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Evaluation of Superiority of FEV1/VC Over FEV1/FVC for Classification of Pulmonary Disorders

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ABSTRACT

Introduction: Forced expiratory value in one score (FEV1)/ Forced vital capacity (FVC) was used in classical literature for primary classifications of pulmonary disorders. American Thoracic Society/ European Respiratory Society guidelines recommended using FEV1/VC instead of FEV1/FVC. The aim of study was determination of the extent of superiority of FEV1/VC over the FEV1/FVC.

Materials and Methods: Two hundred seven subjects whom suffered from different pulmonary disorders were evaluated by standard spirometry, lung volume and Carbon mono-oxide lung diffusion capacity (DLCO). Accuracy of FEV1/VC and FEV1/FVC for diagnosing lung disease was compared by area under the ROC curve, sensitivity and specificity analysis including Kraemer efficiency and likelihood ration methods. Gold standards were diagnosis confirmed by over-all clinical and para-clinical judgment.

Results: Primary classification of FEV1/FVC and FEV1/VC according to gold standards showed that FEV1/FVC detected obstructive and restrictive lung disease better than FEV1/VC. FEV1/FVC was able to detect the obstructive and restrictive lung disease correctly in 61% and 34% and FEV1/VC in 56% and 33% respectively. FEV1/FVC showed 100% agreement with forced expiratory flow (FEF)=25-75%, and Maximum expiratory flow (MEF)=50% but this agreement for FEV1/VC was 95-96%. Accuracy assessments revealed the superiority of FEV/FVC in the likelihood ratio method. Also, based on the ROC curve and Kraemer's coefficient, more accurate results were obtained by FEV1/FVC, compared to FEV1/VC.

Conclusion: FEV1/FVC showed marginally higher accuracy for detecting lung disease than FEV1/VC.

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Introduction

Spirometry is one of the most useful tools for screening, diagnosis, staging and, follow up of patients in pulmonary medicine. Several different approaches were introduced for interpretation of spirometry results but value of forced expiratory volume in one second (FEV1), forced vital capacity (FVC) and FEV1/FVC were the most popular approach in classical literatures and in practice (1). In this approach subjects who show low FEV1 (less than 80% predicted) are considered as sick subjects whom may suffer from either obstructive or restrictive lung disease, at that point they should evaluate for FEV1/FVC ratio in which FEV1/FVC ratio less than 70% (less than 5% of lower limit) considers as obstructive and higher results considers as

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restrictive pattern. "Tiffeneau and Pinelli" introduced FEV1 per vital capacity (VC) in 1947 as a substitution for FEV1/FVC (2). They claimed that FVC during FVC maneuver is usually underestimated due to inability of patients to complete exhale of their lung volume. VC is usually easier maneuver and estimate the lung volume better than FVC therefore FEV1/VC is more accurate than FEV1/FVC for evaluation of obstructive disease. This suggestion is widely used in American thoracic society/European respiratory society guidelines for interpretation of pulmonary function tests (3). Here the question of study was outstretched "Had clinical studies approved the preference of FEV1/VC over FEV1/FVC?" Our search in literature about the studies evaluated this hypothesis in clinical practice was not very conclusive and limited results were found. The aim of this study was to evaluate the accuracy of FEV1/VC and FEV1/FVC for diagnosis and classification of pulmonary disease in clinical practice and to determine the extent of different and benefit from FEV1/VC compare to FEV1/FVC.

Materials and Methods

Patients

Two hundred seven subjects (113 female and 94 male) with average age of 50±15.4 years who complained of dyspnea and cough from different pulmonary diseases were enrolled in this study. Pulmonary function tests and other para-clinical studies were indicated by lung specialists according to the underlying diseases and the necessity of diagnostic work up were discussed to patients and all subjects were signed informed consent. All the subjects with inconclusive clinical diagnosis, un-cooperated subjects and pulmonary function test result of mixed pattern were excluded from study.

Methods

This is a prospective study for detecting the accuracy of diagnostic tests performed in the pulmonary function laboratory of Chronic Obstructive Pulmonary Disease Research Center, Mashhad, Iran, during 2013-2014. The Ethical Committee of Islamic Azad university approved the experiment.

Techniques and protocol

Overall clinical judgment made by a respiratory physician was used as gold standards in this study. In this regard the physician used any recommended paraclinical diagnostic tests required for diagnosing the patient. The respiratory physician classified subjects to obstructive or restrictive lung disease. Minimum clinical evaluation included: Asthmatic subjects mentioned a history of intermittent wheeze or cough that exacerbate after exercise, exposure to air pollution or cold air and night symptoms. Chronic obstructive pulmonary disease (COPD) was diagnosed by the history of cigarette smoking, cough, sputum as defined by Global Initiative for Obstructive Lung Disease (GOLD) criteria and high resolution computed tomography (HRCT) was used to determine the low attenuated lesion for questionable cases of emphysema. Interstitial lung disease and bronchiectasis primary evaluation were performed by HRCT. P 0.1, P I max and P E max was used to detect neuromuscular non-parenchymal restrictive lung disease.

Total lung capacity (TLC) and residual volume (RV) were evaluated for all subjects by body plethysmography (V max, Zan company, Hamburg, Germany). TLC or RV more than 120% predicted was considered as obstructive and values less than 80% predicted considered as restrictive.

Mid expiratory flow parameters as like as $FEF_{25-75\%}$ (Forced expiratory Flow between 25-75% of Vital Capacity) and MEF50% (Maximal expiratory Flow in 50% of Vital Capacity) were used as supplementary criteria for diagnosis of obstructive lung disease especially for small air way disease (4).

Mixed pattern was diagnosed by low FEV1/VC similar to the obstructive pattern (lower than the 5th percentile of the normal distribution) and low lung volumes (TLC less than the 5th percentiles of their relevant predicted values) (1).

STARD checklist for the reporting of studies of diagnostic accuracy was used in this study.

Measurements

Standard spirometry was performed in the beginning of the test at least for three times in sitting position in the body plethysmograph. Slow VC, FEV1, FVC, FEV1/FVC ratio, FEV1/VC ratio, forced expiratory flow (FEF)=25-75%, Maximum expiratory flow (MEF=50%, TLC and RV were determined for all subjects; DLCO (Carbon mono-oxide lung diffusion capacity); P 0.1, P I max and P E max were evaluated as needed. Before the FVC maneuver and lung volumes measurement, the operator demonstrated the required maneuver, and subjects were encouraged and supervised throughout the test performance. Standards outlined by the American Thoracic Society and European Respiratory society (3) were used for determining the acceptability of the test. Percent of predicted was used for evaluation of all parameters except FEV1/FVC ratio and FEV1/VC ratio.

Statistical analysis

Sample size was determined according to alpha risk of 0.05 and 80% power for detecting 10% differences between groups. Normal distribution of the data was checked using Kolmogerov Smirnof test. Student t test was carried out for comparison of spirometric parameters between normal subjects and two major abnormal groups (obstructive and restrictive). Accuracy of FEV1/FVC and FEV1/VC ratios was determined by likelihood ratio and efficiency as discussed by Kraemer (5) and compared with the clinical, mid expiratory flow diagnosis and lung volume gold standards. Receiver operator characteristic (ROC) curve was plotted for three diagnostic categories and the area under the curve was compared. Agreement between FEV1/FVC and FEV1/VC was assessed by Kappa method. Cut off for differentiating between obstructive and restrictive was 0.7 as they were recommended in ATS/ERS guideline. Data are expressed as mean ± SD and P<0.05 was considered statistically significant. EPI INFO 2013 and SPSS version 16 software were used for statistical analysis.

Results

Overall agreement between FEV1/FVC and FEV1/VC

FEV1/FVC and FEV1/VC showed similar results for detecting obstructive and restrictive pattern in 84% of subjects (Kappa = 0.85, P=0.0001), on the contrary in 14% the results of two methods was different (obstructive with FEV1/VC and restrictive with FEV1/FVC test). This agreement was also confirmed in both genders and different age groups.

Primary classification

Comparison of primary classification of FEV1/FVC and FEV1/VC according to gold standards showed that FEV1/FVC detected obstructive and restrictive lung disease better than FEV1/VC (Table 1). According to gold standard of RV, FEV1/FVC was able to detect the obstructive and restrictive lung disease correctly in 61% and 34% respectively. Incorrect diagnosis included 18% of subjects diagnosed as obstructive who were suffered from mixed pattern and 25% of subjects diagnosed as restrictive who suffer from obstructive lung disease (proved by RV evaluation). Correct diagnosis with FEV1/VC was lower (56% and 33% in obstructive and restrictive disease respectively) and mixed pattern was falsely diagnosed in 21% as obstructive which was higher than FEV1/FVC. Table 1 showed the false results in normal subjects but these results were higher in FEV1/VC.

The correct diagnosis according to gold standard of clinical diagnosis was much better for both FEV1/FVC and FEV1/VC (Table 1) but FEV1/FVC showed higher correct result for obstructive lung disease than FEV1/VC (71% for FEV1/FVC compared to 62% for FEV1/VC). False positive result in normal subjects was comparable in FEV1/FVC and FEV1/VC. Overall likelihood ratio was higher in FEV1/FVC in both RV and clinical diagnosis gold standards.

Mid expiratory flows including $FEF_{25-75\%}$ and $MEF_{50\%}$ were used to assess the obstructive lung disease especially in small air way disease (4). FEV1/FVC was able to detect the obstructive lung disease in 100% of subjects according to both $FEF_{25-75\%}$ and $MEF_{50\%}$. In contrast FEV1/VC detected obstruction in 95 and 96% respectively (Table 2). Statistical analysis showed good and significant agreement between $FEF_{25-75\%}$ and $MEF_{50\%}$ and both FEV1/FVC and FEV1/VC for diagnosis of obstructive pattern.

Table 1. Comparison of FEV1/FVC and FEV1/VC for primary classification of lung disease according to gold standard of Residual volume (RV) and overall clinical diagnosis

		FEV1/FVC		FEV1/VC	
		Obstructive	Restrictive	Obstructive	Restrictive
RV	Normal	15 (21%)	56 (41%)	19 (23%)	52 (42%)
	Obstructive	43 (61%)	34 (25%)	47 (56%)	30 (25%)
	Restrictive	12 (18%)	47 (34%)	18 (21%)	41 (33%)
	Likelihood ratio	26.37		21.54	
	P Value	0.0001		0.0001	
Clinical diagnosis	Normal	0 (0%)	9 (7%)	0 (0%)	9 (7%)
	Obstructive	50 (71%)	15 (11%)	52 (62%)	13 (11%)
	Restrictive	20 (29%)	113 (82%)	33 (38%)	101 (82%)
	Likelihood ratio	82.04		67.74	
	P Value	0.0001		0.0001	

Table 2. Agreement of FEV1/FVC with FEV1/VC with parameters of mid expiratory flow for diagnosis of obstructive lung disease

		FEV1/FVC		FEV1/VC	
		Obstructive	Restrictive	Obstructive	Restrictive
MEF_{50}	Normal	0 (0%)	56 (41%)	3 (6%)	53 (43%)
	Obstructive	70 (100%)	81 (59%)	81 (96%)	70 (57%)
	Gamma	1		0.9	
	P Value	0.0001		0.0001	
FEF_{25-75}	Obstructive	70 (100%)	45 (33%)	80 (95%)	35 (28%)
	Restrictive	0 (0%)	92 (67%)	4 (5%)	88 (72%)
	Kappa	0.58		0.63	
	P Value	0.0001		0.0001	

Table 3. Comparison of mean of FEV1/FVC and FEV1/VC in different obstructive and restrictive lung diseases

		FEV1/FVC	FEV1/VC
Obstructive	Asthma	65.4±13.3	63.5±15.4
	COPD	58.5±14.8	55.5±16.4
	Bronchiectasis	75.7±8.5	79.3±12.1
	Kruskal Walis	5.02	6.35
	P value	0.08	0.04
Restrictive	Sarcoidosis	80±7.9	78.8±8.6
	Scleroderma	85.8±8.2	86.9±10.5
	Other ILD	83±8.5	81±12.6
	Kruskal Walis	11.26	11.65
	P value	0.004	0.003

Table 4. Comparison of accuracy of FEV1/FVC and FEV1/VC

	Gold standard	Likelihood ratio	Area	Sensitivity	Specificity	PPV	NPV	Efficiency
FEV1/FVC	RV	26.37	0.685	75%	61%	21%	44%	71%
FEV1/VC		21.54	0.665	42%	77%	27%	52%	57%
FEV1/FVC	Clinical	82.04	0.812	89%	71%	14%	20%	83%
FEV1/VC	diagnosis	67.74	0.771	89%	62%	22%	20%	78%

PPV= positive predicted value, NPV= negative predicted value

Classification in specific lung diseases

Mean of FEV1/FVC and FEV1/VC were compared between three most frequent sub-categories of obstructive and restrictive lung disease. In obstructive lung disease asthma, COPD and bronchiectasis and in restrictive lung disease sarcoidosis, scleroderma and miscellaneous interstitial lung diseases were the main sub-categories (Table 3). Asthma and COPD showed significant and comparable reduction in both FEV1/FVC and FEV1/VC. Reduction of these two parameters in bronchiectasis were not as significant as asthma and COPD, but the result of FEV1/FVC was better for bronchiectasis subjects (Table 3). The results of FEV1/FVC and FEV1/VC were similar for subjects with different type of restrictive pattern.

Accuracy of FEV1/FVC and FEV1/VC

According to gold standard of lung volume (RV), FEV1/FVC showed higher sensitivity and FEV1/VC showed higher specificity (Table 4). Overall the results of accuracy assessment revealed superior results of FEV/FVC in likelihood ratio, area under the curve of ROC and Kraemer efficiency parameters. The accuracy test showed higher results in case of using clinical findings as gold standard. In this method all accuracy assessments showed higher results in FEV1/FVC compared to FEV1/VC (Table 4).

Discussion

In this prospective study, the accuracy of FEV1/FVC and FEV1/VC were evaluated and compared in 207 subjects with different type of lung disease. Gold standards were residual volume (RV) evaluated by body plethysmograph and clinical diagnosis made by a sub-specialist in pulmonary disease according to overall clinical findings, imaging and pulmonary function tests. Although FEV1/FVC and FEV1/VC showed good and significant agreement with each other, RV, mid expiratory flows and clinical diagnosis for

diagnosis of obstructive and restrictive lung disease but in most statistical analysis FEV1/FVC was better than FEV1/VC. FEV1/FVC revealed 61% and 34% correct diagnosis for obstructive and restrictive lung disease according to RV but these results were 10% lower in FEV1/VC. Classifications of patients to two major lung diseases (obstructive and restrictive) and also to three sub-categories of these major classifications were done by precise clinical evaluations. FEV1/FVC was superior for primary classification but FEV1/VC was better for diagnosis of sub-categories. Overall statistical analysis for accuracy showed higher accuracy for FEV1/FVC.

FEV1/FVC is a typical method for classification of lung disease described in most classical references (1) and FEV1/VC is a good substitute for FEV1/FVC in case of incomplete FVC maneuver. The basis for choosing FEV1/VC for primary classification of lung disease in ATS/ERS guidelines is not clear and limited reference about accuracy and superiority of FEV1/VC is available.

Brusasco et al (6) showed that expiratory slow VC is higher than forced expiratory VC in chronic airway obstruction and therefore FEV1/VC should be more precise than FEV1/FVC in COPD subjects. This author was the leading author of ATS/ERS guideline for Interpretation of lung function tests but the basic references for this suggestion were not mentioned in this guideline. Our comprehensive search in literature was also inconclusive and we did not find clinical studies in favor of preference of FEV1/VC over FEV1/FVC. Therefore we conduct this study to determine the superiority of FEV1/VC over FEV1/FVC and determining the necessity of replacing FEV1/FVC by FEV1/VC.

Primary Care Respiratory Alliance of Canada has introduced a new algorithm focuses on the FEV_1 to FVC ratio before and after bronchodilator challenge to differentiate between asthma and COPD (7). The new algorithm includes bronchodilator challenge as it exclude a diagnosis of COPD if the FEV_1-FVC ratio returns to normal after bronchodilator challenge. This algorithm shows further usage of FEV1/FVC for diagnosis of lung diseases.

We believe that these two results (FEV1/FVC and FEV1/VC) should be reported in spirometry reports parallely in which clinician would be able to choose the best result according to clinical findings. As it shows in Table 1 the likelihood ratio for detecting and classification of lung diseases were higher for clinical diagnosis than RV. Therefore the most impressive decision usually will be made according to clinical findings. In this case clinician could use both FEV1/FVC and FEV1/VC and choose the best result according to clinical decision.

Conclusion

In conclusion the results of the present study showed that FEV1/FVC still is a valuable parameter for primary classification of lung disease and clinician should judge about the results of FEV1/FVC and FEV1/VC and choose the best correlate parameter for diagnosis their subjects.

Conflict of Interest

The authors declare no conflict of interest.

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