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ORIGINAL RESEARCH

The FEV_1/FEV_6 ratio is a good substitute for the FEV_1/FVC ratio in the elderly

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Summary
Aims: To determine the agreement between the FEV_1/FEV_6 ratio and the FEV_1/FVC ratio in an elderly population.
Method: The study sample consisted of 3874 participants in a cross-sectional population survey in Tromsø, Norway, aged 60 years or more, in whom acceptable spirometry had been obtained. Mean differences between the FEV_1/FEV_6 ratio (%) and the FEV_1/FVC ratio (%) were calculated according to age, sex, smoking habit, and the degree of airflow limitation. ROC-curve analysis and Kappa-statistics were used to estimate the utility of the FEV_1/FEV_6 ratio in predicting an FEV_1/FVC ratio < 70%.
Results: The mean difference between FEV_1/FEV_6% and FEV_1/FVC% was 2.7% in both men and women. The difference between the two measures increased somewhat with increasing age, and was more pronounced with smoking and decreasing FEV_1/FVC ratio. The value for the FEV_1/FEV_6 ratio which best predicted an FEV_1/FVC ratio of 70%, was 73%, and a very good agreement was found between these two cut-off values (kappa = 0.86).
Conclusion: The FEV_1/FEV_6 ratio appears to be a good substitute for the FEV_1/FVC ratio in an elderly population.

Introduction

Spirometry is often needed to identify COPD [1], and it is mandatory in determining the severity of the disease [2]. In spite of the increased focus on this examination in general practice over the last decade, spirometry is still used infrequently in many practices, or not at all [3].

It is not always easy to obtain valid results for spirometry testing [4]. The difficulties in expiring fully in order to provide the forced vital capacity (FVC) may be one reason for this. This could well be the case amongst the elderly and in patients with pulmonary diseases, who may need 10–20 seconds to exhale fully to their residual volume. The effort needed to reach a plateau on

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the volume-time curve can cause exhaustion and in some cases syncope [5]. When the expected plateau is not obtained, the measurement is judged to be unacceptable according to current guidelines [6,7]. The GOLD guidelines state that measurement of the FEV_1/FVC ratio is a mandatory element in the diagnosis of COPD [2], thus requiring a valid measurement of FVC. Substituting the FVC with the forced expiratory volume at 6 seconds (FEV_6) in the diagnosis of bronchial airflow limitation has recently been recommended [8–12]; this would reduce the required maximal forced expiratory time to six seconds. In this study, the association between the FEV_1/FEV_6 ratio and the FEV_1/FVC ratio has been evaluated in a population of elderly subjects in order to provide further evidence for the debate.

Methods

Subjects

The study sample were inhabitants of Tromsø, aged 60 years or more, who took part in the Tromsø Study 2001, a population survey undertaken between March 2001 and February 2002. Tromsø is a city in the northern part of Norway, with a current population of 63,000. This is the fifth cross-sectional Tromsø Study conducted by The University of Tromsø in cooperation with the National Health Screening Service. In the fourth survey in 1994, all inhabitants aged 55–74 years of age, and 5–10% samples of other age groups between 25–84 years, were asked to take part in a second phase study that included detailed medical examination. The attendance rate was 77%. In this fifth survey, all phase two participants from the fourth survey, who still lived in Tromsø, were eligible to participate, and, in addition, all inhabitants aged 60 and 75 years were also invited. A total of 5328 subjects aged 60 years or more were eligible; 4713 (88.5%) attended phase one, and 4519 (85%) also attended phase two of this fifth survey. Spirometry, which was part of the second phase examination, was performed in 4102 subjects, 90% of the attendees and 77% of the subjects eligible for participation. Absence of staff and technical problems were the reasons for spirometry not being performed in 10% of the attendees. At the completion of data collection, 25 women and 12 men had withdrawn their consent to participate.

Questionnaire

The participants reported their smoking habits and known diseases on a questionnaire. They allocated themselves into one of following smoking groups: 'current smoker'; 'previous smoker'; or 'never smoker'. Those who reported that they had asthma or chronic bronchitis were classified as having self-reported chronic pulmonary disease, and those who reported that they had been diagnosed with cerebral stroke, myocardial infarction or angina pectoris were classified as having self-reported cardiovascular disease.

Spirometry

The spirometer used was a ''Sensormedics Vmax 20''. The American Thoracic Society criteria for spirometry testing were followed [7]. The subjects were sitting, using a nose clip, and were instructed to blow for as long as possible, and at least for six seconds. At least three blows were required. The differences between the best and next best FEV_1 and FVC values were not to exceed 5% or 200 ml, whichever was the greater. Three trained technicians were involved. Reversibility testing was not performed. Current drug therapy was not interrupted before the test. Height was measured barefoot.

Statistical analysis

The mean difference between the FEV_1/FEV_6 ratio (in %) and the FEV_1/FVC ratio (in %) was calculated, and the statistical significance of differences between subgroups was evaluated by Student's t-test. Bivariate linear regression was used in the evaluation of correlations between the FEV_1/FEV_6% and other continuous variables. ROC (Receiver Operating Characteristics) curve analysis and Kappa-statistics [13] were used in evaluating the agreement between FEV_1/FEV_6% and FEV_1/FVC %. Positive predictive value (PPV) and negative predictive value (NPV) were calculated of the most suitable FEV_1/FEV_6 threshold for diagnosing an FEV_1/FVC ratio < 70%. The 5% percentiles of the two measures were determined among the never smokers who did not report cardiovascular or chronic pulmonary disease. The SPSS 12.0 programme for Windows (SPSS inc, Chicago, Illinois, USA) was used in the statistical analyses. The Regional Committee for Medical Research Ethics in Northern Norway approved the study. All the participants gave informed written consent.

Results

The spirometry was found to be acceptable, including the measurement of FEV_6, in 3874

Table 1 Mean age, smoking habit, reported diseases and mean spirometry results according to sex in 3878 subjects aged 60 years or more participating in the Tromsø Study 2001

	Men	Women
Age (years, mean)	69.5	69.2
Smoking habit		
Current daily smoker (%)	23.4	23.5
Previous smoker (%)	58.4	30.0
Never smoker (%)	18.2	46.6
Self-reported disease		
Asthma or chronic bronchitis (%)	12.2	14.8
Cardiovascular disease (%)	27.5	14.8
Spirometry results		
FEV_1% predicted (mean)[a]	90.6	94.8
FVC% predicted (mean)[a]	95.7	106.0
FEV_1/FVC % (mean)	72.3	73.8
FEV_1/FEV_6% (mean)	75.0	76.5

[a] The ECSC reference equation is used [6].

subjects with a mean age of 69.4 years; 2086 were women, and 1788 were men. Characteristics of the subjects, including smoking habits, reported diseases and mean spirometric results are shown in Table 1.

A mean difference between the FEV_1/FEV_6% and the FEV_1/FVC % of 2.7% was found in both sexes, and was not influenced by height. The difference between the two measures increased somewhat with increasing age ($p < 0.001$), from 2.5% to 2.9% (Figure 1). The difference between the two measures was highly dependent on the degree of airflow limitation as measured by the FEV_1/FVC ratio ($p < 0.001$, Figure 2). The mean difference was 3.1% in 'current' smokers, 2.7% in 'previous' smokers, and 2.5% in 'never smokers'. The differences between the 'current' and 'previous smoking' groups, and the 'never' smokers were statistically significant ($p < 0.001$). Subjects aged 60—70 years were more frequently

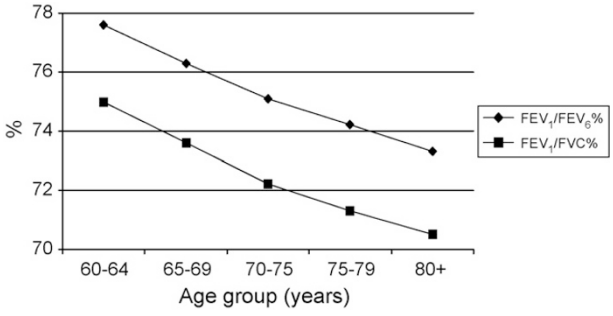

Figure 1 Mean FEV_1/FEV_6% and FEV_1/FVC% by age in 3874 participants in the Tromsø Study 2001.

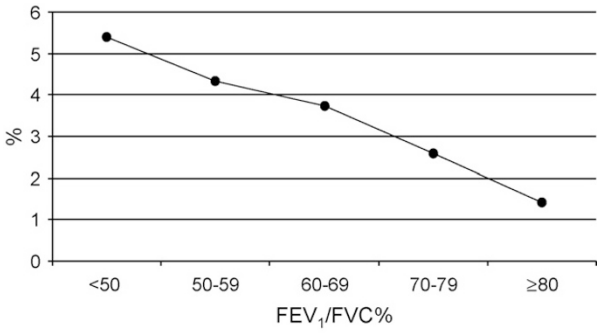

Figure 2 Mean difference between FEV_1/FEV_6% and FEV_1/FVC% (FEV_1/FVC%—FEV_1/FEV_6%) by the degree of airflow limitation as measured by the FEV_1/FVC ratio in 3874 participants aged 60 years or more in the Tromsø Study 2001.

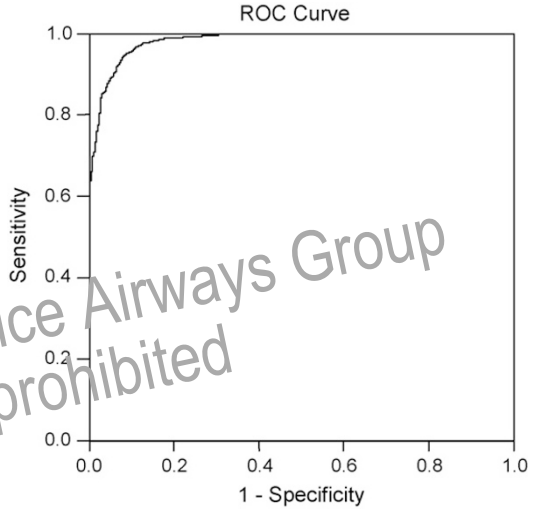

Figure 3 Receiver Operating Characteristics curve showing the ability of the FEV_1/FEV_6% to diagnose $FEV_1/FVC < 70$%. Area under curve is 0.98.

'current' smokers and less frequently 'never smokers' than those who were older ($p < 0.001$).

The ROC curve displaying the test characteristics of the FEV_1/FEV_6 ratio in predicting an FEV_1/FVC ratio < 70% is shown in Figure 3. The area under the curve is 0.98. The highest sum of sensitivity and specificity was found with an FEV_1/FEV_6 threshold of 73% (Table 2). The predictive value of this

Table 2 Sensitivities end specificities of thresholds of the FEV_1/FEV_6 ratio in predicting $FEV_1/FVC < 70$%

FEV_1/FEV_6 ratio	Sensitivity	Specificity
<72%	0.82	0.99
<73%	0.89	0.97
<74%	0.93	0.92
<75%	0.96	0.86

Table 3 Prevalence of $FEV_1/FVC < 70\%$ by smoking habit and predictive values of $FEV_1/FEV_6 < 73\%$ in diagnosing $FEV_1/FVC < 70\%$

	Prevalence of FEV_1/FVC <70% (%)	Positive predictive value of $FEV_1/FEV_6 < 73\%$ (%)	Negative predictive value of $FEV_1/FEV_6 < 73\%$ (%)
Current daily smoker (n = 900)	43.1%	92.6	93.7
Previous smoker (n = 1656)	25.1%	87.8	96.5
Never smoker (n = 1284)	12.2%	83.8	97.5

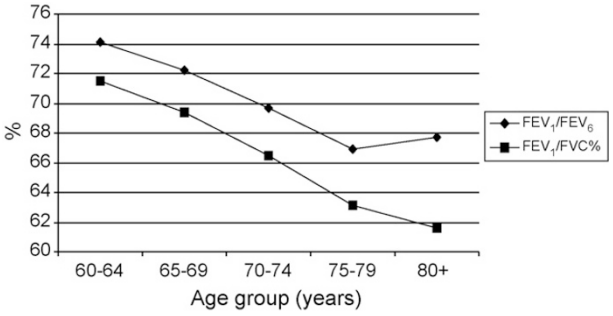

Figure 4 The 5% percentile of the FEV_1/FEV_6% and FEV_1/FVC% by age in 935 healthy never smokers participating in the Tromsø Study 2001. Only 55 subjects older than 80 years were included.

threshold in diagnosing $FEV_1/FVC < 70\%$ is shown in Table 3. Eighty-one percent of those misclassified by using the FEV_1/FEV_6 ratio had an FEV_1/FVC ratio of $70 \pm 2\%$. Kappa-agreement of 0.86 was found between $FEV_1/FEV_6 < 73\%$ and $FEV_1/FVC < 70\%$.

The 5 percentiles among healthy 'never smokers' of the FEV_1/FEV_6 ratio and the FEV_1/FVC ratio decreased steadily and with increasing age, and was below 70% after the age of 70 (Figure 4).

Discussion

The correlation between the FEV_1/FEV_6 ratio and the FEV_1/FVC ratio found in this study is in accordance with the findings of previous studies [8-10,12]. Like Vandevoorde and coauthors we found an FEV_1/FEV_6 cut-off of 73% to be the best substitution for the widely-used FEV_1/FVC threshold of 70% [12]. In Vandevoorde's study, in which younger adults were also included, the Kappa-agreement between the two measures using the 70% and 73% cut-off values was 0.87, compared to 0.86 in this study. Both values are within a range (between 0.8 and 1.0) that has been classified as ''almost perfect agreement'' [13]. Using this cut-off value, 5.4% were misclassified, but the great majority of these had FEV_1/FVC values between 68 and 72%, values that should be interpreted with caution [14]. The risk of over-diagnosis, using this threshold, was particularly low among the 'never smokers' (NPV: 97.5%). The dependence of the difference between the two measures on the airflow limitation, as measured by FEV_1/FVC, was not as strong as found by Enright and co-authors in adults aged 36—60 years [9]. Among subjects with an FEV_1/FVC ratio between 50% and 60% the differences were approximately 4% and 7%, respectively. The elderly with moderate obstruction in our study were probably less able to expire for more than six seconds than the younger adults with the same FEV_1/FEV_6 ratio reported in the American study, resulting in a lower difference between the measures.

We have chosen to present the results for men and women together, since the FEV_1/FVC ratio threshold of 70% is used in both sexes in the GOLD guidelines. Sex and height, and in particular age, certainly have an impact on this ratio [15]. Our Norwegian population may also perform somewhat differently than elderly populations in other parts of the world. The 73% cut-off value of FEV_1/FEV_6 should be regarded as a rough measure that should be interpreted together with other clinical information. This threshold is most useful amongst middle-aged adults [12], and, as shown in this study, lower cut-off values should be used with increasing age.

Although all of the obstacles for spirometry in general practice have not yet been determined, it seems reasonable to assume that a low success rate in obtaining valid test results may play a role. Important reasons for invalid tests are inadequate force and duration of the expiration. The FEV_6 is more easily obtained than the FVC, and substituting the FEV_1/FVC ratio with the FEV_1/FEV_6 ratio may, accordingly, encourage more frequent and better quality spirometry in primary care.

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