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İsmail ÖZSOY, PhD, PT[1]
Serap ACAR, PhD, PT[2]
Sevgi ÖZALEVLİ, PhD, PT[2]
Atila AKKOÇLU, MD[3]
Sema SAVCI, PhD, PT[2]

1 *Kırşehir Ahi Evran University, School of Physical Therapy and Rehabilitation, Kırşehir, Turkey.*
2 *Dokuz Eylül University, School of Physical Therapy and Rehabilitation, İzmir, Turkey.*
3 *Dokuz Eylül University, Faculty of Medicine, Department of Chest Disease, İzmir, Turkey.*

İletişim (Correspondence):

İsmail ÖZSOY, PhD, PT
Kırşehir Ahi Evran University, School of Physical Therapy and Rehabilitation, Kırşehir, Turkey.
Phone: +90-386-2805383
E-mail: ozsoy.ismail@yahoo.com

Serap ACAR
E-mail: serap.acar@deu.edu.tr.
Sevgi ÖZALEVLİ
E-mail: sevgi.ozalevli@deu.edu.tr.
Atila AKKOÇLU
E-mail: atilla.akkoclu@deu.edu.tr.
Sema SAVCI
E-mail: sema.savci@deu.edu.tr.

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CHRONIC OBSTRUCTIVE PULMONARY DISEASE GROUP B AND C: ARE THEY REALLY THE OPPOSITE OF EACH OTHER REGARDING EXERCISE CAPACITY AND MUSCLE STRENGTH?

ORIGINAL ARTICLE

ABSTRACT

Purpose: "Combined COPD Assessment" in the classification of chronic obstructive pulmonary disease (COPD) was proposed as a new method by The Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD). The aim of this study was to evaluate exercise capacity, and muscle strength (respiratory and peripheral muscle strength) between two groups (Group B and C) of the new GOLD combined COPD assessment in this study.

Methods: Patients were categorized into group B (n=18) and C (n=18) according to the GOLD combined COPD assessment. Patients' exercise capacity (the six-minute walk test [6MWT]) and the six-minute pegboard and ring test [6PBRT]), respiratory muscle strength (maximal inspiratory pressure [MIP] and maximal expiratory pressure [MEP]), and peripheral muscle strength (hand-grip and knee extensor strength) were assessed.

Results: The MEP value was significantly higher in group B than in group C (p=0.024). Other values (6MWT distance, 6PBRT score, MIP values, and peripheral muscle strength) were not significantly different between the two groups (p>0.05).

Conclusion: This study shows that comprehensive assessment is very important to evaluate patients with COPD. The GOLD spirometry measures are not solely enough, symptoms and exacerbation history must be evaluated.

Key Words: Chronic Obstructive Pulmonary Disease; Exercise Capacity; Muscle Strength.

KRONİK OBSTRÜKTİF AKCİĞER HASTALIĞI B VE C GRUBU: EGZERSİZ KAPASİTESİ VE KAS KUVVETİ BAKIMINDAN GERÇEKTEN BİRBİRLERİNE ZITLAR MI?

ARAŞTIRMA MAKALESİ

ÖZ

Amaç: Kronik obstrüktif akciğer hastalığı (KOAH)'nın sınıflandırılmasında "Bileşik KOAH Değerlendirilmesi" yeni bir yöntem olarak Kronik Obstrüktif Akciğer Hastalığına Karşı Küresel Girişim (GOLD) tarafından önerilmektedir. Bu çalışmada, yeni GOLD bileşik KOAH değerlendirmesine göre iki grup (Grup B ve C) arasındaki egzersiz kapasitesinin ve kas kuvvetinin (solunum ve periferik kas kuvveti) karşılaştırılması amaçlandı.

Yöntem: Hastalar, GOLD bileşik KOAH değerlendirmesine göre grup B (n=18) ve C (n=18) olarak kategorize edildi. Hastaların egzersiz kapasitesi (altı dakika yürüme testi [6DYT] ve altı dakika pegboard ve ring testi [6PBRT]), solunum kas kuvveti (maksimal inspiratuar basınç [MIP] ve maksimum ekspiratuar basınç [MEP]) ve ekstremite kas kuvveti (el kavrama ve diz ektansiyon kuvveti) değerlendirildi.

Sonuçlar: MEP değeri B grubunda C grubuna göre anlamlı olarak daha yüksekti (p=0,024). Diğer değerler (6DYT mesafesi, 6PBRT skoru, MIP değeri ve ekstremite kas kuvveti) açısından iki grup arasında fark yoktu (p>0,05).

Tartışma: Bu çalışma, KOAH'lı hastaları değerlendirmek için kapsamlı değerlendirmenin çok önemli olduğunu göstermektedir. GOLD spirometre değerlendirilmesi tek başına yeterli değildir, semptomlar ve alevlenme hikayeleri de değerlendirilmelidir.

Anahtar Kelimeler: Kronik Obstrüktif Akciğer Hastalığı; Egzersiz Kapasitesi; Kas Kuvveti.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD), which is a widespread preventable and treatable illness, is one of the important reasons for morbidity and mortality (1). The Global Initiative for Chöronic Obstructive Lung Disease (GOLD) offers a current method to categorize COPD patients that are named 'Combined COPD Assessment'. While conventional COPD categorization is primarily based on airflow obstruction, nowadays GOLD advises regarding exacerbation risk and the symptoms of degree illness level in groups A-D. COPD Assessment Test (CAT) or modified Medical Research Council (mMRC) dyspnea scale are used to assess the symptoms of the patients. Exacerbation risk is evaluated by the patient's spirometric classification and exacerbation history. For symptom assessment, the CAT is primarily recommended by GOLD because of a comprehensive measure of the symptoms. GOLD suggests the evaluation pointing the highest risk should be used for exacerbation risk assessment. Group B is defined high levels symptom and low risk as opposed to group C low levels symptom and high risk of GOLD. The two groups are the opposite of symptom and risk assessment (2).

The 6-minute walking test (6MWT) recommended as the main outcome assessment by the American Thoracic Society (ATS). The 6MWT is an inexpensive and simple but beneficial method for assessing the functional exercise capacity (3). The severity of airflow limitation effects 6MWT distance. As the severity of the airflow limitation increases, the exercise capacity decreases (4). Previously, the lower extremities exercises were often investigated. However, the upper limbs are used commonly to perform varied daily activities, so upper limb exercise is progressively identified as a significant part of pulmonary rehabilitation (5). Patients with COPD often complain of upper limb fatigue and dyspnea during upper extremity activity. Elevating the upper limbs above the shoulders increases lung hyperinflation and functional residual capacity (FRC), both of which conduce to upper extremity exercise intolerance (6).

The six-minute pegboard and ring test (6PBRT) is a reliable and valid method for the assessment of unsupported upper-extremity exercise in patients with COPD, and a positive significant correlation was found between 6PBRT score and airflow limitation degree (7).

An independent predictor of mortality in COPD patients is muscle mass (8). Skeletal muscle strength decreases as the airflow limitation increases (9). Respiratory muscle problems are determined in COPD patients (10) and the weakness of respiratory muscles might be related to many reasons such as deconditioning, malnutrition, electrolyte disturbances, cardiac failure, systemic inflammation, and treatment with corticosteroids (11).

Knee extensor strength relates to mobility and exercise capacity, but the weakness of quadriceps is common in COPD (12). Hand grip strength is an easy method to predict the risk of cardiopulmonary disease and mortality (13).

Although exercise capacity and muscle strength were studied between the subgroup of COPD classification of severity of airflow limitation, there was no study compared the exercise capacity and muscle strength between the COPD group B and C. Group B and C have different clinic feature (spirometry, symptoms, and exacerbation history). Knowing the physical characteristics of groups B and C are important for the treatment methods to be applied. Therefore, the objective of this study was to compare exercise capacity and muscle strength between COPD group B and C. It was hypothesized that exercise capacity and muscle strength would be similar between COPD group B and C.

METHODS

This study was designed as an observational study. Thirty-six patients with stable COPD (group B=18 and group C=18) participated in this study. The study was conducted between September 2013 and May 2014. The diagnosis of COPD made according to GOLD guidelines (medical history, current symptoms, and pulmonary function testing) by an experienced specialist. The inclusion criteria for COPD patients were those who were diagnosed with COPD (forced expiratory volume in one second (FEV_1) <80% of predicted). All patients were in stable clinical condition at the time of the study. Exclusion criteria were using oral corticosteroid for

at least six weeks, acute exacerbation, having significant musculoskeletal or cardiovascular diseases and cognitive impairment. Ethics Committee of Dokuz Eylül University approved the study (1068-GOA). All patients signed a written informed consent form.

To assess pulmonary function test, spirometry (Sensor Medics Vmax 22 machine, SensorMedics Inc., Anaheim, CA, USA) was used according to ATS/European Respiratory Society (ATS/ETS). Percentages of the predicted values of forced vital capacity (FVC), FEV_1, FEV_1/FVC, forced expiratory flow between 25% and 75% of FVC ($FEF_{25-75\%}$) and peak expiratory flow (PEF) were recorded (14).

The COPD Assessment Test (CAT) is a well-known questionnaire. The CAT is suggested to assess symptoms in subjects with COPD. The CAT is a reliable method of the impact of COPD on a patient's health status. The test has eight items to assess symptoms. The score ranges from 0 to 40, and the high score shows symptoms are increased (15).

Maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) values were performed to assess respiratory muscle strength (Sensor Medics Vmax 22 machine, SensorMedics Inc., Anaheim, CA, USA). The subjects performed three to five acceptable and reproducible maximal maneuvers (i.e., differences of 10% or less between values): The recorded value was the highest unless this was obtained from the last effort (16). The MIP and MEP percentages were calculated as a percentage of their predicted values (17).

Hand-grip and knee extensor strength were assessed using a hand-grip dynamometer (Jamar® dynamometer, Patterson Medical, Warrenville, Illinois, USA) and hand-held dynamometer (JTECH, Medical Commander Powertrack II, Salt Lake City, Utah, USA). Measurements were repeated three times from the dominant limbs, and average values were recorded. Handgrip and knee extensor strength percentages were calculated as a percentage of their predicted values (18, 19).

The 6MWT was performed on a 30 m walking course and indoors according to ATS/ERS (3). Blood pressure (Erka Manual Sphygmomanometer, Bad Toelz, Germany), heart rate (Beurer pulse oximeter, Ulm, Germany), oxygen saturation (Beurer pulse oximeter, Ulm, Germany), dyspnea and fatigue (the modified Borg Scale) were recorded before and after the test. The 6MWT distance percentages were calculated as a percentage of their predicted values (20).

Table 1: Patients' Characteristics.

Variables	COPD Group B	COPD Group C	p value
Age (years)	68.83±10.04	66.50±8.20	0.451[a]
Gender (Male/Female)	16/2	16/2	1.00[c]
BMI (kg/m²)	27.17±3.94	26.22±3.71	0.465[a]
Smoking History (pack-years)	46.44±27.29	54.44±30.67	0.414[a]
Duration of Illness (years)	10.11±3.26	10.66±2.54	0.573
GOLD Spirometry Classification	I:2, II:16	III:15, IV:3	
mMRC Score (0–4)	2.00 (2.00-2.00)	1.00 (1.00-1.00)	**<0.001***[b]
CAT Score (0-40)	13.11±1.99	7.78±1.43	**<0.001***[a]
Exacerbation History (n)	1.00 (0.00-1.00)	2.00 (1.00-2.00)	**0.007***[b]
FEV_1 (% predicted)	67.28±12.16	37.39±7.21	**<0.001***[a]
FVC (% predicted)	82.44±12.22	58.33±15.37	**<0.001***[a]
FEV_1/FVC (%)	63.50 (59.50-67.25)	51.50 (46.00-60.00)	**<0.001***[b]
$FEF_{25-75\%}$ (% predicted)	33.50 (24.75-40.00)	15.50 (11.75-17.00)	**<0.001***[b]
PEF (% predicted)	68.50±14.25	42.78±11.34	**<0.001***[a]

*p<0.05. a: Student t Test; b: Mann-Whitney U Test; c: Chi-square Test. Values are expressed as mean±standard deviation or median (25-75 quartiles) for continuous variables and frequencies were reported for categorical variables. BMI: Body Mass Index, mMRC: Modified Medical Research Council Dyspnea Scale, CAT: COPD Assessment Test, FVC: Forced Vital Capacity, FEV_1: Forced Expiratory Volume in One Second, $FEF_{25-75\%}$: Forced Expiratory Flow 25–75%, PEF: Peak Expiratory Flow.

The 6PBRT is a reliable method to assess unsupported upper extremity exercise capacity in COPD patient. The test performed by the method of described Zhan et al. (7). Blood pressure (Erka Manual Sphygmomanometer, Bad Toelz, Germany), heart rate (Beurer pulse oximeter, Ulm, Germany), oxygen saturation (Beurer pulse oximeter, Ulm, Germany), dyspnea and fatigue (modified Borg Scale) were recorded before and after the test.

Statistical Analysis

The data were analyzed using the IBM® SPSS® Statistics for Windows software (ver. 20.0; IBM Corp., New York, USA). Values are expressed as mean± standard deviation and median (25-75 quartiles) for continuous variables, and frequencies were reported for categorical variables. Shapiro-Wilk test and histograms were used to assess distributions for normality of data. If the data is normally distributed, parametric analyses were undertaken. Student t-test, Mann-Whitney U Test, and Chi-square test were used to compare the groups.

There was no previous study, which compared the exercise capacity and muscle strength between the COPD group B and C. However, a previous study has revealed that 6MWT distance was significantly different in COPD spirometric subgroups ($p<0.05$) (21). Based on the results of that study, the minimum required sample size for each group for a comparison analysis was calculated as 17 patients for the probability level as 0.05 and the statistical power level as 80% using G*Power Software (ver. 3.1.9.2 Universität Düsseldorf, Düsseldorf, Germany). "Means: Difference between two independent means (two groups)" test was used to determine the minimum number of participant required for each of two independent groups.

RESULTS

Two patients were GOLD I, 16 patients were GOLD II, 15 patients were GOLD III, and three patients were GOLD IV. The participants' demographic characteristics (age, gender, body mass index), duration of illness, and smoking history of patients were similar between group B and C ($p>0.05$, Table 1). Symptoms levels were significantly higher in group B than group C ($p<0.001$, Table 1). Spirometric values were lower in group C than group B ($p<0.001$, Table 1).

The 6MWT distance, the percentage of 6MWT distance, and 6PBRT score (also difference between final and initial values of heart rate, oxygen saturation, dyspnea, and fatigue) were similar between the groups ($p>0.05$, Table 2).

Only MEP and percentage of MEP values of group C were significantly lower than group B ($p<0.05$, Table 3). Other muscle strength values (MIP, the percentage of MIP values and peripheral muscle

Table 2: Comparison of Exercise Capacity between the Groups.

Variables	COPD Group B	COPD Group C	p value
6MWT Distance (m)	421.39±56.22	385.83±52.78	0.059[a]
6MWT Distance (%)	85.47±10.73	77.59±14.45	0.072[a]
ΔHR (bpm)	22.39±17.68	20.67±11.12	0.729[a]
ΔSpO_2 (%)	1.0 (0.0-3.0)	3.0 (0.7-5.2)	0.084[b]
ΔDyspnea (Modified Borg)	2.0 (1.0-4.0)	2.5 (1.0-5.0)	0.419[b]
ΔLeg Fatigue (Modified Borg)	2.0 (1.0-4.0)	2.5 (1.0-5.2)	0.687[b]
6PBRT score	140.0 (129.0-161.2)	139.5 (117.7-145.0)	0.157[b]
ΔHR (bpm)	7.0 (4.0-11.2)	5.5 (2.7-15.0)	0.680[b]
ΔSpO_2 (%)	0.0 (0.0-1.0)	0.0 (0.0-1.2)	0.414[b]
ΔDyspnea (Modified Borg)	1.0 (0.0-1.0)	1.0 (0.0-2.0)	0.185[b]
ΔArm Fatigue (Modified Borg)	2.5 (1.0-3.2)	3.0 (1.7-4.0)	0.529[b]

Values are expressed as mean±standard deviation or median (25-75 quartiles). a:Student t test, b:Mann-Whitney U test. Δ: Difference (Final-Initial Value), 6MWT: Six-Minute Walk Test, 6PBRT: Six-Minute Pegboard and Ring Test, HR: Heart Rate; SpO_2: Oxygen Saturation.

Table 3: Comparison of Muscle Strength between the Groups.

Variables	COPD Group B	COPD Group C	p value
MIP (cmH_2O)	70.50±35.13	56.50±15.10	0.134
MIP (%)	71.49±34.79	56.89±16.94	0.122
MEP (cmH_2O)	81.06±13.34	71.39±11.18	**0.024***
MEP (%)	44.70±8.28	38.15±8.68	**0.027***
Knee Extensor Strength (kg)	32.11±6.11	28.83±4.59	0.078
Knee Extensor Strength (%)	87.69±9.73	80.60±11.42	0.053
Handgrip Strength (kg)	35.06±7.84	31.11±5.05	0.082
Handgrip Strength (%)	97.70±12.93	88.90±22.98	0.166

*p<0.05. Student t-test. Values are expressed as the mean±standard deviation. MIP: Maximal Inspiratory Pressure, MEP: Maximal Expiratory Pressure.

strength) were similar between group B and C (p>0.05) (Table 3).

DISCUSSION

This study was the first study, which compares exercise capacity and muscle strength between group B and C of GOLD combined COPD assessment. Except for the expiratory muscle strength, other values (exercise capacity, inspiratory and peripheral muscle strength) were similar between groups. These findings show that comprehensive assessment is critical to evaluate patients with COPD. Not only the GOLD spirometry measures were enough, but also symptoms and exacerbation history must be evaluated.

The 6MWT is commonly used to assess functional exercise capacity in COPD patients (3). The studies showed that 6MWT distance decrease with airflow limitation and spirometric disease severity (4,21,22). Additionally, it was demonstrated that FEV_1 was correlated with the dyspnea and desaturation during the 6MWT (23). Although airflow limitation is an important factor to effect 6MWT performance; muscle strength, pulmonary function, symptoms, functional residual capacity, age, and body weight could be listed as factors affecting 6MWT in COPD (24). Similarly, we found that there was no difference in 6MWT distance and difference (final-initial) values between the two groups. Although GOLD spirometric stages were different between group B and C, 6MWT values were similar. These findings support that airflow limitation itself was not enough to determine 6MWT values because several factors such as symptoms might affect the 6MWT.

The 6PBRT is a reliable method to assess unsupported upper extremity exercise capacity in COPD patients (7). During the unsupported upper extremity elevation, respiratory work increase and dyspnea and fatigue occur (25). Previously, most of the studies focused on the lower extremity exercise capacity therefore, studies on upper extremity exercise capacity were limited (26). These studies showed that the relationship between airflow limitation and upper extremity capacity were contradictory (5,7). We found that 6PBRT values were similar between the groups. Although symptoms such as dyspnea are showed to be the major factor to limit unsupported upper extremity exercise capacity, the present study showed that symptoms are not enough to explain upper extremity exercise intolerance.

Skeletal muscle impairment is one of the most important factors of the systemic effects of COPD (27). Muscle mass is an independent determinant of life expectancy in COPD patients (8). Structural changes (atrophy, reduction in oxidative activity, and mitochondrial impairment) cause the development of skeletal muscle dysfunction in people with COPD (28). Studies showed that muscle strength in GOLD spirometry stage from I to IV was decreased (9,29). Contrary to this information in the literature, the study found that skeletal muscle strength was similar between groups GOLD I-II and GOLD III-IV except expiratory muscle strength. Airflow limitation is an essential factor to muscle atrophy, but exacerbation history, malnutrition, systemic inflammation, and physical inactivity are cause muscle dysfunction (30). One study showed that recurrent exacerbations are associated with lower

health status and respiratory weakness (29). The maximal expiratory pressure of group B was significantly higher than group C in our study. This may be caused by the fact that the number of exacerbations in group B was greater than in group C. However, no study comparing muscle strength between groups B and C of COPD have been conducted so far. The further study on this issue is needed.

This study has several limitations. Although there were more participants than the minimum required sample size, the study included men predominantly. Generalizations of these results to women with COPD might not possible. Another limitation of this study was lack of group A and D. There is a need for further study with increased sample size, including COPD A and D groups. In addition, further study examining the response of all groups to pulmonary rehabilitation will provide guidance.

In conclusion, all values were similar in both group B and C patients except the MEP value. This study was the first study comparing exercise capacity and muscle strength between COPD group B and C. This study showed that comprehensive assessment is very important to manage patients with COPD. GOLD spirometry measures are not enough and symptoms and exacerbation history must be evaluated. As COPD progression is heterogeneous, multi-factorial assessments provide different points-of-view in the disease's management.

Sources of Support: None.

Conflict of Interest: None.

Ethical Approval: This study was approved by Dokuz Eylül University Ethics Committee with the number of 1068-GOA.

Informed Consent: Informed consent form was signed by all patients.

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