

CAN FEF 25-75% BE USED AS A VALID ALTERNATIVE TO FEV1% IN COPD DIAGNOSIS?

Saritha Jayachandran Shenoy¹, Neenu Kuruvilla², Kummannoor Parameshwaran Venugopa³, Geethadevi Madhavikutty⁴, Sameena B⁵

¹Assistant Professor, Department of Physiology, Government Medical College, Kottayam.

²Student, Government Medical College, Kottayam.

³Associate Professor, Department of Pulmonary Medicine, Government Medical College, Kottayam.

⁴Associate Professor, Department of Community Medicine, Government Medical College, Kottayam.

⁵PFT Technician, Government Medical College, Kottayam.

ABSTRACT

BACKGROUND

According to American Thoracic Society criteria FEV1% is the gold standard test in the diagnosis of COPD. The prospect of detecting lung disease, at an early stage has led to widespread measurement of FEF 25-75%. This study will provide an alternative to FEV1% in the diagnosis of COPD, so that the difficulties faced by the patients and the technicians in the measurement of FVC and FEV1% can be minimised.

MATERIALS AND METHODS

The study was conducted on 304 patients (194 COPD patients and 110 normal individuals) in the Pulmonary Function Test (PFT) Laboratory of Govt. Medical College; Kottayam. The instrument used was 'Compact Vitalograph'. The results obtained were analysed using SPSS software and the sensitivity and specificity of FEF 25-75% was calculated using 2x2 tables. The positive predictive value (PPV) and negative predictive value (NPV) was also calculated.

RESULTS

Out of the total 304 subjects, 221 (72.70%) are males and 83 (27.30%) are females. 273 subjects (89.8%) came under 'COPD' category and 31 subjects (10.2%) came under 'normal' category based on FEF 25-75. As per our study, FEF 25-75% had a sensitivity of 100%, specificity 28.20% PPV 71.06% and NPV 100%.

CONCLUSION

As per our study, we found that FEF 25-75% has a high sensitivity and low specificity. 71.06% of subjects who test positive will have COPD and 100% of subjects who test negative do not have the disease, hence its validity in COPD diagnosis is very less compared to FEV1%.

KEYWORDS

Pulmonary function test, COPD, FEF 25-75%, FEV1%.

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BACKGROUND

Spirometry is the best standardized and most reproducible diagnostic test for COPD and should be performed on every individual with suspected COPD. Various studies have concluded the importance of using FEV1% in the diagnosis of airways obstruction.^{1,2} But the task of measuring FVC was found to be physically as well as mentally exhausting for both the patient and the examiner. Thus, it became essential to find out an acceptable surrogate for FEV1% in diagnosis of COPD especially when COPD have grown to be a major

cause of morbidity among the people of both developing and developed countries.^{3,4} A study was conducted based on the spirometric test results of 22767 patients routinely tested in the Children's Hospital of Pittsburgh, the Austin Hospital, the John Hunter Hospital, and the National Research Institute Of Tuberculosis and Lung Diseases. The aim of this study was to determine the advantage of using FEF 25-75% and FEF 75% over FEV1, FVC and FEV1/FVC ratio in detecting airways obstruction. Predicted values and lower limits of normal, were calculated for FEV1, FVC FEV1/FVC ratio, FEF 25-75% and FEF 75% using prediction equations from the Global Lung Function Initiative. The result of the study was that FEF 25-75% was below the normal range in only 2.75% cases when FEV1, FVC and FEV1/FVC ratio were within normal limits. Also, airways obstruction went undetected by FEF 25-75% in 2.9% of cases. The study concluded that maximum mid expiratory flow (FEF 25-75%) do not contribute usefully to clinical decision making on airways obstruction as compared to information from FEV1, FVC and FEV1/FVC ratio.^{5,6,7} The prospect of detecting lung disease, at an early stage has led to widespread measurement of FEF

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Corresponding Author:

Dr. K. P. Venugopal,

*Associate Professor and HOD,
Department of Pulmonary Medicine,
Government Medical College,
Kottayam - 686008, Kerala.*

E-mail: sujavenugopal@gmail.com

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25-75%. However, the greater reproducibility of flows and better sensitivity of FEF 25-75% were also challenged. FEF 25-75% is the mean forced expiratory flow during the middle half of FVC. This is expressed as forced expiratory flow at 25% to 75% of the lung volume. Its value is an indication of the patency of small airways. Our study intends to find the validity of this parameter in COPD diagnosis.^{8,9}

It is hoped that the outcome of this study will provide us with a valid alternative to FEV₁% in the diagnosis of COPD, so that the difficulties faced by the patients and the technicians in the measurement of FVC can be minimized.

Aim

To find out the sensitivity of FEF 25-75% compared to FEV₁% in the diagnosis of COPD.

MATERIALS AND METHODS

Our study attempts to find out the sensitivity of FEF 25-75% and assess if it can be used as a valid alternative to FEV₁% in COPD diagnosis. We decided to study the pulmonary function status of the patients referred to the Pulmonary Function Test (PFT) Laboratory of our Medical College from the Chest Clinic of the same hospital during the months of June and July. A total of 304 subjects were studied (194 COPD and 110 normal). Diagnostic Test Evaluation was the study design used.

Selection of Subjects

This study was conducted from June 1 to August 1 2017. PFT laboratory of our Medical College was the study setting. During this period a total of 304 patients were referred to the PFT lab from the Chest Clinic of the same hospital for spirometric evaluation for respiratory obstruction. Out of this 194 patients were diagnosed of COPD of various degrees and 110 patients were found to be normal. All patients in the age group of 20-60 yrs. who attended the PFT laboratory during the study period were included and the patients with any other respiratory or medical illness were excluded from the study. A total of 221 male patients and 83 female patients were included in the study

Informed Consent

All the patients were referred to the lab for spirometric evaluation. They were familiarized with the PFT machine. Objectives of the study and the procedure of performing spirometry were explained in detail. Also consent was obtained for recording their personal details and spirometric values. All the patients complied to the request and willingly signed the consent form.

Inclusion Criteria

All patients without any other respiratory or medical illness, in the age group of 20-60 yrs., who attended the PFT laboratory for spirometric evaluation during the study period, were included in the study.

Exclusion Criteria

All patients with any other respiratory or medical illness who attended the PFT laboratory for spirometric evaluation during the study period were excluded from the study.

Procedure

Diagnostic test evaluation was the study design used. After obtaining consent, each of the patients were given the proforma. The subjects were seated comfortably in front of the PFT machine. Procedure of the test was demonstrated to each of them and they were taught thoroughly about how to perform the test before the recordings were taken. Subjects were tested while seated, and procedures detailed in the ATS guidelines were followed. Height was measured to the nearest centimetre without shoes, and weight was measured to the nearest kilogram. Particular attention was made to ensure that maximal FEV₁ and FVC efforts were obtained. Three readings of each of the subjects were taken and the best among the three was taken into account. The subjects were provided with a sterile mouthpiece. (Figure 1)



Figure 1

Our Equipment

Equipment selection is very important as accurate spirometric data is essential for the study. Recommendations for spirometer performance and validation have been published by the American Thoracic Society. The instrument used was a computerized spirometer called 'Compact Vitalograph.' Here mouthpiece is attached to a flow resistive pneumotachograph which contain parallel rows of resistive wires. Air forces through this, producing a pressure gradient across the resistive element which is converted into electrical signals and measured by the computer system. Results are displayed on the screen. These can be printed on electro sensitive paper for a permanent record. The system is incorporated with ERS 93 software. The software has the provision to calculate FEF

25-75% in addition to FVC in the same manoeuvre. (Figure 2)



Figure 2

Selection of Tests

A number of criteria should be taken into account while choosing the tests to assess lung function. The tests should be safe, simple, reproducible and easily done by the subject. So the tests should be selected with a view for providing information on different aspects of lung function. A simple method for studying pulmonary ventilation is to record the volume movement of air into and out of lungs, a process called spirometry. A spirogram indicates changes in lung volumes under different conditions of breathing. (Figure 3)

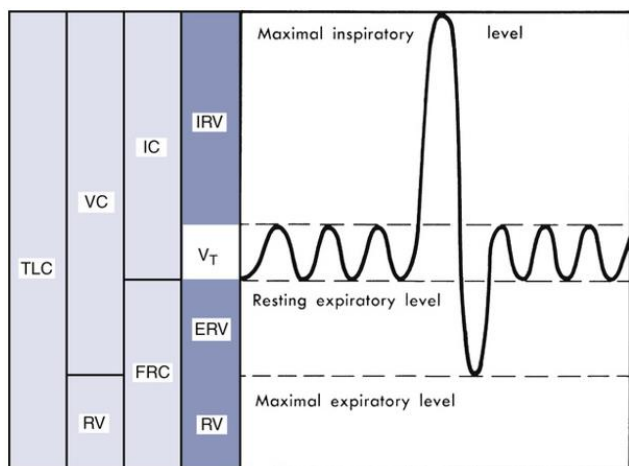


Figure 3

- TLC- Total Lung Capacity.
- IRV-Inspiratory Reserve Volume
- VC- Vital Capacity.
- VT- Tidal Volume.
- RV- Residual Volume.
- ERV- Expiratory Reserve Volume.
- IC- Inspiratory Capacity.
- RV-Residual Volume.
- FRC- Functional Residual Capacity.

For detection of airflow obstruction, the properties of a dynamic lung are studied. Under dynamic conditions, force is not only required to maintain the lung and chest wall at certain volume, but also to overcome the inertia and

resistance of tissues and air molecules. The maximum volume of air that can be exhaled after a maximum inspiration is the Vital Capacity (VC). The normal value of VC in men is about 4 litres and in women, about 3 litres. When expiration is performed as rapidly and as forcibly as possible, the volume is the Forced Vital Capacity. FVC differs very little from VC in the normal subject, but it is proportionately more reduced when there is airway obstruction with air trapping. From FVC, the other important lung functions are obtained: The forced expiratory volume of air exhaled in one second (FEV1) and the maximum mid-expiratory flow rate (FEF 25-75%). (Figure 4)

FEV1% less than 70% of normal is considered as the Gold Standard for the diagnosis of COPD. After recording a few normal tidal respirations, subject inhales to total lung capacity and holds his breath. Then the subject exhales forcefully as maximum as possible. The Graph gives expiratory flow over time in seconds. From the same recording maximum mid-expiratory flow rate (FEF 25-75%) can also be calculated. It is the maximum flow achieved during the middle third of the total expired volume. This is expressed as forced expiratory flow at 25% to 75% of the lung volume. Hence, its value is an indication of the patency of small airways^{10,11,12}

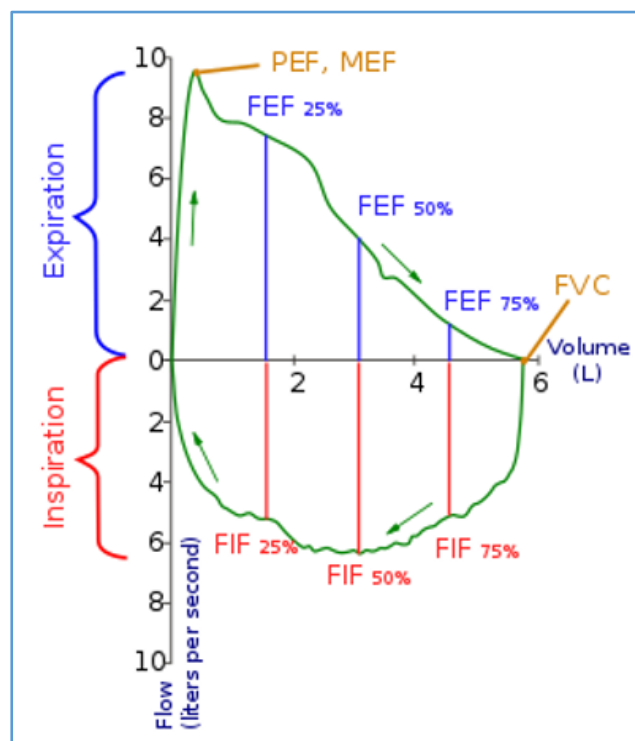


Figure 4

**Pulmonary Mechanics Tests
Forced Vital Capacity (FVC)**

The maximum volume of air that can be exhaled after a maximum inspiration is the Vital Capacity (VC). The normal value of VC in men is about 4 liters and in women, about 3 liters. When expiration is performed as rapidly and as forcibly as possible, the volume is the Forced Vital Capacity. FVC differs very little from VC in the normal subject, but it is proportionately more reduced when there is airway

obstruction with air trapping. The forced expiration causes higher than normal trans pulmonary pressure so that bronchiolar collapse, obstructive lesions and air trapping are all exaggerated. Decreased FVC is common to obstructive conditions like emphysema and bronchial asthma.

Forced Expiratory Volume (FEV_T)

FEV is the volume of air expired over a given time interval during the performance of a forced vital capacity. The time interval is stated in seconds as a subscript to FEV e.g.: -FEV₁, FEV₂, etc. It is normally expressed in litres and time in seconds. Some electronic units compute the FEV_T directly from the exhaled volume or from the instantaneous flow rate by means of appropriate transducers. Since the FEV_T maneuver measures a volume of gas expired over a unit time, it is actually a measure of flow. By assessing the flow at specific intervals, the severity of airway obstruction can be ascertained. Decreased values are common in both obstructive and restrictive patterns.

Forced Expiratory Volume in 1st sec/ Forced Vital Capacity (FEV₁/FVC) %

FEV₁% is the forced expiratory volume for a given interval expressed as a percentage of the forced vital capacity. A normal individual expires 60% of his FVC in 0.5 second, 83% in one second, 94% in 2 seconds and 97% in 3 seconds. Patients with obstructive disease will show a reduced FEV₁% in most cases.

Forced Mid Expiratory Flow Rate (FEF 25-75%)

FEF 25-75% is the mean forced expiratory flow during the middle half of FVC. It was formerly called the maximal mid expiratory flow rate. It is expressed in litre/second. Locating the points on the volume-time curve corresponding to 25% and 75% of the FVC and then passing a straight line through them determine the FEF 25-75%. The slope of this line represents the average rate of airflow over the mid portion of the FVC.^{13,14,15}

Interpretation of Results

Spirometry was performed in the subjects and results were obtained. The proforma was entered with the spirometric data of the subjects. For the vast majority of PFTs, the range of values observed in a population of normal subjects is very broad, making selection of the limits of normal values more difficult. As a rule, the results of PFTs in a particular individual are interpreted with respect to predicted values for normal individuals. Predictive normal values for many of these parameters correlate significantly with selected physical characteristics like age, height, weight, BMI and sex. Regression equations or prediction equations or reference values can be developed from studies of large populations of normal subjects.

Selection of Reference Values

It is essential that care is exercised while selecting prediction equations for clinical use. As the clinical usefulness of decision making is dependent on these predicted values, the

accuracy with which we set the predicted values is important.

Based on the guidelines given by the American Thoracic Society the cut off limit for all the parameters studied under our research were set as 80%. Spirometric values less than 70% for FEV₁% was diagnosed as COPD.

Statistical Analysis

For the entry of statistical data, the computer package used was Microsoft Excel. For analysis SPSS of windows version 10 was used. Cross tabulation of the data was done for FEF 25-75%. Sensitivity and specificity of FEF 25-75% 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.

RESULTS

The results of the study are as follows-

Category	Minimum	Maximum	Mean
Age	25	60	56.67
Height	135	188	161.13
Weight	30	105	55.97
BMI	12.30	33.90	21.59

Table 1. Physical Parameters of the Subjects

The age of the subjects studied is between 25 and 60 years with a mean age of 56.67.

Their height is between 135cm and 188cm, the mean height is 161.13.

The weight of the subjects is between 30kg and 105kg. Mean age is found to be 55.97. The mean BMI of the subjects is 21.59.

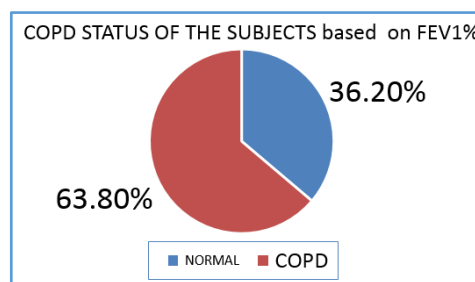


Figure 5

Out of the 304 subjects studied 63.80% are known cases of COPD and 36.20% are normal subjects. (Figure 5)

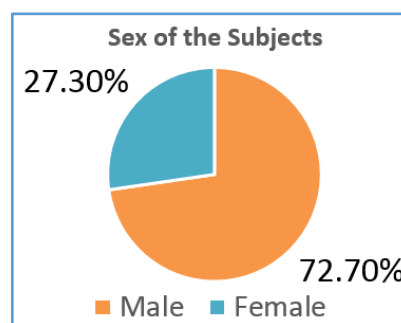


Figure 6

Out of the total 304 subjects, 72.70% are males and 27.30% are females. (Figure 6)

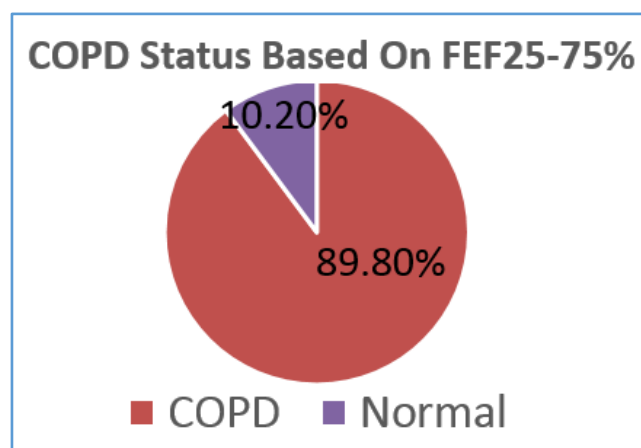


Figure 7

Out of the total 304 subjects studied, 89.80% are diagnosed of COPD and 10.20% as normal based on FEF 25-75%. (Figure 7)

	COPD	Normal
FEF 25-75 < 80%	194	79
FEF 25-75 > 80%	0	31

Table 2. Sensitivity and Specificity of FEF 25-75%

- The Sensitivity of FEF 25-75% is 100%.
- The Specificity of FEF 25-75% is 28.2%.
- The Positive Predictive Value (PPV) is 71.06%
- The Negative Predictive Value (NPV) is 100%.

DISCUSSION

According to American Thoracic Society guidelines for COPD diagnosis, spirometric values less than 70% for FEV1% and less than 80% for FEF 25-75% indicates airway obstruction and is diagnostic of COPD. Sensitivity is defined as the ability of a test to identify correctly all those who have the disease that is 'true positive'. Specificity is defined as the ability of a test to identify correctly those who do not have the disease, who are 'true-negatives'. In addition to sensitivity and specificity, the performance of a screening test is measured by its 'predictive value' which reflects the diagnostic power of the test. The predictive accuracy depends upon sensitivity, specificity and disease prevalence.^{16,17}

A total of 304 subjects referred to the PFT laboratory were studied. Out of the 304 subjects, 194 were diagnosed as COPD and 110 as normal using the Gold Standard spirometric observation 'FEV1%'. Hence, subjects with FEV1% less than 70% are diagnosed as COPD while those with value above 70% are categorized as normal.

Out of the total 304 subjects, 221 (72.70%) are males and 83 (27.30%) are females. So we observed that majority of patients referred to the lab for spirometric evaluation during the study period are males. Hence, the susceptibility

of males more than females to respiratory illness is an area of further research.

We also categorized the 304 subjects using the value of FEF 25-75%. Out of these, 273 subjects (89.8%) came under 'COPD' category and 31 subjects (10.20%) came under 'normal' category. Thus, 79 subjects (25.98%) were misdiagnosed as suffering from COPD. As per our study, FEF 25-75% has a sensitivity of 100%, which means 100% of the diseased people screened by the test has given a true positive result. But the specificity was found to be very low, that is 28.20%, which means only 28.20% of normal subjects screened by the test has given true negative result and 71.80% of normal subjects screened by the test got wrongly classified as COPD subjects. It has a positive predictive value of 71.06% and negative predictive value of 100%. It means that 71.06% of subjects who test positive will actually have COPD and 100% of subjects who test negative actually do not have the disease. As there is a gross disparity between the sensitivity and specificity of FEF 25-75%, the validity of this parameter in diagnosing COPD is very less. Although the spirometric value of this parameter gives a clue to the status of small airways of the subject, its diagnostic efficiency for COPD is extremely poor.

CONCLUSION

Out of the total 304 subjects, 221 (72.70%) are males and 83 (27.30%) are females. So, we observed that majority of patients referred to the lab for spirometric evaluation during the study period are males. Hence, the greater susceptibility of males over females to respiratory illness is an area of further research. As per our results, a gross disparity is seen in the sensitivity and specificity of FEF 25-75%, hence its validity and reproducibility are very less. Also, the variations in predicted and calculated spirometric values and their relationship with the physical measurements of the subject like age, height, weight, BMI etc. also provide a scope for further research.

Summary

Spirometry is a very useful tool to assess lung function and helps in categorising respiratory disease. The Gold Standard for detecting airways obstruction is FEV1%. But the measurement of this parameter can be physically exhausting for older individuals or patients with severe respiratory illness as it requires the patient to empty his or her lungs completely, a process that may take up to 20 seconds. The objective of our research was to study the sensitivity and specificity of FEF 25-75% compared to FEV1% in the diagnosis of COPD.^{18,19,20}

The study was conducted in the Pulmonary Function Test (PFT) Laboratory of our Medical College. PFT data from 304 patients (194 COPD patients and 110 normal individuals) referred to the lab from Chest Clinic of the hospital was studied. The instrument used was a computerized spirometer called 'Compact Vitalograph'. The system is incorporated with 'ERS 93' software. The software has the provision to calculate FEV1 and FEF 25-75% in addition to FVC in the same manoeuvre. The prevalence of

obstruction in the entire study population was 5%. The results obtained were analysed using SPSS software and the sensitivity and specificity was calculated.

As per our study, we found that for the spirometric diagnosis of airways obstruction, FEF 25-75% has a sensitivity of 100%. It has a specificity of only 28.20%. The positive predictive value is 71.06% and the negative predictive value is 100%. It shows a gross disparity in its sensitivity and specificity, hence its validity and reproducibility in COPD diagnosis is very less.

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