

# STUDY OF UTILITY OF FEV1/FEV6 AS A SURROGATE TO FEV1/FVC IN DIAGNOSIS OF COPD

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## Abstract

*Introduction :* COPD remains underdiagnosed in primary health care ,it is due to underutilization of spirometer,which is essential in the diagnosis of COPD.High cost of equipment,need of technically trained personnel to perform spirometry,limited availability contribute lo lack of spirometry in rural areas.Where as some people have difficulty in reaching FVC in spirometry.. It was found that 6 seconds was sufficient to obtain 99% of FVC even for spirograms with FEV1/FVC as low as 50%.

*Aim :* To evaluate the utility of FEV1/FEV6 ratio as a surrogate to FEV1/FVC in diagnosis of COPD,To emphasize the importance of FEF25-75 L/s as an early predictor of COPD.

*Methods , materials :* Study was done on 40 symptomatic patients suspected to have COPD based on clinical,radiological history attending our hospital fulfilling inclusion and exclusion criteria.patients are subjected to PFT by COSMED spirometer.Post bronchodilator FEV1, FEV6, FVC and ratios ,FEV1/FVC and FEV1/FEV6, FEF25-75(L/s) are taken from COSMED spirometry report of tested patients.in our study we compared the utility of post bronchodialator FEV1/FEV6 to gold standard FEV1/FVC in aiding the diagnosis of copd .

*Results :* Out of 40 patients , 37 were diagnosed to have COPD by post bronchodialator FEV1/FVC and 38 by post bronchodialator FEV1/FEV6.Area under curve was obtained was 0.892,The Youden's index was highest at the cut off 0.65 with 100% sensitivity and 86.4 % specificity.

*ROC curve was constructed comparing FEF25-75 l/s to FEV1/FVC. AUC obtained was 0.968.FEF25-75(L/s) < 0.7 had 100% sensitivity and 72% specificity.*

*Conclusion:* Our study concludes that FEV1/FEV6 can be used as a surrogate to FEV1/FVC in diagnosis of COPD. Best cutoff obtained in my study was 0.65.FEF 25-75% can be used as early marker of COPD even if the lung functions are normal thereby predicting the development of COPD

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## I. Introduction/ Background

COPD is now one of the top 3 causes of mortality worldwide and 90 % of these deaths occur in low and middle income countries.<sup>(1)</sup>Global burden is increasing due to continued exposure to risk factors and the aging of population <sup>(2)</sup>.COPD must be considered in patients with signs of dyspnea,chroniccough,sputum production and history of exposure to risk factors for the disease.COPD remains underdiagnosed in primary health care ,it is due to underutilization of spirometer,which is essential in the diagnoosis of COPD<sup>(3)</sup>.High cost of equipment,need of technically trained personnel to perform spirometry,limited availability contribute lo lack of spirometry in rural areas.

Spirometry is a test which always require patient effort and cooperation.the effort to reach FVC is difficult for some patients. As FVC measurement requires the patient to empty lungs completely which may take upto 20 seconds and this can be exhausting for older patients or patients with severe respiratory disease. Also, FVC has a problem of being dependent on the expiratory time which may be increased in COPD.These difficulties encountered in FVC measurement have raised an interest in finding an alternative for FVC, the one which requires shorter exhalation and which offers a discrete end of test criterion. It was found that 6 seconds was sufficient to obtain 99% of FVC even for spirograms with FEV1/FVC as low as 50%. The National Lung Health Education Program proposed using FEV6 and FEV1/FEV6.FEV6 means the amount of air exhaled during whole 6 seconds of spirometry test. FEV1/FEV6 has been proposed as a convenient alternative to FEV1/FVC in the diagnosis of COPD with good reproducibility and sensitivity. The measurement of FEV1/FEV6 can be done by handheld devices like COPD 6 device which is of low cost and needs little training, hence can be made easily available in peripheral settings.FEV6 measurement has a number of advantages, including being easier to perform (using less sophisticated and inexpensive handheld spirometers) and reduction in spirometry complications (such as syncope)<sup>(4-6)</sup>

My study emphasizes the importance of FEV1/FEV6 in diagnosis of COPD. FEV1/FEV6 can be obtained with handheld spirometry which is of low cost compared to the original non portable spirometry, hence can be made easily available in primary care settings. Also, FEV6 can be easily executed for patients and it needs little training for performing technician and there is a reduction in total duration of spirometry test thus decreasing spirometry complications compared to FVC.

### **AIMS AND OBJECTIVES OF THE STUDY**

To evaluate the utility of FEV1/FEV6 ratio as a surrogate to FEV1/FVC in diagnosis of COPD. To determine a fixed cut off of FEV1/FEV6 corresponding to FEV1/FVC < 0.70 for the diagnosis of airflow obstruction.

To emphasize the importance of FEF25-75 L/s as an early predictor of COPD.

### **MATERIALS AND METHODS**

Study design: Hospital based cross sectional study.

Study period: September 2019 –August 2021.

Study setting: Government hospital for chest and communicable diseases, Visakhapatnam, Andhra Pradesh.

Study Population: Patients presenting with symptoms suggestive of COPD attending Government hospital for chest and communicable diseases, Visakhapatnam, Andhra Pradesh.

Sample Size: A total of 40 patients are included in the study.

Sampling technique: Non probability convenient sampling technique.

#### **INCLUSION CRITERIA:**

Patients between age group 40 to 75 years.

Patients willing to participate in the study.

Patients with symptoms suggestive of COPD like cough, expectoration, shortness of breath, wheezing, history of exposure to risk factors for the disease.

#### **EXCLUSION CRITERIA:**

Patients <40 years of age and > 75 years of age.

Patients with acute exacerbation of COPD

Patients with contraindications for spirometry like thoracic or abdominal surgery, myocardial infarction, eye surgery in past 3 years.

Chest radiograph showing parenchymal opacity, mass, scar, cavities.

Patients with other significant respiratory diseases.

Patients not willing to participate in the study.

#### **METHODOLOGY:**

Patients with symptoms suggestive of COPD fulfilling the inclusion criteria are taken into the study.

After taking the informed consent, demographic data, clinical history, comorbidities were noted. A thorough general and systemic examination was done. Routine investigations like CBP, LFT, RFT, CHEST XRAY PA view, sputum CBNAAT were done. Based on the comorbid conditions and clinical history, patients were subjected to specific investigations like ECG, 2D ECHO, HRCT chest, sputum for gram stain and culture sensitivity. All the patients included in the study were subjected to spirometry.

### **STUDY PROCEDURE:**

#### **SPIROMETRY:**

Spirometry is used for objective measurement of airflow limitation. Spirometer is the machine used to record spirometry. COSMED Pulmonary Function Testing (PFT) equipment is used. Post bronchodilator FEV1, FEV6, FVC and ratios, FEV1/FVC and FEV1/FEV6, FEF25-75(L/s) are taken from COSMED spirometry report of tested patients. The device is calibrated every morning using 3 L syringe to ensure that it reads accurate values.

Method of performing spirometry:

The patient is asked to sit straight, with head erect. The patient is asked to hold the mouth piece tightly between lips. Nose clip is kept in place. Initially the patient is asked to breathe in and out at tidal volume (VT) to record tidal flow volume loop. Then the patient is instructed to inhale maximally to TLC and then exhale as fast and as completely as possible to record FVC. The patient is then instructed to inhale fully to TLC to record IVC. Post bronchodilation spirometric reading was taken 15 minutes after the application of 400 mcg salbutamol through spacer.

Spirometry was done according to ATS guidelines. ATS guidelines include both acceptability and reproducibility criterion.

Acceptability:

ATS mandates acceptable maneuvers:

1) Good Start of the test. If the study needs back extrapolation, the extrapolation volume should not exceed

5% of FVC or 150ml whichever is larger.

2) Smooth FV curve free of artifacts.

Artifacts include:

a) Cough during the 1st second of exhalation may significantly affect FEV1

B) Variable effort

C) Glottis closure

D) Early completion of the effort

E) Air leak- Loose tube connections could be the source of air leak or usually, it's because the patient's lips aren't tightly wrapped around the mouthpiece.

3) Good end of the test:

A) Plateau of VT curve of at least 1s

B) Reasonable duration of the effort (FET)-Six seconds is the minimum accepted duration.

C) The patient cannot or should not continue to exhale.

Reproducibility:

After obtaining three acceptable maneuvers, the following reproducibility criteria should be applied:

The two largest values of FVC must be within 150ml of each other.

The two largest values of FEV1 must be within 150ml of each other.

The final values are chosen based on

1) Highest value of FEV1 and FVC from any acceptable/reproducible trial.

2) Based on best test curve.

3) If reproducibility cannot be achieved after eight trials, best test curve is reported.

Reference Values:

The 5th percentile is used to define lower limit of reference range for given age, sex, height and race.

In my study diagnosis of COPD was based on post bronchodilator FEV1/FVC < 0.70 as per GOLD guidelines 2022.

### Analysis

Statistical methods: Statistical analysis, both descriptive and inferential, was performed, in the present study. Results on continuous measurements are presented on mean $\pm$ SD and results on categorical measurements are presented in numbers (%). Scattered plot was performed to find out the correlation between FEV1/FVC and FEV1/FEV6. ROC curve analysis has been performed to find the predictability of study variables for predicting the outcome.

Diagnostic values based on Area under curve:

0.9-1.0 Excellent test

0.8-0.9 Good test

0.7-0.8 Fair test

0.6-0.7 Poor test

0.5-0.6 Fail

Statistical software: The statistical software namely SPSS 17 was used for analysis of the data and Microsoft word and Excel has been used to generate graphs, tables etc.

## II. Discussion :

Out of 40 patients included in the study males were 30 (75%) and females were 10(25%). Majority of the patients belonged to age group between 50-70 years. Mean age of my study population is  $58.55 \pm 8.665$ . In my present study mean height of the patients was  $157 \pm 0.08$  m, and mean weight was  $55.9 \pm 11.3$  kgs and mean BMI was  $22.25 \text{ kg/m}^2$ . Farmers (42.5%) contributed to most of my study population followed by labourers (27.5%).

All the patients in my study had shortness of breath (100%) at presentation to hospital. Cough with expectoration was the next common symptom (87.5%) observed in my study followed by wheezing. In my present study most common chest X-ray finding observed was bilateral hyperinflation (50%), followed by irregular radiolucency (17.5%) and normal chest x-ray (17.5%). Thickened bronchial walls were seen in 10%, and bullae were seen in 2.5%

**Table :1 ,EXOSURES ,HABITS IN COPD PATIENTS**

Personal Habits/ Exposures	Frequency (n)	Percentage
Smoking	29	68
Alcohol	17	42.5

Air pollution	2	5
Biomassfuel exposure	5	12.5
Occupational exposure	4	10

Out of 40 patients in my study 29 patients were current /ex-smokers. Among the exposure history biomass fuel exposure was seen in 5 patients (12.5%).52 % were mild smokers,27% were moderate smokers,21 % were heavy smokers.

Out of total 40 patients taken into the study the diagnosis of COPD was confirmed in 37 patients by spirometry based on post bronchodilator FEV1/FVC.

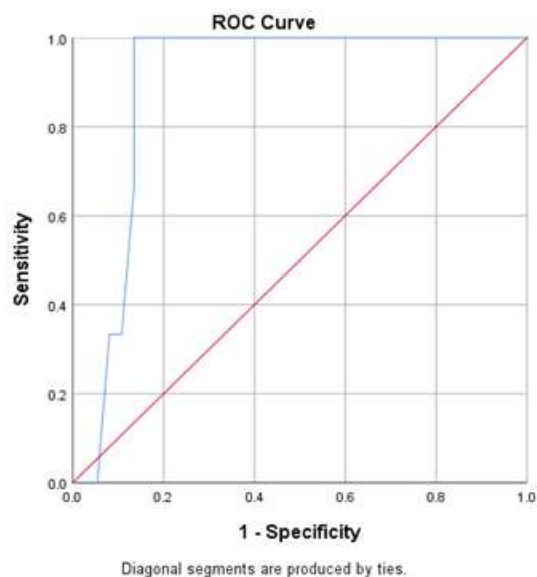
**Table :2,GOLD STAGES OF AIRFLOW LIMITATION IN COPD BASED ON FEV1 FEV1%**

GOLD Severity Stage	Frequency(n)	Percentage
1	4	10 %
2	12	32.5%
3	16	42.5%
4	5	15%
Total	37	100%

Post bronchodilator mean FEV1 obtained in my study was 1.114 L, mean FEV6 obtained in my study was 1.864 L and mean FVC obtained in my study was 2.010 L. The post bronchodilator mean FEV1/FVC and FEV1/FEV6 obtained in my study were 54.29% and 56.55% respectively

Using post bronchodilator FEV1/FEV6 proportion of < 70% as diagnostic method, the diagnosis of COPD was made in 38 patients (95%). Using post bronchodilator FEV1/FVC proportion < 70% as per GOLD guidelines the diagnosis of COPD was made in 37 patients (92.5%).

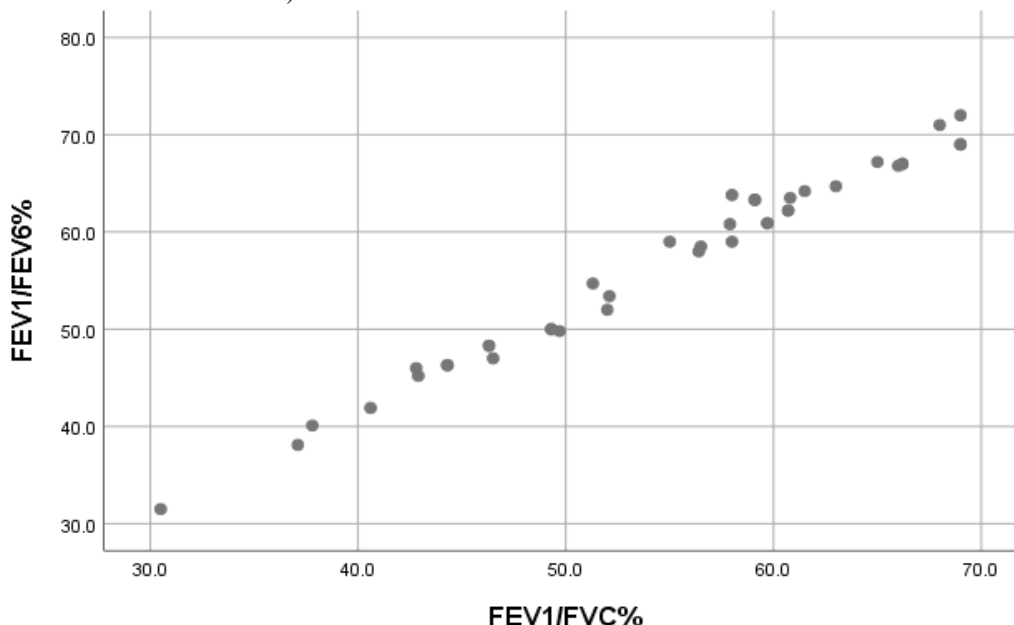
**FIGURE :1 ,RECEIVER OPERATOR CHARACTERISTIC CURVES (ROC CURVE) FOR FEV1/FEV6 RATIO COMPARED TO FEV1/FVC**



Area under curve was obtained was 0.892 when FEV1/FEV6 is compared against the gold standard FEV1/FVC which implies that FEV1/FEV6 can be used as an alternative parameter to diagnose obstructive lung disease. The Youden's index was highest at the cut off 0.65 with 100% sensitivity and 86.4 % specificity.

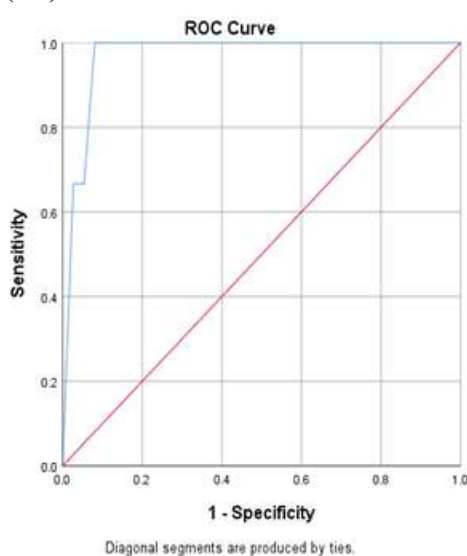
ROC curve can predict the diagnostic accuracy of the study. In my study considering FEV1/FVC<0.7 as gold standard ,ROC was constructed for FEV1/FEV6 ratio comparing with gold standard FEV1/FVC ratios.

The curve showed an excellent diagnostic accuracy with AUC of 0.892 and standard error of 0.051. This implies that FEV1/FEV6 can be applied as a good alternative to FEV1/FVC in diagnosis of COPD. In a study by F.W. Rosa et al on efficacy of FEV1/FEV6 the AUC obtained was 0.98. In a study by Anupam Kumar Singh and Amit Lohia on FEV1/FEV6 the AUC obtained was 0.99. In another study by Surya P Bhatt et al on FEV1/FEV6 the AUC obtained was 0.99

**FIGURE : 2 ,CORRELATION OF FEV1/FVC AND FEV1/FEV6**

There is a positive correlation between FEV1/FVC and FEV1/FEV6 which can be evidenced from the scatter plot above. In my study a scattered plot between FEV1/FEV6 and FEV1/FVC showed a positive correlation. Similar findings of positive correlation was observed in studies done by F.W. Rosa et al, Anupam Kumar Singh and Amit Lohia, Fernando Luiz Cavalcanti Lundgren et al, done on FEV1/FEV6 comparison with FEV1/FVC.<sup>(7-9)</sup>

**FEF 25-75L/s:** It is the flow over the middle half of FVC. It is the average flow from the point where 25% of the FVC has been exhaled to the point where 75% of the FVC has been exhaled. FEF 25-75% measures the airflow in peripheral airways. The peripheral airways are primarily affected in COPD. Hence low FEF 25-75% can be used as early marker of COPD even if the lung functions are normal thereby predicting the development of COPD.

**FIGURE : 3,RECEIVER OPERATOR CHARACTERISTIC CURVES (ROC CURVE) FOR FEF25 - 75 (L/s)RATIO COMPARED TO FEV1/FVC**

In my study the mean FEF25-75 L/s obtained was  $0.5703 \pm 0.30$  L/s ROC curve was constructed comparing FEF25-75 l/s to FEV1/FVC. AUC obtained was 0.968 with 95% confidence interval which shows an excellent predictability in diagnosing the disease. FEF25-75(L/s) < 0.7 had 100% sensitivity and 72% specificity.

Considering FEF25-75 < LLN as low FEF25-75 all the 40 patients had low 25-75 but the spirometric diagnosis of COPD using FEV1/FVC < LLN as low FEF25-75 all the 40 patients had low 25-75 but the spirometric diagnosis of COPD using FEV1/FVC < 0.7 was made in 37 patients. As the remaining 3 patients had abnormal FEF25-75 they have future chance of developing COPD in next 10 years. Thus FEF25-75% is Used as an early marker for COPD.

### III. Conclusion :

Our study concludes that FEV1/FEV6 can be used as a surrogate to FEV1/FVC in diagnosis of COPD. The ROC curve drawn confirms that FEV1/FEV6 can be used as an alternative to diagnose airway obstruction.

In my study the best cutoff obtained was 0.65 which is different from the findings of other studies on FEV1/FEV6 probably because of the low sample size. As its measurement can be done by simple handheld device which is of low cost it can be used in primary care to detect undiagnosed airway obstruction in patients with symptoms of COPD.

My study also concludes that FEF25-75% can be used as early predictor for the disease development

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