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Relationship Between Exercise Capacity and Clinical Measures in Patients with Chronic Obstructive Pulmonary Disease

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ABSTRACT

The aim of this study was to determine the relationship between Minute Walk Distance Test (6MWT), dyspnea, quality of life and disease severity and to identify the predictors of 6MWT among chronic obstructive pulmonary disease (COPD) patients. A total of 36 patients (33 male, 3 female) with mild–to-very severe COPD participated in this study. The 6MWT was performed based on American Thorax Society's protocol. The disease severity was evaluated using spirometery and the health related quality of life was assessed by Persian version of the St George's Respiratory Questionnaire (SGRQ) and the exertional dyspnea was measured by Borg score. The data were analyzed using the Pearson's linear correlation coefficient, Spearman's correlation coefficient and Multivariate linear regression assessments. The 6MWT correlated positively with FEV_1 ($r=0.36$, $p<0.05$) and FVC ($r=0.37$, $p<0.05$), while there was no significant correlation between disease severity based on GOLD classification and 6MWT, also No statistically significant correlation was found between exertional dyspnea and 6MWT. A negative correlation was found between 6MWT and total score of QOL, activity and impact domain, respectively ($r=-0.39$, $r=-0.44$, $r=-0.40$, $P<0.01$). Multiple regression analysis indicated that the age was identified as independent predictor of the 6MWT. This study showed stronger relationship between 6MWT and HRQL (activity and impact) compared with the physiological measures of disease severity such as FEV_1.

Key words: Exercise capacity, Chronic Obstructive Pulmonary Disease, 6 Minute Walk Distance Test.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is an irreversible disease with chronic airflow limitation[1].It'sone of the major causes of mortality and morbidity worldwide[2].COPD patients suffer from relatively severe dyspnea and disability despite regarding their disease severity[3] these problems are usually reason for seeking medical services[4].

Exercise capacity is one of the most important physiologic measures in COPD patients[5]. It can potentially evaluate various limitations and recognize their contributing factors[5]. There are some methods for measuring exercise capacity; one of them is 6 minute walk distance test (6MWT). This measure use for assessing functional status and can predict the prognoses of various respiratory conditions[6]. For many patients with COPD, psychosocial factors may interact with physiologic abnormalities to limit exercise capacity[7].

Many studies are assessed the relationship between exercise capacity and lung function, most of them showed that, there is a weak correlation between exercise capacity and the degree of airway obstruction[4,8]. This finding explains that other factors, except for lung function, play an important role in limiting exercise capacity in COPD patients[4]. Exercise capacity in patients with chronic obstructive pulmonary disease has several determinants[9]. Therefore, understanding the exercise capacity predictors can be create a way to better understanding physical activity limitations[7], the aim of this study is to examine the relationship between dyspnea, quality of life, disease severity and 6MWT to determine those clinical variables predicting functional exercise capacity in patients with chronic obstructive pulmonary disease.

METHODS

Subjects design and population

This cross-sectional study was conducted on 36 patients (33 men & 3 women) with COPD, who were referred to the outpatient pulmonary clinic of the Ahvaz Jundishapur University of Medical Sciences. All of the experimental procedures of the study were approved by the Ethics Committee of the Ahvaz Jundishapur University of Medical Sciences (ruling number: U89295).

Inclusion criteria

Patients with mild to very severe COPD, according to Global Initiative for Chronic Obstructive Lung Disease (GOLD)[10]. Having 40-70 years old, presenting stable clinical condition without episodes of exacerbation in the preceding month.

Exclusion criteria

The cases of comorbid condition likely to reduce exercise capacity such as unstable angina and myocardial infarction during the previous month[11] and body mass index (BMI) >35 $kg.m^{-2}$, weaning dose of oral corticosteroids, having cognitive deficit and musculoskeletal disorders, increasing in FEV_1 greater than or equal to 12% following bronchodilator (salbutamol) therapy and consuming bronchodilator during the 6MWT were excluded.

Measurements

Pulmonary function tests performed using a spirometer (Moose PFT system; Cybermedic, Louisville, CO, USA, software version 3.8D) at the outpatient clinic. The health related quality of life was assessed with Persian version of the St George's Respiratory Questionnaire (SGRQ), Cronbach's alpha was calculated 0.93(12). Three component scores are calculated for the SGRQ: 1) symptoms: included 8 questions about respiratory problems, frequency and severity (e.g. cough, breathlessness, secretion and…); 2) activity: included 2 questions about activities that cause dyspnea (e.g. take shower, walking, dressing and ...); and 3) Impact: included seven questions about How respiratory disease interference in the daily living activities and How to influence on the psychosocial functioning(13). The each component is calculated from the summed weights for the positive responses to its questions. The total score is calculated by summing the scores of three domains of the questionnaire. The result expressed as a percentage, 100% indicated the worst and 0% indicated the best quality of life. The questionnaire completed by patients if they had literacy, for illiterate patients, conducted interview was used and questions explained clearly to better understanding. The exertional dyspnea was measured by a Borg-scale[14], ranging from 0 (not noticeable) to 10 (maximum dyspnea), immediately after 6MWT.

The six minute walk test was performed according to American Thoracic Society guideline. (ATS)[11]. Patients had practiced the 6MWT on two occasions for familiarity with the exercise test and the best one was recorded as the 6MWT. The patients remained seated for 10 minutes before and after the walk test, after the rest period, arterial blood pressure was measured with a mercury sphygmomanometer and a stethoscope (MDF800, Shanghai China) , arterial oxygen saturation and heart rate were assessed with pulse-oximeter (Nellcor – NBP 195).The test was performed indoors, along a flat, straight corridor with 30 meters length. The length of the corridor was marked every 3 meters. The patients were encouraged to walk as far as they could in 6 minutes. Standard phrases of encouragement were used in particular times, during the test. The distance covered was measured as 6 minute walk distance.

Statistical Analysis

Data was analyzed using of Statistical Package for the Social Sciences, version 16.0. Data wasexpressed as mean and standard deviation (Mean±SD). The relationship between numerical variables was examined using Pearson's linear correlation coefficient and Spearman's correlation coefficient was used to determine the association between two ordinal or nominal variables. Multivariate linear regression analysis was used to determine predictors of the 6MWT.The variables found to be significant (P<0.05) on univariate analysis was included in Multivariate linear regression. The level of statistical significance was set at P< 0.05.

RESULTS

Sample Characteristic

A total of 36 patients (33male, 3 female) with COPDparticipated in this study. Demographic data and the baseline lung function are summarized in Table 1. The two factors that worsening the COPD are occupationaldusts and smoking, 14 patients (38.9%) had job contamination (e.g. agronomy, steel workers and oil company workers), 14 patients (38.9%) were current smoker, 14 patients (38.9%) were ex-smoker and 8 patients (22.2%) were none smoker.

Table 2 show severity of COPD based on Global Initiative for Chronic Obstructive Lung Disease (GOLD)(10).

The mean (SD) 6MWT was 455.4 (79.5) m, this was 35.7% (253 m) lower than the expected value (708.7 m), this deference was statically significant (P=0.000). The predicted 6MWT distance was calculated according to the reference equation by Enright *et al,*[15] using patient's age, sex, weight and height.The mean (SD) SGRQ total score was 41.2 (18.4) and mean (SD) 3 dimension of SGRQ; symptom, activity and impact were 46.5(24.9), 57.7 (21.7), 29.7 (19.6) respectively. It should be noted that higher scores indicating worse quality of life.

Table 1: Demographic data and baseline lung function parametersfor subjects with COPD (N=36)

Demographic factors	Mean±SD	95% CI
Age (year)	56.8±8.8	53.8-59.8
BMI ($kg.m^{-2}$)	24.9±4.7	23.2-26.4
Weight (kg)	72.6±14.8	67.4-77.5
Height (cm)	170.7±9.7	167.4-174.1
Pack/Year (year)	28.7±39.2	15.3-42.2
6MWT (m)	455.4±79.5	428.4-482.3
Dyspnea (0-10)	2.98±2.3	2.2-3.7
Total score of SGRQ (0-100)	41.2±18.4	34.9-47.4
Symptoms of SGRQ (0-100)	46.5±24.9	38.08-54.9
Activity of SGRQ (0-100)	57.7±21.7	50.4-65.1
Impact of SGRQ (0-100)	29.7±19.6	23.09-36.4
FEV_1 (L)	1.86±0.89	1.5-2.1
FEV_1% predicted	57.8±24.7	49.2-66.5
FVC (L)	3.19±1.06	2.8-3.5
FVC % predicted	80.0±22.4	72.1-87.8
FEV_1/ FVC %	69.6±16.5	63.9-75.4

BMI= Body Mass Index, 6MWT= 6- Minute Walk Distance, SGRQ= St George's Respiratory Questionnaire, FEV_1= Forced Expiratory Volume in one second, FVC= Forced Vital Capacity

Table 2: Severity disease based on GOLD (N=36)

Severity of COPD	N (%)
Stage I: mild FEV1/FVC , 0.70 FEV1 > 80% predicted	15 (41.66)
Stage II: moderate FEV1/FVC , 0.7050% < FEV1 , 80% predicted	6 (16.66)
Stage III: severe FEV1/FVC , 0.7030% < FEV1 , 50% predicted	6 (16.66)
Stage IV: very severe FEV1/FVC , 0.70FEV1 , 30% predicted or FEV1 , 50%predicted plus chronic respiratory failure	9 (25.0)

FEV_1= Forced Expiratory Volume in one second, FVC= Forced Vital Capacity

Relationships between Clinical Measures and Exercise Capacity

There was no relationship between 6MWT, BMI and severity of disease (table3). Spirometric measures correlated weakly with the 6MWT, showing that persons with less airway obstruction had better exercise capacity. We found that heart rate before walking test presented a negative correlation with 6MWT (table3). No statistically significant correlation was found between exertional dyspnea and 6MWT. Except for symptom, other dimensions (activity and impact) were correlated with 6 minute walk test. Activity dimension was more correlated than the total score and impact (table3). The variables found to be significant on univariate analysis were included: age, weight, pack/year, FEV_1 L, FVC L, pulse rate before 6MWT, O_2 saturation before 6MWT, QOL total, activity and impact domains. Multivariate linear regression was done by these factors. The age was identified as an independent predictor of the 6MWT. A higher 6MWT was associated with lower age.

Table 3: Correlation between 6MWT, clinical variables and HRQL

	6MWT	P-value
Age	-0.60	0.000
Sex	-0.21	NS
BMI	0.35	0.03
Weight	0.54	0.001
Height	0.33	0.049
Pack/Year	-0.38	0.02
Duration of disease	-0.08	NS
Number of hospitalization	-0.32	NS
Heart rate before 6MWT	-0.50	0.002
Heart rate after 6MWT	-0.38	0.02
SPO_2 before 6MWT	0.42	0.01
SPO_2 after 6MWT	0.42	0.01
Systolic blood pressure before 6MWT	-0.20	NS
Systolic blood pressure after 6MWT	-0.23	NS
Severity of disease	-0.26	NS
FEV_1 % predicted	0.36	0.04
FVC % predicted	0.37	0.03
FEV_1/FVC %	0.29	NS
FEF_{25-75} % predicted	0.26	NS
Dyspnea after 6MWT	-0.29	NS
SGRQ symptomscore	-0.03	NS
SGRQ activity score	-0.44	0.007
SGRQ impact score	-0.40	0.01
SGRQ total score	-0.39	0.01

Data expressed as Pearson's or Spearman's rho; NS= non-significant, *6MWT= 6- Minute Walk Distance, BMI= Body Mass Index, FEV_1= Forced Expiratory Volume in one second, FVC= Forced Vital Capacity, FEF_{25-75}=* Forced Expiratory Flow the middle 50% of the FVC, *SGRQ= St George's Respiratory Questionnaire*

DISCUSSION

Our result showed that 6MWT in COPD patients is 35.7% lower than the expected value. De Torres and coworkers reported that limitations of COPD make it difficult to do low resistance activities such as 6MWT[16]. Carters and coworkers[17] showed the ventilatory limitation to exercise in COPD patients based on physiologic gas exchange data, our study and the same studies supported this finding by showing the significant relationship between 6MWT and FEV_1 [18, 19]. In the other study[20] authors reported that 6MWT was positively related with the length of survival, it means that survival was longer among the COPD patients who displayed higher 6MWT value, These relationships

showed that the 6MWT can help in the assessment of pulmonary function and survival in patients with COPD. Although there is a relationship between 6MWT and FEV_1, but it is a weekly correlation[21-23], So that, this limits the use of the FEV_1 as sole indicators of severity and prognoses of disease.

Forced Expiratory Flow (FEF) from 25-75% shows the level of small airway obstruction. Our finding revealed that there was no relationship between FEF_{25-75} and 6MWT, Inal-Ince[24] and Pineda[25] showed that the degree of small airway obstruction contributed to external work of walking rather than the distance, their findings supported our result.

Age is a famous factor influencing the exercise capacity[26, 27].In our study there was a strong negativecorrelation between age and 6MWT.

This study revealed that there was no significant correlation between 6 minute walk distance and exertional dyspnea. Oga and coworkers showed that all of indices of exercise capacity included progressive cycle ergometry, 6MWT and cycle endurance test had moderately correlated with the clinical dyspnea measured by Oxygen Cost Diagram (OCD). However, only cycle endurance test showed weakly correlation with the Borg score at the end of test[5]. Inal-Ince and coworkers showed a significant correlation between dyspnea and 6MWT, in their study, patients had moderately severe and very severe disease[24], but in our study COPD patients were composed mainly of mild to moderate stages, and probably in this stages, airway obstruction does not play an important role in the development of dyspnea. In addition, de Torres showed that women with COPD report more functional dyspnea than men with the same degree of airway obstruction[28]. Most of our samples were men because in Iranian culture women smoking is not acceptable. There was no correlation between 6MWT and dyspnea in low women sample and most patients with mild to moderate disease severity in our study.

Our result showed a significant correlation between quality of life and dyspnea. Negative correlation between SGRQ domains (activity and impact) and 6MWT attributed to the limited functional and physical activity of the studied patients[29].We also observed that the activity score correlated better with 6MWT as previously reported[5, 30].This finding displayed that walking test reflects a good measure of the daily living activities of COPD patients.

No significant correlation was seen between 6MWT and symptom score of the SGRQ, which was consistent with the previous studies[5, 29, 31].

We found that the number of heart rate before of the test had negative correlation with 6MWT, so that increased heart rate before of walking cause to intolerance activity in COPD patients. It seems that one of the ways to improve the exercise capacity is the control of heart rate in the normal range. Camillo and coworkers found that Cardiac autonomic function of patients with COPD is not related to disease severity but mainly to the level of physical activity in daily life[32].

Our result showed a positive correlation between 6MWT and SPO_2 before and after walking test, this means that both of desaturation at the baseline and during the walking test influence on the passed distance, So that oxygen therapy before and during the activity can improve exercise performance in patients with COPD, its consistent with Chatila's findings[33].Casanova et al showed that the 6MWT helps predict mortality primarily in patients with severe COPD, Although the oxygen desaturation profile during the 6MWT improves the predictive ability of the 6MWT[34].

This study was limited by first, the small number of subjects recruited, especially women sample, second, the majority of who demonstrated mild tomoderate COPD, third, it did not assess the respiratory muscle strength.

In conclusion, this study indicates that the 6MWT provides valuable information of functional status in a group of patients with mild to very severe chronic obstructive pulmonary disease. Our result showed that there is a stronger relationship between 6MWT and HRQL (activity and impact) compared to physiological measures of disease severity such as FEV_1. Therefore, organizing management strategies to improve exercise tolerance have a positive impact on HRQL in this patient's population.

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