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Forced expiratory volume in the third second and its derivatives for diagnosis of airway obstruction in obese patients

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Abstract

Background

Spirometry is a simple diagnostic tool for pulmonary diseases, as obstructive pulmonary disorders, especially in obese. Obesity is an increasing worldwide public health concern that contributes to many respiratory problems that affect both large and small airways. The traditional use of forced expiratory volume in the first second (FEV1) and FEV1/forced vital capacity (FVC) in defining large-airflow obstruction may be confined not only by the limitation of FVC maneuver, but also by the long time to reach plateau flow rate in geriatrics and in patients with moderate-to-severe airflow obstruction. FEV3 and its derivatives FEV1/FEV3 and FEV3/FVC are used for better diagnosis of obstruction, especially in deteriorated patients who cannot blow for more than or equal to 6 s even after their best trials. Regarding small-airway obstruction, FEV3/FEV6 abnormality may be used to diagnose it in the early stages, especially with obesity.

Aim

To compare the accuracy of FEV3, FEV1/FEV3, and FEV3/FEV6 with that of FVC, FEV1/FVC, and forced expiratory flow (FEF) 25–75% as indices for large-airway and small-airway obstruction in obese persons, in order to replace the ordinary spirometric maneuvers that are easier to perform.

Patients and methods

In this study, 95 patients were enrolled. All participants were classified according to BMI into normal, overweight, and obese groups. FEV1, FEV3, FEV6, FVC, FEV1/FVC%, FEV1/FEV3%, FEV3/FVC%, and FEV3/FEV6% were determined.

Results

Fifty participants were males, 52.63%, and 45 were females, 47.37%. Acceptable accuracy of FEV1/FEV3 test for diagnosis of large-airway obstruction, if compared with FEV1/FVC. While FEV3/FVC test showed less-satisfied accuracy. FEV3/FEV6 failed to show an acceptable accuracy for diagnosis of small-airway obstruction when compared with FEF25–75%. Regarding the effect of BMI on spirometric values, FEV1/FVC (P = 0.027), FEV1/FEV3 (P = 0.029), and FEF25–75% (P = 0.002) were more significant in obese patients than overweight patients or normal participants. No differences in FEV3/FVC and FEV3/FEV6 were found among the various groups studied.

Conclusion

Targeting obese persons, FEV3 and its derivatives as FEV1/FEV3 and to a lesser extent FEV3/FVC can be used as substitutes for FVC and FEV1/FVC, respectively, for evaluation of large-airway obstruction, while FEV3/FEV6 cannot identify people with small-airflow obstruction.

Keywords: Airway, obesity, obstruction, pulmonary function, spirometry

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Introduction

Spirometry is a procedure used as a diagnostic tool for respiratory diseases, including obstructive pulmonary disorders such as asthma or chronic obstructive pulmonary disease [1]. It is used to monitor progression of lung disorders and response to treatment [2]. It is also suggested as part of the diagnostic workup in patients with supposed as chronic obstructive pulmonary disease or asthma by the American Thoracic Society/European Respiratory Society [3].

The principal indices of spirometry are forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), and FEV1/FVC. In obstructive pulmonary disorders, both small and large airways are influenced. FEV1 mainly reflects large-airway obstruction, while the later fraction of forced expiration reflects small-airway impact [4]. FEV1 less than 80% of the expected value in conjugation with FEV1/FVC less than 70% indicates the presence of airway obstruction [5], while small-airway dysfunction was specified if forced expiratory flow (FEF) 25–75% was lower than 80% [6].

The traditional use of FEV1 and FEV1/FVC in defining airflow obstruction may be restrained not only by the limited maneuver of FVC, but also by the long time taken to reach plateau flow rate, especially in geriatrics and in patients with moderate-to-severe airflow limitation [7].

FEV3 and FEV6 are the second most commonly studied dependable parameters as an alternative to FVC. They are easier because patients are not required to perform maximum end expiration [8]. FEV3 attends its clinical validity for better interpretation of reversibility, especially in deteriorated patients who cannot blow for more than or equal to 6 s even after their best trials [9]. Isolated FEV3/FEV6 abnormality can also be used to diagnose small-airway obstruction in the early stages before emphysematous changes are recognizable [3].

Obesity is one of the most important problems worldwide as it has been associated with many common diseases. It is usually assessed by using BMI, which is a reflection of weight and height [10]. There are obvious mechanical effects of obesity on pulmonary function affecting both large and small airways [11]. To investigate the effect of obesity on the respiratory system, many researchers use the effectiveness of pulmonary-function tests [10].

Identifying alteration in the lung function resulting from obesity is useful since many of these alterations can be reversed by treating obesity in terms of physical exercise, diet regimen, or by surgical treatment of obesity [12].

Aim

The aim of this study was to compare the accuracy of FEV3, FEV1/FEV3, and FEV3/FVC with that of FVC and FEV1/FVC as indices for large-airway obstruction and compare FEV3/FEV6 with FEF25–75% for detection of small-airway obstruction in obese persons, in order to surrogate the usual spirometric maneuvers with others that are easier to perform.

Patients and methods

Patients and study design

This is a cross-sectional study, including 95 inpatients and patients from the chest clinic of Ahmed Maher Teaching Hospital, aged between 14 and 80 years. Participants were provided verified consents and completed a healthy questionnaire about height, weight, smoking status, and medical history. They must be cooperative, and physically and mentally fit. Patients that reported restrictive lung disorders or complained of severe cough or dyspnea were excluded from this study. Pregnant or lactating women and patients using systemic corticosteroid were hindered from the study.

Ethical approval

Local ethical committee approval was obtained from GOTHI (General Organization for Teaching Hospitals and Institutes) with approval number: HAM00135. Patients who accept joining this study signed a well-informed consent form before implying in the study. The study was conducted according to the principles expressed in the Declaration of Helsinki.

Anthropometric evaluation

Anthropometric measurement was performed by well-trained personnel. Height and weight were measured according to recommendations of the International Biological Program [13]. Height was measured to the nearest 0.1 cm using a Holtain portable anthropometer, and weight was determined to the nearest 0.01 kg using a Seca Scale Balance, with the patient wearing minimal clothes. Then, BMI was calculated using the formula:

$$\text{BMI} = \left(\text{weight kg} / \text{height m}^2\right).$$

Normal BMI was defined as less than 25 kg/m^2, overweight as BMI more than 25 kg/m^2, and obesity as BMI more than 30 kg/m^2 for both men and women [14].

Pulmonary-function tests

Pulmonary-function test was done using computerized spirometer (BTL-08 Spiro). Individuals underwent the spirometric test in the sitting position, wearing a nose clip. Three fixed techniques were used for the test. The procedure must be done without air to leak from around the mouthpiece. The flow, volume/timed graphs were taken out in accordance with the criteria predicted by the American Thoracic Society. Flow-volume curves were considered acceptable when forced expiratory time more than 6 s or an obvious plateau in the volume–time curve (end-of-test criterion) without cough, glottis closure, or other significant interruptions.

According to the Global Initiative for Chronic Obstructive Lung Disease criteria for the diagnosis of obstructive pulmonary disease, FEV1/FVC less than 70% as a fixed ratio indicates large-airway obstruction. The severity of airway obstruction was evaluated on the basis of FEV1 expressed as % predicted: mild (>70%), moderate (60–69%), moderately severe (50–59%), severe (35–49%), and very severe (35%) [14].

Study design

All participants were classified according to BMI into normal, overweight, and obese groups. FEV1, FEV3, FEV6, FVC, FEV1/FVC%, FEV1/FEV3%, FEV3/FVC%, and FEV3/FEV6% were determined for each participant. FEV3/FEVC and FEV3/FEV6 values of 95% were taken as the lower limit of these spirometric indices for the diagnosis of an obstructive pattern, while FVC and FEV3 values of 80% were taken as the lower limit of them [15].

Correlation was done between the traditional way of detection of large-airway obstruction by FEV1/FEVC and newer ratios such as FEV1/FEV3 and FEV3/FVC, then another correlation between FEF25–75% and FEV3/FEV6 for detection of small-airway obstruction [16]. Hansen and colleagues redefined the lower limit of normal for FEV3/FEV6 and FEV3/FVC to improve identification of airway obstruction.

Statistical analysis

All data were collected, tabulated, and statistically analyzed using Statistical Package for Social Sciences (SPSS), version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as the mean ± SD and minimum–maximum, and qualitative data were expressed as absolute frequencies (number) and relative frequencies (percentage). One-way analysis of variance was used to compare the normally distributed variables among the three groups of weight. Kruskal–Wallis test was used to compare between them of non-normally distributed variables. Mann–Whitney *U* test was used to compare between each of the two groups of obesity. Receiver-operating characteristic curve and the kappa test were used to detect the diagnosis accuracy of the spirometric parameters used. All tests were two-sided. *P* value (two-tailed) less than 0.05 was considered statistically significant.

Results

Ninety five inpatients and patients from the chest clinic of Ahmed Maher Teaching Hospital were included in this study. Fifty of them were males, 52.63%, and 45 patients, 47.37%, were females as shown in Fig. 1.

Participants' age ranged from 14 to 85 (mean ± SD, 50 ± 15.3 years) and most of them (41.1%) ranged from 50 to 61 years. Among those, 70% were nonsmokers, while others smoked about 4 ± 10 cigarettes. No significant differences in smoking were detected between normal, overweight, or obese groups (Tables 1 and 2).

Regarding diagnosis of large-airway obstruction, different spirometric parameters are compared in Table 3. FEV1/FV3 showed an acceptable accuracy for diagnosis of large-airway obstruction, when compared with FEV1/FVC. While FEV3/FVC showed less acceptable accuracy.

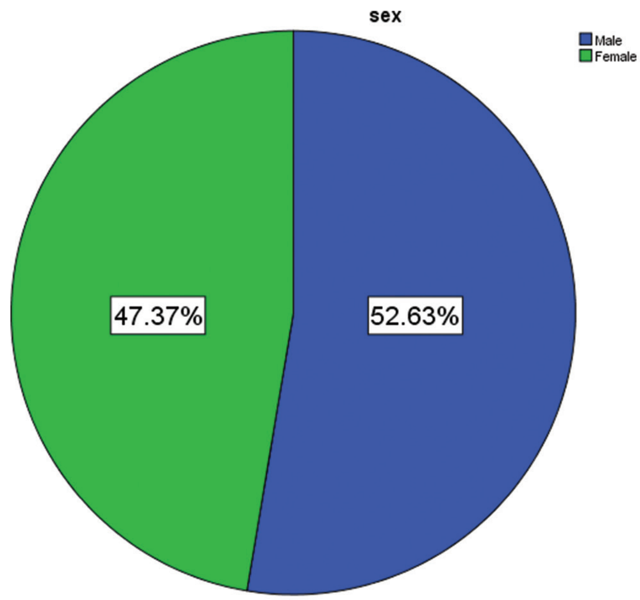

Figure 1: Sex distribution.

Regarding diagnosis of small-airway obstruction, FEV3/FEV6 was used in comparison with FEF25/75% (Table 4). FEV3/FEV6 failed to show an acceptable accuracy for diagnosis of small-airway obstruction.

FEV1/FEV3 can be used as an alternate parameter for FEV1/FVC, for diagnosis of large-airway obstruction evaluations (Table 5). While FEV3/FVC showed less-satisfied specificity value. However, FEV3/FEV6 could not be recommended as a substitute parameter for FEF25/75% in the diagnosis of small-airway obstruction evaluations.

Receiver-operating characteristic curves

Spirometric parameters	AUC
FEV3/FVC test	0.807
FEV1/FEV3 test	0.928
FEV3/FEV6 test	0.701

Figs. 2 and 3 show that FEV1/FEV3 has excellent quality as a diagnostic test for large-airway obstruction more than FEV3/FVC test. While FEV3/FEV6 failed to be considered as a diagnostic test for small-airway obstruction (Table 6).

Regarding the effect of BMI on spirometric values, no differences in FEV1, FVC, and FEV3 were found between normal participants, overweight, and obese patients. FEV1/FVC (P = 0.027), FEV1/FEV3 (P = 0.029), and FEF25–75% (P = 0.002) were more significant in obese patients than overweight patients or normal participants. No differences in FEV3/FVC and FEV3/FEV6 were found among the various groups studied.

As shown in Fig. 4, no differences in all studied spirometric parameters were found between overweight and obese patients. Also, no differences were found between overweight patients and normal participants, except for FEF25–75%. FEF25–75% only increased in overweight patients than in normal participants ($P = 0.043$). FEF25–75%, FEV1/FEV3, FEV1/FVC, and FEV1 ($P = 0.000$, 0.009, 0.009, and .01, respectively) were significantly higher in obese patients than in normal participants. No difference in other spirometric variables was found.

Table 1: Demographic characteristic features of studied patients (*n*=95)

Mean (SD)	Frequency	Percent
Age mean (SD)=50 (15.3)		
14	2	2.1
15-26	6	6.3
27-38	15	15.8
39-49	14	14.7
50-61	39	41.1
62-73	15	15.8
74-85	4	4.2
Height mean (SD)=166.5 (8.5)		
145	1	1.1
146-157	9	9.5
158-170	45	47.4
171-182	38	40.0
183-194	2	2.1
Sex		
Male	50	52.6
Female	45	47.4
Weight mean (SD)=83.7 (29.3)		
Normal weight	30	31.6
Overweight	33	34.7
Obese	32	33.7
Cigarettes' numbers mean (SD)=4 (10)		
0	67	70.5
1-12	16	16.8
13-24	7	7.4
25-36	2	2.1
37-48	2	2.1
49-60	1	1.1

Table 2: Demographic characteristics of groups according to BMI (*n*=95)

	Normal weight *n*=30, Mean (SE)	Overweight *n*=33, Mean (SE)	Obese *n*=32, Mean (SE)	*P*
Weight	59.6 (1.21)	78.3 (1.56)	111.8 (5.8)	<0.001*
Height	167.6 (1.43)	169.0 (1.36)	162.8 (1.54)	0.026*
Cigarettes' numbers	6.80 (2.80)	2.58 (1.20)	3.06 (1.24)	0.307

One-way ANOVA was used to compare the normally distributed variables among the three groups of weight. Kruskal–Wallis test was used to compare between them for non-normally distributed variables. *$P<0.05$ was considered statistically significant among the three groups of weight. (Normal weight: BMI <25, Overweight: BMI ≥25, Obese: BMI ≥30)

Discussion

Preserving lung function in early adult life is important to prevent chronic respiratory diseases, which represent a serious public health problem around the world. There is consistent evidence showing that obesity in adulthood has detrimental effect on lung function [17].

Spirometry is a simple and affordable test that permits measuring the impact of any disease on pulmonary function, monitoring disease progress, identifying the results of therapeutic interventions, and assessing preoperative risk [3]. As an artificial breathing maneuver, spirometry depends on motivation and the ability to cooperate that needs understanding of the examination, sufficient coordination, and a minimal degree of mobility. These requirements are not always sufficiently present in pediatric, geriatric, and obese patients [18].

Lung function is impressed with many factors, such as age, sex, obesity, and smoking status [10]. Obesity as per WHO is defined as 'the abnormal or excessive collection of the fat in the body to the extent that the health is impaired.' Once a nutritional disorder, it is now considered an epidemic even in developing countries [19].

The accumulation of fat in the body affects respiratory physiology, with consequent deterioration of various pulmonary-function parameters [20]. It is known that obese patients have higher risk of respiratory impairments such as dyspnea and airway dysfunction [21]. The relationship between BMI, as a measure of adiposity and lung-function parameters, has conflicting results from different studies [22].

In this study, we classified patients into three groups according to weight category, most of normal-weight participants were at 27–38 years, whereas most of overweight participants were at 50–61 years. However, most of obese participants

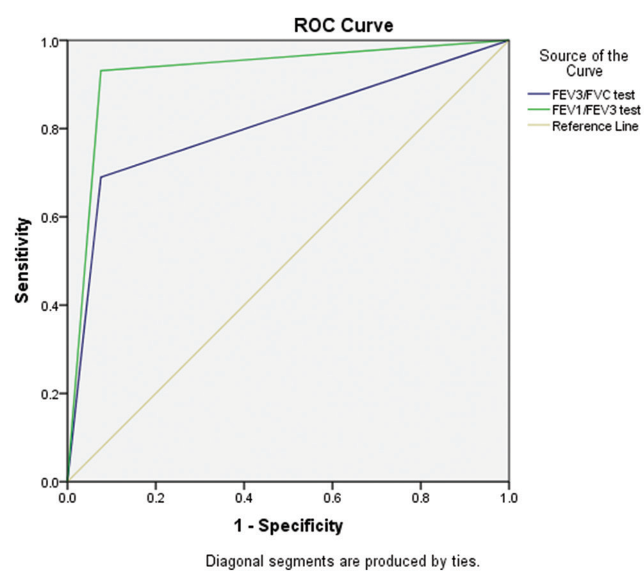

Figure 2: FEV3/FVC and FEV1/FEV3 curve. FEV, forced expiratory volume; FVC, forced vital capacity.

Table 3: Comparison of spirometric tests for diagnosis of large-airway obstruction

Count	FEV1/FVC		Kappa value	P
	Normal spirometry	Abnormal spirometry		
FEV3/FVC	61	9	0.639	0.000
	5	20		
FEV1/FV3	61	2	0.831	0.000
	5	27		

FEV, forced expiratory volume in the first second; FVC, forced vital capacity.

Table 4: Comparison of spirometric tests for diagnosis of small-airway obstruction

Count	FEF25/75 test		Kappa value	P
	Normal spirometry	Abnormal spirometry		
FEV3/FEV6 test	41	27	0.388	0.000
	3	24		

FEF, forced expiratory flow; FEV, forced expiratory volume.

Table 5: Sensitivity, specificity, positive predictive value, and negative predictive value for spirometric parameters

Parameters of accuracy	FEV3/FVC	FEV1/FEV3	FEV3/FEV6
Sensitivity	92.42	92.42	93.18
Specificity	68.97	93.10	47.05
PPV	87.14	96.82	60.29
NPV	80.00	84.37	88.89

FEV, forced expiratory volume; FVC, forced vital capacity; NPV, negative predictive value; PPV, positive predictive value.

Table 6: Summary characteristics and spirometry tests variables in subjects.

	Normal weight n=30, Mean (SE)	Overweight n=33, Mean (SE)	Obese n=32, Mean (SE)	P
FEV1	1.84 (.15)	2.12 (.16)	2.25 (.16)	0.189
FVC	2.57 (.19)	2.70 (.17)	2.68 (.16)	0.849
FEV3	2.41 (.18)	2.61 (.17)	2.61 (.16)	0.614
FEV6	2.58 (.20)	2.69 (.17)	2.73 (.16)	0.814
FEV1/FVC	71.4 (2.89)	76.9 (2.43)	81.8 (2.13)	0.027*
FEV3/FVC	94.7 (1.66)	96.2 (.88)	97.3 (.63)	0.838
FEV1/FEV3	76.2 (2.06)	79.7 (2.06)	84.9 (2.19)	0.029*
FEV3/FEV6	94.4 (1.78)	96.5 (.90)	95.7 (1.6)	0.993
FEF25–75%	55.5 (5.95)	78.7 (7.44)	97.6 (8.95)	0.002*

One-way ANOVA was used to compare the normally distributed variables among the three groups of weight. Kruskal–Wallis test was used to compare between them for non-normally distributed variables. *P<0.05 was considered statistically significant among the three groups of weight. BMI=body mass index, FEF25-75=forced expiratory flow at 25-75%, FEV1=force expiratory volume in first second, FVC=force vital capacity, SEM=standard error of the mean.

were at 50–61 years. No differences in all studied spirometric parameters were found between overweight and obese patients.

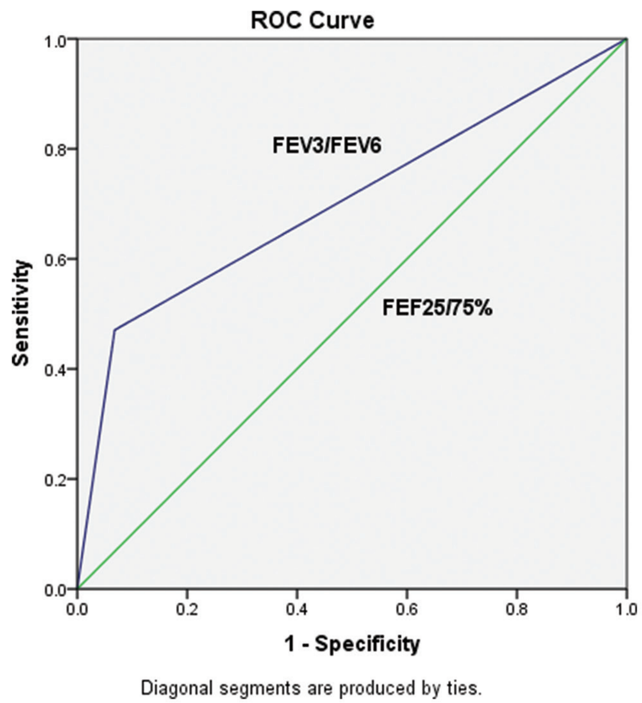

Figure 3: FEV3/FEV6 curve. FEV, forced expiratory volume.

While Lang *et al*. [23] found that the effect of overweight status was considered a minor risk and was not associated with higher risk of asthma. However, obesity was a significant risk factor and was a notable contributor to incident asthma.

Airway obstruction in obese individuals presents a diagnostic obstacle [24]. In the presence of abnormal airflow by spirometry, it may be difficult to differentiate between the effects of increased body size and intrinsic airway disease [25]. In the absence of airway obstruction, obesity influences respiratory-system mechanics through mechanical effect of excess body weight compressing the respiratory system [26].

To the best of our knowledge, this is the first study comparing the accuracy of FEV3, FEV1/FEV3, and FEV3/FVC with that of FVC and FEV1/FVC indices for large-airway obstruction. At the same time, comparing FEV3/FEV6 with that of FEF25–75% as an index for small-airway obstruction in obese persons.

Regarding large-airway obstruction, American Thoracic Society/European Respiratory Society criteria postulated that FVC testing requires a forced expiratory time of more than 6 s or a plateau in the volume–time curve. This often needs a relatively long time to exhale, especially for patients with severe airway limitation, elder patients, obese, and those with severe cough [27].

On the other hand, shorter expiratory time causes FVC underestimation and FEV1/FVC overestimation that may result in false-negative interpretation in patients with mild-airway obstruction [28]. Although the fixed FEV1/FVC ratio as a measure of large-airway obstruction has been established by many researchers and remains the standard diagnostic criterion due to its simplicity, it should be employed carefully [29].

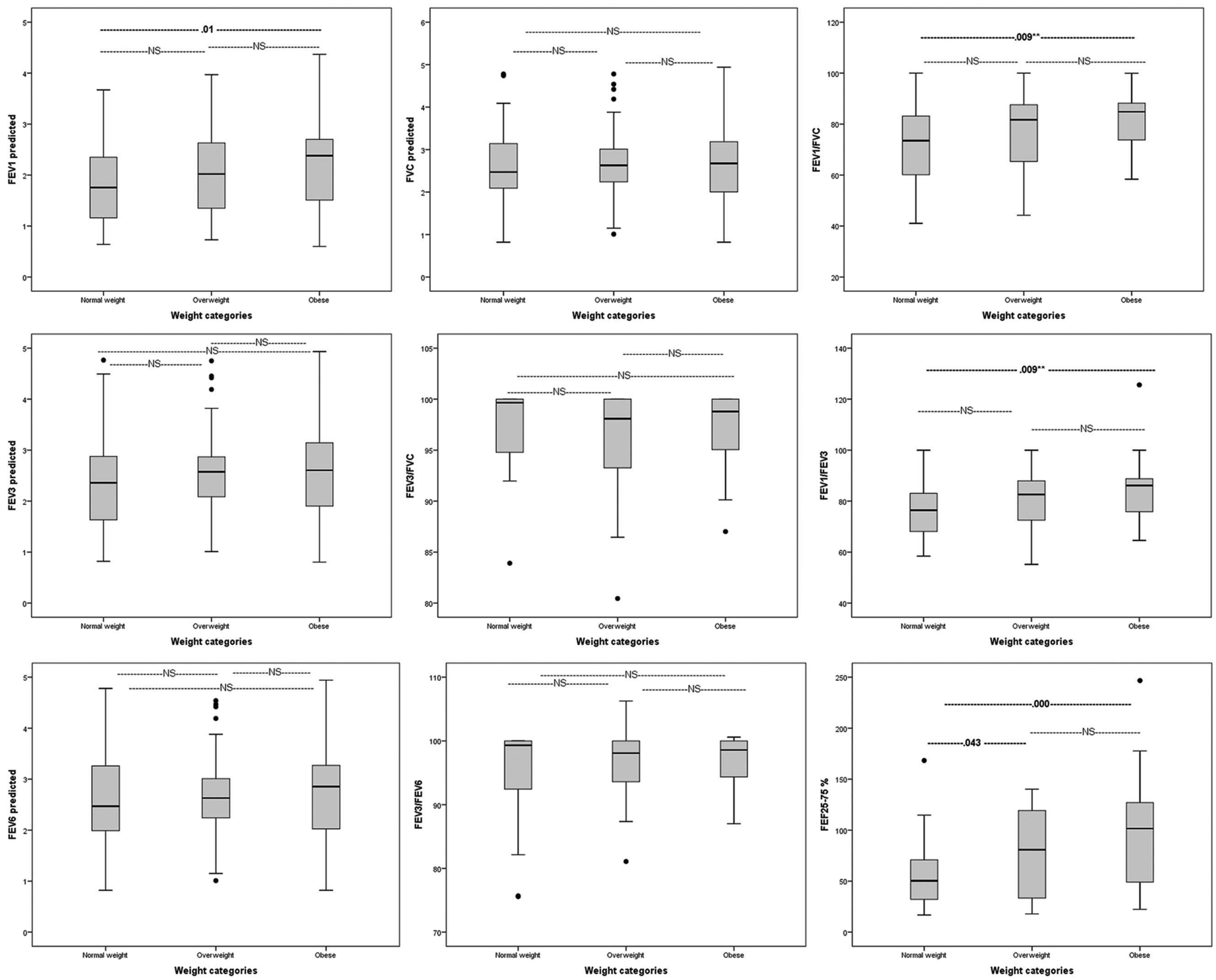

Figure 4: Correlation between spirometric parameters and BMI.

The FEV3 is the rapidly exhaled volume during the first 3 s of a FEV, is reproducible, needs shorter expiratory effort, and provides an accurate outcome. Studies have reported that FEV3 could be considered as a prospective substitute for FVC [7]. FEV3/FVC is influenced by the airflow velocity in both the central and peripheral airway, normally 95% or greater in adults [6]. Some studies have found FEV3 to have acceptable sensitivity and specificity in identifying airflow obstruction, while others have found that its sensitivity is almost low, although specific [30].

In the present study, no differences in FEV1, FVC, and FEV3 were found between normal participants, overweight, and obese patients. Jizar *et al*. [1] had the same opinion, there was no significant difference between FVC and FEV3. These results agree with Pellegrino *et al*. [31] and Demir *et al*. [32] who found that measurement of FEV3 has been proposed as an alternative to the usual forced expiratory maneuver FVC. It is less exhausting for participants to attain, and could minimize the risk of syncope.

In the present study, an acceptable accuracy of FEV1/FEV3 for the diagnosis of large-airway obstruction was detected when compared with FEV1/FVC. While FEV3/FVC showed less-satisfied accuracy. As a result, FEV1/FEV3 can be used as an alternate parameter for FEV1/FVC with excellent quality as a diagnostic test for large-airway obstruction more than FEV3/FVC test.

Vice versa, Pellegrino *et al*. [33] postulated that FEV1/FEV3 could not be recommended as substitute parameters for FEV1/FVC due to low sensitivity and Mehrparvar *et al*. [15] mentioned that FEV1/FEV3 was unsuccessful to show satisfactory accuracy for obstructive lung-disease diagnosis.

Small-airway dysfunction is commonly missed by spirometry and the ratio of FEV1 to FVC is frequently normal [34]. Patients with small-airway obstruction suffer from dysfunction, even though their FEV1 is within the normal range [35].

Obese patients will manifest enhanced small-airway dysfunction as compared with healthy participants [23].

It appears that spirometric abnormalities in patients with mild-to-moderate obesity may be related to small-airway collapse secondary to decreased lung volumes with obesity, or it may be independent [36].

FEF25–75% as a measure for small-airway disease could be falsely low in individuals with obesity and could therefore overdiagnose obstructive airway diseases [37]. One main limitation of FEF25–75% is that it depends on FVC and lung capacity [38].

In our study, FEV3/FEV6 test was used for the diagnosis of small-airway obstruction in comparison with FEF25/75%. FEV3/FEV6 failed to show an acceptable accuracy for diagnosis of small-airway obstruction.

FEV3/FEV6 failed to be considered as a diagnostic test for small-airway obstruction, so it could not be recommended as a substitute parameter for FEF25/75% in the diagnosis of small-airway obstruction evaluations. While Yee *et al*. [39] postulated that there remains a need to identify measures of small-airway disease, believed to be an early pathological lesion in obstructive lung diseases. FEV3/FEV6 has been proposed as a measure of early airflow obstruction.

Graham *et al*. [3] found that participants in whom FEV3/FEV6 was the sole abnormality had significantly greater gas-trapping percentage without significantly greater emphysema percentage, so isolated FEV3/FEV6 abnormality can be used to diagnose chronic airway obstruction in the early stages before emphysematous destruction is detectable. Stringer *et al*. [40] postulated that isolated FEV3/FEV6 abnormalities can be considered to be a diagnostic tool for early detection of chronic airway obstruction.

Lam *et al*. [7] found that FEV3, and its derivatives FEV3/FVC and FEV3/FEV6, are useful adjuncts to FEV1 and FEV1/FVC in identification of airflow obstruction. They could be used to complement, and not to substitute, the standard parameters of FEV1/FVC in the diagnosis of airflow obstruction.

Özbey *et al*. [41] postulated that it would be suitable to refer obese patients with airway obstruction to nutrition and diet clinics for adequate diet control, as decreasing body weight will help in reducing the symptoms and improving quality of life.

Conclusion

FEV3 and its derivatives such as FEV1/FEV3 and to a lesser extent FEV3/FVC can be used as an alternate to FVC and FEV1/FVC, respectively, for evaluation of airway obstruction in obese persons. FEV3/FEV6 cannot identify people with small-airflow obstruction, especially obese persons.

Reference values for FEV3 and its derivatives need to be established for the local population before these parameters, namely FEV3/FVC and FEV1/FEV3 can be tested for performance in the prediction of airflow obstruction.

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Conflicts of interest

There are no conflicts of interest.

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