Original Article

Cardiopulmonary Exercise Testing in Evaluation of Patients of Chronic Obstructive Pulmonary Disease

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ABSTRACT

Background. Objective assessment of severity in patients with chronic obstructive pulmonary disease (COPD) is mainly limited to pulmonary function testing performed at rest. But, accurate assessment of exercise capacity in patients with COPD may be possible with cardiopulmonary exercise testing (CPET).

Methods. Forty-three patients with stable COPD were included and were divided into three groups based upon the spirometry data as per the Global Initiative for Obstructive Lung Disease (GOLD) guidelines as follows: Group A: mild COPD, Group B: moderately severe COPD and Group C: severe COPD. Symptom-limited CPET was performed using treadmill on incremental continuous ramp protocol in all of them.

Results. Five patients (11.6%) had mild COPD; 16 (37.2%) had moderately severe COPD and the remaining 22 (51.6%) patients had severe COPD. Anaerobic threshold was attained in all the 43 patients. The dominant symptom at peak exercise were dyspnoea (n=19) and both dyspnoea and leg fatigue (n=7). The other causes of exercise limitation included dyspnoea with significant oxygen desaturation (n=6); and dyspnoea with severe oxygen desaturation (n=2). Six patients complained only of leg fatigue at peak exercise.

A significant correlation between forced expiratory volume in the first second (FEV_1) percent predicted and the predicted maximum oxygen uptake ($\dot{V}O_2$ max % predicted) was observed in all the three groups (r=0.39, p=0.011) but with marked variability of peak $\dot{V}O_2$ for a given degree of airflow obstruction. Twenty-three (53.5%) patients with low anaerobic threshold (<30%) were identified as potential group likely to benefit from exercise training for pulmonary rehabilitation.

Conclusions. Cardiopulmonary exercise testing is useful to determine the causes of exercise limitation and to assess the maximal exercise capacity of patients with COPD. **[Indian J Chest Dis Allied Sci 2011;53:87-91]**

Key words: Chronic obstructive pulmonary disease, Cardiopulmonary exercise testing.

INTRODUCTION

Exercise intolerance is a hallmark of chronic obstructive pulmonary disease (COPD). Although exertional symptoms may be mild at the outset, exercise limitation is the most disabling and distressing consequence of COPD for majority of the patients.

Presently, objective assessment of severity in cases of COPD is mainly limited to pulmonary function test performed at rest.[1] But it is the integrated influence of multiple factors, e.g., pulmonary mechanics, pulmonary circulation, cardiac, peripheral muscle and psychological factors that determine the functional level of an individual patient. Various types of exercise testing may serve this integrative role and help in objectively assessing the functional outcome in COPD. The exercise tests that are available include stair climbing, walk testing, and cardiac stress testing. These vary widely in terms of reproducibility, cost and information provided.

Of these, cardiopulmonary exercise testing (CPET) is the most comprehensive, and correlates best with the symptoms of COPD with objective evidence of physiologic limitation. It provides the global assessment of the integrative exercise responses involving the pulmonary, cardio-vascular, haematopoetic, neuropsychological and skeletal muscle system, which are not adequately reflected through the measurement of individual organ system function. In patients with COPD, maximal oxygen uptake ($\dot{V}O_2$ max) has been considered to reflect the severity of the disease in contrast to resting pulmonary function test which can not predict exercise performance and exercise

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induced hypoxaemia.[2] This accurate assessment of severity and exercise capacity with CPET in patients of COPD may be useful for the purpose of exercise prescription and determining response to therapy.

Use of CPET in patient management is increasing with the understanding that overall health status correlates better with exercise tolerance rather than with resting measurements. Therefore, the present study aimed to assess the exercise capacity of patients with COPD, determine the cause of exercise limitation and to correlate FEV_1 and $\dot{V}O_2$ max.

MATERIAL AND METHODS

The patients with stable COPD, defined as per the American Thoracic Society (ATS) Guidelines,[3] attending Chest Out-patient Department at Government Medical College, Nagpur were selected for this study. A written consent was obtained from all the participants. The patients were evaluated using a detailed questionnaire.[4] Laboratory investigations, like chest radiograph, electro-cardiogram, blood glucose, haemoglobin estimation were done. Height, weight, heart rate, respiratory rate, blood pressure and oxygen saturation were noted.

Patients with obesity, defined as a body mass index (BMI) greater than $30 kg/m^2$, diabetes mellitus, anaemia, hypertension, history of myocardial infarction, valvular heart diseases, cor-pulmonale, congestive cardiac failure, any other cardiac diseases, musculo-skeletal abnormalities, peripheral vascular disease and very severe COPD were excluded from the study.

The patients, thus, selected in the study were divided into three groups depending upon the spirometry results as per the GOLD guidelines.[5] Group A: mild COPD; Group B: moderately severe COPD; and Group C: severe COPD. Resting pulmonary function test and CPET were performed on the same day as per ATS guidelines.

Symptom-limited CPET was performed on treadmill using Bruce protocol,[6] using cardio-pulmonary exercise machine (Make-Medical Graphics Corporation USA: Software: Breeze Suite Version 6.2). The test was carried out under the supervision of a chest physician with defined criteria for stopping, such as serious cardiac arrhythmias, hypotension, and severe oxygen desaturation.

The various parameters were measured as per the guidelines of the Joint Statement of the ATS/ American College of Chest Physicians (ACCP).[7] Arterial oxygen saturation (SpO_2) and heart rate were recorded via pulse oximetry during exercise and during recovery. Standard 12-lead electro-cardiograms were obtained at rest, every three minutes during exercise and five minutes into the recovery phase. Blood pressure was measured using a standard cuff sphygmomanometer at rest at $\dot{V}O_2$ max and five minutes into the recovery. At the end of exercise the reason(s) for termination of exercise were obtained from the subjects. The $\dot{V}O_2$max was the highest $\dot{V}O_2$ observed during exercise.

Anaerobic threshold was defined as: *(i)* the point at which the ventilatory equivalent for O_2 ($VE/\dot{V}O_2$) was minimal followed by a progressive increase; *(ii)* the point after which the respiratory gas exchange ratio consistently exceeded 1; and *(iii)* the $\dot{V}O_2$ after which expired carbon dioxide increased non-linearly relative to oxygen consumption. The anaerobic threshold percent (%AT) was defined as ($\dot{V}O_2$ at AT/predicted maximal $\dot{V}O_2$) ×100.

The criteria for maximal test in this study were: *(i)* peak $\dot{V}O_2$ equal to or greater than 85% of the predicted value; *(ii)* exercise terminated due to serious electrocardiogram (ECG) abnormality; *(iii)* maximal heart rate attained was greater than 85% predicted; *(iv)* percentage of minute ventilation at peak exercise (VEmax) greater than 85% of MVV; and *(v)* significant decrease in oxygen saturation of greater than four percent[1]. Exercise was considered maximal if one or more of the criteria was reached.

The exercise was also terminated at: *(i)* exhaustion (intolerable dyspnoea as indicated by patient); *(ii)* severe desaturation SpO_2 (<80%); *(iii)* demand by patient for leg cramps, chest pain, discomfort etc; and *(iv)* demand by patients for other reasons.

Statistical Analysis

For statistical analysis the relationship between two sets of data was analysed by computing Pearson's correlation coefficient. Comparison of continuous variables that were normally distributed between groups was done with unpaired 't' test. A p-value of less than 0.05 was considered to be statistically significant.

RESULTS

The anthropometric and pulmonary function data of 43 patients in this study are shown in table 1. The subjects included patients with mild to severe obstructive abnormalities with a wide range of FEV_1 predicted values but the majority of them 38 (88.4%) had moderately severe COPD (n=16; 16%) and/or severe COPD (n=22; 22%) as defined by GOLD guidelines.[5]

Table 1. Anthropometric and pulmonary function data

Variable	Mean±SD	Range
Gender (Male/Female)	29:14	
Age (years)	57.4±11.6	34–76
BMI (kg/m^2)	18.2±3.1	14.2–26.1
Haemoglobin (g/dL)	13.8±0.5	12.5–14.8
FVC% predicted	79.7±21.7	48.0–124.0
FEV_1% predicted	51.1±16.9	24.0–82.0
CPET		
$\dot{V}O_2$max (mL/kg/min)	17.1±5.23	5.4–32.10
$\dot{V}O_2$max(%predicted)	37.2±12.1	14.0–64.0
$\dot{V}O_2$ at AT (mL/kg/min)	11.5±10.2	2.3–32.2
%AT	29.3±15.4	4.4–70.9
Physiological parameters		
Heart rate (per min)(at rest)	84±9	68–110
Heart rate (per min) (at $\dot{V}O_2$max)	113±12	88–140
BP (at rest) systolic (mmHg)	126±7	110–134
BP (at Rest) diastolic (mmHg)	78±6	68–90
BP (at $\dot{V}O_2$max) systolic (mmHg)	158±11	130–176
BP (at $\dot{V}O_2$max) diastolic (mmHg)	89±4	80–100
%SaO_2 (at rest)	97±1	96–99
%SaO_2 (at $\dot{V}O_2$max)	94±3	78–97

BMI=Body mass index; FVC=Forced vital capacity; FEV_1=Forced expiratory volume in the first second; CEPT=Cardio-pulmonary exercise testing; %AT= Anaerobic threshold percent; $\dot{V}O_2$=Maximal oxygen uptake; BP=Blood pressure; SpO_2=Oxygen saturation measured by pulse oximetry

The CPET data for the three groups are as shown in table 2. Statistical analysis showed that the difference between $\dot{V}O_2$ max in Group A (mild COPD) and Group C (severe COPD); Group A (mild COPD) and Group B (moderately severe COPD) was statistically significant (p<0.0001). But difference between $\dot{V}O_2$max of Group B (moderately severe COPD) and Group C (severe COPD) was statistically not significant (p=0.9105). Anaerobic threshold was attained in the study by 43 patients with COPD. The %AT was low (<30%) in 23 (53.5%) patients with COPD.

Relationship between FEV_1 and peak oxygen uptake is shown in the figure. Although there was significant correlation (r=0.39, p=0.011) between FEV_1 % predicted and peak $\dot{V}O_2$% predicted, there was marked variability of peak $\dot{V}O_2$ for a given degree of airflow obstruction.

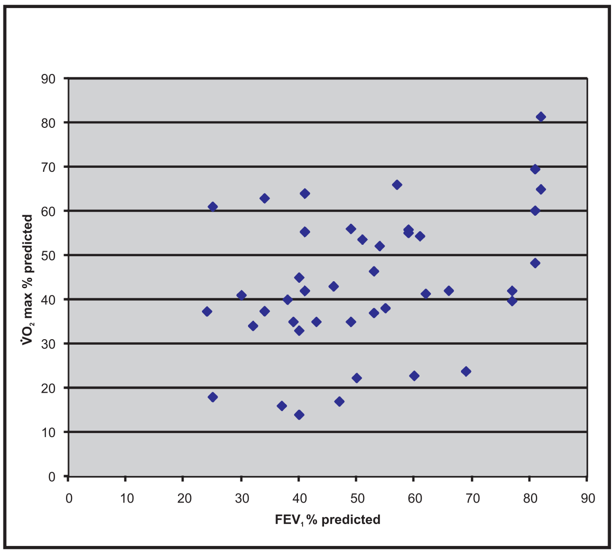

Figure. Correlation between FEV_1 and $\dot{V}O_2$ max.

FEV_1=Forced expiratory volume in the first second; $\dot{V}O_2$max=Maximum oxygen uptake

The dominant symptom at peak exercise were dyspnoea in 19 patients (44.9%), dyspnoea with leg fatigue in 7 patients (16.3%), dyspnoea with significant oxygen desaturation in six (14.0%); dyspnoea oxygen desaturation and leg fatigue in two (4.6%).

The other causes of exercise limitation were severe oxygen desaturation in two (4.7%) and chest pain in one patient (2.3%). Neither cardiovascular limitation nor serious electrocardiographic abnormality was observed in any of the subjects in the study. Termination of exercise by the supervising chest physician was not required for any patient and there were no complications arising from the conduct of CPET in any patient.

Table 2. Cardio-pulmonary exercise testing values for various groups

Group	$\dot{V}O_2$max Predicted	$\dot{V}O_2$max Observed	$\dot{V}O_2$ max % Predicted	$\dot{V}O_2$ at AT	%AT
A (mild COPD)	42.4	26.7±4.0	64.8±12.3	22.6±7.4	47.1±15.8
B (moderately severe COPD)	40.5	16.8±2.2	43.3±12.8	10.2±4.2	27.3±12.3
C (severe COPD)	42.3	15.2±4.7	39.1±14.6	9.9±4.0	25.1±12.4

$\dot{V}O_2$ max=Maximal oxygen uptake; %AT=Anaerobic threshold percent; COPD=Chronic obstructive pulmonary disease

DISCUSSION

Simple physiologic parameters, such as forced expiratory volume have been traditionally used to define the severity of diseases involving the lungs. However, these studies showed only a moderate relationship between the lung function impairment and reduced exercise capacity. We found a significant correlation between FEV_1 % predicted and $\dot{V}O_2$ max % predicted in patients of all three groups of mild, moderately severe and severe COPD, but there was a marked variability of peak $\dot{V}O_2$ for a given degree of airflow obstruction. That is; there is a wide range of exercise performance for a given degree of airflow obstruction. The findings are similar to earlier obsevations[1] inferring that FEV_1 may not adequately characterise the degree of functional impairment that the disease process imposes on the individual.

Though a six-minute walk distance testing is simple, easy, reproducible way to test the patient's functional level; it lacks standardisation in methodology, does not collect basic physiologic data during exercise and its use is limited to moderate or severe disease. Also, it cannot be used for assessing the mechanisms of impairment which the CPET tries to assess objectively.[1]

When the symptoms which contributed directly, or indirectly to exercise limitation during CPET were analysed, dyspnoea was the predominant symptom. The next important cause for exercise limitation in our study was leg fatigue followed by the occurrence of dyspnoea along with leg fatigue. These symptoms were also the dominant symptoms in majority of the studies.[1, 8, 9] While it is expected and well established that patients with COPD become more breathless and show significant oxygen desaturation[1] than controls during exercise at similar work rates (given the limited ventilatory reserve of these patients); the frequency of the complaint of leg fatigue in patients of COPD during CPET raises a possibility of dysfunction of limb muscles in the patients.

The limb muscle strength has often been found to be reduced in patients with COPD.[10] Also there is evidence for muscle wasting and change in muscle fiber types in patients of COPD.[11-14] Possibly secondary to these structural changes the muscle metabolic capacity is reduced. A low activity of mitochondrial enzymes has also been demonstrated in lower limb muscles in patients with COPD.[15]

The exact mechanisms underlying limb muscle dysfunction in patients with COPD are not known but major possibilities include malnutrition, impaired muscle perfusion, hypoxia, inactivity, medications and loss of muscle mass secondary to ageing.[16] Thus, it can be seen that CPET can assist identifying patients with symptom limitation suggestive of limb muscle dysfunction so that therapeutic strategies, such as exercise training, nutritional intervention or anabolic steroids can be considered.[17]

The AT was attained in our study by all 43 patients but the %AT was low (<30%) in 23 (53.5%) patients with COPD. A low AT during CPET can be considered as indicative of deconditioning in sedentary patients with COPD as compared to active patients who have normal AT during CPET. These patients with low AT during CPET have the potential to improve exercise tolerance with exercise training.[1] This group of patients is most likely to benefit from exercise training during pulmonary rehabilitation. Based on the exertional symptoms alone, it would not have been possible to differentiate them from rest of the COPD patients.

To summarise, CPET, non-invasively determines the cause of exercise limitation in majority of patients with COPD. The causes of exercise limitation in this study were dyspnoea and/or oxygen desaturation. Limb muscle dysfunction could be a contributory factor in some of the patients causing exercise limitation. The CPET identifies patients likely to benefit from pulmonary rehabilitation. Spirometry at rest may not accurately predict exercise capacity in COPD patients and CPET ($\dot{V}O_2$max) adds significantly to FEV_1 in determining physical function and maximal exercise capacity.

However, the limitations of the study were a small sample size when divided into groups and marked variability of the data. Further studies on cardiopulmonary testing in patients with COPD are needed to assess the mechanisms limiting exercise and predicting maximal exercise capacity.

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