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KLİNİK ÇALIŞMA
RESEARCH ARTICLE

Does exercise capacity, dyspnea level, or quality of life actually predict mortality in patients with COPD? 8-year follow-up

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SUMMARY

Does exercise capacity, dyspnea level, or quality of life actually predict mortality in patients with COPD? 8-year follow-up

Introduction: *The goals of chronic obstructive pulmonary disease (COPD) treatment are to relieve dyspnea, increase exercise capacity, and improve quality of life. The relation of exercise capacity, dyspnea level, and quality of life with long-term mortality is unclear. Aim of the study was to assess the effect of exercise capacity, dyspnea level and quality of life on long-term mortality risk in patients with COPD.*

Materials and Methods: *Dyspnea level was assessed using the modified Medical Research Council (mMRC), Borg and Baseline Dyspnea Index (BDI) and Body Obstruction Dyspnea Exercise (BODE), health-related quality of life with St. George's Respiratory Questionnaire, and exercise capacity with the 6-minute walking test (6MWT) and cardiopulmonary exercise test. At the end of 8-year follow-up period, the relation between these tests and mortality was examined.*

Results: *A total of 42 patients with stable COPD were included in the study. Sixteen patients died during the approximately 8-year follow-up period. Univariate analysis revealed that VO_2 peak [HR: 1.845; CI: (1.336-2.55); p< 0.001], BODE index [HR: 0.787; CI: (0.703-0.880); p< 0.001], and SGRQ [HR: 1.073; CI: (1.028-1.119); p= 0.001] were significantly correlated to mortality risk. Multivariate Cox regression analysis revealed VO_2 peak [HR: 1.031; CI: (0.683-1.120); p= 0.01] as the single significant predictor of mortality. VO_2 peak less than 22.5 had a sensitivity of 82%, specificity of 80%, and area under the curve of 0.142 [95% CI: (0.027-0.257); p< 0.001] for mortality risk with ROC analysis.*

Conclusion: *Cardiopulmonary disturbances during maximal exercise may be an important indicator of mortality risk.*

Key words: *Chronic obstructive pulmonary disease; cardiopulmonary exercise test; 6-minute walking test; health-related quality of life; St. George's respiratory questionnaire*

ÖZET

Egzersiz kapasitesi, dispne derecesi veya yaşam kalitesi KOAH hastalarında mortaliteyi yansıtır mı? 8-yıllık izlem

Giriş: *Kronik obstrüktif akciğer hastalığı (KOAH)'nda tedavinin amacı dispneyi azaltmak, egzersiz kapasitesini ve yaşam kalitesini arttırmaktır. Egzersiz kapasitesi, dispne düzeyi ve yaşam kalitesi ile uzun dönem mortalite arasındaki ilişki belirsizdir. Bu araştırmanın amacı KOAH hastalarında egzersiz kapasitesi, dispne düzeyi ve yaşam kalitesinin uzun dönem mortalite riskini değerlendirmektir.*

Materyal ve Metod: *Dispne düzeyi "Değiştirilmiş Tıbbi Araştırma Konseyi" (modified Medical Research Council, mMRC), Borg ve Bazal Dispne İndeksi (BDI) ve Vücut Obstrüksiyonu Dispne Egzersizi (BODE), yaşam kalitesi St. George's Solunum Anketi ve egzersiz kapasitesi 6-dakika yürüme testi (6DYT) ve kardiyopulmoner egzersiz testi ile değerlendirildi. Sekiz-yıllık izlem süresinin sonunda bu testler ve mortalite arasındaki ilişki değerlendirildi.*

Bulgular: *Kırk iki stabil KOAH olgusu araştırmaya alındı. Sekiz-yıllık izlemde 16 hasta öldü. Tek değişkenli analizde pik VO_2 [HR: 1.845; CI: (1.336-2.55); p< 0.001], BODE index [HR: 0.787; CI: (0.703-0.880); p< 0.001] ve SGRQ [HR: 1.073; CI: (1.028-1.119); p= 0.001] mortalite riskiyle ilişkili bulundu. Çok değişkenli Cox regresyon analizine gore pik VO_2 mortalitenin en anlamlı göstergesiydi [HR: 1.031; CI: (0.683-1.120); p= 0.01]. ROC analizinde pik VO_2 < 22.5 değerinin %82 duyarlılık, %80 özgüllük ve 0.142 [95% CI: (0.027-0.257); p< 0.001] AUC değeriyle mortalite riskini gösterdiği saptandı.*

Sonuç: *Maksimal egzersiz sırasında ortaya çıkan kardiyopulmoner kısıtlılıklar uzun dönem mortalite riskinin en önemli göstergesidir.*

Anahtar kelimeler: *Kronik obstrüktif akciğer hastalığı; kardiyopulmoner egzersiz testi; 6-dakika yürüme testi; sağlık ilişkili yaşam*

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable disease characterized by persistent airflow limitation, which is usually progressive and associated with an enhanced chronic inflammatory response in the airways and lungs to noxious particles or gases. Exacerbations and comorbidities contribute to the overall disease severity in individual patients (1).

Mortality has been an important outcome in COPD, as it is currently the fourth leading cause of death in the world (2). The relationships of exercise capacity, dyspnea level and health status to mortality have rarely been evaluated.

The six-minute walking test (6MWT) is the most widely recognized test among time-based corridor walking tests. It is widely preferred becuse it is an easy, inexpensive, and practical method to determine submaximal exercise performance. It is used to assess treatment response after medical or surgical treatment or physiotherapy, to determine mortality and morbidity risk, and to determine functional capacity in lung disorders (3).

The cardiopulmonary exercise test (CPET) is considered the gold standard for the quantification of maximum exercise capacity in COPD. It is also used to reveal causes of exercise-limiting symptoms, to prescribe pulmonary rehabilitation programs, and to assess response to any treatment available (4). Respiratory questionnaires and dyspnea scales have been developed to rate the severity of respiratory difficulty, to detect differences between patients with low versus high levels of dyspnea, to evaluate changes in dyspnea level in paralel to disease progression, and to quantify the degree of respiratory difficulty. The modified Medical Research Council dyspnea scale (mMRC), Borg and Baseline Dyspnea Index (BDI) are used to rate dyspnea (5-7). The Body mass, airflow Obstruction, Dyspnea, Exercise capacity (BODE) index is a multidimensional test that uses body mass index (BMI), severity of airway obstruction, and walking distance, in addition to dyspnea severity as assessed using the mMRC (8).

Quality of life reflects the subjective thoughts about one's own health status. Disease or treatment modality alters quality of life by disrupting one's functional status, perceptions, and social status. The St. George's Respiratory Questionnaire (SGRQ) is a 76-item self-reported questionnaire composed of three categories, which assesses the impact of symptoms, activity, and disease on daily life (9).

Some of the goals of COPD treatment are to relieve dsypnea, increase exercise capacity, and improve quality of life. Dyspnea worsened by exertion causes a vicious cycle of reduced exercise capacity and impaired quality of life (10). Exercise tests have been developed to assess exercise capacity; however, it is still unclear how accurate they reflect dyspnea level and quality of life.

In the present study, we aimed to investigate the relation between exercise capacity and dyspnea grade, quality of life, and mortality after 8 years among patients with COPD.

MATERIALS and METHODS

Patients

This prospective single-center study included 42 patients with stable COPD who were under follow-up at the COPD outpatient clinic. Four (9.5%) patients were female and 38 (90.5%) were male. COPD diagnosis was made on the basis of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria (11).

Patients older than 40 years of age who were stable and met the following criteria were included: meeting the COPD clinical diagnostic criteria (chronic dyspnea, cough, sputum expectoration), having air flow limitation according to the GOLD guidelines (FEV_1/FVC ratio 70% or below in spirometry), being able to perform the cardiopulmonary exercise test of sufficient duration and quality, and having no history of COPD exacerbations within the last 4 weeks.

The exclusion criteria were as follows: having acute myocardial infarction, unstable angina, symptomatic and hemodynamically unstable arrhythmias, active endocarditis, acute myocarditis or pericarditis, symptomatic severe aortic stenosis, uncontrolled decompensated heart failure, acute pulmonary embolism, pulmonary infarction, second- or third-degree heart block, orthopedic injuries precluding stress test, dissecting aortic and ventricular aneurysm, severe pulmonary hypertension (PAP > 40 mmHg), neurologic deficit, partial oxygen pressure below 50 mmHg (PaO_2 < 50 mmHg), partial carbondioxide pressure above 70 mmHg ($PaCO_2$ > 70 mmHg), and FEV_1 below 30%, acute exacerbation of COPD, non adherence with the study (mental and psychiatric disorders).

Pulmonary Function Tests And Arterial Blood Gas Analysis

Pulmonary function tests (expiratory air flow rates, static lung volumes, carbon monoxide diffusing testing) were performed. Expiratory flow rates and carbon monoxide diffusing capacity of the lung for were measured using a V_{max} 229 Pulmonary Function/Cardiopulmonary Exercise Test (Sensormedics, Bilthoven, Netherlands).

Arterial blood gas samples were obtained through direct vascular puncture of the radial artery at rest, breathing room air. The samples were instantly studied using an ABL 90 Flex/Blood Gas Analyzer (Radiometer Ltd. Brønshøj, Denmark).

Dyspnea Scores

Disease stage was determined according to the mMRC scale. Postbronchodilator FEV_1 (percentage of predicted) in respiratory function test, mMRC dyspnea scale value, BMI, and 6MWT (m) were used to calculate the BODE index. Functional impairment, magnitude of task and magnitude of effort-related dyspnea were measured, and the BDI score was calculated. Dyspnea severity was assessed using the Borg scale before and after 6MWT and CPET.

Quality of Life

Quality of life was rated using the SGRQ (9). A fixed-format self-complete 76-item questionnaire with three component scores [symptoms, activity, and impact (on daily life), and a total score] was administered to measure health in chronic airflow limitation.

Six-Minute Walking Test

The maximal walking distance (m) at maximal pace along a 20-meter corridor for six minutes was recorded for patients during stable stage (12). The Borg scale was used to score dyspnea grade before and after exercise. Transcutaneous oxygen saturation, heart rate, and blood pressure were measured at the onset and the end of the test. No patient required a portable oxygen delivery system.

Cardiopulmonary Exercise Test

All subjects performed a symptom limited exercise test using bicycle ergometry (Ergometrics 900, SensorMedics™, Bilthoven, Netherlands). They performed incremental exercises by applying workloads that increased by 10-15-20 Watt/minute following a three-minute basal resting period and a three-minute warm-up period (13). During the test, all subjects were monitored to obtain their electrocardiogram, blood pressure, and oxygen saturation (Palce Pulse Oximeter™ 53400, California, USA).

During the test, the following parameters were recorded at basal state, anaerobic treshold, and peak exercise; oxygen consumption (VO_2 peak), peak CO_2 out-put (VCO_2), gas exchange ratio (VCO_2/VO_2), minute ventilation (VE), peak heart rate (HR), heart rate reserve (HRR), oxygen pulse (VO_2/HR), peak workload (Wpeak) during the application of workload. The reason of the termination of the test (dyspnea or leg pain) was recorded. Pre- and post-test dyspnea grade were determined in compliance with the Borg scale. Since the patients reached 85% of the expected pulse rate, their tests were accepted as maximum and recorded.

Follow-up Data

Depending on the clinical indication, patients were followed up for 3- or 6-month periods between 2008-2017, approximately 8 years. In follow-up visits, symptoms of patients, dyspnea score of mMRC, pulmonary function tests were recorded. Patients who did not attend follow-up visits were called via the telephone and any missing information was obtained. This study was approved by University Clinical Research Ethics Committee (Registration number: 06-129-07). All procedures in this study followed were in accordance with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from all patients for being included in the study.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS, Inc. Chicago, IL, USA 20) software package. Data distribution was tested with the Shapiro-Wilk test. The descriptive statistics included mean ± standard deviation for normally distributed variables, median (range) for non-normally distributed variables, and number (percentage) for nominal variables. Statistical significance was set at $p< 0.05$.

The linear correlation between two variables was analyzed using Pearson's or Spearman's corrrelation tests, depending on the normality of distribution. The survival status of the study group after 8 years was determined with life table and Kaplan-Meier survival analysis. Univariate analysis was used to find individual variables predicting mortality; multivariate Cox proportional hazard model regression analysis was used to determine independent variables predicting mortality. Receiver operating characteristics (ROC) analysis was performed to determine the optimal cut-off values for VO_2 peak and to find the area under the curve (AUC), and specificity and sensitivity of VO_2 peak.

RESULTS

The study included 42 patients with stable COPD. The mean age of the study population was 63.36 ± 6.95 years and postbronchodilator FEV_1 was 53.46 ± 14.41 percentage (%) predicted. The general characteristics of the study population are shown on Table 1. The mean walking distance in the 6MWT was 450.34 ± 71.62 m. In the CPET, the mean Wpeak was 95.49 ± 34.57 watt and VO_2 peak was 1.32 ± 0.47 L/min (Table 2).

Sixteen patients died before the end of an approximately 8-year follow-up period. The cause of death was COPD or COPD-related disease in 10 patients, cardiac disorders in four, and malignancy and pulmonary thromboembolism in one patient each.

The mean follow-up duration of the study group was 6.4 ± 2.4 years. The time to mortality was 3.81 ± 2.04 years.

Univariate analysis showed that VO_2 peak [HR: 1.845; CI: (1.336-2.55); p< 0.001], BODE [HR: 0.787; CI: (0.703-0.880); p< 0.001], and SGRQ [HR: 1.073; CI: (1.028-1.119); p= 0.001] increased mortality risk (Table 3). There was no significant relation between 6MWT and mortality.

Cox proportional hazard model analysis was used to determine the relative risk of death with different variables (VO_2 peak, BODE, 6MWT, SGRQ total score) (Table 3). According to that analysis, VO_2 peak [HR: 1.031; CI: (0.683-1.120); p= 0.01] significantly increased the risk of death, but BODE [HR: 0.978; CI: (0.571-1.626); p> 0.05] and SGRQ [HR: 0.827; CI: (0.976-1.090); p> 0.05] were not predictive of mor-

Table 1. General characteristics of the study subjects

	Patients with COPD
Subjects, N	42
Age, years	62.45 ± 8.22
Sex, Male	38 (90.5)
BMI, kg/m^2	22.12 ± 3.13
Smoking, pack/years	40.12 ± 17.32
FEV_1, % pred	53.46 ± 14.41
FVC, % pred	79.31 ± 24.16
FEV_1/FVC	48.24 ± 9.32
mMRC	2.24 ± 0.93
BODE	2.17 ± 1.23
BDI	8.11 ± 4.25
SGRQ, total	51.05 ± 28.34
SGRQ, symptom	58.31 ± 19.33
SGRQ, activity	73.17 ± 11.21
SGRQ, impact	41.4 ± 16.7

tality. A multivariate Cox regression analysis of variables revealed that a significant predictor of mortality was VO_2 peak.

ROC analysis for VO_2 peak was performed (Figure 1). VO_2 peak (pred %) less than 22.5 had a sensitivity of 82%, specificity of 80% and an AUC of 0.858 [95% CI: (0.743-0.973); p< 0.001] for mortality risk. Kaplan-Meier cumulative survival analysis demonstrated significantly higher survival rates of the VO_2 peak ≥ 22.5 group than VO_2 peak < 22.5 study groups during the 8-year follow-up (p< 0.01). Kaplan-Meier survival curves based on VO_2 peak groups are presented in Figure 2.

Table 2. 6MWT and CPET parameters of the study group

Exercise test parameters	Patients with COPD n= 42
6MWT	
6MWT, m	450.34 ± 71.62
Baseline SpO_2, %	91.32 ± 4.21
Final SpO_2, %	85.42 ± 6.54
Desaturation, %	6.72 ± 3.43
Baseline borg	2.56 ± 1.22
Final borg	4.81 ± 2.35
CPET (peak exercise)	
Wpeak, watt	95.49 ± 34.57
VO2, L/min	1.32 ± 0.47
VO2, pred %	49.84 ± 14.35
VO2/kg, mL/kg/min	16.40 ± 4.87
VO2/kg, pred %	59.06 ± 15.09
VCO2, L/min	1.58 ± 0.51
BR	0.34 ± 0.14
VE, L/min	44.98 ± 16.12
VE/VO2	33.15 ± 7.98
VE/VCO2	32.67 ± 8.07
O2 pulse, mL/beat	8.66 ± 4.10
HRR, beats/min	46.92 ± 21.13
Baseline SpO2, %	91.32 ± 4.21
Final SpO2, %	85.42 ± 6.54
Desaturation, %	6.72 ± 3.43
Baseline borg	2.56 ± 1.22
Final borg	4.81 ± 2.35

There was no significant correlation between the 6MWT and dyspnea scales and total (r= -0.036), impact (r= -0.027), symptom (r= -0.102), and activity scores (r= -0.062) of SGRQ questionnaire. Among CPET parameters, VO_2 peak was correlated to SGRQ symptom score (r= -0.382, p= 0.03), activity score (r= -0.440, p= 0.01), impact score (r= -0.395, p=0.03), and total score (r= -0.481, p= 0.01) (Figure 3). O_2 pulse was correlated to SGRQ symptom score (r=

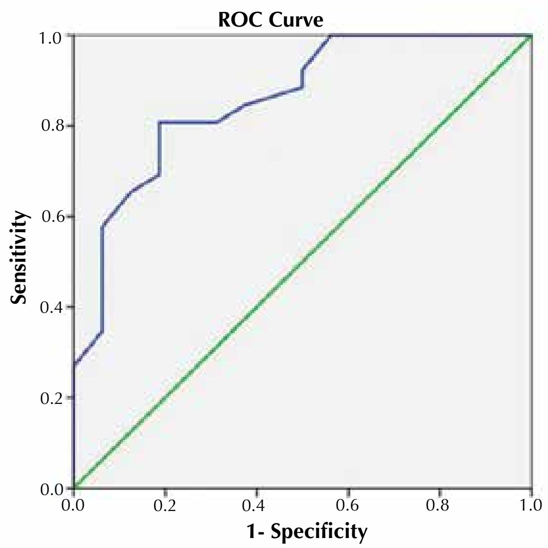

Figure 1. Receiver-operating characteristic (ROC) analysis for VO_2 peak. VO_2 peak (pred %) greater than 22.5 had a sensitivity of 82%, specificity of 80% and an AUC of 0.858 [95% CI: (0.743-0.973); p< 0.001] for mortality risk.

Table 3. Univariate and multivariate Cox proprortional hazards analyses on the relationship between major clinical measurements and all-cause mortality

Variable	Univariate Analysis			Multivariate Analysis		
	HR	95% CI	p	HR	95% CI	p
VO_2 peak	1.845	1.336-2.55	< 0.001	1.031	0.683-1.120	0.01
BODE	0.787	0.703-0.88	< 0.001	0.978	0.571-1.626	NS
SGRQ	1.073	1.028-1.119	0.001	0.827	0.976-1.090	NS
6MWT	0.410	0.129-0.490	NS	0.350	0.165-0.340	NS

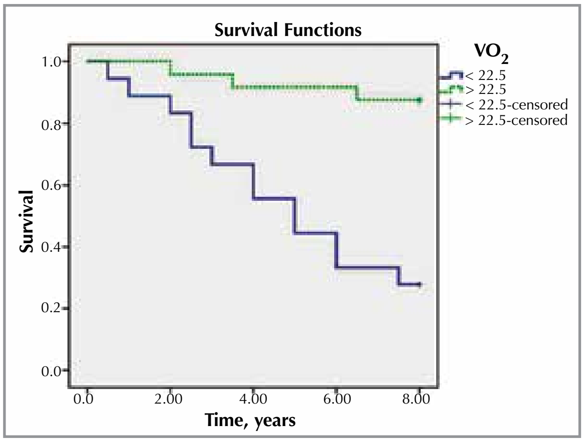

Figure 2. Kaplan-Meier cumulative survival plots demonstrating significantly higher survival rates of the VO_2 peak ≥ 22.5 study groups than VO_2 peak < 22.5 study groups during the 8-year follow-up (p< 0.01).

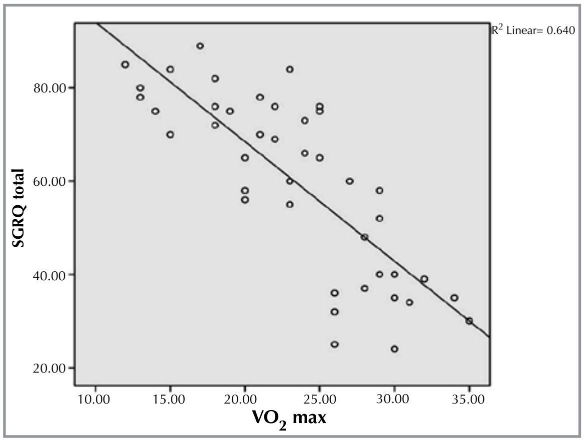

Figure 3. Scatterplot showing significant negative correlation between VO_2 peak and SGRQ total score.

-0.458, p= 0.02), activity score (r= -0.470, p=0.01), impact score (r= -0.497, p= 0.01), and total score (r= -0.510, p= 0.01).

There was a negative correlation between the BODE index and VO_2 peak (r= -0.423, p=0.02), VE (r= -0.388, p= 0.03), and O_2 pulse (r= -0.378, p= 0.03) (Table 4).

DISCUSSION

We evaluated factors related to mortality in COPD, particularly the relationships of exercise capacity, dyspnea level, and health-related quality of life to mortality and found that exercise capacity was the best independent predictor of mortality in patients with COPD.

Patients with COPD have a reduced exercise capacity and quality of life. Dyspnea is the main factor limiting exercise performance, mainly by preventing patients from attaining their maximum exercise capacity (13). Assessment of functional capacity has gained importance in attempts to fully understand the pathogenesis COPD. Exercise capacity of COPD patients is affected by complex factors, including ventilation, muscular function, gas excahange, circulation, nutritional status and dyspnea. Exercise capacity may thus evaluate the severity of COPD more comprehensively than airflow limitation. Peak VO_2 is the primary measure of exercise capacity. The predictor of mortality during an 8-year follow-up of patients with stable COPD were VO_2 peak and SGRQ-determined quality of life with univariate cox proportional hazard analysis. When SGRQ, BODE and VO_2 peak were evaluated in multivariate analysis, the peak VO_2 was the statistically the most significant independent risk factor in determining the mortality risk.

Waschki et al., in a prospective cohort study of 170 outpatients with stable COPD, demonstrated that objectively measured physical activity was the strongest predictor of all-cause mortality in patients with COPD (14).

In the present study, the association between quality of life and mortality was confirmed in univariate analysis. In a multivariate model, VO_2 peak, which is probably the most reliable available index of exercise capacity, was associated with mortality risk. Yoshimura et al. suggested that peak oxygen uptake was preferable in order to investigate the relationship between mortality and COPD because it was more significantly correlated to mortality than any of the other variables (15). Similar results were obtained by Oga et al. and Hiraga et al. with exercise capacity being the most significant predictors of mortality (16,17).

The 6MWT was not found to affect the prognosis of patients with COPD. Most of the disunity in the 6MWT in patients with COPD can be explained by factors that variably reflect the cardiac, respiratory, and metabolic determinants of physical performance (18). Furthermore, the walking distance may be affected by patient motivation and other subjective factors (19).

Table 4. Correlation between six-minute walking test and cardiopulmonary exercise test parameters and respiratory function, dyspnea indexes, and quality of life questionnaire

		CPET							
Parameters	**6MWT m**	**Wmax Watt**	**VO_2 L/min**	**VO_2/kg mL/kg/min**	**VCO_2 L/min**	**VE L/min**	**VE/VO_2**	**VE/VCO_2**	**O_2 pulse**
6MWT, m		0.442*	0.501**	0.401*	0.577**	0.597**	-0.086	-0.038	0.217
FEV_1, %pred	0.206	0.534**	0.626**	0.459**	0.535**	0.524**	-0.014	-0.028	0.057
DLCO, %pred	0.059	0.286	0.455*	0.190	-0.377*	0.360	0.565**	0.369*	0.401*
mMRC	-0.055	0.032	-0.195	-0.117	-0.004	-0.078	0.072	-0.135	-0.358
BODE	-0.384*	-0.227	-0.423*	-0.118	-0.323	-0.388*	-0.082	0.088	-0.378*
BDI	-0.145	-0.120	-0.230	-0.045	-0.158	-0.103	-0.087	-0.046	-0.237
6MWT baseline borg	0.169	0.122	0.208	0.101	0.244	0.075	0.051	-0.139	0.115
6MWT final borg	0.181	0.223	0.243	0.165	0.284	0.108	0.094	-0.251	0.127
CPET baseline borg	0.239	0.147	0.259	0.198	0.262	0.124	0.105	-0.167	0.121
CPET final borg	0.267	0.135	0.256	0.273	0.293	0.217	0.173	-0.272	0.148
SGRQ symptom	-0.102	-0.029	-0.382*	-0.143	-0.155	-0.159	0.095	0.065	-0.458*
SGRQ activity	0.062	-0.180	-0.440*	-0.140	-0.221	-0.117	-0016	0.011	-0.47*
SGRQ impact	-0.027	-0.109	-0.395*	-0.134	-0.216	-0.098	0.102	0.073	-0.497*
SGRQ total	-0.036	-0.149	-0.481*	-0.160	-0.271	-0.161	0.052	0.059	-0.51*

* p< 0.05.
** p< 0.01.

Antonelli-Incalzi et al. found a stronger association between the SGRQ score and mortality [HR: 1.61; 95% CI: (0.91-2.81)]. The association between the SGRQ and mortality attributed to non-pulmonary causes was similar to the one found for total mortality [HR:1.19; 95% CI: (0.99-1.44)] (20). The main finding of their study was that worsening HRQL, as assessed using the SGRQ, was associated with increased mortality in an older population with COPD. Quality of life rated using the SGRQ (especially the impact subscale), helps to identify older patients with COPD at greater risk of death. Domingo-Salvany et al. concluded that SGRQ total and SF-36 physical summary scores were independently associated with total and respiratory mortality in Cox models (21).

Exercise tests instead of static tests are used to rate dyspnea in daily life. In the present study, a significant correlation was found between the two exercise tests among patients with COPD during a stable phase. It was noted that both exercise tests more accurately reflected multidimensional dyspnea level as assessed using BODE. CPET showed significant correlations with all SGRQ domains.

Conflicting results have been obtained by studies investigating the relation between 6MWT and BDI. Our study failed to show any correlation between both exercise tests and mMRC, BDI, and pre- and post-exercise Borg dyspnea index. Pelegrino et al. studied 68 patients with COPD and failed to show any correlation between MRC or BDI and the 6MWT (22). On the other hand, Oga et al. showed a weak correlation between BDI and VO_2 peak (19).

Submaximal and maximal exercise tests may not reflect dyspnea severity during daily life activities. Dyspnea is a subjective symptom that occurs in association with various physiologic and psychological factors (23). Thus, rating dyspnea that occurs during daily life activities is a more accurate method to evaluate the impact of COPD (24). The general view is that self-reported dyspnea rated using the Borg scale during exercise is often poorly reproducible. Moreover, it is difficult to ascertain which dyspnea factor is the primary one in COPD, because dyspnea mechanisms are complex and intertwined (25).

In this study, the BODE index, which is a composite dyspnea index that contains the 6MWT as a parameter, was inversely correlated with the 6MWT and VO_2 peak. The BODE index, a multidimensional scale assessing several factors related to COPD, evaluates a surrogate of nutritional state (BMI), airflow obstruction (FEV_1), dyspnea (mMRC), and exercise capacity (6MWT), and may be a more accurate measure of COPD severity (26,27). The number of studies assessing the association between different exercise tests and quality of life is quite limited (28). Studies have frequently used the 6MWT as the exercise test and SGRQ as the quality of life test. Even studies showing a positive correlation between 6MWT and SGRQ have revealed weak correlations between the SGRQ total and SGRQ activity (29,30).

Our study showed no significant correlation between 6MWT and SGRQ scores, but it revealed a significant correlation between SGRQ's symptom, activity, and impact domains, and VO_2 peak measured by CPET. This significant negative correlation indicates an improved health status with increased exercise performance and reduced SGRQ score. In support of similar studies, our study showed that CPET reflects quality of life more accurately than 6MWT (30,31).

Our study has some limitations including its single-center design and the small number of subjects who were mostly male. The lower number of women is probably related to the lower prevalence of COPD among women in our country.

DISCUSSION

This study demonstrated significant relationships of exercise capacity and quality of life to mortality in patients with COPD. Furthermore, cardiopulmonary disturbances during exercise could be the most important predictors of prognosis. Exercise performance as determined using CPET reflects dyspnea and quality of life more accurately. We concluded that the pathophysiologic mechanisms that primarily affect quality of life in COPD might be ideally detected by cardiopulmonary exercise testing.

CONFLICT of INTEREST

All authors have no conflict of interests.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: All of authors.

Analysis/Interpretation: All of authors.

Data Acquisition: All of authors.

Writting: All of authors.

Critical Revision: All of authors.

Final Approval: All of authors.

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