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## Restrictive pattern in spirometry. Does FEV<sub>1</sub>/FVC need to be increased?

Wykrywanie restrykcyjnego typu zaburzeń wentylacji w spirometrii  
 — czy FEV<sub>1</sub>/FVC musi być podwyższone?

### Abstract

**Introduction:** Spirometry is an excellent tool in the diagnostics of airway obstruction, but is less reliable in restrictive diseases. Diagnosis of lung restriction on the grounds of reduced forced vital capacity (FVC) is burdened with many potential errors. According to the American Thoracic Society/European Respiratory Society (ATS/ERS) 2005 guidelines, restrictive pattern in spirometry consists of a reduction in vital capacity and increase in forced expiratory volume in 1 second/vital capacity (FEV<sub>1</sub>/VC) of > 85–90%. However, to our knowledge, this recommendation has not been validated. The aim of this study was to check how the inclusion of an increased FEV<sub>1</sub>/FVC as a mandatory condition affects the value of spirometry in detecting a restrictive ventilatory defect.

**Materials and methods:** The material consisted of pulmonary test results obtained from consecutive patients referred to our lab during the year 2009, who had undergone spirometry and lung volume measurements at the same visit.

**Results:** Out of 1739 test results, there were 1402 non-obstructive cases (679 females [48.4%] and 723 males [51.6%]) with a mean age of 49.7 ± 14.5 years, included in the analysis. ERS 1993 reference equations were applied to all parameters. The lower limit of normal (LLN) was set at -1.645 of the SR level. Restrictive ventilatory defect (TLC < LLN) was found in 283 patients (20.2%). Reduced FVC only, as a condition of restrictive ventilatory defect diagnosis, was found in 202 patients (14.4%) (sensitivity 59%, specificity 97%). Reduced FVC together with increased FEV<sub>1</sub>/FVC > 85% was found in only 76 patients (5.4%) (sensitivity 23%, specificity 99%). Only 14% of mild, 26% of moderate, and 64% of severe restrictions could be detected with reduced FVC and increased FEV<sub>1</sub>/FVC.

**Conclusions:** Dual condition, i.e. reduced FVC and increased FEV<sub>1</sub>/FVC, significantly diminishes the sensitivity of the test and hampers the diagnosis of restrictive ventilatory defect in spirometry, especially in mild and moderate stages.

**Key words:** spirometry, lung volumes, restrictive lung diseases

**Pneumonol. Alergol. Pol. 2011; 79, 6: 382–387**

### Introduction

Spirometry is the most commonly ordered lung function test. It is a useful, easy method of detection and monitoring of lung function abnormalities. Ventilatory defects may result from an obstruction of airways (obstructive type), decrease of lung volume (restrictive type), or a combination

of both [1]. Spirometry is an excellent tool in the diagnostics of obstructive diseases as it enables detection and assessment of the severity and reversibility of obstruction. Spirometry is less reliable in the diagnostics of restrictive diseases. The main criterion in the diagnosis of restriction is a decrease in total lung capacity (TLC), which cannot be measured during spirometry. Traditional-

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Manuscript received on: 19 Jan 2011  
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 ISSN 0867-7077

ly, it has been established that reduced forced vital capacity (FVC) may correspond to a restrictive ventilatory defect. However, one should be careful about drawing conclusions, as decreased FVC is not specific for restrictive defects. Forced vital capacity may also be decreased in obstructive diseases with coexisting features of lung hyperinflation and air trapping [2]. Diagnosis of restriction on the grounds of FVC reduction is burdened with a large number of misdiagnoses, especially in patients with airway obturation [3–6]. Therefore, the American Thoracic Society (ATS) 1991 guidelines state that restrictive disorders may be suspected when vital capacity (VC) is decreased while FEV<sub>1</sub>/VC (forced expiratory volume in 1 second/vital capacity) index remains within a normal range [7]. At times, airway obstruction may be accompanied by restriction but such situations are rare [4, 5, 8]. Therefore, diagnosis of concomitant obstructive and restrictive disorders is not possible merely on the basis of spirometry testing. The current American Thoracic Society/European Respiratory Society (ATS/ERS) 2005 guidelines on the interpretation of lung function tests recommend that, based on spirometry, restrictive ventilatory defects may be suspected when a decrease in VC is accompanied by an over 85–90% increase in FEV<sub>1</sub>/VC index value [1]. According to our knowledge, introduction of this second condition is not based on published results of clinical trials, but rather on the opinions of the experts, authors of the guidelines.

The aim of this publication was to assess the diagnostic value of spirometry in identification of restrictive ventilation defects based on two criteria: isolated FVC decrease and FVC decrease with concomitant increase in FEV<sub>1</sub>/FVC index value, as well as to assess the influence of an additional criterion of FEV<sub>1</sub>/FVC index increase on the effectiveness of spirometry in diagnosis of restrictive disorders in comparison to FVC reduction only.

### Material and methods

Analysis was carried out on the results of lung function tests performed in the Lung Function Lab at the Institute of Tuberculosis and Lung Diseases in Warsaw from January to December 2009. The results were included in the analysis if both spirometry and plethysmographic lung volume measurements were performed during one visit. In cases of patients who underwent several examinations in the period of that year only, the results of the first test were included in the study (1 result for 1 patient). Examinations were performed using a MasterScreen Body device by Jaeger. Spirometry

and plethysmography were carried out according to the current 2005 ATS/ERS guidelines by two technicians with long experience in this area. Only tests fulfilling the quality criteria presented in the guidelines were included in the study. For spirometry, the criteria constituted at least three correct, repetitive forced expiration measurements. An acceptable measurement comprised a satisfactory expiration start (back extrapolated volume < 150 ml or < 5% of intended FVC), a proper expiration end (expiration time > 6 s with gradual decrease in expiration flow and a plateau at the end), and an absence of artefacts on expiration. Repeatability of measurements was assessed based on the two best measurements of FVC and FEV<sub>1</sub> that did not differ by more than 150 ml. At least three FRC (functional residual capacity) measurements were acquired during plethysmography with 5% repeatability. Predicted values from 1993 ERS guidelines [9] were applied to all measured parameters. The lower limit of normal (LLN) was set at –1.645 of the standardized residual (SR) according to the ATS/ERS 2005 guidelines. Restrictive pattern of ventilation disorders was diagnosed if TLC was decreased below LLN. It was a reference test for comparison of analysed spirometric criteria in the detection of volume restriction. FVC reduction was noted when it was below the LLN. The FEV<sub>1</sub>/FVC index was considered elevated if its absolute value was greater than 0.85 (85%).

Analysis was performed using Statistica software for Windows by Statsoft. Results were presented as means ± standard deviations. Applying the previously mentioned LLN definition, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for the detection of restriction in spirometric testing were calculated using 2 × 2 contingency tables. An  $\chi^2$  test was used in order to compare the number of restrictive disorders detected with spirometry according to the criteria being evaluated in this study. A p-value of < 0.05 was considered significant.

### Results

Initially, the results of 1739 concurrent spirometric and plethysmographic tests fulfilling the quality criteria were identified. The majority of subjects consisted of patients with interstitial lung diseases (90%). Among this group, the greatest number was represented by patients with sarcoidosis (48%). Among the less numerous patients with obstructive diseases (4%) these tests were usually performed after they had received their regular bronchodilatory medication. A total of 336 tests

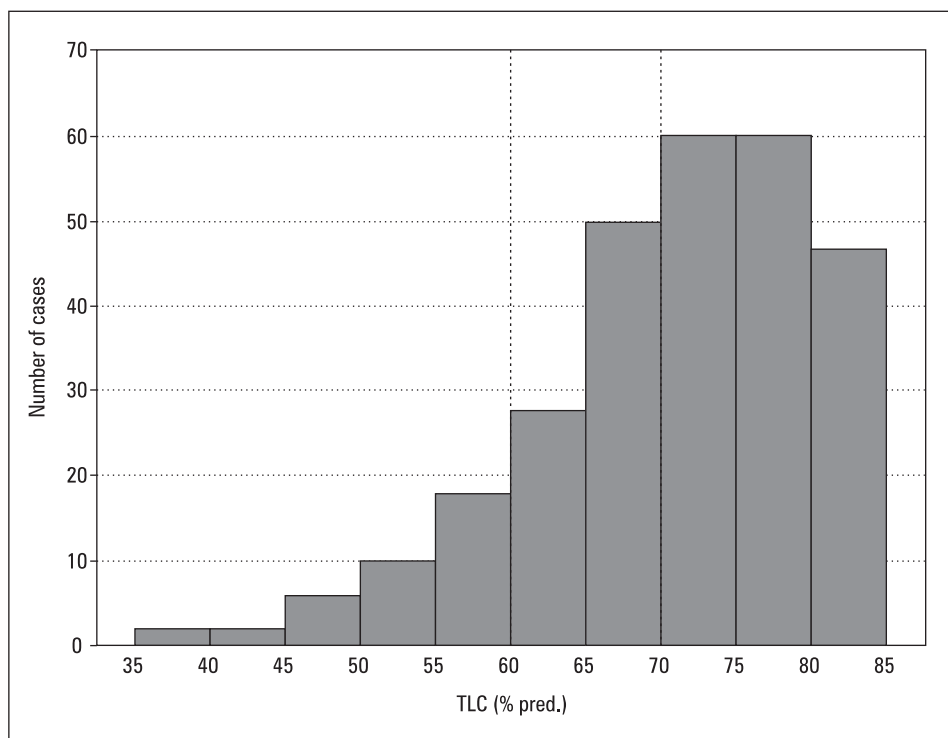


Figure 1. Histogram of TLC (% pred.) in 283 patients with volume restriction (dashed lines indicate restriction severity limits)

Table 1. Test characteristics of spirometry in detecting volume restriction

Condition	Sensitivity	Specificity	PPV	NPV
FVC < DGN	59%	97%	82%	90%
FVC < DGN+ FEV <sub>1</sub> /FVC > 85%	23%	99%	86%	84%

FVC — forced vital capacity; FEV<sub>1</sub> — forced expiratory volume in 1 second; DGN — lower limit of normal; PPV — positive predictive value; NPV — negative predictive value

were excluded from the entire group due to features of airway obstruction (FEV<sub>1</sub>/FVC < LLN). The remaining results from 1402 patients without airway obstruction were subjected to further statistical analysis. This group consisted of 679 females (48.4%) and 723 males (51.6%). Mean age was 49.7 ± 14.5 years and the range of ages was wide — from 21 to 87 years. In 283 (20.2%) patients, restrictive ventilatory defects were diagnosed on the grounds of TLC reduction below LLN. The distribution of TLC results categorized into groups for every 5% of the predicted value (pred.) is presented in Figure 1. The restriction was mild in 169 cases (60% of cases of volume restriction), moderate in 76 (27%), and severe in 38 (13%). Allotment into groups depending on the severity was done according to the scale proposed by ATS. TLC values below LLN but greater or equal to 70% of predicted value indicated mild restriction, values in the range 60–69% of predicted value — moderate restriction and those below 60% of predicted value corresponded to

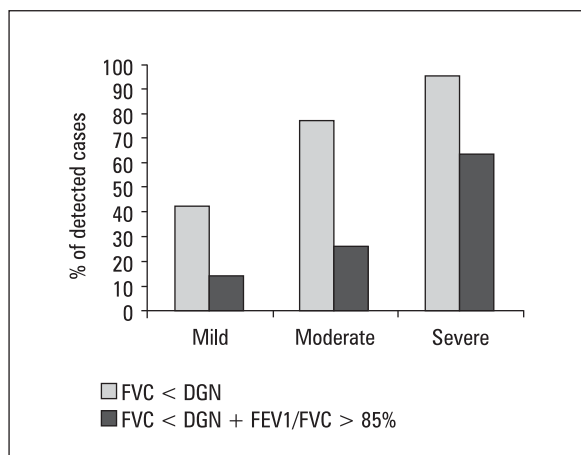
severe restriction [7]. FVC reduction below LLN was noted in 202 cases (14.4% of patients without airway obstruction) and FVC reduction accompanied by an increase in FEV<sub>1</sub>/FVC index only in 76 cases (5.4% of patients without airway obstruction). Among the 202 patients with reduced FVC, in 36 cases (17.8%) TLC remained within the normal range, which did not allow diagnosis of restriction to be made (false-positive test result). The opposite situation was more common: among 283 patients with restriction diagnosed in the reference test (TLC < LLN), in 117 (41.8%) FVC was within the normal range (false-negative test result). In the group of 76 patients with concomitant FVC reduction and FEV<sub>1</sub>/FVC index elevation, features of restriction were not found in 10 cases (13.2%).

Spirometry parameters of detection of restrictive disorders used in the two compared diagnostic criteria are presented in Table 1. Test specificity was 97% for FVC below LLN and 99% for FVC

**Table 2. Detection of volume restriction according to its severity using 2 spirometric criteria**

Severity of restriction according to TLC (% pred.)	Number of cases with FVC < DGN	Number of cases with FVC < DGN + FEV <sub>1</sub> /FVC > 85%
Mild (169 cases)	71 (42%)	23 (14%)
Moderate (76 cases)	59 (78%)	20 (26%)
Severe (cases)	36 (95%)	23 (64%)

TLC — total lung capacity; FVC — forced vital capacity; FEV<sub>1</sub> — forced expiratory volume in 1 second; DGN — lower limit of normal

**Figure 2.** Detection of volume restriction according to its severity using 2 spirometric criteria

below LLN accompanied by an elevated FEV<sub>1</sub>/FVC index. However, sensitivity of sole FVC reduction was 59% while the dual criteria of FVC reduction together with FEV<sub>1</sub>/FVC index elevation were associated with a significantly lower sensitivity (23%). Subsequently, the potential of spirometry in detecting various severity of restriction was evaluated. The results are presented in Table 2 and in Figure 2. There was little chance of detecting restriction of mild degree using spirometry. In almost 2/3 of cases of mild restriction, FVC was normal. As a result of adding a criterion of elevated FEV<sub>1</sub>/FVC index, only 14% of cases of mild restriction were diagnosed in spirometry. Among patients with moderate restriction, FVC reduction was noted in 80%, but concurrent FEV<sub>1</sub>/FVC index elevation was seen in only 26%. In cases of severe restriction, FVC reduction was demonstrated in 95% of patients, but simultaneous FEV<sub>1</sub>/FVC index elevation still could not be found in over 1/3 of patients. A significantly greater number of cases of restriction, especially mild and moderate, could be detected using the isolated FVC reduction parameter than with the double criteria of FVC reduction with concomitant FEV<sub>1</sub>/FVC index elevation ( $\chi^2$  test,  $p < 0.001$ ).

## Discussion

The results of the presented study confirm that spirometry is not a good tool for the diagnostics of ventilation disorders of restrictive type. TLC, the basic parameter for the diagnosis of restriction, cannot be measured during spirometry testing. Airway obstruction poses an additional difficulty in the assessment of FVC reduction in spirometry. A disorder of obstructive type alone may be the cause of secondary FVC reduction through an increase in residual volume (RV) and lung hyperinflation. Our experience, as well as literature data, indicates that in cases of obturation with reduction of vital capacity, the most common cause of decreased FVC is obturation only [4, 5, 8]. Coexistence of obturation and restriction is rare and its diagnosis requires performing plethysmography and measurement of all lung volumes and capacities. Consequently, it is necessary to exclude patients with features of obturation before assessing the value of spirometry in the detection of restrictive disorders.

Aaron et al. [3] demonstrated that the sole FVC reduction in spirometry (as a criterion for diagnosing restriction in patients without features of airway obstruction) is characterized by 68% sensitivity and 93% specificity. These authors stated that, although restriction cannot be confirmed on the basis of spirometry (PPV 58%), normal FVC excludes TLC reduction with a high probability (NPV 93%). Similar conclusions could be drawn from other publications on the topic [6, 10]. The results of our work do not support this suggestion. There were more cases of both FVC reduction with normal TLC and normal FVC accompanied by TLC reduction in our study material. Normal FVC with reduced TLC (41.8% of patients with features of restriction) was noted more often than normal TLC with concomitant decrease in FVC (10% of patients without features of restriction). This is consistent with our earlier results from studies conducted on patients with various interstitial lung diseases [11] as well as on patients

with idiopathic pulmonary fibrosis [12, 13]. In some publications from the literature, the frequency of cases with reduced FVC accompanied by normal TLC (the so-called non-specific pattern of ventilation disorders) amounts to about 10% of patients [14], which is in accordance with the results obtained from our study material described in this publication. In the study by Aaron et al. it was 2.4%, and in the study by Vandevoorde et al. it was 7% of men and 1% of women. Therefore, PPV was higher (82% for the isolated FVC reduction) and NPV lower (90% for the isolated FVC reduction) in our study than in the quoted publications. The population of patients in the study by Aaron was very similar to the one presented here (49.8% of men, mean age of  $50.8 \pm 17.6$  years). In the study by Vandevoorde et al., the subjects were somewhat older and men comprised the majority (60%, mean age of 59 years). These differences do not seem to significantly influence the obtained results. Disparities between the results obtained in the mentioned works may arise from application of different sets of predicted values. In this study, we applied predicted values recommended by ERS in 1993 to all parameters. In the study by Aaron et al., a set of values was used that had been compiled by Knudson in patients below 65 years old in 1983, by Enright in elderly patients in 1993, and by Crapo in 1982 for lung volumes. Furthermore, two methods of measuring lung volumes were applied: plethysmography and helium dilution technique. Vandevoorde et al. used a set of predicted values by NHANES III from 1999 for spirometric parameters and by ERS from 1993 for lung volumes. The results of all the quoted works, as well as those presented in this publication, indicate that volume restriction (especially when mild) cannot be reliably predicted on the basis of spirometry. As demonstrated in this publication, FVC reduction is observed in less than half of patients in this group. However, we did not corroborate the conclusions of other authors that volume restriction may be excluded with great certainty on the grounds of spirometry testing.

Current ATS/ERS recommendations from 2005 on the interpretation of the results of spirometric examination with regard to restrictive ventilatory disorders add an elevation in FEV<sub>1</sub>/FVC index over 85% to the FVC reduction criterion. We are not aware of any publications supporting the validity of this recommendation. It may be indirectly inferred from the study by Aaron et al., in which it was stated that the higher FEV<sub>1</sub>/FVC index, the greater the probability of actual volume

restriction. Results of the study presented here contradict the usefulness of this additional criterion. Its application greatly decreased (to 23%) the sensitivity of spirometry as a test for detection of volume restriction. Such a small sensitivity disqualifies the application of FEV<sub>1</sub>/FVC index elevation as a criterion for diagnosis of restriction. It is particularly disadvantageous in cases of mild and moderate restriction. We observed FVC reduction with concurrent FEV<sub>1</sub>/FVC index elevation in only 14% of cases with mild and 23% with moderate restriction. Therefore, it seems that FVC reduction in the absence of features of obturation (normal value of FEV<sub>1</sub>/FVC index) in spirometry is sufficient to raise suspicion of a restrictive ventilatory defect. Considering spirometry as an easily accessible and inexpensive screening test for the detection of restriction, it should be most useful in groups with a lesser degree of progression of functional abnormalities. It would allow for lowering of the number of plethysmographic examinations, which are expensive and are performed only in specialist facilities.

## Conclusions

1. Spirometric test, regardless of the applied criteria (FVC reduction or FVC reduction with accompanying FEV<sub>1</sub>/FVC index elevation), does not allow for a reliable confirmation or exclusion of a restrictive ventilatory defect.
2. Adding a criterion of FEV<sub>1</sub>/FVC index elevation above 85% to the FVC reduction criterion leads to significant lowering of test sensitivity, which reduces the chances of detecting a restrictive ventilatory defect, especially mild and moderate, using spirometry.

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