2006. Excluded were patients with any of the following conditions: with hemoptysis of unknown origin; pneumothorax; unstable cardiovascular status or recent myocardial infarction or pulmonary embolus; thoracic, abdominal, or cerebral aneurysms; recent eye surgery; presence of an acute disease process that might interfere with test performance; and recent surgery of thorax or abdomen. The following were the study variables in this study:

a. FEV1 = is the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration, expressed in liters.

b. FVC = is the maximal volume of air exhaled with maximally forced effort from a maximal inspiration.

c. FEV6 = forced expiratory volume in six seconds.

d. FEV1/FEV6 = ratio between FEV1 over FEV6

e. FEV1/FVC = ratio between FEV1 over FVC

We analyzed data from consecutive adult Asian patients referred to our Pulmonary Laboratory for routine spirometry over a period of one year using the Sensormedics Vmax Pulmonary Function System. This device is provided with a new software to measure and report FEV6 and FEV1/FEV6 along with all other standard spirometric indices. The spirometer was calibrated daily. Subjects were tested while seated, and procedures detailed in the ATS guidelines were followed. Height was measured to the nearest centimeter without shoes, and weight was measured to the nearest kilogram. Particular attention was made to ensure that maximal FEV1 and FVC efforts were obtained. Each study was screened for technical adequacy. We required at least three acceptable trials, "defined as (1) a good start of test (a well defined early peak in flow and an extrapolated volume of less than 5% of FVC or .15 L, whichever was larger), (2) at least 6s of expiration, and (3) no significant cough or other interruption in the test." The computer report of expiratory time was verified from the volume/time tracings. The highest post-bronchodilator FEV1, FEV6, and FVC from tests of acceptable quality were used for analysis. Only one test per patient was considered, if a subject had undergone multiple spirometric examination over the one year period, the results from their last visit was used.

Each subject was categorized as having "airway obstruction" by comparing both FEV1/FVC and FEV1/FEV6 with the respective lower limits of normal defined by Hankinson and coworkers. We used FEV1/FVC as the "gold standard" for diagnosing airway obstruction. The severity of airway obstruction was graded into one of four categories; possible normal variant (FEV1>100% predicted), mild (FEV1 70-100% predicted), moderate (FEV1 50-70% predicted), and severe (FEV1 <50% predicted).

Statistical Analysis

Sensitivity and specificity of FEV1/ FEV6 in predicting obstruction defined by FEV1/FVC were calculated using 2 x2 tables. The positive predictive value (PPV) and negative predictive value (NPV) were also calculated. The agreement between test result classification based on FVC and FEV6 was calculated using the Kappa test. The patients' age, height , weight and smoking history data were compared with the rest of the groups by paired t-test.

Results

Patients Characteristics

An access to 1553 spirometric test results was made during the study period. We excluded 133 tests (7.27%) from analysis because an expiration time of 6 seconds had not been observed. Three subjects were excluded because of age, seven due to missing FEV6 values, one a Caucasian and 812 with only pre-bronchodilation spirometric results. These left us with post-bronchodilation spirometric data from 597 Asian subjects.

Table 1. Demographic characteristics of included patients

Characteristics	Male N=352	Female N=245
Age (years)*	55 (18-89)	48 (18-82)
Height (cm) *	163 (168-188)	153 (136-173)
Weight (kg)*	67 (24-180)	55 (28-125)
Smoking History		
With Smoking History	273 (78%)	39 (16%)
Without Smoking History	79 (22%)	206 (84%)

*expressed as mean and range

As shown, 352 subjects were males (59%) with a mean age of 55 years and mean weight of 67 kg, while 245 (41%) were females with a mean age of 48 years and a mean weight of 55 kg. Of the 597 subjects, 273 (78%) of the male subjects were smokers while 206 of the females (84%) were not smokers.

Table 2. Distribution of spirometric indices according to sex

Spirometric Indices	Male N=352	Female N=245
FVC %	74	73
FEV1 %	70	75
FEV1/FVC %	70	77
FEV 6 L	2.79	2.10
FEV1/FEV6 %	73	78

Table 2 shows the mean post-bronchodilator FVC%, FEV1%, FEV1/FVC %, FEV6, and FEV1/FEV6 % in all subjects. The mean FEV1/FEV6 % for males and

Table 3. Agreement of FEV1/FEV6 with FEV1/FVC in staging the severity of airway obstruction

	Severity of Airway Obstruction (FEV1/FVC%)				
Severity of Airway Obstruction (FEV1/FEV6%)	Possible Normal Variant	Mild	Moderate	Severe	TOTAL
Possible Normal Variant	1	6	0	0	7
Mild	0	404	30	0	434
Moderate	0	3	101	29	133
Severe	0	1	1	21	23
TOTAL	1	414	132	50	597

Table 3 shows us the agreement of FEV1/ FEV6 with FEV1/FVC with spirometric severity of airway obstruction. There was only one patient with possible normal variant by FEV1/FVC and he was also diagnosed by FEV1/FEV6 as a possible normal variant. Among 414 patients with mild airway obstruction by FEV1/FVC, 404 (97.5%) were diagnosed by FEV1/ FEV6 with mild airway obstruction too. Among 132 patients with moderate airway obstruction by FEV1/ FVC, 101 (76.5%) were classified as moderate airway obstruction by FEV1/FEV6. Among those with severe airway obstruction, 21 (42%) out of 50 patients were diagnosed by FEV1/FEV6 with severe obstruction as well.

Table 4a illustrates the validity of FEV1/FEV6 in diagnosing severe airway obstruction when compared with FEV1/FVC as gold standard. Interpretations based on the FEV6 had a high agreement rate with those based on FVC (Kappa=.0.552; p=0.000). When the values of FEV1/FEV6 % were used, the sensitivity for detecting severe airway obstruction was 42.% and 99.6% specificity. Positive and negative predictive values were 91.3% and 94.9% , respectively.

Table 4a. Validity of FEV1/FEV6 in the Diagnosis of Severe Airway Obstruction

Severity of Airway Obstruction (FEV1/ FEV6)	Severity of Airway Obstruction (FEV1/ FVC) Severe Airway Obstruction	Moderate, Mild, Possible Normal variant	Total
Severe	21	2	23
Moderate	29	545	574
Total	50	547	597

Measure of association and 95% confidence interval

Sensitivity 42.0% *Specificity* 99.6% *PPV* 91.3% *NPV* 94.9%

Kappa Coefficient 0.552 ± .038 p= 0.000

On the other hand, Table 4b demonstrates the validity of FEV1/FEV6 in diagnosing moderate airway obstruction. Interpretations based on the FEV6 had a high agreement rate with those based on FVC (Kappa=.0.694; p=0.000). When the values of FEV1/ FEV6 % were used, the sensitivity for detecting moderate airway obstruction was 76.5% and 93.1% specificity. Positive and negative predictive values were 75.9% and 93.3%, respectively.

Lastly, Table 4c shows the validity of FEV1/FEV6 in diagnosing mild airway obstruction. Interpretations based on the FEV6 had a high agreement rate with those based on FVC (Kappa=.0.837; p=0.000). When the values of FEV1/FEV6 % were used, the sensitivity for detecting mild airway obstruction was 97.6% and 83.6% specificity. Positive and negative predictive values were 93.1% and 93.9% , respectively.

Table 4b. Validity of FEV1/FEV6 in the Diagnosis of Moderate Airway Obstruction

Severity of Airway Obstruction (FEV1/ FEV6)	Severity of Airway Obstruction (FEV1/ FVC) Moderate Airway Obstruction	Moderate, Mild, Possible Normal variant	Total
Moderate	101	32	133
Mild, Possible Normal Variant	31	433	464
Total	132	465	597

Measure of association and 95% confidence interval

Sensitivity 76.5 % *Specificity* 93.1 % *PPV* 75.9 % *NPV* 93.3 %

Kappa Coefficient 0.694 ±0.041, p= 0.000

Table 4c. Validity of FEV1/FEV6 in the Diagnosis of Mild Airway Obstruction

Severity of Airway Obstruction (FEV1/ FEV6)	Severity of Airway Obstruction (FEV1/ FVC) Mild airway Obstruction	Severe, Moderate, and Possible Normal variant	Total
Mild	404	30	434
Severe, Moderate & Possible Normal Variant	10	153	163
Total	414	183	597

Measure of association and 95% confidence interval

Sensitivity 97.6 % *Specificity* 83.6 % *PPV* 93.1% *NPV* 93.9 %

Kappa Coefficient 0.837 ±0.041, p= 0.000

Discussion

Several studies emphasized the importance of spirometry as a screening tool for the early detection of chronic obstructive pulmonary disease in the primary care setting. This has resulted in the need for easy to perform spirometry tests. Increasing evidence showed that the forced expiratory volume in six seconds (FEV6) can be used as a convenient alternative for forced vital capacity (FVC). Spirometric data from 597 Asian subjects were studied, of whom 352 were male and 245 were female. Majority of the males were smokers. Subject characteristics and history of smoking were shown in Tables 1 and 2.

As described in Table 4 above, the FEV1/FVC <70% was used for the diagnosis of obstructive pattern, and it was further classified into four subgroups

according to the severity of airway obstruction: possible normal variant (FEV1> 100% predicted), mild (FEV1 70 -100% predicted), moderate (FEV1 50-70% predicted), and severe (FEV1 <50% predicted).

The main purpose of the present study was to determine if forced expiratory volume at 6s (FEV6) can substitute for force vital capacity (FVC) in spirometric detection of airway obstruction. Indeed, with a kappa value of 0.837, a very good overall performance was obtained for FEV1/FEV6 % in detecting mild airway obstruction. In addition, a kappa value of 0.694 demonstrated a substantial agreement for FEV1/FEV6 in detecting moderate airway obstruction. A kappa value of 1 indicates perfect agreement, while a kappa value of 0 indicates that agreement is no better than chance. Landis and Koch have proposed the following as standards for strength of agreement for the kappa coefficient; 0.01-0.20 slight, 0.21 -0.40 fair, 0.41-0.60 moderate, 0.61-0.80 substantial and 0.81-1.0 almost perfect agreement.[7]

Vandervoorde,[1] in his study involving 11, 676 Caucasian subjects, obtained a kappa value of 0.87 for FEV1/FEV6 <73% and FEV6 <82% as fixed cut offs for the detection of obstructive spirometric patterns. As expected, both FEV6 and FEV1/FEV6 were more reproducible than FVC and FEV1/FVC. The excellent performance of FEV6 and FEV1/FEV6 and their reduced variability suggest they may have a statistical advantage in diagnosing airway obstruction.

FEV1/FEV6 has 97.6% sensitivity and has 83.6% specificity in detecting mild airway obstruction, with a positive and negative predictive values of 93.1% and 93.3% respectively as shown in Table 5c. These findings correlate well with 502 patients studied by Swanney et al.[8] wherein he compared FEV1/FEV6 with FEV1/FVC for diagnosing airway obstruction. He obtained a sensitivity of 95%, specificity of 97.4%, PPV of 91.1% and NPV of 91.1 for FEV1/FEV6 in diagnosing obstruction.

Using FEV6 as a surrogate for FVC has several practical advantages: (1) Spirometry may be less demanding because patients would never have to be pushed to a 15 to 20 sec inhalation. This may be especially important in older and impaired patients; (2) shorter expiratory times require less data storage space, an important issue for smaller, portable spirometers; (3) the end of test is more easily and explicitly defined; and (4) higher sensitivity and specificity for detection of mild airway obstruction.

Conclusion

This study demonstrates that FEV6 is an acceptable surrogate for FVC in detecting airway obstruction in Asians adults, although there were some misclassification when compared with obtaining American Thoracic Society- acceptable maneuvers of longer duration. FEV1/FEV6 has 97.6% sensitivity and has 83.6% specificity in detecting mild airway obstruction, with a positive and negative predictive values of 93.1% and 93.3% respectively. Indeed, with a kappa value of 0.837, a very good overall performance was obtained for FEV1/FEV6 % in detecting mild airway obstruction.

Recommendation

Additional studies are recommended to determine if the current results are generalizable for those using flow-sensing spirometers especially in mass screening as in

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