Accuracy of pulmonary function tests in predicted exercise capacity in COPD patients

G. Efremidis\textsuperscript{a}, M. Tsiamita\textsuperscript{a}, A. Manolis\textsuperscript{b}, K. Spiropoulos\textsuperscript{a,}\textsuperscript{*}

\textsuperscript{a}Division of Pneumonology, Department of Internal Medicine, University of Patras Medical School, Patras 26500, Greece
\textsuperscript{b}Department of Cardiology, Patras Medical School General University Hospital, Rio, Patras, Greece

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Summary

Purpose: The purpose of this study was to examine exercise tolerance in patients with COPD from measurements of resting pulmonary function parameters.

Methods: A total of 57 COPD patients were administered the pulmonary function test (PFT) and cardiopulmonary exercise test. The results were analyzed and essentially linear relationships emerged when each subject’s VO\textsubscript{2} peak was plotted against his individual PFT parameters. Those significant contributors were then introduced in a stepwise multiple regression analysis to determine the best predictor of the VO\textsubscript{2} peak.

Results: Stepwise multiple regressions in variables revealed that peak oxygen consumption (VO\textsubscript{2} peak) was predicted best by the following equation: VO\textsubscript{2} peak\textsuperscript{0.24}=\left(\text{maximum voluntary ventilation}/0.024\right)+\left(\text{forced mid-expiratory flow}/0.47\right)+\left(\text{body surface area}/0.988\right)−0.913\text{ (r}=0.90;\text{ r}^2=0.81\text{ SE}=0.29\text{ L/min}).

Conclusion: We conclude that exercise capacity was predicted from measurements of resting pulmonary function parameters with excellent accuracy in the COPD patient.

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Introduction

Exercise tolerance in patients with COPD has multiple determinants and is difficult to predict from measurements of resting pulmonary function.\textsuperscript{1} Measurements of maximum exercise tolerance have been reported to be useful in disability evaluation\textsuperscript{2} and determination of the cause of exertional symptoms.\textsuperscript{3,4} In addition, understanding the factors which predict exercise capacity will provide clues to a better understanding of physical activity limitations in patients with COPD.
Previous studies in patients with COPD have indicated that ventilatory limitation is a primary determinant of exercise tolerance.\textsuperscript{4,5} However, individual pulmonary function parameters as FEV\textsubscript{1} explain only about half of the variance in measured exercise tolerance.\textsuperscript{6,7}

For many patients with COPD, psychosocial characteristics may interact with physiologic abnormalities to limit physical work capacity. To date, few published studies have closely examined the role of psychosocial variables in the prediction of peak VO\textsubscript{2} in patients with COPD.

This study uses data from a clinical trial of rehabilitation in COPD. The purposes of the analysis were the following: to examine how well exercise tolerance, specifically VO\textsubscript{2} peak, can be predicted from a combination of physiologic and psychosocial measurements, and to provide insight into factors determining and limiting exercise capacity in COPD patients.

**Methods**

**Patient selection:** All the patients recruited from the outpatient clinic before had started the rehabilitation program. We studied 57 clinically stable COPD patients according to GOLD criteria.\textsuperscript{1} All patients signed the informed consent form. The patients were clinically stable and had been receiving optimal medical therapy for at least 8 weeks when they were examined, and had no exacerbation for at least 12 weeks. Patients were excluded if they had: a history suggesting asthma (according to GINA criteria for asthma),\textsuperscript{8} atopy or nasal polyps, a 15% or higher-increase FEV\textsubscript{1} after bronchodilator, active heart disease, musculoskeletal disorders, peripheral vascular diseases or other disabling conditions that would interfere with the tests and could contribute to dyspnea or exercise limitation. All patients had a basal set of spirometry within the last year at our pulmonary function laboratory. The baseline characteristics of the patients are shown in Table 1.

**Study design:** COPD subjects included patients who had performed pulmonary function tests (PFTs) and incremental cycle exercise test during assessment before pulmonary rehabilitation. Subjects were familiarized with all procedures prior to collection of the test results evaluated in this study, and underwent baseline assessment with extensive physiologic and psychosocial tests, prior to beginning the clinical trial.

**Equipment procedures:** Anthropometric and body composition. Body height (cm) was measured with subjects standing barefoot and was determined to the nearest 0.5 cm. Total body mass (kg) was measured with subjects in light clothing and was established to the nearest 0.1 kg. Body surface area (BSA) was measured with Dubois formula:

\[
BSA = 0.007184 \times \text{weight}^{0.425} \times \text{height}^{0.725}.
\]

This formula has remained the standard for calculating BSA.\textsuperscript{9}

PFTs: Each patient underwent PFT including:

1. Spirometry was performed prior to exercise testing, in accordance with the recommended techniques (using a Pulmolab 435 Morgan Data Acquisition System Ver.401).\textsuperscript{10} The subjects completed at least three acceptable maximal forced expiratory maneuvers. Technical procedure acceptability and reproducibility criteria were those recommended by the American Thoracic Society.\textsuperscript{10} The predicted normal values for spirometry were those of Morris and associates.\textsuperscript{11}

2. Maximal voluntary ventilation (MVV) was performed before exercise testing. MVV was directly determined with the subjects using nose
clips and breathing deeply (with a volume greater than the tidal volume preceding the maneuver but less than the vital capacity) and rapidly for a 12-s interval (Pulmolab 435 Morgan Data Acquisition System Ver.401). The subjects were actively encouraged to maintain the same volume and frequency by following an online display of the maneuver on a computer screen, that is, the end expiratory level remained relatively constant. At least two acceptable maneuvers were obtained with values differing by no more than 10% and after flow integration, the highest value recorded by extrapolating the 12-s accumulated volume to 1 min (L/min, BTPS).

3. Lung volumes were determined in a constant volume whole body plethysmography (Master Screen Body, Jaeger, Version 4, 5) before exercise testing. The subjects completed at least three acceptable maneuvers. The predictive values for lung function parameters were derived from those published by the ATS.12,13

4. Arterial blood gases: Arterial blood gas (PaO2 and PaCO2) and pH were measured at rest, before exercise testing, while breathing room air, using a blood gas analyzer (Eschweiler system 2000).

5. Exercise test: The exercise tests (maximal incremental cycle ergometer protocol) were performed on a manual braked cycle ergometer (Pulmolab 505, Exercise test system VS B.42) with the subjects maintaining a pedaling frequency of 60±5 rpm.5 All tests were proceeding by a 1-min baseline of “true” unloaded pedaling, that is, by means of motor-assisted pedaling during this phase. After that exercise began at 25 W for 1 min, with 25 W increments every minute until exhaustion. Normally an increase of 5–10 W is appropriate when testing COPD patients. But Debigare et al.14 conclude that the work rate incremental rate influences only the Wpeak achieved, whereas the peak value for VO2 remains comparable. Subjects breathed through a mouthpiece with nose clips in place. Arterial oxygen saturation was monitored continuously by finger oxymetry. Electrocardiography and pulse oxymetry were monitored continuously during the exercise test and blood pressure was taken manually at periodic intervals. Expired gases were monitored and analyzed by computer for calculation of Vc, VO2, VCO2 and V̇O2/V̇T (as calculated from measurement PaCO2 and PECO2). Peak exercise was defined as the highest work level reached during the incremental exercise test. Patients were included in the analysis without respect to sub-maximal effort, cardiac rate limitation, or ventilatory limitation to exercise. The subjects were actively encouraging every 30 s using two phrases “You are doing well” or “Keep up the good work”. Exercise in the COPD subjects was terminated by any one of the following events:
   a. Subjective complaints (severe dyspnea, fatigue, dizziness, or chest pain);
   b. ECG abnormalities (ST changes, frequent ectopic beats).

Exercise responses were compared with the predicted normal values of ATS5 and ventilation (V̇E) was compared with the predicted maximal ventilatory capacity of Dillard and associates.15

Psychosocial: The following psychosocial measurements were included in this analysis:

1. Quality of life was assessed using the Saint George’s Respiratory Questionnaire.16
2. Depression and anxiety was assessed using the Greek version of the Hospital Anxiety and Depression Scale.17

Statistical analysis

PFT and exercise variables were expressed as means and standard deviations. Relationships between PFT and exercise variables were assessed using the Pearson product moment correlation (R). Correlation between QoL and physiological measures were done using the non-parametric Kendall concordance test. The statistical significant was set at P<0.05. Stepwise multiple regression (r2) was performed on the 57 patients to determine the best predictors of peak VO2 from independent variables (see Table 2 and 3). Computations were made with SPSS 10.1 program.

This analysis identified three variables as the best combination of predictors of peak VO2 (MVV, FEF2575, and BSA).

Results

A total of 57 COPD patients signed informed consent and entered the study. We studied 44 male and 13 female patients. The anthropometric data are presented in Table 1.

Physiologic parameters

Correlations between pulmonary function and exercise test results (VO2 peak) are presented in Table 2, which many variables of PFT correlated
statistically significant with the VO₂ peak. The stepwise multiple regression analysis to predict peak VO₂ from 57 patients elucidates that the best predictor was MVV (describe the 62% in total fluctuation of VO₂ peak, \( F = 46.8, P < 0.001 \)). FEF₂₅₇₅ plus 13% in total fluctuation (\( F = 14.3, P = 0.001 \)) and BSA were responsible for 6.5% in total fluctuation (\( F = 9.4, P = 0.005 \)). The total prediction from the three aforementioned predictors was 81.5%. Using only these variables as independent variables, the best regression equation to predict peak VO₂ was the following equation (\( n = 57 \)):

\[
\text{PeakVO}_2(\text{L/min}) = (\text{MVV} \times 0.024) + (\text{FEF}_{25-75} - 75 \times 0.47) + (\text{BSA} \times 0.988) - 0.913 \quad (r = 0.90; \ r^2 = 0.81, SE=0.29 \text{ L/min}).
\]

All the aforementioned data are presented in Table 3.

### Quality of life

Correlation between quality of life and the VO₂ peak is presented in Table 4. The VO₂ peak correlated significant primarily with activities (\( r = 0.503 \)). Total scores (0.409) of SGRQ, symptoms (\( r = 0.407 \)) and impacts (\( r = 0.298 \)) correlated less than the activities.

HADS score and VO₂ peak were not correlated significant as presented in Table 4.

### Discussion

The results of this study demonstrate that peak VO₂ can be predicted with excellent accuracy (\( r = 0.90; \ r^2 = 0.81 \)),

### Table 2

Correlation between VO₂ peak and resting pulmonary function parameters in 57 patients.

<table>
<thead>
<tr>
<th>Variable</th>
<th>COPD N = 57</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO₂ peak</td>
<td></td>
</tr>
<tr>
<td>Static lung volume</td>
<td>( R )</td>
</tr>
<tr>
<td>VC</td>
<td>0.767</td>
</tr>
<tr>
<td>IC</td>
<td>0.811</td>
</tr>
<tr>
<td>FRC</td>
<td>0.408</td>
</tr>
<tr>
<td>TV</td>
<td>0.430</td>
</tr>
<tr>
<td>Ventilatory output</td>
<td>MVV</td>
</tr>
<tr>
<td>Spirometry</td>
<td>FVC</td>
</tr>
<tr>
<td>FEV₁</td>
<td>0.619</td>
</tr>
<tr>
<td>PEFR</td>
<td>0.647</td>
</tr>
<tr>
<td>FIF₅₀</td>
<td>0.635</td>
</tr>
<tr>
<td>PIFR</td>
<td>0.678</td>
</tr>
<tr>
<td>FEF₂₅</td>
<td>0.474</td>
</tr>
<tr>
<td>FEF₇₅</td>
<td>0.404</td>
</tr>
<tr>
<td>FEF₂₅₇₅</td>
<td>0.381</td>
</tr>
<tr>
<td>FEF₅₀</td>
<td>0.345</td>
</tr>
<tr>
<td>Anthropometric</td>
<td>BSA</td>
</tr>
<tr>
<td>Weight</td>
<td>0.502</td>
</tr>
<tr>
<td>Arterial sample</td>
<td>PH</td>
</tr>
<tr>
<td>( PaO₂ )</td>
<td>0.193</td>
</tr>
<tr>
<td>( PaCO₂ )</td>
<td>−0.219</td>
</tr>
</tbody>
</table>

### Table 3

Stepwise multiple regression analysis to predict VO₂ peak (including only statistical significant variables), \( n = 57 \).

<table>
<thead>
<tr>
<th>Variable examined</th>
<th>Multiple R</th>
<th>Adjusted ( R^2 )</th>
<th>Unstandardized coefficients</th>
<th>Standardized coefficients</th>
<th>( t )</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVV</td>
<td>0.79</td>
<td>0.62</td>
<td>0.024</td>
<td>0.03</td>
<td>0.85</td>
<td>7.13</td>
</tr>
<tr>
<td>FEF₂₅₇₅</td>
<td>0.87</td>
<td>0.75</td>
<td>0.470</td>
<td>0.13</td>
<td>0.37</td>
<td>3.56</td>
</tr>
<tr>
<td>BSA</td>
<td>0.90</td>
<td>0.81</td>
<td>0.988</td>
<td>0.32</td>
<td>0.30</td>
<td>3.06</td>
</tr>
</tbody>
</table>

### Table 4

Relationship between SGRQ scores and HADS score with VO₂ peak (\( n = 57 \)).

<table>
<thead>
<tr>
<th>SGRQ score, % of total disability</th>
<th>VO₂ peak</th>
<th>r</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>40</td>
<td>0.407</td>
<td>0.026</td>
</tr>
<tr>
<td>Activities</td>
<td>52</td>
<td>0.503</td>
<td>0.005</td>
</tr>
<tr>
<td>Impacts</td>
<td>35</td>
<td>0.298</td>
<td>0.05</td>
</tr>
<tr>
<td>Total Score</td>
<td>41</td>
<td>0.409</td>
<td>0.013</td>
</tr>
<tr>
<td>HADS score, % of total disability</td>
<td>Anxiety</td>
<td>30</td>
<td>0.120</td>
</tr>
<tr>
<td></td>
<td>Depression</td>
<td>19</td>
<td>0.187</td>
</tr>
<tr>
<td></td>
<td>Total score</td>
<td>27</td>
<td>0.106</td>
</tr>
</tbody>
</table>
SE=0.29 L/min) in patients with COPD from the independent variables utilized in this analysis. The combination of independent variables found to be most predictive of peak VO$_2$ was MVV, FEF$_{2575}$, and BSA.

The reasons for trying to predict peak VO$_2$ from measures of resting pulmonary function are multiple. Patients could possibly save time, expense, and invasive procedures if an accurate prediction of their maximum exercise tolerance could be made based upon resting pulmonary function parameters. Also, this knowledge may help the patient to get advice about how to do exercises or to be physically active. Reasonably accurate prediction equations could also be used to determine if the measured peak VO$_2$ is consistent with the patient’s physiologic status. This might indicate a need for further evaluation of the patient, with “unexplained” exercise limitation in an individual whose exercise tolerance is reduced out of proportion to that predicted from the resting pulmonary function. This might be especially helpful in the area of disability evaluation.

None of the psychosocial variables measured in this study were found to be significant predictors of peak VO$_2$ once variance associated with physiologic variables was removed. Using multiple regression analysis, Mahler and Harver$^6$ found that the baseline dyspnea index was an important predictor of peak VO$_2$ in a group of patients with COPD. In the present study, neither the measures of SGRQ nor measures of HADs added significantly to the overall prediction equation. The correlations between individual predictor variables and peak VO$_2$ were only slightly lower in the present study than those reported in the study of Mahler and Harver.$^5$

Most similar published studies have examined only patients with COPD.$^6,18-21$ The methodology used in these studies was similar to that used in the present one, namely multiple regression analysis of different parameters of resting and exercise pulmonary function to generate one or more prediction equations of either peak VO$_2$. Differences in results could be related to differences in patients (e.g., disease severity) and to the specific variables examined. For instance, the degree of expiratory obstruction is variable in these studies, with the mean FEV$_1$ between 1.22 and 1.85 L, and the prediction equations explained between 79% and 91% of the variance in measured peak VO$_2$.

Dillard et al. demonstrated a strong relationship between peak VO$_2$ and MIP as well as power output, V$_E$ max DCO and FEV$_1$. This relationship led the authors to conclude that inspiration strength may be an important determinant of exercise capacity in COPD patients. In our prediction equation MVV may well explain the variance in peak VO$_2$ accounted for by MIP and FEV$_1$, as MVV depends upon both inspiration and expiration.

In addition, it is well known that the expiratory airflow limitation is the hallmark of physiological change of COPD.$^1$ The sites of airflow limitation in COPD are the smaller conducting airways (less than 2 mm in internal diameter).$^1$ FEF$_{2575}$ constitutes the parameter that is determined by spirometry, which gives an average flow over the mid-portion of the spirogram. McFarden et al.$^{22}$ postulated that low FEF$_{2575}$ represents the significant obstruction in peripheral bronchioles, despite the variance of FEF$_{2575}$ being generally about 40%, our analysis distinguishes this parameter as the second best predictor. Perhaps, FEF$_{2575}$ represents a more sensitive parameter such as Obliterative Bronchiolitis.$^{22,23}$

The last variable that contributes to our equation is BSA. It is well known that the absolute VO$_2$ peak is strongly influenced by change in body size.$^4$ For that reason, the appropriate adjustment of this parameter for body size should help to explain the impact of other factors. BSA is utilized to measure the metabolic rate in a clinical setting. Obese people have higher total daily energy expenditures because of the excess fat they have to transport when active. Because of the increased metabolic rate to perform a certain amount of external work, i.e., work to move larger body mass, there must be greater than normal cardiorespiratory response to exercise.$^4$ Perhaps BSA contributes to normalizing our equation.

Previous studies found a moderate correlation between maximal exercise capacity and the resting IC$^{24,25}$ but only in patients with flow limitations. In our patients, there was no significant correlation of VO$_2$ peak to IC, because our study may be concluded in flow and non-flow limitation patients.

In summary, maximum exercise tolerance is predicted reasonably well from measurements of resting pulmonary function in these COPD patients. The most consistent predictors of VO$_2$ peak were measurements of expiratory airflow limitation (FEF$_{2575}$) and inspiratory–expiratory strength (MVV); none of the psychosocial variables added significantly to the accuracy of the prediction of peak VO$_2$.

References


