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The significance of FEV1 and FEV1/FVC in COPD diagnosis

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Abstract

Objectives: The forced expiratory volume in the first second (FEV1) and FEV1/FVC ratio alone is limited in its ability to expose COPD's complexity. Given the heterogeneity of the affected population, the use of additional pulmonary function tests (PFTs) in the routine clinical evaluation of COPD patients may be beneficial.

Methods: A total of 598 male individuals aged 25-80+ years were recruited for this study. Spirometry testing was conducted using the SPIROVIT SP-1G2 device manufactured by SCHILLER Switzerland, in accordance with the American Thoracic Society criteria for spirometry. High-intensity interval training (HIIT) was used to evaluate the impact of exercise on respiratory function and dyspnea experienced by COPD patients.

Results: Participants in this study were defined as Non-smoker and healthy if they reported never smoking and did not have asthma, bronchitis, angina pectoris, myocardial infarction, or stroke. FEV1% predicted and FVC% predicted were calculated using the Norwegian equation developed by Langhammer and co-workers. Independent samples T-tests were employed to examine the statistical significance of group differences. The mean and the 5% percentile of FEV1/FVC% were compared with the expected mean and lower limit of normal (LLN) using an equation developed by Enright and co-workers. The statistical analyses were performed using SPSS 16.0 for Windows (SPSS Inc, Chicago, Illinois, USA).

The study results indicated that there was a continuous increase in chances of any respiratory symptom as FEV1/FVC ratios increased and FEV1 in men ≤ 50, reaching a minimum of 0.85 and 0.90, respectively, in all participant characteristics. This would suggest a higher optimal threshold associated with respiratory symptoms than the commonly used threshold of 0.70. Conversely, the chances of any respiratory symptom continued to decrease with lower FEV1/FVC ratios and FEV1 in men >50 and reached a minimum of 0.66 and 0.75, respectively, in all participant characteristics, suggesting a lower optimal threshold associated with respiratory symptoms than the commonly used threshold of 0.70.

Conclusion: Incorporating additional PFTs beyond FEV1 and FEV1/FVC is crucial for a comprehensive evaluation of COPD patients and can lead to more personalized and targeted care.

Keywords: COPD, FEV1, FV1/FVC, GOLD Threshold

1. Introduction

The Global Initiative for Obstructive Lung Diseases (GOLD) recommends using a fixed ratio of FEV1/FVC < 0.70 to diagnose chronic airflow limitation (Cui *et al*., 2019). However, the suggested cut-off limits for this ratio range between 0.60 and 0.75, with many researchers stating that the fixed threshold of 0.70 is based on expert opinion rather than population-based evidence (Cui *et al*., 2019).

The underlying assumption is that this limit is a clinically useful marker of increased morbidity and mortality. There is a lack of population-based evidence to support that the exact threshold < 0.70 for the FEV1/FVC ratio is the most discriminative limit for prediction of morbidity and mortality (Johannessen *et al*., 2005b).

There are limitations to the use of FEV1 alone as a diagnostic tool for COPD (Maldonado-Franco *et al*., 2023). One such limitation is over-diagnosis in older patients as a result of using a fixed FEV1/FVC ratio as a diagnostic cutoff, as their measured FEV1/FVC values may be within the normal range for their age and health status (Vaz Fragoso *et al*., 2016). Conversely, using the fixed FEV1/FVC ratio may result in underestimating the presence of COPD in younger patients, as their measured values may fall within the normal range despite having the disease (Torén *et al*., 2021).

FEV1 measurement alone as a diagnostic tool for COPD also has limitations, including its insensitivity to early-stage COPD. Because small airway narrowing is not yet extensive in early-state COPD, FEV1 measurement may not be an accurate marker of airway obstruction (Kakavas *et al*., 2021). Additionally, FEV1 measurement only provides information on the first second of forced exhalation, during which small airways experience substantial distending forces, meaning that small airway obstruction may not be noted unless extensive narrowing is present (Medbø and Melbye, 2007).

Pulmonary function tests (PFTs) are important tools for COPD phenotyping and individualized care. These tests can provide additional information beyond FEV1 measurement and help guide treatment decisions (Bestall *et al*., 1999).

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Examples of PFTs that contribute to COPD phenotyping and individualized care include diffusion capacity measurements (DLCO), which can help assess the extent of gas exchange abnormalities in COPD patients and guide treatment decisions and field and cardiopulmonary exercise testing (Haynes *et al*., 2023). These tests provide dynamic physiological information and can reveal abnormalities in patients who present with normal spirometry but report respiratory discomfort when engaged in various activities. They can also assess exercise capacity and peak oxygen uptake, which correlates with survival in COPD patients (Bhatt et al., 2019; Bhatt *et al*., 2014).

Another such example is a forced oscillation technique, which measures respiratory impedance and can provide information about airway resistance and lung mechanics. It can be useful in assessing small airway dysfunction in COPD patients. Other PFTs that may contribute to COPD phenotyping and individualized care include lung volume measurements, airway resistance measurements, and bronchodilator responsiveness testing (Lange *et al*., 2016).

Pulmonary function tests (PFTs) can provide a more comprehensive evaluation of COPD patients beyond FEV1 and FEV1/FVC ratio measurement, allowing for a better understanding of the underlying pathophysiological processes and functional profiles. These tests can also help tailor medical management for the specific needs of each patient, thereby optimizing patient care and improving clinical outcomes (Pierson, 2006).

This paper discusses the limitations of the fixed ratio approach for diagnosing chronic airflow limitation (CAL) and the need for alternative thresholds. We are concerned about over-diagnosis and misclassification, particularly in older and younger adult males, where both old individuals with normal lung function but lower FEV1/FVC ratio and FEV1 and young individuals with lung disease and higher FEV1 and FEV1/FVC ratio may be included in the CAL category.

Also, this paper highlights the ongoing debate between the fixed ratio approach and the lower limit of normal (LLN) approach for defining CAL, with the LLN approach considering significant deviation from normality using equations based on different populations.

2. Methods

2.1. Sample size

A total of 598 male individuals were recruited for the purpose of this study.

2.2. Study population

Subjects aged 25-80+ years were recruited. After a thorough explanation of the experiment, each participant provided informed consent. The subjects were asked to fill out questionnaires about their medical history to ensure they had no serious conditions and were a good fit for our study.

2.3. Protocol

We used High-intensity interval training (HIIT) to evaluate the impact of exercise on respiratory function and dyspnea in patients with COPD. All the participants were instructed to perform six cycles of high intensity rebounding for 90 seconds, followed by 60 seconds of recovery (Rawashdeh and Alnawaiseh, 2018a).

2.4. Examinations

Spirometry testing was conducted using the SPIROVIT SP-1G2 device manufactured by SCHILLER Switzerland, in accordance with the spirometry criteria established by the American Thoracic Society (Rawashdeh and Alnawaiseh, 2018b).

The participants were seated, wearing a nose clip, and instructed to exhale for at least six seconds, or as long as possible. They were also asked to take a complete inspiration before inserting the provided mouthpiece. It was necessary to exhale at least three times. The difference in FEV1 and FVC between the best and next best should not be larger than 5% or 200 ml (Medbø and Melbye, 2007).

2.5. Statistical analysis

Using a variety of factors, including sex, age, smoking behaviors, and reported lung and cardiovascular disease, our study utilized the following methods to analyze spirometric results and symptoms:

- Participants were considered healthy non-smokers if they had never smoked and had never had asthma, bronchitis, angina pectoris, myocardial infarction, or stroke.
- FEV1% predicted and FVC% predicted were calculated using the Norwegian equation developed by Langhammer and co-workers (Langhammer *et al*., 2001).
- Independent samples T-tests were conducted to see if there were statistically significant differences between groups.
- The mean and the 5% percentile of FEV1/FVC% were compared with the expected mean and lower limit of normal (LLN) using an equation developed by Enright and co-workers (Enright *et al*., 1993).
- The statistical analyses were performed using SPSS 16.0 for Windows (SPSS Inc, Chicago, Illinois, USA).
- The Ethics Committee/ Mutah University/School of medicine/ Al-Karak, Jordan approved this study, and all participants provided written informed consent.

3. Results

Spirometry was performed in 598 individuals, and the results were analyzed. In men aged 50 or younger. Regardless of age, smoking status, or disease, the predicted mean FEV1% was less than 90% and the predicted FVC% was greater than 90% for all age groups. However, the FEV1/FVC ratio was less than 85%, which decreased significantly with increasing age, regardless of smoking behaviors and any kind of disease (P=0.001 in Table 1).

In men older than 50, the predicted FEV1% was less than 75%, and the predicted FVC% was greater than 75%, which decreased significantly with increasing age (P=0.001 in Table 1). Moreover, the FEV1/FVC ratio was less than 66%, which decreased significantly with increasing age, regardless of smoking behaviors and any kind of disease (P=0.001 in Table 1).

Individuals who reported chronic pulmonary disease had significantly lower lung function measures than those not reporting pulmonary or cardiovascular disease

(P=0.001, Table 1). Furthermore, there was a strong association between reports of cardiovascular illness and decreased lung function in men (P=0.001 in Table 1).

Table 1. Results from spirometric test on 598men, by age, smoking status, reported diseases, and healthy men who never smoked.

Age group	FEV1 % Predicted Mean	FVC % Predicted Mean	FEV1/FVC % Mean
Mean	78.81	82.84	72.84
25-35	88.7	92	84.8
36-40	87.7	91.6	82.8
41-50	85.1	90.2	82.3
51-60	74.7	79.1	65.98
61-70	73.5	78.5	65.50
71-80	72	75.5	64.6
80+	70	73	63.9
Smoking behaviors			
Never Smoked	88	93	78
Ex-Smoker	77	78	72
Flow –Smoker	70.3	75	66
Revealed cardiovascular illness			
Myocardial infarction	78	79	72.5
Angina pectoris	76	80	71.2
Revealed Pulmonary illness			
Asthma	69	71.1	67.4
Chronic Bronchitis	68	74	67.5
Non-smoker and healthy	89	92	77

Of the 598men, 30.86% were aged 50 or younger, while 68.99% were older than 50. Asthma and bronchitis have been recorded. 5% and 3% of men, respectively, while cardiovascular diseases were reported by 3.59% for myocardial infarction and 2% for angina pectoris. The percentage of Never Smoked was 41.75%, former smokers were 3.67%, and flow smokers were 15%. Non-smoker and healthy accounted for 26.35% of the total population (Table 2).

Table 2. Characteristics of the participants in the study

Age (years)	%
25-35	11.6
36-40	12
41-50	7.26
51-60	15.56
61-70	30.63
71-80	8.8
80+	14
Smoking behaviors	
Never Smoked	41.75
Former smokers	3.67
Flow smokers	15
Pack-Years smoked	
<10	12
10-19	11
20-29	13
30+	14
Revealed cardiovascular illness	
Myocardial infarction	3.59
Angina pectoris	2
Revealed Pulmonary illness	
Asthma	5
Chronic bronchitis	3
Non-smoker and healthy	26.53

In Table 3, regardless of smoking behaviors or pulmonary and cardiovascular disease, the incidence of FEV1/FVC ratios <70% and FEV1 <80% increases with age. The frequency is around three times higher among men over 50 years of age who currently smoke than men aged 50 or younger (81.5% and 26%, respectively) (p=0.001) who currently smoke. In Never Smoked over 50 years of age, the incidence of FEV1/FVC ratio <70% and FEV1<80% is five times higher than those aged 50 or younger (53% and 10%, respectively) (p=0.001). The frequency of FEV1/FVC ratio <70% and FEV1<80% among Non-smoker and healthy over 50 years of age is around five times higher than in Non-smoker and healthy aged 50 or younger (54.5% and 12%, respectively) (p=0.001).

Table 3. The percentage of FEV1/FVC 70% and FEV1 80% across all groups, based on age, smoking behaviors, reported disease, and healthy nonsmokers.

Age group	Non-smoker and healthy	Never Smoked	Flow smokers	Pulmonary disease	Cardiovascular disease
25-35	5	3	23	13	11
36-40	11	9	25	14	12
41-50	20	18	30	15	13
51-60	40	38	72	15	15
61-70	48	41	80	16	15
71-80	60	60	86	18	16
80+	70	73	88	20	17

Using FEV1/FVC < 66% and FEV1 < 75% to diagnose COPD in individuals over 50 years of age can significantly reduce the prevalence of COPD. Specifically, the prevalence of COPD would decrease from 81.5% to 40.75% in flow smokers, from 54.5% to 27.25% in Non-smoker and healthy, from 53% to 30.5% in Never Smoked

s, from 17% to 12% in pulmonary disease, and from 15.75% to 11% in cardiovascular disease (P = 0.001-0.005 in Tables 3 and 4). These findings suggest that using a lower threshold for the FEV1/FVC ratio may be more appropriate for diagnosing COPD in older individuals, as the FEV1/FVC ratio declines with age.

Table 4. Percentage (%) of FEV1/FVC< 66 % and FEV1 < 75 by age, smoking behaviors, reported sickness and for the Non-smoker and healthy among men > 50 years.

Age group	Non-smoker and healthy	Never Smoked	Flow smokers	Pulmonary disease	Cardiovascular disease
51-60	20	25	36	11	10
61-70	24	27	40	12	11
71-80	30	33	43	13	11
80+	35	37	44	14	12

While utilizing FEV1/FVC < 85% and FEV1 < 90% to analyze COPD in people under 50 years old, the commonness of COPD would increment from 26% to 36% in flow smokers, from 14% to 22% in pneumonic illness, and from 12%to 22.6% in cardiovascular sickness s(P = 0.001-0.004) (Tables 4 and 5). However, there would be no change in the prevalence of COPD in healthy smokers or Never Smoked. These findings suggest that using a lower threshold for the FEV1/FVC ratio may not be appropriate for diagnosing COPD in younger individuals.

Table 5. Percentage (%) of FEV1/FVC< 85% and FEV1 <90% in men 50 years of age by age, smoking behaviors, reported disease, and for the healthy never smoker.

Age group	Non-smoker and healthy	Never Smoked	Flow smokers	Pulmonary disease	Cardiovascular disease
25-35	7	3	35	20	20
36-40	10	9	36	22	22
41-50	20	18	37	25	26

Table 6 provides evidence supporting the use of a lower threshold in men older than 50 and a higher threshold in men aged 50 or younger for defining COPD. Specifically, the odds for any respiratory symptom, such as dyspnea, decreased with a lower threshold FEV1<75% and FEV1/FVC<66% in men older than 50. Conversely, the odds for any respiratory symptom, such as dyspnea, increased with higher FEV1<85% and FEV1/FVC<95% in men ≤ 50.

Table 6. Observed dyspnea by age group, smoking behaviors, and illnesses.

Age group (years)	Dyspnea Non-smoker and healthy	Dyspnea in Never Smoked	Dyspnea flow smokers	Dyspnea in pulmonary disease	Dyspnea in cardiovascular disease
25-35	5	2	33	22	20
36-40	11	8	35	24	23
41-50	19	17	37	26	25
51-60	22	27	38	12	10
61-70	26	29	42	13	11
71-80	32	35	45	15	12
80+	37	39	46	17	13

Numbers given in %.

4. Discussion

The ongoing investigation discovered that lung capability measures; for example, FEV1% predicted and FVC% predicted are affected by both increasing age and a smoking behavior. This suggests that these factors can contribute to decreased lung function over time. The use of percentages to calculate the predicted values allowed for a more accurate comparison of lung function across different individuals and groups (Table 1) (Medbø and Melbye, 2007).

Moreover, the study found that individuals who reported chronic pulmonary or cardiovascular disease had significantly lower lung function measures compared to those who reported neither pulmonary nor cardiovascular disease (Enright *et al*., 1993, Ramalho *et al*., 2021). This suggests that chronic pulmonary and cardiovascular disease can significantly impact lung function, regardless of age or other factors. Table 1's presentation of these findings enabled for a clear and concise comparison of lung function measures across different groups.

These findings underscore the importance of maintaining healthy lung function through lifestyle choices and disease management. By understanding the factors that can contribute to decreased lung function, individuals can take steps to protect their respiratory health and prevent the development of chronic pulmonary disease (Rawashdeh and Alnawaiseh, 2018a, 2018b).

The study also revealed a significant drop in the FEV1/FVC ratio after the age of 50, and FEV1/FVC<70% and FEV1<80 was more common in older men than those aged 25–50 years (Table 3). The relative increase in frequency in all age groups was markedly higher among flow smokers than Non-smoker and healthy, indicating that smoking has a significant impact on the FEV1/FVC ratio and FEV1, as well as reported pulmonary and cardiovascular disease. However, it is uncertain whether the increase in incidence among healthy smokers with age represents an increase in COPD prevalence or simply the natural aging process (Johannessen *et al*., 2005b; Light and George, 1983).

According to our study, being a smoker is the most significant risk factor for developing COPD. Flow smokers

were significantly more likely to have FEV1/FVC < 70% and FEV1 < 80 than Non-smoker and healthy or Never Smoked s in all age groups (Table 3). Furthermore, a fifty percent decline in lung function can be explained in part by structural changes in the airways that occur with age, such as alveolar dilatation and loss of supporting tissue in the peripheral airways known as "senile emphysema" (Lundbäck *et al*., 2003a, Schneider *et al*., 2021).

Another characteristic of normal aging is muscle atrophy and decreased physical endurance (Hayes *et al*., 2023). Furthermore, the elderly have co-morbidities that might affect lung function, particularly pulmonary and cardiovascular illness, which are known to be related with lower spirometry values, including, in severe cases, the FEV1/FVC ratio and FEV1 (Lundbäck *et al*., 2003b)

Our study provides evidence supporting the use of a lower threshold in men older than 50 and a higher threshold in men aged 50 or younger for defining COPD. Specifically, the odds for any respiratory symptom, such as dyspnea, decreased with a lower threshold FEV1<75% and FEV1/FVC<66% in men older than 50 (Tables 4 and 6). Conversely, the odds for any respiratory symptom, such as dyspnea, increased with higher FEV1<85% and FEV1/FVC<95% in men aged 50 and younger (Tables 5 and 6)

There has been criticism of the use of the fixed ratio approach for diagnosing COPD due to concerns about overdiagnosis and misclassification. Specifically, over-diagnosis may occur in men older than 50, leading to the inclusion of individuals with normal lung function but lower FEV1 and FEV1/FVC ratios. This is because the fifth percentile for the ratio falls below 0.70 near age 45, which means that older patients may be misdiagnosed with airway obstruction if their FEV1/FVC falls below 0.70(Enright *et al*., 1993). Estimates of COPD over-diagnosis due to the fixed ratio ranged from 4.6% to 42.7% in different studies (Ekström *et al*., 2019).

Misclassification in men aged 50 and younger can occur due to the possibility that they are experiencing structural changes in the lungs and their increased respiratory morbidity and mortality is being classified as normal due to higher FEV1 and FEV1/FVC ratios. This is because FEV1 declines more rapidly than FVC with aging, leading to age-dependent decline in FEV1/FVC in healthy, non-smoking, elderly (Lundbäck *et al*., 2003a).

Our study highlights the limitations of using FEV1 and FEV1/FVC ratio alone for diagnosing COPD, as well as the need for additional pulmonary function tests to complement these measurements to provide a more comprehensive assessment of COPD patients. The ongoing debate between using a fixed ratio approach or the lower limit of normal (LLN) approach for defining CAL is discussed in several studies. The LLN approach takes into account reference equations developed from different normal populations and considers significant deviation from normality (Ekström *et al*., 2019; Lundbäck *et al*., 2003b).

In contrast, the fixed ratio approach assumes a certain airflow limitation is normal regardless of age, gender, or body size (Ekberg-Aronsson *et al*., 2005). The flow study suggests that the LLN approach may be more in line with statistical theory and should be further evaluated.

5. Conclusion

Our study highlights the need for further research to evaluate alternative thresholds, such as the LLN approach, for defining CAL and to investigate the clinical implications of different FEV1/FVC ratios and FEV1 in terms of respiratory morbidity and mortality. Incorporating additional PFTs beyond FEV1 and FEV1/FVC is crucial for a comprehensive evaluation of COPD patients and can lead to more personalized and targeted care.

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