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ORIGINAL ARTICLE / ARAŞTIRMA YAZISI

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Assessment of Pulmonary Functions and Peripheral Muscle Strength of COPD Patients in Different GOLD Stages

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ABSTRACT

Purpose: The purpose of this research was to examine the respiratory functions, respiratory muscle strength and peripheral muscle strength of COPD patients with different GOLD stages and to evaluate their correlation with the duration and prognosis of the disease in COPD.

Methods: Patient's demographic information, clinical status, COPD Assessment Test score, mMRC Dyspnea Scale score, emergency and hospital admissions numbers in the last three months, number of exacerbation and hospitalizations in the last one year were recorded. Maximal mouth pressures were used for respiratory muscle strength. Peripheral muscle strength was evaluated with hand grip in the upper extremity. In the lower extremity knee extension and flexion strength were evaluated with a hand-held dynamometer. The findings of PFT performed during the regular hospital controls were obtained. GOLD stages of patients were determined according to GOLD combined assessment.

Results: Total of thirty-one COPD cases (five females, twenty-six males, age 64.80 ± 7.71 years), including nine in Group B, five in Group C and seventeen in Group D, were included in our study. There were statistically significant, negative, moderate correlations between all patients' respiratory functions and disease duration ($p < 0.05$; for FVC% r: -0.410; for FEV_1% r: -0.569; for MEF_{25-75}% r: -0.451). There was statistically significant, moderate, negative correlation between knee extension strength and numbers of exacerbations and hospitalizations over the last one year ($p < 0.05$).

Conclusion: The results of the study suggest that non-respiratory symptoms and GOLD stages should also be considered in the planning of COPD follow-up and pulmonary rehabilitation programs.

Keywords: COPD, pulmonary functions, peripheral muscle strength

Farklı GOLD evrelerindeki KOAH hastalarında pulmoner fonksiyonlar ve periferal kas kuvvetinin değerlendirilmesi

ÖZET

Amaç: Bu araştırmanın amacı, farklı GOLD evrelerdeki KOAH hastalarının solunum fonksiyonlarını, solunum kas kuvvetlerini ve periferal kas kuvvetlerini incelemek ve KOAH'da hastalığın süresi ve prognozu ile ilişkisini değerlendirmekti.

Yöntemler: Hastaların demografik bilgileri, klinik durumları, KOAH Değerlendirme Testi skoru, mMRC dispne skalası skoru, son üç ay içindeki acil servis başvuru ile hastaneye yatış sayıları, son bir yıl içindeki alevlenme öyküsü ile buna bağlı hastaneye yatış bilgileri kaydedildi. Solunum kas kuvveti değerlendirmesi için maksimal ağız içi basınç ölçümü yöntemi kullanıldı. Üst ekstremite periferal kas kuvveti dinamometre ile birlikte el kavrama kuvveti olarak değerlendirildi. Alt ekstremite periferal kas kuvveti değerlendirmesinde el dinamometresi ile diz ekstansiyon ve fleksiyon kuvveti değerlendirmesi yapıldı. Ayrıca tüm hastaların düzenli hastane kontrolleri sırasında yapılan solunum fonksiyon testi sonuçları alındı. KOAH hastalarının GOLD evrelerinin belirlenmesi GOLD birleşik değerlendirmesine göre yapıldı.

Bulgular: Araştırmaya dokuz B Grubu, beş C Grubu ve on yedi D Grubu olmak üzere toplam otuz bir KOAH hastası (beş kadın, yirmi altı erkek; yaş ortalaması 64.80 ± 7.71 yıl) dahil edildi. Tüm hastaların hastalık süresi ile FVC%, FEV_1%, MEF_{25-75}% değerleri arasında istatistiksel olarak anlamlı, negatif, orta dereceli korelasyon vardı ($p < 0.05$; FVC% için r: -0.410; FEV_1% için r: - 0.569; MEF_{25-75}% için r: -0.451). Ayrıca tüm hastaların diz ekstansiyon kuvveti ile son bir yıl içindeki alevlenme öyküsü ve hastaneye yatış sayısı arasında istatistiksel olarak anlamlı, negatif, orta dereceli korelasyon bulundu ($p < 0.05$).

Sonuç: Çalışmanın sonuçlarına göre, KOAH takibi ve pulmoner rehabilitasyon programlarının planlanmasında solunum dışı semptomlar ve KOAH evreleri de dikkate alınabilir.

Anahtar Kelimeler: KOAH, pulmoner fonksiyonlar, periferal kas kuvveti

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Chronic obstructive pulmonary disease (COPD) is a common and progressive disease that characterized by airway obstruction against harmful particles and gases in the airway and lungs, and is treatable and preventable. It develops due to increased chronic inflammatory response in the lungs and airways due to toxic gases and particles. Exacerbations and comorbidities affect the severity of the disease (1, 2).

In 2012, more than three million people (6% of deaths worldwide) died from COPD. COPD is an important preventable and treatable public health problem. It is the leading source of global lifelong morbidity and mortality; many people die due to this disease or its complications. COPD is expected to become more common in the coming years around the world, as the population is older and continues to age. The severity of the disease in COPD is determined according to the GOLD (Global Initiative for Chronic Obstructive Lung Disease) guidelines (2). While determining the severity of airway obstruction with the patient's spirometric values in COPD; combined COPD assessment is made with symptomatic evaluation, number of exacerbations and hospitalizations. Airway restriction is numerically (GOLD 1-4), symptom evaluation and exacerbation risk combined with letter grouping (Group A-D) (2).

COPD causes lung parenchyma injury, resulting in structural changes in the small airways and dynamic collapse. Limitation of expiratory airflow; a reduction of the apposition zone and mechanical side effects in the chest wall, along with changes in diaphragm muscle fibers, cause air trapping and lung hyperinflation. Length of respiratory muscle fibers; shortened due to hyperinflation and increased chest wall expansion resistance, the increase in respiratory work also increases the need for respiratory muscles (3).

A mixture of various local and systemic causes was responsible for respiratory muscle dysfunction in COPD. Respiratory muscle dysfunction is thought to be caused mostly by pulmonary hyperinflation. However, additional structural factors such as tobacco use, systemic inflammation, exacerbations, vigorous exercise, dietary and gas exchange conditions, anabolic insufficiency, comorbidities and medications can also affect muscle function (4). In COPD patients, disturbance of respiratory muscle function can lead to exercise intolerance and hypercapnic respiratory failure. A higher risk of frequent hospital visits has been attributed to respiratory muscle dysfunction (5).

As it is one of COPD physiopathology's most significant extrapulmonary findings, it is the changes in peripheral muscle strength. The loss of muscle mass causes a decrease in muscle strength. Skeletal muscle atrophy is an important cause of weight loss in COPD. The cellular and molecular processes that in these patients contribute to skeletal muscle atrophy remain unclear. Immobility, systemic inflammation, hypoxia of the tissue, oxidative stress and increased apoptosis of the skeletal muscle have been identified as possible pathogenic factors, among others (6, 7). It is also possible to evaluate changes in peripheral muscle strength with hand grip strength. It has been proven that there is a decrease in hand grip strength in COPD compared to healthy individuals (8, 9).

In the light of this information, it was aimed to evaluate the respiratory functions, respiratory muscle strength and peripheral muscle strength of COPD patients in different GOLD stages clinically and to evaluate their correlation with the duration and prognosis of the disease.

MATERIALS AND METHODS

Study Place and Time

The study was held between February 2019 - May 2019 at the Health Sciences University Sureyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital.

Subjects

Inclusion criteria in the study; being in COPD stable period and over the age of 40, the absence of abnormal laboratory findings, not having a mental problem that prevents filling the questionnaires to be used in the study, and the absence of any other respiratory disease such as asthma. The exclusion criteria from the study are; COPD exacerbation (hospitalization with acute exacerbation in the last 15 days), presence of cognitive impairment, pregnancy status, ischemic heart disease, kyphoscoliosis and advanced postural disorder, orthopedic problems and amputation surgery, emphysema, bullous lung disease, presence of bronchiectasis, previous thoracic surgery history, presence of lung cancer, advanced heart failure.

Data Collection

Demographic information of all subjects (age, gender, educational status, occupation, body weight, height, body mass index), clinical (diagnosis period) and medical status, personal history and family history, GOLD stage, COPD Assessment Test (CAT) score, mMRC Dyspnea Scale score, emergency and hospital admissions numbers in the last

three months, exacerbation and hospitalization numbers in the last one year were recorded. Maximal mouth pressures were used for respiratory muscle strength. Peripheral muscle strength in upper extremity was assessed with hand-grip; hand-held dynamometer was used in the lower extremity. In addition, the results of the Pulmonary Function Test performed during the routine controls of all patients were recorded. Informed consent was obtained from the patients who agreed to participate in the study. GOLD stages of patients were determined according to GOLD combined assessment (ABCD Assessment) (2).

Group A: Exacerbation history (0 or 1- not leading to hospital admission), Symptoms (mMRC 0-1 or CAT < 10)

Group B: Exacerbation history (0 or 1- not leading to hospital admission), Symptoms (mMRC ≥ 2 or CAT ≥ 10)

Group C: Exacerbation history (≥ 2 or ≥ 1 leading to hospital admission), Symptoms (mMRC: 0-1 or CAT<10)

Group D: Exacerbation history (≥ 2 or ≥ 1 leading to hospital admission), Symptoms (mMRC ≥ 2 or CAT ≥ 10)

a. Modified Medical Research Council (mMRC) Dyspnea Scale: The patient expresses the degree of shortness of breath according to the score between 0-4. The mMRC dyspnea scale is compatible with the health status score and other dyspnea scales and its application is simple (10, 11). Presence and degree of dyspnea in patients were evaluated with the mMRC Dyspnea Scale.

b. COPD Assessment Test (CAT): The CAT which evaluates the effects of COPD and deterioration in health status, consists of eight items that question "cough, sputum, chest symptoms, fatigue and confidence in leaving home". The reliability and validity of the scale was carried out in Turkey in 2012 by Yorgancıoğlu et al. The minimum score of 0 and the maximum score of 40 can be obtained on the scale. A high score indicates that the severity of COPD is high and the health condition is poor (11).

c. Pulmonary Function Test (PFT): PFT is performed according to American Thoracic Society (ATS) / European Respiratory Society (ERS) statement (12). The PFT results of patients' performed during their routine controls taken into consideration. The percentages of the predicted values for forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), FEV_1/FVC, mid-expiratory flow rate (MEF_{25-75}) and peak expiratory flow (PEF) were used for statistical analysis (12).

d. Respiratory Muscle Strength Assessment: It is a non-invasive test that indirectly demonstrates respiratory muscle strength with maximal inspiratory pressure (PI_{max}) and maximal expiratory pressure ($PE_{max)}$. Tests were done in a sitting position. Patients were asked to perform a maximal inspiration for at least three seconds after expiration while their nose were occluded with a nose clip for evaluation. This cycle was repeated three times and the best score was recorded. In PE_{max} measurement, at least three seconds of maximal expiration was requested after maximal inspiration. The test was repeated three times, and the best score was recorded (13). Measurements were made with a portable mouth pressure measuring device (Micro Medical Micro-RPM, UK). PI_{max} maneuver was done from residual volum (RV) while PE_{max} was from total lung capacity (TLC). The percentage of the predicted values (percent) was used for statistical analysis (14).

e. Peripheral Muscle Strength Assessment:

Upper extremity: For grip strength test a manual hydraulic dynamometer was used according to the recommendations of the American Association of Hand Therapists (AETD). The patients were measured in sitting position, shoulder adduction at 90°, elbow flexion, forearm in prono- supination, neutral and wrist joints in neutral position. Three consecutive measurements were obtained by giving 60-second rest breaks between measurements. The result obtained from the average of three measurements was recorded (15).

Lower extremity: The evaluation was made with a handheld digital dynamometer. M. Quadriceps femoris strength was evaluated for knee extension. The test was applied with the "make test" technique that requires isometric contraction. (Make test is the protocol of the person applying the maximum force against the device while the meter keeps the dynamometer constant). The participant was asked to sustain maximal isometric contraction for 5 seconds after knee extension was done, and the average of three consecutive maximum contraction measurements taken at 30-second intervals was obtained (16). M. Hamstring strength was evaluated for knee flexion. The test also was applied with the "make test" technique. The participant was asked to sustain maximal isometric contraction for five seconds after knee flexion was done, and the average of three consecutive maximum contraction measurements taken at 30-second intervals were obtained (16).

Ethical Considerations

Ethical approval was obtained from the Marmara University Faculty of Medicine Clinical Research Ethics Committee (approval dated 07.09.2018, protocol number 09.2018.613); Approval letter from the İstanbul Provincial Health Directorate, which declared a work permit, was received (the letter dated 12.12.2018 approved was submitted on 25.12.2018).

Statistical Analysis

The data obtained in the study were evaluated with the SPSS (SPSS Inc., Chicago, IL, USA) 11.5 statistical package program at a 95% confidence interval, and the significance level was $p < 0.05$. The compliance of the data to normal distribution was evaluated by One sample Kolmogorov Smirnov and Spiro Wilk tests. Data that did not show normal distribution were evaluated with non-parametric hypothesis tests. Kruskall Wallis test was used for comparison of the groups. According to the results of the test, the group or groups that cause a difference are determined by the Mann-Whitney U test with Bonferroni correction, $\alpha = 0.05/ 3 = 0.0167$ was taken to show statistical significance. In addition, the relationship between respiratory functions, respiratory muscle strength, peripheral muscle strength and duration and prognosis of the disease was evaluated with Spearman's rank correlation coefficient.

RESULTS

A total of thirty-one COPD patients, nine in Group B, five in Group C, and seventeen in Group D, participated in our study. The patients' ages who included in the study were between 45-80 years and their mean age was $\dot{x} = 64.80 \pm 7.71$ years. The results of the gender of the participants 83.9% of the patients were male; 87.1% were right-dominant and 71% were primary school graduates. While three of the cases evaluated in the study were active smokers, twenty-four people quit smoking (Table 1). Twenty-one people were self-employed, eight were civil servants, one patient was retired while another one was a housewife.

Although there was no statistically significant difference between the groups for age, height, body weight, BMI and quantity of smoking (pack*year), it was observed that there was a statistically significant difference between the groups according to the year of diagnosis ($p < 0.05$) (Table 2), Group D significantly differentiated from other groups ($p < 0.0167$).

When respiratory functions and respiratory muscle strengths were compared according to the groups, no statistically significant difference was found ($p > 0.05$) (Table 3).

When the peripheral muscle strength was compared according to the groups, a statistically significant difference was found only in the hand grip strength of the dominant hand ($p < 0.05$) (Table 4). Paired comparisons were made using the Mann Whitney-U test in order to determine which groups caused the significant difference. By applying Bonferroni correction, the new significance level was accepted as 0.0167 and no statistically significant difference was found between the paired groups. When the median value was compared, group B was found to be higher than the other groups, although it was not statistically significant.

The statistically significant relationships between respiratory functions, peripheral muscle strength and disease duration and prognosis for all patients are shown in Table 5. There were negative statistically significant, negative, moderate correlations between disease duration and FVC% (r: -0.410; $p < 0.05$); FEV_1% (r: -0.569; $p < 0.05$); MEF_{25-75}% (r: -0.451; $p < 0.05$) (Table 4). It was found statistically significant, negative, moderate correlations between the number of exacerbations in the last one year and both dominant and non-dominant knee extension strength (r: -0.416; $p < 0.05$; r: -0.411; $p < 0.05$ respectively). Also there were statistically significant, negative, moderate correlations between the number of hospitalization in the last one year and both dominant and non-dominant knee extension strength (r: -0.557; $p < 0.05$; r: -0.523; $p < 0.05$ respectively).

Table 1. Demographic Features of COPD Patients

		Group B		Group C		Group D	
		n	%	n	%	n	%
Gender	Male	8	88.9	2	40	16	94.1
	Female	1	11.1	3	60	1	5.9
Dominant Side	Right	9	100	4	80	14	82.4
	Left			1	20	3	17.6
Cigarettes Use	Active smoker	1	11.1	-	-	2	11.8
	Ex-smoker	7	77.8	4	80	13	76.5
	Non-smoker	1	11.1	1	20	2	11.8
		9	100	5	100	17	100

Table 2. Comparison of Demographic Informations of COPD Groups

	GOLD ABCD	n	Median	Quarters	Chi Square	p
Age (year)	Group B	9	66	56.50-73	0.424	0.809
	Group C	5	68	62.50-70.50		
	Group D	17	65	60-70		
Height (cm)	Group B	9	167	162.50-170.50	2.166	0.339
	Group C	5	161	152.50-160		
	Group D	17	167	165-169.50		
Weight (kg)	Group B	9	72	63.40-81.15	2.48	0.289
	Group C	5	63.4	53.30-71.05		
	Group D	17	68	60.25-73.15		
BMI (kg/m^2)	Group B	9	26.8	23.50-29.95	2.126	0.345
	Group C	5	23.6	22.35-26.10		
	Group D	17	24.3	21.90-26.35		
Quantity of smoking (Pack*Year)	Group B	8	47.5	42.50-60	1.563	0.458
	Group C	4	43	40.25-50		
	Group D	15	45	35-50		
Year of diagnosis	Group B	9	5	3-10	13.837	**0.001***
	Group C	5	5	2-7		
	Group D	17	13	10-15		
	Total	31				

*p<0,05. Kruskall Wallis Test; BMI: body mass index

Table 3. Comparison of Respiratory Functions and Respiratory Muscle Strength According to COPD Groups						
	GOLD ABCD	**n**	**Median**	**Quarters**	**Chi Square**	**p**
PI_{max} %	Group B	9	79.06	59.36-104.64	0.002	0.999
	Group C	5	84.61	53.25-116.25		
	Group D	17	81.35	60.98-102.78		
PE_{max} %	Group B	9	61	46.49-71.82	0.55	0.76
	Group C	5	49.83	46.47-64.54		
	Group D	17	54.53	46.70-63.67		
FVC %	Group B	9	51	38.50-84.50	2.484	0.289
	Group C	5	64	52-68.50		
	Group D	17	47	40-57.50		
FEV_1 %	Group B	9	38	25-58	3.359	0.186
	Group C	5	42	38-47.50		
	Group D	17	33	27-40		
FEV_1 / FVC	Group B	9	55	50-62	0.825	0.662
	Group C	5	53	44.50-72		
	Group D	17	54	47-62		
MEF_{25-75} %	Group B	9	21	9-28.50	3.345	0.188
	Group C	5	21	19-24		
	Group D	17	16	12-18.50		
PEF %	Group B	9	47	35.50-54.50	2.171	0.338
	Group C	5	37	23.50-46.50		
	Group D	17	40	32.50-50.50		
	Total	31				

*p<0,05. Kruskall Wallis Test; PI_{max}: maximal inspiratory pressure, PE_{max}: maximal expiratory pressure, FEV_1: forced expiratory volume in one second, FVC: forced vital capacity, MEF_{25-75}: mid-expiratory flow rate, PEF: peak expiratory flow

Table 4. Comparison of Peripheral Muscle Strength According to COPD Groups						
	GOLD ABCD	**n**	**Median**	**Quarters**	**Chi Square**	**p**
Knee Extension Strength Dominant (kg)	Group B	9	28.62	25.90-32.65	3.145	0.208
	Group C	5	24.2	18.95-27.30		
	Group D	17	29.5	22.05-31.25		
Knee Extension Strength Nondominant (kg)	Group B	9	29.5	24.19-36.25	2.625	0.269
	Group C	5	24.2	18.95-29.20		
	Group D	17	28.5	22.15-30.95		
Knee Flexion Strength Dominant (kg)	Group B	9	19.4	15-23.80	0.137	0.934
	Group C	5	22.1	8.80-23.10		
	Group D	17	18.2	16.05-21.45		
Knee Flexion Strength Nondominant (kg)	Group B	9	18	10.95-24.60	0.361	0.835
	Group C	5	19.7	8.80-20.90		
	Group D	17	18.3	14.75-21.40		
Hand Grip Strength Dominant (kg)	Group B	9	36.1	29.55-41.85	6.335	**0.042***
	Group C	5	25.5	21.60-32.20		
	Group D	17	31.9	26.95-35		
Hand Grip Strength Nondominant (kg)	Group B	9	32.6	27.85-40.55	3.968	0.137
	Group C	5	24.6	20.65-31.75		
	Group D	17	31.5	22.90-33.75		
	Total	31				

*p<0,05. Kruskall Wallis Test

Table 5. Relationship between Respiratory Parameters and Peripheral Muscle Strength of the Patients and Prognosis and Duration of Disease

		Number of Exacerbations in the Last One Year	Hospitalization in the Last One Year	Year of Diagnosis
FVC %	r	-0.224	-0.1	**-.410**
	p	0.226	0.593	**0.022***
FEV_1 %	r	-0.184	-0.079	**-.569**
	p	0.322	0.673	**0.001***
MEF_{25-75} %	r	-0.095	0.061	**-.451**
	p	0.61	0.744	**0.011***
Knee Extension Strength Dominant (kg)	r	**-.416**	**-.557**	0.235
	p	**0.02***	**0.001***	0.203
Knee Extension Strength Nondominant (kg)	r	**-.411**	**-.523**	0.241
		0.022*	**0.003***	0.191

*p<0,05. r: Spearman correlation coefficient, FEV_1: forced expiratory volume in one second, FVC: forced vital capacity, MEF_{25-75}: mid-expiratory flow rate, PEF: peak expiratory flow.

DISCUSSION

In our research; it was foreseen that studies comparing COPD patients at different stages in the relevant literature are limited and their contribution to clarification of the subject in the clinic is anticipated.

When the demographic characteristics of the groups were compared, they showed similarities in terms of age, height, body weight, BMI and smoking. Considering the years of diagnosis, it was seen that the disease duration (median: 13 years) of group D was longer than other groups. The median of duration of disease in groups B and C was 5. According to the combined evaluation, the degree and frequency of exacerbation and symptoms were higher in group D than in the other groups (2). This situation; attributed to increasing frequency and severity of symptoms with increasing duration.

One of the respiratory function test values FEV_1 / FVC value, is the spirometric value used in the diagnosis of the disease. In addition, the expected percentage of FEV_1 is used to evaluate airway restriction (17-19). When respiratory function test results were compared in our groups, no significant difference was found. According to GOLD, it is known that there is a weak relationship between the FEV_1 value and the patient's symptoms and general health status (2). It was thought that the determination of symptoms and exacerbation based on combined assessment in our groups may be the reason for the lack of difference between values of respiratory functions.

In COPD, the function of respiratory muscles is impaired due to pulmonary hyperinflation and loss of strength is observed (20). In addition, the clinical characteristics and risk factors of COPD also affect the respiratory muscle strength. All these considerations contribute to a discrepancy between the respiratory system's mechanical requirements and the respiratory muscle's functional capability, as well as the muscle's metabolic demands and the availability of resources (21). Inspiratory muscle dysfunction is caused by the changes in the thoracic structure due to systemic inflammation that interferes with the structural properties of these muscles. This situation does not limit the ventilation capacity, but it may cause dyspnea, decreased effort capacity and respiratory failure during exacerbation (22). When the respiratory muscle strengths of the COPD patients included in the study were compared, no significant difference was found. Although there was no difference in the group comparison, respiratory muscle strength decreased in all groups compared to the expected values. Since the impairment of respiratory muscle function, especially the diaphragm, is an important predictor of survival in COPD (22), it was accepted as an outcome of our study that respiratory muscle strength evaluations are important in clinical practice.

In COPD, a decrease in peripheral muscle strength is observed along with respiratory muscle strength. In about one third of COPD patients, functional dysfunction of peripheral muscles is seen (4). Decreased peripheral muscle strength has important clinical consequences as it is associated with lower exercise tolerance and higher mortality (23, 24). In many studies conducted with M. Quadriceps, loss of muscle strength in the extremities has been shown in patients with COPD (23, 25). There was no significant difference in the comparison of lower extremity muscle strength of the cases evaluated in our study, according to the groups. It was predicted that this might be due to the difference in the number of cases between the groups.

There is also a decrease in upper extremity muscle strength (4, 23). Although there are studies showing that hand grip strength in COPD is evaluated, it decreases when compared with healthy participants, the relationship between respiratory symptoms has not been clarified (26). Also decrease in hand grip strength is associated with reduced functional capacity and worsening survival (9). In our study, upper extremity muscle strength was evaluated by hand grip strength. When the dominant side hand grip strength values of the groups were compared, a significant difference was found. No significant difference was found when further tests were performed for paired groups. B group hand grip strength median value 36.10; The median value for group C was 25.50 and the median for group D was 31.90. Although it was not statistically significant, it was observed that the hand grip strength values of group B were higher than the other groups. It is also reported in the literature that exacerbations negatively affect muscle strength (27). Parallel to the literature, high hand grip strength in group B; it was thought to be due to the fact that the history of exacerbation in group B was less than in groups C and D according to the combined assessment.

When the relationship between disease duration and respiratory function test results was evaluated, a moderate negative correlation was found with FVC%, FEV_1% and MEF_{25-75}%. As the duration of the illness increased, deterioration in respiratory functions was detected. In the literature, it has been shown that respiratory functions in COPD decrease due to disease prognosis, exacerbations and inflammation (2). Our research results were also in line with the literature.

In the study, it was observed that as the number of exacerbations and hospitalizations in the last one year, there was a decrease in both dominant and non-dominant extremity knee extension strength. It has been shown in the literature that there is a loss of strength in COPD patients, especially in the quadriceps muscle and it has been reported that quadriceps muscle strength is reduced two to four times faster in COPD (4, 25, 28, 29). It was found that the quadriceps muscle strength evaluated on the third day of hospitalization in COPD patients with acute exacerbation was less than those with stable COPD (30, 31). In addition, quadriceps strength decreased by 5% after five days of hospitalization in these patients. The association between reduced strength of quadriceps during hospitalization and less increase in walking time one month after discharge shows that there is a major and long-lasting influence on functional status of loss of strength due to hospitalization (32). Three months after discharge, the loss of quadriceps muscle strength partially improved. In other words, an exacerbation that occurs at any time negatively affects muscle strength and may jeopardize recovery (27, 31). In our study, as the number of exacerbations and hospitalizations increased in the last one year, the decrease in knee extension strength was consistent with the literature.

Study's results are important because it compared respiratory functions, respiratory muscle strength and peripheral muscle strength in different groups of COPD and investigate the relationship between duration and prognosis of the disease. For future researches planning studies including patients in group A who were not included in our study; it will create added value in the COPD clinic in terms of evaluating COPD patients and planning and applying pulmonary rehabilitation programs according to the groups and patients also it will increase the clinical benefit of patients. Muscle strength in COPD; it decreases due to chronic inflammation, exacerbations, comorbidities and drugs used. Especially the late effects of muscle strength loss after exacerbation should be taken into consideration and exercise programs specific to musculoskeletal losses should be structured in these patients. The results of the study show that non-respiratory symptoms and COPD stages should also be considered in the planning of COPD follow-up and pulmonary rehabilitation programs.

DECLARATIONS

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Consent: Informed consent was obtained from all individual participants included in the study.

Availability of Data and Material: Data are not available due to privacy and other restrictions.

Authors' Contributions: All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by BU, SUY and IO. The first draft of the manuscript was written by BU and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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