Assessment of Functional Capacity in Patients with Chronic Obstructive Pulmonary Disease: Correlation between Cardiopulmonary Exercise, 6 Minute Walk and 15 Step Exercise Oximetry Test

Daniel Starobin MD1, Mordechai R. Kramer MD2, Alexander Yarmolovsky MD1, Daniel Bendayan MD2, Izhak Rosenberg MD1, Jacqueline Sulkes PhD2 and Gershon Fink MD1

1Pulmonary Institute, Kaplan Medical Center, Rehovot, Israel
Affiliated to Hebrew University-Hadassah Medical School, Jerusalem, Israel
2Pulmonary Institute, Rabin Medical Center (Beilinson Campus), Petah Tiqva, Israel
Affiliated to Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

Key words: chronic obstructive pulmonary disease, cardiopulmonary exercise test, 6 minute walk, 15 step exercise oximetry test

Abstract

Background: Different exercise tests are used to evaluate the functional capacity in chronic obstructive pulmonary disease. The cardiopulmonary exercise test is considered the gold standard, but the 6 minute walk and the 15 step exercise oximetry test are considerably less expensive.

Objectives: To determine whether reliable data could be obtained at lower cost.

Methods: The study sample consisted of 50 patients with mild to severe stable COPD. All underwent pulmonary function test and the cardiopulmonary exercise test, 6 minute walk and 15 step exercise oximetry test as part of their regular follow-up visit. Functional capacity was graded according to each test separately and the functional capacities obtained were correlated.

Results: The results showed that most of the patients had severe COPD according to pulmonary function tests (mean forced expiratory volume in the first second 46.3 ± 19.9% of predicted value). There was a good correlation between the cardiopulmonary exercise test and the 6 minute walk functional capacity classes (r = 0.44, P = 0.0013). We did not find such correlation between the 15 step exercise oximetry test and the cardiopulmonary exercise test (r = 0.07, P = 0.64).

Conclusions: The study shows that the 6 minute walk is a reliable and accurate test in the evaluation of functional capacity in COPD patients.

Several tests are available for the evaluation of functional capacity in patients with chronic lung diseases. These include the cardiopulmonary exercise test [1], the 6 minute walk [2] and the 15 step exercise oximetry test [3]. The CPXT is considered the gold standard but it is more expensive than other tests that were proven useful for clinical purposes [3-13]. There is scant information in the literature on a correlation between the 6 minute walk and 15 step exercise oximetry, and CPXT [14,15].

The aim of the present study was to correlate the findings of CPXT with the other two tests, and to determine whether reliable functional capacity data can be obtained at a lower cost in patients with chronic obstructive pulmonary disease.

Patients and Methods

An open study design was used. The study population comprised 50 patients with mild to severe COPD attending the Pulmonary Institute at Rabin Medical Center, a tertiary care hospital in central Israel, during a 6 month period from March to August 2003.

Inclusion criteria were age 20–75 years, stable COPD for the 2 months preceding the study, and signed informed consent. COPD was diagnosed according to criteria of the American Thoracic Society [16]. Patients with any acute or chronic cardiac disease, exacerbation of COPD or other pulmonary or infective diseases within 2 months preceding the trial were excluded. Nine COPD patients were not enrolled in the study due to one or more of the above-mentioned exclusion criteria.

As part of their regular follow-up visit, patients first underwent a pulmonary function test, followed on the same day by the upright maximal CPXT, the 6 minute walk and the 15 step exercise oximetry test. The interval between tests was at least one hour. The order of the exercise tests was randomized.

Patients were classified according to the VO2 max results obtained by CPXT as mild, moderate or severe impairment. Separate grading was also done for the 6 minute walk and 15 step exercise oximetry test [Table 1], and the results were compared with the CPXT.

Table 1. Severity of respiratory impairment in patients with COPD, measured by CPXT, 6 minute walk and 15 step exercise oximetry [4-10]

<table>
<thead>
<tr>
<th>Test</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO2 max (ml/kg/min)</td>
<td>20–25</td>
<td>15–20</td>
<td>&lt;15</td>
</tr>
<tr>
<td>6 minute walk distance (m)</td>
<td>&gt;451</td>
<td>301–450</td>
<td>&lt;300</td>
</tr>
<tr>
<td>15 step exercise oximetry test: SaO2 difference (baseline, lowest) (%)</td>
<td>0.5–1.5</td>
<td>1.51–3.0</td>
<td>&gt;3.1</td>
</tr>
</tbody>
</table>

COPD = chronic obstructive pulmonary disease
CPXT = cardiopulmonary exercise test

D. Starobin et al.
Pulmonary function test

This test included spirometry, lung volume, maximal voluntary ventilation and diffusion capacity by single-breath technique. For calibration, a 5 L syringe was used at the beginning of each session on each day. Measurements were corrected for body temperature and pressure saturation. Testing was performed with the Medical Graphics Pulmonary Function System (1070-series 2, St. Paul, MN, USA). Lung volumes were obtained by body plethysmography (model 1085, Medical Graphics). MVV was assessed by asking the patient to breathe as fast and deep as possible for 12 seconds, and the result was multiplied by 5. Diffusion capacity was measured with a gas mixture containing air, 10% helium, and 0.3% carbon monoxide; each diffusion capacity measurement was adjusted to standard temperature and pressure. The predicted values of the parameters were obtained from the regression equations of the European Community for Coal and Steel.

Cardiopulmonary exercise protocol

Exercise testing was done between 8:30 a.m. and 12:00 noon. Patients were encouraged to take their medications as usual. Each participant underwent an incremental exercise test according to the protocol of Wasserman et al. [1]. On arrival at the exercise laboratory patients were connected to a 12-lead electrocardiogram (Cardiofax, Nihon Kohden, Tokyo, Japan) with a single-lead (V5) monitor (VC-22, Nihon Kohden); oxygen saturation (SaO2) was measured by pulse oximetry (Nellcor NPB-190, CA, USA) and blood pressure with a sphygmomanometer. The patient was then positioned on an electrically braked cycle ergometer (Ergoline 800, Germany). After a 2 minute rest (arms at sides) the patients performed unloaded pedaling for 2 minutes at a rate of 60 rpm. The load was then progressively increased by 15 watts/min (ramp protocol). The duration of the test was symptom-limited; the endpoint was defined as the point at which the patient could not maintain a pedaling rate of more than 40 rpm.

Cardiopulmonary data were collected and analyzed with an exercise metabolic unit (CPX, Medical Graphics). Heart rate, minute ventilation, tidal volume (VT), oxygen consumption (VO2), carbon dioxide production (VCO2), oxygen pulse (O2P) and oxygen saturation (SaO2) were recorded and calculated over 30 second intervals using standard formulas. Blood pressure was measured with a sphygmomanometer at rest and every 2 minutes until peak exercise. The dyspnea index (VE/MVV), expressed in percent, was calculated manually.

6 minute walk test

The 6 min walk test was performed along a measured indoor corridor in our institute. Participants were encouraged to cover as much distance as possible.

15 step exercise oximetry test

A finger oximeter (model 8500, Nonin Medical, Plymouth, MN, USA) with continuous online recording of heart rate and oxygen saturation was connected to each patient. Data were sampled every 2 seconds, and the mean value was recorded every 10 seconds. A step measuring 25 x 25 x 20 cm was used. Patients were asked to climb up and down the step 15 times as fast as they could (without any fixed pacing). Each test was repeated twice, and the mean value was taken. When oximeter readings were not optimal, as indicated by yellow or red signals, the data were discarded. The time of exercise was recorded (exercise time), as was the time from start to lowest saturation (desaturation time). The total test time was defined as the time from the start of exercise to complete recovery. Baseline oxygen saturation, lowest saturation, and highest heart rate were recorded as well.

Statistical analysis

Results are reported as mean ± 1 standard deviation. Analysis of variance and the Tukey test for multiple comparisons were used to calculate significant differences between groups by maximum oxygen consumption (VO2max). The BMDP statistical package was used. Kaplan-Meier curves were constructed to compare peak values of VO2max and 6 minute walk ranges or stairs-climbing test parameters with the Mantel-Cox trend-plot statistic. Linear correlation between the desaturation area and the 5 min walk distance was analyzed. Comparison between groups was done using ANOVA. Pearson correlation coefficients (r) and the significance for it (P) were calculated between the variables. To predict VO2max, a stepwise linear regression model was fitted to the data. P ≤ 0.05 was considered statistically significant.

Results

Demographic data

All 50 patients with COPD completed the pulmonary function and the three exercise tests (CPXT: 6 min walk and 15 step oximetry). The mean age of the participants was 64.3 ± 11.7 years (range 27–78 years); 28 were male and 22 female. None had diseases other than COPD that could have influenced the exercise test results (e.g., congestive heart failure, neurologic or orthopedic disorders).

Lung function tests

Pulmonary function test revealed severe COPD in most of the patients, mean FEV1 was 46.3 ± 19.9% of predicted value (range 99% to 16%). There was no statistically significant correlation between the pulmonary function test results and functional capacity by exercise tests. Baseline oxygen saturation was higher than 91% in the study patients (range 91% to 98%). No patient used supplemental oxygen.

Exercise tests

Mean VO2max was 13.5 ± 4.1 ml/kg/min (range 6.9–28.1). According to the pre-selected criteria 37 patients had severe disability (mean VO2max 12.0 ± 3.5 ml/kg/min), 9 had moderate disability (16.2 ± 1.1 ml/kg/min) and 4 had mild disability (21.4 ± 0.5 ml/kg/min).

The mean 6 minute walk distance was 434.7 ± 88.0 m (range

MVV = maximal voluntary ventilation
VE = minute ventilation
FEV1 = forced expiratory volume in the first second
Disability was severe in 19 patients, moderate in 28 and mild in 4.

On the 15 step exercise oximetry test maximal difference in oxygen saturation for the study group was 12%, and the minimal was 0%. Patient classification in accordance with preset criteria yielded 16 with severe disability, 19 with moderate disability and 15 with mild disability.

**Correlation analysis**

There was a good correlation between the CPXT and 6 minute walk disability classes \((r = 0.44, P = 0.0013)\), and an even better correlation between \(VO_2\max\) value and 6 minute walk distance \((r = 0.58, P = 0.0001)\) [Figure 1]. No correlation was noted between the 15 step exercise oximetry test results and either the CPXT \((r = 0.07, P = 0.64)\) or the 6 min walk \((r = 0.13, P = 0.34)\). On multivariate analysis, the 6 minute walk distance and patient's age were statistically significantly correlated with \(VO_2\max\) \((P = 0.0003\) and \(P = 0.032\), respectively). The linear regression model predicted a 0.1 ml/kg decrease in \(VO_2\max\) for every year increase in age, and a 0.02 ml/kg increase in \(VO_2\max\) for every meter increase in 6 min walk distance. The linear regression equation for the calculation of \(VO_2\max\) was fitted to this model

\[
[VO_2\max = 9.99-0.096 \times \text{age}(\text{yr}) + 0.022 \times 6 \text{ min walk}(\text{m})].
\]

**Discussion**

The present study indicates, as is well known, that the pulmonary function test cannot accurately predict exercise performance of patients with COPD [4-7]. FEV1 showed a good correlation only with functional capacity according to the 15 step exercise oximetry test \((r = 0.44, P = 0.0011)\).

Breathing physiology studies during the last decade found that expiratory flow limitation and reduced inspiratory capacity are correlated with severity of disease in COPD patients [17]. These parameters were shown to be accurate tools for predicting functional capacity in COPD patients although no grading system has yet been proposed.

Our analysis of the relationship between the CPXT, the 6 minute walk and the 15 step exercise oximetry test showed a statistically significant correlation for the functional capacity findings between the CPXT and the 6 min walk. As depicted in Figure 1, the strongest correlation was found for the mild and moderate disability classes. Specifically, all patients with mild disability by the CPXT \((VO_2\max > 20 \text{ ml/kg/min})\) achieved a distance of more than 520 m on the 6 min walk, whereas those with moderate disability by the CPXT \((VO_2\max 15-20 \text{ ml/kg/min})\) achieved a distance of not less than 420 m. The correlation was less clear in the severe disability CPXT subgroup \((VO_2\max < 15 \text{ ml/kg/min})\), which had a wide distribution of results on the 6 min walk from 250 to 550 m. Although most of these patients had a distance in the range 300 to 450 m, the uncertainty of the significance of the 6 min walk in patients with severe disability could not be resolved in our small sample.

On the basis of these results, we suggest that the upper limits of the 6 minute walk functional capacity classes be increased by about 50–70 m. Our study confirms the reliability of the 6 min walk in the clinical evaluation and follow-up of patients with COPD. At the same time, the 6 minute walk is both very easy to administer and, of course, less expensive than CPXT. Its results were quite accurate compared to the cardiopulmonary exercise test. Application of the 6 min walk in the evaluation of professional disability was not investigated in this sample. Common sense and previous studies [2-3] indicate that “compensation-orientated” persons are not well motivated to achieve their maximal exercise capacity. We conclude that the 6 minute walk is a relatively reliable and accurate test for the assessment of functional capacity in patients with COPD. The 15 step exercise oximetry test, however, has no correlation to the CPXT in these patients.

**References**

11. Berry MI, Rejeski WJ, Adair NE, Zaccaro D. Exercise rehabilitation

Correspondence: Dr. G. Fink, Pulmonary Institute, Kaplan Medical Center, Rehovot 76100, Israel.
Phone: (972-8) 944-1438
Fax: (972-8) 944-1063
email: daniel_s@clalit.org.il

Our society must make it right and possible for old people not to fear the young or be deserted by them, for the test of a civilization is the way that it cares for its helpless members

Pearl S. Buck (1892-1973), U.S. novelist and winner of the Nobel Prize for Literature. The daughter of Presbyterian missionaries, she grew up in China and later returned there as a teacher. Her most famous novels about China include The Good Earth and The Three Daughters of Madame Liang.

Capsule

Good gut flora

At least 10 trillion microorganisms inhabit our lower intestinal tract; without them, we could not process the bulk of our food and we would be vulnerable to the damaging effects of ingested toxins. Gill and colleagues present a detailed metagenomic analysis of human intestinal microflora. Colonic bacteria and archaea not only help to keep the gut wall intact and healthy; they supply us with a suite of glycoside hydrolases to digest plant carbohydrates, trophic chains of organisms for fermentation of fiber to short chain fatty acids, methanogenesis for hydrogen scrubbing, the means to synthesize amino acids and vitamins, and pathways for the transformation of xenobiotic compounds from plant phenolics to tetrachloroethene.

Science 2006;312:1355
Eilat Israeli

Promoting nerve regeneration

In general, neurons in the mature vertebrate central nervous system fail to regenerate after injury. Intriguingly, however, activation of macrophages in the eye after damage to the optic nerve stimulates the regeneration of retinal ganglion cells (RGCs), so that their axons grow beyond the site of injury. Yin et al., who previously determined that macrophage-secreted proteins less than 20 kDa in size promoted axon regeneration, used mass spectrometry of a prominent component and identified oncomodulin, a calcium-binding protein that has been found in tumors. Although inactive on its own, oncomodulin potentiated the ability of mannose plus forskolin (which elevates cAMP levels) to promote axon outgrowth in cultured RGCs. Pharmacological analysis indicated that oncomodulin activity depended on Ca2/calmodulin-dependent kinase II and on gene transcription. Delivery of oncomodulin and a cAMP analog into the vitreous promoted optic nerve regeneration in vivo. Thus, oncomodulin appears to represent a previously unidentified macrophage-derived trophic factor capable of promoting axonal regeneration in at least some central neurons.

Nat Neurosci 2006;9:843
Eilat Israeli